Health Evidence Review Commission's Value-based Benefits Subcommittee

March 13, 2014

8:30 AM

Meridian Park Hospital
Community Health Education Center, Room 117B&C
19300 SW 65th Avenue, Tualatin, OR 97062

Section 1.0

Call to Order

AGENDA
VALUE-BASED BENEFITS SUBCOMMITTEE
March 13, 2014
8:30am - 1:00pm
Meridian Park Room 117B&C
Community Health Education Center
Tualatin, OR 97062
A working lunch will be served at approximately 12:00 PM
All times are approximate

I. Call to Order, Roll Call, Approval of Minutes – Lisa Dodson 8:30 AM

II. Staff report – Ariel Smits, Cat Livingston, Darren Coffman 8:35 AM

III. Straightforward/Consent Agenda – Ariel Smits 8:45 AM
A. Straightforward Table

IV. Biennial review items– Ariel Smits 9:00 AM
A. Fibromyalgia
B. Somatization/factitious disorder line merge

V. Guidelines – Ariel Smits, Cat Livingston 10:00 AM
A. Lung cancer screening guideline
B. Genetic counseling in the non-prenatal genetic testing guideline
C. Guideline revision for treatment of sleep apnea
D. Fluoride varnish guideline revision
E. Rehabilitation guideline revision

VI. New discussion items – Ariel Smits, Cat Livingston 11:15 AM
A. Transgender hormone therapy
B. Autism
    A. ABA intensity guideline

VII. Previous Discussion Items – Ariel Smits, Cat Livingston 12:20 PM
A. Oral health risk assessment codes
B. Botulinum toxin for chronic migraine

VIII. ICD-10 Conversion – HERC staff 12:40 PM
A. Final approval of October 1 ICD-10 Prioritized List
B. Summary of work to correct errors for ICD-10 List

IX. Public comment 12:55 PM

X. Adjournment – Lisa Dodson 1:00 PM

Value-based Benefits Subcommittee Recommendations Summary
For Presentation to:
Health Evidence Review Commission in January 2014

For specific coding recommendations and guideline wording, please see the text of the 1/9/14 VbBS minutes.

CODE MOVEMENT

- Various straightforward coding changes were made
- 2014 CPT and HCPCS codes placement was finalized
- 2014 CDT code placement was approved
- Sigmoidoscopy with endoscopic ultrasound was moved from the Diagnostic List to the rectal cancer line
- Pediatric trigger thumb treatment was moved to a covered line with a new guideline
- Mastopexy was added to the breast cancer line with modifications to the breast reconstruction guideline
- The Behavioral Health Advisory Panel recommendations for changes to the Prioritized List reflecting DSV-5 were adopted
- Medical nutrition therapy was added to several covered lines
- Invalid HCPCS codes were removed from the diabetes lines
- CDT codes on oral health risk assessment were added to medical preventive lines with a new guideline

ITEMS CONSIDERED BUT NO CHANGES MADE

- Colonoscopy with endoscopic ultrasound was considered for placement on the rectal cancer line but was left on the Excluded List as the more appropriate and lower cost test is the sigmoidoscopy with endoscopic ultrasound
- Changes to the Non-Prenatal Genetic Testing guideline were considered, but discussion was deferred.

GUIDELINE CHANGES

- The continuous blood glucose monitoring guideline was amended to specify when continuous monitoring and when retrospective monitoring is covered.
- The acute otitis media guideline was modified to reflect the AAP and AAO guidelines by making the criteria for recurrent acute otitis media more stringent
- The hydrocele guideline was modified to define children as being age 18 or younger
- The cognitive rehabilitation guideline was modified to clarify that cognitive rehabilitation does not have to start at the time of medical stabilization
- A new guideline specifying when a patient with concussion has persistent symptoms was adopted
- A new guideline for Carotid Artery Stenting was adopted
- A new diagnostic guideline on screening for and monitoring of osteoporosis in adults was adopted
- A new guideline on types of dental restorations was adopted
- A new guideline on the treatment of sleep apnea was adopted

VALUE-BASED BENEFITS SUBCOMMITTEE
Meridian Park Health
Community Health Education Center, Room 117B&C
Tualatin, OR
January 9, 2014
8:30 AM – 1:00 PM

Members Present: Lisa Dodson, MD, Chair; Kevin Olson, MD, Vice-chair; James Tyack, DMD; David Pollack, MD (arrived at 8:40 am); Susan Williams, MD; Mark Gibson; Irene Croswell RPh; Laura Ocker, Lac

Members Absent:

Staff Present: Darren Coffman; Ariel Smits, MD, MPH; Cat Livingston, MD, MPH; Jason Gingerich; Dorothy Allen

Also Attending: Denise Taray, DMAP; Jesse Little, OHA Actuarial Services Unit; *Camille Kerr, Allergan; *Karen Kovak MS, OHA, OHSU; * Ginerva Liptan and Tom Jenkins, MD, Legacy Health; *Tami Stacklehouse and *Tamera Stapes, Fibromyalgia - ME/CFS Support Center, Inc; Matt Krebs, Pfizer; Mike Willett, CGC; Jason Parks and Bridget Kiene, American Cancer Society; Bruce Dubley, OHSU student; *Kim Jones, OHSU Faculty; Jodi Sundberg; *BJ Cavnor, One in Four Chronic Health; Carol Kelly; Dianne Danowski-Smith, Publix Northwest; * Dr. Robert Bennett, OHSU

*Offered testimony

Roll Call/Minutes Approval/Staff Report

The meeting was called to order at 8:35 am and roll was called. Minutes from the October, 2013 VbBS meeting were reviewed and approved.

MOTION: To approve the October, 2013 VbBS minutes as presented. CARRIES 7-0 (Pollack absent).

ACTION: HERC staff will post the approved minutes on the website as soon as possible.

There was no staff report.

- **Topic: Straightforward/Consent Agenda**

  Discussion: There was no discussion.

Actions:

1) Add 45339 to line 173
2) Add 250.41, 250.43, 250.81 and 250.83 to line 10
3) Add 38770 to line 252
4) Remove 519.4 from line 49
5) Add 519.4 to line 689
6) Add 11740 to line 382
7) Add 32110 to line 153
8) Add 50398 to line 78
9) Add 43274-43277 to line 340
10) Add 62100 to line 448
11) Add 63275, 63277, 63278, 63280, 63282, 63283, 63285-63290 to line 137
12) Add 67882 to line 497
13) Add 34825 and 34826 to line 307
14) Add 45384 to line 62
15) Add 28715 to line 384
16) Remove 197.0 from line 278
17) Add 65870 to line 362
18) Add 66682 to line 362
19) Add 67405 to line 84
20) Add 69000 to line 450
21) Add 69540 to line 405
22) Add 27829 to line 297
23) Add 52310 to line 308
24) Add 38747 to line 229
25) Add 50605 to line 186
26) Add 26567 to line 467
27) Add 51050, 51060, and 51065 to line 379
28) Remove 51050, 51060, and 51065 from line 96
29) Add 55831 to line 351
30) Add 58700 to line 260
31) Add 25028 to line 214
32) Add 29540 to line 550
33) Add 23430, 26350, 26352, 26410, 26412 to line 406
34) Add 50546 to line 88
35) Add 29405 to lines 318 and 467
36) Add 43196 and 43226 to line 71
37) Add 44314 to line 308
38) Add 59200 to line 69
39) Add 24635 to line 382
40) Add 61107 to line 101
41) Add 33217, 33220, 33222, and 33226 to line 308
42) Add 77014 to line 277
43) Add 62165 to line 162
44) Add 32124 to line 153
45) Add 26567 to line 467

46) Add 62272 to line 308
47) Add line 312 to GN#6
48) Add 96150-96154 to line 22
49) Add 32110 to line 153
50) Remove S0270-S0274 from all lines on Prioritized List
51) Advise DMAP to add S0270-S0274 to Excluded List
52) Add 92081 and 92082 to line 136
53) Add 66825 to line 448
54) Add 718.44 to line 297
55) Remove 718.44 from line 318
56) Add 14020-14302 to line 308
57) Restrict neonatal specific CPT codes (99468, 99469, 99477, 99478, 99479, 99480, 99481, 99482) to neonatal lines (2, 11, 15, 16, 17, 18, 19, 22, 23, 27, 31, 34, 36, 43, 45, 77, 92, 105, 106, 146, 149, 282, 296, 351, 653)

MOTION: To approve the straightforward/consent agenda items as presented. CARRIES 7-0 (Gibson absent).

- **Topic: 2014 CPT code review**

Discussion: Testimony was heard from Camille Kerr from Allergan. She requested clarification of the omission of 63642-64647 from line 388 DYSTONIA (UNCONTROLLABLE); LARYNGEAL SPASM AND STENOSIS. The code these new codes are replacing was on this line. Smits explained that the old code was more generic; the newer codes are more specific and do not belong on this line.

The placement of CPT codes 34846, 34847 and 87661did not have any discussion. Placement of CPT code 94669 (mechanical chest wall oscillation) involved discussion of what types of therapy would be available to home-bound patients if 94669 was excluded. The response was that other durable medical devices with equal efficacy would be covered.

The new carotid artery stenting guideline was modified to reflect that this procedure will not be covered for patients who have suffered a disabling stroke (modified Rankin scale ≥ 3) to be consistent with the WTA coverage guidance. The term “high risk” was clarified to be “high risk for complications during” CEA. The anatomic risk factors placing a patient at high risk for CEA were defined as recurrent stenosis and/or previous radical neck dissection to be consistent with the WTA coverage guidance.

There was no discussion regarding intravascular stents.

Actions:
1) Place 34846 and 34847 on lines 88, 270, 293, 307, and 349
2) Place 87661 on the Diagnostic List

3) Place 94669 on the Excluded List
4) Place 37217 on lines 342and 440
5) Add a new guideline to lines 342 and 440 as shown in Appendix A
6) Place 37236 and 37237 on lines 270, 307, 349 and 472
7) Place 37238 and 37239 on line 303

- **Topic: 2014 HCPCS code review**

Discussion: The subcommittee had questions about whether G0459 involved a direct patient encounter or could be used for physician-to-physician consultation. It was unclear, but likely could be used for either. The group was comfortable with placing this code on the mental health lines.

Actions:
1) Place G0459 on the mental health lines
2) Place G0460 on the Excluded List
3) Place G0461 and G0462 on the Diagnostic List
4) Place G0463 on lines with E&M outpatient codes
5) Place S9960 and S9961 on the Ancillary List

- **Topic: 2014 CDT code review**

Discussion: Livingston presented the 2014 CDT changes recommended by the OHAP. She highlighted the more controversial code placements. Changes from the proposed placements included the following:

D3427 - periradicular surgery w/o apicoectomy – Tyack discussed that indications and efficacy of this procedure are unclear. The code is instead to be placed on Line 676 Elective Dental.

D3428 and D3429 – after further research, it is clarified that there is insufficient evidence to support use of this in terms of improved outcomes. It is primarily used for volume for implants, which is a low prioritized service. In the future if someone was trying to get an implant a bone graft could also be done at that time. Both were placed on Line 676.

Actions:
1) **Place D0393-D0395 on Line 648**
2) **Place D1999 in Excluded File**
3) **Place D2921 on Line 283**
4) **Place D2941 on Line 372**
5) **Place D2949 on Line 621**
6) **Place D3355-D3357 on Line 676**
7) **Place D3427-D3429 on Line 676**

8) **Place D3431-D3432 on Line 676**
9) **Place D4921 in Excluded File**
10) **Place D5863-D5866 on Line** 631
11) **Place D5994 on Line 676**
12) **Place D6011, 6013, and D6052 on Line 648**
13) **Place D8694 on** Lines 49, 325, and 647
14) **Place D9985 in Excluded File**

MOTION: To approve the CPT, HCPCS, and CDT code placement as noted above. CARRIES 7-0 (Gibson absent).

- **Topic: Colonoscopy with endoscopic ultrasound**

Discussion: The summary document was presented. Olson raised concerns that colonoscopy with endoscopic ultrasound had considerably higher RVUs than sigmoidoscopy, but that this type of ultrasound was only done in the rectal area and would not require a colonoscopy. Smits found a fee statement specifying that sigmoidoscopy with endoscopic ultrasound was 4.68 RVU while colonoscopy with endoscopic ultrasound was 8.81 RVU.

Olson agreed that this procedure was only used for the work up of rectal cancer, not for diagnosis and should be moved from the Diagnostic List to the rectal cancer line.

Actions:
1) Add 45341 and 45342 to line 165 and advise DMAP to remove from the Diagnostic List
2) Keep 45391 and 45392 on the Excluded List

- **Topic: Pediatric trigger thumb**

Discussion: The summary document was presented. There was no discussion.

Actions:
1) Add ICD-9 756.89/ICD-10 M65.31x to line 406
2) Add CPT 26055 to line 406
3) A new guideline was adopted for line 406 as shown in Appendix A

- **Topic: Mastopexy**

Discussion: The summary document was presented. There was no discussion.

Actions:

1) Add 19316 to line 197 and advise DMAP to remove from the Excluded List
2) Modify guideline note 79 as shown in Appendix B

- **Topic: BHAP recommended changes to Prioritized List for DSM-V**

Discussion: There was minimal discussion.

Actions:

For the April 1, 2014 ICD-9 Prioritized List

1) Move ICD-9-CM 296.99 from line 32 to line 212
2) Move ICD-9-CM code 625.4 from line 581 to line 212
3) Move ICD-9 312.39 from 569 to line 487
4) Rename line 133 ~~ATTENTION DEFICIT DISORDERS WITH HYPERACTIVITY OR UNDIFFERENTIATED~~ ATTENTION DEFICIT/HYPERACTIVITY DISORDERS
5) Change GN54: replace "attention deficit disorder (ADD)" with "attention deficit/hyperactivity disorder"
6) Rename line 5 ~~ABUSE OR DEPENDENCE OF PSYCHOACTIVE SUBSTANCE~~ SUBSTANCE USE DISORDER
7) Rename line 457 ~~CHRONIC DEPRESSION (DYSTHYMIA)~~ PERSISTENT DEPRESSIVE DISORDER
8) Rename line 334 ~~PERVASIVE DEVELOPMENTAL DISORDERS, INCLUDING~~ AUTISM SPECTRUM DISORDERS
9) Rename line 483 SIMPLE PHOBIAS AND SOCIAL ANXIETY DISORDER ~~PHOBIAS~~

Changes for the October, 2014 ICD-10 Prioritized List

1) Carry forward line name changes above
2) Add ICD-10-CM F70 to lines 349, 381
3) Add ICD-10-CM F80.89 to line 349 and advise DMAP to remove from the Ancillary File .
4) Add ICD-10-CM code F34.8 to line 207 and advise DMAP to remove from the Excluded File
5) Add ICD-10-CM code N94.3 to line 207 and remove from line 562
6) Add ICD-10 F63.3 to line 467 and remove from 552
7) Add F45.22 to line 467 and remove from line 497
8) Add ICD-10 F50.8 to line 385
   - Add a coding specification to line 385: "ICD-10-CM F50.8 is included on this line only for binge eating disorder. All other diagnoses using this code (i.e. pica in adults) are included on line 640 PICA."
9) Rename line 66 SUBSTANCE-INDUCED MOOD, ANXIETY AND DELUSIONAL AND OBSESSIVE-COMPULSIVE DISORDERS
10) Move code F55.3 from line 5 to line 619

11) Move the [drug] abuse/ dependence with other [drug] induced disorder ICD-10-CM codes to line 66 (F10.188, F10.288, F10.988, F11.188, F11.288, F11.988, F13.188, F13.288, F13.988, F14.188, F14.288, F14.988, F15.188, F15.288, F15.988, F16.188, F16.288, F16.988, F18.188, F18.288, F18.988, F19.188, F19.288, F19.988).
12) Move [substance] use, uncomplicated (F11.90, F12.90, F13.90, F14.90, F15.90, F16.90, F18.90, F19.90) to line 658
13) Rename line 478 ~~USE OF ADDICTIVE SUBSTANCES~~ SEXUAL DYSFUNCTION DUE TO SUBSTANCE USE

Biennial review changes for the October 1, 2016 Prioritized List

1) Delete line 478 SEXUAL DYSFUNCTION DUE TO SUBSTANCE USE and move remaining ICD-10-CM codes for sexual dysfunction due to substance use to line 529 (F10.181, F10.281, F10.981, F11.181, F11.281, F11.981, F13.181, F13.281, F13.981, F14.181, F14.281, F14.981, F15.181, F15.281, F15.981, F16.181, F16.281, F16.981, F18.181, F18.281, F18.981, F19.181, F19.281, F19.981)

- **Topic: Medical nutrition therapy**

Discussion: The summary document was presented. There was minimal discussion.

Actions:

1) Add CPT 97802-97804 to lines 20, 25, 229, 325, 312, 339

MOTION: To approve the new discussion items as presented with the noted change in the recommendations for coverage of colonoscopy with endoscopic ultrasound. CARRIES 7-0 (Gibson absent).

- **Topic: Genetic testing guideline on familial cancer**

Discussion: The staff proposal to change the type of provider who should provide genetic testing in the non-prenatal genetic testing guideline was considered.

Karen Kovak, a genetic counselor from OHSU, testified that there is considerable evidence for a lot of inappropriate genetic testing being done in Oregon. Most of this inappropriate testing is done by non-specialized genetic providers. Based on provider surveys, there is a low level of knowledge and confidence in ordering genetic tests. Ms. Kovak feels that the proposed change to the non-prenatal genetic testing guideline would result in even more inappropriate genetic tests being ordered. Ms. Kovak recommended that USPSTF guidelines be used as NCCN guidelines apply mainly to patients with cancer, rather than non-

symptomatic but at risk individuals. Olson noted that NCCN guidelines do apply to high risk non-symptomatic patients. Ms. Kovak requested that the Oregon Genetics Program have input into this guideline issue.

The problem of access to genetic counseling professionals in parts of Oregon was acknowledged.

Livingston noted that the CCOs are very concerned about inappropriate genetic testing.

Actions:
1) HERC staff will work with the Oregon Genetics Program and Ms. Kovak on types of providers who should be included in the non-prenatal genetic testing guideline and bring this topic back to the March VBBS meeting

- **Topic: Continuous blood glucose monitoring guideline**

Discussion: There was minimal discussion.

Actions:
1) Remove S1030-S1031 from Line 10 Type 1 Diabetes Mellitus
2) Guideline note 108 was modified as shown in Appendix B

- **Topic: Acute otitis media guideline**

Discussion: There was discussion about the deletion of coverage for patients who fail multiple medications. Smits pointed out that these patients need middle ear cultures and therefore would fall under the clause on complicating conditions. There was a suggestion to delete the complicating conditions clause, but it was felt that these are rare conditions and not likely to lead to abuse.

Actions:
1) Guideline note 29 was revised as shown in Appendix B

- **Topic: Hydrocele guideline**

Discussion: The summary document was presented. There was no discussion.

Actions:
1) Guideline note 63 was modified as shown in Appendix B

- **Topic: Cognitive Rehabilitation**

  Discussion: The summary document was presented. There was no discussion.

  Actions:
  1) Guideline note 90 was modified as shown in Appendix B

- **Topic: Concussion guideline**

  Discussion: It was pointed out that the previously recommended changes to the concussion line titles to change the reference from loss of consciousness to persistent symptoms have not been carried out. These were reaffirmed.

  Actions:
  1) A new guideline regarding concussions was adopted as shown in Appendix A
  2) Reaffirm line title changes adopted in December 2010:
     a. 101 SEVERE/MODERATE HEAD INJURY: HEMATOMA/EDEMA WITH ~~LOSS OF CONSCIOU0SNESS~~ PERSISTENT SYMPTOMS, COMPOUND/DEPRESSED FRACTURES OF SKULL
     b. 641 MINOR HEAD INJURY: HEMATOMA/EDEMA WITH NO ~~LOSS OF CONSCIOU0SNESS~~ PERSISTENT SYMPTOMS

- **Topic: Oral health risk assessments**

  Discussion: Livingston presented an issue summary. The question was raised as to whether this would diminish patients seeking dental services if preventive services were provided in primary care offices. Members agreed that barriers to dental evaluations and services were significant and that risk of not having these services is greater than a potential risk of relocation of services. Shaffer raised the concern that there are some implementation issues that may take longer to resolve than by the April 1, 2014 List. The specific concerns are about what would qualify as a training program and which standardized risk assessment tools would be appropriate. There was concern that if risk assessment and counseling codes were added to medical lines prior to establishment of criteria that there would be confusion. There was clarification that DMAP administrative rules would have authority over training and tools. Additionally, there was a question about the choice of 21 as a cutoff for children and it was clarified that was chosen because of the ACA requirements of dental services for up to age 21. After discussion, a guideline was proposed that would enable these codes to be placed on the April 1, 2014 List, and DMAP will go through its administrative rules process to address the implementation issues that may take longer than April 1 to fully define. There was a discussion about the D0191 code which is currently only open for payment for dentists. The decision was made to add this code to Line 3 and Line 1 with a guideline as well. D0145 was discussed and DMAP would need to determine how this

may be opened up to non-dentists given other states have done this, although the coding definition appears specific to dentists.

Dodson suggested OMA, OAFP, AAP society, and OHAP all work together to determine implementation considerations.

Actions:

1) Place D0601-0603 and D0191 on Lines 1,3, and 58
2) Adopt a new guideline:

   Guideline Note XXX Oral Health Risk Assessment
   Line 1,3, 58
   CDT codes D0601-D0603 and D0191 coverage is restricted on these lines as follows:

   Line 1: pregnant women only
   Line 3: children under the age of 6 only
   Line 58: children under the age of 21 only

   These services are included only when performed using approved tools and when performed by a provider who has completed an approved program.
3) Place D0145 on Lines 3 and 58
4) DMAP will address through its rules process:
   a. Appropriate standardized tools that would be required to receive reimbursement for risk assessment
   b. Necessary training for medical providers to bill using these codes
5) Dodson and Tyack to work together with staff on coordinating logistics.

- **Topic: Materials for dental restorations**

Discussion: Livingston presented a summary document. Tyack added that the composites are improving in longevity and catching up to amalgam. Also, some hospitals do not have amalgam separators. It was agreed that In order to keep access at an acceptable level, there needs to be availability of composite fillings.

Actions:

1) Place D2391-D2394 on Line 372 and remove from Line 676.
2) Add a guideline as follows:

   GUIDELINE NOTE XXX DENTAL FILLINGS FOR POSTERIOR TEETH
   Line 372
   For dental fillings in posterior teeth, amalgam is preferred for extensive restorations. If amalgam is unavailable or contraindicated, composite is acceptable.

MOTION: To approve the all guideline changes as presented above, with no decision made on the genetic testing guideline on familial cancer. CARRIES 8-0.

- **Topic: Fibromyalgia**

Discussion: Smits reviewed the evidence summary regarding the efficacy of various therapies for fibromyalgia and the proposal to create a new line for fibromyalgia.

Testimony:

Dr. Robert Bennett, rheumatologist, OHSU, testified that fibromyalgia should be its own line. He testified that fibromyalgia was ubiquitous, with 5% of women, 1% of men with the diagnosis. Fibromyalgia involves changes in the central nervous system. Patients with other types of chronic pain can develop fibromyalgia due to these CNS changes. Fibromyalgia interacts with many other conditions, many of which are covered on the Prioritized List. He feels that fibromyalgia has comparable pain and suffering to rheumatoid arthritis. Other states Medicaid cover fibromyalgia. Fibromyalgia impact scale is a reliable tool to determine the severity of fibromyalgia.

Kim Jones, FNP, OHSU, fibromyalgia researcher, presented several articles to the subcommittee. She stressed that studies should look at more than 1 outcome (not just pain) to determine if a treatment is clinically significant. She reviewed importance of exercise, with PT input, and presented effectiveness studies for trigger point injections.

Dr. Ginerva Lipton, a primary care physician in Legacy, testified that there is no cure for fibromyalgia, need to consider definition of effectiveness. Small reduction in pain or increase in function can have a big impact on patients—on their ability to get back to work, function, etc. In her practice, she finds the following treatments are effective: pregabalin, other medications, trigger point injections (long term and short term relief), specialized PT techniques (myofascial release in particular), PT education on how to exercise/home, myofascial release techniques).

Tamara Staples, Tami Stacklehouse, and Jodie Sundberg patients and advocates, presented a petition signed by persons all over the US requesting coverage for fibromyalgia by OHP. Their testimony stressed the importance of getting the correct treatment and getting it early. They testified that PTSD and rheumatoid arthritis are covered conditions which are similar to fibromyalgia in severity and ability to treat. Not treating fibromyalgia can lead to conditions like hypertension which require treatment. They testified to the frustration of not being able to access treatments and services for their fibromyalgia.

BJ Cavnor testified it is extremely important that OHP recognize fibromyalgia and provide proper treatment. Patients with fibromyalgia have 4 times the risk of suicide (consistent with other chronic pain conditions). Not covering fibromyalgia puts unnecessary burdens for patients and is unfair. He supports a personal multi-modal approach, including alternative therapies. He believes that treatment will make fibromyalgia a chronic manageable condition rather than a chronic disabling condition.

The subcommittee debated whether a new line should be created for fibromyalgia, and there was unanimous consent that such a line should be created. The procedures to be included on this line were debated, particularly PT services. Most members felt that exercise could be done without a specific PT visit or recommendation. Ocker suggested getting input from the PT/OT community. A suggestion was made to put PT codes on the line with a guideline limiting visits to a consult visit and a follow up visit, or 3 visits a year or similar limit. No decision about inclusion of PT services was reached. HERC staff will work with experts to determine if PT services should be included, and have PT community input on a guideline if such services are included on the line.

There was extensive discussion about the scoring of the proposed line. There was debate about the healthy life score. The proposed scores ranged from 2 to 4. Conditions with similar scores were reviewed. The pain and suffering score was debated, with suggested scores ranging from 2 to 4. Effectiveness score proposals ranged from 2 to 3. There was debate about how the "moderate effectiveness" found in the evidence review translated into this score. HERC staff was asked to go back to the literature and try to come up with a percent of patients who improved, and what percent improvement was seen. The need for service was also discussed. Staff proposed 0.8, to account for the fact that those with mild disease did not require treatment. The advocates suggested 1.0 as they felt all patients should receive treatment. The subcommittee generally where in agreement that 0.8 was reasonable for need for service

The decision was made to further discuss this topic at the March VBBS meeting. HERC staff will 1) make a summary of conditions with various healthy life scores between 2 and 4, 2) make a summary of conditions with a pain/suffering score of 2 to 3, and 3) look at the effectiveness of treatment in the literature and try to find a percent score that is more easily translated into the effectiveness score used in the prioritization methodology.

Actions:

1) Further discussion on this topic will be on the March VBBS agenda

- **Topic: Factious disorder and somatization line merge**

  Discussion: Tabled to the March, 2014 VBBS meeting

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- **Topic: Prenatal genetic testing coverage guidance**

  Discussion: This item was informational only for the VbBS, to show committee members the CPT codes included in the guideline. Dr. Tom Jenkins, perinatologist, testified that genetic testing should be covered for elevated risk for aneuploidy (advanced maternal age, etc.). Livingston noted that this topic has already been discussed in great detail. Dr. Jenkins then noted that the current guideline wording does not allow genetic testing for women with elevated risk for aneuploidy based on serum testing or for women who consider CVS or amniocentesis but decide not to proceed with the procedure. The subcommittee agreed with changes to include coverage for these two groups. However, this guideline topic was informational only and this topic needs to be addressed as scheduled at the HERC meeting later today.

  Actions:
  1) The prenatal genetic testing guideline will be discussed further at the January 2014 HERC meeting.

- **Topic: DXA coverage guidance**

  Discussion: Livingston presented an issue summary. She recommended changing this to a diagnostic guideline and specifying that it applies to adults. There was a discussion about this being a significant change from current practice, but derived from the evidence reviewed by HTAS.

  Actions: A new diagnostic guideline was approved as shown in Appendix A.

- **Topic: Coverage guidance on treatment of sleep apnea in adults**

  Discussion: Livingston presented an issue summary. Tyack asked about the removal of mandibular advancement devices. Shaffer discussed how there are differences in up front cost with mandibular advancement devices, versus cpap can be tried and compliance and improvement can be determined. The evidence was stronger for CPAP than for mandibular advancement devices. It was clarified that there would be no change in current coverage of oral appliances for OHP if the coverage guidance remained silent. VbBS was shown new guideline language that was presented to and subsequently revised by HERC later in the day. See the HERC minutes of January 9, 2014 for the approved language.

Actions:

1) Add the following coding specification to Line 210
   42299 Unlisted procedure, palate, uvula (use for laser assisted uvulopalatoplasty (LAUP), somnoplasty, palatal implants) does not pair on Line 210 with obstructive sleep apnea in adults.

- **Public Comment:**

  No additional public comment was received

- **Issues for next meeting:**
  - Non-prenatal genetic testing guideline
  - Screening for lung cancer diagnostic guideline
  - Fibromyalgia prioritization
  - Somatization and factitious disorder line merge

- **Next meeting:** March 13, 2014 at Meridian Park Hospital Health Education Center, Conference Room 117B&C in Tualatin, OR

Appendix A
New Guidelines

GUIDELINE NOTE XXX CAROTID ARTERY STENTING
Lines 342, 440
Carotid artery stenting (CPT 37215-37217) is included on lines 342 and 440 for patients who have not had a disabling stroke (modified Rankin scale ≥ 3) AND

1) who are at high risk for complications during carotid endarterectomy (CEA) due to significant comorbidities and/or anatomic risk factors (i.e., recurrent stenosis and/or previous radical neck dissection) and who also have symptomatic (recent transient ischemic attack or ischemic stroke) carotid artery stenosis >50% OR
2) who are at high risk for complications during CEA due to significant comorbidities and/or anatomic risk factors and have asymptomatic carotid artery stenosis ≥80% only if best current medical therapy is not tolerated or contra-indicated.

GUIDELINE NOTE XXX PEDIATRIC TRIGGER THUMB
Line 406
ICD-9 756.89/ICD-10 M65.31x is included on line 406 for treatment of pediatric trigger thumb only. Surgical treatment should be reserved for trigger thumb that does not spontaneously resolve within 48 months of diagnosis. Immediate surgery may be considered for bilateral trigger thumb or trigger thumb with locking symptoms

GUIDELINE NOTE XXX CONCUSSION AND POST CONCUSSION SYNDROME
Lines 101, 209, 641
ICD-9 diagnosis codes 850.0 and 850.9/ICD-10 diagnosis codes S06.0x0, S06.2x0 and S06.300 are included on line 101 only for concussions with symptoms that persist for more than 7 days but less than 3 months; otherwise, these diagnoses are included on line 641. When concussion symptoms last for more than 3 months, the diagnosis of post-concussive syndrome (ICD-9 310.2/ICD-10 F07.81) should be used, which is included on line 209

DIAGNOSTIC GUIDELINE XX OSTEOPOROSIS SCREENING AND MONITORING IN ADULTS

Osteoporosis screening by dual-energy X-ray absorptiometry (DXA) is covered only for women aged 65 or older, and for men or younger women whose fracture risk is equal to or greater than that of a 65 year old white woman who has no additional risk factors.

Fracture risk should be assessed by the World Health Organization's FRAX tool or similar instrument.

Appendix A

Repeat osteoporosis screening by DXA, for women with normal bone density, is not covered more frequently than once every fifteen years.

Routine osteoporosis screening by DXA is not covered for men.

Unless there has been significant change in the individual's risk factors, such that rapid changes in bone density are expected, monitoring of individuals with low bone density by repeat DXA scanning is covered only at the following frequencies:

- once every two years for those with osteoporosis or advanced osteopenia (T-score of -2.00 or lower)
- once every four years for moderate osteopenia (T-score between -1.50 and -1.99)
- once every fifteen years for mild osteopenia (T-score between -1.01 and -1.49).

Repeat testing is only covered if the results will influence clinical management. For purposes of monitoring osteoporosis medication therapy, testing at intervals of less than two years is not covered.

Appendix B
Modified Guideline Notes

GUIDELINE NOTE 79, BREAST RECONSTRUCTION

Lines 4,197

Breast reconstruction ~~(which may include contralateral reduction mammoplasty)~~ is only covered after mastectomy as a treatment for breast cancer or as prophylactic treatment for the prevention of breast cancer in a woman who qualifies under Guideline Note 3, and must be completed within 5 years of initial mastectomy.

Breast reconstruction may include contralateral reduction mammoplasty (CPT 19318) or contralateral mastopexy (CPT 19316). Mastopexy is only to be covered when contralateral reduction mammaplasty is inappropriate for breast reconstruction and mastopexy will accomplish the desired reconstruction result.

GUIDELINE NOTE 108, CONTINUOUS BLOOD GLUCOSE MONITORING

Line 10

Services related to real-time continuous blood glucose monitoring (for long-term use) or retrospective glucose monitoring (for short-term use) ~~Continuous blood glucose monitoring systems (CPT codes 95250-95251, HCPCS codes S1030-S1031) with real-time or retrospective continuous glucose monitoring systems are only~~ are included on Line 10 ~~for Type 1 diabetics for whom~~ only when insulin pump management is being considered, initiated, or utilized and only when the patient has at least ~~who also have~~ one of the following:

- HbA1c levels greater than 8.0% (despite compliance with treatment), or
- a history of recurrent hypoglycemia.

GUIDELINE NOTE 29, TYMPANOSTOMY TUBES IN ACUTE OTITIS MEDIA

Line 418

Tympanostomy tubes (CPT 69436) are only included on this line as treatment for

1) recurrent acute otitis media (three or more well-documented and separate episodes in six months or four or more well-documented and separate episodes in ~~one year~~ the past 12 months with at least 1 episode in the past 6 months) ~~that fail appropriate medical management~~ in patients who have unilateral or bilateral middle ear effusion at the time of assessment for tube candidacy, or

~~2) for patients who fail medical treatment secondary to multiple drug allergies or who fail two or more consecutive courses of antibiotics, or~~

3) 2) for patients with complicating conditions (immunocompromised host, meningitis by lumbar puncture, acute mastoiditis, sigmoid sinus/jugular vein thrombosis by CT/MRI/MRA, cranial nerve paralysis, sudden onset dizziness/vertigo, need for middle ear culture, labyrinthitis, or brain abscess).

Appendix B

Patients with craniofacial anomalies, Down's syndrome, cleft palate, permanent hearing loss of 25dB or greater independent of otitis media with effusion, and patients with speech and language delay may be considered for tympanostomy if unresponsive to appropriate medical treatment or having recurring infections (without needing to meet the strict "recurrent" definition above).

GUIDELINE NOTE 63, HYDROCELE REPAIR
Line 175
Excision of hydrocele is only covered for children age 18 and younger with hydroceles which persist after 18 months of age.

GUIDELINE NOTE 90, COGNITIVE REHABILITATION
Lines 101,185,201,209,308,342,375,407
Once physical stabilization from acute brain injury has occurred, as determined by an attending physician, cognitive rehabilitation (CPT 97532) is ~~covered~~ included on this line for a three month~~s~~ period. This three month period does not have to be initiated immediately following stabilization from the injury. For up to 3 years following the acute event, an additional 6 visits of cognitive rehabilitation are included on this line each time the patient has ~~Whenever there is~~ a major change in status ~~as evidenced by~~ resulting in a significantly improved prognosis ~~for up to 3 years following the acute event, 6 additional visits of cognitive rehabilitation are covered.~~ Cognitive rehabilitation is not ~~covered~~ included on this line for those in a vegetative state or for those who are unable or unwilling to participate in therapy.

Section 2.0

Staff Report

Section 3.0

Consent Agenda-

Straightforward Items

Straightforward Issues—March, 2014

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
E&M codes	Medical visits	**654** DENTAL CONDITIONS WHERE TREATMENT IS CHOSEN PRIMARILY FOR AESTHETIC CONSIDERATIONS **655** DENTAL CONDITIONS WHERE TREATMENT RESULTS IN MARGINAL IMPROVEMENT	Medical visit codes appear on two dental lines. HERC staff recommends removal	Remove E&M codes from lines 654 and 655
26560-26562	Repair of syndactyly (web finger) each web space	**290** COMPLICATIONS OF A PROCEDURE ALWAYS REQUIRING TREATMENT **362** DEFORMITY/CLOSED DISLOCATION OF JOINT **391** DEFORMITY/CLOSED DISLOCATION OF MINOR JOINT AND RECURRENT JOINT DISLOCATIONS **430** ACUTE PERIPHERAL MOTOR AND DIGITAL NERVE INJURY **511** PERIPHERAL ENTHESOPATHIES **534** DEFORMITIES OF UPPER BODY AND ALL LIMBS	Repair of web finger is on 6 lines for the October 1, 2014 List. Syndactyly (ICD-9 755.1x) is on line 362. The repair codes should only be on this line.	Remove 26560-26562 from lines 290, 391, 430, 511, and 534 Keep only on line 362 for October 1, 2014 List
		122 NUTRITIONAL ANEMIAS	Many non-anemia diagnoses are on this line—various vitamin deficiencies, malnutrition, etc.	Rename line 122 NUTRITIONAL ~~ANEMIAS~~ DEFICIENCIES
		364 DYSTONIA (UNCONTROLLABLE); LARYNGEAL SPASM AND STENOSIS	The coding specification on line 364 should be removed. The 2014 CPT codes provided separate codes which allowed differentiation of indication based on CPT code. Therefore, there is no longer any reason to call out certain pairings on this line.	Remove the following coding specification from line 364: Chemodenervation with botulinum toxin injection (CPT 64612-64614) is included on this line only for treatment of blepharospasm (ICD-9 333.81), spasmodic torticollis (ICD-9 333.83), and other fragments of torsion dystonia (ICD-9 333.89).

Section 4.0

biennial review

Fibromyalgia Review for March 2014

Question: Should Fibromyalgia be given higher priority on the Prioritized List?

Question source: National Fibromyalgia and Chronic Pain Association

Issue: Fibromyalgia is currently located on Line 634 DISORDERS OF SOFT TISSUE, which is below the present funding line. Prioritization of fibromyalgia was discussed at the October, 2013 and January, 2014 VBBS meetings. Evidence for effectiveness of various therapies was reviewed, including exercise, medications, cognitive behavioral therapy, and complementary and alternative medical treatments. Expert testimony and patient/advocate testimony was heard. The commissioners agreed that fibromyalgia should be made its own line for the 2016 biennial review Prioritized List. Various scoring options were reviewed for possible line prioritization. HERC staff was charged with providing summary data regarding similar condition scores for impact on healthy life and pain and suffering, and asked to review the literature for a better estimate of treatment efficacy.

Current and HERC and expert proposed scoring for various categories discussed at the January meeting are listed below:

Category	**Current score**	**HERC staff proposal**	**Expert Proposal**	**Committee Suggested Score Range**
Impact on Healthy Life	0	2	3	2-4 range
Pain/Suffering	1	2	3	2-3 range
Effectiveness	1	2	2	Review
Need for treatment	0.2	0.8	1.0	0.8

Healthy Life

Score categories

2 – Nonfatal with a modest impact on health

3 – Nonfatal with a low probability of a significant residual effect or a high probability of a residual effect with a moderate impact on health

4 – Nonfatal with low probability (<20%) of significant disability or at least a moderate probability of a significant residual effect

HL score = 1	
Representative Conditions	Line
Urticaria	551
Mild eczema	559
Allergic rhinitis	566
Minor sprains and strains	616
HL score = 2	
Representative Conditions	Line
Severe cystic acne	377
Otitis externa	431
Urinary incontinence	459
Obsessive compulsive disorder	467
TMJ disorder	555
HL score = 3	
Representative Conditions	Line
Gout	306
Sarcoidosis	353
Chronic skin ulcers	383
Osteoarthritis	468
HL score = 4	
Representative Conditions	Line
Kidney stones	355
Panic disorder	396
Migraines	414
Mononeuritis multiplex	515

HERC staff recommendation: HL=3 to match similar conditions such as osteoarthritis

Pain and Suffering

1 – Intermittent pain of moderate level or frequent pain of low level and/or low level of suffering of the individual, immediate family or caregiver
2 – Frequent pain of moderate level or constant pain of low level and/or modest level of suffering of the individual, immediate family or caregiver
3 – Intermittent pain of high level or constant pain of moderate level and/or moderate level of suffering of the individual, immediate family or caregiver
4 – Frequent pain of high level and/or high level of suffering of the individual, immediate family or caregiver
5 – Constant pain of high level and/or extreme suffering of the individual, immediate family or caregiver

Suffering score = 1	
Representative Conditions	Line
Lyme disease	271
Cirrhosis	338
Dental caries	347
TIA	419
Suffering score = 2	
Representative Conditions	Line
Mild or moderate depression	207
Gout	306
Osteoarthritis	462
Mononeuritis multiplex	515
Suffering score = 3	
Representative Conditions	Line
Multiple sclerosis	255
Chronic osteomyelitis	258
Spinal disc disease with myelopathy	412
Migraines	414
Suffering score = 4	
Representative Conditions	Line
Traumatic amputation of legs	140
Shingles	159
Acute pancreatitis	198
Stroke	322
Trigeminal neuralgia	446

HERC staff recommendation: Suffering=2 to match similar conditions such as osteoarthritis

Effectiveness
0 – No demonstrated effectiveness (<5%) or causes harm
1 - Achieves desired result in 5-25% of cases
2 - Achieves desired result in 25-50% of cases
3 – Achieves desired result in 60-75% of cases
4 – Achieves desired result in 75-95% of cases
5 – Achieves desired result in 95+% of cases

Effectiveness score = 0	
Representative Conditions	Line
Pica	640
Viral conjunctivitis	641
Mastodynia (breast pain)	645
Effectiveness score = 1	
Representative Conditions	Line
Obesity (INTENSIVE NUTRITIONAL/ PHYSICAL ACTIVITY COUNSELING)	325
Bulemia	385
Chronic pelvic pain	536
Mononeuritis multiplex	541
Lymphedema	579
Effectiveness score = 2	
Representative Conditions	Line
Cirrhosis	338
Autism	313
Viral encephalitis	540
Effectiveness score = 3	
Representative Conditions	Line
Dialysis for chronic kidney disease	343
Pacemakers for cardiac arrythmias	350
Generalized anxiety disorder	418
Root canal for periodontal disease	448

Fibromyalgia Review for March 2014

Review of literature for effectiveness of various treatments for fibromyalgia

1) Exercise
    a. Cochrane 2009
        i. Aerobic exercise training compared to no exercise improved overall well-being by 7 points on a scale of 0 to 100 and reduce pain by 1.3 on a scale of 0 to 10.
        ii. Strength training compared to no exercise reduced pain by 49 fewer points on scale of 0 to 100, improved overall well-being by 41 points on a scale of 0 to 100, and lead to 2 fewer active tender points on a scale of 0-18.
            1. **Note**: based on 2 small, low quality studies (N=21, 47 patients)
2) Cognitive behavioral therapy
    a. Cochrane 2013
        i. CBTs were superior to controls in reducing pain at end of treatment by 0.5 points on a scale of 0 to 10 and by 0.6 points at long-term follow-up (median 6 months)
        ii. in reducing negative mood at end of treatment by 0.7 points on a scale of 0 to 10 and by 1.3 points at long-term follow-up (median 6 months)
        iii. in reducing disability at end of treatment by 0.7 points on a scale of 0 to 10 and at long-term follow-up (median 6 months) by 1.2 points
3) Multi-disciplinary therapy
    a. Hauser 2009
        i. Difficult to extract effect level
        ii. Overall effect on pain, fatigue and depression appears quite small based on meta-analysis plots (figures 2-4 in paper)
    b. Arnold 2012
        i. The standardized mean differences (SMDs) of multicomponent therapy vs. controls at the end of therapy were low for pain and fatigue and moderate for quality of life. The SMDs for multicomponent therapy vs. controls at follow-up were low for fatigue and quality of life.
4) Duloxetine
    a. Cochrane 2011
        i. NNT for 30-50% improvement in one person ranged from 5 to 8 patients
5) Pregabalin
    a. Moore 2009 (Cochrane)
        i. NNT for 50% pain relief in one patient was 10-14
    b. Hauser 2010
        i. NNT for 30% pain reduction in one paitent was 8.6
    c. Siler 2011
        i. NNT to reduce pain in 1 patient was 8
        ii. Range of response with pregabalin was 26-50% with range of response to placebo 19-35%
    d. Tzellos 2010
        i. NNT for pain reduction in 1 patient was 7
6) Amitriptyline
    a. Cochrane 2012
        i. amitriptyline provides pain relief in about 1 in 4 (25%) more people than does placebo, and about 1 in 4 (25%) more people than placebo report having at least one adverse event, probably not serious but disconcerting
7) Milnacipran

a. Cochrane 2012
    i. Milnacipran at either dose provided moderate pain relief (at least 30% reduction in pain intensity) to 10% more participants than did placebo

Summary of effectiveness data:
All interventions (other than strength training, which is likely biased by low quality, small studies) appeared to have a 5-20% achievement of desired reduction in pain, fatigue and/or depression.
HERC staff recommendation: effectiveness score of 1

HERC staff recommendations:
1) Re-prioritize fibromyalgia and create a new line for this condition (ICD-9 729.1 Myalgia and myositis, unspecified /ICD-10 M79.7 Fibromyalgia)
2) Adopt a guideline for the treatment of fibromyalgia as shown below

Line XXX Fibromyalgia
Treatment: Medical Therapy
ICD-10: M79.7
CPT: CBT (90785, 90832-90853), medical office visits (98966-99215, 99441-99449, 99487-99489), medical team conference (99366-99368), preventive medicine visit (99381-99429)

Scoring
Category: 7
HL: 3
Suffering: 2
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 0
Effectiveness: 1
Need for service: 0.8
Net cost: 2
Score: 80
Approximate line placement: 549

DRAFT Scoring Criteria for the HERC Individual and Population Health Impact Measures

Impact on Healthy Life

0 – No impact on health
1 – Nonfatal with a marginal impact on health
2 – Nonfatal with a modest impact on health
3 – Nonfatal with a low probability of a significant residual effect or a high probability of a residual effect with a moderate impact on health
4 – Nonfatal with low probability (<20%) of significant disability (e.g., blindness) or at least a moderate probability of a significant residual effect
5 – Nonfatal, but at least moderate (>20%) probability of significant disability; Very low fatality (<1%)
6 – Low fatality (1-5%)
7 – Moderate fatality (5-20%)
8 – Significant fatality (20-50%)
9 – High fatality (50-90%)
10 – Very high fatality (>90%)

Impact on Pain and Suffering

0 – No impact on pain or suffering
1 – Intermittent pain of moderate level or frequent pain of low level and/or low level of suffering of the individual, immediate family or caregiver
2 – Frequent pain of moderate level or constant pain of low level and/or modest level of suffering of the individual, immediate family or caregiver
3 – Intermittent pain of high level or constant pain of moderate level and/or moderate level of suffering of the individual, immediate family or caregiver
4 – Frequent pain of high level and/or high level of suffering of the individual, immediate family or caregiver
5 – Constant pain of high level and/or extreme suffering of the individual, immediate family or caregiver

Population Effects

0 – No impact on population health
1 – Nontreatment would result in limited spread of a significant nonfatal disease or have a low impact on population safety (e.g. due to the nontreatment of a mental health condition)
2 – Nontreatment would result in a moderate spread of a significant nonfatal disease or have a modest impact on population safety
3 – Nontreatment would result in a limited spread of a potentially fatal disease or a wide spread of a significant nonfatal disease or have a moderate impact on population safety
4 – Nontreatment would result in a moderate spread of a potentially fatal disease or have a high impact on population safety
5 – Nontreatment would result in a wide spread of a potentially fatal disease or have a very high impact on population safety

DRAFT Scoring Criteria for the HERC Individual and Population Health Impact Measures

Impact on Vulnerable Populations

0 – No impact on vulnerable populations
1 – Somewhat disproportionate impact of a condition with a moderate impact on health on one or more vulnerable populations (does not include men, women, children, pregnant women considered as separate populations, nor low-income individuals, since methodology is only being applied to Medicaid population at this point)
2 – Moderately disproportionate impact of a condition with a moderate impact on health on one or more vulnerable populations
3– Somewhat disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations
4 – Moderately disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations
5 – Highly disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations

Tertiary Prevention

0 – No tertiary prevention provided by treatment and early treatment does not prevent progression of the disease
1 – Treatment will prevent of moderate complication and/or early treatment may prevent progression of the disease resulting in a moderate impact on health
2 – Low to modest likelihood that treatment will prevent a significant complication or prevent progression of the disease resulting in significant impact on health
3 –Moderate to high likelihood that treatment will prevent a significant complication or prevent progression of the disease resulting in significant impact on health
4 – Low to modest likelihood that treatment will prevent severely debilitating complication and/or early treatment with prevent progression of disease leading to severe disability or death
5 – Moderately to high likelihood that treatment will prevent severely debilitating complication and/or early treatment with prevent progression of disease leading to severe disability or death

Effectiveness

0 – No demonstrated effectiveness (<5%) or causes harm
1 - Achieves desired result in 5-25% of cases
2 - Achieves desired result in 25-50% of cases
3 – Achieves desired result in 50-75% of cases
4 – Achieves desired result in 75-95% of cases
5 – Achieves desired result in 95+% of cases

Net Cost

0 – Very high cost (>$100,000)
1 – High cost ($20,000-$100,000)
2 – Moderate cost ($5,000-$20,000) or higher cost somewhat offset by cost of treatment alternative
3 – Modest cost ($1,000-$5,000) or higher cost significantly offset by cost of treatment alternative
4 – Low cost (<$1,000) or higher cost nearly offset by cost of treatment alternative
5 – Cost savings

OHSU/Good Samaritan/ National Fibromyalgia and Chronic Pain Association
Proposal for Fibromyalgia Scoring Criteria
for the HSC Individual and
Population Health Impact Measures
2/26/2014

Impact on Healthy Life

0 – No impact on health
1 – Nonfatal with a marginal impact on health
2 – Nonfatal with a modest impact on health
3 – Nonfatal with a low probability of a significant residual effect or a high probability of a residual effect with a moderate impact on health
4 – Nonfatal with low probability (<20%) of significant disability or at least a moderate probability of a significant residual effect
5 – Nonfatal, but at least moderate (>20%) probability of significant disability (e.g., blindness); Low fatality with onset in elderly
6 – Moderately fatal with onset in elderly; low fatality with onset in middle age
7 – Highly fatal with onset in elderly; moderately fatal with onset in middle age; low fatality with onset in young adulthood
8 – Highly fatal with onset in middle aged; moderately fatal with onset in young adulthood; low fatality with onset in childhood/newborn
9 – Highly fatal with onset in young adulthood; moderately fatal with onset in childhood/newborn
10 – Highly fatal with onset in childhood/newborn

Impact on Pain and Suffering

0 – No impact on pain or suffering
1 – Intermittent pain of moderate level or frequent pain of low level and/or low level of suffering of the individual, immediate family or caregiver
2 – Frequent pain of moderate level or constant pain of low level and/or modest level of suffering of the individual, immediate family or caregiver
3 – Intermittent pain of high level or constant pain of moderate level and/or moderate level of suffering of the individual, immediate family or caregiver
4 – Frequent pain of high level and/or high level of suffering of the individual, immediate family or caregiver
5 – Constant pain of high level and/or extreme suffering of the individual, immediate family or caregiver

Population Effects

0 – No impact on population health
1 – Nontreatment would result in limited spread of a significant nonfatal disease or have a low impact on population safety (e.g. due to the nontreatment of a mental health condition)
2 – Nontreatment would result in a moderate spread of a significant nonfatal disease or have a modest impact on population safety
3 – Nontreatment would result in a limited spread of a potentially fatal disease or a wide spread of a significant nonfatal disease or have a moderate impact on population safety
4 – Nontreatment would result in a moderate spread of a potentially fatal disease or have a high impact on population safety
5 – Nontreatment would result in a wide spread of a potentially fatal disease or have a very high impact on population safety

Impact on Vulnerable Populations

0 – No impact on vulnerable populations
1 – Somewhat disproportionate impact of a condition with a moderate impact on health on one or more vulnerable populations (does not include men, women, children or pregnant women considered as separate populations or low-income individuals, since methodology is only being applied to Medicaid population at this point)

OHSU/Good Samaritan/ National Fibromyalgia and Chronic Pain Association
Proposal for Fibromyalgia Scoring Criteria
for the HSC Individual and
Population Health Impact Measures
2/26/2014

2 – Moderately disproportionate impact of a condition with a moderate impact on health on one or more vulnerable populations
3– Somewhat disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations
4 – Moderately disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations
5 – Highly disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations

Tertiary Prevention
0 – No tertiary prevention provided by treatment and early treatment does not prevent progression of the disease
1 – Treatment will prevent of moderate complication and/or early treatment may prevent progression of the disease resulting in a moderate impact on health
2 – Low to modest likelihood that treatment will prevent a significant complication or prevent progression of the disease resulting in significant impact on health
3 –Moderate to high likelihood that treatment will prevent a significant complication or prevent progression of the disease resulting in significant impact on health
4 – Low to modest likelihood that treatment will prevent severely debilitating complication and/or early treatment with prevent progression of disease leading to severe disability or death
5 – Moderately to high likelihood that treatment will prevent severely debilitating complication and/or early treatment with prevent progression of disease leading to severe disability or death

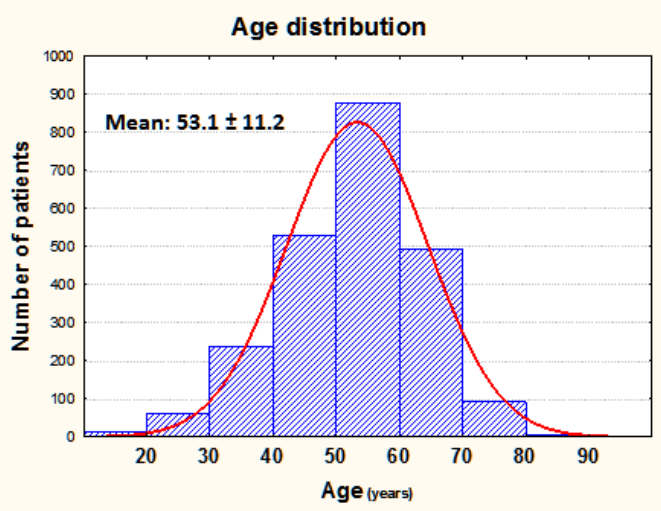
Effectiveness
0 – No demonstrated effectiveness (<5%) or causes harm
1 - Achieves desired result in 5-25% of cases
2 - Achieves desired result in 25-50% of cases
3 – Achieves desired result in 50-75% of cases
4 – Achieves desired result in 75-95% of cases
5 – Achieves desired result in 95+% of cases

Net Cost
0 – Very high cost (>$100,000)
1 – High cost ($20,000-$100,000)
2 – Moderate cost ($5,000-$20,000) or higher cost somewhat offset by cost of treatment alternative
3 – Modest cost ($1,000-$5,000) or higher cost significantly offset by cost of treatment alternative
4 – Low cost (<$1,000) or higher cost nearly offset by cost of treatment alternative
5 – Cost savings

The NFMCPA survey conducted for presentation to the FDA (part one)

During a couple of weeks at the end of November 2013 some 3,200 National Fibromyalgia & Chronic Pain Association (**NFMCPA)** members completed a questionnaire designed by Dr. Rob Bennett (Prof. of Medicine OHSU). The intent of this questionnaire was to provide information for the Federal Drug Administration (FDA) on common symptoms encountered by fibromyalgia patients, other than pain.

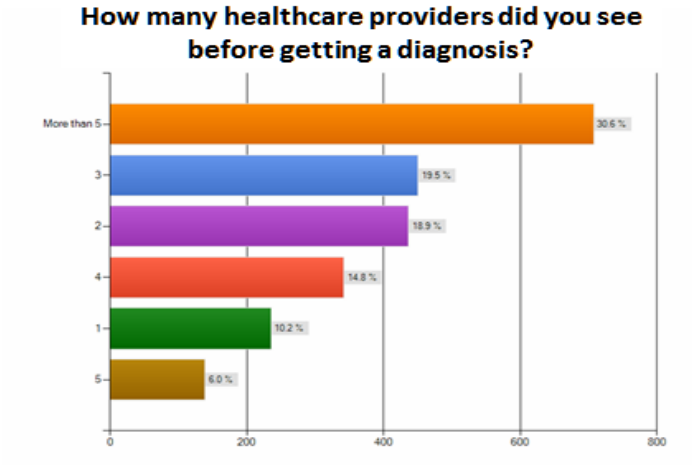
Age



Most of the subjects completing the survey were middle-aged with a mean age of 53. The age distribution can be seen in the accompanying histogram:

However, as you can see, there was a normal distribution of ages ranging from the late teens to 80-year-olds.

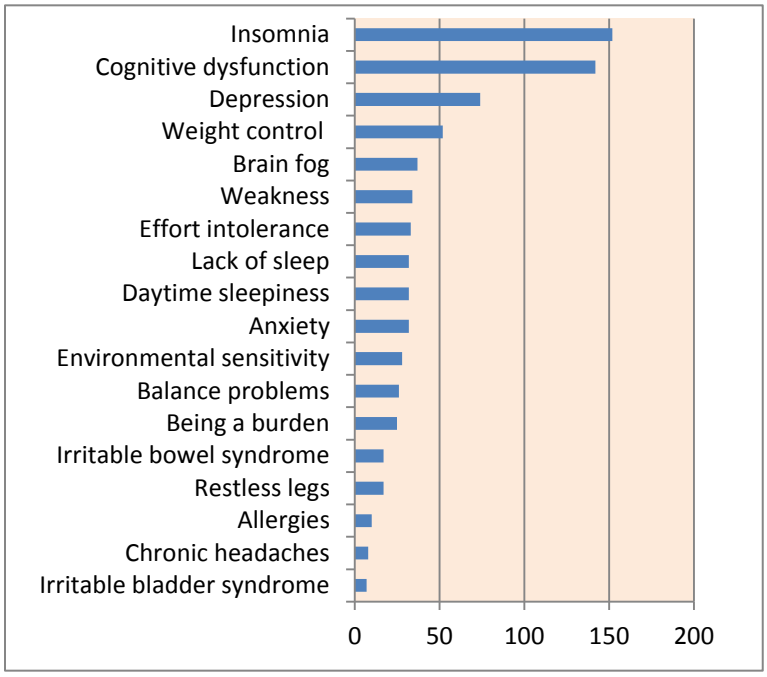
Getting a diagnosis of fibromyalgia



Getting a definitive diagnosis of fibromyalgia can be time-consuming and frustrating. One of the questions we asked in the survey was how many healthcare providers did you see before getting fibromyalgia. Approximately one third of the respondents had to see more than 5 healthcare professionals before getting a definite diagnosis of fibromyalgia.

Non-Pain problems

The FDA was particularly interested in learning about the problems experienced by fibromyalgia patients, other than pain.



One of the questions in the survey asked: *"Out of all your non-pain symptoms, which one causes you most distress?"* Replies are seen in the following chart (the numbers in the lower axis have a number of subjects reporting each problem).

By far the commonest non-pain problems were insomnia and problems with memory and concentration (i.e. cognitive dysfunction). Note the question asked was "which one non-pain problem caused most distress". Thus a patient with insomnia could also have problems with balance, but such additive problems are not captured in this chart.

Some of the individual comments were:

Fearing that being with people will aggravate pain later.
Feel like I am a burden to my children.
Feeling a burden and nonproductive, I can't meet simple goals.
Sometimes feel suicidal
Feeling as if I am living a "less than" life; not the life I envisioned.
Feeling exhausted and completely overwhelmed by the smallest tasks.
Feeling guilty that I can't fix symptoms without medication.
Feeling hopeless because I cannot be who I was or do the things I love.
Feeling like a burden due to loss of productivity.
Feeling that I am not understood and that my physical/energy limitations interfere with living a full life.
Feeling worthless, that my life no longer matters, having to leave my job because my symptoms were intolerable.
Fear of getting worse as I get older.
Unable to do what I used to do, because of brain fog and fear of the unknown.
Everything seems such an effort.
Being a burden to my family; my future looks bleak and full of a lifetime of pain.
Difficulty focusing on the task at hand.
Afraid to commit to do things because I don't know how capable I will be from day to day.
Not being as sharp as I used to be, can't remember something I may have been told a day ago.
Not feeling like I any longer belong with "normal" people.
Sensitivity to all stimuli. Hard to be around other people due to smells, movement, multiple noise sources.
There is no more pleasure or enjoyment in life.
Thinking problems. I "know" what I want to say but can't put it together.

Whereas the last question asked about the non-pain problem that caused most distress, there was also another question regarding the prevalence of non-pain problems in general. As is seen in the chart below, stiffness was the most common non-pain problem (96% of respondents reported stiffness). This was shortly followed by physical weakness, effort intolerance, reduced mental abilities and a weather changes effect. Environmental intolerance to noise, perfumes and cold was reported in 75 to 92% of subjects.

Non-pain problems (%)

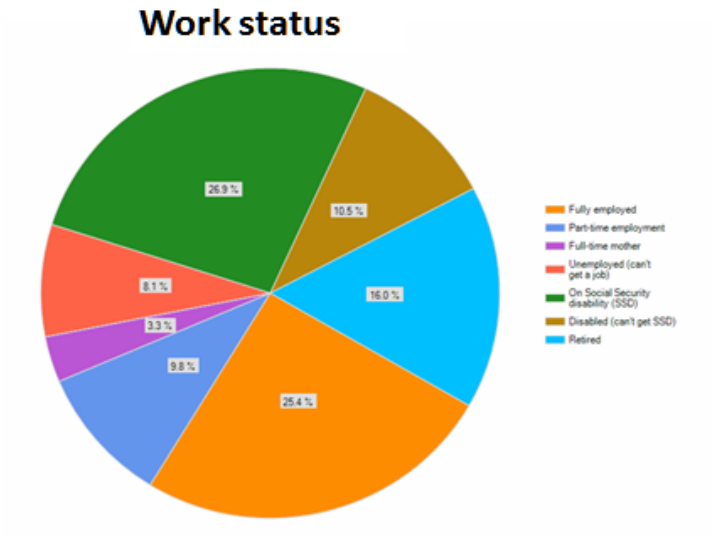
Severe stiffness	96	Irritable bowel syndrome	84
Physical weakness	95	Easily agitated	83
Everything is an effort	94	Chronic headaches	82
Reduce mental acuity	94	Guilt about being a burden	81
Weather change affect	94	Friends do not understand	79
Being productive	93	Low sex drive	77
Difficulty focusing	92	Has many allergies	76
Cold intolerance	92	Perfume intolerance	75
Insomnia	92	Difficulties with intimacy	73
Daytime sleepiness	91	Overactive bladder	72
Poor balance	90	Restless leg syndrome	65
Noise intolerance	90	Oversleeping	64
Effort intolerance	88	Wonders how will it all end?	54
Difficult controlling weight	87	Dr is not helpful	53
Dislike of using drugs	86	Dr doesn't Rx pain meds	49
Reduced pleasure	85	Sometimes feel suicidal	39
Neck extension symptoms	85	Sleep apnea	39
Feeling hopeless/depressed	85		

This chart confirms the high frequency of existential problems such as feeling guilty about being a burden, feeling hopeless and depressed, friends inability to understand, wondering how it will all end and sometimes feeling suicidal (39%), and provide a vivid picture of what it means to be a fibromyalgia patient. Suicidal ideation has been described in several recent papers; and this current survey adds to the increasing recognition that the frustration of having a poorly recognized chronic pain disorder to lead to thoughts as to “where it all end” and “may be ending my life is one way out”.

What are your sources of information about fibromyalgia

Medical practice has been forever changed by the ability of patients to consult the Internet. This means that doctors and other health care professionals are not the only fount of knowledge. In general, this is to the good, as many studies have associated education with a better outcome. It certainly appears that fibromyalgia patients are not an exception, with 82% obtaining information from the Internet and 48% obtaining information from the doctor. Please note these numbers are not mutually exclusive, and most patients are using the Internet in addition to consultations with healthcare professionals, as well as reading books and publications.

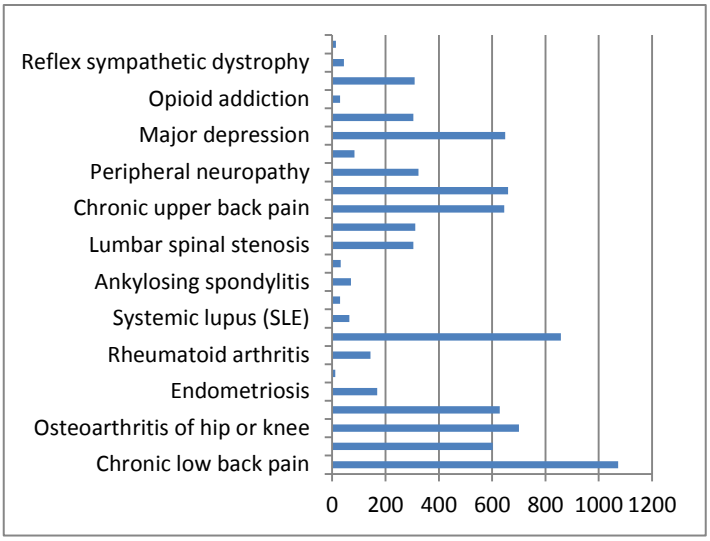
What is your work status



Fibromyalgia patients often have difficulty remaining productively employed on account increased pain on activity, severe fatigue and problems with memory and concentration. As you can see in this survey 25% of the subjects were fully employed and 10 % had part-time employment. Eight percent were unemployed and unable to get a job. Some 11% of subjects rated themselves disabled, but could not qualify for Social Security Disability (SSD). However, 27% of subjects were receiving SSD payments. Some 16% subjects were retired. Overall these figures are very similar to publish data.

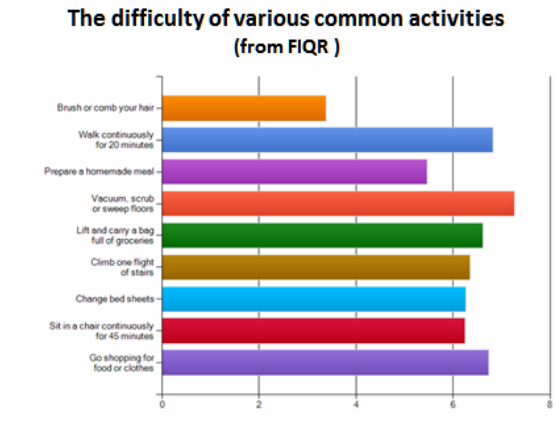
Other Diagnoses

Nearly all fibromyalgia patients have developed some other medical problems by the time they reach middle age.



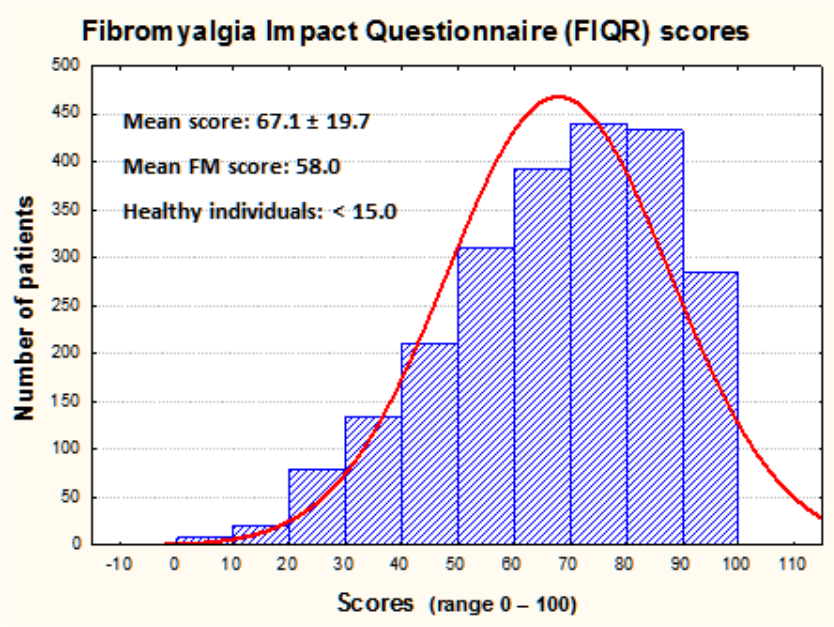
As you can see in the current survey over 1,000 of the 2,178 subjects had low back pain and over 800 suffered from migraine headaches. About 30% of subjects had osteoarthritis of the hands knees and hips; in many subjects this will considerably add to the burden of disability. There is a great deal of current interest in the concept that persistent pain arising in the periphery from joints, myofascial trigger points, headaches etc. lead to the changes in the nervous system characteristic of fibromyalgia. This is often referred to as “central sensitization”.

Dysfunction related to fibromyalgia



In research on fibromyalgia we commonly asked patients how difficult it is to form a simple everyday activities. The chart shown here is taken from the questions in the Fibromyalgia Impact Questionnaire (FIQR). The degree of difficulty is rated on a scale of 0 to 10. You can see that the 3 most problematic tasks are of vacuuming/scrubbing floors, working continuously for 20 minutes and going shopping for food or clothes. Interestingly, sitting in a chair continuously for 45 minutes has a rating similar to changing bedsheets or climbing one flight of stairs.

The activities shown in the above chart have taken from the functional component of the FIQR. In this survey subjects completed the total FIQR with the results shown below:



The mean score for the subjects in this survey was 67.1 with a standard deviation of 19.7. This score is significantly higher than the score we typically see in fibromyalgia patients, which is about 58. Note that healthy individuals usually have a total FIQR score of less than 15.

There are many potential reasons for the discrepancy between the subjects taking the survey in the typical fibromyalgia patient we see in our clinical studies; for instance subjects who decide to join a fibromyalgia organization such as the NFMPCA may in general general have more severe fibromyalgia.

If you would like to take the FIQR yourself, press “control” and click here **Take the FIQR**

Biennial Review—Somatization and Factitious Disorders

Issue: The Behavioral Health Advisory Panel (BHAP) has recommended that line 497 SOMATIZATION DISORDER, SOMATOFORM PAIN DISORDER, CONVERSION DISORDER and line 462 FACTITIOUS DISORDERS be merged. They requested that this merged line be named "SOMATIC SYMPTOMS AND RELATED DISORDERS" and contain consultation, office-based interventions, health and behavior procedure codes. The advisory group requested that the merged line be placed at line 462 (in the funded region of this version of the Prioritized List). During the last biennial review, the Mental Health and Chemical Dependency advisory group (MHCD) had re-prioritized Somatization below the funding line. BHAP requested that HERC staff devise a proposal for this line merge.

Prioritized List lines for the October 1, 2014 ICD-10 List

Line: 462

Condition: FACTITIOUS DISORDERS (See Guideline Notes 64,65)
Treatment: CONSULTATION
ICD-10: F68.1x (Factitious disorder)
CPT: Psychiatric visit (90785-90887), psychological testing (96101), Telephone/on-line assessment (98966-98969, 99441-99449), other office services (99051,99060,90970, 90978), office visits (99201-99215), ER (99281-99285), Rest home/domiciliary (99324-99340), home visit (99341-99350), prolonged service (99354-99360), anticoagulation monitoring (99363-99364), medical team conference (99366-99368), supervision of home health (99374-99375), supervision of hospice (99377-99378), preventive care visit (99381-99397), risk reduction (99401-99404, 99411-99412), SBIRT (99408-99409), complex chronic care co-ordination (99487-99489), transitional care management (99495-99496), medication therapy management (99605-99607)
HCPCS: G0410,G0411,G0425-G0427,H0004,H0023,H0032-H0037, H2010, H2011, H2013, H2021 ,H2022,H2033,S0270-S0274,S9484,T1016

Line: 497

Condition: SOMATIZATION DISORDER; SOMATOFORM PAIN DISORDER, CONVERSION DISORDER (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY
ICD-10: F44.x (conversion disorder), F45x (somatization disorder), F52.5 (vaginismus)
CPT: limited psychiatric services (90846, 90849, 90853, 90882, 90887), Telephone/on-line assessment (98966-98969, 99441-99449), other office services (99051,99060,90970, 90978), office visits (99201-99215), ER (99281-99285), Rest home/domiciliary (99324-99340), home visit (99341-99350), prolonged service (99354-99360), anticoagulation monitoring (99363-99364), medical team conference (99366-99368), supervision of home health (99374-99375), supervision of hospice (99377-99378), preventive care visit (99381-99397), risk reduction (99401-99404, 99411-99412), SBIRT (99408-99409), complex chronic care co-ordination (99487-99489), transitional care management (99495-99496), medication therapy management (99605-99607)

HCPCS: G0410,G0411,G0425-G0427,H0004,H0017-H0019,H0023,H0032-H0034, H0037, H0038, H2010,H2021-H2023,H2027,H2033,S0270-S0274,S9484,T1016

HERC staff recommendation:

1) Merge lines 462 and 497
    1) Include consultation only, as this was the factitious disorder line restriction and somatization was below the funding line prior to this proposed merger
    2) Re-score this combined line as shown below

Line XXX
Condition: SOMATIC SYMPTOMS AND RELATED DISORDERS
Treatment: CONSULTATION
ICD-10 F68.1x (Factitious disorder), F44.x (conversion disorder), F45x (somatization disorder), F52.5 (vaginismus)
CPT: from line 462 (has full set of psychiatric visit types) + 96150-96154 (health and behavior assessment codes)
HCPCS: from line 497 (more comprehensive set)

Scoring (current scoring for Somatization Disorder line in parentheses)
Category :7 (7)
HL: 2 (2)
Suffering: 2 (2)
Population effects: 0 (0)
Vulnerable population: 0 (0)
Tertiary prevention: 0 (0)
Effectiveness: 1 (2)
Need for service: 0.8 (1)
Net cost: 2 (3)
Score: 64
Approximate line placement: 558

Section 5.0

Guidelines

Lung Cancer Screening

Question: Should a diagnostic guideline be added to the Prioritized List regarding screening for lung cancer?

Question source: HERC staff

Issue: The USPSTF has recently issued new recommendations regarding CT scans for screening for lung cancer in older smokers with at least a 30 pack year smoking history. The CT scan code is diagnostic. NCCN has also recently issues new screening recommendations for lung cancer.

USPSTF 2013
Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

NCCN 2014
Recommends screening with annual lose dose CT scan for asymptomatic persons who are potential candidates for definitive treatment and who are aged 55-74 with ≥30 pack year history of smoking who currently smoke or quit <15 years ago (category 1) OR who are aged ≥50 years with ≥20 pack year history of smoking and one additional risk factor (category 2B).

CPT code	**Code description**	**List/Line**
71250	Computed tomography, thorax; without contrast material	Diagnostic
ICD-9		
V15.82	Personal history of tobacco use	Ancillary
V76.0	Special screening for malignant neoplasms of respiratory organs	4 PREVENTIVE SERVICES, OVER AGE OF 10
ICD-10		
Z12.2	Encounter for screening for malignant neoplasm of respiratory organs	Excluded
Z87.891	Personal history of nicotine dependence	Ancillary

HERC staff recommendations:

1) Add Z12.2 to line 3 Preventive Services for the October 1, 2014 Prioritized List and advise DMAP to remove from the Excluded List
2) Add the following Diagnostic Guideline:

DIAGNOSTIC GUIDELINE DXX LUNG CANCER SCREENING

Low dose computed tomography is included for annual screening for lung cancer in persons aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Annals of Internal Medicine | CLINICAL GUIDELINE

Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy of low-dose computed tomography, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) and the benefits and harms of these screening tests and of surgical resection of early-stage non–small cell lung cancer. The USPSTF also commissioned modeling studies to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

Ann Intern Med. www.annals.org

For author affiliation, see end of text.

* For a list of the members of the USPSTF, see the **Appendix** (available at www.annals.org).

This article was published online first at www.annals.org on 31 December 2013.

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendation and Evidence

The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

See the Clinical Considerations section for suggestions for implementation in practice.

See the **Figure** for a summary of the recommendation and suggestions for clinical practice.

Appendix Table 1 describes the USPSTF grades, and **Appendix Table 2** describes the USPSTF classification of levels of certainty about net benefit (both tables are available at www.annals.org).

Rationale

Importance

Lung cancer is the third most common cancer and the leading cause of cancer-related death in the United States (1). The most important risk factor for lung cancer is smoking, which results in approximately 85% of all U.S. lung cancer cases (2). Although the prevalence of smoking has decreased, approximately 37% of U.S. adults are current or former smokers (2). The incidence of lung cancer increases with age and occurs most commonly in persons

See also:

Print
Related article 1
Summary for Patients 2

Web-Only
CME quiz

Figure. **Screening for lung cancer: clinical summary of U.S. Preventive Services Task Force recommendation.**

Annals of Internal Medicine

U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

SCREENING FOR LUNG CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic adults aged 55 to 80 y who have a 30 pack-year smoking history and currently smoke or have quit smoking within the past 15 y
Recommendation	Screen annually for lung cancer with low-dose computed tomography. Discontinue screening when the patient has not smoked for 15 y. Grade: B

Risk Assessment	Age, total cumulative exposure to tobacco smoke, and years since quitting smoking are the most important risk factors for lung cancer. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease.
Screening Tests	Low-dose computed tomography has high sensitivity and acceptable specificity for detecting lung cancer in high-risk persons and is the only currently recommended screening test for lung cancer.
Treatment	Non–small cell lung cancer is treated with surgical resection when possible and also with radiation and chemotherapy.
Balance of Benefits and Harms	Annual screening for lung cancer with low-dose computed tomography is of moderate net benefit in asymptomatic persons who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on counseling and interventions to prevent tobacco use and tobacco-caused disease. These recommendations are available at www.uspreventiveservicestaskforce.org.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

aged 55 years or older. Increasing age and cumulative exposure to tobacco smoke are the 2 most common risk factors for lung cancer.

Lung cancer has a poor prognosis, and nearly 90% of persons with lung cancer die of the disease. However, early-stage non–small cell lung cancer (NSCLC) has a better prognosis and can be treated with surgical resection.

Detection

Most lung cancer cases are NSCLC, and most screening programs focus on the detection and treatment of early-stage NSCLC. Although chest radiography and sputum cytologic evaluation have been used to screen for lung cancer, LDCT has greater sensitivity for detecting early-stage cancer (3).

Benefits of Detection and Early Treatment

Although lung cancer screening is not an alternative to smoking cessation, the USPSTF found adequate evidence that annual screening for lung cancer with LDCT in a defined population of high-risk persons can prevent a substantial number of lung cancer–related deaths. Direct evidence from a large, well-conducted, randomized, controlled trial (RCT) provides moderate certainty of the benefit of lung cancer screening with LDCT in this population (4). The magnitude of benefit to the person depends on that person's risk for lung cancer because those who are at highest risk are most likely to benefit. Screening cannot prevent most lung cancer–related deaths, and smoking cessation remains essential.

Harms of Detection and Early Intervention and Treatment

The harms associated with LDCT screening include false-negative and false-positive results, incidental findings, overdiagnosis, and radiation exposure. False-positive LDCT results occur in a substantial proportion of screened persons; 95% of all positive results do not lead to a diagnosis of cancer. In a high-quality screening program, further imaging can resolve most false-positive results; however, some patients may require invasive procedures.

The USPSTF found insufficient evidence on the harms associated with incidental findings. Overdiagnosis of lung cancer occurs, but its precise magnitude is uncertain. A modeling study performed for the USPSTF estimated that 10% to 12% of screen-detected cancer cases are overdiagnosed—that is, they would not have been detected in the patient's lifetime without screening. Radiation harms, including cancer resulting from cumulative exposure to radiation, vary depending on the age at the start of screening; the number of scans received; and the person's exposure to other sources of radiation, particularly other medical imaging.

USPSTF Assessment

The USPSTF concludes with moderate certainty that annual screening for lung cancer with LDCT is of moderate net benefit in asymptomatic persons who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking. The moderate net benefit of screening depends on limiting screening to persons who are at high risk, the accuracy of image interpretation being similar to that found in the NLST (National Lung Screening Trial), and the resolution of most false-positive results without invasive procedures (4).

Clinical Considerations

Patient Population Under Consideration

The risk for lung cancer increases with age and cumulative exposure to tobacco smoke and decreases with time since quitting smoking. The best evidence for the benefit of screening comes from the NLST, which enrolled adults aged 55 to 74 years who had at least a 30 pack-year smoking history and were current smokers or had quit within the past 15 years. As with all screening trials, the NLST tested a specific intervention over a finite period. Because initial eligibility extended through age 74 years and participants received 3 annual screening computed tomographic scans, the oldest participants in the trial were aged 77 years.

The USPSTF used modeling studies to predict the benefits and harms of screening programs that use different screening intervals, age ranges, smoking histories, and times since quitting. A program that annually screens adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years is projected to have a reasonable balance of benefits and harms. The model assumes that persons who achieve 15 years of smoking cessation during the screening program discontinue screening. This model predicts the outcomes of continuing the screening program used in the NLST through age 80 years.

Screening may not be appropriate for patients with substantial comorbid conditions, particularly those who are in the upper end of the screening age range. The NLST excluded persons who were unlikely to complete curative lung cancer surgery and those with medical conditions that posed a substantial risk for death during the 8-year trial. The baseline characteristics of the NLST showed a relatively healthy sample, and fewer than 10% of enrolled participants were older than 70 years (5). Persons with serious comorbid conditions may experience net harm, no net benefit, or at least substantially less net benefit. Similarly, persons who are unwilling to have curative lung surgery are unlikely to benefit from a screening program.

Assessment of Risk

Age, total exposure to tobacco smoke, and years since quitting smoking are important risk factors for lung cancer and were used to determine eligibility in the NLST. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease. The incidence of lung cancer is relatively low in persons younger than 50 years but increases with age, especially after age 60 years. In current and former smokers, age-specific incidence rates increase with age and cumulative exposure to tobacco smoke.

Smoking cessation substantially reduces a person's risk for developing and dying of lung cancer. Among persons enrolled in the NLST, those who were at highest risk because of additional risk factors or a greater cumulative exposure to tobacco smoke experienced most of the benefit (6). A validated multivariate model showed that persons in the highest 60% of risk accounted for 88% of all deaths preventable by screening.

Screening Tests

Low-dose computed tomography has shown high sensitivity and acceptable specificity for the detection of lung cancer in high-risk persons. Chest radiography and sputum cytologic evaluation have not shown adequate sensitivity or specificity as screening tests. Therefore, LDCT is currently the only recommended screening test for lung cancer.

Treatment

Surgical resection is the current standard of care for localized NSCLC. This type of cancer is treated with surgical resection when possible and also with radiation and chemotherapy. Annual LDCT screening may not be useful for patients with life-limiting comorbid conditions or poor functional status who may not be candidates for surgery.

Other Approaches to Prevention

Smoking cessation is the most important intervention to prevent NSCLC. Advising smokers to stop smoking and preventing nonsmokers from being exposed to tobacco smoke are the most effective ways to decrease the morbidity and mortality associated with lung cancer. Current smokers should be informed of their continuing risk for lung cancer and offered cessation treatments. Screening with LDCT should be viewed as an adjunct to tobacco cessation interventions.

Useful Resources

Clinicians have many resources to help patients stop smoking. The Centers for Disease Control and Prevention has developed a Web site with many such resources, including information on tobacco quit lines, available in several languages (www.cdc.gov/tobacco/campaign/tips). Quit lines provide telephone-based behavioral counseling and support to tobacco users who want to quit smoking. Counseling is provided by trained cessation specialists who follow standardized protocols that may include several sessions and are generally provided at no cost to users. The content has been adapted for specific populations and can be tailored for individual clients. Strong evidence shows

that quit lines can expand the use of evidence-based tobacco cessation treatments in populations that may have limited access to treatment options.

Combination therapy with counseling and medications is more effective at increasing cessation rates than either component alone. The U.S. Food and Drug Administration has approved several forms of nicotine replacement therapy (gum, lozenge, transdermal patch, inhaler, and nasal spray), as well as bupropion and varenicline. More information on the treatment of tobacco dependence can be found in the U.S. Public Health Service Reference Guide "Treating Tobacco Use and Dependence: 2008 Update" (available at www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/reference/tobaqrg.pdf). The National Cancer Institute has developed a patient and physician guide for shared decision making for lung cancer screening based on the NLST (available at www.cancer.gov/newscenter/qa/2002/NLSTstudyGuidePatientsPhysicians). This 1-page resource may be a useful communication tool for providers and patients.

In addition, the National Comprehensive Cancer Network has developed guidelines for the follow-up of lung nodules (7). The appropriate follow-up and management of abnormalities found on LDCT scans are important given the high rates of false-positive results and the potential for harms. Lung cancer screening with LDCT should be implemented as part of a program of care, as outlined in the next section.

Other Considerations

Implementation of a Lung Cancer Screening Program

Screening Eligibility, Screening Intervals, and Starting and Stopping Ages

The NLST, the largest RCT to date with more than 50 000 patients, enrolled participants aged 55 to 74 years at the time of randomization who had a tobacco use history of at least 30 pack-years and were current smokers or had quit within the past 15 years (4). The USPSTF recommends extending the program used in the NLST through age 80 years. Screening should be discontinued once the person has not smoked for 15 years.

The NLST enrolled generally healthy persons, and the findings may not accurately reflect the balance of benefits and harms in those with comorbid conditions. The USPSTF recommends discontinuing screening if a person develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Clinicians will encounter patients who are interested in screening but do not meet the criteria of high risk for lung cancer as described previously. The balance of benefits and harms of screening may be unfavorable in these lower-risk patients. Current evidence is lacking on the net benefit of expanding LDCT screening to include lower-risk patients. It is important that persons who are at lower risk for lung cancer be aware of the potential harms of screening. Future improvements in risk assessment tools will help clinicians better individualize patients' risks (6).

Smoking Cessation Counseling

All persons enrolled in a screening program should receive smoking cessation interventions. To be consistent with the USPSTF recommendation on counseling and interventions to prevent tobacco use and tobacco-caused disease, persons who are referred to a lung cancer screening program through primary care should receive these interventions before referral. Because many persons may enter screening through pathways besides referral from primary care, the USPSTF encourages incorporating such interventions into the screening program.

Shared Decision Making

Shared decision making is important for persons within the population for whom screening is recommended. The benefit of screening varies with risk because persons who are at higher risk because of smoking history or other risk factors are more likely to benefit. Screening cannot prevent most lung cancer deaths, and smoking cessation remains essential. Lung cancer screening has substantial harms, most notably the risk for false-positive results and incidental findings that lead to a cascade of testing and treatment that may result in more harms, including the anxiety of living with a lesion that may be cancer. Overdiagnosis of lung cancer and the risks of radiation are real harms, although their magnitude is uncertain. The decision to begin screening should be the result of a thorough discussion of the possible benefits, limitations, and known and uncertain harms.

Standardization of LDCT Screening and Follow-up of Abnormal Findings

The evidence for the effectiveness of screening for lung cancer with LDCT comes from RCTs done in large academic medical centers with expertise in using LDCT and diagnosing and managing abnormal lung lesions. Clinical settings that have high rates of diagnostic accuracy using LDCT, appropriate follow-up protocols for positive results, and clear criteria for doing invasive procedures are more likely to duplicate the results found in trials. The USPSTF supports adherence to quality standards for LDCT (8) and establishing protocols to follow up abnormal results, such as those proposed by the National Comprehensive Cancer Network (7). A mechanism should be implemented to ensure adherence to these standards.

In the context of substantial uncertainty about how best to manage individual lesions, as well as the magnitude of some of the harms of screening, the USPSTF encourages the development of a registry to ensure that appropriate data are collected from screening programs to foster continuous improvement over time. The registry should also

compile data on incidental findings and the testing and interventions that occur as a result of these findings.

Research Needs and Gaps

Smoking prevalence and lung cancer incidence are higher among socioeconomically disadvantaged populations, and more research is needed in these groups. In addition, if lung cancer screening with LDCT is implemented more widely in diverse community settings, it is important to evaluate whether variability in follow-up protocols of positive results on LDCT scans results in a different balance of benefits and harms than that observed in RCTs.

More research is also needed on the use of biomarkers to focus LDCT efforts in persons who are at highest risk for lung cancer. The role of biomarkers in accurately discriminating between benign and malignant nodules and in identifying more aggressive disease needs to be determined.

Discussion

Burden of Disease

Lung cancer is the third most common cancer in the United States. Age-adjusted incidence rates per 100 000 persons are higher in men and vary according to the duration of and exposure to tobacco smoke. The most important risk factor for lung cancer is smoking, which results in approximately 85% of all lung cancer cases in the United States. Although the prevalence of smoking has decreased, approximately 37% of U.S. adults are current or former smokers. In 2008, an estimated 7 million U.S. adults aged 55 to 75 years had a 30 pack-year or more smoking history (2).

The incidence of lung cancer increases with age, occurring most commonly in adults aged 55 years or older. Lung cancer is the leading cause of cancer-related death in the United States, accounting for approximately 28% of all deaths from cancer. Death from lung cancer is often related to the initial stage of diagnosis. The average 5-year survival rate for lung cancer is among the lowest (17%) of all types of cancer but is higher when the disease is diagnosed at an early stage (52%). However, only 15% of lung cancer cases are diagnosed at such a stage (2).

Scope of Review

To update the 2004 recommendation, the USPSTF commissioned a systematic evidence review to assess the efficacy of LDCT, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) (3). The review focused on new evidence from RCTs to determine the effectiveness of these screening tests in improving health outcomes. Information about the harms associated with these screening tests was obtained from RCTs and cohort studies. The benefits and harms associated with surgical resection of early-stage NSCLC were also examined.

In addition to the evidence review, the USPSTF commissioned modeling studies from the Cancer Intervention and Surveillance Modeling Network (CISNET) to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies (9, 10). The modeling studies complement the evidence that the systematic review provides.

Accuracy of Screening Tests

The sensitivity of chest radiography for detecting lung cancer varies depending on the size and location of the lesion, image quality of the scan, and skill of the radiologist who interprets the scan. Low-dose computed tomography has emerged as a test with higher sensitivity and specificity for lung cancer than chest radiography. In 2004, the USPSTF found inadequate evidence to recommend for or against screening for lung cancer with LDCT, chest radiography, sputum cytologic evaluation, or a combination of these tests (I statement). Since then, many RCTs have been done and published, resulting in more data on the benefits and harms of screening. Recent data from the NLST showed a sensitivity of 93.8% and specificity of 73.4% for LDCT and a sensitivity of 73.5% and specificity of 91.3% for chest radiography (11). Sputum cytologic evaluation is now rarely used for lung cancer screening, and no studies reported on the test characteristics of this screening method.

Effectiveness of Early Detection and Treatment

Four RCTs reported the effectiveness of LDCT for lung cancer screening. The largest trial, the NLST, showed a reduction in lung cancer mortality of 16% (95% CI, 5.0% to 25.0%) (12) and a reduction in all-cause mortality of 6.7% (CI, 1.2% to 13.6%) (4). This trial included more than 50 000 asymptomatic adults aged 55 to 74 years who had at least a 30 pack-year smoking history.

Participants were current or former smokers and were randomly assigned to LDCT or chest radiography. They received annual testing at baseline and years 1 and 2 and were followed for a median of 6.5 years. After 6 to 7 years of follow-up, 2.06% of patients in the chest radiography group and 1.75% of those in the LDCT group had died of lung cancer, for an absolute difference of 0.31% and a number needed to screen of about 320 (4). The number needed to screen is based on 3 annual screenings; screening the same sample over a longer period will result in a much lower estimate.

In contrast to the NLST, 3 small European trials showed potential harm or no benefit of screening. Two small fair-quality trials, the DANTE (Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays) trial and the DLCST (Danish Lung Cancer Screening Trial), showed no benefit associated with LDCT compared with no LDCT (13–15). However, these were smaller trials (n = 2472 and 4104,

Table. **Screening Scenarios From CISNET Models***

Screening Scenario†				Benefit		Harm‡			CT Screens per Lung Cancer Death Averted, *n*
Minimum Pack-Years at Screening, *n*	Minimum Age at Which to Begin Screening, *y*	Time Since Last Cigarette, *y*	Population Ever Screened, %	Lung Cancer Deaths Averted, %	Lung Cancer Deaths Averted, *n*	Total CT Screens, *n*	Radiation-Induced Lung Cancer Deaths, *n*	Overdiagnosis, %§	
40	60	25	13.0	11.0	410	171 924	17	11.2	437
40	55	25	13.9	12.3	458	221 606	20	11.1	506
30	60	25	18.8	13.3	495	253 095	21	11.9	534
30	**55**	**15**	**19.3**	**14.0**	**521**	**286 813**	**24**	**9.9**	**577**
20	60	25	24.8	15.4	573	327 024	25	9.8	597
30	55	25	20.4	15.8	588	342 880	25	10.0	609
20	55	25	27.4	17.9	664	455 381	31	10.4	719
10	55	25	36.0	19.4	721	561 744	35	9.5	819

CISNET = Cancer Intervention and Surveillance Modeling Network; CT = computed tomography.
* All scenarios model the results of following a cohort of 100 000 persons from age 45 to 90 y or until death from any cause, with a varying number of smokers and former smokers screened on the basis of smoking history, age, and years since stopping smoking. Bold text indicates the screening scenario with a reasonable balance of benefits and harms and that is recommended by the U.S. Preventive Services Task Force.
† In all scenarios, screening is continued through age 80 y.
‡ Number of CT screenings is a measure of harm because it relates to the number of patients who will have risk for overdiagnosis and potential consequences from false-positive results.
§ Percentage of screen-detected cancer that is overdiagnosis; that is, cancer that would not have been diagnosed in the patient's lifetime without screening.

respectively) that may have had limited power to detect a true benefit.

Of note, the inclusion criteria in the DLCST resulted in younger and healthier participants than in other trials. The relative risk for all-cause mortality in the DLCST was 1.46 (CI, 0.99 to 2.15). This finding raises the possibility of potential harm of screening a young, healthy population. Follow-up in the DLCST was 4.7 years (15). Combined data from the DLCST and the NELSON (Dutch–Belgian Randomised Lung Cancer Screening) trial will be reported soon (2).

When these 3 fair- or good-quality trials were combined in a meta-analysis, the relative risk for lung cancer mortality was 0.81 (CI, 0.72 to 0.91) (2). Another European trial, the MILD (Multicentric Italian Lung Detection) study, was rated as poor quality because of concerns about the adequacy of randomization; its results were not included in the final meta-analysis (16).

Two fair- to good-quality trials found no benefits associated with chest radiography screening (2). The larger of these trials, the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial, evaluated more than 150 000 participants from the general population and found no benefits of this type of screening in this group or in a subgroup that had tobacco smoke exposure (17).

Smaller RCTs from Europe had different eligibility criteria and have not yet duplicated the findings of the NLST; therefore, only moderate certainty exists about the magnitude of benefit from screening (3). As with all screening trials, these studies were done over a limited time frame, with the NLST evaluating the effect of 3 annual screenings. Modeling is required to estimate the effect of screening beyond that evaluated in a clinical trial. Estimates of the results of different screening intervals, ages at which to start and stop screening, and thresholds for smoking history come from modeling studies that CISNET conducted for the USPSTF.

Annual screening with LDCT provides the greatest benefit in decreasing lung cancer mortality compared with biennial or triennial screening (9, 10). The **Table** shows the results of annual screening strategies between the ages of 55 and 80 years that had a better balance of benefits and harms than other strategies in this age range. Focusing screening efforts on the highest-risk persons, those with at least a 40 pack-year smoking history, results in the lowest number of screening scans per death averted and, therefore, the least harm to patients in terms of risk for overdiagnosis and consequences of false-positive results.

Screening progressively larger proportions of the population by lowering the screening threshold increases the number of deaths averted but with a progressively higher number of screening scans per death averted, therefore increasing harm. The **Table** shows that increasing the proportion of the population screened from 13% to 36% increases the number of deaths averted by 75% but increases the number of screening scans by 327%, greatly increasing the probability of an untoward event after the evaluation of a false-positive result and the number of radiation-induced cancer deaths. The highlighted program—screening current or former smokers aged 55 to 80 years who have at least a 30 pack-year smoking history and discontinuing (or not starting) screening after 15 years of smoking abstinence—most closely resembles the strategy applied to participants in the NLST and offers a reasonable balance of benefits and harms.

The CISNET modeling studies show similar life-years gained per death averted and proportion of cancer cases detected at an early stage across the screening strategies.

The modeling studies estimate that 9.5% to 11.9% of screen-detected cancer cases are overdiagnosed—that is, they would not have been detected in the patient's lifetime without screening (9, 10).

Potential Harms of Screening and Treatment

Harms associated with LDCT screening include false-negative and false-positive results, incidental findings, overdiagnosis, radiation exposure, and psychological distress. The sensitivity of LDCT ranged from 80% to 100%, suggesting a false-negative rate of 0% to 20%. The specificity of LDCT ranged from 28% to 100%.

The positive predictive value for lung cancer of an abnormal test result ranged from 2% to 42% (2). As mentioned previously, the NLST is the largest trial of lung cancer screening to date, and recent results showed a sensitivity of 93.8% and specificity of 73.4% for LDCT. In the NLST, the positive predictive value for a positive finding of a pulmonary nodule measuring 4 mm or larger was 3.8% (11).

Over the 3 rounds of screening in the NLST, 24.2% of screening test results were positive; 96.4% of these were false-positives. Most positive test results were followed by additional imaging. Approximately 2.5% of positive test results required additional invasive diagnostic procedures, such as bronchoscopy, needle biopsy, or thoracoscopy. Of the 17 053 positive test results evaluated, there were approximately 61 complications and 6 deaths after a diagnostic procedure. Recently published data from the first round of screening in the NLST showed an average of 1 follow-up scan per positive screening test result. Approximately 1.9% of NLST participants had a biopsy (11).

The most common incidental findings on LDCT were emphysema and coronary artery calcifications. Other pulmonary findings included bronchiectasis, pulmonary fibrosis, carcinoid tumors, and hamartomas. The NLST reported that 7.5% of non–lung cancer abnormalities were clinically significant. None of the studies reported data on the evaluations that may have occurred in response to the incidental findings. Therefore, the harms and benefits associated with incidental findings cannot currently be determined (2).

Overdiagnosis was not formally reported in any study. The NLST found 119 more lung cancer cases in approximately 26 000 participants in the LDCT group than in the chest radiography group after 6.5 years of follow-up, which suggests some overdiagnosis. Recent data from the Italian Continuing Observation of Smoking Subjects cohort study of approximately 5000 participants showed that of the 120 incident cancer cases, 25% were slow-growing or indolent (based on volume-doubling time), thus possibly indicating some overdiagnosis with LDCT (18).

Radiation exposure associated with LDCT ranged from 0.61 to 1.5 mSv per scan. To provide context, annual background radiation exposure in the United States averages 2.4 mSv, radiation exposure from mammography is 0.7 mSv, and radiation exposure from head computed tomography is 1.7 mSv. The risk for radiation-induced lung cancer depends on the age at which a person begins screening and the amount of cumulative radiation received. On the basis of modeling studies, starting annual LDCT screening before age 50 years may result in more radiation-related lung cancer deaths than starting annual screening after age 50 years (9, 10).

Overall, LDCT screening did not seem to result in substantial long-term psychological distress, although assessment has been limited. No studies reported long-term differences in anxiety or distress levels associated with LDCT in participants.

No RCTs compared treatment of stage IA or IB lung cancer with surgical resection versus no treatment. Surgical resection is the standard of care in the United States for early-stage NSCLC. Studies of symptomatic and unselected patients reported 5-year survival rates associated with surgical resection of 71% to 90% for stage IA cancer and 42% to 75% for stage IB cancer. No RCTs of LDCT screening evaluated the harms associated with screen-detected cancer. Studies that reported the harms of surgical resection were done in patients who were identified in clinical practice and had comorbid conditions (3).

Estimate of Magnitude of Net Benefit

On the basis of data from the systematic evidence review and modeling studies, the USPSTF determined with moderate certainty that annual LDCT screening provides substantial net benefit in persons aged 55 to 80 years at high risk for lung cancer. Evidence from the NLST supports this recommendation because participants in that trial were in this age range and had a similar degree of lung cancer risk from cumulative tobacco exposure. Persons who do not meet the minimum eligibility criteria for the NLST may have less net benefit and more harms from screening (persons aged 55 to 74 years at enrollment who have a ≥30 pack-year smoking history and are current smokers or have quit in the past 15 years). For these persons, the absolute benefit of screening is strongly associated with their age and smoking history.

Modeling studies conducted by CISNET investigators for the USPSTF showed that annual LDCT screening yielded the greatest net benefit (compared with biennial or triennial screening) (9, 10). Benefits were measured as percentage of early-stage detection of lung cancer, percentage and absolute number of lung cancer deaths averted, and number of life-years gained. Harms were measured as number of total LDCT screenings per 100 000 persons and per person, number of cases of overdiagnosed lung cancer, and number of radiation-induced lung cancer deaths. The microsimulation models used standardized data on smoking history and non–lung cancer mortality to simulate the effects of various screening programs on the mortality rate of a U.S. cohort born in 1950. This cohort was chosen because these persons reach age 63 years (ap-

proximate midrange of participants' ages in the NLST) in 2013.

Modeling evidence suggests that an annual screening program starting at age 55 years and ending after age 80 years (in persons who have a 30 pack-year smoking history and currently smoke or have quit in the past 15 years) resulted in approximately 50% of lung cancer cases detected at an early stage (9, 10). This screening protocol would result in a 14% reduction in lung cancer mortality, or an estimated 521 lung cancer deaths prevented per 100 000 persons in the population. The harms associated with this screening protocol are an estimated overdiagnosis of 10% of screen-detected cases and radiation-induced lung cancer deaths of less than 1%. As mentioned previously, a person's absolute net benefit from screening may depend not just on age but functional status and the presence of other comorbid conditions.

How Does Evidence Fit With Biological Understanding?

Lung cancer is a proliferation of malignant cells arising in the tissues or airways of the lungs. In addition to age and exposure to tobacco smoke, other risk factors for lung cancer include family history; chronic obstructive pulmonary disease; pulmonary fibrosis; and exposure to indoor cooking fumes, radon, asbestos, arsenic, chromium, and coal tar. Non–small cell lung cancer is a heterogeneous category that includes adenocarcinoma, squamous cell carcinoma, large cell carcinoma, and undifferentiated carcinoma. Adenocarcinoma is the most common subtype, encompassing 36% of all lung cancer cases.

Currently, 75% of patients with lung cancer present with symptoms of advanced local or metastatic disease that result in poor prognosis (2). At the earliest stage, median 5-year survival for NSCLC is 77%. Patients with localized disease (defined as cancer limited to the lung without metastasis to other organs or lymph nodes) have a median 5-year survival of 52% compared with 25% for those with regional spread and 4% for those with distant metastasis. Thus, earlier detection and treatment of lung cancer give patients a greater chance for cure.

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 30 July to 26 August 2013. Most of the comments generally agreed with the recommendation statement, although some suggested restricting screening to a higher-risk group and others suggested expanding eligibility criteria beyond those used in the NLST. Many comments expressed concerns about implementation of a screening program, predicting substantially greater harm in the community setting than was found in the NLST. Some comments expressed concern about the cost of implementing a screening program and the potential paradoxical effect of enabling persons to continue smoking with the perception that medical care can mitigate the risks of smoking.

In response to these comments, the USPSTF further emphasized the importance of tobacco cessation as the primary way to prevent lung cancer and provided links to resources that clinicians can use to help their patients quit smoking. A section on implementation of a screening program was added, emphasizing the need for monitoring this implementation, quality assurance in diagnostic imaging, and appropriate follow-up to replicate the benefits observed in the NLST in the general population. The USPSTF also clarified that, in addition to age and smoking history, such risk factors as occupational exposure, family history, and history of other lung diseases are important when assessing patients' risks for lung cancer.

The USPSTF acknowledges the importance of accurately identifying persons who are at highest risk to maximize the benefits and minimize the harms of screening and calls for more research to improve risk assessment tools. The USPSTF did not incorporate the costs of a screening program or the potential savings from a reduction in treatment of advanced lung cancer into the recommendation.

Update of Previous USPSTF Recommendation

This recommendation updates the 2004 recommendation, in which the USPSTF concluded that the evidence was insufficient to recommend for or against screening for lung cancer in asymptomatic persons with LDCT, chest radiography, sputum cytologic evaluation, or a combination of these tests. In the current recommendation, the USPSTF recommends annual screening for lung cancer with LDCT in persons who are at high risk based on age and cumulative tobacco smoke exposure.

Recommendations of Others

In 2012, the American College of Chest Physicians, the American Society of Clinical Oncology, and the American Thoracic Society (19) recommended screening for lung cancer with LDCT primarily on the basis of results from the NLST, using eligibility criteria that closely modeled those of the NLST (persons aged 55 to 74 years who have a ≥30 pack-year smoking history and currently smoke or have quit in the past 15 years). The recommendations also stipulated that screening should be offered only in clinical settings similar to those in the trial.

The American Association for Thoracic Surgery (20) recommends annual screening with LDCT in current and former smokers aged 55 to 79 years who have a 30 pack-year smoking history. It also recommends annual screening starting at age 50 to 79 years in patients who have a 20 pack-year smoking history and additional comorbid conditions that produce a cumulative risk for cancer of at least 5% over the next 5 years. Furthermore, it recommends annual screening in long-term cancer survivors aged 55 to 79 years.

In 2013, the American Cancer Society (21) also began recommending screening for lung cancer with LDCT in

high-risk patients who are in relatively good health and meet the NLST criteria (persons aged 55 to 74 years who have a ≥30 pack-year smoking history and currently smoke or have quit in the past 15 years). It recommends against the use of chest radiography and strongly suggests that all adults who receive screening enter an organized screening program that has experience in LDCT.

In addition, the National Comprehensive Cancer Network (7) recommends LDCT screening in selected patients who are at high risk for lung cancer. High risk is defined as persons aged 55 to 74 years who have at least a 30 pack-year smoking history and, if a former smoker, 15 years or less since quitting or persons aged 50 years or older who have at least a 20 pack-year smoking history and 1 additional risk factor. It does not recommend lung cancer screening in persons who are at moderate risk (aged ≥50 years and ≥20 pack-year smoking history or secondhand smoke exposure but no additional lung cancer risk factors) or low risk (younger than 50 years or smoking history of <20 pack-years).

From the U.S. Preventive Services Task Force, Rockville, Maryland.

Disclaimer: Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

References

1. **American Cancer Society.** Cancer Facts & Figure 2013. Atlanta, GA: American Cancer Society; 2013. Accessed at www.cancer.org/research/cancerfactsfigures/cancerfactsfigures/cancer-facts-figures-2013 on 21 November 2013.

2. **Humphrey L, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, et al.** Screening for Lung Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation Statement. Evidence synthesis no. 105. AHRQ publication no. 13-05196-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

3. **Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, et al.** Screening for lung cancer with low-dose computed tomography: a systematic review to update the U.S. Preventive Services Task Force recommendation. Ann Intern Med. 2013;159:411-20. [PMID: 23897166]

4. **Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al; National Lung Screening Trial Research Team.** Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365:395-409. [PMID: 21714641]

5. **Aberle DR, Adams AM, Berg CD, Clapp JD, Clingan KL, Gareen IF, et al; National Lung Screening Trial Research Team.** Baseline characteristics of participants in the randomized National Lung Screening Trial. J Natl Cancer Inst. 2010;102:1771-9. [PMID: 21119104]

6. **Kovalchik SA, Tammemagi M, Berg CD, Caporaso NE, Riley TL, Korch M, et al.** Targeting of low-dose CT screening according to the risk of lung-cancer death. N Engl J Med. 2013;369:245-54. [PMID: 23863051]

7. **National Comprehensive Cancer Network.** National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Lung Cancer Screening. Fort Washington, PA: National Comprehensive Cancer Network; 2014.

8. Medicare Improvements for Patients and Providers Act, 42 U.S.C. §101-304 (2008).

9. **de Koning HJ, Plevritis S, Hazelton WD, ten Haaf K, Munshi V, Jeon J, et al.** Benefits and Harms of Computed Tomography Lung Cancer Screening Programs for High-Risk Populations. AHRQ publication no. 13-05196-EF-2. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

10. **de Koning HJ, Meza R, Plevritis SK, ten Haaf K, Munshi VD, Jeon J, et al.** Benefits and harms of lung cancer screening: modeling strategies for the U.S. Preventive Services Task Force. Ann Intern Med. 2014;160:●●●-●●●.

11. **Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, Duan F, et al; National Lung Screening Trial Research Team.** Results of initial low-dose computed tomographic screening for lung cancer. N Engl J Med. 2013;368:1980-91. [PMID: 23697514]

12. **Pinsky PF, Church TR, Izmirlian G, Kramer BS.** The National Lung Screening Trial: Results stratified by demographics, smoking history, and lung cancer histology. Cancer. 2013. [PMID: 24037918]

13. **Infante M, Lutman FR, Cavuto S, Brambilla G, Chiesa G, Passera E, et al; DANTE Study Group.** Lung cancer screening with spiral CT: baseline results of the randomized DANTE trial. Lung Cancer. 2008;59:355-63. [PMID: 17936405]

14. **Infante M, Cavuto S, Lutman FR, Brambilla G, Chiesa G, Ceresoli G, et al; DANTE Study Group.** A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial. Am J Respir Crit Care Med. 2009;180:445-53. [PMID: 19520905]

15. **Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, et al.** CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. Thorax. 2012;67:296-301. [PMID: 22286927]

16. **Pastorino U, Rossi M, Rosato V, Marchianò A, Sverzellati N, Morosi C, et al.** Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. Eur J Cancer Prev. 2012;21:308-15. [PMID: 22465911]

17. **Oken MM, Hocking WG, Kvale PA, Andriole GL, Buys SS, Church TR, et al; PLCO Project Team.** Screening by chest radiograph and lung cancer mortality: the Prostate, Lung, Colorectal, and Ovarian (PLCO) randomized trial. JAMA. 2011;306:1865-73. [PMID: 22031728]

18. **Veronesi G, Maisonneuve P, Bellomi M, Rampinelli C, Durli I, Bertolotti R, et al.** Estimating overdiagnosis in low-dose computed tomography screening for lung cancer: a cohort study. Ann Intern Med. 2012;157:776-84. [PMID: 23208167]

19. **Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al.** Benefits and harms of CT screening for lung cancer: a systematic review. JAMA. 2012;307:2418-29. [PMID: 22610500]

20. **Jaklitsch MT, Jacobson FL, Austin JH, Field JK, Jett JR, Keshavjee S, et al.** The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. J Thorac Cardiovasc Surg. 2012;144:33-8. [PMID: 22710039]

21. **Wender R, Fontham ET, Barrera E Jr, Colditz GA, Church TR, Ettinger DS, et al.** American Cancer Society lung cancer screening guidelines. CA Cancer J Clin. 2013;63:107-17. [PMID: 23315954]

Appendix: U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Virginia A. Moyer, MD, MPH, *Chair* (American Board of Pediatrics, Chapel Hill, North Carolina); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veterans Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); and Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina).

† For a list of current Task Force members, go to www.uspreventiveservicestaskforce.org/members.htm.

Appendix Table 1. **What the USPSTF Grades Mean and Suggestions for Practice**

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Appendix Table 2. **USPSTF Levels of Certainty Regarding Net Benefit**

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.

Genetic Testing for Hereditary Cancers

Question: Should the non-prenatal Genetic Testing Guideline be modified to allow more flexibility regarding the types of professionals allowed to provide genetic counseling?

Question source: Gregory Sindmack, MD, OB-Gyn, Klamath Fall and colleagues

Issue: The current non-prenatal Genetic Testing Guideline specifies that genetic counseling must be performed prior to genetic testing for such familial cancer genes as BRCA and Lynch syndrome. Such counseling must be performed by providers with certain credentials in order to be covered. Dr. Sindmack and colleagues are requesting that pre-test genetic counseling be allowed when provided by a "qualified and appropriately trained practitioner." This is consistent with CMS requirements and the requirements of most major insurers.

The Health Services Commission (HERC's predecessor) has reviewed genetic counseling and appropriate providers at several prior meetings, and their intent had been to have professionals with specific training in genetic counseling provide pre/post-test genetic counseling.

This issue was discussed at the January, 2014 VBBS meeting. The proposal discussed was to change the non-prenatal genetic testing guideline to allow counseling by "a suitably trained health professional with expertise and experience in cancer genetics." This wording is consistent with NCCN recommendations. Testimony was heard from the Oregon Genetics Group that specific genetic training is required for genetics counseling. The group requested that HERC staff get more input from them about specific training requirements. Specifically, the group requested that USPSTF recommendations be considered.

Also, Dr. Sindmack and colleagues raised concerns about the requirement to provide genetic counseling both before and after testing. His group's concern was that if the patient was lost to follow up and did not receive the after counseling, there would be an issue with reimbursement.

USPSTF recommendation 2012

> Screen women whose family history may be associated with an increased risk for potentially harmful BRCA mutations. Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. Grade: B
>
> Genetic risk assessment and BRCA mutation testing are generally multistep processes involving identification of women who may be at increased risk for potentially harmful mutations, followed by genetic counseling by suitably trained health care providers and genetic testing of selected high-risk women when indicated.

Genetic Counseling

Genetic counseling about BRCA mutation testing may be done by trained health professionals, including trained primary care providers. Several professional organizations describe the skills and training necessary to provide comprehensive genetic counseling. The process of genetic counseling includes detailed kindred analysis and risk assessment for potentially harmful BRCA mutations; education about the possible results of testing and their implications; identification of affected family members who may be preferred candidates for testing; outlining options for screening, risk-reducing medications, or surgery for eligible patients; and follow-up counseling for interpretation of test results.

NCCN 2013 Breast and/or Ovarian Cancer Genetic Assessment

Genetic counseling is highly recommended when genetic testing is offered and after resulted are disclosed. A genetic counselor, medical geneticist, oncologist, surgeon, oncology nurse, or other health professional with expertise and experience in cancer genetics should be involved early in counseling patients who potentially meet criteria for an inherited syndrome.

American College of Surgeons Commission on Cancer 2012 standards

A genetics professional has experience and an educational background in genetics, cancer genetics, counseling, and hereditary cancer syndromes to provide accurate risk assessment and empathetic genetic counseling to patients with cancer and their families. Genetics professionals include people certified in any of the following ways:

- American Board of Genetic Counseling or American Board of Medical Genetics board certified/board eligible or a licensed genetic counselor
- American College of Medical Genetics physician board certified in medical genetics
- Genetics Clinical Nurse or Advanced Practice Nurse in Genetics
- Advanced practice oncology nurse who is prepared at the graduate level with specialized education in cancer genetics and hereditary cancer predispostition syndromes
- Board-certified physician with experience in cancer genetics

Genetic Testing for Hereditary Cancers

Relevant portion of current non-prenatal Genetic Testing Guideline

DIAGNOSTIC GUIDELINE D1, NON-PRENATAL GENETIC TESTING GUIDELINE

A) Related to genetic testing for patients with breast/ovarian and colon/endometrial cancer suspected to be hereditary, or patients at increased risk to due to family history.
   1) Services are provided according to the Comprehensive Cancer Network Guidelines.
      a) Lynch syndrome (hereditary colorectal and endometrial cancer) services (CPT 81292-81300, 81317-81319) and familial adenomatous polyposis (FAP) services (CPT 81201-81203) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Screening. V.1.2013 (5/13/13). ***www.nccn.org***
      b) BRCA1/BRCA2 testing services (CPT 81211-81217) for women without a personal history of breast and/or ovarian cancer should be provided to high risk women as defined in Guideline Note 3 or as otherwise defined by the US Preventive Services Task Force.
      c) BRCA1/BRCA2 testing services (CPT 81211-81217) for women with a personal history of breast and/or ovarian cancer and for men with breast cancer should be provided according to the NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V.1.2011 (4/7/11). ***www.nccn.org***
      d) PTEN (Cowden syndrome) services (CPT 81321-81323) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Screening. V.1.2013 (5/13/13). ***www.nccn.org.***
   2) Genetic counseling should precede genetic testing for hereditary cancer. Very rarely, it may be appropriate for a genetic test to be performed prior to genetic counseling for a patient with cancer. If this is done, genetic counseling should be provided as soon as practical.
      a) Pre and post-test genetic counseling by the following providers should be covered.
         i) Medical Geneticist (M.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics
         ii) Clinical Geneticist (Ph.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics.
         iii) Genetic Counselor - Board Certified or Active Candidate Status from the American Board of Genetic Counseling, or Board Certified by the American Board of Medical Genetics.
         iv) Advance Practice Nurse in Genetics - Credential from the Genetic Nursing Credentialing Commission.
   3) If the mutation in the family is known, only the test for that mutation is covered. For example, if a mutation for BRCA 1 has been identified in a family, a single site mutation analysis for that mutation is covered (CPT 81215), while a full sequence BRCA 1 and 2 (CPT 81211) analyses is not. There is one exception, for individuals of Ashkenazi Jewish ancestry with a known mutation in the family, the panel for Ashkenazi Jewish BRCA mutations is covered (CPT 81212).

Expert Input
From the Oregon Genetics Program:

Recommend no change to current guidelines (See attached document for full details). Also made multiple suggestions for updating the current genetic testing guideline and the BRCA/high risk for breast cancer guideline.

Executive Summary
In response to the proposal to broaden the language regarding coverage for cancer genetic services, the Oregon Genetics Program (OGP) recommends that genetic counseling and testing services be covered when ordered by a genetics provider as per the current guidelines for these reasons:
1) Cancer risk assessment and genetic counseling are rapidly becoming standards of care for patients with a personal history of cancer and/or a family history of cancer.
2) In Oregon, non-genetics specialist providers are already ordering cancer genetic testing and Oregonians are not receiving recommended care according to guidelines.
3) The right cancer genetic tests are not being ordered in the Oregon Medicaid population.
4) The standard practice of genetic specialists allows *all* close blood relatives who choose to be tested to receive the much less expensive single site testing.
5) Testing may be being ordered on the wrong individuals, such that the provider is not testing the right family member for informative results and/or is ordering the wrong test.
6) Current Medicaid guidelines state that only single site testing is covered when a family *BRCA* mutation is known. This guideline is either not being followed or many providers who are doing genetic testing are not determining the mutation status in the family before proceeding with testing of their patients.
7) Non-genetic specialist providers do not have the knowledge or confidence needed for accurate risk assessment. (
8) Aggressive marketing increases provider awareness of available genetic tests, but does not increase knowledge of heritable cancers.
9) Access to cancer genetic services is improving in the state, with new clinics in eastern Oregon and new telemedicine services in southern Oregon and the Salem area. Expansion into other underserved areas is under discussion.

From Cori Feist, genetic counselor at OHSU:

Suitably trained means (as stated in section 2, part a):

2a) Pre and post-test genetic counseling by the following providers should be covered.
   i) Medical Geneticist (M.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics
   ii) Clinical Geneticist (Ph.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics.
   iii) Genetic Counselor - Board Certified or Active Candidate Status from the American Board of Genetic Counseling, or Board Certified by the American Board of Medical Genetics.

iv) Advance Practice Nurse in Genetics - Credential from the Genetic Nursing Credentialing Commission.

In other words, an OB/Gyn or Oncologist is not considered "suitably trained" to provide genetic counseling.

Expertise and experience is implied when an individual has completed the necessary training and board examination to become on of the above (MD, PhD, CGC, APNG). You could say that successful completion of board certification or credentialing by an accredited program qualifies as "expertise/experience".

HERC staff recommendations:

1) Modify diagnostic guideline D1 as shown below
   a. Incorporates suggestions from the Oregon Genetics Program and from other genetics professional input as well as USPSTF and NCCN guideline language
   b. Alternate: keep section A2a unchanged
2) Modify guideline note 3 as shown below
   a. Incorporates suggestions from the Oregon Genetics Program

DIAGNOSTIC GUIDELINE D1, NON-PRENATAL GENETIC TESTING GUIDELINE

Coverage of genetic testing in a non-prenatal setting shall be determined by the algorithm shown in Figure D1 unless otherwise specified below.

A) Related to genetic testing for patients with breast/ovarian and colon/endometrial cancer or other related cancers suspected to be hereditary, or patients at increased risk to due to family history.
   1) Services are provided according to the Comprehensive Cancer Network Guidelines.
      a) Lynch syndrome (hereditary colorectal and endometrial cancer, and other cancers associated with Lynch syndrome) services (CPT 81292-81300, 81317-81319) and familial adenomatous polyposis (FAP) services (CPT 81201-81203) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Screening. V.1.2013 (5/13/13). ***www.nccn.org***
      b) BRCA1/BRCA2 testing services (CPT 81211-81217) for women without a personal history of breast, ~~and/or~~ ovarian, and other associated cancers should be provided to high risk women as defined in Guideline Note 3 or as otherwise defined by the US Preventive Services Task Force.
      c) BRCA1/BRCA2 testing services (CPT 81211-81217) for women with a personal history of breast, ~~and/or~~ ovarian, and other associated cancers and for men with breast cancer should be provided according to the NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V.1.2011 (4/7/11). ***www.nccn.org***

d) PTEN (Cowden syndrome) services (CPT 81321-81323) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Screening. V.1.2013 (5/13/13). ***www.nccn.org.***

2) Genetic counseling should precede genetic testing for hereditary cancer whenever possible. ~~Very rarely, it may be appropriate for a genetic test to be performed prior to genetic counseling for a patient with cancer. If this is done, genetic counseling should be provided as soon as practical~~.

a) Pre and post-test genetic counseling ~~by the following providers~~ should be covered when provided by a suitably trained health professional with expertise and experience in cancer genetics

i) "Suitably trained" is defined as board certified or active candidate status from the American Board of Medical Genetics, American Board of Genetic Counseling, or Genetic Nursing Credentialing Commission.

~~ii) Medical Geneticist (M.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics~~

~~iii) Clinical Geneticist (Ph.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics.~~

~~iv) Genetic Counselor - Board Certified or Active Candidate Status from the American Board of Genetic Counseling, or Board Certified by the American Board of Medical Genetics.~~

~~v) Advance Practice Nurse in Genetics - Credential from the Genetic Nursing Credentialing Commission.~~

~~b)~~ If timely pre-test genetic counseling is not possible, appropriate genetic testing accompanied by pre- and post- test informed consent and post-test disclosure performed by a board-certified physician with experience in cancer genetics should be covered.

~~i)~~ i) Post-test genetic counseling should be performed as soon as is practical.

GUIDELINE NOTE 3, PROPHYLACTIC TREATMENT FOR PREVENTION OF BREAST CANCER IN HIGH RISK WOMEN

Line 195

Bilateral prophylactic breast removal is included on Line 195 for women without a personal history of invasive breast cancer who are at high risk for breast cancer. Prior to surgery, women without a personal history of breast cancer must have a genetics consultation as defined in section A2 of the DIAGNOSTIC GUIDELINE D1, NON-PRENATAL GENETIC TESTING GUIDELINE. High risk is defined as:

A) Having a BRCA1/BRCA2 mutation;

B) Having a strong family history of breast cancer, defined as one of the following:

1) 2 first-degree or second degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative);

2) 3 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative);

3) 4 relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative);
4) 1 relative with ovarian cancer at any age and, on the same side of the family, either 1 first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years, or 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years, or another ovarian cancer at any age;
5) 1 first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years;
6) 1 first-degree or second-degree relative diagnosed with bilateral breast cancer and one first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years; or,
7) a male relative with breast cancer at any age and on the same side of the family at least 1 first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years, or 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years.

C) A history of LCIS with a family history of breast cancer; or,
D) A history of treatment with thoracic radiation between ages 10 and 30.

Contralateral prophylactic mastectomy is included on Line 195 for women with a personal history of breast cancer and any of the high risk categories listed above. In addition, contralateral prophylactic mastectomy of the unaffected breast is indicated for women with invasive lobular carcinoma.

Prophylactic oophorectomy is included on Line 195 for women who have the BRCA1/BRCA2 mutation

Annals of Internal Medicine | Review

Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer in Women: A Systematic Review to Update the U.S. Preventive Services Task Force Recommendation

Heidi D. Nelson, MD, MPH; Miranda Pappas, MA; Bernadette Zakher, MBBS; Jennifer Priest Mitchell, BA; Leila Okinaka-Hu, MD; and Rongwei Fu, PhD

Background: Mutations in breast cancer susceptibility genes (*BRCA1* and *BRCA2*) are associated with increased risks for breast, ovarian, and other types of cancer.

Purpose: To review new evidence on the benefits and harms of risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women.

Data Sources: MEDLINE and PsycINFO between 2004 and 30 July 2013, the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews from 2004 through the second quarter of 2013, Health Technology Assessment during the fourth quarter of 2012, Scopus, and reference lists.

Study Selection: English-language studies about accuracy of risk assessment and benefits and harms of genetic counseling, genetic testing, and interventions to reduce cancer incidence and mortality.

Data Extraction: Individual investigators extracted data on participants, study design, analysis, follow-up, and results, and a second investigator confirmed key data. Investigators independently dual-rated study quality and applicability by using established criteria.

Data Synthesis: Five referral models accurately estimate individual risk for BRCA mutations. Genetic counseling increases the accuracy of risk perception and decreases the intention for genetic testing among unlikely carriers and cancer-related worry, anxiety, and depression. No trials evaluated the effectiveness of intensive screening or risk-reducing medications in mutation carriers, although false-positive rates, unneeded imaging, and unneeded surgeries were higher with screening. Among high-risk women and mutation carriers, risk-reducing mastectomy decreased breast cancer by 85% to 100% and breast cancer mortality by 81% to 100% compared with women without surgery; risk-reducing salpingo-oophorectomy decreased breast cancer incidence by 37% to 100%, ovarian cancer by 69% to 100%, and all-cause mortality by 55% to 100%.

Limitation: The analysis included only English-language articles; efficacy trials in mutation carriers were lacking.

Conclusion: Studies of risk assessment, genetic counseling, genetic testing, and interventions to reduce cancer and mortality indicate potential benefits and harms that vary according to risk.

Primary Funding Source: Agency for Healthcare Research and Quality.

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For author affiliations, see end of text.

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The U.S. Preventive Services Task Force (USPSTF) recommended in 2005 that women whose family histories are associated with increased risks for clinically significant, or deleterious, mutations in the *BRCA1* or *BRCA2* gene be referred for genetic counseling and evaluation for mutation testing (1). This recommendation was intended for primary prevention of cancer and applies to women without previous diagnoses of breast or ovarian cancer.

Deleterious mutations in the *BRCA1* and *BRCA2* genes are associated with increased risks for breast, ovarian, fallopian tube, and peritoneal cancer in women and breast cancer in men (2). They are also, to a lesser degree, associated with pancreatic and early-onset prostate cancer, and *BRCA2* mutations are associated with melanoma. Mutations in BRCA genes cluster in families exhibiting an autosomal dominant pattern of transmission and account for 5% to 10% of cases of breast cancer overall (3, 4).

Specific BRCA mutations, known as founder mutations, occur among certain ethnic groups, including Ashkenazi Jewish (5–7), black (8), and Hispanic persons (9, 10), and in identified families (11–15). Other genes are associated with hereditary susceptibility to breast and ovarian cancer but are not commonly tested, such as *PTEN* (the Cowden syndrome) and *TP53* (the Li–Fraumeni syndrome) (2, 16).

Genetic risk assessment and testing involve determining individual risk for BRCA mutations, followed by selective testing of high-risk persons. Characteristics associated with an increased likelihood of BRCA mutations (17–20) include breast and ovarian cancer in relatives and a young age of onset. These and other individual and family characteristics can be used to assess personal mutation risk and the need for referral for additional evaluation. Genetic counseling is the process of identifying and counseling persons at risk for familial or inherited cancer and is recommended before testing (21, 22).

Guidelines recommend testing for mutations only when an individual has a personal or family history of cancer suggestive of inherited cancer susceptibility and the

See also:

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results can be adequately interpreted and will aid in management (23). The type of mutation analysis that is required depends on family history. Persons without links to families or groups with known mutations (5–10, 12–14) generally have direct DNA sequencing. For appropriate candidates, interventions to reduce cancer risk include earlier, more frequent, or intensive cancer screening; risk-reducing medications; and risk-reducing surgery, including bilateral mastectomy and salpingo-oophorectomy.

This systematic review is an update of a prior review (1, 24, 25) for the USPSTF on the effectiveness and adverse effects of risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women. Its purpose is to evaluate and summarize research addressing specific key questions important to the USPSTF as it considers new recommendations for primary care practice.

METHODS

This research is part of a comprehensive systematic review that includes an additional analysis of studies of the prevalence and penetrance of BRCA mutations that is not included in this manuscript (26). We followed a standard protocol consistent with the Agency for Healthcare Research and Quality (AHRQ) methods for systematic reviews (27). On the basis of evidence gaps identified from a prior review (24, 25), the USPSTF and AHRQ determined the key questions for this update by using the methods of the USPSTF (28). Investigators created an analytic framework incorporating the key questions and outlining the patient populations, interventions, outcomes, and potential adverse effects (**Appendix Figure 1**, available at www.annals.org). A work plan was externally reviewed and modified.

The target population includes women without cancer or known BRCA mutations who are seen in clinical settings applicable to U.S. primary care practice, although the ideal candidate for mutation testing could be a male or female relative with cancer. The conditions of interest are mutation carrier status and BRCA-related cancer (predominantly breast, ovarian, fallopian tube, and peritoneal). Although other types of cancer are also considered during familial risk assessment, studies with these cancer outcomes are outside the scope of this review.

Data Sources

We searched MEDLINE from 2004 to 30 July 2013, the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews from 2004 through the second quarter of 2013, and Health Technology Assessment during the fourth quarter of 2012 for relevant English-language studies, systematic reviews, and meta-analyses. We manually reviewed reference lists of articles and reviewed citations of key studies by using Scopus.

Study Selection

Research published in 2004 or later and done in the United States or in populations that receive services and interventions applicable to medical practice in the United States was reviewed. Randomized, controlled trials (RCTs); systematic reviews; prospective and retrospective cohort studies; case–control studies; and diagnostic accuracy evaluations were included if they addressed the accuracy of risk assessment methods, outcomes of genetic counseling and testing, and the effectiveness of interventions to reduce BRCA-related cancer and mortality among mutation carriers.

Risk assessment methods were included if they were designed to guide referrals to genetic counselors or other genetic specialists and were usable by nonspecialists in genetics in clinical settings (that is, methods that were brief and nontechnical and did not require special training to administer or interpret). Evaluation of comprehensive models used in the practice of genetic counseling was outside the scope of this review, which focuses on primary care practice. Interventions included intensive screening, risk-reducing medications, and risk-reducing surgery. Only risk-reducing medications approved by the U.S. Food and Drug Administration (that is, tamoxifen and raloxifene) were considered, consistent with the scope of the USPSTF.

Studies of any design were included if they described potential adverse effects, including inaccurate risk assessment; inappropriate testing; false-positive and false-negative results; false reassurance; incomplete testing; misinterpretation of results; anxiety; cancer-related worry; immediate and long-term harms associated with interventions; and ethical, legal, and social implications. For adverse effects of interventions, studies were included that enrolled women at high risk for BRCA-related cancer regardless of their mutation status.

After an initial review of abstracts, we reviewed full-text articles by using additional inclusion criteria. Studies from the prior review that met inclusion criteria for the update were included to build on previous relevant research. **Appendix Figure 2** (available at www.annals.org) shows the results of the search and selection process.

Data Abstraction and Quality Assessment

An investigator abstracted data about the study design and setting; participant characteristics; procedures for data collection; number of participants enrolled and lost to follow-up; methods of exposure and outcome ascertainment; analytic methods, including adjustment for confounders; and outcomes. A second investigator confirmed the accuracy of key data. Two investigators used predefined criteria for RCTs; systematic reviews; and cohort, case–control, and diagnostic accuracy studies developed by the USPSTF (28, 29) to rate the quality of studies (good, fair, or poor) and resolved discrepancies by consensus.

Quality could not be assessed for many studies with designs that did not have predefined criteria, such as de-

scriptive, cross-sectional, and pre–post studies, and case series. The applicability of studies was determined using the population, intervention, comparator, outcomes, timing of outcomes measurement, and setting format adapted to this topic (30).

Data Synthesis and Analysis

Because of heterogeneity across studies, results were not combined in a quantitative meta-analysis. We assessed the aggregate quality of the body of evidence (good, fair, or poor) by using methods that the USPSTF developed on the basis of the number, quality, and size of studies and consistency of results between studies (28). Studies were considered consistent if outcomes were generally in the same direction of effect and ranges of effect sizes were narrow.

Role of the Funding Source

This research was funded by the AHRQ. Investigators worked with AHRQ staff and USPSTF members to define the scope, analytic framework, and key questions; resolve issues arising during the project; and review the final report to ensure that it met basic methodological standards for systematic reviews. The draft report was reviewed by content experts, USPSTF members, AHRQ program officers, and collaborative partners and was posted for public comment for 4 weeks during April 2013. The funding source had no role in the selection, critical appraisal, or synthesis of evidence. The investigators were solely responsible for the content and the decision to submit the manuscript for publication.

Results

Accuracy and Adverse Effects of Referral Models to Estimate Individual Risk for BRCA Mutations

Risk models estimate the likelihood of BRCA mutations in individual persons, and some were developed to guide patient referrals to genetic counselors or other genetic specialists for more comprehensive evaluations. Ten studies describing performance characteristics of the Ontario Family History Assessment Tool (FHAT) (31–33), Manchester scoring system (33–36), Referral Screening Tool (RST) (37, 38), Pedigree Assessment Tool (PAT) (39), and Family History Screen-7 (FHS-7) (40) met inclusion criteria for this review (**Appendix Table 1**, available at www.annals.org). Included studies met criteria for fair or good quality and determined the sensitivity and specificity of models by comparing results of mutation carriers versus noncarriers or referral models versus more complex models, such as the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (41, 42), BRCAPRO (43–45), and Myriad II (18) (**Appendix Table 2**, available at www.annals.org). No studies described adverse effects of the risk models. Studies of the RST, PAT, and FHS-7 were published after the prior USPSTF systematic review.

Models were evaluated in patient populations in the United States (RST and PAT), Canada (FHAT), the United Kingdom (Manchester scoring system), and Brazil (FHS-7). Most studies defined the referral threshold as 10% estimated probability of a BRCA mutation. The FHAT and Manchester scoring system were evaluated in selected populations of known mutation carriers and noncarriers. Sensitivity was high for both models in most studies (94% for the FHAT [31, 32] and 87% to 93% for the Manchester scoring system [34–36]). Lower sensitivity estimates (70% for the FHAT and 58% for the Manchester scoring system) came from a study of both models that included 200 mutation carriers and 100 noncarriers (33), which represented a patient spectrum different from that of the other studies.

The RST, PAT, and FHS-7 were evaluated in large samples of women having screening mammography or visiting primary care clinics. The sensitivity of the RST was high compared with that of the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (89%), BRCAPRO (91%), and Myriad II (91%) (37). A revised Web-based version that includes more information on family history reported slightly higher sensitivity values (38). The PAT had 100% sensitivity compared with Myriad II (39), and the FHS-7 had 88% sensitivity compared with a genetic evaluation that included kindred analysis, risk estimates using multiple models, and clinical criteria (40).

Benefits and Adverse Effects of Genetic Counseling to Determine Eligibility for Genetic Testing

Twenty-seven studies met inclusion criteria, including 16 published since the prior review (46–63) and 11 included previously (64–74) (**Appendix Table 3**, available at www.annals.org). Studies provided data about accuracy of risk perception; intention for genetic testing; and distress, measured as breast cancer–related worry, anxiety, or depression.

Risk Perception

Although studies included in the prior USPSTF review were inconclusive (64, 66–69, 71–74), 8 new studies consistently reported improved accuracy of the perception of risk for breast cancer after genetic counseling (50, 54–56, 58, 59, 61, 72). A single study reported decreased accuracy (51). Only 1 study evaluated perception of risk for ovarian cancer and reported decreased accuracy after counseling (57). A fair-quality systematic review of 19 studies published before February 2007 indicated that risk perception was accurate for 42% of women before counseling and for 58% after (63). Accuracy improved when counseling provided information about family history, heredity, and personal risk estimates and facilitated informed decision making and adaptation to personal risk.

Intention to Participate in Genetic Testing

Two new studies reported decreased intention to have genetic testing after genetic counseling among women unlikely to be carriers (50, 55), which is consistent with prior studies (64, 67, 70). These include a study comparing telephone counseling, in-person counseling, and no counseling that indicated that women in the 2 counseling groups were less likely to pursue genetic testing than those in the noncounseling group (55). A fair-quality RCT reported decreased interest in genetic testing 6 months after group and individual counseling compared with no counseling (50).

Cancer-Related Worry, Anxiety, and Depression

No new studies reported increased breast cancer–related worry among women who received genetic counseling, and 8 studies reported decreases (48, 50–53, 55, 56, 60); 1 poor-quality RCT reported no changes (49). These results are consistent with prior studies indicating that breast cancer–related worry usually decreases after genetic counseling (65–67, 69–71, 73, 74). No studies reported statistically significant increases in anxiety and depression after genetic counseling; 3 reported statistically significant decreases (52, 61, 62), and 3 reported no changes (48, 56, 60). Studies in the prior review also indicated that measures of anxiety and depression generally decreased or did not differ with counseling (65, 66, 68, 69, 72–74).

Adverse Effects of Genetic Testing

Thirteen new observational studies (75–89) and 1 included previously (90) (**Appendix Table 4**, available at www.annals.org) provided data about distress due to BRCA testing, measured as breast cancer–related worry, anxiety, or depression or other psychosocial outcomes. No studies described other adverse effects of testing, such as false-positive or false-negative results or unneeded risk-reducing interventions.

Five studies reported statistically significant increases in breast cancer–related worry after receipt of BRCA test results (76, 87–90). These results were confined to mutation carriers before versus after testing (88), mutation carriers compared with noncarriers (87, 89) or compared with women who were not tested (90), and women with a family history that indicates high risk for breast cancer compared with untested low-risk women (76). One study reported a decrease in breast cancer–related worry for both carriers and noncarriers (78).

Studies reported decreased anxiety scores after testing regardless of mutation status (75) and among noncarriers only (82). Prospective cohort studies found statistically significantly higher anxiety scores for mutation carriers versus noncarriers (83, 87), women with family histories of breast cancer who were not tested versus mutation carriers (79, 80), and mutation carriers and noncarriers (78). Although all women in 1 study had high anxiety scores, noncarriers had lower anxiety scores at 1-week follow-up than carriers and women who were not tested (90). Four studies reported no differences in anxiety over 1 year (77, 85) or among carriers, noncarriers, and age-matched control participants (76, 84).

Women with family histories of breast cancer who did not have genetic testing had higher depression scores than mutation carriers in 1 study, although scores did not reach the threshold for clinical depression (80). Noncarriers had lower depression scores at 4-month follow-up than carriers and women who were not tested in another study (90). Four studies reported no differences in depression over time (75, 85) or among carriers, noncarriers, and age-matched control participants (76, 84), with all scores below the case threshold.

Mutation carriers had more subjective sleep problems than noncarriers and age-matched control participants, although actual sleep duration, latency, and wakefulness, as measured by a wrist monitor, showed no differences among groups (86).

Effectiveness and Adverse Effects of Risk-Reducing Interventions in BRCA Mutation Carriers

Intensive Screening

Breast Cancer. No studies of the effectiveness of intensive screening met inclusion criteria. Five studies that enrolled mutation carriers and other high-risk women described adverse effects (91–95). The Dutch MRISC (Magnetic Resonance Imaging [MRI] Screening) study reported statistically significantly higher false-positive rates with MRI than with mammography on the first and subsequent screening rounds (first, 14.0% vs. 5.5%; subsequent, 8.2% vs. 4.6%; $P < 0.001$ for both comparisons) (91). False-negative rates for MRI were lower than those for mammography, although numbers were small (91). A study of every-6-month screening found similar false-positive rates for MRI (11%) and mammography (15%) (92). Recall rates for annual MRI were higher than those for annual mammography in a descriptive study conducted in the United Kingdom (MRI, 11.0% per woman-year; mammography, 3.9%; combined, 13.0%) (93). In that study, 245 of 279 total recalls were for benign findings, amounting to 8.5 recalls per cancer case detected.

These studies also reported additional imaging procedures or biopsies that may have been unnecessary because final results were benign and women may never have had these procedures if the original screening test had not been done (92, 96). In the Dutch MRISC study, 43% of women with unneeded biopsies had preceding screening MRIs and 28% had mammography (96). Alternating MRI with mammography screening every 6 months yielded a greater proportion of unneeded imaging (targeted ultrasonography) in women screened with mammography than with MRI (mammography, 8 of 11; MRI, 4 of 8), although rates of unneeded biopsies were similar (mammography, 3 of 11; MRI, 2 of 8) (92).

Discomfort, pain, and anxiety of women having intensive screening with annual mammography, MRI, and bi-

annual clinical breast examination were similar to those of women having only biannual clinical breast examination in a fair-quality prospective cohort study (94). Most women had no anxiety after each type of screening. In a pre–post study of screening with MRI, mammography, ultrasonography, and clinical breast examination, women who were recalled reported higher anxiety scores approximately 1 month after screening than those who were not recalled (8.8 vs. 5.9; $P = 0.03$) (95). Among-group differences were not statistically significant after 6 months.

Ovarian Cancer. No studies of the effectiveness of intensive screening met inclusion criteria. Adverse effects were described in a study of annual measurements of serum cancer antigen-125 (CA-125) and transvaginal ultrasonography in 459 BRCA mutation carriers (mean, 2.4 screening visits [1.6 per year]) (97). Abnormalities were detected in 3% (38 of 1116) of screening visits. Of 26 diagnostic procedures, cancer was not detected in 67% (4 of 6) after abnormal serum CA-125 measurement compared with 100% (9 of 9) after abnormal transvaginal ultrasound. Combined methods resulted in an unneeded rate of diagnostic surgery of 55% (6 of 11) (97). In a study of screening with annual serum CA-125 measurements and transvaginal ultrasonography, women with abnormal results had statistically significantly higher cancer-related distress 1 week after receiving results than those with normal results, although long-term distress, anxiety, and depression scores were not higher (98).

Risk-Reducing Medications

Breast Cancer. No trials evaluated the efficacy of risk-reducing medications in BRCA mutation carriers, although placebo-controlled trials of tamoxifen and raloxifene indicated reduced risk for estrogen receptor–positive breast cancer for women at various risk levels (26, 99, 100).

Adverse effects for trial participants are relevant to mutation carriers. Women using tamoxifen and raloxifene had more thromboembolic events than women using placebo (tamoxifen risk ratio [RR], 1.93 [95% CI, 1.41 to 2.64]; 4 trials and raloxifene RR, 1.60 [CI, 1.15 to 2.23]; 2 trials) (99, 100). Coronary heart disease events and stroke were not increased in placebo-controlled trials, although women randomly assigned to raloxifene had higher stroke mortality than placebo recipients in the RUTH (Raloxifene Use for the Heart) trial (RR, 1.49 [CI, 1.00 to 2.24]) (101). Tamoxifen caused more cases of endometrial cancer (RR, 2.13 [CI, 1.36 to 3.32]; 3 trials) and was related to more benign gynecologic conditions; surgical procedures, including hysterectomy; and uterine bleeding than placebo (99, 100). Women receiving tamoxifen had more cataract surgeries than those receiving placebo in the NSABP (National Surgical Adjuvant Breast and Bowel Project) P-1 trial (102). The most common adverse effects were vasomotor symptoms and vaginal discharge, itching, or dryness for tamoxifen and vasomotor symptoms and leg cramps for raloxifene (99, 100).

Risk-Reducing Surgery

Bilateral Mastectomy. A prospective cohort study of women with BRCA mutations indicated that none of 75 women with risk-reducing mastectomies was diagnosed with breast cancer during follow-up compared with 34 of 585 (5.8%) without mastectomies (103). A cohort study of mutation carriers in Denmark found that 3 of 96 women who had mastectomies were diagnosed with breast cancer versus 16 of 211 who did not (hazard ratio [HR], 0.39 [CI, 0.12 to 1.36]), although the study was inadequately powered for this outcome (104). A descriptive study found that none of 307 women who had BRCA mutations or were otherwise considered to be at high risk and had mastectomies was diagnosed with breast cancer during follow-up, whereas 21.3 were expected (105), consistent with results of an earlier study of 18 mutation carriers (106, 107).

Adverse effects include surgical complications, long-term physical effects, and distress. In a case series of 122 women who had risk-reducing mastectomy, 64.4% reported postsurgical numbness, pain, tingling, infection, swelling, breast hardness, bleeding, organizing hematoma, failed reconstruction, breathing problems, thrombosis, and pulmonary embolism (108). Most women (87.3%) reported postmastectomy pain and discomfort, and 21.8% reported that pain affected their daily lives in a follow-up study of 59 high-risk women (109). Women's pain scores did not statistically significantly differ before mastectomy, 6 months after mastectomy, and 1 year after mastectomy in another study (110).

In a study of 90 high-risk women with risk-reducing bilateral mastectomies, including 50 mutation carriers, anxiety scores statistically significantly decreased after surgery (mean Hospital Anxiety and Depression Scale scores: before surgery, 5.59; 6 months after surgery, 3.80; 1 year after surgery, 3.83; $P < 0.001$) (110, 111). Women also reported less pleasure in sexual activity 1 year after surgery than 6 months after surgery and before surgery (mean Sexual Activity Questionnaire scores: before surgery, 12.28; 6 months after surgery, 12.21; 1 year after surgery, 11.18; $P = 0.005$). Depression scores, body image, and other concerns did not change. Other studies indicated no statistically significant changes in psychological or sexual activity measures after mastectomy (108, 109, 112).

Salpingo-Oophorectomy and Oophorectomy. In a prospective study of 1557 BRCA mutation carriers, salpingo-oophorectomy was statistically significantly associated with reduced incidence of ovarian or primary peritoneal cancer (1.3% vs. 5.8%; HR, 0.28 [CI, 0.12 to 0.69]), breast cancer (11.6% vs. 21.6%; HR, 0.54 [CI, 0.37 to 0.79]), and all-cause mortality (1.8% vs. 5.9%; HR, 0.45 [CI, 0.21 to 0.95]) (103). In this study, salpingo-oophorectomy did not reduce breast cancer– and ovarian cancer–specific mortal-

ity, although the study may have been underpowered for these outcomes. Oophorectomy was also associated with reduced breast cancer incidence in a prospective study of women from families with known *BRCA1* mutation carriers (18% vs. 42%; HR, 0.38 [CI, 0.15 to 0.97]) (113). Risk reduction was most pronounced for women who had the procedure at younger ages in this study, as well as in a retrospective study of risk-reducing oophorectomy (114).

Few studies described adverse effects. Most women reported worse vasomotor symptoms and sexual function after risk-reducing salpingo-oophorectomy in a small pre–post study of mutation carriers (115). In another small pre–post study, mutation carriers reported an increase in somatization; a decrease in cancer-related distress; and no change in health-related quality of life, anxiety, or depression after salpingo-oophorectomy (116).

DISCUSSION

No studies directly addressed the effectiveness of risk assessment, genetic counseling, and genetic testing in reducing cancer incidence and mortality (**Table**). Five referral models accurately estimated individual risk for BRCA mutations, with most sensitivity measures greater than 85%. However, reference standards and study designs varied, and some models have been evaluated only in single studies. Risk was based on self-reported information, which potentially compromises model accuracy. The sensitivity and specificity of self-reported history of cancer in first-degree relatives have been estimated as 65% and 99% for breast cancer (117) and 50% and 99% for ovarian cancer, respectively (118).

Genetic counseling increases the accuracy of risk perception; decreases intention for mutation testing among women who are unlikely carriers; and decreases cancer-related worry, anxiety, and depression. Limitations of studies included differences in designs and measures, dissimilar comparison groups, and small sizes. Risk perception improved after receipt of test results, and breast cancer–related worry and anxiety increased for women with positive results and decreased for others, although results were inconsistent. Studies were limited by high loss to follow-up and differences between comparison groups. Other relevant adverse effects of genetic testing were not studied, including false-positive or false-negative results, genetic discrimination, and insurability.

No trials evaluated the effectiveness of intensive screening in reducing the incidence of BRCA-related cancer and mortality. Higher rates of false-positive test results, unneeded imaging, and unneeded surgeries with screening were reported. No trials of risk-reducing medications provided results for BRCA mutation carriers, and whether efficacy in carriers differs from that in noncarriers is unclear. In trials, tamoxifen and raloxifene increased thromboembolic events and tamoxifen increased endometrial cancer and cataracts. Both caused undesirable effects for some women, such as vasomotor symptoms.

For high-risk women and mutation carriers, risk-reducing bilateral mastectomy reduced breast cancer incidence and mortality and oophorectomy or salpingo-oophorectomy reduced breast and ovarian cancer incidence and all-cause mortality. Comparison groups varied among studies, although results were consistent. Some women had physical complications of risk-reducing surgery, postsurgical symptoms, or changes in body image, whereas some women had less anxiety. Studies were descriptive and lacked important outcomes, and the few available studies had small numbers of participants and no comparison groups.

Limitations of this review include the use of only English-language articles and studies applicable to the United States, although these studies are most relevant to the USPSTF. The review focused on 5 key questions that restricted its scope, and men were not explicitly included except as family members of the women under evaluation. The number, quality, and applicability of included studies varied widely. Data were not available to determine the optimum age for testing and how the age at testing influences benefits and harms. Whether testing for BRCA mutations reduces cause-specific or all-cause mortality and improves quality of life is unknown. The harms associated with receiving a false-negative result or a result indicating mutations of unknown significance are unknown. Evidence of harms often relied on small descriptive studies with brief follow-up, and the long-term effect of risk assessment, counseling, and testing is unknown.

Several factors not evaluated in studies influence treatment effects. Effectiveness of salpingo-oophorectomy for reducing breast cancer risk depends on the age at which the procedure is done and decreases after menopause. However, how and when the benefit–harm ratio shifts for women facing this decision is uncertain. Also, the type of risk-reducing intervention that a mutation carrier selects may depend on her specific mutation. For example, women with *BRCA1* mutations have higher risks for ovarian cancer than those with *BRCA2* mutations (119, 120) and may consider their surgical options differently. Medications reduce risk for estrogen receptor–positive breast cancer (100) and consequently may be a more favorable choice for women with *BRCA2* mutations, for whom 77% of breast cancer cases are estrogen receptor–positive (121). How these factors influence patient decision making and eventual clinical outcomes is unknown.

To determine the appropriateness of risk assessment and testing for BRCA mutations in primary care, research on access to testing; effectiveness of screening approaches, including risk stratification; use of system supports; and patient acceptance and education is needed. Trials comparing types of providers and protocols could address who should perform these services, how they should be performed , and what skills are required. The consequences of

Table. **Summary of Evidence**

New Studies*	Design	Limitation	Consistency	Applicability	Overall Quality	Finding
Effectiveness of risk assessment, genetic counseling, and genetic testing to reduce BRCA-related cancer and mortality						
None	–	–	–	–	–	–
Accuracy and adverse effects of referral models to estimate individual risk for BRCA mutations						
8 studies of 5 models; no studies of adverse effects	Diagnostic accuracy	Reference standards and study designs varied; risk was based on self-reported information	Consistent	High	Good	Risk models report sensitivity estimates >85% for the FHAT, Manchester scoring system, RST, PAT, and FHS-7.
Benefits and adverse effects of genetic counseling to determine eligibility for genetic testing						
16 studies of the accuracy of risk perception, intention for genetic testing, and distress	RCT, cohort, case–control, pre–post	Noncomparable groups; small size; outcome measures varied	Consistent	High	Fair	Counseling increased the accuracy of risk perception and decreased intention for mutation testing among unlikely carriers as well as cancer-related worry, anxiety, and depression.
Adverse effects of genetic testing						
13 studies of risk perception and distress	Cohort, case–control, pre–post	No studies of other outcomes; high loss to follow-up; comparison groups and measures varied	Mixed	High	Fair	Breast cancer–related worry and anxiety increased for women with positive results and decreased for others, although results differed across studies. Risk perception improved after receipt of test results.
Effectiveness of risk-reducing interventions						
No studies of intensive screening or risk-reducing medications among BRCA mutation carriers	–	–	–	–	–	–
Risk-reducing surgery: 3 studies of mastectomy and 3 of oophorectomy or salpingo-oophorectomy	Cohort	Comparison groups varied	Consistent	High	Fair	For high-risk women, including mutation carriers, mastectomy reduced breast cancer by 85% to 100% and breast cancer mortality by 81% to 100%; salpingo-oophorectomy reduced breast cancer by 37% to 100%, ovarian cancer by 69% to 100%, and all-cause mortality by 55% to 100%.
Adverse effects of risk-reducing interventions in BRCA mutation carriers						
Intensive screening: 3 studies of physical harms of breast cancer screening and 2 of anxiety; 1 study of physical harms of ovarian cancer screening and 1 of cancer-related distress	Cohort	No RCTs; screening intervals and false-positive calculations varied among studies; some studies lacked within-cohort comparison groups	Consistent	High	Poor	False-positive rates, unnecessary imaging, and unneeded surgeries were higher with screening. Some women had transient cancer-related distress or anxiety if screening results were abnormal.

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Table—Continued

New Studies*	Design	Limitation	Consistency	Applicability	Overall Quality	Finding
Risk-reducing medications: 6 placebo-controlled trials (4 of tamoxifen and 2 of raloxifene) and 1 head-to-head trial in a systematic review	RCT	No results for BRCA mutation carriers; trials were heterogeneous; data on long-term effects were incomplete	Consistent	High	Good	Tamoxifen and raloxifene increased thromboembolic events compared with placebo. Tamoxifen increased endometrial cancer and cataracts compared with raloxifene. Both caused adverse effects for some women.
Risk-reducing surgery: 6 studies of complications, physical effects, or distress	Case series, pre–post	Lack of studies; small numbers of participants; no comparison groups	NA	Low	Poor	Some women had physical complications of surgery, postsurgical symptoms, changes in body image, and less anxiety.

FHAT = Ontario Family History Assessment Tool; FHS-7 = Family History Screen-7; NA = not applicable; PAT = Pedigree Assessment Tool; RCT = randomized, controlled trial; RST = Referral Screening Tool.
* Studies published in 2004 or later.

identifying women as high-risk, as well as genetic testing of women and their relatives, require more study. Well-designed investigations using standardized measures and enrolling participants that reflect the general population, including women from minority groups, are needed.

An expanded database or registry of patients receiving genetic counseling and testing for BRCA mutations would provide essential information about predictors of cancer, response to interventions, and other modifying factors. Traditionally, all patients clinically tested through direct DNA sequencing in the United States used a single private laboratory and patient data were inaccessible. Developing a centralized accessible database with key variables to address these issues as testing practices change in the wake of the recent U.S. Supreme Court decision on DNA patents (122) would be a major advance in this field.

Additional research on interventions is needed. Practice standards for screening have preceded supporting evidence despite known harms of overscreening. For example, although intensive screening with annual transvaginal ultrasonography and serum CA-125 measurement is recommended for high-risk women (21), no efficacy trials are available. The PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial reported no mortality benefit of screening average-risk women by using transvaginal ultrasonography and serum CA-125 measurement compared with usual care after 12 years of follow-up (123) and did not report outcomes for high-risk women, including BRCA mutation carriers. Also, a study of 3532 European women who were at increased risk for ovarian cancer, had unknown BRCA status, received transvaginal ultrasonography and CA-125 measurement, and were followed for up to 16 years indicated no stage shifts in disease incidence (124).

Trials of risk-reducing medications in mutation carriers, including aromatase inhibitors, and measurement of long-term outcomes are also needed. Comparisons of salpingo-oophorectomy versus more limited surgeries, such as salpingectomy alone, would inform current practice. Studies of factors related to acceptance of risk-reducing interventions based on genetic information would be useful, such as determining whether cancer incidence in relatives is reduced because they adopt risk-reducing interventions. This information could improve patient decision making and lead to better health outcomes.

The process of risk assessment and referral, evaluation by genetic counselors, genetic testing, and use of intensive screening and risk-reducing medications and surgeries is complex. Each step requires careful interpretation of information, consideration of risks, weighing of benefits and harms, and shared decision making before moving to the next step. Services must be well-integrated and highly personalized to optimize benefits and minimize harms for women as well as their families. Additional studies are necessary to better inform practice.

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Disclaimer: The findings and conclusions in this review are those of the authors, who are responsible for its content, and do not necessarily represent the views of the AHRQ. No statement in this review should be construed as an official position of the AHRQ or of the U.S. Department of Health and Human Services.

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References

1. **U.S. Preventive Services Task Force.** Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Ann Intern Med. 2005;143:355-61. [PMID: 16144894]

2. **Lindor NM, McMaster ML, Lindor CJ, Greene MH; National Cancer Institute, Division of Cancer Prevention, Community Oncology and Prevention Trials Research Group.** Concise handbook of familial cancer susceptibility syndromes - second edition. J Natl Cancer Inst Monogr. 2008:1-93. [PMID: 18559331]

3. **Whittemore AS, Gong G, John EM, McGuire V, Li FP, Ostrow KL, et al.** Prevalence of *BRCA1* mutation carriers among U.S. non-Hispanic Whites. Cancer Epidemiol Biomarkers Prev. 2004;13:2078-83. [PMID: 15598764]

4. Prevalence and penetrance of *BRCA1* and *BRCA2* mutations in a population-based series of breast cancer cases. Anglian Breast Cancer Study Group. Br J Cancer. 2000;83:1301-8. [PMID: 11044354]

5. **Neuhausen S, Gilewski T, Norton L, Tran T, McGuire P, Swensen J, et al.** Recurrent *BRCA2 6174delT* mutations in Ashkenazi Jewish women affected by breast cancer. Nat Genet. 1996;13:126-8. [PMID: 8673092]

6. **Struewing JP, Hartge P, Wacholder S, Baker SM, Berlin M, McAdams M, et al.** The risk of cancer associated with specific mutations of *BRCA1* and *BRCA2* among Ashkenazi Jews. N Engl J Med. 1997;336:1401-8. [PMID: 9145676]

7. **Roa BB, Boyd AA, Volcik K, Richards CS.** Ashkenazi Jewish population frequencies for common mutations in *BRCA1* and *BRCA2*. Nat Genet. 1996;14:185-7. [PMID: 8841191]

8. **Weitzel JN, Lagos V, Blazer KR, Nelson R, Ricker C, Herzog J, et al.** Prevalence of BRCA mutations and founder effect in high-risk Hispanic families. Cancer Epidemiol Biomarkers Prev. 2005;14:1666-71. [PMID: 16030099]

9. **Weitzel JN, Lagos VI, Herzog JS, Judkins T, Hendrickson B, Ho JS, et al.** Evidence for common ancestral origin of a recurring *BRCA1* genomic rearrangement identified in high-risk Hispanic families. Cancer Epidemiol Biomarkers Prev. 2007;16:1615-20. [PMID: 17646271]

10. **Mefford HC, Baumbach L, Panguluri RC, Whitfield-Broome C, Szabo C, Smith S, et al.** Evidence for a *BRCA1* founder mutation in families of West African ancestry [Letter]. Am J Hum Genet. 1999;65:575-8. [PMID: 10417303]

11. **Peelen T, van Vliet M, Petrij-Bosch A, Mieremet R, Szabo C, van den Ouweland AM, et al.** A high proportion of novel mutations in *BRCA1* with strong founder effects among Dutch and Belgian hereditary breast and ovarian cancer families. Am J Hum Genet. 1997;60:1041-9. [PMID: 9150151]

12. **Arason A, Jonasdottir A, Barkardottir RB, Bergthorsson JT, Teare MD, Easton DF, et al.** A population study of mutations and LOH at breast cancer gene loci in tumours from sister pairs: two recurrent mutations seem to account for all *BRCA1*/*BRCA2* linked breast cancer in Iceland. J Med Genet. 1998;35:446-9. [PMID: 9643283]

13. **Thorlacius S, Olafsdottir G, Tryggvadottir L, Neuhausen S, Jonasson JG, Tavtigian SV, et al.** A single *BRCA2* mutation in male and female breast cancer families from Iceland with varied cancer phenotypes. Nat Genet. 1996;13:117-9. [PMID: 8673089]

14. **Einbeigi Z, Bergman A, Kindblom LG, Martinsson T, Meis-Kindblom JM, Nordling M, et al.** A founder mutation of the *BRCA1* gene in Western Sweden associated with a high incidence of breast and ovarian cancer. Eur J Cancer. 2001;37:1904-9. [PMID: 11576847]

15. **Tonin PN, Mes-Masson AM, Futreal PA, Morgan K, Mahon M, Foulkes WD, et al.** Founder *BRCA1* and *BRCA2* mutations in French Canadian breast and ovarian cancer families. Am J Hum Genet. 1998;63:1341-51. [PMID: 9792861]

16. **National Cancer Institute.** Genetics of Breast and Ovarian Cancer (PDQ). Bethesda, MD: National Institutes of Health; 2013. Accessed at www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional on 9 September 2013.

17. **Couch FJ, DeShano ML, Blackwood MA, Calzone K, Stopfer J, Campeau L, et al.** *BRCA1* mutations in women attending clinics that evaluate the risk of breast cancer. N Engl J Med. 1997;336:1409-15. [PMID: 9145677]

18. **Frank TS, Deffenbaugh AM, Reid JE, Hulick M, Ward BE, Lingenfelter B, et al.** Clinical characteristics of individuals with germline mutations in *BRCA1* and *BRCA2*: analysis of 10,000 individuals. J Clin Oncol. 2002;20:1480-90. [PMID: 11896095]

19. **Shattuck-Eidens D, Oliphant A, McClure M, McBride C, Gupte J, Rubano T, et al.** *BRCA1* sequence analysis in women at high risk for susceptibility mutations. Risk factor analysis and implications for genetic testing. JAMA. 1997;278:1242-50. [PMID: 9333265]

20. **Srivastava A, McKinnon W, Wood ME.** Risk of breast and ovarian cancer in women with strong family histories. Oncology (Williston Park). 2001;15:889-902. [PMID: 11499690]

21. **National Comprehensive Cancer Network.** Genetic/Familial High-Risk Assessment: Breast and Ovarian. Fort Washington, PA: National Comprehensive Cancer Network; 2013. Accessed at www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf on 27 February 2013.

22. **National Comprehensive Cancer Network.** NCCN Clinical Practice Guidelines in Oncology: Breast Cancer Screening and Diagnosis. Fort Washington, PA: National Comprehensive Cancer Network; 2011. Accessed at www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf on 10 December 2013.

23. Statement of the American Society of Clinical Oncology: genetic testing for cancer susceptibility, Adopted on February 20, 1996. J Clin Oncol. 1996;14:1730-6. [PMID: 8622094]

24. **Nelson HD, Huffman LH, Fu R, Harris EL, Walker M, Bougatsos C.** Genetic Risk Assessment and BRCA Mutation Testing for Breast and Ovarian Cancer Susceptibility: Evidence Synthesis. 375th ed. Rockville, MD: Agency for Healthcare Research and Quality; 2005.

25. **Nelson HD, Huffman LH, Fu R, Harris EL:** U.S. Preventive Services Task Force. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2005;143:362-79. [PMID: 16144895]

26. **Nelson HD, Fu R, Goodard K, Mitchell JP, Okinaka-Hu L, Pappas M, et al.** Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA Related Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

27. **U.S. Preventive Services Task Force.** Procedure Manual. Rockville, MD: U.S. Preventive Services Task Force; 2008. Accessed at www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanual.htm on 3 April 2013.

28. **Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al. Methods Work Group, Third US Preventive Services Task Force.** Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20:21-35. [PMID: 11306229]

29. **Leeflang MM, Deeks JJ, Gatsonis C, Bossuyt PM; Cochrane Diagnostic Test Accuracy Working Group.** Systematic reviews of diagnostic test accuracy. Ann Intern Med. 2008;149:889-97. [PMID: 19075208]

30. **Atkins D, Chang SM, Gartlehner G, Buckley DI, Whitlock EP, Berliner E, et al.** Assessing applicability when comparing medical interventions: AHRQ and the Effective Health Care Program. J Clin Epidemiol. 2011;64:1198-207. [PMID: 21463926]

31. **Gilpin CA, Carson N, Hunter AG.** A preliminary validation of a family history assessment form to select women at risk for breast or ovarian cancer for referral to a genetics center. Clin Genet. 2000;58:299-308. [PMID: 11076055]

32. **Parmigiani G, Chen S, Iversen ES Jr, Friebel TM, Finkelstein DM, Anton-Culver H, et al.** Validity of models for predicting *BRCA1* and *BRCA2* mutations. Ann Intern Med. 2007;147:441-50. [PMID: 17909205]

33. **Panchal SM, Ennis M, Canon S, Bordeleau LJ.** Selecting a BRCA risk assessment model for use in a familial cancer clinic. BMC Med Genet. 2008;9:116. [PMID: 19102775]

34. **Evans DG, Eccles DM, Rahman N, Young K, Bulman M, Amir E, et al.** A new scoring system for the chances of identifying a *BRCA1/2* mutation outperforms existing models including BRCAPRO. J Med Genet. 2004;41:474-80. [PMID: 15173236]

35. **Barcenas CH, Hosain GM, Arun B, Zong J, Zhou X, Chen J, et al.** Assessing BRCA carrier probabilities in extended families. J Clin Oncol. 2006; 24:354-60. [PMID: 16421416]
36. **Antoniou AC, Hardy R, Walker L, Evans DG, Shenton A, Eeles R, et al.** Predicting the likelihood of carrying a *BRCA1* or *BRCA2* mutation: validation of BOADICEA, BRCAPRO, IBIS, Myriad and the Manchester scoring system using data from UK genetics clinics. J Med Genet. 2008;45:425-31. [PMID: 18413374]
37. **Bellcross CA, Lemke AA, Pape LS, Tess AL, Meisner LT.** Evaluation of a breast/ovarian cancer genetics referral screening tool in a mammography population. Genet Med. 2009;11:783-9. [PMID: 19752737]
38. **Bellcross C.** Further development and evaluation of a breast/ovarian cancer genetics referral screening tool [Letter]. Genet Med. 2010;12:240. [PMID: 20395744]
39. **Hoskins KF, Zwaagstra A, Ranz M.** Validation of a tool for identifying women at high risk for hereditary breast cancer in population-based screening. Cancer. 2006;107:1769-76. [PMID: 16967460]
40. **Ashton-Prolla P, Giacomazzi J, Schmidt AV, Roth FL, Palmero EI, Kalakun L, et al.** Development and validation of a simple questionnaire for the identification of hereditary breast cancer in primary care. BMC Cancer. 2009;9: 283. [PMID: 19682358]
41. **Antoniou AC, Cunningham AP, Peto J, Evans DG, Lalloo F, Narod SA, et al.** The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions. Br J Cancer. 2008;98:1457-66. [PMID: 18349832]
42. **Antoniou AC, Pharoah PD, McMullan G, Day NE, Stratton MR, Peto J, et al.** A comprehensive model for familial breast cancer incorporating *BRCA1*, *BRCA2* and other genes. Br J Cancer. 2002;86:76-83. [PMID: 11857015]
43. **Berry DA, Parmigiani G, Sanchez J, Schildkraut J, Winer E.** Probability of carrying a mutation of breast-ovarian cancer gene *BRCA1* based on family history. J Natl Cancer Inst. 1997;89:227-38. [PMID: 9017003]
44. **Parmigiani G, Berry D, Aguilar O.** Determining carrier probabilities for breast cancer-susceptibility genes *BRCA1* and *BRCA2*. Am J Hum Genet. 1998; 62:145-58. [PMID: 9443863]
45. **Berry DA, Iversen ES Jr, Gudbjartsson DF, Hiller EH, Garber JE, Peshkin BN, et al.** BRCAPRO validation, sensitivity of genetic testing of *BRCA1*/*BRCA2*, and prevalence of other breast cancer susceptibility genes. J Clin Oncol. 2002;20: 2701-12. [PMID: 12039933]
46. **Armstrong K, Micco E, Carney A, Stopfer J, Putt M.** Racial differences in the use of *BRCA1*/*2* testing among women with a family history of breast or ovarian cancer. JAMA. 2005;293:1729-36. [PMID: 15827311]
47. **Bennett P, Wilkinson C, Turner J, Edwards RT, France B, Griffith G, et al.** Factors associated with intrusive cancer-related worries in women undergoing cancer genetic risk assessment. Fam Cancer. 2009;8:159-65. [PMID: 19011994]
48. **Bennett P, Wilkinson C, Turner J, Brain K, Edwards RT, Griffith G, et al.** Psychological factors associated with emotional responses to receiving genetic risk information. J Genet Couns. 2008;17:234-49. [PMID: 18259848]
49. **Bloom JR, Stewart SL, Chang S, You M.** Effects of a telephone counseling intervention on sisters of young women with breast cancer. Prev Med. 2006;43: 379-84. [PMID: 16916540]
50. **Bowen DJ, Burke W, Culver JO, Press N, Crystal S.** Effects of counseling Ashkenazi Jewish women about breast cancer risk. Cultur Divers Ethnic Minor Psychol. 2006;12:45-56. [PMID: 16594854]
51. **Brain K, Parsons E, Bennett P, Cannings-John R, Hood K.** The evolution of worry after breast cancer risk assessment: 6-year follow-up of the TRACE study cohort. Psychooncology. 2011;20:984-91. [PMID: 20677331]
52. **Braithwaite D, Sutton S, Mackay J, Stein J, Emery J.** Development of a risk assessment tool for women with a family history of breast cancer. Cancer Detect Prev. 2005;29:433-9. [PMID: 16055276]
53. **Fry A, Cull A, Appleton S, Rush R, Holloway S, Gorman D, et al.** A randomised controlled trial of breast cancer genetics services in South East Scotland: psychological impact. Br J Cancer. 2003;89:653-9. [PMID: 12915873]
54. **Gurmankin AD, Domchek S, Stopfer J, Fels C, Armstrong K.** Patients' resistance to risk information in genetic counseling for *BRCA1*/*2*. Arch Intern Med. 2005;165:523-9. [PMID: 15767527]
55. **Helmes AW, Culver JO, Bowen DJ.** Results of a randomized study of telephone versus in-person breast cancer risk counseling. Patient Educ Couns. 2006;64:96-103. [PMID: 16427245]
56. **Hopwood P, Wonderling D, Watson M, Cull A, Douglas F, Cole T, et al.** A randomised comparison of UK genetic risk counselling services for familial cancer: psychosocial outcomes. Br J Cancer. 2004;91:884-92. [PMID: 15305197]
57. **Kelly KM, Senter L, Leventhal H, Ozakinci G, Porter K.** Subjective and objective risk of ovarian cancer in Ashkenazi Jewish women testing for *BRCA1*/*2* mutations. Patient Educ Couns. 2008;70:135-42. [PMID: 17988821]
58. **Matloff ET, Moyer A, Shannon KM, Niendorf KB, Col NF.** Healthy women with a family history of breast cancer: impact of a tailored genetic counseling intervention on risk perception, knowledge, and menopausal therapy decision making. J Womens Health (Larchmt). 2006;15:843-56. [PMID: 16999640]
59. **Mikkelsen EM, Sunde L, Johansen C, Johnsen SP.** Risk perception among women receiving genetic counseling: a population-based follow-up study. Cancer Detect Prev. 2007;31:457-64. [PMID: 18061369]
60. **Mikkelsen EM, Sunde L, Johansen C, Johnsen SP.** Psychosocial consequences of genetic counseling: a population-based follow-up study. Breast J. 2009;15:61-8. [PMID: 19120380]
61. **Pieterse AH, Ausems MG, Spreeuwenberg P, van Dulmen S.** Longer-term influence of breast cancer genetic counseling on cognitions and distress: smaller benefits for affected versus unaffected women. Patient Educ Couns. 2011;85: 425-31. [PMID: 21316181]
62. **Roshanai AH, Rosenquist R, Lampic C, Nordin K.** Does enhanced information at cancer genetic counseling improve counselees' knowledge, risk perception, satisfaction and negotiation of information to at-risk relatives?—a randomized study. Acta Oncol. 2009;48:999-1009. [PMID: 19636983]
63. **Smerecnik CM, Mesters I, Verweij E, de Vries NK, de Vries H.** A systematic review of the impact of genetic counseling on risk perception accuracy. J Genet Couns. 2009;18:217-28. [PMID: 19291376]
64. **Bowen DJ, Burke W, Yasui Y, McTiernan A, McLeran D.** Effects of risk counseling on interest in breast cancer genetic testing for lower risk women. Genet Med. 2002;4:359-65. [PMID: 12394349]
65. **Bowen DJ, Burke W, McTiernan A, Yasui Y, Andersen MR.** Breast cancer risk counseling improves women's functioning. Patient Educ Couns. 2004;53: 79-86. [PMID: 15062908]
66. **Brain K, Norman P, Gray J, Rogers C, Mansel R, Harper P.** A randomized trial of specialist genetic assessment: psychological impact on women at different levels of familial breast cancer risk. Br J Cancer. 2002;86:233-8. [PMID: 11870512]
67. **Burke W, Culver JO, Bowen D, Lowry D, Durfy S, McTiernan A, et al.** Genetic counseling for women with an intermediate family history of breast cancer. Am J Med Genet. 2000;90:361-8. [PMID: 10706356]
68. **Cull A, Miller H, Porterfield T, Mackay J, Anderson ED, Steel CM, et al.** The use of videotaped information in cancer genetic counselling: a randomized evaluation study. Br J Cancer. 1998;77:830-7. [PMID: 9514066]
69. **Hopwood P, Keeling F, Long A, Pool C, Evans G, Howell A.** Psychological support needs for women at high genetic risk of breast cancer: some preliminary indicators. Psychooncology. 1998;7:402-12. [PMID: 9809331]
70. **Lerman C, Hughes C, Benkendorf JL, Biesecker B, Kerner J, Willison J, et al.** Racial differences in testing motivation and psychological distress following pretest education for *BRCA1* gene testing. Cancer Epidemiol Biomarkers Prev. 1999;8:361-7. [PMID: 10207641]
71. **Lerman C, Schwartz MD, Miller SM, Daly M, Sands C, Rimer BK.** A randomized trial of breast cancer risk counseling: interacting effects of counseling, educational level, and coping style. Health Psychol. 1996;15:75-83. [PMID: 8681923]
72. **Lobb EA, Butow PN, Barratt A, Meiser B, Gaff C, Young MA, et al.** Communication and information-giving in high-risk breast cancer consultations: influence on patient outcomes. Br J Cancer. 2004;90:321-7. [PMID: 14735171]
73. **Watson M, Lloyd S, Davidson J, Meyer L, Eeles R, Ebbs S, et al.** The impact of genetic counselling on risk perception and mental health in women with a family history of breast cancer. Br J Cancer. 1999;79:868-74. [PMID: 10070883]
74. **Watson M, Duvivier V, Wade Walsh M, Ashley S, Davidson J, Papaikonomou M, et al.** Family history of breast cancer: what do women understand and recall about their genetic risk? J Med Genet. 1998;35:731-8. [PMID: 9733031]
75. **Arver B, Haegermark A, Platten U, Lindblom A, Brandberg Y.** Evaluation of psychosocial effects of pre-symptomatic testing for breast/ovarian and colon cancer pre-disposing genes: a 12-month follow-up. Fam Cancer. 2004;3:109-16. [PMID: 15340261]

76. **Dagan E, Shochat T.** Quality of life in asymptomatic *BRCA1/2* mutation carriers. Prev Med. 2009;48:193-6. [PMID: 19084553]
77. **Ertmanski S, Metcalfe K, Trempala J, Glowacka MD, Lubinski J, Narod SA, et al.** Identification of patients at high risk of psychological distress after *BRCA1* genetic testing. Genet Test Mol Biomarkers. 2009;13:325-30. [PMID: 19405874]
78. **Foster C, Watson M, Eeles R, Eccles D, Ashley S, Davidson R, et al; Psychosocial Study Collaborators.** Predictive genetic testing for *BRCA1/2* in a UK clinical cohort: three-year follow-up. Br J Cancer. 2007;96:718-24. [PMID: 17285126]
79. **Geirdal AØ, Dahl AA.** The relationship between coping strategies and anxiety in women from families with familial breast-ovarian cancer in the absence of demonstrated mutations. Psychooncology. 2008;17:49-57. [PMID: 17385192]
80. **Geirdal AØ, Reichelt JG, Dahl AA, Heimdal K, Maehle L, Stormorken A, et al.** Psychological distress in women at risk of hereditary breast/ovarian or HNPCC cancers in the absence of demonstrated mutations. Fam Cancer. 2005; 4:121-6. [PMID: 15951962]
81. **Julian-Reynier C, Mancini J, Mouret-Fourme E, Gauthier-Villars M, Bonadona V, Berthet P, et al.** Cancer risk management strategies and perceptions of unaffected women 5 years after predictive genetic testing for *BRCA1/2* mutations. Eur J Hum Genet. 2011;19:500-6. [PMID: 21267012]
82. **Kinney AY, Bloor LE, Mandal D, Simonsen SE, Baty BJ, Holubkov R, et al.** The impact of receiving genetic test results on general and cancer-specific psychologic distress among members of an African-American kindred with a *BRCA1* mutation. Cancer. 2005;104:2508-16. [PMID: 16222692]
83. **Low CA, Bower JE, Kwan L, Seldon J.** Benefit finding in response to *BRCA1/2* testing. Ann Behav Med. 2008;35:61-9. [PMID: 18347905]
84. **Reichelt JG, Heimdal K, Møller P, Dahl AA.** *BRCA1* testing with definitive results: a prospective study of psychological distress in a large clinic-based sample. Fam Cancer. 2004;3:21-8. [PMID: 15131402]
85. **Reichelt JG, Møller P, Heimdal K, Dahl AA.** Psychological and cancer-specific distress at 18 months post-testing in women with demonstrated *BRCA1* mutations for hereditary breast/ovarian cancer. Fam Cancer. 2008;7:245-54. [PMID: 18219587]
86. **Shochat T, Dagan E.** Sleep disturbances in asymptomatic *BRCA1/2* mutation carriers: women at high risk for breast-ovarian cancer. J Sleep Res. 2010;19: 333-40. [PMID: 20337906]
87. **van Dijk S, Timmermans DR, Meijers-Heijboer H, Tibben A, van Asperen CJ, Otten W.** Clinical characteristics affect the impact of an uninformative DNA test result: the course of worry and distress experienced by women who apply for genetic testing for breast cancer. J Clin Oncol. 2006;24:3672-7. [PMID: 16877736]
88. **Metcalfe KA, Mian N, Enmore M, Poll A, Llacuachaqui M, Nanda S, et al.** Long-term follow-up of Jewish women with a *BRCA1* and *BRCA2* mutation who underwent population genetic screening. Breast Cancer Res Treat. 2012;133: 735-40. [PMID: 22240989]
89. **Graves KD, Vegella P, Poggi EA, Peshkin BN, Tong A, Isaacs C, et al.** Long-term psychosocial outcomes of *BRCA1*/*BRCA2* testing: differences across affected status and risk-reducing surgery choice. Cancer Epidemiol Biomarkers Prev. 2012;21:445-55. [PMID: 22328347]
90. **Meiser B, Butow P, Friedlander M, Barratt A, Schnieden V, Watson M, et al.** Psychological impact of genetic testing in women from high-risk breast cancer families. Eur J Cancer. 2002;38:2025-31. [PMID: 12376208]
91. **Kriege M, Brekelmans CT, Boetes C, Muller SH, Zonderland HM, Obdeijn IM, et al; Dutch MRI Screening (MRISC) Study Group.** Differences between first and subsequent rounds of the MRISC breast cancer screening program for women with a familial or genetic predisposition. Cancer. 2006;106: 2318-26. [PMID: 16615112]
92. **Le-Petross HT, Whitman GJ, Atchley DP, Yuan Y, Gutierrez-Barrera A, Hortobagyi GN, et al.** Effectiveness of alternating mammography and magnetic resonance imaging for screening women with deleterious BRCA mutations at high risk of breast cancer. Cancer. 2011;117:3900-7. [PMID: 21365619]
93. **Leach MO, Boggis CR, Dixon AK, Easton DF, Eeles RA, Evans DG, et al; MARIBS study group.** Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet. 2005;365:1769-78. [PMID: 15910949]
94. **Rijnsburger AJ, Essink-Bot ML, van Dooren S, Borsboom GJ, Seynaeve C, Bartels CC, et al.** Impact of screening for breast cancer in high-risk women on health-related quality of life. Br J Cancer. 2004;91:69-76. [PMID: 15199386]
95. **Spiegel TN, Esplen MJ, Hill KA, Wong J, Causer PA, Warner E.** Psychological impact of recall on women with BRCA mutations undergoing MRI surveillance. Breast. 2011;20:424-30. [PMID: 21612928]
96. **Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, et al; Magnetic Resonance Imaging Screening Study Group.** Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med. 2004;351:427-37. [PMID: 15282350]
97. **Hermsen BB, Olivier RI, Verheijen RH, van Beurden M, de Hullu JA, Massuger LF, et al.** No efficacy of annual gynaecological screening in BRCA1/2 mutation carriers; an observational follow-up study. Br J Cancer. 2007;96:1335-42. [PMID: 17426707]
98. **Brain KE, Lifford KJ, Fraser L, Rosenthal AN, Rogers MT, Lancastle D, et al.** Psychological outcomes of familial ovarian cancer screening: no evidence of long-term harm. Gynecol Oncol. 2012;127:556-63. [PMID: 22943881]
99. **Nelson HD, Fu R, Humphrey L, Smith M, Griffin JC, Nygren P.** Comparative Effectiveness of Medications to Reduce Risk of Primary Breast Cancer in Women. Rockville, MD: Agency for Healthcare Research and Quality; 2009.
100. **Nelson HD, Smith ME, Griffin JC, Fu R.** Use of medications to reduce risk for primary breast cancer: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013;158:604-14. [PMID: 23588749]
101. **Barrett-Connor E, Mosca L, Collins P, Geiger MJ, Grady D, Kornitzer M, et al; Raloxifene Use for The Heart (RUTH) Trial Investigators.** Effects of raloxifene on cardiovascular events and breast cancer in postmenopausal women. N Engl J Med. 2006;355:125-37. [PMID: 16837676]
102. **Fisher B, Costantino JP, Wickerham DL, Cecchini RS, Cronin WM, Robidoux A, et al.** Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. J Natl Cancer Inst. 2005;97:1652-62. [PMID: 16288118]
103. **Domchek SM, Friebel TM, Singer CF, Evans DG, Lynch HT, Isaacs C, et al.** Association of risk-reducing surgery in *BRCA1* or *BRCA2* mutation carriers with cancer risk and mortality. JAMA. 2010;304:967-75. [PMID: 20810374]
104. **Skytte AB, Crüger D, Gerster M, Laenkholm AV, Lang C, Brøndum-Nielsen K, et al.** Breast cancer after bilateral risk-reducing mastectomy. Clin Genet. 2011;79:431-7. [PMID: 21199491]
105. **Evans DG, Baildam AD, Anderson E, Brain A, Shenton A, Vasen HF, et al.** Risk reducing mastectomy: outcomes in 10 European centres. J Med Genet. 2009;46:254-8. [PMID: 18996907]
106. **Hartmann LC, Schaid DJ, Woods JE, Crotty TP, Myers JL, Arnold PG, et al.** Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. N Engl J Med. 1999;340:77-84. [PMID: 9887158]
107. **Hartmann LC, Sellers TA, Schaid DJ, Frank TS, Soderberg CL, Sitta DL, et al.** Efficacy of bilateral prophylactic mastectomy in *BRCA1* and *BRCA2* gene mutation carriers. J Natl Cancer Inst. 2001;93:1633-7. [PMID: 11698567]
108. **Metcalfe KA, Esplen MJ, Goel V, Narod SA.** Psychosocial functioning in women who have undergone bilateral prophylactic mastectomy. Psychooncology. 2004;13:14-25. [PMID: 14745742]
109. **Gahm J, Wickman M, Brandberg Y.** Bilateral prophylactic mastectomy in women with inherited risk of breast cancer—prevalence of pain and discomfort, impact on sexuality, quality of life and feelings of regret two years after surgery. Breast. 2010;19:462-9. [PMID: 20605453]
110. **Brandberg Y, Sandelin K, Erikson S, Jurell G, Liljegren A, Lindblom A, et al.** Psychological reactions, quality of life, and body image after bilateral prophylactic mastectomy in women at high risk for breast cancer: a prospective 1-year follow-up study. J Clin Oncol. 2008;26:3943-9. [PMID: 18711183]
111. **Brandberg Y, Arver B, Johansson H, Wickman M, Sandelin K, Liljegren A.** Less correspondence between expectations before and cosmetic results after risk-reducing mastectomy in women who are mutation carriers: a prospective study. Eur J Surg Oncol. 2012;38:38-43. [PMID: 22032910]
112. **Wasteson E, Sandelin K, Brandberg Y, Wickman M, Arver B.** High satisfaction rate ten years after bilateral prophylactic mastectomy—a longitudinal study. Eur J Cancer Care (Engl). 2011;20:508-13. [PMID: 20597955]
113. **Kramer JL, Velazquez IA, Chen BE, Rosenberg PS, Struewing JP, Greene MH.** Prophylactic oophorectomy reduces breast cancer penetrance during prospective, long-term follow-up of *BRCA1* mutation carriers. J Clin Oncol. 2005; 23:8629-35. [PMID: 16314625]
114. **Olson JE, Sellers TA, Iturria SJ, Hartmann LC.** Bilateral oophorectomy and breast cancer risk reduction among women with a family history. Cancer Detect Prev. 2004;28:357-60. [PMID: 15542261]

115. **Finch A, Metcalfe KA, Chiang JK, Elit L, McLaughlin J, Springate C, et al.** The impact of prophylactic salpingo-oophorectomy on menopausal symptoms and sexual function in women who carry a BRCA mutation. Gynecol Oncol. 2011;121:163-8. [PMID: 21216453]

116. **Finch A, Metcalfe KA, Chiang J, Elit L, McLaughlin J, Springate C, et al.** The impact of prophylactic salpingo-oophorectomy on quality of life and psychological distress in women with a BRCA mutation. Psychooncology. 2013;22:212-9. [PMID: 21913283]

117. **Mai PL, Garceau AO, Graubard BI, Dunn M, McNeel TS, Gonsalves L, et al.** Confirmation of family cancer history reported in a population-based survey. J Natl Cancer Inst. 2011;103:788-97. [PMID: 21562245]

118. **Kerber RA, Slattery ML.** Comparison of self-reported and database-linked family history of cancer data in a case-control study. Am J Epidemiol. 1997;146:244-8. [PMID: 9247008]

119. **Antoniou A, Pharoah PD, Narod S, Risch HA, Eyfjord JE, Hopper JL, et al.** Average risks of breast and ovarian cancer associated with *BRCA1* or *BRCA2* mutations detected in case series unselected for family history: a combined analysis of 22 studies. Am J Hum Genet. 2003;72:1117-30. [PMID: 12677558]

120. **Chen S, Parmigiani G.** Meta-analysis of *BRCA1* and *BRCA2* penetrance. J Clin Oncol. 2007;25:1329-33. [PMID: 17416853]

121. **Mavaddat N, Barrowdale D, Andrulis IL, Domchek SM, Eccles D, Nevanlinna H, et al; HEBON.** Pathology of breast and ovarian cancers among *BRCA1* and *BRCA2* mutation carriers: results from the Consortium of Investigators of Modifiers of *BRCA1/2* (CIMBA). Cancer Epidemiol Biomarkers Prev. 2012;21:134-47. [PMID: 22144499]

122. Association for Molecular Pathology v. Myriad Genetics, Inc., No. 12-398, slip op. (2013).

123. **Buys SS, Partridge E, Black A, Johnson CC, Lamerato L, Isaacs C, et al; PLCO Project Team.** Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. JAMA. 2011;305:2295-303. [PMID: 21642681]

124. **Evans DG, Lennard F, Pointon LJ, Ramus SJ, Gayther SA, Sodha N, et al; UK Study of MRI Screening for Breast Cancer in Women at High Risk (MARIBS).** Eligibility for magnetic resonance imaging screening in the United Kingdom: effect of strict selection criteria and anonymous DNA testing on breast cancer incidence in the MARIBS Study. Cancer Epidemiol Biomarkers Prev. 2009;18:2123-31. [PMID: 19567506]

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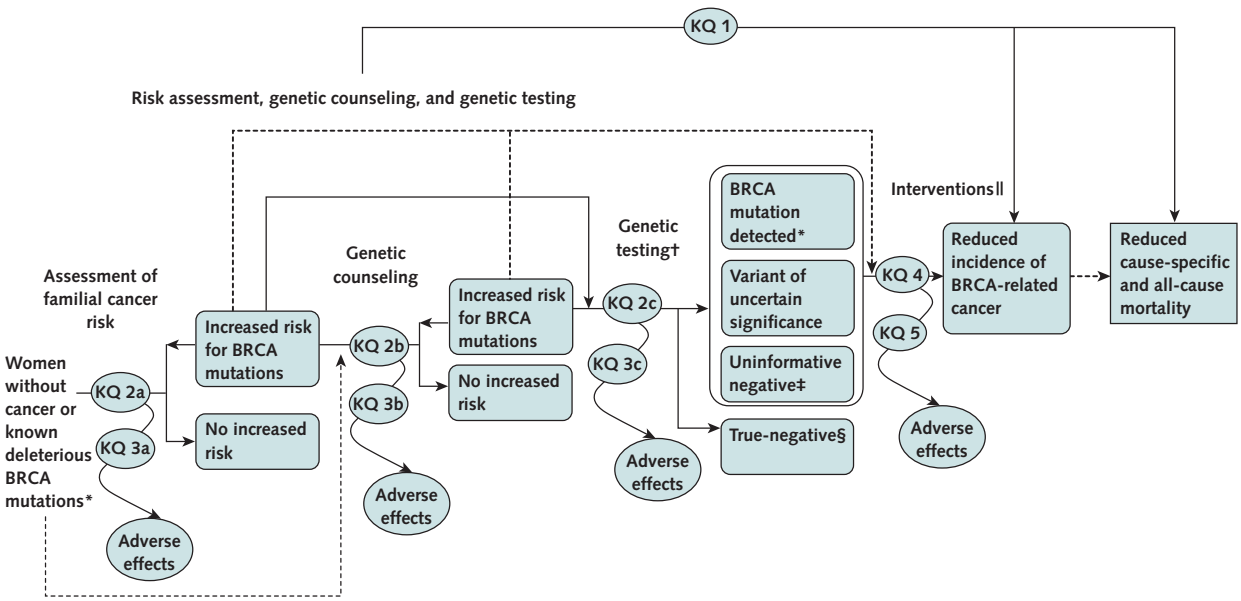
125. **Antoniou AC, Pharoah PP, Smith P, Easton DF.** The BOADICEA model of genetic susceptibility to breast and ovarian cancer. Br J Cancer. 2004;91:1580-90. [PMID: 15381934]
126. **Euhus DM BD, Parmigiani G, Iversen ES, Frawley W.** CancerGene [computer program]. Version 4.3. Dallas, TX: University of Texas Southwestern Medical Center at Dallas; 2006.
127. Penn II *BRCA1* and *BRCA2* Mutation Risk Evaluation Model [computer program]. Accessed at www.afcri.upenn.edu/itacc/penn2/ on 9 September 2013.

Appendix Figure 1. **Analytic framework and key questions.**



Key Questions

1. **Do risk assessment, genetic counseling, and genetic testing lead to reduced incidence of BRCA-related cancer and reduced cause-specific and all-cause mortality?**

2a. What is the accuracy of methods to assess familial cancer risk for BRCA-related cancer when done by a nonspecialist in genetics in a clinical setting?

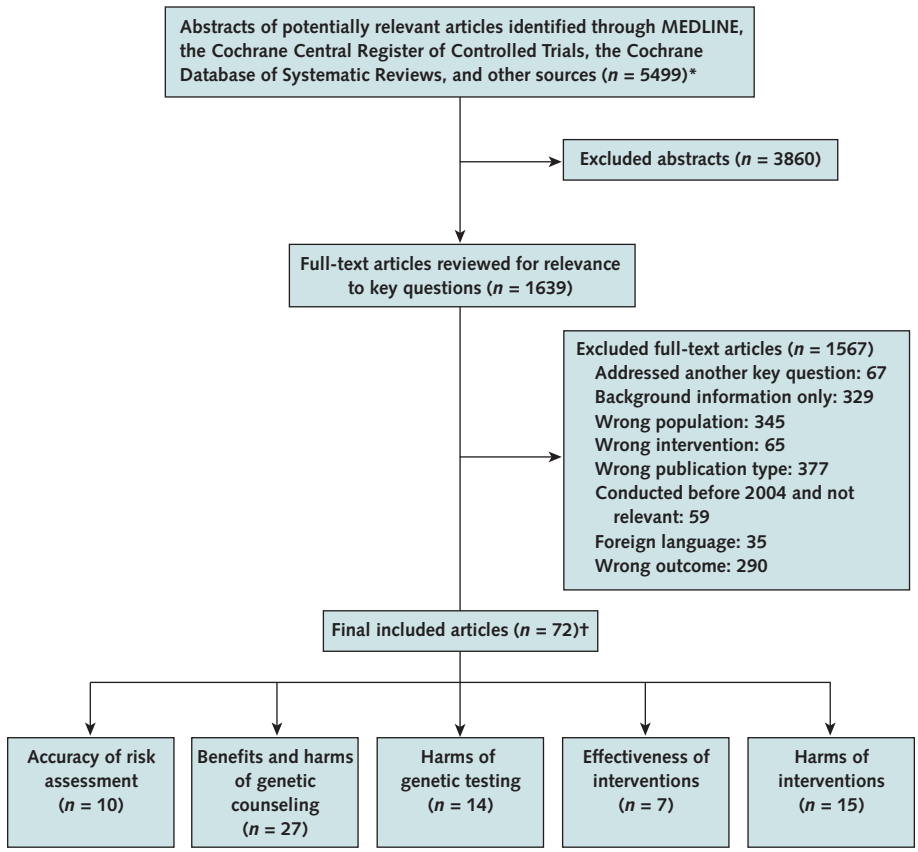
2b. What are the benefits of genetic counseling in determining eligibility for genetic testing for BRCA-related cancer? Potential benefits include improved accuracy of risk assessment and pretest probability for testing and improved patient knowledge, risk perception, satisfaction, and health and psychological outcomes.

2c. Among women with increased risk for BRCA-related cancer, what is the clinical validity of genetic testing for deleterious mutations?

3. **What are the potential adverse effects of 3a) risk assessment, 3b) genetic counseling, and 3c) genetic testing? Adverse effects include, but may not be limited to, inaccurate risk assessment; inappropriate testing; false-positive and false-negative results; adverse effect on the patient's relationships with family; false reassurance; incomplete testing; misinterpretation of the test result; anxiety; worry about cancer; and ethical, legal, and social implications.**
4. **Do interventions reduce the incidence of BRCA-related cancer and death for women with increased risk? Interventions include intensive screening (earlier and more frequent mammography and breast MRI), use of risk-reducing medications (tamoxifen and raloxifene), and risk-reducing surgery (mastectomy and salpingo-oophorectomy).**
5. **What are the potential adverse effects of interventions to reduce risk for BRCA-related cancer? Adverse effects include, but may not be limited to, immediate and long-term harms associated with breast imaging, risk-reducing medications, and risk-reducing surgery and ethical, legal, and social implications.**

KQ = key question; MRI = magnetic resonance imaging.
* Clinically significant mutations of the *BRCA1* or *BRCA2* gene or related syndromes.
† Testing may be done on the unaffected woman, the relative with cancer, or the relative with the highest risk, as appropriate.
‡ No known mutation in relatives and none detected in the patient.
§ Known mutation in relatives but none detected in the patient.
‖ Interventions include increased early detection through intensive screening (earlier and more frequent mammography and breast MRI), risk-reducing medications (tamoxifen and raloxifene), and risk-reducing surgery (mastectomy and salpingo-oophorectomy).

Appendix Figure 2. **Summary of evidence search and selection.**



* Identified from reference lists, hand-searching, suggestions from experts, and other methods.
† Studies that provided data and contributed to the body of evidence were considered to be "included." Studies may contribute data to >1 key question. This number includes studies included from the prior review as well as this updated review.

Appendix Table 1. Models Estimating Individual Risk for BRCA Mutations to Guide Referrals

Model	Data Collection and Calculation*	Relatives With Breast or Ovarian Cancer	Additional Risk Factors in Model	Accuracy Studies						
				Study, Year (Reference)	Population	Reference Standard	Sensitivity, %	Specificity, %	PPV	NPV
FHAT	Clinical scoring tool; referral threshold of 10 is equivalent to a 2-fold increase in risk for breast or ovarian cancer.	First-, second-, and third-degree	Age at diagnosis, bilateral breast cancer, breast and ovarian cancer in the same person, breast cancer in men, colon and prostate cancer	Gilpin et al, 2000 (31)	35 carriers and 149 noncarriers	10% threshold	94	51	0.31	0.97
				Parmigiani et al, 2007 (32)	33 carriers and 559 noncarriers	10% threshold	94	32	†	‡
				Panchal et al, 2008 (33)	200 carriers and 100 noncarriers	10% threshold	70	63	–	–
Manchester scoring system	Clinical scoring tool; referral threshold of 10 for *BRCA1*- or *BRCA2*-specific scores or 15 combined. Not intended for Ashkenazi Jewish persons.	First-, second-, and third-degree	Type of cancer (breast, ovarian, pancreatic, or prostate), affected family members, age at diagnosis	Evans et al, 2004 (34)	23 carriers and 235 noncarriers	10% threshold	87	66	0.20	0.98
				Barcenas et al, 2006 (35)	69 carriers and 306 noncarriers	10% threshold	93	41	0.28	0.96
				Panchal et al, 2008 (33)	200 carriers and 100 noncarriers	15% threshold	58	71	–	–
				Antoniou et al, 2008 (36)	365 carriers and 1569 noncarriers	15% threshold	92	33	0.24	0.95
RST	Clinical checklist of 13 items; referral threshold of 2 positive responses.	First- and second-degree	Breast cancer in women ≤50 y (self or relatives), ovarian cancer at any age (self or relatives), ≥2 cases of breast cancer in women aged >50 y on the same side of the family; breast cancer in men; Jewish ancestry	Bellcross et al, 2009 (37)	296 women randomly selected from 2462 tested while having screening mammography	Correctly assigns to high mutation probability compared with BOADICEA, BRCAPRO, and Myriad II models at 10% thresholds	BOADICEA: 89 BRCAPRO: 91 Myriad II: 91 Overall: 81§	BOADICEA: 77 BRCAPRO: 76 Myriad II: 78 Overall: 92§	BOADICEA: 0.28 BRCAPRO: 0.24 Myriad II: 0.34 Overall: 0.80§‖	BOADICEA: 0.99 BRCAPRO: 0.98 Myriad II: 0.99 Overall: 0.92§¶
PAT	Clinical scoring tool; optimum referral threshold of 8.	First-, second-, and third-degree	Breast cancer in women aged ≤50 y or >50 y, ovarian cancer at any age, breast cancer in men, Ashkenazi Jewish ancestry	Hoskins et al, 2006 (39)	737 women identified at potentially increased risk from 3906 tested while having screening mammography**	Correctly assigns to high mutation probability compared with the Myriad II model at the 10% threshold	100	93	0.63	1.00
FHS-7	Clinical checklist of 7 items; referral threshold of 1 positive response.	First-degree	Any relatives with breast cancer at age ≤50 y, bilateral breast cancer, breast and ovarian cancer in the same person, breast cancer in men, ≥2 relatives with breast and/or ovarian cancer, ≥2 relatives with breast and/or colon cancer	Ashton-Prolla et al, 2009 (40)	885 women with ≥1 positive response and 910 with no positive responses from 9218 women tested in primary care clinics	Correctly assigns to high mutation probability compared with genetic evaluation††	88	56	0.63	1.00

BOADICEA = Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm; FHAT = Ontario Family History Assessment Tool; FHS-7 = Family History Screen-7; NPV = negative predictive value; PAT = Pedigree Assessment Tool; PPV = positive predictive value; RST = Referral Screening Tool.

* Referral threshold indicates estimated probability to initiate a referral, most set at 10%.

† Positive likelihood ratio of 1.38.

‡ Negative likelihood ratio of 0.18.

§ Defined as high-risk by any of the models.

‖ Corrected for general populations: 0.39.

¶ Corrected for general populations: 0.78.

** Defined as potentially at increased risk by the Gail model for 5-y risk for breast cancer of 6.7%, lifetime risk of 15%, or ≥1 case of breast or ovarian cancer in any family member.

†† Evaluation included kindred analysis, breast cancer risk estimates, Penn II *BRCA1* and *BRCA2* Mutation Risk Evaluation Model mutation risk estimate, and American Society of Clinical Oncology criteria.

Appendix Table 2. **Models Used as Reference Standards to Estimate Individual Risks for BRCA Mutations**

Model	Administration	Application	Description
BOADICEA (42, 125)	Web-based	All persons	Includes breast, ovarian, prostate, and pancreatic cancer. Family history data for first-, second-, and third-degree relatives are entered for persons with and without cancer.
BRCAPRO (43–45)	CaGene computer program (126)	All persons	Includes breast cancer in men and women and ovarian cancer. Bayesian model using first- and second-degree family history includes age at diagnosis, ethnicity, and size of family to estimate the age-specific probability of a BRCA mutation. Generates conditional or posterior probabilities.
Myriad II (18)	CaGene computer program (126) or tables	All persons	Includes breast cancer in men and women and ovarian cancer. Logistic regression model developed from data on women with early-onset breast cancer and/or ovarian cancer with ≥2 first- or second-degree relatives with early breast or ovarian cancer.
Penn II (127)	Web-based	Families with cases of breast cancer	Includes breast, ovarian, prostate, and pancreatic cancer. Uses a 1-page questionnaire to solicit data for first-, second-, and third-degree relatives. Determines the probability of a BRCA mutation in the person as well as family members with cancer.

BOADICEA = Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm; CaGene = Cancer Gene; Penn II = Penn II *BRCA1* and *BRCA2* Mutation Risk Evaluation Model.

Appendix Table 3. Studies of Genetic Counseling

Study, Year (Reference)	Participants, *n*	Design	Genetic Counseling Provider	Setting	Measure	Outcome					Quality Rating
						Accuracy of Risk Perception	Intention to Participate in Testing	Worry	Anxiety	Depression	
Current report											
Bennett et al, 2008 (48)	128	Pre–post	Genetic counselor	Cancer genetics service center	DUKE-SSQ, HADS, IES, MCMQ, NSI	–	–	Decrease	NS	NS	NA
Bennett et al, 2009 (47)	128	Pre–post	Genetic counselor	Cancer genetics service center	DUKE-SSQ, IES, MCMQ	–	–	NS	–	–	NA
Bloom et al, 2006 (49)	163	RCT	Counselor	Telephone counseling	NSI	NS	–	NS	–	–	Poor*†‡
Bowen et al, 2006 (50)	221	RCT	Psychologist, genetic counselor	University	NSI, BSI	Increase	Decrease	Decrease	–	–	Fair*
Brain et al, 2011 (51)	263	Pre–post	Clinician	NR	CWS-R	–	–	Decrease	–	–	NA
Braithwaite et al, 2005 (52)	72	RCT	Clinical nurse specialist	NR	NSI, STAI, HADS	Increase	–	Decrease	Decrease	–	Fair*
Fry et al, 2003 (53)	263	RCT	Genetic specialist, breast surgeon	Familial breast cancer clinic	CWS	Increase	–	Decrease	–	–	Fair§
Gurmankin et al, 2005 (54)	125	Pre–post	Clinician	University cancer risk evaluation program	STAI, NSI	Increase	–	–	–	–	NA
Helmes et al, 2006 (55)	340	RCT	Genetic counselor	NR	NSI	Increase	Decrease	Decrease	–	–	Fair*
Hopwood et al, 2004 (56)	256	Pre–post	Genetic counselor	Cancer genetic service centers	NSI, GHQ, CWS	NS	–	Decrease	NS	–	NA
Kelly et al, 2008 (57)	78	Pre–post	Genetic counselor	NR	NSI	Decrease	–	–	–	–	NA
Matloff et al, 2006 (58)	64	RCT	Genetic counselor	NR	NSI	Increase	–	–	–	–	Fair*
Mikkelsen et al, 2007 (59)	1971	Prospective	Physician	Clinical department	IES	NS	–	–	–	–	Fair†
Mikkelsen et al, 2009 (60)	1971	Prospective	Physician	Clinical department	HADS	–	–	Decrease	NS	NS	Fair†
Pieterse et al, 2011 (61)	77	Pre–post	Clinical geneticist, genetic counselor	Department of medical genetics	VAS, NSI, PPC, STAI, IES	Increase	–	–	Decrease	–	NA
Roshanai et al, 2009 (62)	163	RCT	Specialist nurse	Cancer genetic clinic	SPIKES, HADS	Increase	–	–	Decrease	Decrease	Fair*
Prior report											
Bowen et al, 2002 (64)	354	RCT	Genetic or health counselor	NR	NSI	–	Decrease	–	–	–	Fair‖¶
Bowen et al, 2004 (65)	354	RCT	Genetic or health counselor	NR	NSI	Increase	–	NS	Decrease	NS	Fair§¶
Brain et al, 2002 (66)	740	RCT	Clinical geneticist, genetic nurse specialist	NR	STAI, NSI	Increase	–	Mixed**	Decrease	–	Good
Burke et al, 2000 (67)	356	RCT	Genetic counselor	Medical office	NSI	Increase	Decrease	NS	–	–	Fair‖¶
Cull et al, 1998 (68)	144	RCT	Geneticist, breast surgeon	Breast cancer family clinic	NSI, STAI, GHQ	Mixed§	–	–	NS	NS	Good
Hopwood et al, 1998 (69)	174	Prospective	Clinician	Family history clinics	NSI, GHQ, PAS	Increase	–	NS	NS	–	Fair††
Lerman et al, 1996 (71)	227	RCT	Genetic counselor	Cancer centers	IES	Increase	–	NS	–	–	Fair‖¶
Lerman et al, 1999 (70)	364	RCT	Oncology nurse, genetic counselor	Hospital cancer center	IES	–	Increase	NS	–	–	Fair§‖¶
Lobb et al, 2004 (72)	193	Longitudinal	Clinical geneticist, oncologist, genetic counselor	NR	NSI, IES, HADS	NS	–	–	NS	NS	Good

Continued on following page

Appendix Table 3—Continued

Study, Year (Reference)	Participants, *n*	Design	Genetic Counseling Provider	Setting	Measure	Outcome					Quality Rating
						Accuracy of Risk Perception	Intention to Participate in Testing	Worry	Anxiety	Depression	
Watson et al, 1998 (74)	115	RCT	Clinical geneticist	Hospitals	GHQ-12, CWS, VAS	Increase	–	NS	NS	NS	Good
Watson et al, 1999 (73)	283	Prospective	Clinical geneticist	Genetic counseling centers	NSI, GHQ, IES, STAI	NS	–	NS	NS	–	Good

BSI = Brief Symptom Inventory; CWS = Cancer Worry Scale; CWS-R = Cancer Worry Scale-Revised; Duke-UNC SSQ = Duke-University of North Carolina Functional Social Support Questionnaire; GHQ = General Health Questionnaire; GHQ-12 = 12-item General Health Questionnaire; HADS = Hospital Anxiety and Depression Scale; IES = Impact of Events Scale; MCMQ = Medical Coping Modes Questionnaire; NA = not available; NR = not reported; NS = not statistically significant; NSI = Non Standard Instrument; PAS = Psychiatric Assessment Schedule; PPC = Perceived Personal Control; RCT = randomized, controlled trial; SPIKES = Setting, Patient's Perception, Invitation, Knowledge, Exploring/Empathy, Strategy/Summary; STAI = State-Trait Anxiety Inventory; VAS = visual analog scale.

* Inadequate reporting of randomization technique (49, 50, 52, 55, 58, 62).

† Noncomparable groups at baseline (49, 59, 60).

‡ No specified eligibility criteria (49).

§ High attrition (53, 68) or attrition not reported (65).

‖ Allocation concealment not reported (64, 65, 70, 71).

¶ No intention-to-treat analysis (65, 67, 70, 71).

** Results varied by group.

†† Unclear whether participants were from random or consecutive groups (69).

Appendix Table 4. Studies of Distress After Genetic Testing

Study, Year (Reference)	Participants, *n*	Design	Mutation Status	Genetic Counseling Provider	Comparison	Measure	Outcome			Quality Rating
							Worry	Anxiety	Depression	
Current report										
Arver et al, 2004 (75)	63	Pre–post	Positive or negative	Genetically trained oncologist, oncology nurse	A: Before test B: 2 mo after test C: 1 y after test	HADS, SF-36	–	Decrease (B, C vs. A)	NS	NA
Dagan and Shochat, 2009 (76)	73	Case–control	Positive or negative	NR	A: Carriers B: Noncarriers C: Age-matched control participants	HRQOL, CRW, BSI	Increase (A, B vs. C)	NS	NS	Fair*
Ertmanski et al, 2009 (77)	56	Pre–post	Positive	NR	A: Before test B: 1 mo after test C: 1 y after test	STAI, IES	–	NS	–	NA
Foster et al, 2007 (78)	154	Prospective	Positive or negative	NR	A: Carriers B: Noncarriers	GHQ, CWS-R	Decrease (A, B)	Increase (A, B)	–	Fair*†
Geirdal et al, 2005 (80)	10 244	Prospective	Positive or unknown	NR	A: Positive B: Not tested but family history C: Not tested, 10 000 age-matched control participants	HADS, GHQ, BHS, IES	–	Increase (B vs. A)	Increase (B vs. A)	Good
Geirdal and Dahl, 2008 (79)	242	Prospective	Positive or unknown	NR	A: Positive B: Not tested but family history	HADS, COPE	–	Increase (B vs. A)	–	Good
Kinney et al, 2005 (82)	52	Prospective	Positive or negative	Genetic professional	A: Carriers B: Noncarriers	STAI, IES, CES-D	–	Decrease (B)	–	Poor*†
Low et al, 2008 (83)	47	Prospective	Positive or negative/uncertain	Genetic counselor	A: Positive B: True-negative and uncertain	IES-R, COPE, PTGI	–	Increase (A vs. B)	–	Fair*†‡
Metcalfe et al, 2012 (88)	17	Pre–post	Positive	NR	A: Before test B: 1 y after test C: 2 y after test	IES	Increase (B vs. A, C)	–	–	NA
Reichelt et al, 2004 (84)	209	Prospective	Positive, negative, or unknown	Medical geneticist, genetic counselor	A: Carriers B: Noncarriers	HADS, GHQ, BHS, IES	–	NS	NS	Good
Reichelt et al, 2008 (85)	181	Pre–post	Positive or true-negative	Genetic counselor	A: Before test B: 6 wk after test C: 18 mo after test	HADS, IES	–	NS	NS	NA
van Dijk et al, 2006 (87)	132	Prospective	Positive, true-negative, or uncertain	NR	A: Positive B: True-negative C: Uninformative	IES, NSI	Increase (A vs. B, C)	Increase (A vs. B, C)	–	Good
Prior report										
Meiser et al, 2002 (90)	143	Prospective	Positive or negative	NR	A: Carriers B: Noncarriers C: Not tested	BDI, IES, MBSS, STAI, NSI	Increase (A vs. C)	Decrease (B vs. A, C)	Decrease (B vs. A, C)	Good

BDI = Beck Depression Inventory; BHS = Beck Hopelessness Scale; BSI = Brief Symptom Inventory; CES-D = Center for Epidemiologic Studies-Depression Scale; COPE = Emotional Approach Coping Scale; CRW = Cancer-Related Worry Scale; CWS-R = Cancer-Related Worry Scale-Revised; GHQ = General Health Questionnaire; HADS = Hospital Anxiety and Depression Scale; HRQOL = Health-Related Quality of Life; IES = Impact of Events Scale; IES-R = Impact of Events Scale-Revised; MBSS = Miller Behavioral Style Scale; NA = not applicable; NR = not reported; NS = not statistically significant; NSI = Non Standard Instrument; PTGI = Post-Traumatic Growth Inventory; SF-36 = Swedish 36-Item Short Form Health Survey; STAI = State-Trait Anxiety Inventory.

* Unclear enrollment (76, 78, 82, 83).

† Differences between groups at baseline or lack of reporting of baseline participant characteristics (78, 82, 83).

‡ High loss to follow-up (83).

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Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer in Women: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2005 U.S. Preventive Services Task Force (USPSTF) recommendation on genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility.

Methods: The USPSTF reviewed the evidence on risk assessment, genetic counseling, and genetic testing for potentially harmful BRCA mutations in asymptomatic women with a family history of breast or ovarian cancer but no personal history of cancer or known potentially harmful BRCA mutations in their family. The USPSTF also reviewed interventions aimed at reducing the risk for BRCA-related cancer in women with potentially harmful BRCA mutations, including intensive cancer screening, medications, and risk-reducing surgery.

Population: This recommendation applies to asymptomatic women who have not been diagnosed with BRCA-related cancer.

Recommendation: The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with 1 of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (*BRCA1* or *BRCA2*). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. (B recommendation)

The USPSTF recommends against routine genetic counseling or BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes. (D recommendation)

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* For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).

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The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendations and Evidence

The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with 1 of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (*BRCA1* or *BRCA2*). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. (B recommendation)

The USPSTF recommends against routine genetic counseling or BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes. (D recommendation)

See the Clinical Considerations section for additional information on screening tools.

See the **Figure** for a summary of the recommendation and suggestions for clinical practice.

See also:

Print

Related article 1

Summary for Patients 2

Web-Only

Supplement

Figure. **Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: clincal summary of U.S. Preventive Services Task Force recommendation.**

Annals of Internal Medicine

U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

RISK ASSESSMENT, GENETIC COUNSELING, AND GENETIC TESTING FOR BRCA-RELATED CANCER IN WOMEN CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women who have not been diagnosed with BRCA-related cancer and who have no signs or symptoms of the disease	
Recommendation	Screen women whose family history may be associated with an increased risk for potentially harmful BRCA mutations. Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. Grade: B	Do not routinely recommend genetic counseling or BRCA testing to women whose family history is not associated with an increased risk for potentially harmful BRCA mutations Grade: D

Risk Assessment	Family history factors associated with increased likelihood of potentially harmful BRCA mutations include breast cancer diagnosis before age 50 years, bilateral breast cancer, family history of breast and ovarian cancer, presence of breast cancer in ≥1 male family member, multiple cases of breast cancer in the family, ≥1 family member with 2 primary types of BRCA-related cancer, and Ashkenazi Jewish ethnicity. Several familial risk stratification tools are available to determine the need for in-depth genetic counseling, such as the Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, and FHS-7.	
Screening Tests	Genetic risk assessment and BRCA mutation testing are generally multistep processes involving identification of women who may be at increased risk for potentially harmful mutations, followed by genetic counseling by suitably trained health care providers and genetic testing of selected high-risk women when indicated. Tests for BRCA mutations are highly sensitive and specific for known mutations, but interpretation of results is complex and generally requires posttest counseling.	
Treatment	Interventions in women who are BRCA mutation carriers include earlier, more frequent, or intensive cancer screening; risk-reducing medications (e.g., tamoxifen or raloxifene); and risk-reducing surgery (e.g., mastectomy or salpingo-oophorectomy).	
Balance of Benefits and Harms	In women whose family history is associated with an increased risk for potentially harmful BRCA mutations, the net benefit of genetic testing and early intervention is moderate.	In women whose family history is not associated with an increased risk for potentially harmful BRCA mutations, the net benefit of genetic testing and early intervention ranges from small to moderate.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on medications for the reduction of breast cancer risk and screening for ovarian cancer. These recommendations are available at www.uspreventiveservicestaskforce.org.	

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

Appendix Table 1 describes the USPSTF grades, and **Appendix Table 2** describes the USPSTF classification of levels of certainty about net benefit (both tables are available at www.annals.org).

Rationale

Importance

The cancer types related to potentially harmful mutations of the BRCA genes are predominantly breast, ovarian, and fallopian tube cancer, although other types are also associated (1). In the general population, 12.3% of women will develop breast cancer during their lifetime and 2.74% will die of the disease, whereas 1.4% of women will develop ovarian cancer and 1.0% will die of the disease (2). A woman's risk for breast cancer increases to 45% to 65% by age 70 years if there are clinically significant mutations in either BRCA gene (3, 4). Mutations in the *BRCA1* gene increase ovarian cancer risk to 39% by age 70 years, and *BRCA2* mutations increase ovarian cancer risk to 10% to 17% by age 70 years (3, 4). In the general population, these mutations occur in an estimated 1 in 300 to 500 women (0.2% to 0.3%) (5–8). In a meta-analysis con-

ducted for the USPSTF, the combined prevalence of *BRCA1* and *BRCA2* mutations was 2.1% in a general population of Ashkenazi Jewish women (9).

Detection of Potentially Harmful BRCA Mutations

Genetic risk assessment and BRCA mutation testing is generally a multistep process involving identification of individuals who may be at increased risk for potentially harmful mutations, followed by genetic counseling from suitably trained health care providers and genetic testing of selected high-risk individuals when indicated. Several familial risk stratification tools are clinically useful for selecting patients who should be offered genetic counseling to further determine their candidacy for possible BRCA mutation testing.

Benefits of Testing for Potentially Harmful BRCA Mutations

For women whose family history is associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, adequate evidence suggests that the benefits of testing for potentially harmful BRCA mutations are moderate.

For women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, there is adequate evidence that the benefits of testing for potentially harmful BRCA mutations are few to none.

Harms of Detection of Potentially Harmful BRCA Mutations and Early Intervention and Treatment

Adequate evidence suggests that the overall harms of detection of and early intervention for potentially harmful BRCA mutations are small to moderate.

USPSTF Assessment

For women whose family history is associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, there is moderate certainty that the net benefit of testing for potentially harmful BRCA mutations and early intervention is moderate.

For women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, there is moderate certainty that the net benefit of testing for potentially harmful BRCA mutations and early intervention ranges from minimal to potentially harmful.

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic women who have not been diagnosed with BRCA-related cancer.

Women who have 1 or more family members with a known potentially harmful mutation in the *BRCA1* or *BRCA2* genes should be offered genetic counseling and testing.

The USPSTF recognizes the potential importance of further evaluating women who have a diagnosis of breast or ovarian cancer. Some women receive genetic testing as part of a cancer evaluation at the time of diagnosis of breast cancer. The USPSTF did not review the appropriate use of BRCA testing in the evaluation of women who are newly diagnosed with breast cancer. That assessment is part of disease management and is beyond the scope of this recommendation. Women who have been diagnosed with breast cancer in the past and who did not receive BRCA testing as part of their cancer care but have a family history of breast or ovarian cancer should be encouraged to discuss further evaluation with their clinician.

These recommendations do not apply to men, although male family members may be identified for testing during evaluation.

Family History Screening and Risk Assessment

Mutations in the BRCA genes cluster in families, exhibiting an autosomal dominant pattern of transmission in maternal or paternal lineage. During standard elicitation of family history information from patients, primary care providers should ask about specific types of cancer, primary cancer sites, which family members were affected, relatives with multiple types of primary cancer, and the age at diagnosis and sex of affected family members.

For women who have at least 1 family member with breast, ovarian, or other types of BRCA-related cancer, primary care providers may use 1 of several brief familial risk stratification tools to determine the need for in-depth genetic counseling.

Although several risk tools are available, the tools evaluated by the USPSTF include the Ontario Family History Assessment Tool (**Table 1**), Manchester Scoring System (**Table 2**), Referral Screening Tool (**Table 3**), Pedigree Assessment Tool (**Table 4**), and FHS-7 (**Table 5**) (10–19). The Referral Screening Tool (available at www.breastcancergenescreen.org) and FHS-7 are the simplest and quickest to administer. All of these tools seem to be clinically useful predictors of which women should be referred for genetic counseling due to increased risk for potentially harmful BRCA mutations (most sensitivity estimates were >85%), although some models have been evaluated in only 1 study (9, 20). To determine which patients would benefit from BRCA risk assessment, primary care providers should not use general breast cancer risk assessment models (for example, the National Cancer Institute Breast Cancer Risk Assessment Tool, which is based on the Gail model) because they are not designed to determine which women should receive genetic counseling or BRCA testing.

In general, these tools elicit information about factors that are associated with increased likelihood of BRCA mutations. Family history factors associated with increased likelihood of potentially harmful BRCA mutations include breast cancer diagnosis before age 50 years, bilateral breast cancer, presence of breast and ovarian cancer, presence of breast cancer in 1 or more male family members, multiple cases of breast cancer in the family, 1 or more family mem-

Table 1. **Ontario Family History Assessment Tool***

Risk Factor	Points
Breast and ovarian cancer	
Mother	10
Sibling	7
Second-/third-degree relative	5
Breast cancer relative	
Parent	4
Sibling	3
Second-/third-degree relative	2
Male relative (add to above)	2
Breast cancer characteristics	
Onset at age 20–29 y	6
Onset at age 30–39 y	4
Onset at age 40–49 y	2
Premenopausal/perimenopausal	2
Bilateral/multifocal	3
Ovarian cancer relative	
Mother	7
Sibling	4
Second-/third-degree relative	3
Age at ovarian cancer onset	
<40 y	6
40–60 y	4
>60 y	2
Age at prostate cancer onset	
<50 y	1
Age at colon cancer onset	
<50 y	1
Family total	
Referral†	≥10

* From reference 19.
† Referral with a score of ≥10 corresponds to doubling of lifetime risk for breast cancer (22%).

bers with 2 primary types of BRCA-related cancer, and Ashkenazi Jewish ethnicity. The USPSTF recognizes that each risk assessment tool has limitations and found insufficient comparative evidence to recommend one tool over another. The USPSTF also found insufficient evidence to support a specific risk threshold for referral for testing.

Genetic Counseling

Genetic counseling about BRCA mutation testing may be done by trained health professionals, including trained primary care providers. Several professional organizations describe the skills and training necessary to provide comprehensive genetic counseling. The process of genetic counseling includes detailed kindred analysis and risk assessment for potentially harmful BRCA mutations; education about the possible results of testing and their implications; identification of affected family members who may be preferred candidates for testing; outlining options for screening, risk-reducing medications, or surgery for eligible patients; and follow-up counseling for interpretation of test results.

Table 2. **Manchester Scoring System***

Risk Factor	*BRCA1* Score	*BRCA2* Score
Age at onset of female breast cancer†		
<30 y	6	5
30–39 y	4	4
40–49 y	3	3
50–59 y	2	2
≥60 y	1	1
Age at onset of male breast cancer†		
<60 y	5‡	8§
≥60 y	5‡	5§
Age at onset of ovarian cancer†		
<60 y	8	5
≥60 y	5	5
Pancreatic cancer	0	1
Age at onset of prostate cancer†		
<60 y	0	2
≥60 y	0	1

* From reference 13. Developed so that a score of 10 in either column or a combined score of 15 for both columns would be equivalent to a 10% chance of identifying a *BRCA1* or *BRCA2* mutation.
† For relatives in direct lineage.
‡ If *BRCA2* tested.
§ If *BRCA1* tested.

BRCA Mutation Testing

Adequate evidence suggests that current genetic sequencing tests can accurately detect BRCA mutations. Testing for BRCA mutations should be done only when an individual has personal or family history that suggests an inherited cancer susceptibility, when an individual has access to a health professional who is trained to provide genetic counseling and interpret test results, and when test results will aid in decision making. Initial testing of a family member who has breast or ovarian cancer is the preferred strategy in most cases, but it is reasonable to test if

Table 3. **Referral Screening Tool***

Risk Factor	Breast Cancer at Age ≤50 y	Ovarian Cancer at Any Age
Yourself		
Mother		
Sister		
Daughter		
Mother's side		
Grandmother		
Aunt		
Father's side		
Grandmother		
Aunt		
≥2 cases of breast cancer after age 50 y on the same side of the family		
Male breast cancer at any age in any relative		
Jewish ancestry		

* From reference 16. A patient completes the checklist if she has a family history of breast or ovarian cancer and receives a referral if she checks ≥2 items.

Table 4. **Pedigree Assessment Tool***

Risk Factor	Score†
Breast cancer at age ≥50 y	3
Breast cancer at age <50 y	4
Ovarian cancer at any age	5
Male breast cancer at any age	8
Ashkenazi Jewish heritage	4

* From reference 17. A score of ≥8 is the optimum referral threshold.
† For every family member with a breast or ovarian cancer diagnosis, including second- or third-degree relatives.

no affected relative is available. It is essential that before testing, the individual is fully informed about the implications of testing and has expressed a desire for it.

The type of mutation analysis required depends on family history. Individuals from families with known mutations or from ethnic groups in which certain mutations are more common (for example, Ashkenazi Jewish women) can be tested for these specific mutations.

Individuals without linkages to families or groups with known mutations receive more comprehensive testing. In these cases, when possible, testing should begin with a relative who has breast or ovarian cancer to determine whether affected family members have a clinically significant mutation.

Tests for BRCA mutations are highly sensitive and specific for known mutations, but interpretation of results is complex and generally requires posttest counseling. Test results for genetic mutations are reported as positive (that is, potentially harmful mutation detected), variants of uncertain clinical significance, uninformative-negative, or true-negative. Women who have relatives with known BRCA mutations can be reassured about their inherited risk for a potentially harmful mutation if the results are negative (that is, a true negative). Some studies suggest increased breast cancer risk in some women with true-negative results (21–24). However, a comprehensive meta-analysis conducted for the USPSTF that included these studies found that breast cancer risk is generally not increased in women with true-negative results (9). An uninformative-negative result occurs when a woman's test does not detect a potentially harmful mutation but no relatives have been tested or no mutations have been detected in tested relatives. Available tests may not be able to identify mutations in these families. Risk for breast cancer is increased in women with uninformative-negative results (9).

Table 5. **FHS-7***

Did any of your first-degree relatives have breast or ovarian cancer?
Did any of your relatives have bilateral breast cancer?
Did any man in your family have breast cancer?
Did any woman in your family have breast and ovarian cancer?
Did any woman in your family have breast cancer before age 50 y?
Do you have 2 or more relatives with breast and/or ovarian cancer?
Do you have 2 or more relatives with breast and/or bowel cancer?

* From reference 18. One positive response initiates referral.

Timing of Screening

Consideration of screening for potentially harmful BRCA mutations should begin once women have reached the age of consent (18 years). Primary care providers should periodically assess all patients for changes in family history (for example, comprehensive review at least every 5 to 10 years [25]).

Interventions for Women Who Are BRCA Mutation Carriers

Interventions that may reduce risk for cancer or cancer-related death in women who are BRCA mutation carriers include earlier, more frequent, or intensive cancer screening; risk-reducing medications (for example, tamoxifen or raloxifene); and risk-reducing surgery (for example, mastectomy or salpingo-oophorectomy). However, the strength of evidence varies across the types of interventions.

Evidence is lacking on the effect of intensive screening for BRCA-related cancer on clinical outcomes in women who are BRCA mutation carriers. Medications, such as tamoxifen and raloxifene, have been shown to reduce the incidence of invasive breast cancer in high-risk women in the general population, but they have not been studied specifically in women who are BRCA mutation carriers (9, 20, 26).

In high-risk women and those who are BRCA mutation carriers, cohort studies of risk-reducing surgery (mastectomy and salpingo-oophorectomy) showed substantially reduced risk for breast or ovarian cancer. Breast cancer risk was reduced by 85% to 100% with mastectomy (27–29) and by 37% to 100% with oophorectomy, and ovarian cancer risk was reduced by 69% to 100% with oophorectomy or salpingo-oophorectomy (26). Salpingo-oophorectomy was also associated with a 55% relative reduction in all-cause mortality (as measured during the course of the study) in women with *BRCA1* or *BRCA2* mutations and without a history of breast cancer (27).

Other Approaches to Prevention

The USPSTF recommendations on medications for breast cancer risk reduction are available on the USPSTF Web site (www.uspreventiveservicestaskforce.org).

The USPSTF recommends against screening for ovarian cancer in women. This recommendation does not apply to women with known genetic mutations that increase their risk for ovarian cancer (for example, BRCA mutations).

Useful Resources

The National Cancer Institute Cancer Genetics Services Directory provides a list of professionals who offer services related to cancer genetics, including cancer risk assessment, genetic counseling, and genetic sus-

ceptibility testing (available at www.cancer.gov/search/geneticsservices).

Other Considerations

Although some studies have reported that women prefer in-person genetic counseling, telephone- or computer-based counseling may be considered for women who would not otherwise have access to these services.

Research Needs and Gaps

Research on risk assessment and testing for BRCA mutations has focused on short-term outcomes for highly selected women in referral centers. Additional studies are needed, including comparative effectiveness trials of approaches to risk screening and strategies to improve access to genetic counseling and BRCA testing for high-risk individuals.

Another unresolved question is what specific training is needed (for persons other than trained genetic counselors) to provide genetic counseling. It would be helpful to understand which methods of delivery of genetic counseling are most effective, including those that can increase access to genetic counseling in rural or other settings. Trials comparing types of providers and protocols could address these questions.

What happens after patients are identified as high-risk in clinical settings is unknown. The consequences of genetic testing for individuals and their relatives require more study. Well-designed investigations using standardized measures and diverse study populations are needed.

An expanded database or registry of patients receiving genetic counseling for inherited breast and ovarian cancer susceptibility or who are tested for BRCA mutations would provide useful information about predictors of cancer and response to interventions. Additional data are needed from women of varying socioeconomic, racial, and ethnic groups.

For women who are mutation carriers, studies about the effectiveness of intensive cancer screening and risk-reducing medications and the effects of age at intervention on improving long-term outcomes are needed. This research would increase knowledge of the relative benefits and harms of interventions that are provided on the basis of genetic risk information.

Discussion

Burden of Disease

Breast cancer is the second most common cancer in women in the United States and is the second leading cause of cancer death (30, 31). In 2013, an estimated 232 340 women in the United States will be diagnosed with breast cancer and 39 620 women will die of the disease (32). According to lifetime risk estimates for the general population, 12.3% of women will develop breast cancer during their lives and 2.74% will die of it (2).

Ovarian cancer is the fifth leading cause of cancer death in women in the United States (31), accounting for an estimated 22 240 new cases and 14 030 deaths in 2013 (33). According to lifetime risk estimates for the general population, 1.4% of women will develop ovarian cancer during their lives and 1.0% will die of it (2).

Estimates of the prevalence of potentially harmful BRCA mutations vary by population. The estimated prevalence is 0.2% to 0.3% in the general population of women (5–8), 6.0% in women with cancer onset before age 40 years (8, 34, 35), and 2.1% in the general population of Ashkenazi Jewish women (36–39). In a meta-analysis of studies in which recruitment was based on family history of breast or ovarian cancer, *BRCA1* mutation prevalence was 13.6%, *BRCA2* mutation prevalence was 7.9%, and prevalence of either mutation was 19.8% (9).

Scope of Review

This recommendation applies to women who have no signs or symptoms of BRCA-related cancer. For its updated evidence review, the USPSTF considered risk assessment, genetic counseling, and genetic testing for potentially harmful *BRCA1* or *BRCA2* mutations in asymptomatic women with a family history of breast or ovarian cancer but no personal history of cancer or known potentially harmful BRCA mutations in their family. The USPSTF also reviewed interventions aimed at reducing the risk for BRCA-related cancer in women with potentially harmful BRCA mutations, including intensive cancer screening (for example, earlier and more frequent mammography or magnetic resonance imaging of the breast), medications (for example, tamoxifen or raloxifene), and risk-reducing surgery (for example, mastectomy or oophorectomy). Studies about patients with current or past breast or ovarian cancer were excluded unless they were designed to address screening issues in women without cancer (for example, retrospective or case–control studies).

Accuracy of Familial Risk Assessment

The USPSTF reviewed several tools that could be used in primary care settings to predict individual risk for breast cancer and potentially harmful BRCA mutations.

Tools specifically designed to determine risk for BRCA-related cancer are primarily intended for use by nongeneticist health care providers to guide referral to genetic counselors for more definitive evaluation. Models that have been validated in studies include the Ontario Family History Assessment Tool (**Table 1**), Manchester Scoring System (**Table 2**), Referral Screening Tool (**Table 3**), Pedigree Assessment Tool (**Table 4**), and FHS-7 (**Table 5**) (10–19). In general, these tools elicit information about factors associated with increased likelihood of BRCA mutations. They are clinically useful predictors of which women should be referred for genetic counseling because of increased risk for potentially harmful BRCA mutations (most sensitivity estimates were >85%), although some models have been evaluated in only 1 study (9, 20). The

USPSTF recognizes that each risk assessment tool has limitations and found insufficient evidence to recommend one tool over another.

Accuracy of BRCA Mutation Testing

The type of mutation analysis done depends on family history. Individuals from families with known mutations or from ethnic groups with common mutations (for example, Ashkenazi Jewish women) can be tested specifically for these mutations. The sensitivity and specificity of analysis techniques are measured by individual clinical laboratories and are not publicly available. Individuals without linkages to families or groups with known mutations receive more comprehensive testing. In these cases, guidelines recommend initial testing of a relative with known breast or ovarian cancer, when possible, to check for the presence of clinically significant mutations.

Effectiveness of BRCA Mutation Testing and Early Detection and Treatment

To understand the potential benefits and harms of genetic counseling, the USPSTF reviewed 18 studies (40–57) published since its previous review. Studies generally reported positive (or no negative) psychological effects, increased accuracy of risk perception, or decreased intention to have genetic testing.

Genetic counseling significantly decreased breast cancer worry in 8 studies (44–46, 48, 50, 53–55). Three studies (41, 44, 49) reported decreased or no changes in general anxiety and depression after genetic counseling, whereas other studies found no significant differences in anxiety scores (48, 50). However, 1 of these studies noted an increase in state anxiety scores after genetic counseling (44). Eight studies published since 2004 reported improved accuracy of risk perception after genetic counseling (41, 42, 44–47, 49, 50, 52). Two studies reported decreased intention to have genetic testing after genetic counseling (45, 46).

Interventions that may reduce risk for cancer in women who are BRCA mutation carriers include: earlier, more frequent, or intensive cancer screening; use of selective estrogen receptor modulators as risk-reducing medications (for example, tamoxifen or raloxifene); and risk-reducing surgery (for example, mastectomy or salpingo-oophorectomy).

Evidence is lacking on the effect of intensive screening for BRCA-related cancer on clinical outcomes in women who are BRCA mutation carriers.

Selective estrogen receptor modulators reduced the incidence of invasive breast cancer in several randomized, controlled trials (58–64), although clinical trials of tamoxifen and raloxifene have not been conducted specifically in women who are BRCA mutation carriers. In a meta-analysis of trials published to date (26, 65), tamoxifen and raloxifene reduced the incidence of estrogen receptor–positive invasive breast cancer, with 7 fewer events per 1000 women for tamoxifen (4 trials) and 9 fewer events per 1000 women for raloxifene (2 trials), assuming 5 years of treatment. Selective estrogen receptor modulators do not reduce risk for estrogen receptor–negative breast cancer, which includes 69% of breast cancer cases associated with *BRCA1* mutations and 16% associated with *BRCA2* mutations (66).

In cohort studies of high-risk women and those who are BRCA mutation carriers, risk-reducing surgery (for example, mastectomy or salpingo-oophorectomy) substantially reduced risk for breast or ovarian cancer. Mastectomy reduced breast cancer risk by 85% to 100%, and oophorectomy or salpingo-oophorectomy reduced ovarian cancer risk by 69% to 100% and breast cancer risk by 37% to 100% (9). In 1 fair-quality prospective cohort study (27), salpingo-oophorectomy was also associated with a 55% relative reduction in all-cause mortality (as measured during the course of the study) in women with *BRCA1* and *BRCA2* mutations without a history of breast cancer. Breast cancer risk reduction associated with oophorectomy was more pronounced in women who were premenopausal at the time of surgery (27, 67).

Potential Harms of Cancer Screening and Treatment

Intensive screening for breast and ovarian cancer is associated with false-positive results, unnecessary imaging, and unneeded surgery. In 2 studies comparing mammography with magnetic resonance imaging for breast cancer screening in which 18% to 100% of study participants were BRCA mutation carriers, mammography was associated with higher false-positive rates (14% vs. 5.5% in the first round of screening; $P < 0.001$ [68]; 15% vs. 11% in another study [69]) and more false-negative results (12 vs. 1 case in the first round of screening; 12 vs. 4 cases in subsequent rounds [68]). In a retrospective analysis of a cohort of women with potentially harmful BRCA mutations or first-degree relatives with BRCA mutations, those who were screened with mammography were more likely to have unneeded imaging than those who were screened with magnetic resonance imaging; however, rates of unneeded biopsy were similar (69).

Risk-reducing medications (for example, tamoxifen or raloxifene) can increase risk for thromboembolic events (4 to 7 events per 1000 women over 5 years). Tamoxifen increased the risk for endometrial cancer (4 to 5 cases per 1000 women) compared with placebo or raloxifene, and it also increased risk for cataracts (15 per 1000 women) compared with raloxifene (26, 63).

Data on the long-term physical harms of risk-reducing mastectomy are limited. In high-risk women having risk-reducing mastectomy with immediate reconstruction, 21% in 1 series had complications (for example, hematoma, contracture, or implant rupture) (70). In another series, 64% reported postsurgical symptoms (for example, numbness, pain, tingling, infection, swelling, breast hardness, bleeding, organizing hematoma, failed reconstruction, breathing problems, thrombosis, and pulmonary embo-

lism) (71). After risk-reducing oophorectomy, 5% of women in 1 study had postsurgical complications (for example, wound infection, bladder or uterine perforation, or small-bowel obstruction) (72).

Seven observational studies provided data on psychological distress due to risk-reducing mastectomy (71, 73–76) or oophorectomy (25, 77). In 1 study of 90 women who had risk-reducing bilateral mastectomy (73, 74), there were significant reductions in scores for anxiety and sexual pleasure and no significant differences in depression scores, body image concerns, or other measures. In another study (75), there were no significant differences in psychological measures between women who had risk-reducing mastectomy and a reference sample that did not have the procedure. Ten years after risk-reducing mastectomy, most women in another study reported that their family lives were unchanged, but 39% reported negative effects on spousal relationships because of decreased sensation and changed body appearance (76). After risk-reducing salpingo-oophorectomy, premenopausal women reported significant worsening of vasomotor symptoms and decreased sexual function (77).

Estimate of Magnitude of Net Benefit

For women whose family history is associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, the USPSTF found adequate evidence that the benefits of testing, detection, and early intervention are moderate. For women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, the USPSTF found adequate evidence that the benefits of testing, detection, and early intervention are few to none. The USPSTF found adequate evidence that the overall harms of testing, detection, and early intervention are small to moderate.

For women whose family history is associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, the USPSTF concludes with moderate certainty that the net benefit of testing, detection, and early intervention is moderate. For women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, the USPSTF concludes with moderate certainty that the net benefit of testing, detection, and early intervention ranges from minimal to potentially harmful.

How Does Evidence Fit With Biological Understanding?

The *BRCA1* and *BRCA2* genes are tumor suppressor genes. Mutations of these genes have been linked to hereditary breast and ovarian cancer. Risks for breast, ovarian, and other types of BRCA-related cancer are greatly increased in patients who have inherited potentially harmful *BRCA1* or *BRCA2* mutations. Genetic testing may identify such mutations. Several options are available to manage cancer risk in patients who are found to be mutation carriers.

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 2 April through 29 April 2013. In response to comments, the USPSTF clarified that this recommendation statement applies to women. It also expanded the recommendation to include women who have family members with tubal or peritoneal (in addition to breast or ovarian) cancer. The USPSTF clarified that it recognizes the potential importance of further evaluating women who have a diagnosis of breast or ovarian cancer; however, that assessment is part of disease management and is beyond the scope of this recommendation.

The USPSTF added that it found insufficient evidence to recommend one risk assessment tool over another or to support a specific risk threshold for referral for genetic counseling and BRCA testing. It also added a compilation of risk assessment tools (**Tables 1 to 5**). Although the preferred BRCA testing strategy is initial testing of a family member with breast or ovarian cancer, the USPSTF clarified that it is reasonable to start testing in an unaffected individual if no affected relative is available. Because of the complexity of BRCA test results, the USPSTF also suggests posttest counseling. It also clarified and updated information on BRCA testing, other resources, and recommendations of other groups.

Update of Previous USPSTF Recommendation

In 2005, the USPSTF recommended that women whose family history is associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes be referred for genetic counseling and evaluation for BRCA testing. It also recommended against routine referral for genetic counseling or routine BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes (78).

This recommendation statement reaffirms the USPSTF's previous recommendation. Since 2005, family history risk stratification tools have been developed and validated for use in primary care practice to guide referral for BRCA genetic counseling (**Tables 1 to 5**). In addition, the potential benefits and harms of medications for breast cancer risk reduction have been studied for longer follow-up periods, and more information is available about the potential psychological effects of genetic counseling and risk-reducing surgery.

Recommendations of Other Groups

The National Comprehensive Cancer Network provides specific criteria for genetic counseling and testing (1). The American Congress of Obstetricians and Gynecologists recommends genetic risk assessment for women who have more than a 20% to 25% risk for an inherited predisposition to breast and ovarian cancer and states that it

may be helpful for patients with more than a 5% to 10% risk (79). The American Society of Clinical Oncology recommends genetic testing when there is personal or family history suggestive of genetic cancer susceptibility, the test can be adequately interpreted, and the results will aid in diagnosis or medical management of the patient or family member who has hereditary risk for cancer. It also recommends genetic testing only when pretest and posttest counseling are included (80). The National Society of Genetic Counselors has issued practice guidelines for risk assessment and genetic counseling for hereditary breast and ovarian cancer. It recommends that genetic testing should be offered to individuals with a personal or family history suggestive of an inherited cancer syndrome, when the test can be adequately interpreted, if testing will influence medical management of the patient or relative, when potential benefits outweigh potential risks, if testing is voluntary, and when the individual seeking testing or a legal proxy can provide informed consent (81). The European Society for Medical Oncology recommends that all patients who may be referred for BRCA testing should first complete informed consent and genetic counseling and patients who are mutation carriers should be encouraged to advise close family members to obtain genetic counseling (82). The Society of Gynecologic Oncologists recommends genetic risk assessment for individuals with a personal risk of more than approximately 20% to 25% for an inherited predisposition to cancer and states that it may be helpful for patients with more than approximately 5% to 10% risk. Genetic testing for cancer predisposition requires informed consent that should encompass pretest education and counseling about the risks, benefits, and limitations of testing, including the implications of both positive and negative genetic test results (83).

From the U.S. Preventive Services Task Force, Rockville, Maryland.

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Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

References

1. **Lindor NM, McMaster ML, Lindor CJ, Greene MH; National Cancer Institute, Division of Cancer Prevention, Community Oncology and Prevention Trials Research Group.** Concise handbook of familial cancer susceptibility syndromes - second edition. J Natl Cancer Inst Monogr. 2008:1-93. [PMID: 18559331]

2. **Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, et al, eds.** SEER Cancer Statistics Review, 1975–2010. Bethesda, MD: National Cancer Institute; 2013. Accessed at http://seer.cancer.gov/csr/1975_2010 on 14 November 2013.

3. **Antoniou A, Pharoah PD, Narod S, Risch HA, Eyfjord JE, Hopper JL, et al.** Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies. Am J Hum Genet. 2003;72:1117-30. [PMID: 12677558]

4. **Chen S, Parmigiani G.** Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol. 2007;25:1329-33. [PMID: 17416853]

5. Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series of breast cancer cases. Anglian Breast Cancer Study Group. Br J Cancer. 2000;83:1301-8. [PMID: 11044354]

6. **Antoniou AC, Gayther SA, Stratton JF, Ponder BA, Easton DF.** Risk models for familial ovarian and breast cancer. Genet Epidemiol. 2000;18:173-90. [PMID: 10642429]

7. **Antoniou AC, Pharoah PD, McMullan G, Day NE, Stratton MR, Peto J, et al.** A comprehensive model for familial breast cancer incorporating BRCA1, BRCA2 and other genes. Br J Cancer. 2002;86:76-83. [PMID: 11857015]

8. **Peto J, Collins N, Barfoot R, Seal S, Warren W, Rahman N, et al.** Prevalence of BRCA1 and BRCA2 gene mutations in patients with early-onset breast cancer. J Natl Cancer Inst. 1999;91:943-9. [PMID: 10359546]

9. **Nelson HD, Fu R, Goddard K, Priest Mitchell J, Okinaka-Hu L, Pappas M, et al.** Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation. Evidence synthesis no. 101. AHRQ publication no. 12-05164-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

10. **Panchal SM, Ennis M, Canon S, Bordeleau LJ.** Selecting a BRCA risk assessment model for use in a familial cancer clinic. BMC Med Genet. 2008;9:116. [PMID: 19102775]

11. **Parmigiani G, Chen S, Iversen ES Jr, Friebel TM, Finkelstein DM, Anton-Culver H, et al.** Validity of models for predicting BRCA1 and BRCA2 mutations. Ann Intern Med. 2007;147:441-50. [PMID: 17909205]

12. **Oros KK, Ghadirian P, Maugard CM, Perret C, Paredes Y, Mes-Masson AM, et al.** Application of BRCA1 and BRCA2 mutation carrier prediction models in breast and/or ovarian cancer families of French Canadian descent. Clin Genet. 2006;70:320-9. [PMID: 16965326]

13. **Evans DG, Eccles DM, Rahman N, Young K, Bulman M, Amir E, et al.** A new scoring system for the chances of identifying a BRCA1/2 mutation outperforms existing models including BRCAPRO. J Med Genet. 2004;41:474-80. [PMID: 15173236]

14. **Barcenas CH, Hosain GM, Arun B, Zong J, Zhou X, Chen J, et al.** Assessing BRCA carrier probabilities in extended families. J Clin Oncol. 2006;24:354-60. [PMID: 16421416]

15. **Antoniou AC, Hardy R, Walker L, Evans DG, Shenton A, Eeles R, et al.** Predicting the likelihood of carrying a BRCA1 or BRCA2 mutation: validation of BOADICEA, BRCAPRO, IBIS, Myriad and the Manchester scoring system using data from UK genetics clinics. J Med Genet. 2008;45:425-31. [PMID: 18413374]

16. **Bellcross CA, Lemke AA, Pape LS, Tess AL, Meisner LT.** Evaluation of a breast/ovarian cancer genetics referral screening tool in a mammography population. Genet Med. 2009;11:783-9. [PMID: 19752737]

17. **Hoskins KF, Zwaagstra A, Ranz M.** Validation of a tool for identifying women at high risk for hereditary breast cancer in population-based screening. Cancer. 2006;107:1769-76. [PMID: 16967460]

18. **Ashton-Prolla P, Giacomazzi J, Schmidt AV, Roth FL, Palmero EI, Kalakun L, et al.** Development and validation of a simple questionnaire for the identification of hereditary breast cancer in primary care. BMC Cancer. 2009;9:283. [PMID: 19682358]

19. **Gilpin CA, Carson N, Hunter AG.** A preliminary validation of a family history assessment form to select women at risk for breast or ovarian cancer for referral to a genetics center. Clin Genet. 2000;58:299-308. [PMID: 11076055]

20. **Nelson H, Pappas M, Zakher B, Mitchell J, Okinaka-Hu L, Fu R.** Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: a systematic review to update the U.S. Preventive Services Task Force recommendation. Ann Intern Med. 2013.

21. **Gronwald J, Cybulski C, Lubinski J, Narod SA.** Phenocopies in breast cancer 1 (BRCA1) families: implications for genetic counselling [Letter]. J Med Genet. 2007;44:e76. [PMID: 17400795]
22. **Rowan E, Poll A, Narod SA.** A prospective study of breast cancer risk in relatives of BRCA1/BRCA2 mutation carriers. J Med Genet. 2007;44:e89. [PMID: 17673443]
23. **Smith A, Moran A, Boyd MC, Bulman M, Shenton A, Smith L, et al.** Phenocopies in BRCA1 and BRCA2 families: evidence for modifier genes and implications for screening. J Med Genet. 2007;44:10-15. [PMID: 17079251]
24. **Vos JR, de Bock GH, Teixeira N, van der Kolk DM, Jansen L, Mourits MJ, et al.** Proven non-carriers in BRCA families have an earlier age of onset of breast cancer. Eur J Cancer. 2013. [PMID: 23490645]
25. **Finch A, Metcalfe KA, Chiang J, Elit L, McLaughlin J, Springate C, et al.** The impact of prophylactic salpingo-oophorectomy on quality of life and psychological distress in women with a BRCA mutation. Psychooncology. 2013;22: 212-9. [PMID: 21913283]
26. **Nelson HD, Smith ME, Griffin JC, Fu R.** Use of medications to reduce risk for primary breast cancer: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013;158:604-14. [PMID: 23588749]
27. **Domchek SM, Friebel TM, Singer CF, Evans DG, Lynch HT, Isaacs C, et al.** Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. JAMA. 2010;304:967-75. [PMID: 20810374]
28. **Skytte AB, Crüger D, Gerster M, Laenkholm AV, Lang C, Brøndum-Nielsen K, et al.** Breast cancer after bilateral risk-reducing mastectomy. Clin Genet. 2011;79:431-7. [PMID: 21199491]
29. **Evans DG, Gaarenstroom KN, Stirling D, Shenton A, Maehle L, Dørum A, et al.** Screening for familial ovarian cancer: poor survival of BRCA1/2 related cancers. J Med Genet. 2009;46:593-7. [PMID: 18413372]
30. **Centers for Disease Control and Prevention.** Breast Cancer Statistics. Atlanta, GA: Centers for Disease Control and Prevention; 2013. Accessed at www.cdc.gov/cancer/breast/statistics on 14 November 2013.
31. **Centers for Disease Control and Prevention, National Cancer Institute, North American Association of Central Cancer Registries.** United States Cancer Statistics: 1999–2010 Cancer Incidence and Mortality Data. Atlanta, GA: Centers for Disease Control and Prevention; 2013. Accessed at http://apps.nccd.cdc.gov/uscs on 9 December 2013.
32. **National Cancer Institute.** Breast Cancer. Bethesda, MD: National Cancer Institute; 2013. Accessed at www.cancer.gov/cancertopics/types/breast on 14 November 2013.
33. **National Cancer Institute.** Ovarian Cancer. Bethesda, MD: National Cancer Institute; 2013. Accessed at www.cancer.gov/cancertopics/types/ovarian on 14 November 2013.
34. **FitzGerald MG, MacDonald DJ, Krainer M, Hoover I, O'Neil E, Unsal H, et al.** Germ-line BRCA1 mutations in Jewish and non-Jewish women with early-onset breast cancer. N Engl J Med. 1996;334:143-9. [PMID: 8531968]
35. **Malone KE, Daling JR, Neal C, Suter NM, O'Brien C, Cushing-Haugen K, et al.** Frequency of BRCA1/BRCA2 mutations in a population-based sample of young breast carcinoma cases. Cancer. 2000;88:1393-402. [PMID: 10717622]
36. **Fodor FH, Weston A, Bleiweiss IJ, McCurdy LD, Walsh MM, Tartter PI, et al.** Frequency and carrier risk associated with common BRCA1 and BRCA2 mutations in Ashkenazi Jewish breast cancer patients. Am J Hum Genet. 1998; 63:45-51. [PMID: 9634504]
37. **Hartge P, Struewing JP, Wacholder S, Brody LC, Tucker MA.** The prevalence of common BRCA1 and BRCA2 mutations among Ashkenazi Jews. Am J Hum Genet. 1999;64:963-70. [PMID: 10090881]
38. **Metcalfe KA, Poll A, Royer R, Llacuachaqui M, Tulman A, Sun P, et al.** Screening for founder mutations in BRCA1 and BRCA2 in unselected Jewish women. J Clin Oncol. 2010;28:387-91. [PMID: 20008623]
39. **Roa BB, Boyd AA, Volcik K, Richards CS.** Ashkenazi Jewish population frequencies for common mutations in BRCA1 and BRCA2. Nat Genet. 1996; 14:185-7. [PMID: 8841191]
40. **Armstrong K, Micco E, Carney A, Stopfer J, Putt M.** Racial differences in the use of BRCA1/2 testing among women with a family history of breast or ovarian cancer. JAMA. 2005;293:1729-36. [PMID: 15827311]
41. **Roshanai AH, Rosenquist R, Lampic C, Nordin K.** Does enhanced information at cancer genetic counseling improve counselees' knowledge, risk perception, satisfaction and negotiation of information to at-risk relatives?—a randomized study. Acta Oncol. 2009;48:999-1009. [PMID: 19636983]
42. **Matloff ET, Moyer A, Shannon KM, Niendorf KB, Col NF.** Healthy women with a family history of breast cancer: impact of a tailored genetic counseling intervention on risk perception, knowledge, and menopausal therapy decision making. J Womens Health (Larchmt). 2006;15:843-56. [PMID: 16999640]
43. **Bloom JR, Stewart SL, Chang S, You M.** Effects of a telephone counseling intervention on sisters of young women with breast cancer. Prev Med. 2006;43: 379-84. [PMID: 16916540]
44. **Braithwaite D, Sutton S, Mackay J, Stein J, Emery J.** Development of a risk assessment tool for women with a family history of breast cancer. Cancer Detect Prev. 2005;29:433-9. [PMID: 16055276]
45. **Helmes AW, Culver JO, Bowen DJ.** Results of a randomized study of telephone versus in-person breast cancer risk counseling. Patient Educ Couns. 2006;64:96-103. [PMID: 16427245]
46. **Bowen DJ, Burke W, Culver JO, Press N, Crystal S.** Effects of counseling Ashkenazi Jewish women about breast cancer risk. Cultur Divers Ethnic Minor Psychol. 2006;12:45-56. [PMID: 16594854]
47. **Mikkelsen EM, Sunde L, Johansen C, Johnsen SP.** Risk perception among women receiving genetic counseling: a population-based follow-up study. Cancer Detect Prev. 2007;31:457-64. [PMID: 18061369]
48. **Mikkelsen EM, Sunde L, Johansen C, Johnsen SP.** Psychosocial consequences of genetic counseling: a population-based follow-up study. Breast J. 2009;15:61-8. [PMID: 19120380]
49. **Pieterse AH, Ausems MG, Spreeuwenberg P, van Dulmen S.** Longer-term influence of breast cancer genetic counseling on cognitions and distress: smaller benefits for affected versus unaffected women. Patient Educ Couns. 2011;85: 425-31. [PMID: 21316181]
50. **Hopwood P, Wonderling D, Watson M, Cull A, Douglas F, Cole T, et al.** A randomised comparison of UK genetic risk counselling services for familial cancer: psychosocial outcomes. Br J Cancer. 2004;91:884-92. [PMID: 15305197]
51. **Kelly KM, Senter L, Leventhal H, Ozakinci G, Porter K.** Subjective and objective risk of ovarian cancer in Ashkenazi Jewish women testing for BRCA1/2 mutations. Patient Educ Couns. 2008;70:135-42. [PMID: 17988821]
52. **Gurmankin AD, Domchek S, Stopfer J, Fels C, Armstrong K.** Patients' resistance to risk information in genetic counseling for BRCA1/2. Arch Intern Med. 2005;165:523-9. [PMID: 15767527]
53. **Bennett P, Wilkinson C, Turner J, Brain K, Edwards RT, Griffith G, et al.** Psychological factors associated with emotional responses to receiving genetic risk information. J Genet Couns. 2008;17:234-41. [PMID: 18259848]
54. **Brain K, Parsons E, Bennett P, Cannings-John R, Hood K.** The evolution of worry after breast cancer risk assessment: 6-year follow-up of the TRACE study cohort. Psychooncology. 2011;20:984-91. [PMID: 20677331]
55. **Fry A, Cull A, Appleton S, Rush R, Holloway S, Gorman D, et al.** A randomised controlled trial of breast cancer genetics services in South East Scotland: psychological impact. Br J Cancer. 2003;89:653-9. [PMID: 12915873]
56. **Smerecnik CM, Mesters I, Verweij E, de Vries NK, de Vries H.** A systematic review of the impact of genetic counseling on risk perception accuracy. J Genet Couns. 2009;18:217-28. [PMID: 19291376]
57. **Bennett P, Wilkinson C, Turner J, Edwards RT, France B, Griffith G, et al.** Factors associated with intrusive cancer-related worries in women undergoing cancer genetic risk assessment. Fam Cancer. 2009;8:159-65. [PMID: 19011994]
58. **Fisher B, Costantino JP, Wickerham DL, Cecchini RS, Cronin WM, Robidoux A, et al.** Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. J Natl Cancer Inst. 2005;97:1652-62. [PMID: 16288118]
59. **Powles TJ, Ashley S, Tidy A, Smith IE, Dowsett M.** Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. J Natl Cancer Inst. 2007;99:283-90. [PMID: 17312305]
60. **Veronesi U, Maisonneuve P, Rotmensz N, Bonanni B, Boyle P, Viale G, et al; Italian Tamoxifen Study Group.** Tamoxifen for the prevention of breast cancer: late results of the Italian Randomized Tamoxifen Prevention Trial among women with hysterectomy. J Natl Cancer Inst. 2007;99:727-37. [PMID: 17470740]
61. **Cuzick J, Forbes JF, Sestak I, Cawthorn S, Hamed H, Holli K, et al; International Breast Cancer Intervention Study I Investigators.** Long-term results of tamoxifen prophylaxis for breast cancer—96-month follow-up of the randomized IBIS-I trial. J Natl Cancer Inst. 2007;99:272-82. [PMID: 17312304]

62. **Grady D, Cauley JA, Geiger MJ, Kornitzer M, Mosca L, Collins P, et al; Raloxifene Use for The Heart Trial Investigators.** Reduced incidence of invasive breast cancer with raloxifene among women at increased coronary risk. J Natl Cancer Inst. 2008;100:854-61. [PMID: 18544744]

63. **Lippman ME, Cummings SR, Disch DP, Mershon JL, Dowsett SA, Cauley JA, et al.** Effect of raloxifene on the incidence of invasive breast cancer in postmenopausal women with osteoporosis categorized by breast cancer risk. Clin Cancer Res. 2006;12:5242-7. [PMID: 16951244]

64. **Vogel VG, Costantino JP, Wickerham DL, Cronin WM, Cecchini RS, Atkins JN, et al; National Surgical Adjuvant Breast and Bowel Project.** Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. Cancer Prev Res (Phila). 2010;3:696-706. [PMID: 20404000]

65. **Nelson HD, Fu R, Humphrey L, Smith M, Griffin JC, Nygren P.** Comparative Effectiveness of Medications to Reduce Risk of Primary Breast Cancer in Women. Comparative effectiveness review no. 17. Rockville, MD: Agency for Healthcare Research and Quality; 2009.

66. **Kurian AW, Gong GD, John EM, Johnston DA, Felberg A, West DW, et al.** Breast cancer risk for noncarriers of family-specific BRCA1 and BRCA2 mutations: findings from the Breast Cancer Family Registry. J Clin Oncol. 2011; 29:4505-9. [PMID: 22042950]

67. **Eisen A, Lubinski J, Klijn J, Moller P, Lynch HT, Offit K, et al.** Breast cancer risk following bilateral oophorectomy in BRCA1 and BRCA2 mutation carriers: an international case-control study. J Clin Oncol. 2005;23:7491-6. [PMID: 16234515]

68. **Kriege M, Brekelmans CT, Boetes C, Muller SH, Zonderland HM, Obdeijn IM, et al; Dutch MRI Screening (MRISC) Study Group.** Differences between first and subsequent rounds of the MRISC breast cancer screening program for women with a familial or genetic predisposition. Cancer. 2006;106: 2318-26. [PMID: 16615112]

69. **Le-Petross HT, Whitman GJ, Atchley DP, Yuan Y, Gutierrez-Barrera A, Hortobagyi GN, et al.** Effectiveness of alternating mammography and magnetic resonance imaging for screening women with deleterious BRCA mutations at high risk of breast cancer. Cancer. 2011;117:3900-7. [PMID: 21365619]

70. **Contant CM, Menke-Pluijmers MB, Seynaeve C, Meijers-Heijboer EJ, Klijn JG, Verhoog LC, et al.** Clinical experience of prophylactic mastectomy followed by immediate breast reconstruction in women at hereditary risk of breast cancer (HB(O)C) or a proven BRCA1 and BRCA2 germ-line mutation. Eur J Surg Oncol. 2002;28:627-32. [PMID: 12359199]

71. **Metcalfe KA, Esplen MJ, Goel V, Narod SA.** Psychosocial functioning in women who have undergone bilateral prophylactic mastectomy. Psychooncology. 2004;13:14-25. [PMID: 14745742]

72. **Kauff ND, Satagopan JM, Robson ME, Scheuer L, Hensley M, Hudis CA, et al.** Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. N Engl J Med. 2002;346:1609-15. [PMID: 12023992]

73. **Brandberg Y, Arver B, Johansson H, Wickman M, Sandelin K, Liljegren A.** Less correspondence between expectations before and cosmetic results after risk-reducing mastectomy in women who are mutation carriers: a prospective study. Eur J Surg Oncol. 2012;38:38-43. [PMID: 22032910]

74. **Brandberg Y, Sandelin K, Erikson S, Jurell G, Liljegren A, Lindblom A, et al.** Psychological reactions, quality of life, and body image after bilateral prophylactic mastectomy in women at high risk for breast cancer: a prospective 1-year follow-up study. J Clin Oncol. 2008;26:3943-9. [PMID: 18711183]

75. **Gahm J, Wickman M, Brandberg Y.** Bilateral prophylactic mastectomy in women with inherited risk of breast cancer—prevalence of pain and discomfort, impact on sexuality, quality of life and feelings of regret two years after surgery. Breast. 2010;19:462-9. [PMID: 20605453]

76. **Wasteson E, Sandelin K, Brandberg Y, Wickman M, Arver B.** High satisfaction rate ten years after bilateral prophylactic mastectomy - a longitudinal study. Eur J Cancer Care (Engl). 2011;20:508-13. [PMID: 20597955]

77. **Finch A, Metcalfe KA, Chiang JK, Elit L, McLaughlin J, Springate C, et al.** The impact of prophylactic salpingo-oophorectomy on menopausal symptoms and sexual function in women who carry a BRCA mutation. Gynecol Oncol. 2011;121:163-8. [PMID: 21216453]

78. **Nelson HD, Huffman LH, Fu R, Harris EL; U.S. Preventive Services Task Force.** Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2005;143:362-79. [PMID: 16144895]

79. **American College of Obstetricians and Gynecologists.** ACOG Practice Bulletin No. 103: Hereditary breast and ovarian cancer syndrome. Obstet Gynecol. 2009;113:957-66. [PMID: 19305347]

80. **Robson ME, Storm CD, Weitzel J, Wollins DS, Offit K; American Society of Clinical Oncology.** American Society of Clinical Oncology policy statement update: genetic and genomic testing for cancer susceptibility. J Clin Oncol. 2010; 28:893-901. [PMID: 20065170]

81. **Berliner JL, Fay AM, Cummings SA, Burnett B, Tillmanns T.** NSGC practice guideline: risk assessment and genetic counseling for hereditary breast and ovarian cancer. J Genet Couns. 2013;22:155-63. [PMID: 23188549]

82. **Balmaña J, Díez O, Rubio IT, Cardoso F; ESMO Guidelines Working Group.** BRCA in breast cancer: ESMO Clinical Practice Guidelines. Ann Oncol. 2011;22 Suppl 6:vi31-4. [PMID: 21908500]

83. **Lancaster JM, Powell CB, Kauff ND, Cass I, Chen LM, Lu KH, et al; Society of Gynecologic Oncologists Education Committee.** Society of Gynecologic Oncologists Education Committee statement on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol. 2007;107:159-62. [PMID: 17950381]

Appendix: U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Virginia A. Moyer, MD, MPH, *Chair* (American Board of Pediatrics, Chapel Hill, North Carolina); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veterans Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); and Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina).

† For a list of current Task Force members, go to www.uspreventiveservicestaskforce.org/members.htm.

Appendix Table 1. **What the USPSTF Grades Mean and Suggestions for Practice**

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Appendix Table 2. **USPSTF Levels of Certainty Regarding Net Benefit**

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.

Oregon Genetics Program Response to Proposed Changes to Diagnostic Guideline D1

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Executive Summary

In response to the proposal to broaden the language regarding coverage for cancer genetic services, the Oregon Genetics Program (OGP) recommends that genetic counseling and testing services be covered when ordered by a genetics provider as per the current guidelines for these reasons:

1) Cancer risk assessment and genetic counseling are rapidly becoming standards of care for patients with a personal history of cancer and/or a family history of cancer. (Pg 4)

2) In Oregon, non-genetics specialist providers are already ordering cancer genetic testing and Oregonians are not receiving recommended care according to guidelines. (Pg 6)

3) The right cancer genetic tests are not being ordered in the Oregon Medicaid population. (Pg 7)

4) The standard practice of genetic specialists allows *all* close blood relatives who choose to be tested to receive the much less expensive single site testing. (Pg 8)

5) Testing may be being ordered on the wrong individuals, such that the provider is not testing the right family member for informative results and/or is ordering the wrong test. (Pg 8)

6) Current Medicaid guidelines state that <u>only</u> single site testing is covered when a family *BRCA* mutation is known. This guideline is either not being followed or many providers who are doing genetic testing are not determining the mutation status in the family before proceeding with testing of their patients. (Pg 9)

7) Non-genetic specialist providers do not have the knowledge or confidence needed for accurate risk assessment. (Pg 9)

8) Aggressive marketing increases provider awareness of available genetic tests, but does not increase knowledge of heritable cancers. (Pg 12)

9) Access to cancer genetic services is improving in the state, with new clinics in eastern Oregon and new telemedicine services in southern Oregon and the Salem area. Expansion into other underserved areas is under discussion. (Pg 13)

In summary, the Oregon Genetics Program believes that patients and their families are better served when genetic services are provided by qualified providers wherever possible, as is outlined in the current Medicaid guidelines.

- Our goal is to improve the quality and economy of genetic testing by emphasizing that referral for genetic consultation before testing is preferred wherever possible. The level of expertise needed in the current climate with a rapidly changing array of testing available and increasing complex results interpretation in cancer argues for enforcing the current guideline rather than diluting it.
- We believe that genetic consultation before testing is crucial in indicating if testing is necessary, what test is appropriate and who in the family is appropriate to test, as well as to interpret test results.

- American College of Surgeons' Commission on Cancer (CoC) Standards define who should be considered a genetic specialist and also define pre- and post-test genetic counseling. These standards are being adopted by CoC credentialed cancer centers and health insurance companies such as Cigna and Priority Health.
- If there is intent to broaden the type of provider that can order testing and provide informed consent for testing, we recommend that the language be in line with CoC Standards, as well as evidence-based guidelines such as the National Comprehensive Cancer Network (NCCN) guidelines and the U.S. Preventive Services Task Force (USPSTF) recommendations.

If the Healthcare Evidence Review Committee decides to broaden the current cancer genetic services policies, we recommend adding information to the guidelines, instead of removing information. There is clear evidence that non-genetic specialist providers are generally unable to provide appropriate risk assessment and genetic counseling services.

We recommend retaining the guideline for genetic counseling as the best option, but expanding coverage of genetic testing to allow more flexibility regarding the types of professionals allowed to order genetic testing. Our suggested draft wording can be found on pages 18 - 20. The following pages provide more details describing the state of genetic services in Oregon and nationally.

We sincerely thank you for your time and attention to this matter. We highly regard the important work you do and appreciate any opportunity we have to work with you on matters relating to the health of Oregonians and genetics. Please let us know if you have any questions or would like to discuss this or other topics.

Kind regards,

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In response to the proposal to broaden the language regarding coverage for cancer genetic services, the Oregon Genetics Program (OGP) recommends that genetic counseling and testing services be covered when provided by a genetics specialist as per the current guidelines for these reasons:

1) **Cancer risk assessment and genetic counseling are rapidly becoming standards of care for patients with a personal history of cancer and/or a family history of cancer.**

→**The American College of Surgeons' Commission on Cancer (CoC) has a very clear definition of who should be considered a genetics specialist and what pre- and post-test counseling entail.**

CoC Definition: Genetics professionals include people with the following:

- *An American Board of Genetic Counseling (ABGC) or American Board of Medical Genetics (ABMG) board-certified/board-eligible or (in some states) a licensed genetic counselor*
- *An American College of Medical Genetics physician board certified in medical genetics*
- *A Genetics Clinical Nurse (GCN) or an Advanced Practice Nurse in Genetics (APNG), credentialed through the Genetics Nursing Credentialing Commission (GNCC). Credentialing is obtained through successful completion of a professional portfolio review process*
- *An advanced practice oncology nurse who is prepared at the graduate level (master or doctorate) with specialized education in cancer genetics and hereditary cancer predisposition syndromes*; certification by the Oncology Nursing Certification Corporation is preferred*
- *A board-certified physician with experience in cancer genetics (defined as providing cancer risk assessment on a regular basis)*

  **Please note, specialized training in cancer genetics should be ongoing; <u>educational seminars offered by commercial laboratories about how to perform genetic testing are not considered adequate training for cancer risk assessment and genetic counseling</u>.*

CoC Definition: Pretest Counseling

- *Collecting relevant information needed to assess a patient's personal and family medical history*
  - *A three- to four-generation pedigree, including detailed medical information about the patient's first-, second-, and third-degree relatives should be obtained. Gathering information about paternal and maternal family history, ancestry/ethnicity, and consanguinity, as available, is necessary.*
- *Evaluating the patient's risk*

- *One aspect of risk assessment is discussing the absolute risk that the patient will develop a specific type of cancer or cancers based on the family history. The second aspect is the risk that the patient carries a heritable or germ line mutation in a cancer susceptibility gene.*

- *Performing a psychosocial assessment*
- *Educating the patient about the suspected hereditary cancer syndrome, if appropriate*
  - *The provider reviews and discusses with the patient the cancer risks associated with gene mutations, including basic concepts such as genes and inheritance patterns and more advanced concepts of penetrance and variable expressivity and the possibility of genetic heterogeneity.*
- *Obtaining informed consent for genetic testing (if genetic testing is recommended).*

CoC Definition: Posttest Counseling

- *Disclosure of the results and posttest counseling include a discussion of the results, significance and impact of the test results, medical management options, informing other relatives, future contact, and available resources. The test results and interpretation will be communicated to the provider.*

  See Supplemental Material , page 16, for an excerpt of the CoC Risk Assessment and Genetic Counseling Standard or go to: http://www.facs.org/cancer/coc/programstandards2012.pdf for the full Cancer Program Standards 2012: Ensuring Patient-Centered Care v1.2.1

→Recent research studies by Bellcross (2011), Brierley (2012), and Riley (2012) outline the process of genetic counseling to include:

- Detailed personal and three-generational family health history
- Pre-test informed consent and post-test result disclosure and interpretation
- Informed consent include testing options, implications of test results, whom to test in the family, options for cancer screening and risk reduction, and economic considerations and psychosocial assessment.
- A genetic specialist can also explain questions and understand practice issues related to genetic ethics, law, privacy, and insurance coverage.

→There are existing model health insurance policies that require pre- and post-test genetic counseling and identifying that genetic specialists are the only providers appropriate to perform genetic counseling and genetic testing.

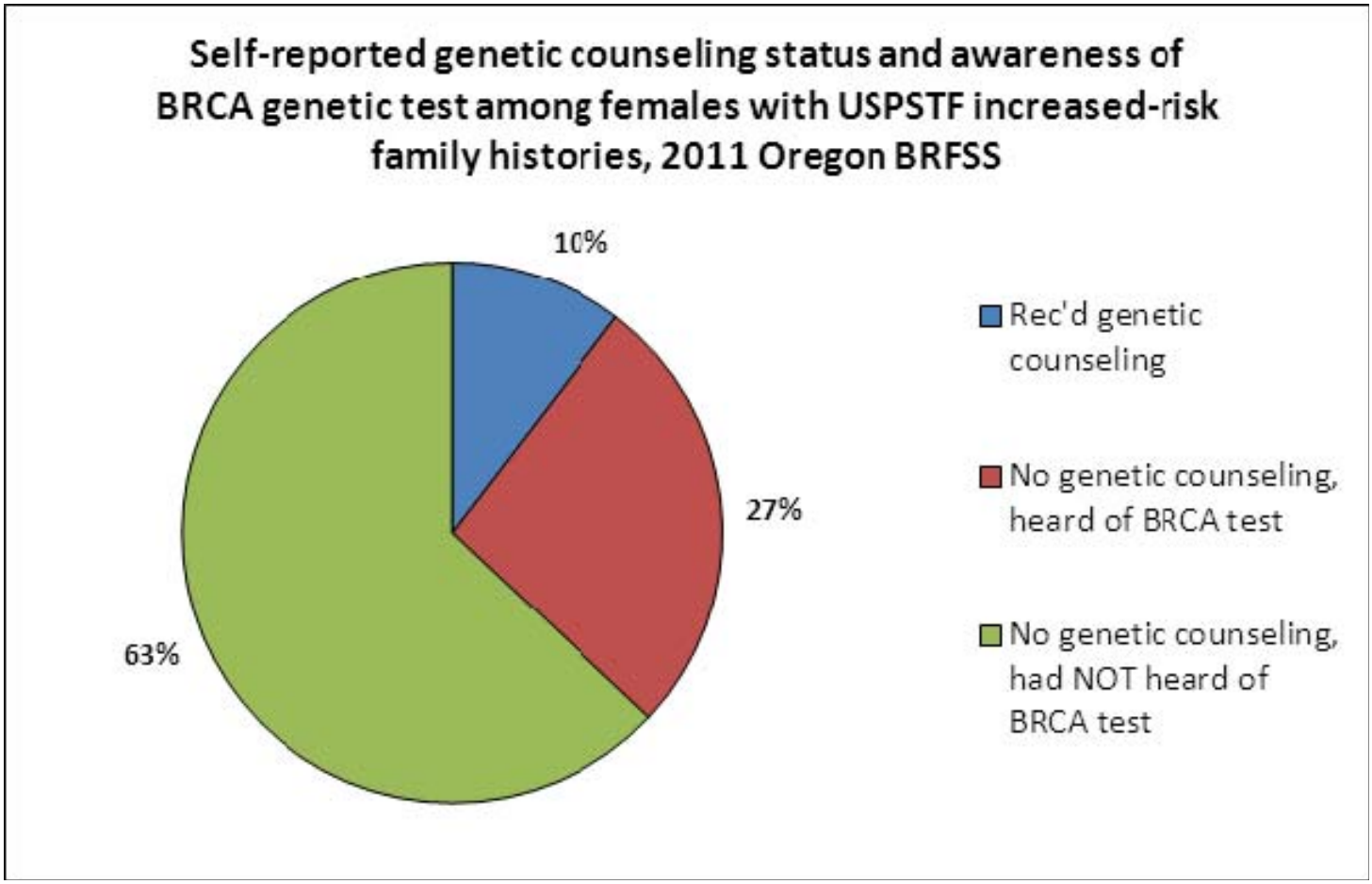
- Please see Supplemental Material , page 56, for Cigna's full policy on Genetic Testing for Susceptibility to Breast & Ovarian Cancer and Genetic Testing for Susceptibility to Colorectal Cancer or find multiple links to Cigna policies on genetic testing of heritable disorders:

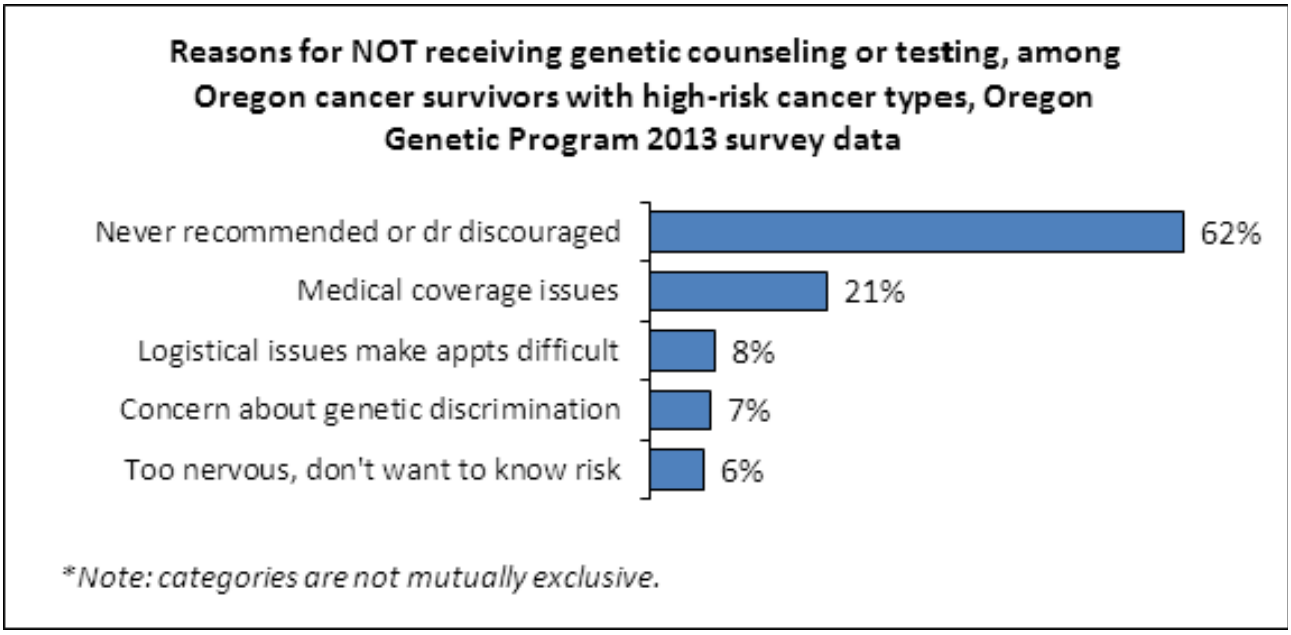
https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/mm_0052_coveragepositioncriteria_genetic_testing.pdf

- Please see the Supplemental Material , page 120, for the full Priority Health policy on Genetics: Counseling, Testing and Screening or go to: http://www.priorityhealth.com/provider/manual/auths/~/media/documents/medical-policies/91540.pdf.

2) In Oregon, cancer genetic testing is already being ordered by non-genetics specialist providers and Oregonians are also not receiving recommended care according to guidelines.

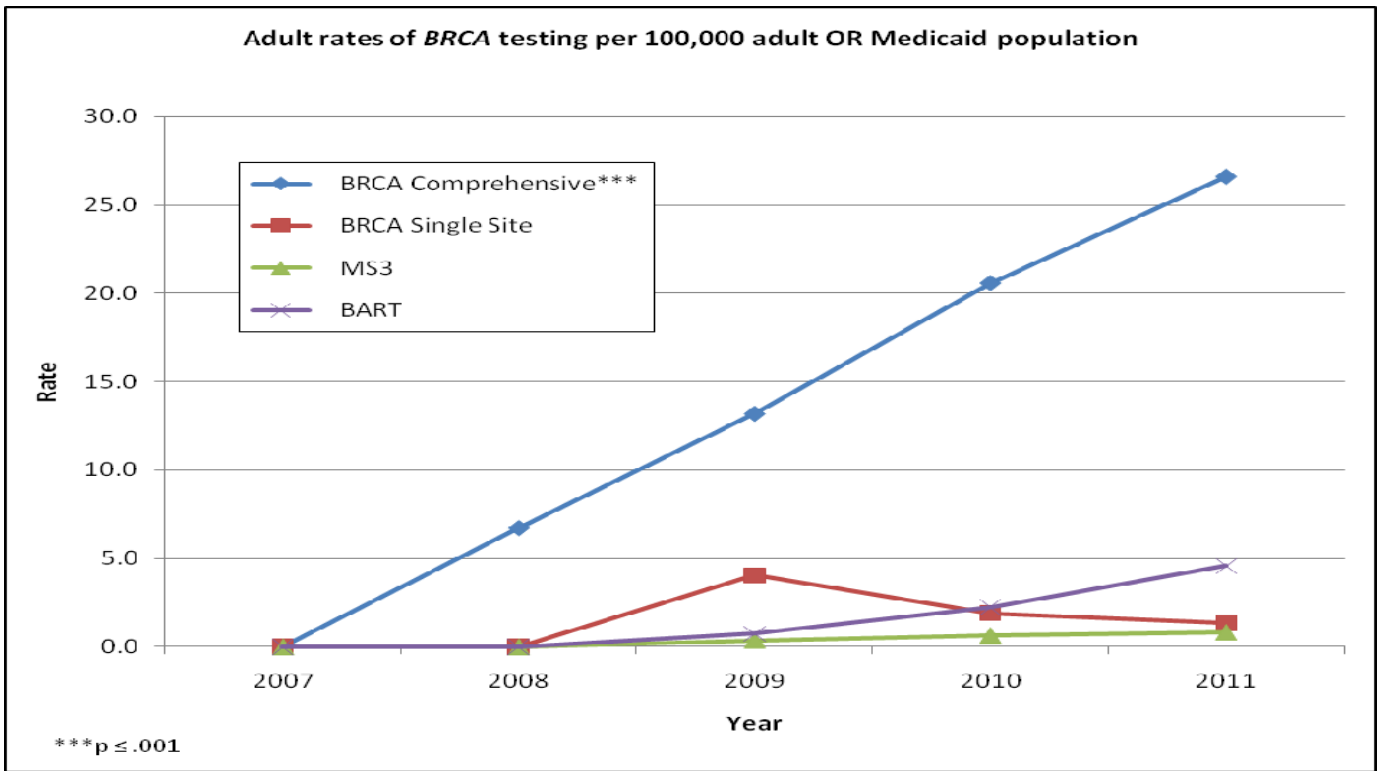
The OGP estimates that about 60% of cancer genetic testing in Oregon is ordered by non-genetic specialist providers. In addition, Oregon data indicates that patients who are appropriate for genetic counseling (such as females who fit U.S. Preventive Task Force Services guidelines for *BRCA* genetic counseling, shown in the next two charts) are not given the option of seeking genetic counseling or being referred to a genetic specialist.





3) The right cancer genetic tests are not being ordered in the Oregon Medicaid population. This graph of Medicaid testing ordered over several years' shows that comprehensive *BRCA* testing is growing quickly while single site testing is actually declining. The trend and shape of these lines is consistent whether we look at Medicaid data alone or all *BRCA* testing done in Oregon. If the correct testing is being ordered, we would expect comprehensive testing to decline and site specific testing to increase, as only one person in each family needs to receive the comprehensive testing if testing is done in accordance with standard care.

Data from preliminary 2007-2011 Medicaid Analysis, unpublished



4) **The cost of comprehensive genetic testing is much higher than the cost of site specific testing.** For example, comprehensive *BRCA* testing costs approximately $2,200 to $4,000 (or more, if multi-gene panels are ordered, an increasingly common practice (Ambry Genetics, 2014; Smith, 2013). **The standard practice of genetic specialists** is to find a symptomatic family member available for testing, so that a positive result not only allows opportunities for prevention and early diagnosis of future primary cancers in the individual, but also **allows *all* close blood relatives who choose to be tested to receive the much less expensive single site testing.** This is illustrated by *BRCA* single site testing, which costs approximately $400 (Ambry Genetics, 2014). In addition, any subsequent family member who has a negative test result for the familial mutation will know that they are not at increased risk of developing HBOC syndrome-related cancers and can return to the low risk cancer screenings recommended for the general public.

5) In addition, the upward trend in comprehensive testing in the Medicaid population suggests that comprehensive **testing may be being ordered on the wrong individuals, that the provider is not testing the right family member for informative results and/or is ordering the wrong test.**

Nationally, there is strong evidence that misinterpretation of results is common when a non-genetics specialist provider is involved in ordering and interpreting cancer genetic test results. These references provide some data:

➔ **Adverse events in cancer genetic testing: medical, ethical, legal, and financial implications** (Brierley, 2012).

Abstract: *Cancer genetic counseling and testing are now integral services in progressive cancer care. There has been much debate over whether these services should be delivered by providers with specialized training in genetics or by all clinicians. Adverse outcomes resulting from cancer genetic counseling and testing performed by clinicians without specialization in genetics have been reported, but formal documentation is sparse.* ***In this review, we present a series of national cases illustrating major patterns of errors in cancer genetic counseling and testing and the resulting impact on medical liability, health care costs, and the patients and their families.***

Cancer J. 2012 Jul-Aug;18(4):303-9. doi: 10.1097/PPO.0b013e3182609490.

See Supplemental Material , page 49, for the full article.

➔ **ARUP Laboratories: Value of Genetic Counselors in the Laboratory**

Introduction: *Genetic counselors (GCs) employed by diagnostic laboratories may write medical papers, coordinate research, create and maintain genetic databases, educate clients and health care providers, and review test orders. Of these duties, the one that most directly benefits patients, medical institutions, and insurers is the rigorous reviewing of genetic test orders. GCs at ARUP Laboratories, a national reference laboratory, collectively save ordering institutions more than $30,000 per month by modifying test orders to improve utilization.*

Seven GCs at ARUP Laboratories performed a review of all genetic test modifications over an 11-month period, reviewing clinical information that accompanied test orders for complex genetic tests (i.e., sequencing, large duplication/deletion analysis, or array-based technologies) before testing was performed. The GCs considered the clinical utility and cost-effectiveness of the ordered tests and contacted the ordering institution and/or health care provider to collect additional clinical information, confirm testing, or suggest alternative testing based on the provided clinical information or family history.

The GCs identified and cancelled or changed inappropriately ordered genetic tests for an average cost savings of $36,500 per month, representing approximately 30 percent of all complex genetic tests ordered. Among frequently misordered tests were requests for full-gene sequencing when a familial mutation was known or when a screening panel would have been more appropriate (e.g., cystic fibrosis testing in expectant individuals with no family history).

Erroneously ordered genetic testing delays medical decision-making and increases diagnostic costs. In 2008, U.S. health care spending was the highest of all industrialized countries, about $7,681 per resident, and accounted for 16.2 percent of the nation's gross domestic product (GDP). Reducing the growth in health care costs is thus a priority.

http://www.aruplab.com/files/resources/genetics/White-paper-1-value-of-GCs-in-lab.pdf

See Supplemental Material , page 19, for the full white paper.

6) **Current Medicaid guidelines state that only single site testing is covered when a family *BRCA* mutation is known. However, considering the rapid growth of comprehensive testing and the decline of single site testing (as seen in #3), either this guideline is not being followed or many providers who are doing genetic testing are not determining the mutation status in the family before proceeding with testing of their patients.** The same pattern of comprehensive and site testing is also seen in Oregon cancer genetic testing as a whole, indicating that the genetic testing practice of providers is likely consistent regardless of which payor is covering a given patient.

> *Diagnostic Guideline D1, Non-prenatal Genetic Testing Guideline, A) 3) If the mutation in the family is known, only the test for that mutation is covered. For example, if a mutation for BRCA 1has been identified in a family, a single site mutation analysis for that mutation is covered (CPT 81215),while a full sequence BRCA 1 and 2 (CPT 81211) analyses is not. There is one exception, for individuals of Ashkenazi Jewish ancestry with a known mutation in the family, the panel for Ashkenazi Jewish BRCA mutations is covered (CPT 81212).*

7) In general, non-genetic specialist providers do not have the knowledge or confidence needed for accurate risk assessment, though aggressive marketing is increasing their awareness of available genetic tests, many of which have not had their analytic validity, clinical validity, and clinical utility evaluated.

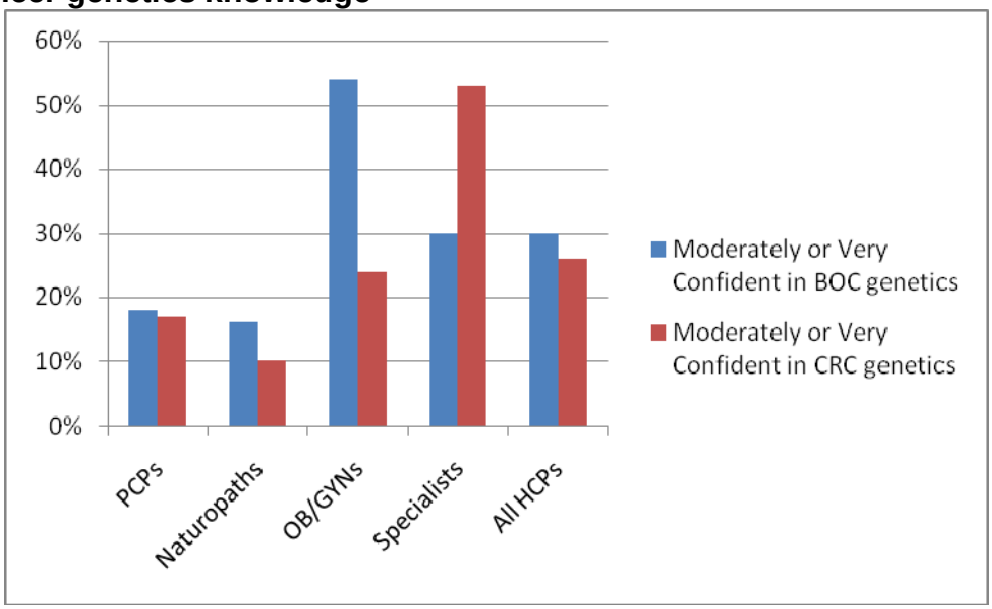
➔**Genetic testing has limitations when conducted by healthcare providers without genetic credentials** (Bensend, 2014; Brierley, 2012; Radford, 2013; Wood, 2008).

- Errors and inadequate genetic counseling occur due to limited expertise and restrictive time structure.
- The average time given to see patients by a non-genetics specialist provider is 20 minutes, while the average time given to see patients by a genetics specialist is 57 minutes.
    - *Genetic counselors spent half of their time on patient-related activities, one-fourth on direct patient care, and the remainder on all other activities. The total professional time averaged 7 hours per new patient and 3.5 hours per follow-up with nearly 60% of this time devoted to patient-related activities. (McPherson, 2008)*
- There are great time pressures that make it difficult for detailed risk assessment, test interpretation and making recommendations for genetic counseling and testing of family members.

➔**Providers have low confidence in their knowledge of genetics**

- The Oregon Genetic Program conducted a Health Care Provider Survey (N=1211) in 2010 and found that only **30% of clinicians reported that they felt moderately or very confident in their genetics knowledge on breast and ovarian cancer and 26% respectively for colorectal cancer genetics** (Cox, 2012).
- OB/GYNs were the most confident in their breast and ovarian cancer genetics knowledge, just over 50% of OB/GYNs were moderately or very confident in their breast and ovarian cancer genetics knowledge.
- Specialists were the most confident in their colorectal cancer genetics knowledge, just over 50% of specialists were moderately or very confident.

Percent of each healthcare provider group that is moderately or very confident in their cancer genetics knowledge



➔ **Provider confidence in genetics is directly associated with whether a non-genetics specialist provider will suspect a *BRCA* or *MMR* mutation.**

- Confidence in breast, ovarian, and colorectal cancer genetics played a role in whether providers suspected *BRCA* and *MMR* mutations.
- Providers who were the most confident in cancer genetics had the highest proportions who both suspected *BRCA* and *MMR* mutations and ordered/recommended genetic testing. This association was strongest when looking at confidence in colorectal cancer genetics.

Suspect Mutation by Confidence in Medical Genetics

	Moderately/Very Confident in breast and ovarian cancer genetics knowledge	Moderately/Very Confident in colorectal cancer genetics knowledge
Ever suspected *BRCA/MMR* mutation in patients w/o cancer (Yes vs. No)	43% vs. 20%, p=0.0000	44% vs. 19%, p=0.0000
Always/usually ordered/recommended *BRCA/MMR* genetic testing for patients w/o cancer (vs. sometimes/never)	42% vs. 22%, p=0.0024	66% vs. 21%, p=0.0000
Ever suspected *BRCA/MMR* mutation in patients w/cancer (Yes vs. No)	40% vs. 17%, p=0.0008	56% vs. 19%, p=0.0000
Always/usually ordered/recommended *BRCA/MMR* genetic testing for patients w/cancer (vs. sometimes/never)	45% vs. 18%, p=0.0038	68% vs. 19%, p=0.0003

➔ **Physicians are not collecting the full family history information to conduct an appropriate cancer risk assessment.**

- Although 98% of health care providers reported that they collected family history to assess risk of hereditary cancers in patients without cancer, approximately 20% reported that they did not collect family history of second degree relatives and 10% did not ask about age of cancer diagnosis of their patient's family members (Cox, 2012).
- A majority of health care providers have not been able to identify and differentiate between low/medium and high risk case scenarios. It's easier for clinicians to determine

who is at low risk then at high risk for hereditary breast and ovarian cancer (Bellcross, 2011; Trivers, 2011; Wood, 2008). See Supplemental Material , page 27/141/151.

➔ **National data shows low cancer genetics knowledge among primary providers, including OB/Gyns (Bellcross, 2011)**

Awareness and utilization of BRCA1/2 testing among U.S. primary care physicians.

Background: *Testing for mutations in the breast and ovarian cancer susceptibility genes BRCA1 and BRCA2 (BRCA) has been commercially available since 1996.* ***PURPOSE:*** *This study sought to determine, among U.S. primary care physicians, the level of awareness and utilization of BRCA testing and the 2005 U.S. Preventive Services Task Force (USPSTF) recommendations.* ***Methods:*** *In 2009, data were analyzed on 1500 physician respondents to the 2007 DocStyles national survey (515 family practitioners, 485 internists, 250 pediatricians, and 250 obstetricians/gynecologists).* ***Results:*** *Overall, 87% of physicians were aware of BRCA testing, and 25% reported having ordered testing for at least one patient in the past year. Ordering tests was most prevalent among obstetricians/gynecologists in practice for more than 10 years, with more affluent patients. Physicians were asked to select indications for BRCA testing from seven different clinical scenarios representing increased (4) or low-risk (3) situations consistent with the USPSTF guidelines. Among ordering physicians (pediatricians excluded), 45% chose at least one low-risk scenario as an indication for BRCA testing. Only 19% correctly selected all of the increased-risk and none of the low-risk scenarios.* ***Conclusions: A substantial majority of primary care physicians are aware of BRCA testing and many report having ordered at least one test within the past year. A minority, however, appear to consistently recognize the family history patterns identified by the USPSTF as appropriate indications for BRCA evaluation.*** *These results suggest the need to improve providers' knowledge about existing recommendations-particularly in this era of increased BRCA direct-to-consumer marketing.*

Am J Prev Med. 2011 Jan;40(1):61-6. doi: 10.1016/j.amepre.2010.09.027.

See Supplemental Material , page 27, for the full article.

➔ **The low knowledge of genetics, the low confidence in their genetic knowledge, and the association between confidence in medical genetics and not having suspected a *BRCA* or *MMR* mutation highlights the connection between provider confidence, knowledge and the quality of care.**

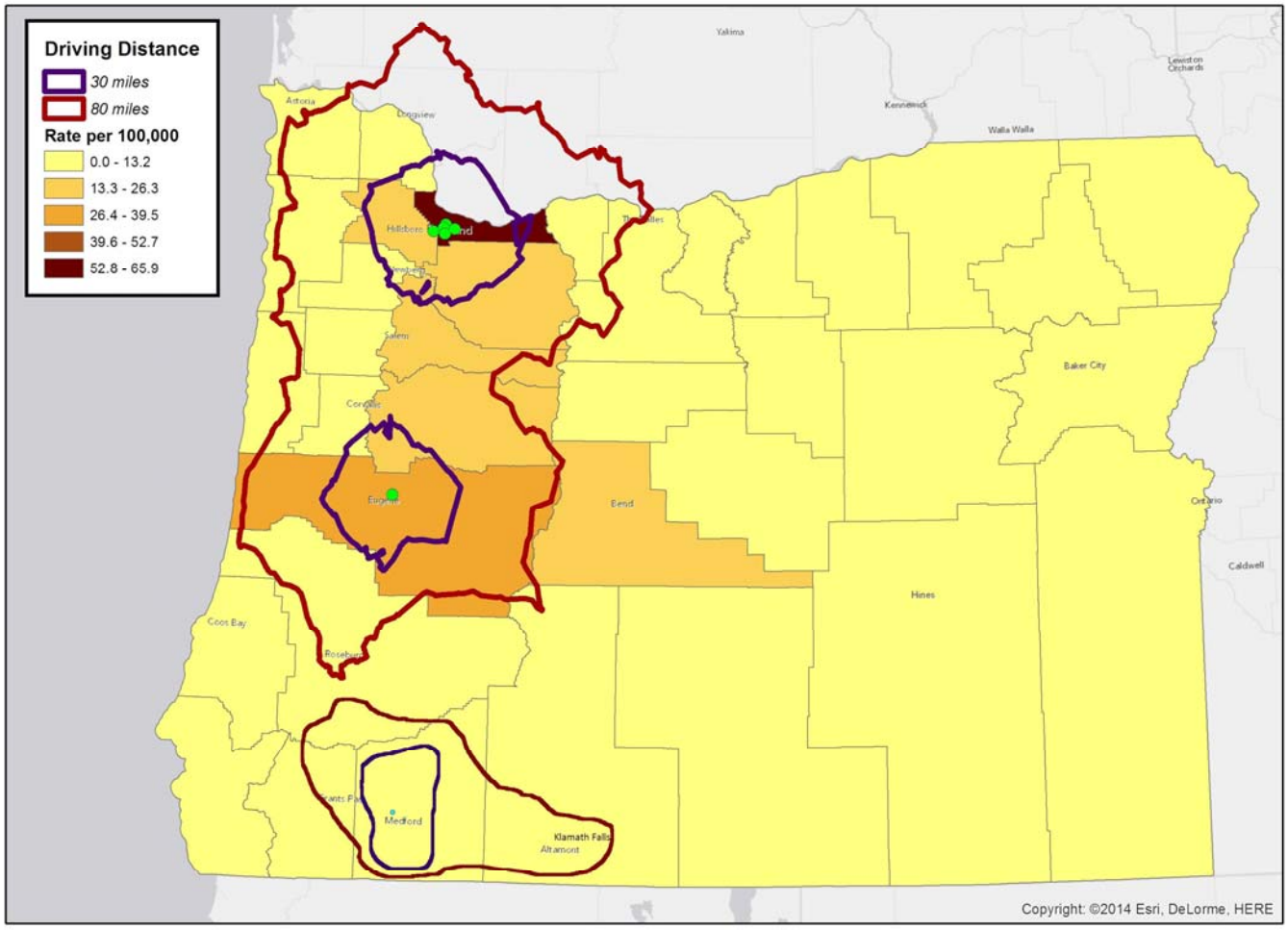
- **With the goal of assuring consistent and high-quality care to all Oregonians, we strongly recommends that any predisposition or presymptomatic genetic testing, including *BRCA* & *MMR* testing, be accompanied with pre- & post-test genetic counseling and conducted by a qualified health care professional with training in genetics.**

8) Aggressive marketing increases provider awareness of available genetic tests, but does not increase knowledge of heritable genetic cancers. The CoC standards, discussed in #1, state clearly that marketing events is not considered adequate training.

- …“educational seminars offered by commercial laboratories about how to perform genetic testing are not considered adequate training for cancer risk assessment and genetic counseling.”
- Oregon providers are regularly being approached by sales representatives, receiving marketing information in the mail, and going to presentations sponsored by genetic testing companies. In addition, patients are also receiving mailings and viewing pharmaceutical commercials. All of this activity is increasing the awareness of available genetic testing, but is not increasing the knowledge about cancer genetic medicine.

9) We recognize that access to genetic services is challenging for many Oregonians, yet **access to cancer genetic services is improving in the state, with new clinics in eastern Oregon and new telemedicine services in Southern Oregon and the Salem area. Expansion into other underserved areas is under discussion.**

Adult Medicaid Cancer Genetic Testing Rates per 100,000 Adult Medicaid Clients, Oregon, 2007-2010



Among the adult Medicaid population who are receiving genetic testing, the majority live within the 80 mile driving distance (red line) of a cancer genetics clinic, and many live within a 30 mile driving distance (blue line). Anecdotal evidence from conversations with cancer

genetic counselors indicate that many individuals are willing to drive long distances to get quality information, risk assessment, and genetic services.

Oregon data indicates that patients who are appropriate for genetic counseling (shown on page 8 & 9) are not given the option of seeking genetic counseling or being referred to a genetic specialist because their providers do not mention genetic counseling or discourage them from seeking genetic counseling.

In summary, the Oregon Genetics Program feels strongly that patients and their families are better served when genetic services are provided by qualified providers wherever possible, as is outlined in the current Medicaid guidelines.

- Our goal is to improve the quality and economy of genetic testing by emphasizing that referral for genetic consultation before testing is preferred wherever possible. The level of expertise needed in the current climate with a rapidly changing array of testing available and increasing complexity of results interpretation in cancer argues for enforcing the current guideline rather than diluting it.
- We feel that genetic consultation before testing is crucial in indicating if testing is necessary, what test is appropriate and who in the family is appropriate to test, as well as to interpret test results.
- CoC Standards define who should be considered a genetic specialist and also define pre- and post-test genetic counseling. These standards are being adopted by CoC credentialed cancer centers and health insurance companies such as Cigna and Priority Health.
- If there is intent to broaden the type of provider that can order testing and provide informed consent for testing, we suggest that the language be in line with CoC Standards, as well as evidence-based guidelines such as the National Comprehensive Cancer Network *(*NCCN) guidelines and the U.S. Preventive Services Task Force (USPSTF) recommendations.

  The current NCCN guidelines state:

  "*Genetic counseling is highly recommended when genetic testing is offered and after results are disclosed. A genetic counselor, medical geneticist, oncologist, surgeon, oncology nurse, or other health professional <u>with expertise and experience in cancer genetics</u> should be involved early in counseling patients who potentially meet criteria for an inherited syndrome."* (p.13, NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Breast and Ovarian version 4.2013, NCCN.org)

If the Healthcare Evidence Review Committee decides to broaden the current cancer genetic services policies, we strongly recommend adding information to the guidelines, instead of removing information. There is clear evidence that non-genetic specialist providers are generally unable to provide appropriate risk assessment and genetic counseling services. We recommend retaining the guideline for genetic counseling as the best option, but expanding

coverage of genetic testing to allow more flexibility regarding the types of professionals allowed to provide genetic testing. Our suggested draft wording is as follows:

DIAGNOSTIC GUIDELINE D1, NON-PRENATAL GENETIC TESTING GUIDELINE

Coverage of genetic testing in a non-prenatal setting shall be determined by the algorithm shown in Figure D1 unless otherwise specified below.

A) Related to genetic testing for patients with breast/ovarian and colon/endometrial cancer or other related cancers suspected to be hereditary, or patients at increased risk to due to family history.

1) Services are provided according to the Comprehensive Cancer Network Guidelines.

a) Lynch syndrome (hereditary colorectal and endometrial cancer, and other cancers associated with Lynch syndrome) services (CPT 81292-81300, 81317-81319) and familial adenomatous polyposis (FAP) services (CPT 81201-81203) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Screening. V.1.2013 (4/13/13). www.nccn.org

b) BRCA1/BRCA2 testing services (CPT 81211-81217) for women without a personal history of breast, ~~and/or~~ ovarian, and other associated cancers should be provided to high risk women as defined in Guideline Note 3 or as otherwise defined by the US Preventive Services Task Force.

c) BRCA1/BRCA2 testing services (CPT 81211-81217) for women with a personal history of breast, ~~and/or~~ ovarian, and other associated ~~-~~cancers and for men with breast cancer or other associated cancers should be provided according to the NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V.1.2011 (4/7/11). www.nccn.org

d) PTEN (Cowden syndrome) services (CPT 81321-81323) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Screening V.1.2013 (5/13/13). www.nccn.org.

2) Genetic counseling should precede genetic testing for hereditary cancer whenever possible. Very rarely, it may be appropriate for a genetic test to be performed prior to genetic counseling for a patient with cancer. If this is done, genetic testing should be accompanied by pre- and post- test informed consent and genetic counseling should be provided as soon as practical.

a) Pre and post-test genetic counseling by the following providers should be covered.

i) Medical Geneticist (M.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics

ii) Clinical Geneticist (Ph.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics.

iii) Genetic Counselor - Board Certified or Active Candidate Status from the American Board of Genetic Counseling, or Board Certified by the American Board of Medical Genetics.

iv) Advance Practice Nurse in Genetics - Credential from the Genetic Nursing Credentialing Commission.

b) If timely pre-test genetic counseling is not possible, appropriate genetic testing accompanied by pre- and post- test informed consent and post-test disclosure performed by a board-certified physician with experience in cancer genetics should be covered.

i) Post-test genetic counseling should be performed as soon as is practical.

GUIDELINE NOTE 3, PROPHYLACTIC TREATMENT FOR PREVENTION OF BREAST CANCER IN HIGH RISK WOMEN

Lines 4,197

Bilateral prophylactic breast removal is included on Line 4 for women without a personal history of invasive breast cancer who are at high risk for breast, ovarian, and other related cancers. Prior to surgery, women without a personal history of breast , ovarian, and other related cancers must have a genetics consultation by the providers outlined in section 2) a). High risk is defined as:

A) Having a BRCA1/BRCA2 mutation;

B) Having a strong family history of breast cancer, defined as one of the following:

1) 2 first-degree or second degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative);

2) 3 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative);

3) 4 relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative);

4) 1 relative with ovarian cancer at any age and, on the same side of the family, either 1 first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years, or 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years, or another ovarian cancer at any age;

5) 1 first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years;

6) 1 first-degree or second-degree relative diagnosed with bilateral breast cancer and one first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years; or,

7) a male relative with breast cancer at any age and on the same side of the family at least 1 first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years, or 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years.

C) A history of LCIS with a family history of breast cancer; or,

D) A history of treatment with thoracic radiation between ages 10 and 30.

Contralateral prophylactic mastectomy is included on Lines 4 and 197 for women with a personal history of breast, ovarian, or other associated cancers and any of the high risk categories listed above. In addition, contralateral prophylactic mastectomy of the unaffected breast is indicated for women with invasive lobular carcinoma.

Prophylactic oophorectomy is included on Line 4 for women who have the BRCA1/BRCA2 mutation.

We also recommend that you keep Figure D1 (Non-Prenatal Genetic Testing Algorithm) as is.

We sincerely thank you for your time and attention to this matter. We highly regard the important work you do and appreciate any opportunity we have to work with you on matters relating to the health of Oregonians and genetics. Please let us know if you have any questions or would like to discuss this or other topics.

Kind regards,

Karen Kovak & Summer Lee Cox

References

Ambry Genetics (2014, January 17). *2014 CPT Codes and Client Pricing*. Retrieved from: https://www.ambrygen.com/sites/default/files/Master_Pricelist_testName_1_17_2014_0.pdf
See Supplemental Material_OGP References page 1

(CoC) American College of Surgeons, Commission on Cancer (2014, January 28). *Cancer program standards 2012: Ensuring patient-centered care (V 1.2.1).* Retrieved from: http://www.facs.org/cancer/coc/programstandards2012.pdf
See Supplemental Material_OGP References page 16

ARUP Laboratories: Value of Genetic Counselors in the Laboratory. Retrieved from: http://www.aruplab.com/files/resources/genetics/White-paper-1-value-of-GCs-in-lab.pdf
See Supplemental Material_OGP References page 19

Bellcross, C., Kolor, K., Goddard, K., Coates, R., Reyes, M., & Khoury, M. (2011). Awareness and utilization of BRCA1/2 testing among U.S. primary care physicians. *American Journal of Preventive Medicine*, 40(1), 61-66. doi:10.1016/j.amepre.2010.09.027
See Supplemental Material_OGP References page 27

Bensend, T., Veach, P., & Niendorf, K. (2014). What's the Harm? Genetic counselor perceptions of adverse effects of genetics service provision by non-genetics professionals. *Journal of Genetic Counseling*, 23(1), 48-63. doi:10.1007/s10897-013-9605-3
See Supplemental Material_OGP References page 33

Brierley, K. L., Blouche, E., Cogswell, W., Homer JP, Pencarinha D, Stanislaw CL, & Matloff ET. (2012). Adverse events in cancer genetic testing: medical, ethical, legal, and financial implications. *Cancer Journal* (Sudbury, Mass.), 18(4), 303-309. doi:10.1097/PPO.0b013e3182609490
See Supplemental Material_OGP References page 49

Cigna - Genetic Testing for Breast & Ovarian Cancer and Genetic Testing for Colorectal Cancer Policies, the full Genetic Testing of Heritable Disorders can be found at: https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/mm_0052_coveragepositioncriteria_genetic_testing.pdf
See Supplemental Material_OGP References page 56

Cox, S., Zlot, A., Silvey, K., Elliott, D., Horn, T., Johnson, A., & Leman, R. (2012). Patterns of cancer genetic testing: a randomized survey of Oregon clinicians. *Journal of Cancer Epidemiology*, 2012294730. doi:10.1155/2012/294730
See Supplemental Material_OGP References page 100

McPherson E, Zaleski C, Benishek K, McCarty CA, Giampietro PF, Reynolds K, Rasmussen K. Clinical genetics provider real-time workflow study. Genet Med. 2008 Sep;10(9):699-706. doi: 10.1097GIM.0b013e318182206f. PubMed PMID: 18978682.

See Supplemental Material_OGP References page 112

Priority Health policy on Genetics: Counseling, Testing and Screening, retrieved from: http://www.priorityhealth.com/provider/manual/auths/~/media/documents/medical-policies/91540.pdf
See Supplemental Material_OGP References page 120

Radford, C., Prince, A., Lewis, K., & Pal, T. (2013). Factors which impact the delivery of genetic risk assessment services focused on inherited cancer genomics: Expanding the role and reach of certified genetics professionals. *Journal of Genetic Counseling*. doi 10.1007/s10897-013-9668-1
See Supplemental Material_OGP References page 146

Riley, B., Culver, J., Skrzynia, C., Senter, L., Peters, J., Costalas, J., & ... Trepanier, A. (2012). Essential elements of genetic cancer risk assessment, counseling, and testing: updated recommendations of the National Society of Genetic Counselors. Journal of Genetic Counseling, 21(2), 151-161. doi:10.1007/s10897-011-9462-x
See Supplemental Material_OGP References page 155

Smith, S. V. (2013, May 14). *The cost of Angelina Jolie's cancer testing? More than $4,000* | *Marketplace.org*. Retrieved from http://www.marketplace.org/topics/business/cost-angelina-jolies-cancer-testing-more-4000
See Supplemental Material_OGP References page166

Trivers, K., Baldwin, L., Miller, J., Matthews, B., Andrilla, C., Lishner, D., & Goff, B. (2011). Reported referral for genetic counseling or BRCA 1/2 testing among United States physicians: a vignette-based study. *Cancer*, 117(23), 5334-5343. doi:10.1002/cncr.26166
See Supplemental Material_OGP References page 168

Wood, M., Stockdale, A., & Flynn, B. (2008). Interviews with primary care physicians regarding taking and interpreting the cancer family history. *Family Practice*, 25(5), 334-340. doi:10.1093/fampra/cmn053
See Supplemental Material_OGP References page 178

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Mary K. Harada, M.D.

Subject: Support Modification to OHP policy

February 18, 2014

To whom it may concern,

The following comments are regarding "The Genetic Counseling Restriction for Non-Prenatal Testing" to be discussed at the Value-based Benefits Subcommittee meeting scheduled for March 13, 2014.

I am writing in support of an OHP policy modification requiring that OHP patients be required to see a Medical Geneticist, Clinical Geneticist, Genetics Counselor or Advanced Practice Nurse in Genetics prior to having BRCA testing.

I am a breast cancer surgeon in Oregon and I have over 27 years of experience in treating breast cancer surgically. Additionally, I am a breast cancer survivor. In my practice, it is a necessity for me to be able to counsel and collect patient samples for the Hereditary Breast and Ovarian Cancer Syndrome (BRCA) prior to making a recommendation for surgery.
If a patient has a BRCA mutation, then they have up to an 87% chance of having breast cancer in either breast in their lifetime. Therefore, if a patient has a BRCA mutation, then I must counsel them about having a double mastectomy. If the patient does not have a BRCA mutation, then I can discuss either having a lumpectomy or a unilateral mastectomy. As you can see, the BRCA test results may have a profound effect on the choices for breast cancer surgery.
I am not a Geneticist, but I feel very competent about discussing the BRCA issues with patients and their families. I service a rural area, so there are no geneticists locally. And to require that a patient see a Geneticist prior to having a BRCA test is poor patient care for two important reasons. Firstly, patients have a very poor follow through on referrals for genetic counseling out of town. Secondly, adding this additional requirement for the patient will delay their treatment and therefore may contribute to a poor outcome. And it may even contribute to their death.

I encourage you to change the OHP policy regarding BRCA testing requirements.

Thank you for your attention and consideration.

Best Regards,

DR. Mary Harada

Dr. Mary Harada

Treatment of sleep apnea in adults - guideline revision

Question: Should the recently approved guideline on sleep apnea in adults be revised?

Question source: Christine Seals, MD, and other Medical Directors from CCOs

Issue: On 1/9/14 HERC approved Prioritized List changes regarding the treatment of sleep apnea in adults, based on an approved Coverage Guidance. The CCO Medical Directors have had concerns with the proposed and approved language. They are most concerned with the allowance of coverage for an AHI from 5 to 14 in the face of limited evidence. They suggested adding language that would clarify the coverage of CPAP for this AHI range if sleep disturbance is not otherwise explainable.

Prioritized list changes approved by HERC 1/9/2014:

GUIDELINE NOTE 27, TREATMENT OF SLEEP APNEA IN ADULTS

Line 210

CPAP is covered initially when all of the following conditions are met:

- 12 week 'trial' period to determine benefit. This period is covered if apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) is greater than or equal to 15 events per hour; or if between 5 and 14 events with additional symptoms including one or more of the following:
    - excessive daytime sleepiness (Epworth Sleepiness Scale score > 10), or
    - documented hypertension, or
    - ischemic heart disease, or
    - history of stroke;
- Providers must provide education to patients and caregivers prior to use of CPAP machine to ensure proper use; and
- Positive diagnosis through polysomnogram (PSG) or Home Sleep Test (HST).

CPAP coverage subsequent to the initial 12 weeks is based on documented patient tolerance, compliance, and clinical benefit. Compliance (adherence to therapy) is defined as use of CPAP for at least four hours per night on 70% of the nights during a consecutive 30 day period.

Mandibular advancement devices (oral appliances) are covered for those for whom CPAP fails or is contraindicated.

Surgery for sleep apnea in adults is not covered.

Treatment of sleep apnea in adults - guideline revision

HERC Staff Recommendations:

Either

1) **Make no change**
   OR
2) **Modify Guideline Note 27 as follows:**

GUIDELINE NOTE 27, TREATMENT OF SLEEP APNEA IN ADULTS

Line 210

CPAP is covered initially when all of the following conditions are met:

- 12 week 'trial' period to determine benefit. This period is covered if apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) is greater than or equal to 15 events per hour; or if between 5 and 14 events with additional symptoms including one or more of the following:
  - excessive daytime sleepiness (Epworth Sleepiness Scale score > 10) that is not attributable to another modifiable sedating condition (e.g. narcotic dependence) or, excessive daytime sleepiness and they are engaged a high risk occupation (e.g. commercial truck driving), or
  - documented hypertension, or
  - ischemic heart disease, or
  - history of stroke;
- Providers must provide education to patients and caregivers prior to use of CPAP machine to ensure proper use; and
- Positive diagnosis through polysomnogram (PSG) or Home Sleep Test (HST).

CPAP coverage subsequent to the initial 12 weeks is based on documented patient tolerance, compliance, and clinical benefit. Compliance (adherence to therapy) is defined as use of CPAP for at least four hours per night on 70% of the nights during a consecutive 30 day period.

Mandibular advancement devices (oral appliances) are covered for those for whom CPAP fails or is contraindicated.

Surgery for sleep apnea in adults is not covered.

Fluoride varnish guideline revision

Question: Fluoride varnish guideline revision

Question source: Deborah Loy, Capitol Dental Care

Issue:
Deborah Loy submitted a letter about fluoride varnish coverage in medical settings (see letter) expressing concerns about coverage of varnish in medical settings in adolescents up to age 18. There was concern about decreasing dental visits because this service was provided in medical offices, as well as inappropriate application in lower risk patients.

Prioritized List background
At the August 8, 2013 VBBS meeting, the D1206 code was added to Lines 3 and 4 (3 only on the ICD-10 List).

Code	Code Description	Current Lines
D1206	Topical application of fluoride varnish	57,3
D1208	Topical application of fluoride	57 PREVENTIVE DENTAL SERVICES

8/8/2013
The evidence reviewed included a MED 2009 report and the ADA 2006 guidelines on the efficacy of fluoride varnish.

1) **MED 2009**
    a. Evidence based review
    b. Good evidence of effectiveness of fluoride varnish twice per year through age 16
2) **American Dental Association 2006**
    a. Recommends fluoride varnish through age 18 for moderate and high risk children twice per year

The adopted guideline note was as follows:

> **GUIDELINE NOTE 17, PREVENTIVE DENTAL CARE**
> *Lines 3,4,58*
>
> Dental cleaning is limited to once per 12 months for adults and twice per 12 months for children up to age 19 (D1110, D1120). More frequent dental cleanings may be required for certain higher risk populations. Additionally, assessment (D0191) may be performed once per 12 months for adults and twice per 12 months for children up to age 19.
>
> Fluoride varnish (D1206) is included on Lines 3 and 4 for use with children 18 and younger during well child preventive care visits. Fluoride

treatments (D1206 and D1208) are included on line Line 58 PREVENTIVE DENTAL SERVICES for use with adults and children during dental visits. The total number of fluoride applications provided in all settings is not to exceed four per twelve months for a child at high risk for dental caries and two per twelve months for a child not at high risk. The number of fluoride treatments is limited to once per 12 months for average risk adults and up to four times per 12 months for high risk adults.

Evidence review on the application of fluoride varnish in medical settings

USPSTF, 2013 DRAFT Assessment of benefit

1. The USPSTF concludes with moderate certainty that there is a moderate net benefit to prescribing oral fluoride supplementation at recommended doses starting at age 6 months to children with inadequate fluoride in their water, and there is a moderate net benefit to applying fluoride varnish to the primary teeth of infants and children starting at the age of primary tooth eruption.
2. The USPSTF found adequate evidence that primary care clinicians can effectively identify dental caries in children age 5 years or younger; however, the USPSTF found inadequate evidence on the effectiveness of screening to improve outcomes and on the harms of screening or treatment. Therefore, the USPSTF concluded that the evidence on the benefits and harms of screening is lacking, and the balance of benefits and harms could not be determined.

USPSTF, 2013 DRAFT Recommendation statement

3. The U.S. Preventive Services Task Force (USPSTF) recommends that primary care clinicians prescribe oral fluoride supplementation starting at age 6 months for children whose water supply is deficient in fluoride, and apply fluoride varnish to the primary teeth of infants and children starting at the age of primary tooth eruption. **B recommendation.**
4. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine screening for dental caries in children from birth to age 5 years by primary care clinicians. **I statement.**

Pahel, 2011

1. Claims review
2. Involved entire North Carolina Medicaid program, childrens aged 72 months or younger from 2000 through 2006.
3. Results: “Children enrolled in North Carolina Medicaid with ≥ 4 IMB visits experienced, on average, a 17% reduction in dental-caries-related treatments up to 6 years of age compared with children with no IMB visits. When we simulated data for initial IMB visits at 12 and 15 months of age,

there was a cumulative 49% reduction in caries-related treatments at 17 months of age. The cumulative effectiveness declined because of an increase in treatments from 24 to 36 months, an increase in referrals for dental caries occurred with increasing time since fluoride application, and emergence of teeth not initially treated with fluoride."

4. Conclusions:
    a. Reduced caries related treatments for children with ≥ 4 IMB visits. Multiple applications of fluoride at the time of primary tooth emergence seem to be most beneficial. Referrals to dentists for treatment of existing disease detected by physicians during IMB implementation limited the cumulative reductions in caries-related treatments, but also contributed to improved oral health.

Stearns, 2012

1. Cost effectiveness analysis
2. Into the Mouths of Babes – model in North Carolina involving screening, parental counseling, topical fluoride application, and referral to dentists, if needed
3. N = 209 285 children enrolled in Medicaid at age 6 months
4. compared children with 4 or more vs 0 IMB visits
5. Results: "Into the Mouths of Babes is 32% likely to be cost-saving, with discounting of benefits and payments. On average, IMB visits cost $11 more than reduced dental treatment payments per person. The program almost breaks even if future benefits from prevention are not discounted, and it would be cost-saving with certainty if IMB services could be provided at $34 instead of $55 per visit. The program is cost-effective with 95% certainty if Medicaid is willing to pay $2331 per hospital episode avoided."

<u>Recommendations from others</u>

Health Resources and Services Administration (HRSA)

- One of HRSA's top strategic priorities and a goal of the 2010-2015 HHS Strategic Plan is the integration of oral health into primary care

AAPD, 2012

Guideline on Infant Oral Health Care

1. *Oral health risk assessment:* Every infant should receive an oral health risk assessment from his/her primary health care pro-vider or qualified health care professional by six months of age.
2. *Establishment of a dental home:* Parents should establish a dental home for infants by 12 months of age.
3. Health care professionals and all other stakeholders in children's oral health should support the identification of a dental home for all infants by 12 months of age.

4. Professionally-applied topical fluoride, such as fluoride varnish, should be considered for children at risk for caries

Bright Futures Guideline Promoting Oral Health

1. Encourage establishment of dental home by age 1
2. Oral health risk assessment in primary care office by age 6 months (policy adopted 2003)
3. in the absence of a dental home program that is able to see the 1- to 4-year-old child, the primary care child health care professional should continue to perform oral health risk assessments in the 1- to 4-year-old child.
4. The AAPD also recommends that health care professionals use the Caries-Risk Assessment Tool (CAT) beginning at age 1 year (Table 1) as part of the oral risk assessment.
5. Some child health care professionals also may provide enhanced oral health counseling or apply fluoride varnish to help with caries prevention in high risk children

HERC staff assessment

The guideline enables coverage of varnish in medical offices for up to ages 18. This is based on evidence up to age 16 in moderate and high risk children and adolescents and the ADA professional guidelines support this, and extend the age up to 18. The 16 to 18 age gap is not supported by evidence, however, there is evidence of efficacy for under 16, the cost is relatively low, and harms are few and 18 is more consistent with other age cutoffs in the Prioritized List.

Medicaid eligibility (i.e. low socioeconomic status) is one of the qualifying definitions of moderate to high risk for which varnish is indicated. All patients under OHP would thus meet this definition of risk.

There is good data that varnish application in primary care settings is effective, and possibly cost-saving. Recommending establishment with a dental provider is part of the risk assessment and fluoride varnish treatment.

HERC Staff Recommendations:

1) Make no change to the current guideline

February 11, 2014

Oregon Health Policy & Research
Health Evidence Review Commission
1225 Ferry Street
Suite C
Salem, Oregon 97301

RE: Dental Procedure Codes D01206, D0145, and D0191

Dear Darren Coffman:

The Health Evidence Review Commission (HERC) has made some recent decisions regarding dental procedure coverage and line placement. I do not feel these decisions have necessarily included input from the Oral Health Advisory Panel (OHAP) and/or if they were discussed the subjects were not well vetted before HERC made a decision. There is a great deal of broad based oral health expertise on the advisory panel to not use it to full advantage.

A decision was made by the HERC to expand coverage in a medical setting of fluoride varnish D1206 up through age 18. As an oral health advisory panel member I do not dispute the evidence and value of fluoride varnish in a medical setting for younger children. It is questionable on its impact for older school age children. This HERC decision was made without input from the OHAP. Having a dental home is a key factor in a child's oral health. It is for this reason that the American Academy of Pediatrics 'Oral Health Risk Assessment Tool' lists 'existing dental home' first on its 'protective factors'. Oregon Health Plan (OHP) utilization shows low penetration rates for young children however, penetration numbers rise significantly for school aged children.

Families covered under OHP struggle with environmental barriers (i.e. transportation, time off from work/school, arranging child care for children not scheduled to be seen etc.). It is for these reasons that medical-dental collaboration surrounding the young child is seen as a best practice. Young children during the first years of life are seeing medical providers for well child checks and immunizations. Incorporating oral health assessment, anticipatory guidance and fluoride varnish during these visits makes good practical sense. It makes less sense to do so with older children and potential confuse parents or through the convenience of not having to seek services from yet one more provider (a dentist) negatively impact either an established dental home or motivation to acquire one. If I am a stressed out mom and my medical provider looks into my child's mouth, gives some hygiene instructions and applies fluoride varnish I am going to think why do I have to make that 'extra visit' to see the dentist.

A medical provider should need to do an oral health risk assessment in order to bill D01206. If a child has an existing dental home (at age?? to be determined in conjunction with input from the OHAP) the OHP member should be found low risk and fluoride varnish in a medical setting after that age would not be covered. If the child does not have an existing dental home vanish would be covered. However, in addition to applying varnish the medical provider would need to make a referral to the coordinated care organization (CCO) for a dental home to be established. One of the CCO metrics being proposed is dental service penetration. Services delivered by a medical provider are not per Medicaid counted as dental services they are oral health services. The CCO has a wonderful opportunity to coordinate care across delivery systems. The HERC's decision to cover fluoride varnish in a medical setting for the older age child seems counter intuitive to Triple Aim goals of better care, services and lower costs. Tearing down delivery system silos versus building new ones is a vision of transformation.

Another decision by the HERC was to place D0145 (oral evaluation for a patient under three years of age) on a medical line to cover this procedure being done by medical providers. I wholeheartedly disagree with this decision. With the Health Insurance Portability and Accountability Act (HIPPA) it not only included privacy rules but also mandated use of national coding standards. For dental that would be the American Dental Association (ADA) Current Dental Terminology (CDT) coding manual. In the CDT under the 'Diagnostic' section are found the clinical evaluation codes. The evaluation codes descriptors state 'the codes in this section recognize the cognitive skills necessary for **patient evaluation**. The collection and recording of some data and components of the dental examination may be delegated, however, the **evaluation, which includes diagnosis and treatment planning, is the responsibility of the dentist…**

The CDT is a copy-write manual. No other procedure code descriptors other than the evaluation codes so clearly calls out the dentist and him/her not delegating this diagnostic component. These evaluation codes are not simply an assessment and/or screening they encompasses the full breadth of dental diagnosing, and treatment planning including development of a preventive oral health regimen. Although I have the utmost respect for the cognitive skills of medical providers the ADA code descriptor requirements of D0145 cannot be met by a medical provider.

Under the OHP and any other Medicaid program requirements a provider must bill the '**most accurate code**' that describes the service delivered. ADA recognized the importance of non-dentists in conducting oral health pre-diagnostic services such as screening and/or assessment. Unlike the evaluation codes the new screening and assessment codes can be done by non-dentists (i.e. medical and/or mid-level dental providers). My recommendation is that HERC remove D0145 from a medical line and instead D0191 (assessment of a patient) described as 'a limited clinical inspection that is performed to identify possible signs of oral or systemic disease, malformation, or injury, and the potential need for referral for diagnosis and treatment should be added to a medical line in its place.

Although Oregon does allow physicians to do dental services it does not relieve a medical provider from being held to the cognitive skills and standard of care expected to do the service as described. It also does not relieve a provider from billing the most accurate code that describes the service. It makes dill or beans to me if some states are allowing medical providers to bill D0145. Many states made this well intentioned but ill resulted decision trying to fill a void of not having any other dental screening and/or assessment codes to choose from. That is not the case today with D0190 and D0191 added to the CDT coding manual. I feel medical providers should be paid in addition to a well child check for doing D0191.

In closing, many in dental have anxiously awaited risk assessment codes. The new risk assessment codes are D0601 (low), D0602 (moderate) and D0603 (high) risk come with a flurry of expectations. The risk assessment that will take place in a medical setting will look very different than those in a dental setting. The average medical encounter has a lot to squeeze in a limited duration of time. Dental will be working out what we hope to see done in utilizing risk assessment codes. Some of those decisions will need additional evidence and debate. Medical on the other hand has an acceptable tool in the oral health risk assessment proposed by the American Academy of Pediatrics. This is the same tool recommended by 'Smiles for Life' a training program with wide support from the medical community. I would recommend its use for medical providers.

I have recommended to the Division of Medical Assistance Programs that medical provider has oral health training available to them similar to what is done in other states. Oregon's 'First Tooth' program or 'Smiles for Life' could be the training curriculum for medical providers. A medical provider who wishes to receive higher reimbursement for oral prevention codes would in states like Washington and North Carolina be required to complete training. Ones who do not want to complete training still may bill the codes but will not be reimbursed at the higher level.

I sincerely hope the HERC reconsiders recent decisions and reconvenes the OHAP for further discussion and vetting.

Sincerely,

Deborah Loy
Capitol Dental Care

Studies assessing impact of enhanced oral health services in medical setting

I did not find many studies measuring the effectiveness of oral health programs in medical settings. I no doubt missed some, so please feel free to send along others.-Weston

Arch Pediatr Adolesc Med. 2012 Oct;166(10):945-51. Available**:** **http://www.ncbi.nlm.nih.gov/pubmed/22926203:**

Cost-effectiveness of preventive oral health care in medical offices for young Medicaid enrollees.

Stearns SC, Rozier RG, Kranz AM, Pahel BT, Quiñonez RB.

Abstract

OBJECTIVE:

To estimate the cost-effectiveness of a medical office-based preventive oral health program in North Carolina called Into the Mouths of Babes (IMB).

DESIGN:

Observational study using Medicaid claims data (2000-2006).

SETTING:

Medical staff delivered IMB services in medical offices, and dentists provided dental services in offices or hospitals.

PARTICIPANTS:

A total of 209 285 children enrolled in Medicaid at age 6 months.

INTERVENTIONS:

Into the Mouths of Babes visits included screening, parental counseling, topical fluoride application, and referral to dentists, if needed. The cost-effectiveness analysis used the Medicaid program perspective and a propensity score-matched sample with regression analysis to compare children with 4 or more vs 0 IMB visits.

MAIN OUTCOME MEASURES:

Dental treatments and Medicaid payments for children up to age 6 years enabled assessment of the likelihood of whether IMB was cost-saving and, if not, the additional payments per hospital episode avoided.

RESULTS:

Into the Mouths of Babes is 32% likely to be cost-saving, with discounting of benefits and payments. On average, IMB visits cost $11 more than reduced dental treatment payments per person. The program almost breaks even if future benefits from prevention are not discounted, and it would be cost-saving with certainty if IMB services could be provided at $34 instead of $55 per visit. The program is cost-effective with 95% certainty if Medicaid is willing to pay $2331 per hospital episode avoided.

CONCLUSIONS:

Into the Mouths of Babes improves dental health for additional payments that can be weighed against unmeasured hospitalization costs.

Pediatrics. 2011 Mar;127(3):e682-9. Available**:** **http://www.ncbi.nlm.nih.gov/pubmed/21357343:**

Effectiveness of preventive dental treatments by physicians for young Medicaid enrollees.

Pahel BT, Rozier RG, Stearns SC, Quiñonez RB.

Abstract

OBJECTIVE:

To estimate the effectiveness of a medical office-based preventive dental program (Into the Mouths of Babes [IMB]), which included fluoride varnish application, in reducing treatments related to dental caries.

METHODS:

We used longitudinal claims and enrollment data for all children aged 72 months or younger enrolled in North Carolina Medicaid from 2000 through 2006. Regression analyses compared subgroups of children who received up to 6 IMB visits at ages 6 to 35 months with children who received no IMB visits. Analyses were adjusted for child and area characteristics.

RESULTS:

Children enrolled in North Carolina Medicaid with ≥ 4 IMB visits experienced, on average, a 17% reduction in dental-caries-related treatments up to 6 years of age compared with children with no IMB visits. When we simulated data for initial IMB visits at 12 and 15 months of age, there was a cumulative 49% reduction in caries-related treatments at 17 months of age. The cumulative effectiveness declined because of an increase in treatments from 24 to 36 months, an increase in referrals for dental caries occurred with increasing time since fluoride application, and emergence of teeth not initially treated with fluoride.

CONCLUSIONS:

North Carolina's IMB program was effective in reducing caries-related treatments for children with ≥ 4 IMB visits. Multiple applications of fluoride at the time of primary tooth emergence seem to be most beneficial. Referrals to dentists for treatment of existing disease detected by physicians during IMB implementation limited the cumulative reductions in caries-related treatments, but also contributed to improved oral health.

Prim Dent Care. 2010 Apr;17(2):53-60 available**: http://www.ncbi.nlm.nih.gov/pubmed/20353653**

A review of effective methods of delivery of care: skill-mix and service transfer to primary care settings.

Williams DM[1], Medina J, Wright D, Jones K, Gallagher JE.

Abstract

AIMS:

Health policy in England is seeking to minimise hospital use and provide access to services in a primary healthcare setting and maximise skill-mix, driven by issues such as cost and access. The aim of this review was to determine the effectiveness of increased use of skill-mix and service transfer within general and oral healthcare. Secondary outcome measures were related to cost, quality, access, health outcomes and satisfaction.

METHODS:

Data sources were the Cochrane Database of Systematic Reviews, Centre for Reviews and Dissemination DARE, British Nursing Index, CINAHL, EMBASE, MEDLINE, and PsycINFO from 1996 to August 2008. The reference lists of relevant papers were scanned to identify additional studies. Data selection: A rapid appraisal of systematic reviews, randomised controlled trials, controlled trials and service evaluations in relation to specialist services, practitioners with a special interest, medical and dental, nursing and dental care professionals, together with evidence of service shifts from secondary to primary care was undertaken.

RESULTS:

A total of 206 papers were reviewed. All titles and abstracts of articles and papers found were extracted and validated according to predefined criteria. They were screened for relevance by two researchers, who assessed

trial quality and extracted data. Twenty-six papers met the inclusion criteria. The literature demonstrated limited evidence of the cost-effectiveness and health outcomes associated with changes in setting and skill-mix. However, there was evidence of improved access, patient and professional satisfaction.

CONCLUSIONS:

There is an overwhelming need for well-designed interventions with robust evaluation to examine cost-effectiveness and benefits to patients and the health workforce.

Evid Based Dent. 2011;12(2):51. Available: **http://www.ncbi.nlm.nih.gov/pubmed/21701550**

Skill-mix and service transfer to primary care settings.

Richards D.

Abstract

DATA SOURCES:

British Nursing Index, CINAHL, Cochrane Database of Systematic Reviews, DARE (Database of Abstracts of Reviews of Effects), EMBASE, Medline, PsycINFO and the reference lists of eligible papers were searched.

STUDY SELECTION:

Studies that focused on practitioners with special interests (PwSIs) or roles clearly created/defined to be practising with special interests, detailing innovative ways of working with a special interest with evidence of formal evaluation of changing role of location of service from systematic reviews or interventions were included. Surveys of views on changing skill-mix or location of services, studies that did not concern dental or medical professionals, dental care or nursing professionals were excluded. Only studies in English and with a UK focus were included.

DATA EXTRACTION AND SYNTHESIS:

All titles and abstracts identified were screened for relevance. Two authors assessed quality and extracted data, queries were reviewed by a third author and a narrative synthesis was presented.

RESULTS:

Twenty-six papers met the criteria with a strong bias towards the medical literature. Five categories emerged:(i) specialist outreach; (ii) general practitioners with a special interest; (iii) nurse practitioners with a special interest; (iv) dental care professionals; (v) out-of-hospital services. Evidence showed specialist outreach clinics to be effective in relation to access and patient satisfaction with some having a higher quality of care but higher cost. However there may be cost-benefits associated with this care, particularly when part of a multifaceted intervention. There is controversy and a limited evidence as to whether the services provided by medical PwSIs are effective, and whether the benefits outweigh the risk and the cost. From the evidence obtained through early innovation, it appears that these services can increase access and are more satisfying for patients, and that these roles have the potential to bring more work satisfaction to the practitioners. Overall, the findings do support the view that moving specialist care into the primary care setting via appropriately trained nurse practitioners is an effective use of resources, but with the caveat that nurse practitioners in primary care are not necessarily cost-effective. There is evidence that professionals complementary to dentistry (PCDs) are able to diagnose a range of conditions and, with appropriate training, complete a wide range of dental procedures as well as dentists, but much of the evidence for other aspects of substitution was of lower quality, weak or insufficient.

CONCLUSIONS:

There was limited evidence of the cost-effectiveness and health outcomes associated with changes in setting and

skill-mix. However, there was evidence of improved access, patient and professional satisfaction. There is an overwhelming need for well-designed interventions with robust evaluation to examine cost-effectiveness and benefits to patients and the health workforce.

J Public Health Dent. 2004 Summer;64(3):164-72. Available: **http://www.ncbi.nlm.nih.gov/pubmed/15341140**

Efficacy of educational interventions targeting primary care providers' practice behaviors: an overview of published systematic reviews.

Sohn W, Ismail AI, Tellez M.

Abstract

OBJECTIVES:

Primary care providers (e.g., family physicians, pediatricians, registered nurses, physician assistants, and nurse practitioners) could play a pivotal role in the provision of preventive services, especially for very young children (younger than 3 years old) and population groups with limited access to dental care. Given the current problems with access to dental care among low-income Americans, we contend there is a need to involve nondental primary health care providers in screening for and preventing oral health problems. The objective of this overview is to present findings from systematic reviews on the efficacy of continuing medical education, printed educational material, academic outreach, reminders, and local opinion leaders on the adoption of new knowledge and practices by primary care providers.

METHODS:

A search was conducted using the Cochrane Library and MEDLINE. The search aimed to locate systematic reviews published between January 1988 and March 2003. Two researchers independently extracted data and assessed study quality using a modified version of the QUOROM statement.

RESULTS:

Eleven systematic reviews were included in this overview. The evidence from the included systematic reviews showed that formal continuing medical education (CME) and distributing educational materials did not effectively change primary care providers' behaviors. There are effective interventions available to increase knowledge and change behaviors of primary care providers, such as small group discussion, interactive workshops, educational outreach visits, and reminders.

CONCLUSION:

There is a limited knowledge base on the efficacy of the selected interventions on oral health screening by primary care providers. Considering the potential role of primary care providers in improving oral health of underserved populations, this research area should receive more attention.

Am J Prev Med. 2004 May;26(4):315-25. Available**: http://www.ncbi.nlm.nih.gov/pubmed/15110059**

Physicians' roles in preventing dental caries in preschool children: a summary of the evidence for the U.S. Preventive Services Task Force.

Bader JD1, Rozier RG, Lohr KN, Frame PS.

Abstract

CONTEXT:

Almost 20% of children aged 2 to 5 years have untreated dental caries. Physician interventions to prevent and

manage dental caries in preschool children could help address this common problem.

OBJECTIVE:

To review the evidence for effectiveness of five possible physician interventions- (1) screening and risk assessment, (2) referral, (3) provision of dietary supplemental fluoride, (4) application of fluoride varnish, and (5) counseling-for the prevention of dental caries for the U.S. Preventive Services Task Force.

DATA SOURCES:

Articles from 1966 to 2001 addressing the effectiveness of primary care clinicians' interventions to prevent or manage dental caries were identified in MEDLINE. The evidence for effectiveness of supplemental fluorides, fluoride varnish, and counseling for caries prevention performed by dental personnel was also examined through existing and new systematic reviews.

DATA SYNTHESIS:

For most key questions related to the five interventions, the evidence for primary care clinician effectiveness was rated as poor owing to the scarcity of studies. Ten surveys of physicians' knowledge and behavior about fluoride supplementation provided fair evidence, suggesting that supplementation decisions were often made without consideration of other fluoride exposures. Reviews of the dental literature identified fair evidence supporting the effectiveness of both fluoride supplements and varnish, although information describing effectiveness and adverse outcomes of supplementation with the most recent dosage schedule is not available.

CONCLUSIONS:

Evidence for the effectiveness of traditionally recommended primary care clinician interventions (screening, referral, counseling) to prevent dental caries in preschool children is lacking. There is fair evidence for the effectiveness of two fluoride-based interventions (fluoride supplementation and varnish) applicable in primary care practice. However, there is also fair evidence indicating that physicians' consideration of fluoride exposure is incomplete, thus increasing the risk for fluorosis among those prescribed supplements.

This is a 2008 dissertation from one of the authors in the North Carolina studies. Not sure it belongs on this list, but it is interesting (and long).

Available: HERE

REFERRALS FOR DENTAL CARE IN A MEDICAL OFFICE-BASED PREVENTIVE DENTAL PROGRAM

BHAVNA TALEKAR PAHEL

A dissertation submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Health Policy and Administration, UNC School of Public Health. Chapel Hill

SPECIAL JADA INSERT

ADA

American Dental Association
www.ada.org

Professionally Applied Topical Fluoride
Executive Summary of Evidence-Based Clinical Recommendations

The ADA Council on Scientific Affairs

May 2006

These evidence-based clinical recommendations were developed by an expert panel established by the American Dental Association Council on Scientific Affairs (CSA) that evaluated the collective body of scientific evidence on the effectiveness of professionally applied topical fluoride for caries prevention. The recommendations are intended to assist dentists in clinical decision-making. The dentist, knowing the patient's health history and vulnerability to oral disease, is in the best position to make treatment decisions in the interest of each patient. For this reason, evidence-based clinical recommendations are intended to provide guidance and are not a standard of care, requirements or regulations. These clinical recommendations must be balanced with the practitioner's professional expertise and the individual patient's preferences.

MedLine and the Cochrane Database of Systematic Reviews were searched for systematic reviews and clinical studies of professionally applied topical fluoride—including gel, foam and varnish forms—through October 2005. The American Dental Association Council on Scientific Affairs formed a panel of experts to evaluate the collective evidence and develop these clinical recommendations. Panelists were selected on the basis of their expertise in the relevant subject matter. They were required to sign a disclosure stating that neither they nor their spouse or dependent children had a significant financial interest that would reasonably appear to affect the development of these recommendations. The panel's recommendations are detailed in a document titled "Professionally Applied Topical Fluoride: Evidence-Based Clinical Recommendations," for which this is the executive summary. The document was submitted for review to scientists with expertise in fluoride and caries, ADA agencies and 46 organizations representing academia, professional organizations, industry and third-party payers. The clinical recommendations are approved by the ADA Council on Scientific Affairs.

GRADING THE EVIDENCE AND CLASSIFYING THE STRENGTH OF THE RECOMMENDATIONS

The scientific evidence was classified according to the following format:

GRADE	CATEGORY OF EVIDENCE
Ia	Evidence from systematic reviews of randomized controlled trials
Ib	Evidence from at least one randomized controlled trial
IIa	Evidence from at least one controlled study with out randomization
IIb	Evidence from at least one other type of quasi-experimental study
III	Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities

The strength of the recommendations were classified according to the following format:

CLASSIFICATION	STRENGTH OF RECOMMENDATIONS
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendation from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence

Amended with permission of BMJ Publishing Group from Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. Brit Med J 1999;318(7183):593-96.

PANEL CONCLUSIONS BASED ON THE EVIDENCE

The following evidence statements and corresponding classification of evidence (in parentheses) represent the conclusions of the expert panel.

1. Fluoride gel is effective in preventing caries in school-aged children (Ia).

2. Patients whose caries risk is low, as defined in this document, may not receive additional benefit from professional topical fluoride application (Ia).

3. There are considerable data on caries reduction for professionally applied topical fluoride gel treatments of 4 minutes or more (Ia). In contrast, there is laboratory, but no clinical equivalency data on the effectiveness of 1-minute fluoride gel applications (IV).

4. Fluoride varnish applied every six months is effective in preventing caries in the primary and permanent dentition of children and adolescents (Ia).

5. Two or more applications of fluoride varnish per year are effective in preventing caries in high-risk populations (Ia).

6. Fluoride varnish applications take less time, create less patient discomfort and achieve greater patient acceptability than does fluoride gel, especially in preschool-aged children (III).

7. Four-minute fluoride foam applications, every 6 months, are effective in caries prevention in the primary dentition and newly erupted permanent first molars (Ib).

8. There is insufficient evidence to address whether or not there is a difference in the efficacy of NaF versus APF gels (IV).

CARIES RISK CATEGORIES

The panel encourages dentists to employ caries risk assessment strategies in their practices. Appropriate preventive dental treatment (including topical fluoride therapy) can be planned after identification of caries risk status. It also is important to consider that risk of developing dental caries exists on a continuum and changes over time as risk factors change. Therefore, caries risk status should be re-evaluated periodically.

The panel understands that there is no single system for caries risk assessment that has been shown to be valid and reliable. However, there is evidence that dentists can use simple clinical indicators to classify caries risk status that is predictive of future caries experience. The panel offers the system outlined below, which is modified from systems that were tested in a clinical setting to classify patients with either low, moderate or high caries risk. This system is offered for guidance and, as stated above, must be balanced with the practitioner's professional expertise. Other resources for assessing caries risk exist and are referenced in the full document.

Low caries risk

All age groups

No incipient or cavitated primary or secondary carious lesions during the last three years and no factors that may increase caries risk*

Moderate caries risk

Younger than 6 years

No incipient or cavitated primary or secondary carious lesions during the last three years but presence of at least one factor that may increase caries risk*

Older than 6 years (any of the following)

One or two incipient or cavitated primary or secondary carious lesions in the last three years

No incipient or cavitated primary or secondary carious lesions in the last three years but presence of at least one factor that may increase caries risk*

High caries risk

Younger than 6 years (any of the following)

Any incipient or cavitated primary or secondary carious lesion during the last three years

Presence of multiple factors that may increase caries risk*

Low socioeconomic status†

Suboptimal fluoride exposure

Xerostomia‡

Older than 6 years (any of the following)

Three or more incipient or cavitated primary or secondary carious lesions in the last three years

Presence of multiple factors that may increase caries risk*

Suboptimal fluoride exposure

Xerostomia‡

*Factors increasing risk of developing caries also may include, but are not limited to

- high titers of cariogenic bacteria;
- poor oral hygiene;
- prolonged nursing (bottle or breast);
- poor family dental health;
- developmental or acquired enamel defects;
- genetic abnormality of teeth;
- many multisurface restorations;
- chemotherapy or radiation therapy;
- eating disorders;
- drug or alcohol abuse;
- irregular dental care;
- cariogenic diet;
- active orthodontic treatment;
- presence of exposed root surfaces;
- restoration overhangs and open margins;
- physical or mental disability with inability or unavailability of performing proper oral health care.

† On the basis of findings from population studies, groups with low socioeconomic status have been found to have an increased risk of developing caries. In children too young for their risk to be based on caries history, low socioeconomic status should be considered as a caries risk factor.

‡ Medication-, radiation- or disease-induced xerostomia.

When reviewing the systematic reviews and clinical trials, the panel considered the caries risk status of the individuals who participated in the studies.

EVIDENCE-BASED CLINICAL RECOMMENDATIONS FOR PROFESSIONALLY APPLIED TOPICAL FLUORIDE

The following table summarizes the evidence-based clinical recommendations for the use of professionally applied topical fluoride. The clinical recommendations are a resource for dentists to use. These clinical recommendations must be balanced with the practitioner's professional judgment and the individual patient's preferences.

It is recommended that all age and risk groups use an appropriate amount of fluoride toothpaste when brushing twice a day, and that the amount of toothpaste used for children under 6 years of age not exceed the size of a pea. For patients at moderate and high risk of caries, additional preventative interventions should be considered, including use of additional fluoride products at home, pit-and-fissure sealants and antibacterial therapy.

RISK CATEGORY	AGE CATEGORY FOR RECALL PATIENTS								
	< 6 Years			6 To 18 Years			18 + Years		
	Recommendation	Grade of Evidence	Strength of Recommendation	Recommendation	Grade of Evidence	Strength of Recommendation	Recommendation	Grade of Evidence	Strength of Recommendation
Low	May not receive additional benefit from professional topical fluoride application*	Ia	B	May not receive additional benefit from professional topical fluoride application*	Ia	B	May not receive additional benefit from professional topical fluoride application*	IV	D
Moderate	Varnish application at 6-month intervals	Ia	A	Varnish application at 6-month intervals OR Fluoride gel application at 6-month intervals	Ia Ia	A A	Varnish application at 6-month intervals OR Fluoride gel application at 6-month intervals	IV IV	D§ D‡
High	Varnish application at 6-month intervals OR Varnish application at 3-month intervals	Ia Ia	A D†	Varnish application at 6-month intervals OR Varnish application at 3-month intervals OR Fluoride gel application at 6-month intervals OR Fluoride gel application at 3-month intervals	Ia Ia Ia IV	A A† A D‡	Varnish application at 6-month intervals OR Varnish application at 3-month intervals OR Fluoride gel application at 6-month intervals OR Fluoride gel application at 3-month intervals	IV IV IV IV	D§ D§ D‡ D‡

* Fluoridated water and fluoride toothpastes may provide adequate caries prevention in this risk category. Whether or not to apply topical fluoride in such cases is a decision that should balance this consideration with the practitioner's professional judgment and the individual patient's preferences.

† Emerging evidence indicates that applications more frequent than twice per year may be more effective in preventing caries.

‡ Although there are no clinical trials, there is reason to believe that fluoride gels would work similarly in this age group.

§ Although there are no clinical trials, there is reason to believe that fluoride varnish would work similarly in this age group.

Laboratory data demonstrate foam's equivalence to gels in terms of fluoride release; however, only two clinical trials have been published evaluating its effectiveness. Because of this, the recommendations for use of fluoride varnish and gel have not been extrapolated to foams.

Because there is insufficient evidence to address whether or not there is a difference in the efficacy of NaF versus APF gels, the clinical recommendations do not specify between these two formulations of fluoride gels. Application time for fluoride gel and foam should be 4 minutes. A 1-minute fluoride application is not endorsed.

ACKNOWLEDGMENTS

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The complete document, "Professionally Applied Topical Fluoride: Evidence-Based Clinical Recommendations," is available online at "www.ada.org/goto/ebd" or by calling the ADA's toll-free number, Ext. 2878.

ADA.
American Dental Association
www.ada.org

Evidence Synthesis
Number 104

Prevention of Dental Caries in Children Younger Than Age 5 Years: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation

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Disclaimer

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The information in this report is intended to help clinicians, employers, policymakers, and others make informed decisions about the provision of health care services. This report is intended as a reference and not as a substitute for clinical judgment.

The final report may be used, in whole or in part, as the basis for the development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. AHRQ or U.S. Department of Health and Human Services endorsement of such derivative products may not be stated or implied.

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Structured Abstract

Background: A 2004 U.S. Preventive Services Task Force (USPSTF) review recommended that primary care clinicians prescribe oral fluoride supplementation to preschool children older than age 6 months whose primary water source is deficient in fluoride, but found insufficient evidence to recommend for or against risk assessment of preschool children by primary care clinicians for the prevention of dental caries.

Purpose: To systematically update the 2004 USPSTF review on prevention of dental caries in children younger than age 5 years by medical primary care clinicians.

Methods: We searched the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the 1st quarter of 2013), and Ovid MEDLINE (1999 through March 8, 2013) and manually reviewed references lists.

Results: No randomized trial or observational study compared clinical outcomes between children younger than age 5 years screened and not screened by primary care clinicians for dental caries. One good-quality cohort study found primary care pediatrician examination following 2 hours of training associated with a sensitivity of 0.76 for identifying a child with one or more cavities and 0.63 for identifying children younger than age 36 months in need of a dental referral, compared with a pediatric dentist evaluation. No study evaluated the accuracy of risk assessment tools applied by primary care clinicians to identify children younger than age 5 years at increased risk for future dental caries. We identified no new trials on the effects of oral fluoride supplementation in children younger than age 5 years on dental caries outcomes. Three randomized trials published since the prior USPSTF review were consistent with three previous trials in finding fluoride varnish more effective than no fluoride varnish in reducing caries incidence in higher-risk children younger than age 5 years (percent reduction in caries increment, 18 to 59 percent), though in all trials fluoride varnish was applied by dental personnel. Three trials reported no clear effects of xylitol versus no xylitol on caries incidence in children younger than age 5 years. Five new observational studies in an updated systemic review were consistent with previous findings of an association between early childhood exposure to systemic fluoride and enamel fluorosis. Other than diarrhea reported in two trials of xylitol, harms were poorly reported in trials of caries prevention interventions. Evidence on the effectiveness of educational or counseling interventions and the effectiveness of primary care referral to a dentist remains sparse or unavailable

Limitations: Only English-language articles were included. Due to limited evidence from randomized trials, we included non-randomized trials. Studies conducted in resource-poor settings may be of limited applicability to screening in the U.S.

Conclusions: Evidence previously reviewed by the USPSTF found oral fluoride supplementation effective at reducing caries incidence in children younger than age 5 years, but associated with risk of enamel fluorosis. New evidence supports the effectiveness of professionally applied fluoride varnish at preventing caries in higher-risk children younger than age 5 years. Research is needed to understand the accuracy of primary care oral health

examination and caries risk assessment, primary care referral to dental care, and effective parental and caregiver/guardian educational and counseling interventions.

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CHAPTER 1. INTRODUCTION

Purpose of Review and Previous USPSTF Recommendation

This report was commissioned by the U.S. Preventive Services Task Force (USPSTF), in order to update its 2004 recommendation on prevention of dental caries by medical primary care clinicians in children younger than age 5 years.[1]

In 2004, the USPSTF recommended that primary care clinicians prescribe dietary fluoride supplementation to children older than age 6 months whose primary water source is deficient in fluoride (**B recommendation**).[1] This recommendation was based on fair evidence that in young children with low fluoride exposure, prescription of dietary fluoride supplements by primary care clinicians is associated with reduced risk of dental caries that outweighs potential harms of enamel fluorosis, which in the United States (U.S.) is primarily manifested as mild cosmetic discoloration of teeth.[2]

In 2004, the USPSTF also concluded that the evidence was insufficient to recommend for or against routine risk assessment of children younger than age 5 years by primary care clinicians for the prevention of dental disease (**I statement**). The USPSTF found no validated risk-assessment tools or algorithms for assessing dental disease risk by primary care clinicians, and little evidence on the accuracy of primary care clinicians in assessing dental disease risk or on performing oral examinations.[3] In addition, the USPSTF found little evidence on the effectiveness of counseling parents or referring high-risk children to dental care providers in reducing risk of caries and related dental disease. Therefore, the USPSTF concluded that there was insufficient evidence to determine the balance between benefits and harms of routine risk assessment to prevent dental disease among children younger than age 5 years.

Condition Definition

Dental caries, or tooth decay, is an infectious process involving breakdown of the tooth enamel. Caries form through a complex interaction between cariogenic, acid-producing bacteria in combination with fermentable carbohydrates and other dietary, genetic, behavioral, social, and cultural factors.[3-5]

Children are susceptible to caries as soon as the first teeth appear, which usually occurs around 6 months of age. Early childhood caries is defined as the presence of one or more *decayed* (non-cavitated or cavitated), *missing* (due to caries), or *filled* tooth surfaces (dmf) in preschool-age children.[6] The abbreviation dmfs refers to decayed, missing, or filled primary tooth *surfaces*, and dmft refers to decayed, missing, or filled primary *teeth* (one tooth may have more than one affected surface).

Prevalence and Burden of Disease

Dental caries is the most common chronic disease of children in the U.S., and is increasing in prevalence among young children.[7,8] The National Health and Nutrition Examination Study (NHANES) found the prevalence of caries experience in primary teeth in 2- to 5-year-olds increased from approximately 24 to 28 percent between 1988 to 1994 and 1999 to 2004.[9] Approximately three quarters of children with caries had not received treatment for the condition.

Dental caries disproportionately affects minority and economically disadvantaged children. NHANES found that among children ages 2 to 11 years, 54 percent of children in families below the federal poverty threshold experienced primary tooth dental caries, compared to one third of children in families with incomes above 200 percent of the poverty threshold.[9] Mexican American children were more likely to experience dental caries in primary teeth (55 percent) than were black children (43 percent) or white children (39 percent), and were more likely to have untreated dental caries (33, 28, and 20 percent, respectively). In addition to higher prevalence, the severity of dental caries is also greater in economically disadvantaged and minority children.[9]

Early childhood caries is associated with pain and loss of teeth, as well as impaired growth, decreased weight gain, and negative effects on quality of life.[3,10] Repairs or extractions of carious teeth can be traumatic experiences for young children, and occasionally result in serious complications. Early childhood caries is also associated with failure to thrive and can affect appearance, self-esteem, speech, and school performance, and is associated with future caries in both the primary and permanent dentitions.[11] Premature loss of primary molars due to early childhood caries can result in loss of arch space, leading to crowding of the permanent teeth, affecting aesthetics and potentially requiring orthodontic correction.[3] In 2000, the U.S. Surgeon General estimated that over 50 million school hours are lost each year nationally due to dental related concerns.[8] More recent data indicate that more than 4 million school hours are lost each year due to dental care in the state of North Carolina, with over 700,000 of these hours lost due to dental pain or infection.[12]

Etiology and Natural History

Dental caries is a disease that occurs when bacteria, predominantly *Streptococcus mutans*, colonize the tooth surface and metabolize dietary carbohydrates (especially refined sugars) to produce lactic and other acids, resulting in demineralization of teeth.[3,13] In children ages 12 to 30 months, caries typically initially affects the maxillary primary incisors and first primary molars, reflecting the pattern of eruption. Dental caries first manifests as white spot lesions, which are small areas of demineralization under the enamel surface. At this stage, the caries lesion is usually reversible. If oral conditions do not improve, demineralization progresses, and eventually results in irreversible cavities, with a loss of the normal tooth shape and contour. Continued progression of the caries process leads to pulpitis and tooth loss, and can be associated with complications such as facial cellulitis and systemic infections.[13,14]

Risk Factors/Indicators

Risk factors for dental caries in young children include high levels of cariogenic bacterial colonization, frequent exposure to dietary sugar and refined carbohydrates, inappropriate bottle feeding, low saliva flow rates, developmental defects of tooth enamel, low socioeconomic status, previous caries, maternal caries, high maternal levels of cariogenic bacteria, and poor maternal oral hygiene.[13,15] Other risk factors include lack of access to dental care, low community water fluoride levels, inadequate tooth brushing or use of fluoride-containing toothpastes, and lack of parental knowledge regarding oral health.[8]

Rationale for Screening/Screening Strategies

Screening for dental caries and risk for caries in young children prior to school entry could identify caries at an earlier and reversible stage and lead to interventions to treat existing caries, prevent progression of caries, and reduce incidence of future lesions. Screening strategies typically include oral health risk assessment and visual examination to identify high-risk children, including those already with caries. Primary care clinicians can play an important role in screening for dental caries because many young children routinely see a primary care provider starting shortly after birth, but do not see a dentist until they are older.[16] Approximately three quarters of children younger than age 6 years did not have at least one visit to a dentist in the previous year, though the proportion with a visit increased from 21 percent in 1996 to 25 percent in 2004.[17] Access to dental care is limited by many factors, including shortages in dentists treating young children, particularly children who are not insured or who are publicly insured.[18] Once children enter school, there are additional opportunities for screening and treatment.[19]

Interventions/Treatment

In young children at risk for dental caries, interventions focus on reducing the burden of bacteria, reducing the intake of refined sugars, and increasing the resistance of teeth to caries development.[3,15] Strategies to reduce the burden of bacteria include the use of fluoride, parental counseling to improve oral hygiene, xylitol, and topical antimicrobials such as chlorhexidine or povidone-iodine. Educational and behavioral interventions can reduce intake of refined sugars through changes in diet and feeding practices. Children with caries or at risk of caries can also be referred for needed dental care.

Fluoride increases the resistance of teeth to caries development. Fluoride exposure can be topical (fluoride dentifrices, rinses, gels, foams, varnishes) or systemic (dietary fluoride supplements).[3,15] Effects of fluoridated water are both topical and systemic. After exposure, fluoride is incorporated into dental plaque, saliva and tooth enamel and increases tooth resistance to acid decay, acts as a reservoir for remineralization of caries lesions, and inhibits cariogenic bacteria.[3,14] A potential harm of excessive systemic fluoride exposure is enamel fluorosis, a visible change in enamel opacity due to altered mineralization. The severity of change depends on the dose, duration and timing of fluoride intake, and is most strongly associated with cumulative intake during enamel development. Mild fluorosis manifests as small opaque white

streaks or specks in the tooth enamel.[2] Severe fluorosis results in discoloration and pitted or rough enamel.[14] The prevalence of severe enamel fluorosis in the U.S. was estimated at less than 1 percent in 1999 to 2004.[2]

Topical fluoride is typically applied as a varnish in young children. Unlike fluoride gels, which are commonly used in older, school-aged children, fluoride varnish does not require specialized dental devices or equipment and can be applied quickly without the risk of the child swallowing large amounts, which can cause transient gastric irritation.[3] Compared to other topical fluoride application methods (such as acidulated phosphate fluoride or sodium fluoride gel), systemic exposure to fluoride is low following application of fluoride varnish.[20,21] The varnish results in prolonged contact time between the fluoride and the tooth surface, enhancing incorporation into the tooth surface layers and more prolonged release. Fluoride varnish is typically available in the U.S. as 5 percent sodium fluoride (2.26 percent F).

Xylitol is a naturally occurring sugar with properties that reduce levels of caries-forming *S. mutans* in the plaque and saliva.[22] In young children, xylitol can be administered as a syrup or topically via wipes. In older children, xylitol can also be administered in gum, lozenges, or snack foods. Other topical antimicrobials such as chlorhexidine varnish and povidone-iodine rinses are not in common use in young children in the U.S. or are not available, as in the case of chlorhexidine varnish.

Current Clinical Practice

Since the publication of the Surgeon General's Report on Oral Health in 2000,[8] many organizations (see below) have emphasized the importance of preventive oral health care for young children, particularly in the primary care setting. The American Academy of Pediatrics (AAP) has developed an oral health risk assessment tool for use in primary care settings starting at the 6-month visit, along with suggested interventions for children at risk.[23] The American Academy of Pediatric Dentistry (AAPD) developed the Caries-risk Assessment Tool (CAT), designed for use by dental and non-dental personnel.[24] Although the vast majority of pediatricians agree with recommendations on oral health screening, only about half report examining the teeth of more than half of their 0- to 3-year-old patients, and few (4 percent) reported regularly applying fluoride varnish.[18]

Recommendations of Other Groups

In 2003, the AAP issued a policy statement that encouraged practitioners to incorporate oral health-related services into their practice by engaging in oral health assessments, anticipatory guidance, and preventive services, including making referrals to dentists. More specifically, an oral health assessment was recommended for all children by age 6 months and a first dental visit by age 1 year.[25] These recommendations were re-affirmed in 2009 and were also endorsed by the Bright Futures program.[26,27] In a second policy statement, the AAP supported the use of dietary fluoride supplementation and the application of fluoride varnish for children at risk for dental caries.[28] The American Dental Association (ADA) recommends the application of fluoride

varnish every 6 months in preschool children at moderate risk of dental caries and every 3 to 6 months in those at high risk.[29] The American Academy of Family Physicians, the ADA, and others recommend that clinicians consider the use of dietary fluoride supplementation in children ages 6 months to 16 years who lack access to adequately fluoridated drinking water.[30,31] Recommended doses of dietary fluoride supplementation range from 0.25 to 1.0 mg per day, depending on age, the level of community or household water fluoridation, and ingestion of other dietary fluoride sources.[31,32] Dietary fluoride supplementation is not recommended when water fluoridation levels are greater than 0.6 ppm F or when caries risk is low.[31]

The Centers for Disease Control and Prevention recommend that clinicians counsel parents about appropriate use of fluoride toothpaste, especially in children younger than age 2 years, prescribe dietary fluoride supplements in children at high risk of dental caries and whose drinking water lacks adequate fluoride, and limit the use of high fluoride concentration products like varnish and gel to high-risk individuals.[14] It recommends that clinicians account for overall ingestion of fluoride through diet, drinking water, and other sources and to consider the risk of dental fluorosis before prescribing supplements or applying high fluoride concentration products.
The AAPD recommends use of xylitol in age-appropriate formulations for moderate- and high-risk children.[22] The ADA recommends xylitol in children age 5 years or older, recommends against use of chlorhexidine varnish, and found insufficient evidence to determine effectiveness of povidone-iodine.[33]

CHAPTER 2. METHODS

Key Questions and Analytic Framework

Using methods developed by the USPSTF,[34,35] representatives from the USPSTF and the Agency for Healthcare Research and Quality (AHRQ) determined the scope and key questions for this review. Investigators created an analytic framework with the key questions and the patient population, interventions, and outcomes reviewed (**Figure 1**). The target population was asymptomatic children younger than age 5 years, including children with existing dental caries who need additional preventive or restorative interventions for untreated disease. Community interventions for prevention of dental caries and school-based interventions for older children are addressed elsewhere by the Community Preventive Services Task Force.[36]

We also addressed a "contextual question" requested by the USPSTF to help inform the report. Contextual questions address background areas deemed important by the USPSTF for informing its recommendations. Contextual questions are not reviewed using systematic review methodology, but rather summarize the evidence from key informative studies.

Key Questions

1. How effective is oral screening (including risk assessment) by the primary care clinician in preventing dental caries in children younger than age 5 years?
2. How accurate is screening by the primary care clinician in identifying children younger than age 5 years who:
    a. Have cavitated or non-cavitated caries lesions?
    b. Are at increased risk for future dental caries?
3. What are the harms of oral health screening by the primary care clinician?
4. How effective is parental or caregiver/guardian oral health education by the primary care clinician in preventing dental caries in children younger than age 5 years?
5. How effective is referral by a primary care clinician to a dentist in preventing dental caries in children younger than age 5 years?
6. How effective is preventive treatment (dietary fluoride supplementation, topical fluoride application, or xylitol) in preventing dental caries in children younger than age 5 years?
7. What are the harms of specific oral health interventions for prevention of dental caries in children younger than age 5 years (parental or caregiver/guardian oral health education, referral to a dentist, and preventive treatments)?

Contextual Question

What percentage of children younger than age 5 years in the U.S. has access to dental care,* and what factors are associated with access to dental care in this population?

*Access to dental care is defined as the ability of a child to receive dental care services, based on availability of dental care providers and/or ability to pay for those services.

Key question 1 focuses on direct evidence on the effectiveness of oral screening (defined to include oral examination as well as risk assessment for future caries) by medical primary care clinicians in preventing future dental caries and associated complications, compared with not screening. Such direct evidence on the effectiveness of screening interventions may be limited. Therefore, the remainder of the analytic framework (key questions 2 through 7) evaluates the chain of indirect evidence needed to link screening with improvement in important health outcomes. Links in the chain of indirect evidence include the accuracy of screening by primary care clinicians for identifying children with dental caries or at increased risk of developing caries, the effectiveness of primary care interventions for reducing the incidence of dental caries and associated complications, and harms (including dental fluorosis) associated with screening and preventive treatments. Implicit in the indirect chain of evidence is that, to understand benefits and harms of screening, it is necessary but not sufficient to show that children at risk for dental caries can be identified; it is also necessary to show that there are effective treatments for those identified.

Search Strategies

We searched Ovid MEDLINE (January 1999 to March 8, 2013) and the Cochrane Library Database (through the first quarter of 2013) for relevant articles. Search strategies are shown in **Appendix A1**. We also reviewed reference lists of relevant articles.

Study Selection

At least two reviewers independently evaluated each study to determine inclusion eligibility. We selected studies on the basis of inclusion and exclusion criteria developed for each key question (**Appendix A2**). Articles were selected for full review if they were about dental caries in preschool children, were relevant to a key question, and met the pre-defined inclusion criteria. We restricted inclusion to English-language articles and excluded studies only published as abstracts. Studies of non-human subjects were also excluded, and studies had to report original data.

For all key questions, we included studies of children younger than 5 years of age, including those with dental caries at baseline. We focused on studies of screening or diagnostic accuracy performed in primary care settings. For preventive treatments (key question 6), we also included studies of primary care feasible treatments (treatments not requiring extensive dental specific training) performed in non-primary care settings, but noted whether the treatment was administered by persons with dental training. Interventions were parental or caregiver education, referral to a dentist by a primary care clinician, and preventive treatments including dietary fluoride supplementation, topical fluoride application, xylitol, and antimicrobial rinses and varnishes. Outcomes were decreased incidence of dental caries and associated complications, and harms, including dental fluorosis. We included randomized controlled trials, non-randomized controlled clinical trials, and cohort studies for all key questions. We also included an updated systematic review of observational studies on risk of enamel fluorosis that was originally included in the 2004 USPSTF review.[37,38] **Appendix A3** shows the results of our

literature search and selection process and **Appendix A4** lists excluded studies with reasons for exclusion.

Data Abstraction and Quality Rating

One investigator abstracted details about each article's study design, patient population, setting, screening method, treatment regimen, analysis, followup, and results. A second investigator reviewed data abstraction for accuracy. Two investigators independently applied criteria developed by the USPSTF[34,35] to rate the quality of each study as good, fair, or poor (**Appendix A5**). Discrepancies were resolved through a consensus process.

Data Synthesis

We assessed the aggregate internal validity (quality) of the body of evidence for each key question ("good," "fair," "poor") using methods developed by the USPSTF, based on the number, quality and size of studies, consistency of results among studies, and directness of evidence.[34,35] Meta-analysis was not attempted due to methodological shortcomings in the studies and differences across studies in design, interventions, populations, and other factors.

External Review

The draft report was reviewed by content experts, USPSTF members, AHRQ Project Officers, and collaborative partners and revised prior to finalization (**Appendix A6**).

CHAPTER 3. RESULTS

Key Question 1. How Effective Is Oral Screening (Including Risk Assessment) by the Primary Care Clinician in Preventing Dental Caries in Children Younger Than Age 5 Years?

No randomized trial or observational study compared clinical outcomes between children younger than age 5 years screened and not screened by primary care clinicians.

Key Question 2a. How Accurate Is Screening by the Primary Care Clinician in Identifying Children Younger Than Age 5 Years Who Have Cavitated or Non-Cavitated Caries Lesions?

Summary

One good-quality study found primary care pediatrician examination of children younger than age 36 months following 2 hours of oral health education associated with a sensitivity of 0.76 for identifying a child with one or more cavities and 0.63 for identifying children in need of a dental referral, compared with a pediatric dentist evaluation.[39] Specificity was 0.95 and 0.98, respectively. A study included in the 2004 USPSTF review found pediatrician examination following 4 hours of oral health education associated with a sensitivity of 1.0 and specificity of 0.87 for identifying nursing caries in children ages 18 to 36 months.[40]

Evidence

The 2004 USPSTF review[3] included one fair-quality study that found a pediatrician oral health exam of children ages 18 to 36 months following 4 hours of training associated with a sensitivity of 1.0 and specificity of 0.87 for identifying nursing caries (defined as caries involving one or more of the maxillary central or lateral incisors or the primary molars, but excluding the mandibular incisors) compared with a pediatric dentist exam.[40] A second study included in the prior USPSTF review found a non-dental nurse exam associated with high sensitivity and specificity, but enrolled children ages 5 to 12 years and is therefore of limited applicability to younger children.[41]

One good-quality study not included in the prior USPSTF review evaluated the accuracy of caries screening of children younger than age 36 months (n=258) by primary care pediatricians following 2 hours of oral health education (**Appendixes B1** and **B2**).[39] The study enrolled Medicaid-eligible children (9.7 percent with a cavity at baseline, mean 0.3 cavities/child) attending a private pediatric group practice in North Carolina. Compared to a pediatric dentist evaluation, it found a sensitivity of 0.76 (19/25) and specificity of 0.95 (222/233) for identifying a child with one or more cavities, a sensitivity of 0.49 (39/80) and specificity of 0.99

(3210/3235) for identifying a tooth with a cavity, and a sensitivity of 0.63 (17/27) and specificity of 0.98 (225/231) for identifying children in need of a dental referral. The need for referral was determined by the presence of a cavity, soft tissue of pathology, or evidence of tooth or mouth trauma.

No study evaluated the accuracy of primary care screening for non-cavitated caries (e.g., white spot) lesions.

Key Question 2b. How Accurate Is Screening by the Primary Care Clinician in Identifying Children Younger Than Age 5 Years Who Are at Increased Risk for Future Dental Caries?

The prior USPSTF review found no study on the accuracy of assessment by primary care clinicians for identifying children at risk for future dental caries.[3] Although risk assessment tools for use in primary care settings are available from the AAP,[24] the AAPD,[24] and the ADA,[42] we found no study on the accuracy of risk assessment by primary care clinicians using these or other instruments.

Key Question 3. What Are the Harms of Oral Health Screening by the Primary Care Clinician?

No randomized trial or observational study compared harms between children younger than age 5 years screened and not screened by primary care clinicians.

Key Question 4. How Effective Is Parental or Caregiver/Guardian Oral Health Education by the Primary Care Clinician in Preventing Dental Caries in Children Younger Than Age 5 Years?

Summary

No trial specifically evaluated an educational or counseling intervention by a primary care clinician to prevent dental caries. One fair-quality and one poor-quality non-randomized trial found multifactorial interventions that included an educational component associated with decreased caries outcomes in underserved children younger than age 5 years.[43-45]

Evidence

The 2004 USPSTF review found no studies on the effectiveness of oral health educational or counseling interventions administered by a primary care clinician.[3] We identified no trials published since the 2004 review that specifically evaluated an educational or counseling intervention, though two non-randomized, controlled clinical trials (reported in three

publications) evaluated oral health educational interventions as a part of multicomponent interventions (**Appendixes B3** and **B4**).[43-45] One study was rated fair-quality[45] and the other poor-quality.[43,44] In addition to using a non-randomized design, other methodological shortcomings in the poor-quality study were high attrition and failure to adjust for confounders.

The fair-quality trial found a multicomponent intervention including additional pediatrician training, provision of an educational brochure, and electronic medical record reminders associated with decreased incidence of cavities versus usual care after 1 year (18 vs. 32 percent, adjusted hazard ratio [HR], 0.23 [95 percent confidence interval [CI], 0.09 to 0.62]).[45] Children were ages 6 months to 5 years at enrollment and recruited from an urban, underserved setting. Results were adjusted for age, race/ethnicity, socioeconomic status, and dietary and oral health risk. The trial used a cluster design, with one intervention and one demographically similar control clinic. Baseline caries prevalence was about 6 percent.

The poor-quality trial also found a multicomponent intervention (including provision of educational materials, counseling on oral hygiene, and provision of toothbrush and toothpaste) associated with a lower prevalence of caries compared to usual care (54 vs. 64 percent; $p=0.03$), dental extraction (3 vs. 12 percent; $p<0.0001$), and mean dmft score (2.2 vs. 3.7; $p<0.001$).[43,44] The intervention was administered between ages 8 and 32 months to children recruited from primary care clinics in an urban, deprived setting and outcomes were assessed at age 5 years. The intervention was administered by health visitors (registered nurses with further training in children health, health promotion, prevention, and education) at healthy child visits.

Key Question 5. How Effective Is Referral by a Primary Care Clinician to a Dentist in Preventing Dental Caries in Children Younger Than Age 5 Years?

Summary

No study directly evaluated the effects of referral by a primary care clinician to a dentist on caries incidence. A fair-quality retrospective cohort study (n=14,389) found that having a first dental preventive visit after age 18 months in children with existing dental disease was associated with increased risk of subsequent dental procedures compared with having a first visit before age 18 months, but was not designed to determine referral source.[46]

Evidence

The 2004 USPSTF report identified no studies on the effects of referral by a primary care clinician to a dentist on dental caries outcomes.[3] We identified no study published since the 2004 USPSTF report that specifically evaluated effects of primary care referral on dental caries outcomes. However, one study may provide indirect evidence on the effects of earlier referral for untreated dental disease. It was a fair-quality retrospective cohort study that found that, among Medicaid children with existing dental disease (n=14,389), having a first dental visit after age 18 months was associated with increased risk of subsequent dental procedures between ages 43 and

72 months compared with having an earlier (before age 18 months) first visit (incidence density ratio ranged from 1.1 to 1.4, depending on time of first dental visit), after adjusting for sex, race, number of well-child visits, and other factors (**Appendixes B5** and **B6**).[46] There was no difference in risk of subsequent dental procedures among children without existing dental disease at baseline. The study does not directly address the key question because it was not designed to determine whether a primary care referral was the source of the initial preventive visit.

Key Question 6. How Effective Is Preventive Treatment in Preventing Dental Caries in Children Younger Than Age 5 Years?

Summary

We identified no trials published since the 2004 USPSTF review on effects of dietary fluoride supplementation in children younger than age 5 years on dental caries incidence. One randomized trial and four other trials included in the 2004 USPSTF review found dietary fluoride supplementation in settings with water fluoridation levels below 0.6 ppm F associated with decreased caries incidence versus no fluoridation (percent reduction in caries increment ranged from 48 to 72 percent for primary teeth and from 51 to 81 percent for tooth surfaces).[3]

We identified three randomized trials published since the 2004 USPSTF review that found fluoride varnish more effective than no fluoride varnish in reducing caries incidence (percent reduction in caries increment, 18 to 59 percent).[47-49] Results were consistent with three randomized trials included in the prior USPSTF review (percent reduction in caries increment, 37 to 63 percent).[3] Most trials were conducted in low socioeconomic status settings with low community water fluoridation levels, but benefits were also observed in studies conducted in adequately fluoridated settings.

Three trials reported no clear effects of xylitol versus no xylitol on caries outcomes in children younger than age 5 years and one trial found no difference between xylitol and tooth brushing, but the trials varied with respect to dosing and formulation of xylitol.[50-53] The most promising results were from a single, small trial of xylitol wipes.[50] Evidence from single trials of chlorhexidine varnish or povidone-iodine solution in children younger than age 5 years was too limited to determine effectiveness.[54,55]

Evidence

Dietary Fluoride Supplementation. We identified no trials published since the 2004 USPSTF review on effects of dietary fluoride supplementation on dental caries outcomes in children younger than age 5 years. The 2004 USPSTF review[3] included six trials[56-61] of dietary fluoride supplements. Sample sizes ranged from 140 to 815 children. Only one of the trials was clearly randomized.[60] None of the non-randomized trials adjusted for potential confounders. Other methodological limitations were inadequate blinding and high or unreported attrition. The trials were also clinically heterogeneous, and varied with respect to age at enrollment (ranging from 2

to 3 weeks to 18 to 39 months), duration of followup (range, 2 to 6 years), dose of fluoride (range, 0.25 to 1.0 mg, varying in part based on child's age), and setting, including one Chinese trial that recruited 2-year-old children from kindergarten.[59]

The single randomized trial (n=140; fluoridation <0.1 ppm F) found use of 0.25 mg fluoride drops or chews associated with decreased incidence of caries versus no fluoride supplementation in Taiwanese children age 2 years at enrollment.[60] Percentage reduction in incidence ranged from 52 to 72 percent for dmft and from 51 to 81 percent for dmfs, depending on whether fluoride was given as tablets or drops. Across all six trials, percentage reductions in incidence with fluoride supplementation ranged from 32 to 72 percent for dmft and 38 to 81 percent for dmfs versus placebo (vitamin drops) or no supplementation. Five trials were conducted in settings with water fluoridation levels below current thresholds for supplementation (<0.6 ppm F).[32,56,58-61] Excluding the trial conducted in a setting above this fluoridation threshold, incidence reductions ranged from 48 to 72 percent for dmft and 51 to 81 percent for dmfs.[57] Two trials with extended followup also found dietary fluoride supplementation in early childhood associated with decreased incidence of caries at ages 7 to 10 years (reductions ranged from 33 to 80 percent).[56,62]

Topical Fluoride. The 2004 USPSTF review included six trials[63-68] on the effectiveness of professionally applied fluoride varnish in preventing dental caries in primary teeth. Two trials[63,64] were randomized and one[66] used alternate allocation; the other three were not randomized. Sample sizes in these three trials ranged from 142 to 225. All of the trials enrolled children between ages 3 and 5 years and followed patients for 2 years[64,66] or 9 months.[63] Community water fluoridation status met recommended thresholds in one trial[63] and was not reported in the other two. Fluoride varnish was applied as 2.26 percent F (Duraphat®) for two applications separated by 4[63] or 6 months,[66] or as four applications over 2 years.[64] No trial utilized a placebo or control treatment and only one[63] clearly reported blinded outcomes assessment. The percent reduction in incident caries lesions ranged from 37 to 63 percent ($p<0.01$ in all trials), with an absolute reduction in the mean number of cavities per child of 0.67 to 1.24 per year.

We identified seven trials published since the 2004 USPSTF review on professionally applied topical fluoride in children younger than age 5 years (**Table 1** and **Appendix B7**).[47-49,69-72] We rated three trials good-quality,[47,48,70] three fair-quality,[49,71,72] and one poor-quality (**Appendix B4**).[69] Six trials were randomized; the poor-quality trial used alternate allocation. Shortcomings in the fair-quality trials included high loss to followup, failure to describe adequate blinding, and failure to describe adequate allocation concealment.

Three trials (two good-quality and one fair-quality) evaluated fluoride varnish (2.26 percent F) applied every 6 months versus no fluoride varnish.[47-49] Sample sizes ranged from 280 to 1146 children. Two trials were conducted in rural Aboriginal populations in Canada (no fluoridation)[47] and Australia (<0.6 ppm F for >90 percent of children, baseline dmfs scores of 3.8 and 11)[48] and used a cluster design. The third trial enrolled underserved, primarily Hispanic and Chinese children in an urban U.S. setting with adequate fluoridation (1 ppm F) who were caries-free at baseline.[49] As in the trials included in the 2004 USPSTF review, fluoride varnish was applied by dental personnel in all studies.

All three trials found use of fluoride varnish associated with decreased caries incidence after 2 years, although the difference was not statistically significant in the Canadian study.[47] Percent reductions in dmfs increment were 18 and 24 percent in the studies of rural Aboriginal populations[47,48] and 59 percent in the U.S. trial.[49] Absolute mean reductions in the number of affected surfaces ranged from 1.0 to 2.4. Fluoride varnish was also associated with decreased risk of having any cavity. The poor-quality trial, which evaluated 2.26 percent F varnish applied every 3 months in Chinese children (with or without removal of carious tissue) reported findings consistent with the fair-quality trials.[69]

Two trials evaluated effectiveness of other methods for administering topical fluoride.[69,70] Both were conducted in China. One good-quality trial found 1.23 percent acidulated phosphate fluoride foam applied every 6 months more effective ($p=0.03$) than placebo (mean percent reduction in dmfs increment, 24 percent; absolute mean reduction in affected surfaces, 1.2).[70] A poor-quality trial found 38 percent silver diamine fluoride solution every 12 months somewhat more effective than 2.26 percent F varnish every 3 months.[69]

Two trials found multiple fluoride varnish applications within a 2-week period associated with no clear differences versus a standard application schedule of every 6 months,[71,72] and one trial found no clear difference between a once- versus twice-yearly schedule.[49]

Xylitol. Xylitol was not an included intervention in the 2004 USPSTF review. We identified four fair-quality[50-52,73] and two poor-quality trials[53,74] of xylitol in children ages 6 months to 5 years (**Table 2**, **Appendixes B4** and **B7**). Two trials enrolled children from settings in which water was not fluoridated[73] or inadequately fluoridated,[53] and the other four did not report water fluoridation status. Five trials were randomized[50-52,73,74] and one used a non-randomized design.[53]

Three trials compared xylitol to no xylitol.[50,52,53] They varied with respect to dosing and formulation of xylitol. A fair-quality randomized trial (n=115) found xylitol tablets (0.48 g) associated with reduced dmfs increment after 2 years, but the difference was not statistically significant (mean percent reduction, 52 percent; absolute mean reduction in affected surfaces, 0.42).[52] The trial enrolled 2-year-old Swedish children, with the intervention consisting of a xylitol tablet at bedtime for 6 months, followed by two tablets daily. One small (n=37) fair-quality randomized trial found xylitol wipes used three times per day for 1 year markedly more effective than placebo wipes in reducing caries among children ages 6 to 35 months (reduction in dmfs increment, 91 percent; $p<0.05$).[50] A poor-quality, non-randomized trial found no effect of xylitol chewing gum (1.33 g) four times daily on incidence of caries in 4-year-old children in Japan.[53]

Two studies compared xylitol to topical fluoride.[51,74] A cluster randomized trial found no difference between 65 percent xylitol gum three times per day versus tooth brushing with fluoride, but was conducted in a supervised daycare setting, and enrolled children up to age 6 years, potentially limiting its applicability to younger children.[51] A poor-quality trial found xylitol chewable tablets (1.2 g three times daily) more effective than fluoride varnish once every 6 months.[74]

One fair-quality randomized trial found xylitol syrup 8 g per day in two or three divided doses

more effective than one 2.67 g dose daily in reducing incidence of caries outcomes.[73]

Other Interventions. One fair-quality cluster randomized trial (n=290) of children ages 4 to 5 years in rural China found 40 percent chlorhexidine acetate varnish associated with decreased caries outcomes versus placebo varnish, with a 37 percent reduction in dmfs incidence in the molar teeth (mean absolute dmfs-molar reduction of 0.6) (**Table 3**, **Appendixes B4** and **B7**).[54]

A fair-quality randomized trial (n=83) of high-risk children age 16 months in Puerto Rico found 0.2 mL of 10 percent povidone-iodine solution applied every 2 months associated with decreased incidence of white spot lesions on maxillary teeth after 1 year (8 vs. 32 percent; relative risk [RR], 0.24 [95 percent CI, 0.1 to 0.8]).[55]

Key Question 7. What Are the Harms of Specific Oral Health Interventions for Prevention of Dental Caries in Children Younger Than Age 5 Years?

Summary

Five new studies in an updated systematic review were consistent with previous studies in finding an association between early childhood ingestion of systemic fluoride and enamel fluorosis of the permanent dentition.[38] Studies were observational and had methodological shortcomings, including use of retrospective recall to determine exposures. Other than diarrhea reported in two trials of xylitol,[53,73] harms were poorly reported in other trials of caries prevention interventions, including no trials reporting incidence or prevalence of fluorosis with fluoride varnish.

Evidence

No trial reported risk of dental fluorosis associated with early childhood ingestion of dietary fluoride supplements. The 2004 USPSTF review included a systematic review of 14 observational studies on risk of fluorosis, based on literature searches conducted through September 1997.[37] Ten of the studies relied on retrospective parental recall of early childhood fluoride ingestion to determine subsequent risk of fluorosis in the permanent dentition. In the other four, early childhood supplemental fluoride use had been recorded at the time of exposure. The dosages of fluoride supplementation in the studies generally exceeded current recommendations. Prevalence of fluorosis ranged from 10 to 49 percent in the studies that relied on retrospective parental recall, and from 15 (on central incisors only) to 67 percent in the studies that recorded supplement use during early childhood. The odds ratios (ORs) for dental fluorosis associated with regular early childhood use ranged from 1.3 to 10.7 in the studies that relied on retrospective recall, and RRs ranged from 4.2 to 15.6 in the studies that recorded supplement use at the time of exposure.

The systematic review included in the 2004 USPSTF review has subsequently been updated with searches conducted through June 2006 (**Appendixes B8** and **B9**).[38] The update included five

additional observational studies on the association between early childhood intake of fluoride supplements and risk of fluorosis.[75-79] Determinations of early childhood exposures were all based on retrospective parental recall, with fluorosis assessed at ages 8 to 14 years. Results of the new studies were consistent with the original systematic review, with intake of fluoride supplements prior to age 7 years (primarily before age 3 years) associated with increased risk of fluorosis. Risk estimates ranged from an OR of 10.8 (95 percent CI, 1.9 to 62) with intake during the first 2 years of life[78] to a slight increase in risk (OR, 1.1 to 1.7; depending on comparison).[75] One study reported a dose-dependent association, with an OR of 1.8 (95 percent CI, 1.4 to 2.4) for each year of supplementation.[79] We identified no studies published since the updated systematic review on the association between early childhood intake of dietary fluoride supplements and risk of enamel fluorosis.

No study reported the risk of fluorosis associated with use of fluoride varnish. However, the degree of systemic exposure following application of fluoride varnish is believed to be low. Two trials reported diarrhea in 11 percent of children allocated to xylitol chewing gum[53] or syrup.[73] Other trials of xylitol[50-52,74] did not report rates of diarrhea.

Contextual Question. What Percentage of Children Younger Than Age 5 Years in the U.S. Has Access to Dental Care, and What Factors Are Associated With Access to Dental Care in This Population?

Based on a national telephone survey (n=89,071) of parents performed in 2003 to 2004, 23 percent of children ages 1 to 5 years lacked dental insurance coverage in the previous year, 51 percent did not receive dental care, and 3.5 percent had a perceived unmet dental need.[80] Children who lacked dental insurance were also less likely to receive preventive care and more likely to have a perceived unmet need for care. In multivariate analyses, factors associated with lack of dental insurance coverage among all children ages 1 to 17 years were being Hispanic and foreign-born, having a non-English primary language spoken at home, having three or more children in the family, lower socioeconomic status, rural residence, living in the South, and lower household education level. An analysis based on 2004 Medical Expenditure Panel Survey (MEPS) data also found that a primary care provider's recommendation for dental care was associated with a threefold increased likelihood (OR, 2.9 [95 percent CI, 2.2 to 3.9]) of having a subsequent dental visit.[81] In 2009, based on MEPS data, the proportion of children ages 1 to 5 years with a dental visit in the prior year was 31 percent (95 percent CI, 28 to 34 percent).[82]

Several studies have shown that expanding access to dental coverage for low-income families through the State Children's Health Insurance Program (SCHIP) and Medicaid programs was associated with an increase in preventive dental visits in eligible children.[83-85] Higher Medicaid payment levels were associated with higher rates of receipt of care.[86]

CHAPTER 4. DISCUSSION

Summary of Review Findings

Dental caries is highly prevalent in children younger than age 5 years. A high proportion of children in this age group do not receive recommended dental care,[80] suggesting a potential role for primary care providers in dental caries prevention. However, as in the 2004 USPSTF review,[3] we found no direct evidence on the effects of screening for dental caries by primary care clinicians in children younger than age 5 years versus no screening on caries incidence and related outcomes. Other evidence reviewed for this update is summarized in **Table 4**.

Newer evidence identified for this update was consistent with findings from the 2004 USPSTF review in showing that fluoride varnish in children younger than age 5 years is effective at reducing caries incidence.[47-49] Because trials were primarily conducted in higher-risk children (based on community water fluoride levels or socioeconomic status), the applicability of these findings to children not at increased risk may be limited, particularly for studies conducted in countries and settings in which sources of fluoride and health behaviors differ markedly from the U.S. In all trials, the varnish was applied by dental personnel, though fluoride varnish is believed to be easily applied with minimal training.[87,88]

We identified no new trials on the effectiveness of dietary fluoride supplementation in children younger than age 5 years. Although the 2004 USPSTF review found dietary fluoride supplementation to be effective at reducing caries incidence in children younger than age 5 years primarily in settings with water fluoridation levels less than 0.6 ppm F, conclusions were mostly based on non-randomized trials.[3] Newer observational studies were consistent with the 2004 USPSTF review in finding an association between early childhood intake of dietary fluoride supplementation and risk of enamel fluorosis.[38] Risk of enamel fluorosis appears to be impacted by total intake of fluoride (from supplements, drinking water, other dietary sources, and dentifrices), as well as age at intake, with intake before age 2 to 3 years appearing to confer highest risk.[89] Although the prevalence of enamel fluorosis has increased in the U.S., severe fluorosis is uncommon, with a prevalence of less than 1 percent.[2,90,91]

Trials of xylitol in children younger than age 5 years found no clear effects on caries incidence, though studies differed in the doses and formulations evaluated.[50,52,53] The most promising results were from a small trial of xylitol wipes that reported a marked decrease in caries incidence, but require confirmation.[50] Evidence on the effectiveness of other interventions not in common use in the U.S. in young children, such as chlorhexidine varnish and povidone-iodine solution, is limited to single trials, precluding reliable conclusions.[54,55]

Evidence remains limited on the accuracy of primary care clinicians in identifying caries lesions in children younger than age 5 years or in predicting caries incidence. One study not included in the prior USPSTF review found that primary care pediatricians missed 24 percent of children in need of a dental referral and 37 percent of children with a cavity, compared to a pediatric dentist exam, though specificity was high.[39] No study evaluated the diagnostic accuracy of caries risk assessment instruments administered by primary care clinicians, despite the availability of

instruments designed for use in primary care settings.[24] Some studies have assessed caries risk assessment instruments in children younger than age 5 years, but the instruments were not administered by primary care providers or in primary care settings. In addition, these instruments often incorporate findings from an oral examination by dental personnel, and include tests not commonly obtained in primary care (such as *S. mutans* levels, saliva secretion level, or saliva buffer capacity),[92,93] potentially limiting applicability of findings to primary care settings.[94,95]

No trial specifically evaluated the effectiveness of parental or caregiver/guardian education on caries outcomes, though limited evidence from two trials suggests that multifactorial interventions in which education was a component could be effective.[43-45] Although some evidence indicates that health care providers' recommendation for dental care increases the likelihood of subsequent dental visits in young children,[81] no trial evaluated the effectiveness of primary care referral to a dentist on caries outcomes. One retrospective cohort study found an association between an early (prior to age 18 months) dental visit and fewer subsequent dental procedures in children with dental disease at baseline.[46]

Limitations

We excluded non-English language articles, which could result in language bias, though we identified no non-English language studies that would have met inclusion criteria. We did not search for studies published only as abstracts and could not formally assess for publication bias with graphical or statistical methods because of the small number of studies for each key question and differences in study design, populations, and outcomes assessed. We found few or no randomized trials for a number of key questions. Therefore, we included non-randomized trials, as well as observational studies (for harms), which are more susceptible to bias and confounding than well-conducted randomized trials.

Emerging Issues

The increasing prevalence of dental caries in young children is an important emerging issue.[9] The reasons for this trend are not completely understood, but could include changes in dietary patterns access to dental care, demographics or socioeconomic status.

Future Research

Research is needed to identify effective oral health educational and counseling interventions for parents and caregiver/guardians of young children. Research is also needed to validate the accuracy and utility of caries risk assessment instruments for use in primary care settings, and to determine how referral by primary care clinicians of young children for dental care affects caries outcomes. Additional trials would strengthen conclusions regarding the effectiveness of dietary fluoride supplementation in young children, especially in the current U.S. context of exposure to multiple sources of fluoride, and trials are needed to demonstrate that results from trials of fluoride varnish applied by dental personnel can be reproduced in primary care settings.

Conclusions

Dietary fluoride supplementation and fluoride varnish appear to be effective at preventing caries outcomes in higher-risk children younger than age 5 years. Dietary fluoride supplementation in early childhood is associated with risk of enamel fluorosis, which is usually mild. More research is needed to understand the accuracy of oral health examination and caries risk assessment by primary care clinicians, primary care referral for dental care, and effective parental and caregiver/guardian educational and counseling interventions.

REFERENCES

1. U.S. Preventive Services Task Force. Prevention of dental caries in preschool children: recommendations and rationale. *Am J Prev Med*. 2004;26(4):326-9. PMID: 15110060
2. Beltran-Aguilar D, Barker LK, Dye BA. Prevalence and Severity of Dental Fluorosis in the United States, 1999–2004. National Center for Health Statistics Data Brief. Hyattsville, MD: National Center for Health Statistics; 2010.
3. Bader JD, Rozier RG, Lohr KN, et al. Physicians' roles in preventing dental caries in preschool children: a summary of the evidence for the U.S. Preventive Services Task Force. *Am J Prev Med*. 2004;26(4):315-25. PMID: 15110059
4. Centers for Disease Control and Prevention. Dental Caries: Hygiene-Related Diseases. Atlanta: Centers for Disease Control and Prevention; 2009. Accessed at http://www.cdc.gov/healthywater/hygiene/disease/dental_caries.html on 23 May 2012.
5. Selwitz RH, Ismail AI, Pitts NB. Dental caries. *Lancet*. 2007;369(9555):51-9. PMID: 17208642
6. American Dental Association. Statement on Early Childhood Caries. Chicago: American Dental Association; 2000. Accessed at http://www.ada.org/2057.aspx on 13 December 2012.
7. National Center for Health Statistics. Healthy People 2010 Final Review. Hyattsville, MD: National Center for Health Statistics; 2012.
8. U.S. Department of Health and Human Services. Oral Health in America: A Report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health; 2000.
9. Dye BA, Tan S, Smith V, et al. Trends in oral health status: United States, 1988–1994 and 1999–2004. *Vital Health Stat 11*. 2007;(248):1-92. PMID: 17633507
10. Kawashita Y, Kitamura M, Saito T. Early childhood caries. *Int J Dent*. 2011;2011:725320. PMID: 22007218
11. Casamassimo PS, Thikkurissy S, Edelstein BL, et al. Beyond the dmft: the human and economic cost of early childhood caries. *J Am Dent Assoc*. 2009;140(6):650-7. PMID: 19491160
12. Jackson SL, Vann WF Jr, Kotch JB, et al. Impact of poor oral health on children's school attendance and performance. *Am J Public Health*. 2011;101(10):1900-6. PMID: 21330579
13. Caulfield PW, Griffen AL. Dental caries: an infectious and transmissible disease. *Pediatr Clin North Am*. 2000;47(5):1001-19. PMID: 11059347
14. Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. *MMWR Recomm Rep*. 2001;50(RR-14):1-42. PMID: 11521913
15. Tinanoff N, Reisine S. Update on early childhood caries since the Surgeon General's report. *Acad Pediatr*. 2009;9(6):396-403. PMID: 19945074
16. American Academy of Pediatrics. Profile of Pediatric Visits: Annualized Estimates 2000–2004. Elk Grove Village, IL: American Academy of Pediatrics; 2007.
17. Edelstein BL, Chinn CH. Update on disparities in oral health and access to dental care for America's children. *Acad Pediatr*. 2009;9(6):415-9. PMID: 19945076

18. Lewis CW, Boulter S, Keels MA, et al. Oral health and pediatricians: results of a national survey. *Acad Pediatr*. 2009;9(6):457-61. PMID: 19945080
19. Community Preventive Services Task Force. Recommendations on selected interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. *Am J Prev Med*. 2002;23(1 Suppl):16-20. PMID: 12091092
20. Ekstrand J, Koch G, Lindgren LE, et al. Pharmacokinetics of fluoride gels in children and adults. *Caries Res*. 1981;15(3):213-20. PMID: 6938306
21. Ekstrand J, Koch G, Petersson LG. Plasma fluoride concentration and urinary fluoride excretion in children following application of the fluoride-containing varnish Duraphat. *Caries Res*. 1980;14(4):185-9. PMID: 6929729
22. American Academy of Pediatric Dentistry. Guideline on Xylitol Use in Caries Prevention. Chicago: American Academy of Pediatric Dentistry: 2011.
23. American Academy of Pediatrics. Oral Health Risk Assessment Tool. Elk Grove Village, IL: American Academy of Pediatrics; 2011. Accessed at http://www2.aap.org/oralhealth/docs/RiskAssessmentTool.pdf on 13 December 2012.
24. American Academy on Pediatric Dentistry Council on Clinical Affairs. Policy on use of a caries-risk assessment tool (CAT) for infants, children, and adolescents. *Pediatr Dent*. 2008;30(7 Suppl):29-33. PMID: 19216377
25. Hale KJ; American Academy of Pediatrics Section on Pediatric Dentistry. Oral health risk assessment timing and establishment of the dental home. *Pediatrics*. 2003;111(5 Pt 1):1113-6.
26. American Academy of Pediatrics. Policy statement—AAP publications retired and reaffirmed. *Pediatrics*. 2009;124(2):845. PMID: 19651598
27. American Academy of Pediatrics. Recommendations for Preventive Pediatric Health Care. Elk Grove Village, IL: American Academy of Pediatrics; 2008.
28. American Academy of Pediatrics, Section on Pediatric Dentistry and Oral Health. Preventive oral health intervention for pediatricians. *Pediatrics*. 2008;122(6):1387-94. PMID: 19015205
29. American Dental Association Council on Scientific Affairs. Professionally applied topical flouride: evidence-based clinical recommendations. *J Dent Educ*. 2007;71(3):393-402. PMID: 17389574
30. American Academy of Family Physicians. Flouridation of Public Water Supplies. Leawood, KS: American Academy of Family Physicians; 2008. Accessed at http://www.aafp.org/online/en/home/policy/policies/f/fluoridationofpublicwatersupplies.html on 12 January 2013.
31. Rozier RG, Adair S, Graham F, et al. Evidence-based clinical recommendations on the prescription of dietary fluoride supplements for caries prevention: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc*. 2010;141(12):1480-9. PMID: 21158195
32. American Academy of Pediatric Dentistry. Guideline on Fluoride Therapy. Chicago: American Academy of Pediatric Dentistry; 2012. Accessed at http://www.aapd.org/media/Policies_Guidelines/G_fluoridetherapy.pdf on 3 May 2013.
33. Rethman MP, Beltran-Aguilar ED, Billings RJ, et al. Nonfluoride caries-preventive agents: executive summary of evidence-based clinical recommendations. *J Am Dent Assoc*. 2011;142(9):1065-71. PMID: 21987836

34. Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. *Am J Prev Med*. 2001;20(Suppl 1):21-35. PMID: 11306229
35. U.S. Preventive Services Task Force. Procedure Manual. Rockville, MD: U.S. Preventive Services Task Force; 2011. Accessed at http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanual.htm on 3 April 2013.
36. Community Preventive Services Task Force. Improving Oral Health: Dental Caries (Cavities). Atlanta: Centers for Disease Control and Prevention; 2010. Accessed at http://www.thecommunityguide.org/oral/caries.html on 27 March 2013.
37. Ismail AI, Bandekar RR. Fluoride supplements and fluorosis: a meta-analysis. *Community Dent Oral Epidemiol*. 1999;27(1):48-56. PMID: 10086926
38. Ismail AI, Hasson H. Fluoride supplements, dental caries and fluorosis: a systematic review. *J Am Dent Assoc*. 2008;139(11):1457-68. PMID: 18978383
39. Pierce KM, Rozier RG, Vann WF Jr. Accuracy of pediatric primary care providers' screening and referral for early childhood caries. *Pediatrics*. 2002;109(5):e82. PMID: 11986488
40. Serwint JR, Mungo R, Negrete VF, et al. Child-rearing practices and nursing caries. *Pediatrics*. 1993;92(2):233-7. PMID: 8337022
41. Beltrán ED, Malvitz DM, Eklund SA. Validity of two methods for assessing oral health status of populations. *J Public Health Dent*. 1997;57(4):206-14. PMID: 9558624
42. American Dental Association. Caries Risk Assessment Form (Age 0-6). Chicago: American Dental Association; 2011. Accessed at http://www.ada.org/sections/professionalResources/pdfs/topics_caries_under6.pdf on 27 March 2013.
43. Davies GM, Duxbury JT, Boothman NJ, et al. A staged intervention dental health promotion programme to reduce early childhood caries. *Community Dent Health*. 2005;22(2):118-22. PMID: 15984138
44. Davies GM, Duxbury JT, Boothman NJ, et al. Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area. *Community Dent Health*. 2007;24(2):117-21. PMID: 17615828
45. Kressin NR, Nunn ME, Singh H, et al. Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention. *Med Care*. 2009;47(11):1121-8. PMID: 19786919
46. Beil H, Rozier RG, Preisser JS, et al. Effect of early preventive dental visits on subsequent dental treatment and expenditures. *Med Care*. 2012;2012:749-56. PMID: 22525611
47. Lawrence HP, Binguis D, Douglas J, et al. A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children. *Community Dent Oral Epidemiol*. 2008;36(6):503-16. PMID: 18422711
48. Slade GD, Bailie RS, Roberts-Thomson K, et al. Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial. *Community Dent Oral Epidemiol*. 2011;39(1):29-43. PMID: 20707872
49. Weintraub JA, Ramos-Gomez F, Jue B, et al. Fluoride varnish efficacy in preventing early childhood caries. *J Dent Res*. 2006;85(2):172-6. PMID: 16434737

50. Zhan L, Cheng J, Chang P, et al. Effects of xylitol wipes on cariogenic bacteria and caries in young children. *J Dent Res*. 2012;91(7 Suppl):85S-90. PMID: 22699675
51. Kovari H, Pienihakkinen K, Alanen P. Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland. *Acta Odontol Scand*. 2003;61(6):367-70. PMID: 14960009
52. Oscarson P, Lif Holgerson P, Sjostrom I, et al. Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children. *Eur Arch Paediatr Dent*. 2006;7(3):142-7. PMID: 17140543
53. Seki M, Karakama F, Kawato T, et al. Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomised trial. *Int Dent J*. 2011;61(5):274-80. PMID: 21995376
54. Du MQ, Tai BJ, Jiang H, et al. A two-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children. *J Dent Res*. 2006;85(6):557-9. PMID: 16723655
55. Lopez L, Berkowitz R, Spiekerman C, et al. Topical antimicrobial therapy in the prevention of early childhood caries: a follow-up report. *Pediatr Dent*. 2002;24(3):204-6. PMID: 12064491
56. Hamberg L. Controlled trial of fluoride in vitamin drops for prevention of caries in children. *Lancet*. 1971;1(7696):441-2. PMID: 4100412
57. Hennon DK, Stookey GK, Beiswanger BB. Fluoride-vitamin supplements: effects on dental caries and fluorosis when used in areas with suboptimum fluoride in the water supply. *J Am Dent Assoc*. 1977;95(5):965-71. PMID: 269878
58. Hennon DK, Stookey GK, Muhler JC. Prophylaxis of dental caries: relative effectiveness of chewable fluoride preparations with and without added vitamins. *J Pediatr*. 1972;80(6):1018-21. PMID: 5026023
59. Hu D, Wan H, Li S. The caries-inhibiting effect of a fluoride drop program: a 3-year study on Chinese kindergarten children. *Chin J Dent Res*. 1998;1(3):17-20. PMID: 10557167
60. Lin YT, Tsai CL. Comparative anti-caries effects of tablet and liquid fluorides in cleft children. *J Clin Dent*. 2000;11(4):104-6. PMID: 11460274
61. Margolis FJ, Macauley J, Freshman E. The effects of measured doses of fluoride. A five-year preliminary report. *Am J Dis Child*. 1967;113(6):670-2. PMID: 4381737
62. Margolis FJ, Reames HR, Freshman E, et al. Flouride. Ten-year prospective study of deciduous and permanent dentition. *Am J Dis Child*. 1975;129(7):794-800. PMID: 1096595
63. Autio-Gold JT, Courts F. Assessing the effect of fluoride varnish on early enamel carious lesions in the primary dentition. *J Am Dent Assoc*. 2001;132(9):1247-53. PMID: 1665349
64. Frostell G, Birkhed D, Edwardsson S, et al. Effect of partial substitution of invert sugar for sucrose in combination with Duraphat® treatment on caries development in preschool children: the Malmo study. *Caries Res*. 1991;25(4):304-10. PMID: 1913770
65. Grodzka K, Augustyniak L, Budny J. Caries increment in primary teeth after application of Duraphat® fluoride varnish. *Community Dent Oral Epidemiol*. 1982;10(2):55-9. PMID: 6952970
66. Holm AK. Effect of a fluoride varnish (Duraphat®) in preschool children. *Community Dent Oral Epidemiol*. 1979;7(5):241-5. PMID: 295702

67. Petersson LG, Twetman S, Pakhomov GN. The efficiency of semiannual silane fluoride varnish applications: a two-year clinical study in preschool children. *J Public Health Dent*. 1998;58(1):57-60. PMID: 9608447
68. Twetman S, Petersson LG, Pakhomov GN. Caries incidence in relation to salivary mutans streptococci and fluoride varnish applications in preschool children from low- and optimal-fluoride areas. *Caries Res*. 1996;30(5):347-53. PMID: 8877088
69. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. *J Dent Res*. 2002;81(11):767-70. PMID: 12407092
70. Jiang H, Bian Z, Tai BJ, et al. The effect of a bi-annual professional application of APF foam on dental caries increment in primary teeth: 24-month clinical trial. *J Dent Res*. 2005;84(3):265-8. PMID: 15723868
71. Weinstein P, Riedy CA, Kaakko T, et al. Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years. *Eur J Paediatr Dent*. 2001;2:91-6.
72. Weinstein P, Spiekerman C, Milgrom P. Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition. *Caries Res*. 2009;43(6):484-90. PMID: 20016179
73. Milgrom P, Ly KA, Tut OK, et al. Xylitol pediatric topical oral syrup to prevent dental caries: a double-blind randomized clinical trial of efficacy. *Arch Pediatr Adolesc Med*. 2009;163(7):601-7. PMID: 19581542
74. Alamoudi NM, Hanno AG, Masoud MI, et al. Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs. An 18-month clinical trial. *Saudi Med J*. 2012;33(2):186-92. PMID: 22327761
75. Bottenberg P, Declerck D, Ghidey W, et al. Prevalence and determinants of enamel fluorosis in Flemish schoolchildren. *Caries Res*. 2004;38(1):20-8. PMID: 14684973
76. Hiller KA, Wilfart G, Schmalz G. Developmental enamel defects in children with different fluoride supplementation: a follow-up study. *Caries Res*. 1998;32(6):405-11. PMID: 9745112
77. Pendrys DG. Risk of enamel fluorosis in nonfluoridated and optimally fluoridated populations: considerations for the dental professional. *J Am Dent Assoc*. 2000;131(6):746-55. PMID: 10860326
78. Pendrys DG, Katz RV. Risk factors for enamel fluorosis in optimally fluoridated children born after the US manufacturers' decision to reduce the fluoride concentration of infant formula. *Am J Epidemiol*. 1998;148(10):967-74. PMID: 9829868
79. Wang NJ, Gropen AM, Øgaard B. Risk factors associated with fluorosis in a non-fluoridated population in Norway. *Community Dent Oral Epidemiol*. 1997;25(6):396-401. PMID: 9429811
80. Liu J, Probst JC, Martin AB, et al. Disparities in dental insurance coverage and dental care among US children: the National Survey of Children's Health. *Pediatrics*. 2007;119(Suppl 1):S12-21. PMID: 17272579
81. Beil HA, Rozier RG. Primary health care providers' advice for a dental checkup and dental use in children. *Pediatrics*. 2010;126(2):e435-41. PMID: 20660547
82. Agency for Healthcare Research and Quality. MEPS HC-126B: 2009 Dental Visits. Rockville, MD: Agency for Healthcare Research and Quality; 2011. Accessed at

http://meps.ahrq.gov/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-126B on 27 March 2013.

83. Kaakko T, Skaret E, Getz T, et al. An ABCD program to increase access to dental care for children enrolled in Medicaid in a rural county. *J Public Health Dent*. 2002;62(1):45-50. PMID: 14700089
84. Lave JR, Keane CR, Lin CJ, et al. The impact of dental benefits on the utilization of dental services by low-income children in western Pennsylvania. *Pediatr Dent*. 2002;24(3):234-40. PMID: 12064498
85. Liao CC, Ganz ML, Jiang H, et al. The impact of the public insurance expansions on children's use of preventive dental care. *Matern Child Health J*. 2010;14(1):58-66. PMID: 19067137
86. Decker SL. Medicaid payment levels to dentists and access to dental care among children and adolescents. *JAMA*. 2011;306(2):187-93. PMID: 21750296
87. Autio-Gold J. Recommendations for fluoride varnish use in caries management. *Dent Today*. 2008;27(1):64-7. PMID: 18240633
88. Bawden JW. Fluoride varnish: a useful new tool for public health dentistry. *J Public Health Dent*. 1998;58(4):266-9. PMID: 10390707
89. Hong L, Levy SM, Broffitt B, et al. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. *Community Dent Oral Epidemiol*. 2006;34(4):299-309. PMID: 16856950
90. Beltran-Aguilar ED, Barker LK, Canto MT, et al. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis—United States, 1988-1994 and 1999-2002. *MMWR Surveill Summ*. 2005;54(3):1-43. PMID: 16121123
91. Pendrys DG. The fluorosis risk index: a method for investigating risk factors. *J Public Health Dent*. 1990;50(5):291-8. PMID: 2231522
92. Bratthall D, Hansel Petersson G. Cariogram—a multifactorial risk assessment model for a multifactorial disease. *Community Dent Oral Epidemiol*. 2005;33(4):256-64. PMID: 16008632
93. MacRitchie HM, Longbottom C, Robertson M, et al. Development of the Dundee Caries Risk Assessment Model (DCRAM)—risk model development using a novel application of CHAID analysis. *Community Dent Oral Epidemiol*. 2012;40(1):37-45. PMID: 21838824
94. Harris R, Nicoll AD, Adair PM, et al. Risk factors for dental caries in young children: a systematic review of the literature. *Community Dent Health*. 2004;21(Suppl 1):71-85. PMID: 15072476
95. Holgerson PL, Twetman S, Stecksen-Blicks C. Validation of an age-modified caries risk assessment program (Cariogram) in preschool children. *Acta Odontol Scand*. 2009;67(2):106-12. PMID: 19152150

Figure 1. Analytic Framework

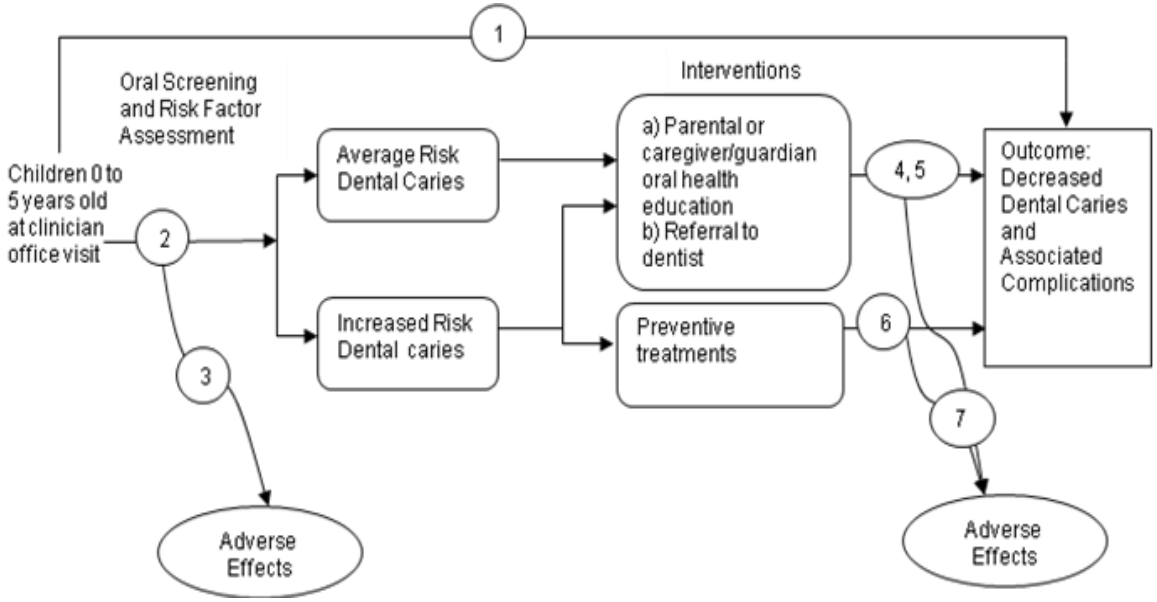

Table 1. Summary of Topical Fluoride Preventive Treatments

Author, year, quality	Study design	Interventions	Country; Setting; Fluoridation status	Age at enrollment	Sample size	Follow-up (yrs)	Mean caries increment	Absolute reduction in caries increment	Reduction in caries increment	Other dental caries outcomes
Chu et al, 2002[69] Poor	Controlled clinical trial	A: Removal of carious tissue plus 38% silver diamine fluoride solution every 12 months B: 38% silver diamine fluoride solution every 12 months C: Removal of carious tissue plus 5% sodium fluoride varnish every 3 months D: 5% sodium fluoride varnish every 3 months E: Placebo (water)	China; Kindergarten; Water fluoridation status: <0.2 ppm	4.0 years	308	2.5	New caries surfaces A: 0.26 B: 0.47 C: 0.89 D: 0.70 E: 1.58 p for ANOVA <0.001, E vs. others	A: 1.32 B: 1.11 C: 0.69 D: 0.88 E vs. others	A: 84% B: 70% C: 44% D: 56% E vs. others	Arrested caries surfaces A: 2.49 B: 2.82 C: 1.45 D: 1.54 E: 1.27 p for ANOVA <0.001, E vs. others
Jiang et al, 2005[70] Good	Cluster RCT (15 clusters)	A: 0.6-0.8 g of 1.23% acidulated phosphate fluoride foam applied every 6 months, max 4 applications B: Placebo foam	China; Kindergarten; Water fluoridation status: 0.1-0.3 ppm	3.5-3.6 years	318	2	dmfs A: 3.8 B: 5.0 p=0.03	1.2	24%	A vs. B No increase in dmfs: 38% (64/167) vs. 26% (40/151) dmfs increase of 1 to 5: 34% (56/167) vs. 38% (58/151) dmfs increase of 6 to 10: 17% (28/167) vs. 18% (27/151) dmfs increase of >10: 11% (19/167) vs. 17% (26/151)
Lawrence et al, 2008[47] Good	Cluster RCT (20 clusters)	A: 0.3-0.5 ml 5% sodium fluoride varnish applied to full primary dentition every 6 months B: No fluoride varnish	Canada; Rural Aboriginal communities; Water fluoridation status: No fluoridation	2.5 years	1146	2	dmfs A: 11.0 (4.3)* B: 13.4 (6.1)* p=0.24 (p=0.18)*	2.4 (1.8)*	18% (29%)*	A vs. B Dental caries in aboriginal cohort: 72% (595/832) vs. 75% (247/328), adjusted OR 0.72 (95% CI 0.42 to 1.25); NNT 26 Dental caries in those caries free at baseline: 44% (157/354) vs. 58% (73/126); adjusted OR 0.63 (95% CI 0.33 to 1.1); NNT 7.4

Table 1. Summary of Topical Fluoride Preventive Treatments

Author, year, quality	Study design	Interventions	Country; Setting; Fluoridation status	Age at enrollment	Sample size	Follow-up (yrs)	Mean caries increment	Absolute reduction in caries increment	Reduction in caries increment	Other dental caries outcomes
Slade et al, 2011[48] Good	Cluster RCT (30 clusters)	A: 0.25 ml of 5% sodium fluoride varnish to maxillary anterior teeth/molars, mandibular molars/incisors every 6 months, education/advice to caregiver with toothbrush/paste provided, community oral health promotion program B: No interventions	Australia; Rural Aboriginal communities; Water fluoridation status: 81-92% had <0.6 ppm F	2.8 years	666	2	dmfs A: 7.3 B: 9.6† p<0.05	2.3	24%	
Weinstein et al, 2001[71] Fair	RCT with 3 treatment groups	A: One application of 5% fluoride varnish at baseline and six months B: Three applications of 5% fluoride varnish within two weeks of baseline C: Three applications of 5% fluoride varnish within two weeks of baseline and six months	United States; Head Start programs; Water fluoridation status: NR	3-5 years	111	1	Clinical dmfs A: 4.6 B: 3.2 C: 4.7 p=0.65 Radiographic mean dmfs A: 0.9 B: 0.5 C: 0.1 p=0.28	Not calculated	Not calculated	
Weinstein et al, 2009[72] Fair	RCT with 2 treatment groups	A: One 5% fluoride varnish treatment and two placebo treatments every six months B: One set of three 5% fluoride varnish treatments over two weeks once per year and three placebo treatments over two weeks six months later	United States Recruitment setting: Head Start programs Water fluoridation status: NR (Yakima voters approved fluoridation in 1999)	55-56 months	515	3	dmfs A: 7.4 B: 9.8 p=0.001	2.4	24%	Adjusted rate ratio of new tooth decay in primary surfaces 1.13 (95% CI 0.94 to 1.37)

Table 1. Summary of Topical Fluoride Preventive Treatments

Author, year, quality	Study design	Interventions	Country; Setting; Fluoridation status	Age at enrollment	Sample size	Follow-up (yrs)	Mean caries increment	Absolute reduction in caries increment	Reduction in caries increment	Other dental caries outcomes
Weintraub et al, 2006[49, ‡] Fair	RCT	A: 0.1 mL of 5% sodium fluoride varnish per arch applied twice per year with four intended applications B: 0.1 mL of 5% sodium fluoride varnish per arch applied once per year with two intended applications C: No fluoride varnish	United States; Family dental center and public health center serving primarily low-income, underserved Hispanic and Chinese populations Water fluoridation status: ~1 ppm	1.8 years	280	2	$d_{2+}fs$[§] A: 0.7 B: 0.7 C: 1.7 p<0.01 for A or B vs. C	1.0	59% (A + B vs. C)	A vs. B vs. C Caries lesions at 12 months: 13% (11/83) vs. 15% (13/86) vs. 29% (27/92); RR 0.45 (95% CI 0.24 to 0.85); NNT 7 for A vs. C and 0.52 (95% CI 0.28 to 0.93); NNT 8 for B vs. C Caries lesions at 24 months: 4.3% (3/70) vs. 14% (10/69) vs. 24% (15/63); RR 0.18 (95% CI 0.06 to 0.59); NNT 6 for A vs. C and 0.61 (95% CI 0.30 to 1.26); NNT 11 for B vs. C

*Children caries free at baseline
[†]Adjusted
[‡]In the fluoride varnish treatment group some children received a placebo varnish instead of fluoride varnish due to protocol errors
[§]Participants were caries-free at baseline

Abbreviations: ANOVA = Analysis of Variance; CI = confidence interval; $d_{2+}fs$ = number of decayed or filled surfaces; dmfs = number of decayed, missing and filled surfaces; F = fluoride; F-U = followup; g = gram; mL = milliliter; NNT = number needed to treat; NR = not reported; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; ppm = parts per million; yrs = years

Table 2. Summary of Xylitol Preventive Treatments

Author, year, quality	Study design	Interventions	Country; Setting; Fluoridation status	Age at enrollment	Sample size	Follow-up (yrs)	Mean caries increment	Absolute reduction in caries increment	Reduction in caries increment	Other dental caries outcomes
Alamoudi et al., 2012[74] Poor	RCT	A: Xylitol chewable tablets (1.2 grams, 84% xylitol) chewed for 5 minutes three times daily B: Fluoride varnish, every 6 months throughout study	Saudi Arabia Recruitment setting: Well baby clinics and dental clinics Water fluoridation status: Not reported	2 to 5 years	34	1.5	dmft A: 0.8 B: 4.4 p=not reported	3.6	82%	A vs. B dmft at baseline: 8.4 vs. 10.3 (p=0.19) dmft at 18 months: 9.2 vs. 14.7 (p=0.001)
Kovari et al., 2003[51, *] Fair	Cluster RCT (11 clusters)	A: 65% Xylitol gum three times per day, chewed for 3-5 minutes, for total of 2.5 g/day B: Tooth brushing with 0.05% NaF toothpaste after lunch	Finland Recruitment setting: Daycare centers Water fluoridation status: Not reported	3 to 6 years	786	3-6	Not reported	Not reported	Not reported	A vs. B Caries at 7 years old: 31% (98/316) vs. 35% (149/427), RR 0.88 (95% CI 0.72 to 1.10) Caries at 9 years old: 43% (133/310) vs. 51% (221/434), RR 0.84 (95% CI 0.72 to 0.99) dmft: 1.1 vs. 1.0 at 7 years, 1.2 vs. 1.6 at 9 years
Milgrom et al., 2009[73, *] Fair	RCT	A: Xylitol 8 gram per day syrup, divided into 2 doses (4 gram per dose) B: Xylitol 8 gram per day syrup, divided into 3 doses (2.67 gram per dose) C: Xylitol 2.67 gram dose syrup one dose per day	Marshall Islands Recruitment setting: Community based Water fluoridation status: Drinking water not fluoridated (supplemental and topical fluoride not available)	14 to 16 months	94	1	Number of decayed teeth A: 0.6 B: 1.0 C: 1.9 p<0.05 for A or B vs. C	A: 1.3 B: 0.9 vs. C	A: 68% B: 47% vs. C	A vs. B vs. C Tooth decay: 24.2% (8/33) vs. 40.6% (13/32) vs. 51.7% (15/29), RR 0.47 (95% CI 0.23 to 0.94) for A vs. C and 0.79 (95% CI 0.45 to 0.1.4) for B vs. C Incidence rates for decayed primary teeth per year: 0.66 vs. 1.10 vs. 2.20

Table 2. Summary of Xylitol Preventive Treatments

Author, year, quality	Study design	Interventions	Country; Setting; Fluoridation status	Age at enrollment	Sample size	Follow-up (yrs)	Mean caries increment	Absolute reduction in caries increment	Reduction in caries increment	Other dental caries outcomes
Oscarson et al., 2006[52] Fair	RCT	A: One 0.48 gram xylitol tablet at bedtime after brushing for 6 months; then one tablet twice daily to age 3 years and 6 months B: No tablets	Sweden Recruitment setting: Public dental clinic Water fluoridation status: Not reported	25 months	115	2	dmfs A: 0.38 B: 0.80 p>0.05	0.42	52%	A vs. B Dental caries: 18% (10/55) vs. 25% (16/63), OR 0.65 (95% CI 0.27 to 1.59)
Seki et al., 2011[53] Poor	Cluster, non-randomized controlled clinical trial (3 clusters)	A: Xylitol chewing gum (100% xylitol, 1.33 grams); one pellet chewed 5 minutes four times daily B: No intervention	Japan Recruitment setting: Preschool Water fluoridation status: Not reported (states fluoridation "limited" in Japan)	66-72% 4 years old	161	1	dfs A: 3.3 B: 3.4 p>0.05	0.1	3%	A vs. B Development of caries from baseline to 6 months: 1.7 vs. 1.6 (p>0.05) Development of caries from 6 months to 1 year: 1.6 vs. 1.8 (p>0.05)
Zhan et al., 2012[50] Fair	RCT	A: Xylitol wipes, two at a time, three times per day (estimated daily dosage 4.2 g) every 3 months B: Placebo wipes	U.S. Recruitment setting: University pediatric clinic Water fluoridation status: Not reported	6-35 months	37	1	dmfs† A: 0.05 B: 0.53 p=0.01	0.48	91%	A vs. B New caries lesions at 1 year†: 5% vs. 40% (p=0.03); NNT 3 ITT analysis of new caries lesions at 1 year: 5% vs. 32%; RR 0.14 (95% CI 0.02 to 1.07); NNT 4

*Baseline caries status not defined
†Numbers based on per protocol analysis

Abbreviations: CI = confidence interval; dfs = decayed and filled services; dmfs = decayed, missing, and filled surfaces; dmft = decayed, missing, and filled teeth; F-U = followup; g = grams; NaF = sodium fluoride; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; U.S. = United Sates; yrs = years; NNT = number needed to treat

Table 3. Summary of Other Preventive Treatments

Author, year, quality	Study design	Interventions	Country; Setting; Fluoridation status	Age at enrollment	Sample size	F-U (yrs)	Mean caries increment	Absolute reduction in caries increment	Reduction in caries increment	Other dental caries outcomes
Du et al., 2006[54] Fair	Cluster RCT (14 clusters)	A: 40% w/w chlorhexidine acetate varnish every 6 months B: Placebo varnish	China; Kindergartens in rural communities; Water fluoridation status: 0.1-0.3 ppm	4-5 years	290	2	dmfs-molar: A: 1.0 B: 1.6 p=0.036	0.6	37%	
Lopez et al., 2002[55] Fair	RCT	A: 0.2 ml of 10% povidone-iodine solution every 2 months B: Placebo solution	United States; Women, infant and children clinic in Puerto Rico; Water fluoridation status: NR	16 months	83	1	Not reported	Not reported	Not reported	A vs. B* White spot lesions - maxillary primary incisors: 8% (3/39) vs. 32% (14/44); RR 0.24 (95% CI 0.1 to 0.8)

*Participants were caries-free at baseline

Abbreviations: CI = confidence interval; dmfs = decayed, missing, filled surfaces; F-U = followup; mL = milliliter; NR = not reported; ppm = parts per million; RCT = randomized controlled trial; RR = relative risk; w/w = weight/weight; yrs = years

Table 4. Summary of Evidence

Main findings from 2005 USPSTF review	Number and type of studies identified for update *Overall quality**	Limitations	Consistency	Applicability	Summary of findings
Key Question 1. How effective is oral screening (including risk assessment) by the primary care clinician in preventing dental caries in children younger than 5 years of age?					
No evidence	No studies	No studies	No studies	No studies	No randomized trial or observational study compared clinical outcomes between children younger than 5 years of age screened and not screened by primary care clinicians.
Key Question 2a. How accurate is screening by the primary care clinician in identifying children younger than 5 years of age who have cavitated or non-cavitated caries lesions?					
One study found pediatrician examination following 4 hours of oral health education associated with a sensitivity of 1.0 and specificity of 0.87 for identifying nursing caries in children 18 to 36 months of age.	One cohort study *Overall quality: Fair*		N/A	Study conducted in a primary care setting	One study found primary care pediatrician examination following 2 hours of oral health education associated with a sensitivity of 0.76 for identifying a child with one or more cavities and 0.63 for identifying children <36 months of age in need of a dental referral, compared with a pediatric dentist evaluation.
Key Question 2b. How accurate is screening by the primary care clinician in identifying children younger than 5 years of age who are at increased risk for future dental caries?					
No evidence	No studies	No studies	No studies	No studies	No study evaluated the accuracy of risk assessment tools applied by primary care clinicians to identify children at increased risk for future dental caries.
Key Question 3. What are the harms of oral health screening by the primary care clinician?					
No evidence	No studies	No studies	No studies	No studies	No randomized trial or observational study compared harms between children younger than 5 years of age screened and not screened by primary care clinicians.
Key Question 4. How effective is parental or caregiver/guardian oral health education by the primary care clinician in preventing dental caries in children younger than 5 years of age?					
No evidence	1 randomized trial, 1 non-randomized trial *Overall quality: Poor*	Non-randomized design, high attrition, failure to adjust for confounders.	Moderate inconsistency	Education evaluated as part of a multifactorial intervention	No trial specifically evaluated an educational or counseling intervention to prevent dental caries. Two studies found multifactorial interventions that included an educational component associated with decreased incidence or prevalence of cavities in underserved children younger than 5 years of age.
Key Question 5. How effective is referral by a primary care clinician to a dentist in preventing dental caries in children younger than 5 years of age?					
No evidence	1 cohort study *Overall quality: Poor*	Study not designed to determine whether a primary care referral was the source of the initial preventive visit	N/A	Medicaid population, higher risk children	No study directly evaluated the effects of referral by a primary care clinician to a dentist on caries incidence. One study found a first dental preventive visit after 18 months of age in children with existing dental disease associated with increased risk of subsequent dental procedures compared with a first visit before 18 months of age, but was not designed to determine referral source.

Table 4. Summary of Evidence

Main findings from 2005 USPSTF review	Number and type of studies identified for update *Overall quality**	Limitations	Consistency	Applicability	Summary of findings
Key Question 6. How effective is preventive treatment with *dietary fluoride supplementation* in preventing dental caries in children younger than 5 years of age?					
6 trials of dietary fluoride supplements. One randomized trial and four other trials found oral fluoride supplementation in settings with water fluoridation levels below 0.6 ppm F associated with decreased caries incidenceversus no fluoridation (ranges of 48 percent to 72 percent for primary teeth and 51 percent to 81 percent for primary tooth surface).	No studies *Overall quality: Fair*	Limitations in previously reviewed studies include use of non-randomized design, not controlling for confounders, inadequate blinding and high or unreported attrition	N/A	No studies	We identified no new trials on the effects of dietary fluoride supplementation in children younger than 5 years of age on dental caries incidence.
Key Question 6. How effective is preventive treatment with *topical fluoride* application (fluoride varnish) in preventing dental caries in children younger than 5 years of age?					
Three randomized trials found fluoride varnish more effective than no fluoride varnish in reducing caries incidence (percent reduction 37 percent to 63 percent, with an absolute reduction in the mean number of cavities per child of 0.67 to 1.24 per year.)	6 randomized trials, 1 trial using alternate allocation *Overall quality: Fair*	High loss to followup, failure to describe adequate blinding, and failure to describe adequate allocation concealment	Consistent	Rural settings with inadequate fluoridation or low socioeconomic status settings	Three randomized trials published since the prior review found fluoride varnish more effective than no fluoride varnish in reducing caries incidence (percent reduction in caries increment 18 to 59 percent). Other trials evaluated methods of topical fluoride application not used in the United States or compared different doses or frequencies of topical fluoride.
Key Question 6. How effective is preventive treatment with *xylitol* in preventing dental caries in children younger than 5 years of age?					
No studies (not included in the prior review)	5 randomized trials; 1 non-randomized *Overall quality: Fair*	Variability in xylitol formulation and dosing	Some inconsistency	Children from settings where water was not fluoridated or fluoridation limited	Three trials reported no clear effects of xylitol versus no xylitol on caries incidence in children younger than 5 years, with the most promising results from a small (n=37) trial of xylitol wipes. One trial found no difference between xylitol and toothbrushing.

Table 4. Summary of Evidence

Main findings from 2005 USPSTF review	Number and type of studies identified for update *Overall quality**	Limitations	Consistency	Applicability	Summary of findings
Key Question 7. What are the harms of specific oral health interventions for prevention of dental caries in children younger than 5 years of age (parental or caregiver/guardian oral health education, referral to a dentist, and preventive treatments)?					
1 systematic review of 14 observational studies found dietary fluoride supplementation in early childhood associated with increased risk of fluorosis; odd ratios ranged from 1.3 to 15.6 and prevalence ranged from 10 percent to 67 percent.	5 observational studies in an updated systematic review *Overall quality: Fair*	Use of retrospective parental recall to determine exposures	Consistent	Doses of fluoride generally higher than currently recommended	Five observational studies in an updated systemic review were consistent with previously reported findings in showing an association between early childhood ingestion of systemic fluoride and enamel fluorosis. Other than diarrhea reported in two trials of xylitol, harms were poorly reported in other trials of caries prevention interventions in children younger than 5 years of age.

* "Overall quality" is based on new evidence identified for this update plus previously reviewed evidence.

Abbreviations: CT = randomized controlled trial; USPSTF = United States Preventive Services Task Force.

Appendix A1. Search Strategies

Database: Ovid MEDLINE(R) without Revisions <1999 to March 8 2013>
Search Strategy:
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1 exp physicians/
2 exp pediatrics/ or pediatrician$.mp.
3 exp nurse practitioners/
4 exp nurse's aides/
5 exp physician assistants/
6 exp nurse clinicians/
7 nurses/
8 Primary care physician$.mp.
9 General practitioner$.mp.
10 Primary care clinician$.mp.
11 exp ambulatory care facilities/
12 exp primary health care/
13 exp physician's role/
14 exp physician's practice patterns/
15 exp mass screening/
16 exp health behavior/
17 exp health promotion/
18 exp infant welfare/
19 exp health services accessibility/
20 exp child health services/
21 exp "referral and consultation"/
22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 limit 22 to (english language and humans)
24 limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or technical report or validation studies)
25 exp epidemiologic study characteristics/
26 exp epidemiologic research design/
27 exp questionnaires/
28 (25 or 26 or 27) and 23
29 24 or 28
30 exp dental caries/
31 Dental screening.mp. or exp dental care for children/
32 dental care/ or dental examination.mp. or exp diagnosis, oral/
33 30 or 31 or 32
34 29 and 33
35 limit 34 to (infant <1 to 23 months> or preschool child <2 to 5 years>)

Database: Ovid MEDLINE(R) without Revisions <1999 to March 8, 2013>
Search Strategy:
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1 exp physicians/

Appendix A1. Search Strategies

2 exp pediatrics/ or pediatrician$.mp.
3 exp nurse practitioners/
4 exp nurse's aides/
5 exp physician assistants/
6 exp nurse clinicians/
7 nurses/
8 Primary care physician$.mp.
9 General practitioner$.mp.
10 Primary care clinician$.mp.
11 exp ambulatory care facilities/
12 exp primary health care/
13 exp physician's role/
14 exp physician's practice patterns/
15 exp mass screening/
16 exp health behavior/
17 exp health promotion/
18 exp infant welfare/
19 exp health services accessibility/
20 exp child health services/
21 exp "referral and consultation"/
22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 limit 22 to (english language and humans)
24 limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or technical report or validation studies)
25 exp epidemiologic study characteristics/
26 exp epidemiologic research design/
27 exp questionnaires/
28 (25 or 26 or 27) and 23
29 24 or 28
30 exp MOTHERS/
31 exp PARENTS/
32 30 or 31
33 exp dental health services/ or dental utilization.mp. or exp dental care/
34 29 and 33
35 limit 34 to (infant <1 to 23 months> or preschool child <2 to 5 years>)

Database: Ovid MEDLINE(R) without Revisions <1999 to March 8, 2013>
Search Strategy:
---
1 exp physicians/
2 exp pediatrics/ or pediatrician$.mp.
3 exp nurse practitioners/
4 exp nurse's aides/
5 exp physician assistants/

Appendix A1. Search Strategies

6 exp nurse clinicians/
7 nurses/
8 Primary care physician$.mp.
9 General practitioner$.mp.
10 Primary care clinician$.mp.
11 exp ambulatory care facilities/
12 exp primary health care/
13 exp physician's role/
14 exp physician's practice patterns/
15 exp mass screening/
16 exp health behavior/
17 exp health promotion/
18 exp infant welfare/
19 exp health services accessibility/
20 exp child health services/
21 exp "referral and consultation"/
22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 limit 22 to (english language and humans)
24 limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or technical report or validation studies)
25 exp epidemiologic study characteristics/
26 exp epidemiologic research design/
27 exp questionnaires/
28 (25 or 26 or 27) and 23
29 24 or 28
30 exp mothers/
31 exp parents/
32 30 or 31
33 exp fluorides, topical/
34 exp fluorides/
35 exp cariostatic agents/
36 Supplemental fluoride$.mp.
37 Fluoride tab$.mp.
38 Fluoride drop$.mp.
39 Fluoride varnish$.mp.
40 33 or 34 or 35 or 36 or 37 or 38 or 39
41 29 and 40
42 limit 41 to (newborn infant <birth to 1 month> or infant <1 to 23 months> or preschool child <2 to 5 years>)

Database: Ovid MEDLINE(R) without Revisions <1999 to March 8, 2013>
Search Strategy:
---
1 exp physicians/

Appendix A1. Search Strategies

2 exp pediatrics/ or pediatrician$.mp.
3 exp nurse practitioners/
4 exp nurse's aides/
5 exp physician assistants/
6 exp nurse clinicians/
7 nurses/
8 Primary care physician$.mp.
9 General practitioner$.mp.
10 Primary care clinician$.mp.
11 exp ambulatory care facilities/
12 exp primary health care/
13 exp physician's role/
14 exp physician's practice patterns/
15 exp mass screening/
16 exp health behavior/
17 exp health promotion/
18 exp infant welfare/
19 exp health services accessibility/
20 exp child health services/
21 exp "referral and consultation"/
22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 limit 22 to (english language and humans)
24 limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or technical report or validation studies)
25 exp epidemiologic study characteristics/
26 exp epidemiologic research design/
27 exp questionnaires/
28 (25 or 26 or 27) and 23
29 24 or 28
30 exp MOTHERS/
31 exp PARENTS/
32 30 or 31
33 exp dental care for children/
34 exp dental caries/
35 exp oral hygiene/
36 exp oral health/
37 exp health education, dental/
38 exp diet, cariogenic/
39 exp dental care/
40 33 or 34 or 35 or 36 or 37 or 38 or 39
41 29 and 40
42 limit 41 to (infant <1 to 23 months> or preschool child <2 to 5 years>)

Database: Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) <1946 to March 8, 2013>

Appendix A1. Search Strategies

Search Strategy:

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1 exp "Pit and Fissure Sealants"/
2 exp Dental Caries/
3 exp fluorosis, dental/
4 2 or 3
5 1 and 2
6 limit 5 to "all child (0 to 18 years)"
7 ((tooth or teeth or pit or pits or fissur$) adj5 seal$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
8 2 and 7
9 limit 8 to "all child (0 to 18 years)"
10 ((tooth or teeth or enamel$ or crown or root or dental$ or molar$ or incisor$ or bicuspid$ or canine$ or premolar$) adj5 (decay$ or carie$ or fluorosis)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
11 1 and 10
12 limit 11 to "all child (0 to 18 years)"
13 6 or 9 or 12
14 (201206$ or 201207$ or 201208$ or 201209$ or 20121$).ed.
15 13 and 14
16 exp Tooth Demineralization/
17 ((tooth or teeth or root$ or crown$ or dental$ or dentist$) adj5 (caries or cario$ or decay$ or cavit$ or fluorosis)).mp.
18 16 or 17
19 xylitol.mp.
20 18 and 19
21 limit 20 to "all child (0 to 18 years)"

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <February 2013>
Search Strategy:

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1 (physician$ or pediatrician$ or general practi$ or primary care or primary health care or nurse or nurses or (nurs$ adj3 (care or caring or cared or cares)) or screen$ or (health$ adj3 (behav$ or promot$ or access$)) or referral$ or consult$ or counsel$ or parent$ or mother$ or father$ or guardian$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (62097)
2 ((dental$ or tooth or teeth$) adj7 (caries or decay$ or fluorid$ or xylitol or sealant$ or sealing or cariostat$ or fluorosis) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (968)
3 ((dental or dentist$ or oral) adj7 (screen$ or fluorid$ or checkup$ or (check$ adj up) or exam or exams or examine$ or examination$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (343)
4 ((dental or dentist$ or oral) adj3 (hygien$ or health$ or prophyla$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (384)

Appendix A1. Search Strategies

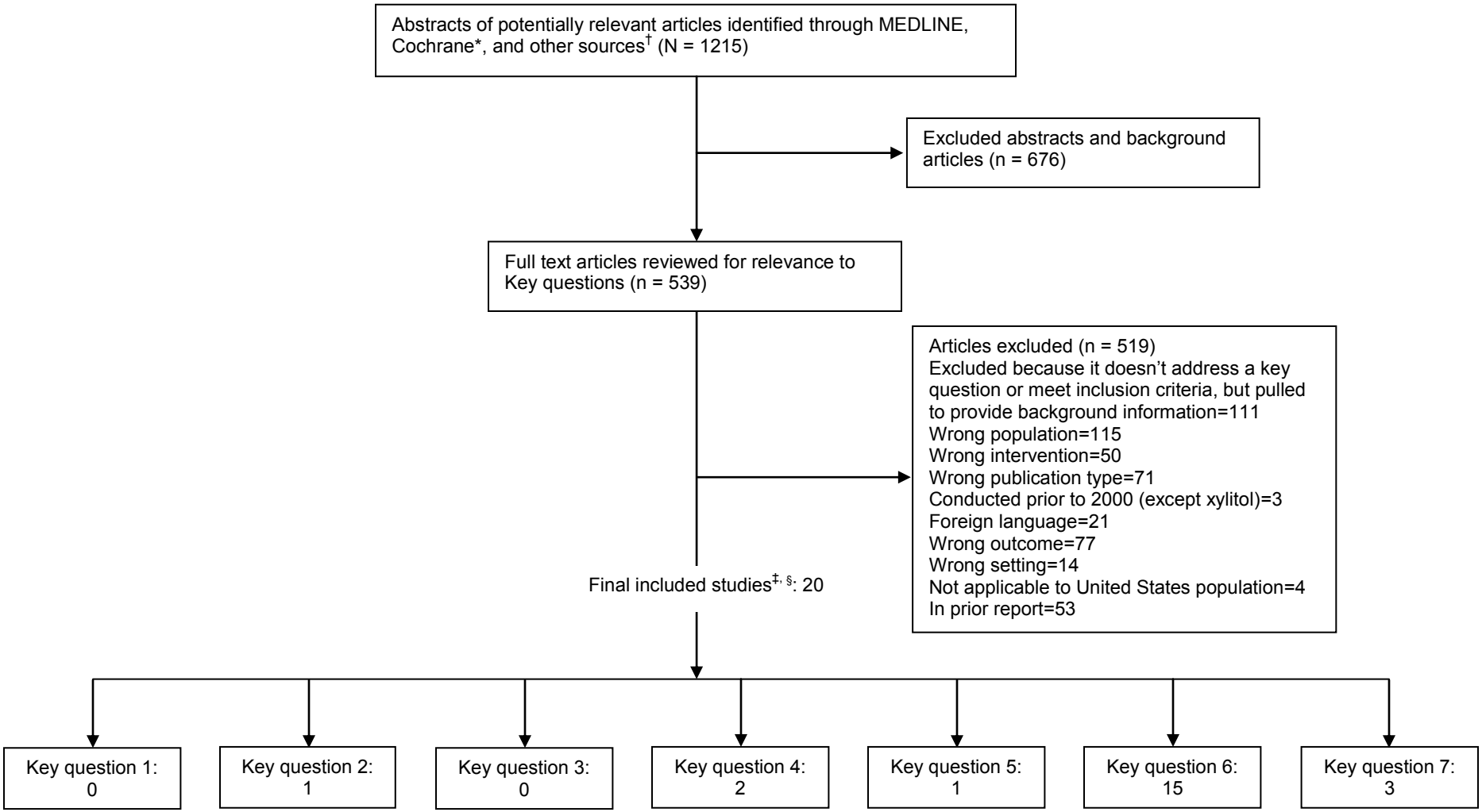
5 2 or 3 or 4 (1263)
6 1 and 5 (239)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <1999 to February 2013>
Search Strategy:
---
1 (physician$ or pediatrician$ or general practi$ or primary care or primary health care or nurse or nurses or (nurs$ adj3 (care or caring or cared or cares)) or screen$ or (health$ adj3 (behav$ or promot$ or access$)) or referral$ or consult$ or counsel$ or parent$ or mother$ or father$ or guardian$).mp. [mp=title, abstract, full text, keywords, caption text] (6578)
2 ((dental$ or tooth or teeth$) adj7 (caries or decay$ or fluorid$ or xylitol or sealant$ or sealing or cariostat$ or fluorosis) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, abstract, full text, keywords, caption text] (43)
3 ((dental or dentist$ or oral) adj7 (screen$ or fluorid$ or checkup$ or (check$ adj up) or exam or exams or examine$ or examination$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, abstract, full text, keywords, caption text] (39)
4 ((dental or dentist$ or oral) adj3 (hygien$ or health$ or prophyla$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, abstract, full text, keywords, caption text] (47)
5 2 or 3 or 4 (78)
6 1 and 5 (75)

Appendix A2. Inclusion and Exclusion Criteria

	Include	Exclude
Population	All key questions: Asymptomatic children less than 5 years of age	All key questions Animal studies, adults, children older than preschool age (>5 years), symptomatic
Interventions	Key questions 1-3: Oral screening and risk factor assessment performed by primary care clinicians Key questions 4 and 5: Parent/caregiver/guardian oral health education and/or referral to dentist Key questions 6 and 7: Preventive treatments: including oral fluoride supplementation, topical fluoride application, or xylitol	Key questions 1-3: Community or school-based interventions Key questions 4 and 5: Interventions not performed in primary care settings Key questions 6 and 7: Treatments not available for preschool children or not available in the United States
Outcomes	All key questions Reduced dental caries and associated outcomes Key questions 2 and 3: Diagnostic accuracy and measures of risk prediction Key question 7: Dental fluorosis, emotional stress, acute toxicity, and other associated complications	All key questions Cost-effectiveness
Study types and designs	Key questions 1, 4, 5, and 6: Randomized controlled trials, non-randomized controlled clinical trials, and cohort studies Key question 2: Studies of diagnostic accuracy or risk prediction Key questions 3 and 7: Randomized controlled trials, cohort studies, case-control studies, and systematic reviews	Key questions 1, 2, 4, 5, and 6: Case-control studies, uncontrolled intervention studies All key questions: Opinion, editorials, or case reports

Appendix A3. Literature Flow Diagram



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Identified from reference lists, hand searching, suggested by experts, etc.
‡Studies that provided data and contributed to the body of evidence were considered 'included'.
§Studies may have provided data for more than one key question.

Appendix A4. Excluded Studies List

Key to exclusion codes

2	Excluded because it doesn't address a key question or meet inclusion criteria, but pulled to provide background information
3	Wrong population
4	Wrong intervention
5	Wrong publication type
6	Conducted prior to 2000 (except xylitol)
7	Foreign language, otherwise included
8	Wrong outcome
9	Wrong setting
10	Not applicable to United States population
11	In prior report

List of excluded studies

Diet, nutrition, and oral health: a rational approach for the dental practice. *J Am Dent Assoc.* 1984;109(1):20-32, [PMID: 6589288]
Exclusion code: 5

NIH Consensus Development Conference on Diagnosis and Management of Dental Caries Throughout Life. Bethesda, MD, March 26-28, 2001. Conference Papers. *J Dent Educ.* 2001;65(10):935-1179., [PMID: 11706839]
Exclusion code: 11

The endless learning curve: 2005 Table Clinic winners. *Northwest Dent.* 2005;84(3):23-27, [PMID: 16044850]
Exclusion code: 2

Xylitol-containing oral syrup may prevent caries in children. *J Am Dent Assoc.* 2009;140(8):972, [PMID: 19654247]
Exclusion code: 5

Aaltonen AS, Suhonen JT, Tenovuo J, Inkila-Saari I. Efficacy of a slow-release device containing fluoride, xylitol and sorbitol in preventing infant caries. *Acta Odontol Scand.* 2000;58(6):285-292, [PMID: 11196405]
Exclusion code: 4

Aasenden R, DePaola PF, Brudevold F. Effects of daily rinsing and ingestion of fluoride solutions upon dental caries and enamel fluoride. *Archives of Oral Biology.* 1972;17(12):1705-1714, [PMID: 4405216]
Exclusion code: 3

Ad Hoc Committee on Fluoride, Committee to Coordinate Environmental Health and Related Programs. Review of Fluoride: Benefits and Risks. Washington, DC: US Department of Health and Human Services; 1991: http://health.gov/environment/ReviewofFluoride/.
Exclusion code: 11

Adair PM, Pine CM, Burnside G, et al. Familial and cultural perceptions and beliefs of oral hygiene and dietary practices among ethnically and socio-economicall diverse groups. *Community Dent Health.* 2004;21(1 Suppl):102-111, [PMID: 15072479]
Exclusion code: 4

Adams SH, Hyde S, Gansky SA. Caregiver acceptability and preferences for early childhood caries preventive treatments for Hispanic children. *J Public Health Dent.* 2009;69(4):217-224, [PMID: 19486461]
Exclusion code: 8

Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey. 2011; http://meps.ahrq.gov/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-126B. Accessed 27 March, 2013
Exclusion code: 2

Akerblom HK, Koivukangas T, Puukka R, Mononen M. The tolerance of increasing amounts of dietary xylitol in children. *International journal for vitamin and nutrition research. Supplement.* 1982;22:53-66, [PMID: 6802776]
Exclusion code: 3

Al Ghanim NA, Adenubi JO, Wyne AA, Khan NB. Caries prediction model in pre-school children in Riyadh, Saudi Arabia. *Int J Paediatr Dent.* 1998;8(2):115-122, [PMID: 9728096]
Exclusion code: 8

Appendix A4. Excluded Studies List

Alaluusua S, Malmivirta R. Early plaque accumulation – a sign for caries risk in young children. *Comm Dent Oral Epidemiol* 1994;22:273-276, [PMID: 7813174]
Exclusion code: 8

Alanen P, Holsti ML, Pienihakkinen K. Sealants and xylitol chewing gum are equal in caries prevention. *Acta Odontol Scand.* 2000;58(6):279-284, [PMID: 11196404]
Exclusion code: 3

Alanen P, Isokangas P, Gutmann K. Xylitol candies in caries prevention: results of a field study in Estonian children. *Community Dent Oral Epidemiol.* 2000;28(3):218-224, [PMID: 10830649]
Exclusion code: 3

Alonge OK, Williamson DD, Narendran S. Dental fluorosis among third graders in Harris County, Texas--1998 study findings. *Texas dental journal.* 2000;117(9):22-29, [PMID: 11857845]
Exclusion code: 3

American Academy of Family Physicians. Flouridation of public water supplies. *Policies* 2008; http://www.aafp.org/online/en/home/policy/policies/f/fluoridationofpublicwatersupplies.html. Accessed 12 January, 2013
Exclusion code: 2

American Academy of Pediatric Dentistry. Caries risk assessment for infants, children, and adolescents. *Pediatr Dent.* 2011;33:110-117.
Exclusion code: 2

American Academy of Pediatric Dentistry. Guideline on Caries-risk Assessment and Management for Infants, Children, and Adolescents. *American Academy of Pediatric Dentistry Reference Manual.* 2011;32(6):101-108.
Exclusion code: 2

American Academy of Pediatric Dentistry. Guideline on fluoride therapy. *AAPD 2012-2013 Clinical Guidelines.* 2012;34(6). http://www.aapd.org/media/Policies_Guidelines/G_FluorideTherapy.pdf.
Exclusion code: 11

American Academy of Pediatric Dentistry. Guideline on Xylitol Use in Caries Prevention. *American Academy of Pediatric Dentistry Reference Manual.* 2012/2013;34(6):166-169.
Exclusion code: 2

American Academy of Pediatric Dentistry. *Guideline on Fluoride Therapy.* 2012/2013Exclusion code: 2

American Academy of Pediatric Dentistry. Guideline on Caries-risk Assessment and Management for Infants, Children, and Adolescents. *American Academy of Pediatric Dentistry Reference Manual.* 2012/2013;34(6):118-125.
Exclusion code: 2

American Academy of Pediatrics. Policy Statement - AAP Publications Retired and Reaffirmed. *Policy Statement* http://pediatrics.aappublications.org/content/124/2/845.full. Accessed 12 January, 2013
Exclusion code: 2

American Academy of Pediatrics. *Oral health risk assessment timing and establishment of the dental home.* 2003Exclusion code: 2

American Academy of Pediatrics. *Profile of pediatric visits: Annualized estimates 2000-2004.* Elk Grove Village, Illinois 2007Exclusion code: 2

American Academy of Pediatrics. *Recommendations for Preventive Pediatric Health Care.* 2008.
Exclusion code: 2

American Academy of Pediatrics. Preventive oral health intervention for pediatricians: Section on pediatric dentistry and oral health. *Pediatrics.* 2008;122(6):1387-1394, [PMID: 19015205]
Exclusion code: 2

American Academy of Pediatrics. Oral Health Risk Assessment Tool. 2011. http://www2.aap.org/oralhealth/docs/RiskAssessmentTool.pdf. Accessed 13 Dec 2012
Exclusion code: 2

American Academy on Pediatric Dentistry Council on Clinical Affairs. Policy on use of a caries-risk assessment tool (CAT) in infants, children, and adolescents. *Pediatr Dent.* 2002;24(Suppl):15-17.
Exclusion code: 5

American Academy on Pediatric Dentistry Council on Clinical Affairs. Policy on Use of a Caries-risk Assessment Tool (CAT) for Infants, Children and Adolescents. *Pediatr Dent.* 2006;31(6).
Exclusion code: 2

American Academy on Pediatric Dentistry Council on Clinical Affairs. Policy on the use of xylitol in caries

Appendix A4. Excluded Studies List

prevention. *Pediatr Dent.* 2008;30(7 Suppl):36-37, [PMID: 19216379]
Exclusion code: 2

American Academy on Pediatric Dentistry Council on Clinical Affairs. Policy on use of a caries-risk assessment tool (CAT) for infants, children, and adolescents. *Pediatr Dent.* 2008;30(7 Suppl):29-33, [PMID: 19216377]
Exclusion code: 2

American Dental Association. Statement on Early Childhood Caries. 2000; http://www.ada.org/2057.aspx. Accessed 13 Dec, 2012
Exclusion code: 2

American Dental Association. ADA Caries Risk Assessment Forms. 2009; http://www.ada.org/5157.aspx?currentTab=2. Accessed 23 Oct 2012.
Exclusion code: 2

American Dental Association. Caries Risk Assessment Form (Age 0-6). 2011; http://www.ada.org/sections/professionalResources/pdfs/topics_caries_under6.pdf. Accessed 27 March, 2013
Exclusion code: 2

American Dental Association Council on Scientific Affairs. Professionally applied topical flouride: Evidence-based clinical recommendations. *J Dent Educ.* 2007;71(3):393-402, [PMID: 17389574]
Exclusion code: 2

Ammari AB, Bloch-Zupan A, Ashley PF. Systematic review of studies comparing the anti-caries efficacy of children's toothpaste containing 600 ppm of fluoride or less with high fluoride toothpastes of 1,000 ppm or above. *Caries Res.* 2003;37(2):85-92, [PMID: 12652045]
Exclusion code: 3

Ananaba N, Malcheff S, Briskie D, Inglehart MR. Infant oral health examinations: attitudes and professional behavior of general and pediatric dentists in Michigan and pediatric dentists in the U.S. *J Mich Dent Assoc.* 2010;92(12):38-43, [PMID: 21291093]
Exclusion code: 2

Andruskeviciene V, Milciuviene S, Bendoraitiene E, et al. Oral health status and effectiveness of caries prevention programme in kindergartens in Kaunas city (Lithuania). *Oral health prev.* 2008;6(4):343-348, [PMID: 19178101]
Exclusion code: 4

Ansai T, Yamashita Y, Shibata Y, et al. Relationship between dental caries experience of a group of Japanese kindergarten children and the results of two caries activity tests conducted on their saliva and dental plaque. *International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children.* 1994;4(1):13-17, [PMID: 7748842]
Exclusion code: 8

Anttonen V, Larmas M, Raitio M. Children were guaranteed regular check ups in dental study. *Bmj.* 1999;319(7222):1432, [PMID: 10574873]
Exclusion code: 5

Armfield JM. Community effectiveness of public water fluoridation in reducing children's dental disease. *Public Health Rep.* 2010;125(5):655-664, [PMID: 20873281]
Exclusion code: 4

Arora A, Scott JA, Bhole S, Do L, Schwarz E, Blinkhorn AS. Early childhood feeding practices and dental caries in preschool children: a multi-centre birth cohort study. *BMC Public Health.* 2011;11:28, [PMID: 21223601]
Exclusion code: 5

Arruda AO, Senthamarai Kannan R, Inglehart MR, Rezende CT, Sohn W. Effect of 5% fluoride varnish application on caries among school children in rural Brazil: A randomized controlled trial. *Community Dentistry and Oral Epidemiology.* 2012;40(3):267-276, [PMID: 22150341]
Exclusion code: 3

Assael LA. Should dentists become 'oral physicians'? No, dentistry must remain dentistry. *J Am Dent Assoc.* 2004;135(4):439+441+443+445+447-449, [PMID: 15127866]
Exclusion code: 5

Autio JT. Effect of xylitol chewing gum on salivary Streptococcus mutans in preschool children. *J Dent Child.* 2002;69(1):81-86, 13, [PMID: 12119821]
Exclusion code: 8

Autio JT, Courts FJ. Acceptance of the xylitol chewing gum regimen by preschool children and teachers in a Head Start program: a pilot study. *Pediatr Dent.* 2001;23(1):71-74, [PMID: 11242737]
Exclusion code: 8

Autio-Gold J. Recommendations for fluoride varnish use in caries management. *Dent Today.* 2008;27(1):64-67; quiz 67, 58, [PMID: 18240633]

Appendix A4. Excluded Studies List

Exclusion code: 2

Autio-Gold JT, Courts F. Assessing the effect of fluoride varnish on early enamel carious lesions in the primary dentition. *J Am Dent Assoc.* 2001;132(9):1247-1253, [PMID: 1665349]
Exclusion code: 11

Azarpazhooh A, Limeback H, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. *Cochrane Database Syst Rev.* 2011(11):CD007095, [PMID: 22071833]
Exclusion code: 8

Baca P, Muñoz MJ, Bravo M, Junco P, Baca AP. Effectiveness of chlorhexidine-thymol varnish in preventing caries lesions in primary molars. *J Dent Child.* 2004;71(1):61-65, [PMID: 15272659]
Exclusion code: 3

Bader JD, Rozier RG, Lohr KN, Frame PS. Physicians' roles in preventing dental caries in preschool children: a summary of the evidence for the U.S. Preventive Services Task Force. *Am J Prev Med.* 2004;26(4):315-325, [PMID: 15110059]
Exclusion code: 2

Bader JD, Shugars DA, Bonito AJ. Systematic reviews of selected dental caries diagnostic and management methods. *J Dent Educ.* 2001;65(10):960-968, [PMID: 11699997]
Exclusion code: 5

Badet MC, Richard B, Dorignac G. An in vitro study of the pH-lowering potential of salivary lactobacilli associated with dental caries. *J Appl Microbiol.* 2001;90(6):1015-1018, [PMID: 11412333]
Exclusion code: 8

Balaban R, Aguiar CM, Da Silva Araújo AC, Dias Filho EBR. Knowledge of paediatricians regarding child oral health. *Int J Paediatr Dent.* 2012;22(4):286-291, [PMID: 22092596]
Exclusion code: 3

Baldani MH, Antunes JLF. Inequalities in access and utilization of dental services: a cross-sectional study in an area covered by the Family Health Strategy. *Cad Saude Publica.* 2011;27 Suppl 2:S272-283, [PMID: 21789419]
Exclusion code: 2

Baldani MH, Mendes YBE, Lawder JAdC, de Lara API, Rodrigues MMAdS, Antunes JLF. Inequalities in dental services utilization among Brazilian low-income children: the role of individual determinants. *J Public Health Dent.* 2011;71(1):46-53, [PMID: 21667543]
Exclusion code: 2

Banoczy J, Scheinin A, Esztari I, Szoke J, Hadas E, Zimmermann P. [Caries-preventing action of xylitol-containing sweets, studied in children's institutions]. *Orv Hetil.* 1985;126(40):2447-2451, [PMID: 4047645]
Exclusion code: 7

Banoczy J, Scheinin A, Esztari I, et al. [3-year results of a WHO-supported caries-prevention program, using xylitol, in Hungarian children's homes. I. Clinical caries studies]. *Fogorv Sz.* 1985;78(11):329-338, [PMID: 3914420]
Exclusion code: 7

Bär A. Caries prevention with xylitol. A review of the scientific evidence. *World review of nutrition and dietetics.* 1988;55:183-209, [PMID: 3287773]
Exclusion code: 5

Barber LR, Wilkins EM. Evidence-based prevention, management, and monitoring of dental caries. *J Dent Hyg.* 2002;76(4):270-275, [PMID: 12592918]
Exclusion code: 2

Barmes D, Barnaud J, Khambonanda S, Infirri JS. Field trials of preventive regimens in Thailand and French Polynesia. *Int Dent J.* 1985;35(1):66-72, [PMID: 3888852]
Exclusion code: 3

Bawden JW. Fluoride varnish: a useful new tool for public health dentistry. *J Public Health Dent.* 1998;58(4):266-269, [PMID: 10390707]
Exclusion code: 2

Beil H, Mayer M, Rozier RG. Dental care utilization and expenditures in children with special health care needs. *J Am Dent Assoc.* 2009;140(9):1147-1155, [PMID: 19723949]
Exclusion code: 3

Beil HA, Rozier RG. Primary health care providers' advice for a dental checkup and dental use in children. *Pediatrics.* 2010;126(2):e435-441, [PMID: 20660547]
Exclusion code: 8

Bell JF, Huebner CE, Reed SC. Oral health need and access to dental services: evidence from the National Survey of Children's Health, 2007. *Maternal and Child Health Journal.* 2012;16 Suppl 1:S27-34, [PMID: 22456986]
Exclusion code: 2

Appendix A4. Excluded Studies List

Beltrán ED, Malvitz DM, Eklund SA. Validity of two methods for assessing oral health status of populations. *J Public Health Dent.* 1997;57(4):206-214, [PMID: 9558624]
Exclusion code: 6

Beltran-Aguilar D, Barker LK, Dye BA. *Prevalence and severity of dental fluorosis in the United States, 1999-2004. National Center for Health Statistics Data Brief.* Hyattsville, MD. 2010.
Exclusion code: 2

Beltran-Aguilar ED, Barker LK, Canto MT, et al. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis--United States, 1988-1994 and 1999-2002. *MMWR Surveill Summ.* 2005;54(3):1-43, [PMID: 16121123]
Exclusion code: 4

Beltran-Aguilar ED, Goldstein JW, Lockwood SA. Fluoride varnishes. A review of their clinical use, cariostatic mechanism, efficacy and safety. *J Am Dent Assoc.* 2000;131(5):589-596, [PMID: 10832252]
Exclusion code: 11

Beltran-Aguilar ED, Griffin SO, Lockwood SA. Prevalence and trends in enamel fluorosis in the United States from the 1930s to the 1980s. *J Am Dent Assoc.* 2002;133(2):157-165, [PMID: 11868834]
Exclusion code: 11

Beltrán-Valladares PR, Cocom-Tun H, Casanova-Rosado JF, Vallejos-Sánchez AA, Medina-Solís CE, Maupomé G. Prevalence of dental fluorosis and additional sources of exposure to fluoride as risk factors to dental fluorosis in schoolchildren of Campeche, Mexico. *Rev Invest Clin.* 2005;57(4):532-539, [PMID: 16315637]
Exclusion code: 7

Bentley EM, Holloway PJ. An evaluation of the role of health visitors in encouraging dental attendance of infants. *Community Dent Health.* 1993;10(3):243-249., [PMID: 8269339]
Exclusion code: 11

Berg JH. Early dental caries detection as a part of oral health maintenance in young children. *Compend Contin Educ Dent.* 2005;26(5 Suppl 1):24-29, [PMID: 17036541]
Exclusion code: 5

Binkley CJ, Garrett B, Johnson KW. Increasing dental care utilization by Medicaid-eligible children: A dental care coordinator intervention. *J Public Health Dent.* 2010;70(1):76-84, [PMID: 19765202]
Exclusion code: 2

Blackwell DL, Tonthat L. Summary health statistics for U.S. children: National Health Interview Survey, 1999. *Vital Health Stat [10].* 2003(210):1-50, [PMID: 15789511]
Exclusion code: 2

Blair Y, Macpherson L, McCall D, McMahon A. Dental health of 5-year-olds following community-based oral health promotion in Glasgow, UK. *Int J Paediatr Dent.* 2006;16(6):388-398, [PMID: 17014536]
Exclusion code: 9

Blair Y, Macpherson LMD, McCall DR, McMahon AD, Stephen KW. Glasgow nursery-based caries experience, before and after a community development-based oral health programme's implementation. *Community Dent Health.* 2004;21(4):291-298, [PMID: 15617414]
Exclusion code: 9

Bloom B, Cohen RA, Freeman G. Summary health statistics for U.S. children: National Health Interview Survey, 2010. *Vital and health statistics. Series 10, Data from the National Health Survey.* 2011(250):1-80, [PMID: 22338334]
Exclusion code: 2

Bonanato K, Paiva SM, Pordeus IA, Ramos-Jorge ML, Barbabela D, Allison PJ. Relationship between mothers' sense of coherence and oral health status of preschool children. *Caries Res.* 2009;43(2):103-109, [PMID: 19321987]
Exclusion code: 8

Bonanato K, Pordeus IA, Moura-Leite FR, Ramos-Jorge ML, Vale MP, Paiva SM. Oral disease and social class in a random sample of five-year-old preschool children in a Brazilian city. *Oral health prev.* 2010;8(2):125-132, [PMID: 20589245]
Exclusion code: 4

Borutta A, Reuscher G, Hufnagl S, Möbius S. Caries prevention with fluoride varnishes among preschool children. *Kariesprophylaxe mit fluoridlacken bei vorschulkindern.* 2006;68(11):731-734, [PMID: 17199209]
Exclusion code: 7

Bottenberg P, Declerck D, Ghidey W, Bogaerts K, Vanobbergen J, Martens L. Prevalence and determinants of enamel fluorosis in Flemish schoolchildren. *Caries Res.* 2004;38(1):20-28, [PMID: 14684973]

Appendix A4. Excluded Studies List

Exclusion code: 8

Bottenberg P, Melckebeke LV, Louckx F, Vandenplas Y. Knowledge of Flemish paediatricians about children's oral health - Results of a survey. *Acta Paediatrica, International Journal of Paediatrics.* 2008;97(7):959-963, [PMID: 18474066]
Exclusion code: 4

Braga MM, Oliveira LB, Bonini GAVC, Bönecker M, Mendes FM. Feasibility of the international caries detection and assessment system (icdas-ii) in epidemiological surveys and comparability with standard world health organization criteria. *Caries Res.* 2009;43(4):245-249, [PMID: 19439944]
Exclusion code: 4

Bratthall D, Hansel Petersson G. Cariogram--a multifactorial risk assessment model for a multifactorial disease. *Community Dent Oral Epidemiol.* 2005;33(4):256-264, [PMID: 16008632]
Exclusion code: 3

Brickhouse TH, Unkel JH, Kancitis I, Best AM, Davis RD. Infant oral health care: A survey of general dentists, pediatric dentists, and pediatricians in Virginia. *Pediatr Dent.* 2008;30(2):147-153, [PMID: 18481580]
Exclusion code: 2

Brown LF. Research in dental health education and health promotion: a review of the literature. *Health Educ Q.* 1994;21(1):83-102, [PMID: 8188495]
Exclusion code: 11

Bubna S, Perez-Spiess S, Cernigliaro J, Julliard K. Infant oral health care: Beliefs and practices of American Academy of Pediatric Dentistry members. *Pediatr Dent.* 2012;34(3):203-209, [PMID: 22795152]
Exclusion code: 3

Busuttil Naudi A, Mooney G, El-Bahannasawy E, et al. The dental health and preventative habits of cardiac patients attending the Royal Hospital for Sick Children Glasgow. *Eur Arch Paediatr Dent.* 2006;7(1):23-30, [PMID: 17140524]
Exclusion code: 3

Calonge N, U.S. Preventive Services Task Force. Prevention of Dental Caries in Preschool Children: Recommendations and Rationale. *Am J Prev Med.* 2004;26(4):326-329, [PMID: 15110060]
Exclusion code: 2

Campus G, Cagetti MG, Sacco G, Solinas G, Mastroberardino S, Lingstrom P. Six months of daily high-dose xylitol in high-risk schoolchildren: a randomized clinical trial on plaque pH and salivary mutans streptococci. *Caries Res.* 2009;43(6):455-461, [PMID: 20016175]
Exclusion code: 3

Campus G, Solinas G, Strohmenger L, et al. National pathfinder survey on children's oral health in Italy: pattern and severity of caries disease in 4-year-olds. *Caries Res.* 2009;43(2):155-162, [PMID: 19365120]
Exclusion code: 8

Carvalho DM, Salazar M, Oliveira BH, Coutinho ES. Fluoride varnishes and decrease in caries incidence in preschool children: a systematic review. *Rev Bras Epidemiol.* 2010;13(1):139-149, [PMID: 20683562]
Exclusion code: 5

Casamassimo P, Holt K. *Bright Futures in Practice: Oral Health—Pocket Guid.* Washington, D.C.: National Maternal and Child Oral Health Resource Center; 2004.
Exclusion code: 5

Casamassimo PS, Thikkurissy S, Edelstein BL, Maiorini E. Beyond the dmft: the human and economic cost of early childhood caries. *J Am Dent Assoc.* 2009;140(6):650-657, [PMID: 19491160]
Exclusion code: 5

Caufield PW, Griffen AL. *DENTAL CARIES: An Infectious and Transmissible Disease.* 2000. 0031-3955
Exclusion code: 2

Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. . *MMWR* 2001;50(RR-14):1-42, [PMID: 11521913]
Exclusion code: 11

Centers for Disease Control and Prevention. Dental Caries: Hygiene-related diseases. 2009; http://www.cdc.gov/healthywater/hygiene/disease/dental_caries.html. Accessed May 23, 2012
Exclusion code: 2

Centers for Medicare & Medicaid Services (CMS). *Use of Dental Services in Medicaid and CHIP.* Baltimore, MD: CMS.gov; 2011.
Exclusion code: 2

Chan SCL, Tsai JSJ, King NM. Feeding and oral hygiene habits of preschool children in Hong Kong and their caregivers' dental knowledge and attitudes. *Int J Paediatr Dent.* 2002;12(5):322-331, [PMID: 12199891]
Exclusion code: 4

Appendix A4. Excluded Studies List

Chandiwal S, Yoon RK. Assessment of an infant oral health education program on resident physician knowledge. *J Dent Child.* 2012;79(2):49-52, [PMID: 22828757]
Exclusion code: 3

Clark DC. Trends in prevalence of dental fluorosis in North America. *Community Dent Oral Epidemiol.* 1994;22(3):148-152, [PMID: 8070241]
Exclusion code: 11

Clark DC, Stamm JW, Quee TC, Robert G. Results of the Sherbrooke-Lac Mégantic fluoride varnish study after 20 months. *Community Dentistry and Oral Epidemiology.* 1985;13(2):61-64, [PMID: 3857148]
Exclusion code: 3

Clark DC, Stamm JW, Robert G, Tessier C. Results of a 32-month fluoride varnish study in Sherbrooke and Lac-Megantic, Canada. *The Journal of the American Dental Association.* 1985;111(6):949-953, [PMID: 3905917]
Exclusion code: 3

Clark DC, Stamm JW, Tessier C, Robert G. The final results of the Sherbrooke-Lac Mégantic fluoride varnish study. *J Can Dent Assoc.* 1987;53(12):919-922, [PMID: 3319099]
Exclusion code: 3

Cleaton-Jones P, Hargreaves JA, Beere D, Matejka J, Hargreaves V. Use of DI-S and CPITN as predictors in dental caries studies in the primary dentition. *The Journal of the Dental Association of South Africa = Die Tydskrif van die Tandheelkundige Vereniging van Suid-Afrika.* 1991;46(10):503-505, [PMID: 1820667]
Exclusion code: 8

Close K, Rozier RG, Zeldin LP, Gilbert AR. Barriers to the adoption and implementation of preventive dental services in primary medical care. *Pediatrics.* 2010;125(3):509-517, [PMID: 20123767]
Exclusion code: 2

Collins RJ, Nehring ME, Maas WR, et al. Toward improving the oral health of Americans: An overview of oral health status, resources, and care delivery. *Public Health Rep.* 1993;108(6):657-672, [PMID: 8265750]
Exclusion code: 5

Committee on Fluoride in Drinking Water NRC. *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*: The National Academies Press; 2006.
Exclusion code: 2

Community Preventive Services Task Force. Improving Oral Health: Dental Caries (Cavities). 2010; http://www.thecommunityguide.org/oral/caries.html. Accessed 27 March, 2013
Exclusion code: 2

Conway DI, Macpherson LMD, Stephen KW, Gilmour WH, Petersson LG. Prevalence of dental fluorosis in children from non-water-fluoridated Halmstad, Sweden: Fluoride toothpaste use in infancy. *Acta Odontol Scand.* 2005;63(1):56-63, [PMID: 16095064]
Exclusion code: 4

Cruxen B, Volschan G. Getting to know the early childhood caries through qualitative analysis. *J Clin Pediatr Dent.* 2006;31(1):48-51, [PMID: 17091659]
Exclusion code: 8

Cutress T, Howell PT, Finidori C, Abdullah F. Caries preventive effect of high fluoride and xylitol containing dentifrices. *J Dent Child.* 1992;59(4):313-318, [PMID: 1430505]
Exclusion code: 3

da Silva BDM, Forte FDS. Access to dental treatment, mothers perception of oral health and intervention strategies in the city of Mogeiro, PB, Brazil. *Pesquisa Brasileira em Odontopediatria e Clinica Integrada.* 2009;9(3):313-319.
Exclusion code: 10

Damiano PC, Willard JC, Momany ET, Chowdhury J. The impact of the Iowa S-SCHIP program on access, health status, and the family environment. *Ambul Pediatr.* 2003;3(5):263-269, [PMID: 12974660]
Exclusion code: 2

Davenport C, Elley K, Salas C, et al. The clinical effectiveness and cost-effectiveness of routine dental checks: a systematic review and economic evaluation. *Health Technol Assess.* 2003;7(7):iii-v, [PMID: 12709293]
Exclusion code: 4

Davies G, Health CD. A randomised controlled trial of the effectiveness of providing free fluoride toothpaste form the age of 12 months on reducing caries in 5-6 year old children. *Community Dent Health.* 2002;19:131-136, [PMID: 12269458]
Exclusion code: 4

Davies GM, Duxbury JT, Boothman NJ, Davies RM, Blinkhorn AS. A staged intervention dental health promotion programme to reduce early childhood caries.

Appendix A4. Excluded Studies List

Community Dent Health. 2005;22(2):118-122, [PMID: 15984138]
Exclusion code: 5

Davies GN. Early childhood caries - A synopsis. *Community Dentistry and Oral Epidemiology.* 1998;26(1 SUPPL.):106-116, [PMID: 9671208]
Exclusion code: 5

de Silva-Sanigorski AM, Waters E, Calache H, et al. Splash!: a prospective birth cohort study of the impact of environmental, social and family-level influences on child oral health and obesity related risk factors and outcomes. *BMC Public Health.* 2011;11:505, [PMID: 21708037]
Exclusion code: 5

De Soet JJ, Gruythuysen RJM, Bosch JA, Van Amerongen WE. The effect of 6-monthly application of 40% chlorhexidine varnish on the microflora and dental caries incidence in a population of children in Surinam. *Caries Res.* 2002;36(6):449-455, [PMID: 12459619]
Exclusion code: 3

Decker SL. Medicaid payment levels to dentists and access to dental care among children and adolescents. *Jama.* 2011;306(2):187-193, [PMID: 21750296]
Exclusion code: 2

Declerck D, Leroy R, Martens L, et al. Factors associated with prevalence and severity of caries experience in preschool children. *Community Dent Oral Epidemiol.* 2008;36(2):168-178, [PMID: 18333881]
Exclusion code: 8

Deinard A, Johnson B. Ending an epidemic: physicians' role in primary caries prevention. *Minn Med.* 2009;92(3):38-39, [PMID: 19400385]
Exclusion code: 2

dela Cruz GG, Rozier RG, Slade G. Dental screening and referral of young children by pediatric primary care providers. *Pediatrics.* 2004;114(5):e642-652, [PMID: 15520094]
Exclusion code: 8

Demers M, Brodeur JM, Mouton C, Simard PL, Trahan L, Veilleux G. A multivariate model to predict caries increment in Montreal children aged 5 years. *Community Dent Health.* 1992;9(3):273-281, [PMID: 1451000]
Exclusion code: 8

DePaola PF, Lax M. The caries-inhibiting effect of acidulated phosphate-fluoride chewable tablets: a two-year double-blind study. *The Journal of the American Dental Association.* 1968;76(3):554-557, [PMID: 4865754]
Exclusion code: 3

DeVoe JE, Tillotson CJ, Wallace LS, Angier H, Carlson MJ, Gold R. Parent and child usual source of care and children's receipt of health care services. *Ann Fam Med.* 2011;9(6):504-513, [PMID: 22084261]
Exclusion code: 2

Di Giuseppe G, Nobile CGA, Marinelli A, Angelillo IF. Knowledge, attitude and practices of pediatricians regarding the prevention of oral diseases in Italy. *BMC Public Health.* 2006;6:176, [PMID: 16822318]
Exclusion code: 8

Dillenberg JS, Levy SM, Schroeder DC, Gerston EN, Andersen CJ. Arizona providers' use and knowledge of fluoride supplements. *Clin Prev Dent.* 1992;14(5):15-26, [PMID: 1291183]
Exclusion code: 11

Dimitrova MM, Kukleva MP, Stoykova MS. A study of dentists' opinion about caries treatment of 1-3- year-old children. *Folia Med (Plovdiv).* 2001;43(1-2):25-27, [PMID: 15354461]
Exclusion code: 8

Dincer E, Ligouri AL, Rayman S, Rivera A. Parental perceptions about children's oral health care and toothpaste in New York City neighborhoods. *N Y State Dent J.* 2009;75(2):44-48, [PMID: 19418881]
Exclusion code: 8

Do LG, Spencer AJ. Decline in the prevalence of dental fluorosis among South Australian children. *Community Dentistry and Oral Epidemiology.* 2007;35(4):282-291, [PMID: 17615015]
Exclusion code: 4

Doméjean S, White JM, Featherstone JD. Validation of the CDA CAMBRA caries risk assessment--a six-year retrospective study. *J Calif Dent Assoc.* 2011;39(10):709-715, [PMID: 22132582]
Exclusion code: 3

Donahoe JF, Powers RJ. Xylitol. Clinical pharmacology in normal adult volunteers. *Journal of Clinical Pharmacology.* 1974;14(5-6):255-260, [PMID: 4829518]
Exclusion code: 3

dos Santos APP, Nadanovsky P, de Oliveira BH. Inconsistencies in recommendations on oral hygiene

Appendix A4. Excluded Studies List

practices for children by professional dental and paediatric organisations in ten countries. *Int J Paediatr Dent.* 2011;21(3):223-231, [PMID: 21332850]
Exclusion code: 8

Douglass JM, Douglass AB, Silk HJ. Infant oral health education for pediatric and family practice residents. *Pediatr Dent.* 2005;27(4):284-291, [PMID: 16317967]
Exclusion code: 5

Douglass JM, Tinanoff N, Tang JM, Altman DS. Dental caries patterns and oral health behaviors in Arizona infants and toddlers. *Community Dent Oral Epidemiol.* 2001;29(1):14-22, [PMID: 11153558]
Exclusion code: 2

Doull J, Boekelheide K, Farishian BG, et al. *Fluoride in drinking water: a scientific review of EPA's standards [Internet]*. Washington, DC: The National Academies Press; 2006.
Exclusion code: 2

Driscoll WS, Heifetz SB, Korts DC. Effect of acidulated phosphate-fluoride chewable tablets on dental caries in schoolchildren: results after 30 months. *The Journal of the American Dental Association.* 1974;89(1):115-120, [PMID: 4151915]
Exclusion code: 3

Dye BA, Barker LK, Li X, Lewis BG, Beltran-Aguilar ED. Overview and quality assurance for the oral health component of the National Health and Nutrition Examination Survey (NHANES), 2005-08. *J Public Health Dent.* 2011;71(1):54-61, [PMID: 21667544]
Exclusion code: 3

Dye BA, Tan S, Smith V, et al. Trends in oral health status: United States, 1988–1994 and 1999–2004. *Vital Health Stat.* 2007;1(248), [PMID: 17633507]
Exclusion code: 2

Eckersley AJ, Blinkhorn FA. Dental attendance and dental health behaviour in children from deprived and non-deprived areas of Salford, north-west England. *Int J Paediatr Dent.* 2001;11(2):103-109, [PMID: 11310132]
Exclusion code: 8

Edelstein BL. Solving the problem of early childhood caries: a challenge for us all. *Arch Pediatr Adolesc Med.* 2009;163(7):667-668, [PMID: 19581553]
Exclusion code: 2

Edelstein BL, Chinn CH. Update on Disparities in Oral Health and Access to Dental Care for America's Children. *Acad Pediatr.* 2009;9(6):415-419, [PMID: 19945076]
Exclusion code: 2

Eklund SA, Burt BA, Ismail AI, Calderone JJ. High-fluoride drinking water, fluorosis, and dental caries in adults. *J Am Dent Assoc.* 1987;114(3):324-328, [PMID: 3470353]
Exclusion code: 11

Ekman A, Persson B. Effect of early dental health education for Finnish immigrant families. *Swed Dent J.* 1990;14(3):143-151, [PMID: 2255993]
Exclusion code: 11

Ekstrand J, Koch G, Lindgren LE, Petersson LG. Pharmacokinetics of fluoride gels in children and adults. *Caries Res.* 1981;15(3):213-220, [PMID: 6938306]
Exclusion code: 11

Ekstrand J, Koch G, Petersson LG. Plasma fluoride concentration and urinary fluoride excretion in children following application of the fluoride-containing varnish Duraphat. *Caries Res.* 1980;14(4):185-189, [PMID: 6929729]
Exclusion code: 11

Elkind A, Blinkhorn FA, Mackie IC, Tickle M, Duxbury JT, Blinkhorn AS. Service quality implications of dental undergraduate outreach teaching for Primary Care Trusts in England, UK. *Community Dent Health.* 2006;23(2):75-79, [PMID: 16800361]
Exclusion code: 3

Emerich K, Wyszowski J. Oral health prevention in view of Polish paediatricians. *Dental and Medical Problems.* 2009;46(2):157-161.
Exclusion code: 8

Englander HR, Mellberg JR, Engler WO. Observations on dental caries in primary teeth after frequent fluoride toplications in a program involving other preventives. *J Dent Res.* 1978;57(9-10):855-860, [PMID: 281356]
Exclusion code: 5

Fanning EA, Cellier KM, Leadbeater MM, Somerville CM. South Australian kindergarten children: fluoride tablet supplements and dental caries. *Aust Dent J.* 1975;20(1):7-9, [PMID: 1057890]
Exclusion code: 11

Featherstone JD, . Delivery challenges for fluoride, chlorhexidine, and xylitol. *BMC Oral Health.* 2006;Jun 6 Suppl 1:S8:1-5, [PMID: 16934125]
Exclusion code: 5

Appendix A4. Excluded Studies List

Featherstone JD, Adair SM, Anderson MH, et al. Caries management by risk assessment: consensus statement, April 2002. *J Calif Dent Assoc.* 2003;31(3):257-269, [PMID: 12693825]
Exclusion code: 5

Feldens CA, Giugliani ER, Duncan BB, Drachler Mde L, Vitolo MR. Long-term effectiveness of a nutritional program in reducing early childhood caries: a randomized trial. *Community Dent Oral Epidemiol.* 2010;38(4):324-332, [PMID: 20406273]
Exclusion code: 9

Feltman R, Kosel G. Prenatal and postnatal ingestion of fluorides – Fourteen years of investigation – Final report. *Journal of Dental Medicine.* 1961;16:190-199.
Exclusion code: 8

Fennis-Le YL, Verdonschot EH, Burgersdijk RCW, König KG, Van't Hof MA. Effect of 6-monthly applications of chlorhexidine varnish on incidence of occlusal caries in permanent molars: A 3-year study. *J Dent.* 1998;26(3):233-238, [PMID: 9594475]
Exclusion code: 3

Fisher-Owens S, Platt LJ, Weintraub JA, et al. Influences on children's oral health: a conceptual model. *Pediatrics.* 2007;e510-520:510-520, [PMID: 17766495]
Exclusion code: 5

Fontana M, Catt D, Eckert GJ, et al. Xylitol: effects on the acquisition of cariogenic species in infants. *Pediatr Dent.* 2009;31(3):257-266, [PMID: 19552232]
Exclusion code: 3

Fontana M, Jackson R, Eckert G, et al. Identification of caries risk factors in toddlers. *J Dent Res.* 2011;90(2):209-214, [PMID: 21173434]
Exclusion code: 8

Fontana M, Wolff M. Translating the caries management paradigm into practice: challenges and opportunities. *J Calif Dent Assoc.* 2011;39(10):702-708, [PMID: 22132581]
Exclusion code: 5

Franco S, Theriot J, Greenwell A. The influence of early counselling on weaning from a bottle. *Community Dent Health.* 2008;25(2):115-118, [PMID: 18637324]
Exclusion code: 4

Franzman MR, Levy SM, Warren JJ, Broffitt B. Fluoride dentifrice ingestion and fluorosis of the permanent incisors. *J Am Dent Assoc.* 2006;137(5):645-652, [PMID: 16739545]
Exclusion code: 4

Frostell G, Birkhed D, Edwardsson S, et al. Effect of partial substitution of invert sugar for sucrose in combination with duraphat® treatment on caries development in preschool children: The malmo study. *Caries Res.* 1991;25(4):304-310, [PMID: 1913770]
Exclusion code: 11

Gabris K, Nyarasdy I, Banoczy J. [Significance of assessing risk factors for caries in their prevention]. *Orv Hetil.* 2002;143(24):1467-1473, [PMID: 12138644]
Exclusion code: 7

Gabris K, Pienihakkinen K, Nyarasdy I, Rigo O, Banoczy J, Scheinin A. [3-year results of the WHO xylitol caries-prevention program in Hungarian homes for children. IV. Microbiological studies: changes in salivary Lactobacillus and Candida albicans counts]. *Fogorv Sz.* 1987;80(3):71-76, [PMID: 3549372]
Exclusion code: 7

Gagnon F, Catellier P, Arteau-Gauthier I, et al. Compliance with fluoride supplements provided by a dental hygienist in homes of low-income parents of preschool children in Quebec. *J Public Health Dent.* 2007;67(1):60-63, [PMID: 17436981]
Exclusion code: 8

Galganny-Almeida A, Queiroz MC, Leite AJ. The effectiveness of a novel infant tooth wipe in high caries-risk babies 8 to15 months old. *Pediatr Dent.* 2007;29(4):337-342, [PMID: 17867402]
Exclusion code: 8

Gallagher IH, Pearce EI. The sugar alcohols. Non-cariogenic sweeteners. *N Z Dent J.* 1977;73(334):200-206, [PMID: 351471]
Exclusion code: 3

Gao XL, Hsu CYS, Xu Y, Hwarng HB, Loh T, Koh D. Building caries risk assessment models for children. *J Dent Res.* 2010;89(6):637-643, [PMID: 20400721]
Exclusion code: 10

Gao XL, Hsu CYS, Xu YC, Loh T, Koh D, Hwarng HB. Behavioral pathways explaining oral health disparity in children. *J Dent Res.* 2010;89(9):985-990, [PMID: 20554887]
Exclusion code: 10

Garbutt JM, Leege E, Sterkel R, Gentry S, Wallendorf M, Strunk RC. What are parents worried about? Health problems and health concerns for children. *Clinical Pediatrics.* 2012;July 26, 2012, [PMID: 22843294]

Appendix A4. Excluded Studies List

Exclusion code: 5

Gibbons RJ, van Houte J. Dental caries. *Annual Review of Medicine.* 1975;26:121-136, [PMID: 1096752]
Exclusion code: 5

Gift HC, Milton B, Walsh V. Physicians and caries prevention. Results of a physician survey on preventive dental services. *Jama.* 1984;252(11):1447-1448, [PMID: 6471271]
Exclusion code: 11

Goldberg E, Lewis P, Ferguson F. Oral health status and access-to-care concerns of Suffolk County Head Start children. *N Y State Dent J.* 2011;77(1):20-22, [PMID: 21417161]
Exclusion code: 2

Gomez SS, Weber AA. Effectiveness of a caries preventive program in pregnant women and new mothers on their offspring. *Int J Paediatr Dent.* 2001;11(2):117-122, [PMID: 11310134]
Exclusion code: 2

Gomez SS, Weber AA, Emilson CG. A prospective study of a caries prevention program in pregnant women and their children five and six years of age. *J Dent Child.* 2001;68(3):191-195, 152, [PMID: 11693012]
Exclusion code: 3

Gosnell E, Casamassimo PS. Restoration and Post-Surgical Prevention Will Not Solve Early Childhood Caries. *Clinical Dentistry and Research.* 2012;36(1):35-40.
Exclusion code: 2

Graber TM, Muller TP, Bhatia VD. The effect of xylitol gum and rinses on plaque acidogenesis in patients with fixed orthodontic appliances. *Swedish dental journal. Supplement.* 1982;15:41-55, [PMID: 6963783]
Exclusion code: 3

Grant JS, Kotch JB, Quinonez RB, Kerr J, Roberts MW. Evaluation of knowledge, attitudes, and self-reported behaviors among 3-5 year old school children using an oral health and nutrition intervention. *J Clin Pediatr Dent.* 2010;35(1):59-64, [PMID: 21189766]
Exclusion code: 8

Grant JS, Roberts MW, Brown WD, Quinonez RB. Integrating dental screening and fluoride varnish application into a pediatric residency outpatient program: clinical and financial implications. *J Clin Pediatr Dent.* 2007;31(3):175-178, [PMID: 17550042]
Exclusion code: 8

Graves RC, Abernathy JR, Disney JA, Stamm JW, Bohannan HM. University of North Carolina caries risk assessment study. III. Multiple factors in caries prevalence. *J Public Health Dent.* 1991;51(3):134-143, [PMID: 1920265]
Exclusion code: 8

Greene-McIntyre M, Finch MH, Searcy J. Smile Alabama! Initiative: interim results from a program to increase children's access to dental care. *J Rural Health.* 2003;19 Suppl:407-415, [PMID: 14526525]
Exclusion code: 2

Grembowski D, Spiekerman C, Milgrom P. Linking mother and child access to dental care. *Pediatrics.* 2008;122(4):e805-814, [PMID: 18829778]
Exclusion code: 2

Grenby TH, Bashaarat AH. A clinical trial to compare the effects of xylitol and sucrose chewing-gums on dental plaque growth. *Br Dent J.* 1982;152(10):339-343, [PMID: 6953972]
Exclusion code: 3

Grillaud M, Bandon D, Nancy J, Delbos Y, Vaysse F. [The polyols in pediatric dentistry: advantages of xylitol]. *Arch Pediatr.* 2005;12(7):1180-1186, [PMID: 15964535]
Exclusion code: 7

Grindefjord M, Dahllöf G, Nilsson B, Modéer T. Prediction of dental caries development in 1-year-old children. *Caries Res.* 1995;29(5):343-348, [PMID: 8521434]
Exclusion code: 8

Grocholewicz K. [The effect of selected prophylactic-educational programs on oral hygiene, periodontium and caries in school children during a 4-year observation]. *Annales Academiae Medicae Stetinensis.* 1999;45:265-283, [PMID: 10909495]
Exclusion code: 7

Grodzka K, Augustyniak L, Budny J. Caries increment in primary teeth after application of Duraphat® fluoride varnish. *Community Dentistry and Oral Epidemiology.* 1982;10(2):55-59, [PMID: 6952970]
Exclusion code: 11

Günay H, Dmoch-Bockhorn K, Günay Y, Geurtsen W. Effect on caries experience of a long-term preventive program for mothers and children starting during pregnancy. *Clin Oral Investig.* 1998;2(3):137-142, [PMID: 9927915]
Exclusion code: 3

Appendix A4. Excluded Studies List

Hamberg L. Controlled trial of fluoride in vitamin drops for prevention of caries in children. *Lancet.* 1971;1(7696):441-442, [PMID: 4100412]
Exclusion code: 11

Hamilton FA, Davis KE, Blinkhorn AS. An oral health promotion programme for nursing caries. *International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children.* 1999;9(3):195-200, [PMID: 10815576]
Exclusion code: 4

Hanno AG, Alamoudi NM, Almushayt AS, Masoud MI, Sabbagh HJ, Farsi NM. Effect of xylitol on dental caries and salivary Streptococcus mutans levels among a group of mother-child pairs. *J Clin Pediatr Dent.* 2011;36(1):25-30, [PMID: 22900440]
Exclusion code: 5

Hanson J, Campbell L. Xylitol and caries prevention. *J Mass Dent Soc.* 2011;60(2):18-21, [PMID: 22128472]
Exclusion code: 2

Hardman MC, Davies GM, Duxbury JT, Davies RM. A cluster randomised controlled trial to evaluate the effectiveness of fluoride varnish as a public health measure to reduce caries in children. *Caries Res.* 2007;41(5):371-376, [PMID: 17713337]
Exclusion code: 3

Harris R, Nicoll AD, Adair PM, Pine CM. Risk factors for dental caries in young children: A systematic review of the literature. *Community Dent Health.* 2004;21(1 SUPPL.):71-85, [PMID: 15072476]
Exclusion code: 8

Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: A review of the process. *Am J Prev Med.* 2001;20(3, Supplement 1):21-35, [PMID: 11306229]
Exclusion code: 2

Hartlmaier KM. [Sweet, yet harmless]. *Zahnarztl.* 1977;67(14):882-883, [PMID: 268111]
Exclusion code: 7

Havenaar R, Huis in 't Veld JHJ, de Stoppelaar JD, Backer Dirks O. Anti-cariogenic and remineralizing properties of xylitol in combination with sucrose in rats inoculated with Streptococcus mutans. *Caries Res.* 1984;18(3):269-277, [PMID: 6584218]
Exclusion code: 3

Hecksher AS, Luiz RR, Costa AJL, Moraes NM. Reliability analysis of visual examinations carried out by school-teachers and a dental assistant in the detection of dental caries. *Community Dent Health.* 2010;27(2):89-93, [PMID: 20648885]
Exclusion code: 3

Hefti A. [Sugar substitutes in caries prevention]. *Schweiz Med Wochenschr.* 1980;110(7):269-273, [PMID: 7367846]
Exclusion code: 7

Heifetz SB, Horowitz HS, Meyers RJ, Li SH. Evaluation of the comparative effectiveness of fluoride mouthrinsing, fluoride tablets, and both procedures in combination: interim findings after two years. *Pediatr Dent.* 1987;9(2):121-125, [PMID: 3475680]
Exclusion code: 3

Hennon DK, Stookey GK, Beiswanger BB. Fluoride-vitamin supplements: effects on dental caries and fluorosis when used in areas with suboptimum fluoride in the water supply. *J Am Dent Assoc.* 1977;95(5):965-971, [PMID: 269878]
Exclusion code: 11

Hennon DK, Stookey GK, Muhler JC. Prophylaxis of dental caries: Relative effectiveness of chewable fluoride preparations with and without added vitamins. *J Pediatr.* 1972;80(6):1018-1021, [PMID: 5026023]
Exclusion code: 2

Herndon JB, Tomar SL, Lossius MN, Catalanotto FA. Preventive oral health care in early childhood: Knowledge, confidence, and practices of pediatricians and family physicians in florida. *Journal of Pediatrics.* 2010;157(6):1018-1024.e1012, [PMID: 20655542]
Exclusion code: 3

Herrmann HJ, Roberts MW. Preventive dental care: The role of the pediatrician. *Pediatrics.* 1987;80(1):107-110, [PMID: 3601505]
Exclusion code: 5

Hiller KA, Wilfart G, Schmalz G. Developmental Enamel Defects in Children with Different Fluoride Supplementation - A Follow-Up Study. *Caries Res.* 1998;32(6):405-411, [PMID: 9745112]
Exclusion code: 4

Hochstetter AS, Lombardo MJ, D'eramo L, Piovano S, Bordoni N. Effectiveness of a preventive educational programme on the oral health of preschool children. *Promotion & education.* 2007;14(3):155-158, [PMID: 18154225]
Exclusion code: 9

Appendix A4. Excluded Studies List

Hoeft KS, Barker JC, Masterson EE. Maternal beliefs and motivations for first dental visit by low-income Mexican American children in California. *Pediatr Dent.* 2011;33(5):392-398, [PMID: 22104706]
Exclusion code: 8

Holbrook WP, de Soet JJ, de Graaff J. Prediction of dental caries in pre-school children. *Caries Res.* 1993;27(5):424-430, [PMID: 8242681]
Exclusion code: 8

Holgerson PL, Twetman S, Stecksen-Blicks C. Validation of an age-modified caries risk assessment program (Cariogram) in preschool children. *Acta Odontol Scand.* 2009;67(2):106-112, [PMID: 19152150]
Exclusion code: 2

Holm AK. Effect of a fluoride varnish (Duraphat ®) in preschool children. *Community Dentistry and Oral Epidemiology.* 1979;7(5):241-245, [PMID: 295702]
Exclusion code: 11

Holm GB, Holst K, Koch G, Widenheim J. Fluoride chewing tablets--a new aid in caries prevention. Comparative effect of a weekly mouthrinse with 0.2% NaF and daily chewing of a fluoride tablet (Gostrimant (R)). 2. year clinical test in schoolchildren. *Tandlakartidningen.* 1975;67(6):354-361, [PMID: 1057274]
Exclusion code: 7

Holm GB, Holst K, Mejare I. The caries-preventive effect of a fluoride varnish in the fissures of the first permanent molar. *Acta Odontol Scand.* 1984;42(4):193-197, [PMID: 6594021]
Exclusion code: 3

Holst A, Braune K. Dental assistants' ability to select caries risk-children and to prevent caries. *Swed Dent J.* 1994;18(6):243-249, [PMID: 7725238]
Exclusion code: 9

Holst A, Mårtensson I, Laurin M. Identification of caries risk children and prevention of caries in pre-school children. *Swed Dent J.* 1997;21(5):185-191, [PMID: 9472147]
Exclusion code: 9

Holt RD, Winter GB, Fox B, Askew R. Effects of dental health education for mothers with young children in London. *Community Dentistry and Oral Epidemiology.* 1985;13(3):148-151, [PMID: 860335]
Exclusion code: 4

Holt RD, Winter GB, Fox B, Askew R. Second assessment of London children involved in a scheme of dental health education in infancy. *Community Dent Oral Epidemiol.* 1989;17(4):180-182, [PMID: 2758790]
Exclusion code: 11

Holve S. An observational study of the association of fluoride varnish applied during well child visits and the prevention of early childhood caries in American Indian children. *Maternal and Child Health Journal.* 2008;12(SUPPL. 1):S64-S67, [PMID: 17957458]
Exclusion code: 5

Hong L, Levy SM, Broffitt B, et al. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. *Community Dentistry and Oral Epidemiology.* 2006;34(4):299-309, [PMID: 16856950]
Exclusion code: 4

Hong L, Levy SM, Warren JJ, Broffitt B, Cavanaugh J. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. *Caries Res.* 2006;40(6):494-500, [PMID: 17063020]
Exclusion code: 4

Horowitz HS. Research issues in early childhood caries. *Community Dentistry and Oral Epidemiology.* 1998;26(1 SUPPL.):67-81, [PMID: 9671202]
Exclusion code: 5

Horowitz HS. The role of dietary fluoride supplements in caries prevention. *J Public Health Dent.* 1999;59(4):205-210, [PMID: 10682325]
Exclusion code: 11

Howell E, Trenholm C, Dubay L, Hughes D, Hill I. The impact of new health insurance coverage on undocumented and other low-income children: lessons from three California counties. *J Health Care Poor Underserved.* 2010;21(2 Suppl):109-124, [PMID: 20453380]
Exclusion code: 2

Hu D, Wan H, Li S. The caries-inhibiting effect of a fluoride drop program: a 3-year study on Chinese kindergarten children. *Chin J Dent Res* 1998;1(3):17-20, [PMID: 10557167]
Exclusion code: 11

Hujoel PP, Makinen KK, Bennett CA, et al. The optimum time to initiate habitual xylitol gum-chewing for obtaining long-term caries prevention. *J Dent Res.* 1999;78(3):797-803, [PMID: 10096456]

Appendix A4. Excluded Studies List

Exclusion code: 3

Huntington NL, Kim IJ, Hughes CV. Caries-risk factors for Hispanic children affected by early childhood caries. *Pediatr Dent.* 2002;24(6):536-542, [PMID: 12528946]
Exclusion code: 8

Huston JP. Preventing dental disease. *J Calif Dent Assoc.* 2006;34(7):491-492, [PMID: 16995607]
Exclusion code: 5

Huttunen JK. Serum lipids, uric acid and glucose during chronic consumption of fructose and xylitol in healthy human subjects. *Int Z Vitam Ernahrungsforsch Beih.* 1976;15:105-115, [PMID: 1066327]
Exclusion code: 8

Imfeld TN. Clinical caries studies with polyalcohols. A literature review. *Schweiz Monatsschr Zahnmed.* 1994;104(8):941-945, [PMID: 8091172]
Exclusion code: 5

Institute of Medicine. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*: The National Academies Press; 1997.
Exclusion code: 2

Ismail AI, Bandekar RR. Fluoride supplements and fluorosis: A meta-analysis. *Community Dent Oral Epidemiol.* 1999;27(1):48-56, [PMID: 10086926]
Exclusion code: 2

Ismail AI, Nainar SMH, Sohn W. Children's first dental visit: Attitudes and practices of US pediatricians and family physicians. *Pediatr Dent.* 2003;25(5):425-430, [PMID: 14649605]
Exclusion code: 8

Ismail AI, Ondersma S, Jedele JMW, Little RJ, Lepkowski JM. Evaluation of a brief tailored motivational intervention to prevent early childhood caries. *Community Dent Oral Epidemiol.* 2011;39(5):433-448, [PMID: 21916925]
Exclusion code: 9

Ismail AI, Sohn W, Tellez M, et al. The International Caries Detection and Assessment System (ICDAS): an integrated system for measuring dental caries. *Community Dent Oral Epidemiol.* 2007;35(3):170-178, [PMID: 17518963]
Exclusion code: 5

Ismail AI, Sohn W, Tellez M, Willem JM, Betz J, Lepkowski J. Risk indicators for dental caries using the International Caries Detection and Assessment System (ICDAS). *Community Dentistry and Oral Epidemiology.* 2008;36(1):56-68, [PMID: 18205641]
Exclusion code: 3

Isogangas P, Makinen KK, Tiekso J, Alanen P. Long-term effect of xylitol chewing gum in the prevention of dental caries: a follow-up 5 years after termination of a prevention program. *Caries Res.* 1993;27(6):495-498, [PMID: 8281565]
Exclusion code: 3

Isokangas P. [Xylitol chewing gum in caries prevention. A longitudinal study on Finnish school children]. *Proc Finn Dent Soc.* 1987;83(5-6):285-288, [PMID: 3432257]
Exclusion code: 7

Isokangas P, Alanen P, Tiekso J. The clinician's ability to identify caries risk subjects without saliva tests--a pilot study. *Community Dentistry and Oral Epidemiology.* 1993;21(1):8-10, [PMID: 8432109]
Exclusion code: 5

Isokangas P, Alanen P, Tiekso J, Makinen KK. Xylitol chewing gum in caries prevention: a field study in children. *J Am Dent Assoc.* 1988;117(2):315-320, [PMID: 3166474]
Exclusion code: 3

Isokangas P, Soderling E, Pienihakkinen K, Alanen P. Occurrence of dental decay in children after maternal consumption of xylitol chewing gum, a follow-up from 0 to 5 years of age. *J Dent Res.* 2000;79(11):1885-1889, [PMID: 11145360]
Exclusion code: 3

Isokangas P, Tenovuo J, Soderling E, Mannisto H, Makinen KK. Dental caries and mutans streptococci in the proximal areas of molars affected by the habitual use of xylitol chewing gum. *Caries Res.* 1991;25(6):444-448, [PMID: 1810656]
Exclusion code: 3

Isokangas P, Tiekso J, Alanen P, Makinen KK. Long-term effect of xylitol chewing gum on dental caries. *Community Dent Oral Epidemiol.* 1989;17(4):200-203, [PMID: 2758793]
Exclusion code: 3

Jackson SL, Vann WF, Jr., Kotch JB, Pahel BT, Lee JY. Impact of poor oral health on children's school attendance and performance. *Am J Public Health.* 2011;101(10):1900-1906, [PMID: 21330579]
Exclusion code: 2

Appendix A4. Excluded Studies List

Jiang H, Tai B, Du M, Peng B. Effect of professional application of APF foam on caries reduction in permanent first molars in 6-7-year-old children: 24-month clinical trial. *J Dent.* 2005;33(6):469-473, [PMID: 15935266]
Exclusion code: 3

Joharji RM, Adenubi JO. Prevention of pit and fissure caries using an antimicrobial varnish: 9 month clinical evaluation. *J Dent.* 2001;29(4):247-254, [PMID: 1525226]
Exclusion code: 3

Johnsen DC. The role of the pediatrician in identifying and treating dental caries. *Pediatric Clinics of North America.* 1991;38(5):1173-1181, [PMID: 1886741]
Exclusion code: 5

Jones K, Tomar SL. Estimated impact of competing policy recommendations for age of first dental visit. *Pediatrics.* 2005;115(4):906-914, [PMID: 15805363]
Exclusion code: 2

Jones KF, Berg JH. Fluoride supplementation. A survey of pediatricians and pediatric dentists. *Am J Dis Child.* 1992;146(12):1488-1491, [PMID: 1456266]
Exclusion code: 11

Juric H, Dukic W, Jankovic B, Karlovic Z, Pavelic B. Suppression of salivary Streptococcus mutans and lactobacilli by topical caries preventive agents. *Cent Eur J Public Health.* 2003;11(4):219-222, [PMID: 14768786]
Exclusion code: 8

Kaakko T, Skaret E, Getz T, et al. An ABCD program to increase access to dental care for children enrolled in Medicaid in a rural county. *J Public Health Dent.* 2002;62(1):45-50, [PMID: 14700089]
Exclusion code: 2

Källestål C. Evaluation of caries preventive, measures. *Swed Dent J.* 2000;24(1-2):1-11, [PMID: 10997757]
Exclusion code: 5

Kandelman D, Bar A, Hefti A. Collaborative WHO xylitol field study in French Polynesia. I. Baseline prevalence and 32-month caries increment. *Caries Res.* 1988;22(1):55-62, [PMID: 3422062]
Exclusion code: 3

Kandelman D, Gagnon G. Clinical results after 12 months from a study of the incidence and progression of dental caries in relation to consumption of chewing-gum containing xylitol in school preventive programs. *J Dent Res.* 1987;66(8):1407-1411, [PMID: 3476611]
Exclusion code: 3

Kawashita Y, Fukuda H, Kawasaki K, et al. Pediatrician-recommended use of sports drinks and dental caries in 3-year-old children. *Community Dent Health.* 2011;28(1):29-33, [PMID: 21485231]
Exclusion code: 8

Kawashita Y, Kitamura M, Saito T. Early childhood caries. *Int J Dent.* 2011;2011:725320, [PMID: 22007218]
Exclusion code: 2

Kay E, Locker D. A systematic review of the effectiveness of health promotion aimed at improving oral health. *Community Dent Health.* 1998;15(3):132-144, [PMID: 10645682]
Exclusion code: 11

Kay EJ, Locker D. Is dental health education effective? A systematic review of current evidence. *Community Dent Oral Epidemiol.* 1996;24(4):231-235, [PMID: 8871028]
Exclusion code: 11

Kebriaei A, Rothe V, Pitner S, Balluff M, Salama F. Effectiveness of a basic training presentation on infant oral health care for pediatric medicine residents. *J Clin Pediatr Dent.* 2008;33(2):143-146, [PMID: 19358382]
Exclusion code: 3

Kertesz P, Schuder L, Szoke J, et al. [3 years' results of the WHO xylitol caries-preventing program in Hungarian children's homes. VI. Changes in the carbohydrate-protein ratio in dental plaque]. *Fogorv Sz.* 1988;81(2):33-37, [PMID: 3268440]
Exclusion code: 7

Khambanonda S, Chandravejjsmarn R, Barmes DE, Sardo Infirri J, Moller I. [Prevention of dental caries in Thailand: 3 fluoridated products submitted for comparative tests]. *J Biol Buccale.* 1983;11(3):255-263, [PMID: 6581163]
Exclusion code: 7

Kobayashi M, Chi D, Coldwell SE, Domoto P, Milgrom P. The effectiveness and estimated costs of the access to baby and child dentistry program in Washington State. *J Am Dent Assoc.* 2005;136(9):1257-1263, [PMID: 16196230]
Exclusion code: 3

Appendix A4. Excluded Studies List

Kopycka-Kedzierawski DT, Bell CH, Billings RJ. Prevalence of dental caries in Early Head Start children as diagnosed using teledentistry. *Pediatr Dent.* 2008;30(4):329-333, [PMID: 18767513]
Exclusion code: 4

Kopycka-Kedzierawski DT, Billings RJ. Teledentistry in inner-city child-care centres. *J Telemed Telecare.* 2006;12(4):176-181, [PMID: 16774697]
Exclusion code: 4

Kopycka-Kedzierawski DT, Billings RJ. Prevalence of dental caries and dental care utilisation in preschool urban children enrolled in a comparative-effectiveness study. *European archives of paediatric dentistry : official journal of the European Academy of Paediatric Dentistry.* 2011;12(3):133-138, [PMID: 21640057]
Exclusion code: 2

Kopycka-Kedzierawski DT, Billings RJ, McConnochie KM. Dental screening of preschool children using teledentistry: a feasibility study. *Pediatr Dent.* 2007;29(3):209-213, [PMID: 17688017]
Exclusion code: 2

Kowash MB, Pinfield A, Smith J, Curzon ME. Effectiveness on oral health of a long-term health education programme for mothers with young children. *Br Dent J.* 2000;188(4):201-205, [PMID: 10740903]
Exclusion code: 9

Kramer PF, Ardenghi TM, Ferreira S, Fischer LDA, Cardoso L, Feldens CA. Use of dental services by preschool children in Canela, Rio Grande do Sul State, Brazil. *Utilização de serviços odontológicos por crianças de 0 a 5 anos de idade no Município de Canela, Rio Grande do Sul, Brasil.* 2008;24(1):150-156, [PMID: 18209843]
Exclusion code: 7

Kranz AM, Rozier RG, Zeldin LP, Preisser JS. Oral health activities of early head start teachers directed toward children and parents. *J Public Health Dent.* 2011;71(2):161-169, [PMID: 21774140]
Exclusion code: 9

Kruger E, Dyson K, Tennant M. Pre-school child oral health in rural Western Australia. *Aust Dent J.* 2005;50(4):258-262, [PMID: 17016892]
Exclusion code: 8

Kumar J, Swango P, Haley V, Green E. Intra-oral distribution of dental fluorosis in Newburgh and Kingston, New York. *J Dent Res.* 2000;79(7):1508-1513, [PMID: 11005736]
Exclusion code: 4

Kuthy RA, McTigue DJ. Fluoride prescription practices of Ohio physicians. *J Public Health Dent.* 1987;47(4):172-176, [PMID: 3478487]
Exclusion code: 11

Kutsch VK, Young DA. New directions in the etiology of dental caries disease. *J Calif Dent Assoc.* 2011;39(10):716-721, [PMID: 22132583]
Exclusion code: 5

Lam M, Riedy CA, Coldwell SE, Milgrom P, Craig R. Children's acceptance of xylitol-based foods. *Community Dent Oral Epidemiol.* 2000;28(2):97-101, [PMID: 10730717]
Exclusion code: 8

Lave JR, Keane CR, Lin CJ, Ricci EM. The impact of dental benefits on the utilization of dental services by low-income children in western Pennsylvania. *Pediatr Dent.* 2002;24(3):234-240, [PMID: 12064498]
Exclusion code: 2

Law V, Seow WK. A longitudinal controlled study of factors associated with mutans streptococci infection and caries lesion initiation in children 21 to 72 months old. *Pediatr Dent.* 2006;28(1):58-65, [PMID: 16615377]
Exclusion code: 4

Law V, Seow WK. A longitudinal study of 0.2% chlorhexidine gel for removal of mutans streptococci infection in preschool children. *Aust Dent J.* 2007;52(1):26-32, [PMID: 17500161]
Exclusion code: 8

Lawrence A. Dental health educators in general practice have small impact. *Evidence-based dentistry.* 2004;5(1):15, [PMID: 15238970]
Exclusion code: 5

Lee B, Sue D. Xylitol for prevention of dental caries. *Dicp.* 1989;23(9):691-692, [PMID: 2800584]
Exclusion code: 5

Lee JY, Bouwens TJ, Savage MF, Vann Jr WF. Examining the cost-effectiveness of early dental visits. *Pediatr Dent.* 2006;28(2):102-105, [PMID: 16708783]
Exclusion code: 4

Lepore LM, Yoon RK, Chinn CH, Chussid S. Evaluation of behavior change goal-setting action plan on oral health activity and status. *N Y State Dent J.* 2011;77(6):43-47, [PMID: 22338818]

Appendix A4. Excluded Studies List

Exclusion code: 9

Levy SM. Systemic fluoride supplementation in an academic family practice setting. *J Fam Pract.* 1987;24(5):532, 534, 536, [PMID: 3572325]
Exclusion code: 11

Levy SM, Kiritsy MC, Slager SL, Warren JJ. Patterns of dietary fluoride supplement use during infancy. *J Public Health Dent.* 1998;58(3):228-233, [PMID: 10101699]
Exclusion code: 11

Lewis CW, Boulter S, Keels MA, et al. Oral health and pediatricians: results of a national survey. *Acad Pediatr.* 2009;9(6):457-461, [PMID: 19945080]
Exclusion code: 2

Lewis CW, Grossman DC, Domoto PK, Deyo RA. The role of the pediatrician in the oral health of children: A national survey. *Pediatrics.* 2000;106(6):E84, [PMID: 11099627]
Exclusion code: 11

Liao C-C, Ganz ML, Jiang H, Chelmow T. The impact of the public insurance expansions on children's use of preventive dental care. *Matern Child Health J.* 2010;14(1):58-66, [PMID: 19067137]
Exclusion code: 2

Lin DL, Harrison R, Aleksejuniene J. Can a prenatal dental public health program make a difference? *J Can Dent Assoc.* 2011;77:b32, [PMID: 21507285]
Exclusion code: 4

Lin YTJ, Tsai CL. Comparative Anti-Caries Effects of Tablet and Liquid Fluorides in Cleft Children. *J Clin Dent.* 2000;11(4):104-106, [PMID: 11460274]
Exclusion code: 11

Liu J, Probst JC, Martin AB, Wang J-Y, Salinas CF. Disparities in dental insurance coverage and dental care among US children: the National Survey of Children's Health. *Pediatrics.* 2007;119 Suppl 1:S12-21, [PMID: 17272579]
Exclusion code: 2

Liu M, Zhu L, Zhang B, Petersen PE. Changing use and knowledge of fluoride toothpaste by schoolchildren, parents and schoolteachers in Beijing, China. *Int Dent J.* 2007;57(3):187-194, [PMID: 17695741]
Exclusion code: 8

Loesche WJ, Grossman NS, Earnest R, Corpron R. The effect of chewing xylitol gum on the plaque and saliva levels of Streptococcus mutans. *The Journal of the American Dental Association.* 1984;108(4):587-592, [PMID: 6427315]
Exclusion code: 3

Loftus R. Advancing the practice of dental disease management. *J Calif Dent Assoc.* 2011;39(10):701-708.
Exclusion code: 5

Ly KA, Milgrom P, Rothen M. The potential of dental-protective chewing gum in oral health interventions. *J Am Dent Assoc.* 2008;139(5):553-563, [PMID: 18451371]
Exclusion code: 2

Lynch H, Milgrom P. Xylitol and dental caries: an overview for clinicians. *J Calif Dent Assoc.* 2003;31(3):205-209, [PMID: 12693818]
Exclusion code: 2

Machiulskiene V, Nyvad B, Baelum V. Caries preventive effect of sugar-substituted chewing gum. *Community Dent Oral Epidemiol.* 2001;29(4):278-288, [PMID: 11515642]
Exclusion code: 3

Machiulskiene V, Nyvad B, Baelum V. Determinants of dropout in a community intervention trial on the caries-preventive effect of chewing gums. *J Public Health Dent.* 2002;62(1):21-27, [PMID: 14700085]
Exclusion code: 3

MacRitchie HM, Longbottom C, Robertson M, et al. Development of the Dundee Caries Risk Assessment Model (DCRAM)--risk model development using a novel application of CHAID analysis. *Community Dent Oral Epidemiol.* 2012;40(1):37-45, [PMID: 21838824]
Exclusion code: 2

Maguire A, Rugg-Gunn AJ. Xylitol and caries prevention--is it a magic bullet? *Br Dent J.* 2003;194(8):429-436, [PMID: 12778091]
Exclusion code: 2

Makinen KK. Biochemical principles of the use of xylitol in medicine and nutrition with special consideration of dental aspects. *Experientia Suppl.* 1978(30):1-160, [PMID: 357173]
Exclusion code: 5

Makinen KK, Chen CY, Makinen PL, et al. Properties of whole saliva and dental plaque in relation to 40-month consumption of chewing gums containing xylitol, sorbitol of sucrose. *Caries Res.* 1996;30(3):180-188, [PMID: 8860027]
Exclusion code: 3

Appendix A4. Excluded Studies List

Makinen KK, Chiego DJ, Jr., Allen P, et al. Physical, chemical, and histologic changes in dentin caries lesions of primary teeth induced by regular use of polyol chewing gums. *Acta Odontol Scand.* 1998;56(3):148-156, [PMID: 9688223]
Exclusion code: 3

Makinen KK, Hujoel PP, Bennett CA, et al. A descriptive report of the effects of a 16-month xylitol chewing-gum programme subsequent to a 40-month sucrose gum programme. *Caries Res.* 1998;32(2):107-112, [PMID: 9544858]
Exclusion code: 3

Makinen KK, Hujoel PP, Bennett CA, Isotupa KP, Makinen PL, Allen P. Polyol chewing gums and caries rates in primary dentition: a 24-month cohort study. *Caries Res.* 1996;30(6):408-417, [PMID: 8946097]
Exclusion code: 3

Makinen KK, Isotupa KP, Makinen P-L, et al. Six-month polyol chewing-gum programme in kindergarten-age children: a feasibility study focusing on mutans streptococci and dental plaque. *Int Dent J.* 2005;55(2):81-88, [PMID: 15880962]
Exclusion code: 8

Makinen KK, Makinen PL, Pape HR, Jr., et al. Stabilisation of rampant caries: polyol gums and arrest of dentine caries in two long-term cohort studies in young subjects. *Int Dent J.* 1995;45(1 Suppl 1):93-107, [PMID: 7607749]
Exclusion code: 3

Makinen KK, Scheinin A. Turku sugar studies. II. Preliminary biochemical and general findings. *Acta Odontol Scand.* 1974;32(6):413-421, [PMID: 4533573]
Exclusion code: 5

Makinen KK, Scheinin A. Turku sugar studies. VI. The administration of the trial and the control of the dietary regimen. *Acta Odontol Scand.* 1976;34(4):217-239, [PMID: 795261]
Exclusion code: 3

Makinen KK, Soderling E, Hurttia H, Lehtonen OP, Luukkala E. Biochemical, microbiologic, and clinical comparisons between two dentifrices that contain different mixtures of sugar alcohols. *The Journal of the American Dental Association.* 1985;111(5):745-751, [PMID: 3905908]
Exclusion code: 3

Makinen KK, Soderling E, Isokangas P, Tenovuo J, Tiekso J. Oral biochemical status and depression of Streptococcus mutans in children during 24- to 36-month use of xylitol chewing gum. *Caries Res.* 1989;23(4):261-267, [PMID: 2790861]
Exclusion code: 3

Makinen KK, Tenovuo J, Scheinin A. Xylitol-induced increase of lactoperoxidase activity. *J Dent Res.* 1976;55(4):652-660, [PMID: 777061]
Exclusion code: 8

Malcheff S, Pink TC, Sohn W, Inglehart MR, Briskie D. Infant oral health examinations: Pediatric dentists' professional behavior and attitudes. *Pediatr Dent.* 2009;31(3):202-209, [PMID: 19552224]
Exclusion code: 3

Mamber E. Baby clinic: a comprehensive project to promote oral health in expecting mothers and their babies. *Alpha Omegan.* 2004;97(3):33-34, [PMID: 15641758]
Exclusion code: 5

Mandel ID. Caries Prevention: Current Strategies, New Directions. *J Am Dent Assoc.* 1996;127(10):1477-1488, [PMID: 8908917]
Exclusion code: 5

Marcucci M, Bandettini MV, Panattoni E, Nucci N, Patane F. [Sugar substitutes and dental caries]. *Prev Stomatol.* 1984;10(1):9-25, [PMID: 6382242]
Exclusion code: 7

Margolis FJ, Burt BA, Schork MA, Bashshur RL, Whittaker BA, Burns TL. Fluoride supplements for children. A survey of physicians' prescription practices. *Am J Dis Child.* 1980;134(9):865-868, [PMID: 7416113]
Exclusion code: 11

Margolis FJ, Chesney BK, Schork A. Fluoride supplements. Changes in physicians' attitudes and practices following an intensive, multifaceted educational program. *Am J Dis Child.* 1987;141(1):72-76, [PMID: 3788885]
Exclusion code: 11

Margolis FJ, Macauley J, Freshman E. The effects of measured doses of fluoride. A five-year preliminary report. *Am J Dis Child.* 1967;113(6):670-672, [PMID: 4381737]
Exclusion code: 11

Margolis FJ, Reames HR, Freshman E, MaCauley CD, Mehaffey H. Flouride. Ten-year prospective study of deciduous and permanent dentition. *American Journal*

Appendix A4. Excluded Studies List

of Diseases of Children. 1975;129(7):794-800, [PMID: 1096595]
Exclusion code: 2

Marinho CV, Higgins PJ, Logan S, Sheiham A. Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents [Systematic Review]. *Cochrane Database Syst Rev.* 2009(1), [PMID: 14583954]
Exclusion code: 3

Marinho CV, Higgins PJ, Logan S, Sheiham A. Fluoride mouthrinses for preventing dental caries in children and adolescents [Systematic Review]. *Cochrane Database Syst Rev.* 2009(4), [PMID: 12917928]
Exclusion code: 3

Marinho CV, Higgins PJ, Logan S, Sheiham A. Fluoride gels for preventing dental caries in children and adolescents [Systematic Review]. *Cochrane Database Syst Rev.* 2009(4), [PMID: 12076446]
Exclusion code: 3

Marinho CV, Higgins PJ, Sheiham A, Logan S. One topical fluoride (toothpastes, or mouthrinses, or gels, or varnishes) versus another for preventing dental caries in children and adolescents [Systematic Review]. *Cochrane Database Syst Rev.* 2009(1), [PMID: 14583954]
Exclusion code: 3

Marinho CV, Higgins PJ, Sheiham A, Logan S. Combinations of topical fluoride (toothpastes, mouthrinses, gels, varnishes) versus single topical fluoride for preventing dental caries in children and adolescents [Systematic Review]. *Cochrane Database Syst Rev.* 2009(1), [PMID: 14973992]
Exclusion code: 3

Marinho VC, Higgins JP, Logan S, Sheiham A. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane database of systematic reviews (Online).* 2002(3), [PMID: 12137653]
Exclusion code: 3

Marinho VC, Higgins JP, Logan S, Sheiham A. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane database of systematic reviews (Online).* 2009, [PMID: 12137653]
Exclusion code: 6

Marshall TA, Levy SM, Broffitt B, et al. Dental caries and beverage consumption in young children. *Pediatrics.* 2003;112(3 Pt 1):e184-191, [PMID: 12949310]
Exclusion code: 8

Martin AB, Probst J, Wang J-Y, Hale N. Effect of having a personal healthcare provider on access to dental care among children. *J Public Health Manag Pract.* 2009;15(3):191-199, [PMID: 19363398]
Exclusion code: 2

Massoth D, Massoth G, Massoth IR, et al. The effect of xylitol on Streptococcus mutans in children. *J Calif Dent Assoc.* 2006;34(3):231-234, [PMID: 16895079]
Exclusion code: 3

McCunniff MD, Damiano PC, Kanellis MJ, Levy SM. The impact of WIC dental screenings and referrals on utilization of dental services among low-income children. *Pediatr Dent.* 1998;20(3):181-187., [PMID: 9635314]
Exclusion code: 11

McDonagh MS, Whiting PF, Wilson PM, et al. Systematic review of water fluoridation. *Bmj.* 2000;321(7265):855-859, [PMID: 11021861]
Exclusion code: 11

Messimer S, Hickner J. Oral fluoride supplementation: improving practitioner compliance by using a protocol. *J Fam Pract.* 1983;17(5):821-825, [PMID: 6631346]
Exclusion code: 11

Meurman P, Merilainen L, Pienihakkinen K, Alanen P, Trahan L, Soderling E. Xylitol-resistant mutans streptococci strains and the frequency of xylitol consumption in young children. *Acta Odontol Scand.* 2005;63(5):314-316, [PMID: 16419438]
Exclusion code: 8

Meurman P, Pienihakkinen K, Eriksson A-L, Alanen P. Oral health programme for preschool children: a prospective, controlled study. *Int J Paediatr Dent.* 2009;19(4):263-273, [PMID: 19320915]
Exclusion code: 4

Meyer K, Geurtsen W, Gunay H. An early oral health care program starting during pregnancy: results of a prospective clinical long-term study. *Clin Oral Investig.* 2010;14(3):257-264, [PMID: 19543927]
Exclusion code: 3

Milgrom P, Chi DL. Prevention-centered caries management strategies during critical periods in early childhood. *J Calif Dent Assoc.* 2011;39(10):735-741, [PMID: 22132585]
Exclusion code: 2

Appendix A4. Excluded Studies List

Milgrom P, Tut OK. Evaluation of Pacific Islands Early Childhood Caries Prevention Project: Republic of the Marshall Islands. *J Public Health Dent.* 2009;69(3):201-203, [PMID: 19486466]
Exclusion code: 3

Milgrom P, Weinstein P, Huebner C, Graves J, Tut O. Empowering Head Start to improve access to good oral health for children from low income families. *Matern Child health.* 2011;15:876-882, [PMID: 18246416]
Exclusion code: 8

Milgrom P, Zero DT, Tanzer JM. An examination of the advances in science and technology of prevention of tooth decay in young children since the Surgeon General's Report on Oral Health. *Acad Pediatr.* 2009;9(6):404-409, [PMID: 19837019]
Exclusion code: 2

Minah G, Lin C, Coors S, Rambob I, Tinanoff N, Grossman LK. Evaluation of an early childhood caries prevention program at an urban pediatric clinic. *Pediatr Dent.* 2008;30(6):499-504, [PMID: 19186776]
Exclusion code: 4

Mofidi M, Slifkin R, Freeman V, Silberman P. The impact of a state children's health insurance program on access to dental care. *J Am Dent Assoc.* 2002;133(6):707-714; quiz 767-708, [PMID: 12083646]
Exclusion code: 2

Mohebbi SZ, Virtanen JI, Vahid-Golpayegani M, Vehkalahti MM. A cluster randomised trial of effectiveness of educational intervention in primary health care on early childhood caries. *Caries Res.* 2009;43(2):110-118, [PMID: 19321988]
Exclusion code: 4

Mouradian WE, Wehr E, Crall JJ. Disparities in children's oral health and access to dental care. *Journal of the American Medical Association.* 2000;284(20):2625-2631, [PMID: 11086371]
Exclusion code: 2

Nagarkar S, Kumar J, Moss M. Early childhood caries-related visits to emergency departments and ambulatory surgery facilities and associated charges in New York state. *JADA.* 2012;143:59-65, [PMID: 22207670]
Exclusion code: 4

Nakai Y, Shinga-Ishihara C, Kaji M, Moriya K, Murakami-Yamanaka K, Takimura M. Xylitol gum and maternal transmission of mutans streptococci. *J Dent Res.* 2010;89(1):56-60, [PMID: 19948944]
Exclusion code: 3

National Center for Health Statistics. Healthy People 2010 Final Review. *Healthy People.* 2010.
Exclusion code: 2

Newburn E. The potential role of alternative sweeteners in caries prevention. *Isr J Dent Sci.* 1991;2(4):200-213, [PMID: 1958328]
Exclusion code: 5

Nietert PJ, Bradford WD, Kaste LM. The impact of an innovative reform to the South Carolina dental medicaid system. *Health Serv Res.* 2005;40(4):1078-1091, [PMID: 16033493]
Exclusion code: 2

Nord A, Haugejorden O. [Two-year trial of the fluoride-containing varnishes Duraphat and Carex]. *Nor Tannlaegeforen Tid.* 1991;101(2):46-49, [PMID: 1861962]
Exclusion code: 7

Nordblad A, Suominen-Taipale L, Murtomaa H, Vartiainen E, Koskela K. Smart Habit Xylitol campaign, a new approach in oral health promotion. *Community Dent Health.* 1995;12(4):230-234, [PMID: 8536087]
Exclusion code: 3

North Carolina Department of Health and Human Services. Medical Providers: Partner with us to improve your child patients' oral health *Into the Mouths of Babes* 2012; http://www.ncdhhs.gov/dph/oralhealth/partners/IMB.htm. Accessed 20 Feb, 2013
Exclusion code: 5

Nowak AJ, PS. C. Using anticipatory guidance in pediatric dentistry: a developmentally paced prevention philosophy. *JADA.* 1995;126:1156-1164.
Exclusion code: 5

Ogard B, Seppä L, Rølla G. Professional topical fluoride applications--clinical efficacy and mechanism of action. *Adv Dent Res.* 1994;8(2):190-201, [PMID: 7865075]
Exclusion code: 8

Okunseri C, Szabo A, Jackson S, Pajewski NM, Garcia RI. Increased children's access to fluoride varnish treatment by involving medical care providers: effect of a Medicaid policy change. *Health Serv Res.* 2009;44(4):1144-1156, [PMID: 19453390]
Exclusion code: 2

Oliveira M, Paiva S, Martins L, Ramos-Jorge M, Lima Y, Cury J. Fluoride intake by children at risk for the development of dental fluorosis: comparison of regular

Appendix A4. Excluded Studies List

dentifrices and flavoured dentifrices for children. *Caries Res.* 2007;41(6):460-466, [PMID: 17823508]
Exclusion code: 8

O'Rourke CA, Attrill M, Holloway PJ. Cost appraisal of a fluoride tablet programme to Manchester primary schoolchildren. *Community Dentistry and Oral Epidemiology.* 1988;16(6):341-344, [PMID: 3144446]
Exclusion code: 8

Pahel BT, Rozier RG, Stearns SC, B. QR. Effectiveness of preventive dental treatments by physicians for young Medicaid enrollees. *Pediatrics.* 2011;127(3):e682-689, [PMID: 21357343]
Exclusion code: 5

Passson C. Xylitol: a sugar that fights tooth decay. *J Colo Dent Assoc.* 1993;71(3):19-23, [PMID: 8408742]
Exclusion code: 5

Peldyak J, Makinen KK. Xylitol for caries prevention. *J Dent Hyg.* 2002;76(4):276-285, [PMID: 12592919]
Exclusion code: 2

Pendrys DG. The fluorosis risk index: a method for investigating risk factors. *J Public Health Dent.* 1990;50(5):291-298, [PMID: 2231522]
Exclusion code: 8

Pendrys DG. Risk of enamel fluorosis in nonfluoridated and optimally fluoridated populations: considerations for the dental professional. *J Am Dent Assoc.* 2000;131(6):746-755, [PMID: 10860326]
Exclusion code: 11

Pendrys DG, Katz RV. Risk factors for enamel fluorosis in optimally fluoridated children born after the US manufacturers' decision to reduce the fluoride concentration of infant formula. *Am J Epidemiol.* 1998;148(10):967-974, [PMID: 9829868]
Exclusion code: 8

Pereira AC, Da Cunha FL, Meneghim MDC, Werner CW. Dental caries and fluorosis prevalence study in a nonfluoridated Brazilian community: Trend analysis and toothpaste association. *J Dent Child.* 2000;67(2):132-135, [PMID: 10826050]
Exclusion code: 3

Peretz B, Gluck G. Early childhood caries (ECC): a preventive-conservative treatment mode during a 12-month period. *J Clin Pediatr Dent.* 2006;30(3):191-194, [PMID: 16683664]
Exclusion code: 3

Petersson LG, Arthursson L, Ostberg C, Jonsson G, Gleerup A. Caries-inhibiting effects of different modes of duraphate varnish reapplication: A 3-year radiographic study. *Caries Res.* 1991;25(1):70-73, [PMID: 2070384]
Exclusion code: 3

Petersson LG, Birkhed D, Gleerup A, Johansson M, Jonsson G. Caries-preventive effect of dentifrices containing various types and concentrations of fluorides and sugar alcohols. *Caries Res.* 1991;25(1):74-79, [PMID: 2070385]
Exclusion code: 3

Petersson LG, Twetman S, Pakhomov GN. The efficiency of semiannual silane fluoride varnish applications: A two-year clinical study in preschool children. *J Public Health Dent.* 1998;58(1):57-60, [PMID: 9608447]
Exclusion code: 11

Peyron M, Matsson L, Birkhed D. Progression of approximal caries in primary molars and the effect of Duraphat treatment. *Scand J Dent Res.* 1992;100(6):314-318, [PMID: 1465563]
Exclusion code: 8

Pickett FA. Nonfluoride caries-preventive agents: new guidelines. *J Contemp Dent Pract.* 2011;12(6):469-474, [PMID: 22269228]
Exclusion code: 2

Pienihakkinen K, Jokela J. Clinical outcomes of risk-based caries prevention in preschool-aged children. *Community Dent Oral Epidemiol.* 2002;30(2):143-150, [PMID: 12000355]
Exclusion code: 2

Pienihäkkinen K, Jokela J, Alanen P. Assessment of Caries Risk in Preschool Children. *Caries Res.* 2004;38(2):156-162, [PMID: 14767173]
Exclusion code: 4

Pinkerton RE, Tinanoff N, Willms JL, Tapp JT. Resident physician performance in a continuing education format. Does newly acquired knowledge improve patient care? *Jama.* 1980;244(19):2183-2185, [PMID: 7420722]
Exclusion code: 11

Pita-Fernández S, Pombo-Sánchez A, Suárez-Quintanilla J, Novio-Mallón S, Rivas-Mundiña B, Pértega-Díaz S. Clinical relevance of tooth brushing in relation to dental caries. *Relevancia clínica del cepillado*

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dental y su relación con la caries. 2010;42(7):372-379, [PMID: 20116887]
Exclusion code: 7

Pitts NB, Boyles J, Nugent ZJ, Thomas N, Pine CM. The dental caries experience of 5-year-old children in Great Britain (2005/6). Surveys co-ordinated by the British Association for the study of community dentistry. *Community Dent Health.* 2007;24(1):59-63, [PMID: 17405473]
Exclusion code: 8

Plonka KA, Pukallus ML, Barnett A, Holcombe TF, Walsh LJ, Seow WK. A controlled, longitudinal study of home visits compared to telephone contacts to prevent early childhood caries. *Int J Paediatr Dent.* 2012, [PMID: 22251427]
Exclusion code: 4

Plotzitza B, Kneist S, Berger J, Hetzer G. Efficacy of chlorhexidine varnish applications in the prevention of early childhood caries. *European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry.* 2005;6(3):149-154, [PMID: 16216096]
Exclusion code: 8

Plutzer K, Keirse MJNC. Incidence and prevention of early childhood caries in one- and two-parent families. *Child Care Health Dev.* 2011;37(1):5-10, [PMID: 20533911]
Exclusion code: 3

Plutzer K, Spencer AJ. Efficacy of an oral health promotion intervention in the prevention of early childhood caries. *Community Dent Oral Epidemiol.* 2008;36(4):335-346, [PMID: 19145720]
Exclusion code: 3

Plutzer K, Spencer AJ, Keirse MJNC. Reassessment at 6-7 years of age of a randomized controlled trial initiated before birth to prevent early childhood caries. *Community Dent Oral Epidemiol.* 2012;40(2):116-124, [PMID: 22022927]
Exclusion code: 4

Poulsen S, Gadegaard E, Mortensen B. Cariostatic effect of daily use of a fluoride-containing lozenge compared to fortnightly rinses with 0.2% sodium fluoride. *Caries Res.* 1981;15(3):236-242, [PMID: 6938308]
Exclusion code: 3

Prakash P, Lawrence HP, Harvey BJ, McIsaac WJ, Limeback H, Leake JL. Early childhood caries and infant oral health: Paediatricians' and family physicians' knowledge, practices and training. *Paediatrics and Child Health.* 2006;11(3):151-157, [PMID: 19030271]
Exclusion code: 3

Pukallus ML, Plonka KA, Barnett AG, Walsh LJ, Holcombes TF, Kim Seow W. A randomised, controlled clinical trial comparing chlorhexidine gel and low-dose fluoride toothpaste to prevent early childhood caries. *Int J Paediatr Dent.* 2012(Epub), [PMID: 22713081]
Exclusion code: 4

Raitio M, Mottonen M, Uhari M. Toothbrushing and the occurrence of salivary mutans streptococci children at day care centers. *Caries Res.* 1995;29(4):280-284, [PMID: 7656297]
Exclusion code: 4

Raitio M, Pienihäkkinen K, Scheinin A. Multifactorial modeling for prediction of caries increment in adolescents. *Acta Odontol Scand.* 1996;54(2):118-121, [PMID: 8739144]
Exclusion code: 3

Ramirez JH, Arce R, Contreras A. Why must physicians know about oral diseases? *Teaching and Learning in Medicine.* 2010;22(2):148-155, [PMID: 20614382]
Exclusion code: 2

Ramos-Gomez F, Crystal YO, Ng MW, Tinanoff N, Featherstone JD. Caries risk assessment, prevention, and management in pediatric dental care. *Gen Dent.* 2010;58(6):505-517; quiz 518-509, [PMID: 21062720]
Exclusion code: 5

Ramos-Gomez F, Ng MW. Into the future: keeping healthy teeth caries free: pediatric CAMBRA protocols. *J Calif Dent Assoc.* 2011;39(10):723-733, [PMID: 22132584]
Exclusion code: 3

Ramos-Gomez FJ, Crall J, Gansky SA, Slayton RL, Featherstone JDB. Caries risk assessment appropriate for the age 1 visit (infants and toddlers). *J Calif Dent Assoc.* 2007;35(10):687-702, [PMID: 18044377]
Exclusion code: 5

Ramos-Gomez FJ, Crystal YO, Ng MW, Crall JJ, Featherstone JDB. Pediatric dental care: prevention and management protocols based on caries risk assessment.[Erratum appears in J Calif Dent Assoc. 2010 Nov;38(11):790]. *J Calif Dent Assoc.* 2010;38(10):746-761, [PMID: 21162350]
Exclusion code: 5

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Ramos-Gomez FJ, Gansky SA, Featherstone JDB, et al. Mother and youth access (MAYA) maternal chlorhexidine, counselling and paediatric fluoride varnish randomized clinical trial to prevent early childhood caries. *Int J Paediatr Dent.* 2012;22(3):169-179, [PMID: 21999806]
Exclusion code: 4

Ramseier CA, Leiggener I, Lang NP, Bagramian RA, Inglehart MR. Short-term effects of hygiene education for preschool (kindergarten) children: a clinical study. *Oral health prev.* 2007;5(1):19-24, [PMID: 17366757]
Exclusion code: 9

Rayner JA. A dental health education programme, including home visits, for nursery school children. *Br Dent J.* 1992;172(2):57-62, [PMID: 1739501]
Exclusion code: 11

Reich E, Lussi A, Newbrun E. Caries-risk assessment. *Int Dent J.* 1999;49(1):15-26, [PMID: 10887469]
Exclusion code: 5

Rethman MP, Beltran-Aguilar ED, Billings RJ, et al. *Non-fluoride caries preventive agents: Full report of systematic review and evidence-based recommendations* 5/24/2011 2011.
Exclusion code: 2

Rethman MP, Beltran-Aguilar ED, Billings RJ, et al. Nonfluoride caries-preventive agents: executive summary of evidence-based clinical recommendations. *J Am Dent Assoc.* 2011;142(9):1065-1071, [PMID: 21987836]
Exclusion code: 2

Ribelles Llop M, Guinot Jimeno F, Mayne Acien R, Bellet Dalmau LJ. Effects of xylitol chewing gum on salivary flow rate, pH, buffering capacity and presence of Streptococcus mutans in saliva. *Eur J Paediatr Dent.* 2010;11(1):9-14, [PMID: 20359274]
Exclusion code: 2

Richardson AS. Parental participation in the administration of fluoride supplements. *Can J Public Health.* 1967;58(11):508-513, [PMID: 6077085]
Exclusion code: 11

Rigilano JC, Friedler EM, Ehemann LJ. Fluoride prescribing patterns among primary care physicians. *J Fam Pract.* 1985;21(5):381-385, [PMID: 4056672]
Exclusion code: 11

Riordan PJ. Dental fluorosis decline after changes to supplement and toothpaste regimens. *Community Dentistry and Oral Epidemiology.* 2002;30(3):233-240, [PMID: 12000347]
Exclusion code: 4

Roberts MW. Dental health of children: Where we are today and remaining challenges. *J Clin Pediatr Dent.* 2008;32(3):231-234, [PMID: 18524274]
Exclusion code: 2

Roberts MW, Keels MA, Sharp MC, Lewis JL, Jr. Fluoride supplement prescribing and dental referral patterns among academic pediatricians. *Pediatrics.* 1998;101(1):E6, [PMID: 9417170]
Exclusion code: 11

Roeters FJ, Verdonschot EH, Bronkhorst EM, van 't Hof MA. Prediction of the need for bitewing radiography in detecting caries in the primary dentition. *Community Dentistry and Oral Epidemiology.* 1994;22(6):456-460, [PMID: 7882663]
Exclusion code: 8

Rosenblatt A, Stamford TCM, Niederman R. Silver diamine fluoride: A caries "silver-fluoride bullet". *J Dent Res.* 2009;88(2):116-125, [PMID: 19278981]
Exclusion code: 5

Rozier RG. The prevalence and severity of enamel fluorosis in North American children. *J Public Health Dent.* 1999;59(4):239-246, [PMID: 10682330]
Exclusion code: 11

Rozier RG. Effectiveness of methods used by dental professionals for the primary prevention of dental caries. *J Dent Educ.* 2001;65(10):1063-1072, [PMID: 11699978]
Exclusion code: 11

Rozier RG, Adair S, Graham F, et al. Evidence-based clinical recommendations on the prescription of dietary fluoride supplements for caries prevention: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc.* 2010;141(12):1480-1489, [PMID: 21158195]
Exclusion code: 2

Rozier RG, Slade GD, Zeldin LP, Wang H. Parents' satisfaction with preventive dental care for young children provided by nondental primary care providers. *Pediatr Dent.* 2005;27(4):313-322, [PMID: 16317972]
Exclusion code: 8

Sabbagh H, El-Kateb M, Al Nowaiser A, Hanno A, Alamoudi N. Assessment of pediatricians dental knowledge, attitude and behavior in Jeddah, Saudi

Appendix A4. Excluded Studies List

Arabia. *J Clin Pediatr Dent.* 2011;35(4):371-376, [PMID: 22046694]
Exclusion code: 3

Sakuma S, Nakamura M, Miyazaki H. Predictors of dental caries development in 1.5-year-old high-risk children in the Japanese public health service. *J Public Health Dent.* 2007;67(1):14-19, [PMID: 17436974]
Exclusion code: 10

Scheie AA, Fejerskov OB. Xylitol in caries prevention: what is the evidence for clinical efficacy? *Oral Dis.* 1998;4(4):268-278, [PMID: 10200706]
Exclusion code: 2

Scheinin A. Xylitol: an update. Recent studies, indications. *Oral Health.* 1981;71(8):43-47, [PMID: 6949112]
Exclusion code: 2

Scheinin A. Field studies on sugar substitutes. *Int Dent J.* 1985;35(3):195-200, [PMID: 3902660]
Exclusion code: 3

Scheinin A, Banoczy J. Collaborative WHO xylitol field studies in Hungary. An overview. *Acta Odontol Scand.* 1985;43(6):321-325, [PMID: 3867218]
Exclusion code: 3

Scheinin A, Banoczy J. Xylitol and caries: the collaborative WHO oral disease preventive programme in Hungary. *Int Dent J.* 1985;35(1):50-57, [PMID: 3858229]
Exclusion code: 3

Scheinin A, Banoczy J, Szoke J, et al. Collaborative WHO xylitol field studies in Hungary. I. Three-year caries activity in institutionalized children. *Acta Odontol Scand.* 1985;43(6):327-347, [PMID: 3879082]
Exclusion code: 3

Scheinin A, Makinen KK, Tammisalo E, Rekola M. Turku sugar studies. XVIII. Incidence of dental caries in relation to 1 year consumption of xylitol chewing gum. *Acta Odontol Scand.* 1975;33(5):269-278, [PMID: 1067728]
Exclusion code: 5

Scheinin A, Makinen KK, Ylitalo K. Turku sugar studies. I. An intermediate report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man. *Acta Odontol Scand.* 1974;32(6):383-412, [PMID: 4156819]
Exclusion code: 3

Scheinin A, Makinen KK, Ylitalo K. Turku sugar studies. V. Final report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man. *Acta Odontol Scand.* 1976;34(4):179-216, [PMID: 795260]
Exclusion code: 2

Scheinin A, Pienihakkinen K, Tiekso J, et al. Collaborative WHO xylitol field studies in Hungary. VII. Two-year caries incidence in 976 institutionalized children. *Acta Odontol Scand.* 1985;43(6):381-387, [PMID: 3879087]
Exclusion code: 3

Schinder E, Rosenberg M, Zangwill L. Educational approach to modifying dental habits in pre-school children. *Review Association Odontologica Argentina.* 1992;80(4).
Exclusion code: 7

Schröder U, Granath L. Dietary habits and oral hygiene as predictors of caries in 3-year-old children. *Community Dentistry and Oral Epidemiology.* 1983;11(5):308-311, [PMID: 6578900]
Exclusion code: 8

Schröder U, Widenheim J, Peyron M, Hägg E. Prediction of caries in 1 1/2-year-old children. *Swed Dent J.* 1994;18(3):95-104, [PMID: 8085221]
Exclusion code: 8

Schutze Jr HJ, Forrester DJ, Balis SB. Evaluation of a fluoride prophylaxis paste in a fluoridated community. *Journal of the Canadian Dental Association.* 1974;40(10):675-683, [PMID: 4154056]
Exclusion code: 4

Seale NS, Casamassimo PS. Access to dental care for children in the United States: a survey of general practitioners. *J Am Dent Assoc.* 2003;134(12):1630-1640, [PMID: 14719761]
Exclusion code: 2

Seale NS, Casamassimo PS. U.S. predoctoral education in pediatric dentistry: its impact on access to dental care. *J Dent Educ.* 2003;67(1):23-30, [PMID: 12540102]
Exclusion code: 2

Section on Pediatric D, Oral H. Preventive oral health intervention for pediatricians. *Pediatrics.* 2008;122(6):1387-1394, [PMID: 19015205]
Exclusion code: 2

Selwitz RH, Ismail AI, Pitts NB. Dental caries. *Lancet.* 2007;369(9555):51-59, [PMID: 17208642]
Exclusion code: 5

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Seow WK, Cheng E, Wan V. Effects of oral health education and tooth-brushing on mutans streptococci infection in young children. *Pediatr Dent.* 2003;25(3):223-228, [PMID: 12889697]
Exclusion code: 8

Seppa L, Hausen H, Karkkainen S. Plaque fluoride and mutans streptococci in plaque and saliva before and after discontinuation of water fluoridation. *Eur J Oral Sci.* 1996;104(4 (Pt 1)):353-358, [PMID: 8930582]
Exclusion code: 3

Seppa L, Karkkainen S, Hausen H. Caries frequency in permanent teeth before and after discontinuation of water fluoridation in Kuopio, Finland. *Community Dent Oral Epidemiol.* 1998;26(4):256-262, [PMID: 9758426]
Exclusion code: 3

Seppä L, Leppänen T, Hausen H. Fluoride varnish versus acidulated phosphate fluoride gel: a 3-year clinical trial. *Caries Res.* 1995;29(5):327-330, [PMID: 8521431]
Exclusion code: 3

Serwint JR, Mungo R, Negrete VF, Duggan AK, Korsch BM. Child-rearing practices and nursing caries. *Pediatrics.* 1993;92(2 I):233-237, [PMID: 8337022]
Exclusion code: 6

Sgan-Cohen HD, Mansbach IK, Haver D, Gofin R. Community-oriented oral health promotion for infants in Jerusalem: evaluation of a program trial. *J Public Health Dent.* 2001;61(2):107-113, [PMID: 11474913]
Exclusion code: 8

Shiboski CH, Gansky SA, Ramos-Gomez F, Ngo L, Isman R, Pollick HF. The association of early childhood caries and race/ethnicity among California preschool children.[Erratum appears in J Public Health Dent. 2003 Fall;63(4):264]. *J Public Health Dent.* 2003;63(1):38-46, [PMID: 12597584]
Exclusion code: 8

Shivaprakash PK, Elango I, Baweja DK, Noorani HH. The state of infant oral healthcare knowledge and awareness: Disparity among parents and healthcare professionals. *Journal of Indian Society of Pedodontics and Preventive Dentistry.* 2009;27(1):39-43, [PMID: 19414973]
Exclusion code: 3

Siegel C, Gutgesell ME. Fluoride supplementation in Harris County, Texas. *Am J Dis Child.* 1982;136(1):61-63, [PMID: 7055110]
Exclusion code: 11

Silva PF, Forte FDS, Chaves AMBP, Farias IAP, Castro KS. Reproducibility of caries diagnosis in permanent teeth according to WHO, ICDAS-II and Nyvad criteria. *Brazilian Journal of Oral Sciences.* 2012;11(1):25-29.
Exclusion code: 8

Silva R, Mendes S, Bernardo M, Barros L. Dental caries related practices and knowledge of pediatricians and family doctors. *Revista Portuguesa de Estomatologia, Medicina Dentaria e Cirurgia Maxilofacial.* 2012;53(3):135-142.
Exclusion code: 8

Sintes JL, Elias-Boneta A, Stewart B, Volpe AR, Lovett J. Anticaries efficacy of a sodium monofluorophosphate dentifrice containing xylitol in a dicalcium phosphate dihydrate base. A 30-month caries clinical study in Costa Rica. *Am J Dent.* 2002;15(4):215-219, [PMID: 12572637]
Exclusion code: 3

Sintes JL, Escalante C, Stewart B, et al. Enhanced anticaries efficacy of a 0.243% sodium fluoride/10% xylitol/silica dentifrice: 3-year clinical results. *Am J Dent.* 1995;8(5):231-235, [PMID: 8634157]
Exclusion code: 3

Slade GD, Rozier RG, Zeldin LP, Margolis PA. Training pediatric health care providers in prevention of dental decay: results from a randomized controlled trial. *BMC Health Serv Res.* 2007;7:176, [PMID: 17980021]
Exclusion code: 5

Söderling E, Alaräisänen L, Scheinin A, Mäkinen KK. Effect of xylitol and sorbitol on polysaccharide production by and adhesive properties of Streptococcus mutans. *Caries Res.* 1987;21(2):109-116, [PMID: 3469026]
Exclusion code: 3

Soderling E, Isokangas P, Pienihakkinen K, Tenovuo J. Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants. *J Dent Res.* 2000;79(3):882-887, [PMID: 10765964]
Exclusion code: 3

Soderling E, Scheinin A. Perspectives on xylitol-induced oral effects. *Proc Finn Dent Soc.* 1991;87(2):217-229, [PMID: 1896434]
Exclusion code: 5

Soderling EM. Xylitol, mutans streptococci, and dental plaque. *Adv Dent Res.* 2009;21(1):74-78, [PMID: 19717413]
Exclusion code: 2

Appendix A4. Excluded Studies List

Sohn W, Ismail AI, Tellez M. Efficacy of educational interventions targeting primary care providers' practice behaviors: an overview of published systematic reviews. *J Public Health Dent.* 2004;64(3):164-172, [PMID: 15341140]
Exclusion code: 2

Spittle B. *Fluoride poisoning: Is fluoride from your drinking water and other sources making you sick?*: International Society for Fluoride Research (New Zealand); 2012.
Exclusion code: 5

Splieth CH, Alkilzy M, Schmitt J, Berndt C, Welk A. Effect of xylitol and sorbitol on plaque acidogenesis. *Quintessence Int.* 2009;40(4):279-285, [PMID: 19417872]
Exclusion code: 3

Sprod AJ, Anderson R, Treasure ET. Effective oral health promotion: literature review. 1996. http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?LinkFrom=OAI&ID=12000008300.
Exclusion code: 11

Stecksen-Blicks C, Holgerson PL, Twetman S. Effect of xylitol and xylitol-fluoride lozenges on approximal caries development in high-caries-risk children. *Int J Paediatr Dent.* 2008;18(3):170-177, [PMID: 18341562]
Exclusion code: 3

Stevens GD, Seid M, Tsai K-Y, West-Wright C, Cousineau MR. Improvements in access to care for vulnerable children in California between 2001 and 2005. *Public Health Rep.* 2009;124(5):682-691, [PMID: 19753946]
Exclusion code: 2

Stijacic T, Schroth RJ, Lawrence HP. Are Manitoba dentists aware of the recommendation for a first visit to the dentist by age 1 year? *Journal of the Canadian Dental Association.* 2008;74(10):903+903a-903h, [PMID: 19126358]
Exclusion code: 8

Strippel H. Effectiveness of structured comprehensive paediatric oral health education for parents of children less than two years of age in Germany. *Community Dent Health.* 2010;27(2):74-80, [PMID: 20648883]
Exclusion code: 8

Strohmenger L, Brambilla E. The use of fluoride varnishes in the prevention of dental caries: A short review. *Oral Dis.* 2001;7(2):71-80, [PMID: 11355442]
Exclusion code: 5

Suhonen J, Sener B, Bucher W, Lutz F. Release of preventive agents from pacifiers in vitro. An introduction to a novel preventive measure. *Schweiz Monatsschr Zahnmed.* 1994;104(8):946-951, [PMID: 8091173]
Exclusion code: 8

Svenson D, Bridges D. Xylitol: the sugar that prevents tooth decay. *Dent Hyg (Chic).* 1977;51(9):401, [PMID: 348510]
Exclusion code: 2

Szoke J, Esztari I, Pienihakkinen K, Banoczy J, Scheinin A. [3-year results of the WHO xylitol caries preventive program in Hungarian children's homes]. *Fogorv Sz.* 1986;79(12):368-373, [PMID: 3466810]
Exclusion code: 7

Tabari ED, Ellwood R, Rugg-Gunn AJ, Evans DJ, Davies RM. Dental fluorosis in permanent incisor teeth in relation to water fluoridation, social deprivation and toothpaste use in infancy. *Br Dent J.* 2000;189(4):216-220, [PMID: 11036750]
Exclusion code: 4

Tanabe Y, Park JH, Tinanoff N, Turng BF, Lilli H, Minah GE. Comparison of chairside microbiological screening systems and conventional selective media in children with and without visible dental caries. *Pediatr Dent.* 2006;28(4):363-368, [PMID: 16903447]
Exclusion code: 4

Task Force on Community Preventive Services. Recommendations on selected interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. *Am J Prev Med.* 2002;23(1 Suppl):16-20, [PMID: 12091092]
Exclusion code: 2

Tavener JA, Davies GM, Davies RM, Ellwood RP. The prevalence and severity of fluorosis in children who received toothpaste containing either 440 or 1,450 ppm F from the age of 12 months in deprived and less deprived communities. *Caries Res.* 2006;40(1):66-72, [PMID: 16352884]
Exclusion code: 4

Tenovuo J, Hakkinen P, Paunio P, Emilson C. Effects of chlorhexidine-fluoride gel treatments in mothers on the establishment of mutans streptococci in primary teeth and the development of dental caries in children. *Caries Res.* 1992;26(4), [PMID: 1423442]
Exclusion code: 3

Appendix A4. Excluded Studies List

Thaweboon S, Thaweboon B, Soo-Ampon S. The effect of xylitol chewing gum on mutans streptococci in saliva and dental plaque. *Southeast Asian J Trop Med Public Health.* 2004;35(4):1024-1027, [PMID: 15916109]
Exclusion code: 3

Thomas S, Tandon S, Nair S. Effect of dental health education on the oral health status of a rural child population by involving target groups. *Journal of the Indian Society of Pedodontics and Preventive Dentistry.* 2000;18(3):115-125, [PMID: 11324201]
Exclusion code: 3

Thorild I, Lindau B, Twetman S. Effect of maternal use of chewing gums containing xylitol, chlorhexidine or fluoride on mutans streptococci colonization in the mothers' infant children. *Oral health prev.* 2003;1(1):53-57, [PMID: 15643749]
Exclusion code: 3

Thorild I, Lindau B, Twetman S. Salivary mutans streptococci and dental caries in three-year-old children after maternal exposure to chewing gums containing combinations of xylitol, sorbitol, chlorhexidine, and fluoride. *Acta Odontol Scand.* 2004;62(5):245-250, [PMID: 15841810]
Exclusion code: 3

Thorild I, Lindau B, Twetman S. Caries in 4-year-old children after maternal chewing of gums containing combinations of xylitol, sorbitol, chlorhexidine and fluoride. *Eur Arch Paediatr Dent.* 2006;7(4):241-245, [PMID: 17164069]
Exclusion code: 3

Tickle M. The 80:20 phenomenon: help or hindrance to planning caries prevention programmes? *Community Dent Health.* 2002;19(1):39-42, [PMID: 11922411]
Exclusion code: 8

Tickle M, Milsom KM, Donaldson M, et al. Protocol for Northern Ireland Caries Prevention in Practice Trial (NIC-PIP) trial: a randomised controlled trial to measure the effects and costs of a dental caries prevention regime for young children attending primary care dental services. *BMC Oral Health.* 2011;11:27, [PMID: 21985746]
Exclusion code: 5

Tinanoff N. Dental caries risk assessment and prevention. *Dent Clin North Am.* 1995;39(4):709-719, [PMID: 8522039]
Exclusion code: 5

Tinanoff N, Kanellis MJ, Vargas CM. Current understanding of the epidemiology, mechanisms, and prevention of dental caries in preschool children. *Pediatr Dent.* 2002;24(6):543-551, [PMID: 12528947]
Exclusion code: 5

Tinanoff N, Reisine S. *Update on Early Childhood Caries Since the Surgeon General's Report* .2009.
Exclusion code: 2

Truin GJ, Van't Hof MA. Caries prevention by professional fluoride gel application on enamel and dentinal lesions in low-caries children. *Caries Res.* 2005;39(3):236-240, [PMID: 15914987]
Exclusion code: 3

Truman BI, Gooch BF, Sulemana I, et al. Reviews of evidence on interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. *Am J Prev Med.* 2002;23(1 Suppl):21-54, [PMID: 12091093]
Exclusion code: 4

Tubert-Jeannin S, Auclair C, Amsallem E, et al. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. *Cochrane database of systematic reviews (Online).* 2011;12, [PMID: 22161414]
Exclusion code: 2

Twetman S. Prevention of early childhood caries (ECC)--review of literature published 1998-2007. *Eur Arch Paediatr Dent.* 2008;9(1):12-18, [PMID: 18328233]
Exclusion code: 5

Twetman S, Petersson LG. Influence of xylitol in dentifrice on salivary microflora of preschool children at caries risk. *Swed Dent J.* 1995;19(3):103-108, [PMID: 7676386]
Exclusion code: 8

Twetman S, Petersson LG. Prediction of caries in pre-school children in relation to fluoride exposure. *Eur J Oral Sci.* 1996;104(5-6):523-528, [PMID: 9021320]
Exclusion code: 4

Twetman S, Petersson LG, Pakhomov GN. Caries Incidence in Relation to Salivary Mutans Streptococci and Fluoride Varnish Applications in Preschool Children from Low- and Optimal-Fluoride Areas. *Caries Res.* 1996;30(5):347-353, [PMID: 8877088]
Exclusion code: 11

Appendix A4. Excluded Studies List

Twetman S, Ståhl B, Nederfors T. Use of the strip mutans test in the assessment of caries risk in a group of preschool children. *International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children.* 1994;4(4):245-250, [PMID: 7748864]
Exclusion code: 4

Twetman S, Stecksen-Blicks C. Effect of xylitol-containing chewing gums on lactic acid production in dental plaque from caries active pre-school children. *Oral health prev.* 2003;1(3):195-199, [PMID: 15641497]
Exclusion code: 3

U.S. Department of Health and Human Services. *Oral Health in America: A Report of the Surgeon General.* Rockville, MD: U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health; 2000.
Exclusion code: 2

U.S. Preventive Services Task Force. Procedure Manual. 2011; http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanual.htm. Accessed 3 April, 2013
Exclusion code: 2

Uhari M, Kontiokari T, Koskela M, Niemelä M. Xylitol chewing gum in prevention of acute otitis media: Double blind randomised trial. *British Medical Journal.* 1996;313(7066):1180-1184, [PMID: 8916749]
Exclusion code: 8

Ullbro C, Brown A, Twetman S. Preventive periodontal regimen in Papillon-Lefevre syndrome. *Pediatr Dent.* 2005;27(3):226-232, [PMID: 16173228]
Exclusion code: 3

US Government Accountability Office (GAO). *Efforts Under Way to Imrpove Children's Access to Dental Services, but Sustained Attention Needed to Address Ongoing Concerns.* Washinton, D.C.: Government Accountability Office 2010.
Exclusion code: 5

Vachirarojpisan T, Shinada K, Kawaguchi Y. The process and outcome of a programme for preventing early childhood caries in Thailand. *Community Dent Health.* 2005;22(4):253-259, [PMID: 16379164]
Exclusion code: 4

Van Der Hoek W, Ekanayake L, Rajasooriyar L, Karunaratne R. Source of drinking water and other risk factors for dental fluorosis in Sri Lanka. *International Journal of Environmental Health Research.* 2003;13(3):285-293, [PMID: 12909559]
Exclusion code: 4

Van Rijkom HM, Truin GJ, Van 't Hof MA. Caries-Inhibiting Effect of Professional Fluoride Gel Application in Low-Caries Children Initially Aged 4.5-6.5 Years. *Caries Res.* 2004;38(2):115-123, [PMID: 14767168]
Exclusion code: 3

Vannier R. [Replacement sweetening agents in the prevention of dental caries]. *Actual Odontostomatol (Paris).* 1978(123):403-415, [PMID: 735891]
Exclusion code: 7

Vargas CM, Monajemy N, Khurana P, Tinanoff N. Oral health status of preschool children attending Head Start in Maryland, 2000. *Pediatr Dent.* 2002;24(3):257-263, [PMID: 12064502]
Exclusion code: 8

Virtanen JI, Bloigu RS, Larmas MA. Timing of first restorations before, during, and after a preventive xylitol trial. *Acta Odontol Scand.* 1996;54(4):211-216, [PMID: 8876730]
Exclusion code: 8

Wåler SM, Rölla G. Effect of xylitol on dental plaque in vivo during carbohydrate challenge. *Scand J Dent Res.* 1983;91(4):256-259, [PMID: 6579603]
Exclusion code: 3

Wan AKL, Seow WK, Purdie DM, Bird PS, Walsh LJ, Tudehope DI. The effects of chlorhexidine gel on Streptococcus mutans infection in 10-month-old infants: a longitudinal, placebo-controlled, double-blind trial. *Pediatr Dent.* 2003;25(3):215-222, [PMID: 12889696]
Exclusion code: 8

Wang NJ, Gropen AM, Øgaard B. Risk factors associated with fluorosis in a non-fluoridated population in Norway. *Community Dentistry and Oral Epidemiology.* 1997;25(6):396-401, [PMID: 9429811]
Exclusion code: 8

Warren DP, Henson HA, Chan JT. Dental hygienist and patient comparisons of fluoride varnishes to fluoride gels. *J Dent Hyg.* 2000;74(2):94-101, [PMID: 11314061]
Exclusion code: 11

Warren JJ, Weber-Gasparon iK, Marshall TA, et al. A longitudinal study of dental caries risk among very

Appendix A4. Excluded Studies List

young low SES children. *Comm Dent Oral Epidemiol* 2009;37:116-122, [PMID: 19046332]
Exclusion code: 8

Washington State Department of Health. *Washington State Smile Survey 2010.* Olympia, WA: Division of Community and Family Health, Office of Maternal and Child Health, Oral Health Program, Washington State Department of Health;2010. DOH Pub No 160-099
Exclusion code: 2

Weinstein P. Public health issues in early childhood caries. *Community Dentistry and Oral Epidemiology.* 1998;26(1 SUPPL.):84-90, [PMID: 9671204]
Exclusion code: 5

Weinstein P. Motivational interviewing concepts and the relationship to risk management and patient counseling. *J Calif Dent Assoc.* 2011;39(10):742-745, [PMID: 22132586]
Exclusion code: 5

Weinstein P, Harrison R, Benton T. Motivating parents to prevent caries in their young children: one-year findings. *Journal of the American Dental Association (1939).* 2004;135(6):731-738, [PMID: 15270155]
Exclusion code: 4

Weinstein P, Harrison R, Benton T. Motivating mothers to prevent caries: confirming the beneficial effect of counseling. *J Am Dent Assoc.* 2006;137(6):789-793, [PMID: 16803808]
Exclusion code: 4

Weinstein P, Riedy CA. The reliability and validity of the RAPIDD scale: readiness assessment of parents concerning infant dental decay. *J Dent Child.* 2001;68(2):129-135, 142, [PMID: 11475689]
Exclusion code: 8

Weintraub JA. Prevention of early childhood caries: A public health perspective. *Community Dentistry and Oral Epidemiology.* 1998;26(1 SUPPL.):62-66, [PMID: 9671201]
Exclusion code: 5

Weintraub JA. Fluoride varnish for caries prevention: comparisons with other preventive agents and recommendations for a community-based protocol. *Special care in dentistry : official publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry.* 2003;23(5):180-186, [PMID: 14965184]
Exclusion code: 5

Wendt L, Carlsson E, Hallonsten A, Birkhed D. Early dental caries risk assessment and prevention in pre-school children: evaluation of a new strategy for dental care in a field study. *Acta Odontol Scand.* 2001;59(5):261-266, [PMID: 11680643]
Exclusion code: 9

Wendt LK, Hallonsten AL, Koch G. Dental caries in one- and two-year old children living in Sweden: a longitudinal study. *Swed Dent J.* 1991;15:1-6, [PMID: 2035146]
Exclusion code: 5

Wennhall I, Martensson E, Sjunnesson I, Matsson L, Schroder U, Twetman S. Caries-preventive effect of an oral health program for preschool children in a low socio-economic, multicultural area in Sweden: results after one year. *Acta Odontol Scand.* 2005;63(3):163-167, [PMID: 16191910]
Exclusion code: 4

Whittle J, Whitehead H, Bishop C. A randomised control trial of oral health education provided by a health visitor to parents of pre-school children. *Community Dent Health.* 2008;25(1):28-32, [PMID: 18435231]
Exclusion code: 9

Widenheim J. A time-related study of intake pattern of fluoride tablets among Swedish preschoolchildren and parental attitudes. *Community Dent Oral Epidemiol.* 1982;10(6):296-300, [PMID: 6961977]
Exclusion code: 11

Winter GB, Holt RD, Williams BF. Clinical trial of a low-fluoride toothpaste for young children. *Int Dent J.* 1989;39(4):227-235, [PMID: 2691402]
Exclusion code: 4

Wong MC, Glenny AM, Tsang BW, Lo EC, Worthington HV, Marinho VC. Topical fluoride as a cause of dental fluorosis in children. *Cochrane database of systematic reviews (Online).* 2010(1), [PMID: 20091645]
Exclusion code: 5

World Health Organization. The use of xylitol in the prevention of dental caries. *Bulletin of the World Health Organization.* 1979;57(2):213-214. http://whqlibdoc.who.int/bulletin/1979/Vol57-No2/bulletin_1979_57%282%29_213-225.pdf.
Exclusion code: 5

Yoder KM, Mallatt ME. The status of kindergarten and middle school entry dental examinations in Indiana. *J*

Appendix A4. Excluded Studies List

Indiana Dent Assoc. 2005;84(2):15-18, [PMID: 16359000]
Exclusion code: 3

Yoon RK, Smaldone AM, Edelstein BL. Early childhood caries screening tools: a comparison of four approaches. *J Am Dent Assoc.* 2012;143(7):756-763, [PMID: 22751977]
Exclusion code: 9

Young D, Ricks CS, Featherstone JD, et al. Changing the face and practice of dentistry: a 10-year plan. *J Calif Dent Assoc.* 2011;39(10):746-751, [PMID: 22132587]
Exclusion code: 5

Zero D, Fontana M, Lennon AM. Clinical applications and outcomes of using indicators of risk in caries management. *J Dent Educ.* 2001;65(10):1126-1132, [PMID: 11699989]
Exclusion code: 2

Appendix A5. USPSTF Quality Rating Criteria for Randomized, Controlled Trials and Observational Studies

Randomized Controlled Trials (RCTs)

Criteria:

- Initial assembly of comparable groups**:** RCTs—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; cohort studies—consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention-to-treat analysis for RCTs; for cluster RCTs, correction for correlation coefficient

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (followup at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the important limitations noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for.

Poor: Studies will be graded "poor" if any of the following major limitations exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primary care, adequately described
- Study uses a credible reference standard, performed regardless of test results
- Reference standard interpreted independently of screening test
- Handles indeterminate results in a reasonable manner
- Spectrum of patients included in study
- Sample size
- Administration of reliable screening test
- Random or consecutive selection of patients

Appendix A5. USPSTF Quality Rating Criteria for Randomized, Controlled Trials and Observational Studies

- Screening cutoff pre-determined
- All patients undergo the reference standard

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease; study attempts to enroll a random or consecutive sample of patients who meet inclusion criteria screening cutoffs pre-stated.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients (i.e. applicable to most screening settings).

Poor: Has important limitation such as: uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size of very narrow selected spectrum of patients.

Sources: Harris et al, 2001[34] and USPSTF Procedure Manual[35]

Appendix A6. List of Reviewers

Expert Reviewers

Kevin J. Donly, D.D.S., M.S., Professor and Chair, Department of Developmental Dentistry, University of Texas Health Science Center at San Antonio

William Frese, M.D., M.P.H., Assistant Professor, University of Illinois at Chicago

David M. Krol, M.D., M.P.H., Senior Program Officer, Robert Wood Johnson Foundation

Steven M. Levy, D.D.S., M.P.H., Wright-Bush-Shreves Endowed Professor of Research, Department of Preventive and Community Dentistry, College of Dentistry, University of Iowa

Charlotte W. Lewis, M.D., M.P.H., Associate Professor of Pediatrics, University of Washington School of Medicine

Amr M. Moursi, D.D.S., Ph.D., Chair, Department of Pediatric Dentistry, New York University, College of Dentistry

Francisco Ramos-Gomez, D.D.S., M.S., M.P.H., Professor, Section of Pediatric Dentistry, University of California Los Angeles, School of Dentistry

Federal Reviewers

Joseph Chin, M.D., M.S., Medical Officer, Centers for Medicare and Medicaid Services

Barbara Gooch, D.M.D., M.P.H., Associate Director for Science, Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion, Center for Disease Control and Prevention

Susan Griffin, Ph.D., Health Economist, Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion, Center for Disease Control and Prevention

Gary C. Martin, D.D.S, M.P.H., Military Consultant to the United States Air Force Surgeon General for Dental Public Health, United States Air Force, Uniformed Services University of the Health Sciences

Appendix B1. Diagnostic Accuracy Studies for the Prevention of Dental Caries

Author, year, title	Screening test	Reference standard	Country Setting Screener	Population	Sample size Proportion with condition	Definition of a positive screening exam	Proportion unexaminable by screening test
Beltran et al., 1997[41] *Validity of two methods for assessing oral health status of populations*	Nurse exam (no previous dental experience; received written material on procedures and diagnostic criteria for conditions to be evaluated)	Pediatric dentist exam	U.S. Rural school Nurse	Children 5 to 12 years of age attending school	n=258 children Cavitated lesions: 9.7% (mean 0.3/child)	Identification of untreated decay Identification of need for treatment (urgent or nonurgent)	Appears to be none
Pierce et al., 2002[39] *Accuracy of pediatric primary care providers' screening and referral for early childhood caries*	Primary care pediatrician exam following 2 hours of training	Pediatric dentist exam	U.S. Pediatric group practice Primary care pediatrician	Children <36 months of age with erupted teeth participating in the "Into the Mouths of Babes" program. Excluded if they had received fluoride varnish and oral screening within 3 months or were very ill	n=258 children Cavitated lesions: 9.7% (mean 0.3/child)	Identification of a cavitated lesion Identification of need for referral	Appears to be none
Serwint et al., 1993[40] *Child-rearing practices and nursing caries*	Pediatrician exam (not primary care provider) following 4 hours of training	Pediatric dentist exam	U.S. General pediatric clinic Pediatrician	Children 18-36 months of age, mother primary caretaker. Excluded for developmental delay or facial abnormalities	n=110 children Nursing caries (caries involving one or more teeth including the maxillary central or lateral incisors or the primary molars but sparing the mandibular incisors): 20% (22/110)	Identification of nursing caries	Not reported

Appendix B1. Diagnostic Accuracy Studies for the Prevention of Dental Caries

Author, year, title	Analysis of screening failures	Proportion who underwent reference standard and included in analysis	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality rating
Beltran et al., 1997[41] *Validity of two methods for assessing oral health status of populations*	Not applicable	Appears to be all	Untreated decay: 0.92 (71/77) Any treatment needed: 0.80 (70/88)	Untreated decay: 0.99 (141/142) Any treatment needed: 0.99 (233/235)	Untreated decay: 0.99 (71/72) Any treatment needed: 0.97 (70/72)	Untreated decay: 0.96 (141/147) Any treatment needed: 0.93 (233/251)	Fair
Pierce et al., 2002[39] *Accuracy of pediatric primary care providers' screening and referral for early childhood caries*	Not applicable	Appears to be all	Patient-level analysis: 0.76 (19/25) Tooth-level analysis: 0.49 (39/80) Need for referral: 0.63 (17/27)	Patient-level analysis: 0.95 (222/233) Tooth-level analysis: 0.99 (3210/3235) Need for referral: 0.98 (225/231)	Patient-level analysis: 0.63 (19/30); 0.83 (25/30) if precavitated lesions re-classified as true-positives Tooth-level analysis: 0.61 (39/64) Need for referral: 0.74 (17/23)	Patient-level analysis: 0.97 (222/228) Tooth-level analysis: 0.99 (3210/3251) Need for referral: 0.96 (225/235)	Good
Serwint et al., 1993[40] *Child-rearing practices and nursing caries*	Not reported	55% (61/110)	1.0 (n/N not calculable)	0.87 (n/N not calculable)	Not calculable	Not calculable	Fair

Abbreviations: CI = confidence interval; U.S. = United States

Appendix B2. Quality Ratings for Diagnostic Accuracy Studies

Author, year, title	Representative spectrum	Random or consecutive sample	Screening test adequately described	Screening cutoffs predefined	Credible reference standard	Reference standard applied to all screened patients	Same reference standard applied to all patients	Reference standard and screening examination interpreted independently	High rate of uninterpretable results or noncompliance with screening test	Analysis includes patients with uninterpretable results or noncompliance	Quality rating
Beltran et al., 1997[41] *Validity of two methods for assessing oral health status of populations*	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	No	Not applicable	Fair
Pierce et al., 2002[39] *Accuracy of pediatric primary care providers' screening and referral for early childhood caries*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not applicable	Good
Serwint et al., 1993[40] *Child-rearing practices and nursing caries*	Yes	Unclear	Yes	Yes	Yes	No	Yes	Yes	No	Not applicable	Fair

Appendix B3. Trials of Educational Interventions for the Prevention of Dental Caries

Author, year, title	Study Design	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed	Country
Davies et al., 2007[44] *Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area* Davies et al., 2005[43] *A staged intervention dental health promotion programme to reduce early childhood caries*	Cluster, non-randomized controlled clinical trial (2 clusters)	A: Series of interventions from 8-32 months by health visitor including provision of educational materials, counseling on oral hygiene, and provision of toothbrush and toothpaste B: No intervention	Age at time of initial followup evaluation (mean, years): 4.0 vs. 4.0 Female: 48% vs 49% Non-white: 51% vs 37% Proportion of adults unemployed: 24% vs. 22% Jarman index (underprivileged area score): 39 vs. 40	Children 8 months of age attending a primary care clinic	Number approached: 1545 (839 vs. 706) Number eligible: 1545 (839 vs. 706) Number enrolled: 1545 (839 vs. 706) Number analyzed: 1545 (839 vs. 706)	UK Primary care clinics
Kressin et al., 2009[45] *Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention*	Cluster, non-randomized controlled clinical trial (2 clusters)	A: Multicomponent intervention including training of pediatricians in patient centered counseling, providing parents/caregivers with educational brochure, and editing the electronic medical record to prompt counseling B: Usual care	Age <1 year: 1% vs. 3% Age 1 to <2 year: 55% vs. 55% Age 2 to <3 year: 25% vs. 26% Caregiver employed: 57% vs. 69% (p<0.0001) White: 17% vs. 45% (p<0.0001 for differences in race) Black: 76% vs. 35% Asian: 6% vs. 19% Hispanic: 13% vs. 15% Diet summary score (0-6 scale): 3.2 vs. 3.5 (p<0.0001) Hygiene summary score (0 to 6 scale, higher=better): 4.9 vs. 4.5 (p<0.0001) Tooth-monitoring summary score (0-3 scale): 0.7 vs. 0.9 (p=0.02) Baseline caries: 5.8% vs. 6.4% (p=0.66)	Parents/caregivers of children 6 months to 5 years of age attending well-child visits. Excluded for congential oral anomalies, ectodermal dysplasis, or other disease other than caries	Number approached: Not reported Number eligible: Not reported Number enrolled: 1087 (635 vs. 452) Number analyzed: 1045	U.S.

Appendix B3. Trials of Educational Interventions for the Prevention of Dental Caries

Author, year, title	Sponsor	Duration of followup	Confounders adjusted for in analysis	Outcomes	Adverse events/harms	Attrition	Quality rating
Davies et al., 2007[44] *Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area* Davies et al., 2005[43] *A staged intervention dental health promotion programme to reduce early childhood caries*	National Health Service Research and Development Programme for Primary Dental Care	Evaluated at 3-4 and at 5 years of age	None	A vs. B at 3-4 year old followup; all children and restricted to children who attended developmental check and MMR vaccination (n=1207, 649 vs. 558) Caries experience: 34% vs. 40%, p=0.01; 29% vs. 39%, p=0.001 Nursing caries: 21% vs. 23%, p=0.49; 17% vs. 24%, p=0.003 dmft (mean): 1.5 vs. 1 .7, p=0.09; 1.2 vs. 1.7, p=0.001 dmfs (mean): 3.3 vs. 3.7, p=0.35; 2.6 vs. 3.8, p=0.008 A vs. B at 5 year old followup; restricted to children who attended developmental check and MMR vaccination (n=539, 253 vs. 286) Caries experience: 54% vs. 64%, p=0.03 Nursing caries: 20% vs. 32%, p=0.002 Extraction: 3% vs. 12%, p<0.0001 dmft (mean): 2.2 vs. 3.7, p<0.001	Not reported	At 3-4 years, 22% (338/1545) of potentially eligible cohort did not attend developmental check or MMR vaccination and would not have received all interventions; at 5 years 65% (1006/1545) excluded	Poor
Kressin et al., 2009[45] *Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention*	NIH/NIDCR and VA	1 year	Length of enrollment, sex, race, treatment before 42 months, continuously enrolled in Medicaid number of well child visits	A vs. B Caries (irreversible cavitated lesions): 18% vs. 32%, adjusted HR 0.23 (95% CI 0.09 to 0.62)	Not reported	42/1087 enrolled were not analyzed	Fair

Abbreviations: AHRQ = Agency for Healthcare Research and Quality; CI = confidence interval; dmfs = decayed missing filled surfaces; dmft = decayed missing filled teeth; HR = hazard ratio; MMR = measles, mumps, and rubella; NIDCR = National Institute of Dental and Craniofacial Research; NIH = National Institutes of Health; UK = United Kingdom; U.S. = United States; VA = Veterans Affairs

Appendix B4. Quality Ratings of Randomized, Controlled Trials

Author, year, title	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination
Alamoudi et al., 2012[74] *Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs*	Unclear	Yes	Unclear	Yes	Unclear	No	No	Yes
Chu et al., 2002[69] *Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin carries in Chinese pre-school children*	No	No	Unclear	Yes	Yes	No	Unclear	Yes
Davies et al., 2007[44] *Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area* Davies et al., 2005[43] *A staged intervention dental health promotion programme to reduce early childhood caries*	Not randomized	Unclear	Yes	Yes	Unclear	Unclear	Unclear	No
Du et al., 2006[54] *A 2-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children*	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes
Jiang et al., 2005[70] *The effect of a bi-annual professional application of APF foam on dental caries increment in primary teet: 24-month clinical trial*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kovari et al., 2003[51] *Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland*	NR	NR	Unclear	Yes	Unclear	No	No	Yes

Appendix B4. Quality Ratings of Randomized, Controlled Trials

Author, year, title	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination
Kressin et al., 2009[45] *Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention*	Not randomized	Yes	Yes	Yes	No	No	Yes	Yes
Lawrence et al., 2008[47] *A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children*	Yes	Unclear	Yes	Yes	Yes	No	No	Yes
Milgrom et al., 2009[73] *Xylitol pediatric topical oral syrup to prevent dental caries*	Yes	Unclear	No (age)	Yes	Yes	Yes	Yes	Yes
Oscarson et al., 2006[52] *Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children*	NR	NR	Yes	Yes	Yes	No	No	Yes
Seki et al., 2011[53] *Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomized trial*	No	No	Unclear (dfs index)	Yes	Yes	No	No	Yes
Slade et al., 2011[48] *Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial*	Yes	Yes	Yes; some difference in fluoridation status	Yes	No	No	No	Yes

Appendix B4. Quality Ratings of Randomized, Controlled Trials

Author, year, title	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination
Weinstein et al., 2001[71] *Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years*	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes
Weinstein et al., 2009[72] *Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition*	Yes	Unclear	No; mean dmfs were not balanced	Yes	Yes	Unclear	Unclear	Yes
Weintraub et al., 2006[49] *Fluoride varnish efficacy in preventing early childhood caries*	Yes	Yes	Yes; stated no imbalances apparent	Yes	Yes	No	Yes	Yes
Zhan et al., 2012[50] *Effects of xylitol wipes on carcinogenic bacteria and caries in young children*	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes

Author, year, title	Loss to followup: differential/high	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Outcomes Pre-specified	Funding source	External validity	Quality Rating
Alamoudi et al., 2012[74] *Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs*	Yes (very high)	Yes	Yes	Yes	The Deanship of Scientific Research, King Abdulaziz University, Jeddah, Saudi Arabia (Project No. 429/011-9)	Fair	Poor
Chu et al., 2002[69] *Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin carries in Chinese pre-school children*	No/No	Yes	No	Yes	A research grant from the University of Hong Kong (CRCG)	Limited: Chinese flouridated water, 73% used fuoridated toothpaste	Poor

Appendix B4. Quality Ratings of Randomized, Controlled Trials

Author, year, title	Loss to followup: differential/high	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Outcomes Pre-specified	Funding source	External validity	Quality Rating
Davies et al., 2007[44] *Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area* Davies et al., 2005[43] *A staged intervention dental health promotion programme to reduce early childhood caries*	Yes	No	No	Yes	National Health Service Research and Development Programme for Primary Dental Care	Fair	Poor
Du et al., 2006[54] *A 2-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children*	No/Unclear	Yes	No	Yes	National Key Technologies R&D Program of the tenth 5-Year Plan, Ministry ofScience and Technology, and National Committee for Oral Health, People's Republic of China	Limited: Chinese children in China, no organized oral health care programs, but access to flouridated water	Fair
Jiang et al., 2005[70] *The effect of a bi-annual professional application of APF foam on dental caries increment in primary teet: 24-month clinical trial*	No/No	Yes	No	Yes	National Key Technologies R&D Program of the tenth 5-Year Plan, Ministry of Science and Technology, China (2004BA720A24)	Limited: Chinese chlidren, fluoridated water, no organized health care programs, limited use of fluoride toothpaste	Good
Kovari et al., 2003[51] *Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland*	No	Yes	No	Yes	Not reported	Limited	Fair
Kressin et al., 2009[45] *Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention*	No	Yes	No	Yes	NIH/NIDCR and VA	Fair	Fair

Appendix B4. Quality Ratings of Randomized, Controlled Trials

Author, year, title	Loss to followup: differential/high	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Outcomes Pre-specified	Funding source	External validity	Quality Rating
Lawrence et al., 2008[47] *A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children*	No/No	Yes	No	Yes	Institute of Aboriginal Peoples' Health of the Canadian Institutes of Health Research (Grant #MOP-64215) and Toronto Hospital for Sick Children Foundation (Grant #XG 03-067)	Limited: Aboriginal communities in rural Canada	Good
Milgrom et al., 2009[73] *Xylitol pediatric topical oral syrup to prevent dental caries*	No	Yes	No	Yes	Health Resources and Services Administration Maternal and Child Health Bureau and National Institute of Dental and Craniofacial Research	Fair	Fair
Oscarson et al., 2006[52] *Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children*	No	Yes	No	Yes	Grants from Count of Vasterbotten, Patient Revenue Fund for Dental Prophylaxis and Swedish Dental Society	Fair	Fair
Seki et al., 2011[53] *Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomized trial*	Yes	Yes	Yes	Yes	Uemura Fund, Nihon University School of Dentistry, a grant to promote multi-disciplinary research projects from the Ministry of Education, Science, Sports, Culture and Technology, Japan	Fair	Poor
Slade et al., 2011[48] *Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial*	No/No	Yes	No	Yes	Project grant #320858 from the Australian National Health and Medical Research Council	Limited: Aboriginal communities in rural Australia	Good

Appendix B4. Quality Ratings of Randomized, Controlled Trials

Author, year, title	Loss to followup: differential/high	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Outcomes Pre-specified	Funding source	External validity	Quality Rating
Weinstein et al., 2001[71] *Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years*	Yes/Yes	Yes	No	Yes	Grant No. R03DE012138 from NIDCR/NIH	Head Start program	Fair
Weinstein et al., 2009[72] *Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition*	No/No	Yes	No	Yes	Grants No. R01DE14403 and U54DE14254 from NIDCR, NIH	Head Start program	Fair
Weintraub et al., 2006[49] *Fluoride varnish efficacy in preventing early childhood caries*	Yes/No	Yes	No	Yes	USPHS Research Grants P60 DE13058 and U54 DE142501 from NIDCR and NCMHD, NIH, and by the UCSF Department of Preventive and Restorative Dental Sciences	Limited: Under-serviced community in United States; all non-white	Fair
Zhan et al., 2012[50] *Effects of xylitol wipes on carcinogenic bacteria and caries in young children*	No/Yes (23% in one group)	Yes	No	Yes	California Society of Pediatric Dentistry Foundation, Graduate Scientific Research Award from American Academy of Pediatric Dentistry, and NIH/NIDCR grant U54 DEO19285	Single center	Fair

Abbreviations: dfs = decayed filled surfaces; dmfs = decayed missing filled surfaces; NCMHD = National Center on Minority Health and Health Disparities; NIDCR = National Institute of Dental and Craniofacial Research; NIH = National Institutes of Health; UCSF = University of California San Francisco; USPHS = United States Public Health Service; VA = Veterans Affairs

Appendix B5. Cohort Study of Dental Referral From a Primary Care Clinician for the Prevention of Dental Caries

Author, year, title	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed	Country
Beil et al., 2012[46] *Effect of early preventive dental visits on subsequent dental treatment and expenditures*	A: First preventive dental visit by age 18 months B: First preventive dental visit after age 18 months	Primary or secondary dental preventive visit before 18 months of age vs. between 18 and 42 months of age Female: 46% vs. 48-51% Non-white race: 67% vs. 66-67% Number of well-child visits: 1.8 vs. 1.4-1.7 Percent of population in county under 18 months of age enrolled in Medicaid: 30% vs. 31-33% Dentists per capita in county: 5.1 vs. 4.5-4.9	Children enrolled in North Carolina Medicaid prior to first birthday, enrolled for at least 12 months, with a paid claim for dental care. Excluded if they received dental services in medical office as part of the Into the Mouths fo Babes fluoride varnish program.	Approached: 165,383 Eligible: 19,888 Enrolled: 19,888 Analyzed: 19,888	U.S.

Author, year, title	Sponsor	Duration of followup	Confounders adjusted for in analysis	Outcomes	Adverse events/harms	Attrition	Quality rating
Beil et al., 2012[46] *Effect of early preventive dental visits on subsequent dental treatment and expenditures*	AHRQ and NIDCR	Through 72 months of age	Age, race/ethnicity, caregiver employment, caregiver education, language spoken at home, diet score, hygiene score, tooth monitoring score	First preventive visit at 18-24, 25-30, 31-36, or 37-42 months vs. <18 months (reference) Primary or secondary preventive visit: Incidence density ratio 0.98 (0.87-1.1), 1.1 (0.94-1.2), 1.1 (0.96-1.2), and 1.1 (0.95-1.2) Tertiary preventive visit: Incidence density ratio 1.2 (1.0-1.4), 1.2 (1.1-1.4), 1.1 (0.99-1.3), and 1.4 (1.2-1.6)	Not reported	None reported	Fair

Abbreviations: AHRQ = Agency for Healthcare Research and Quality; NIDCR = National Institute of Dental and Craniofacial Research; U.S. = United States

Appendix B6. Quality Rating of Cohort Study

Author, Year	Did the study attempt to enroll a random sample or consecutive patients meeting inclusion criteria (inception cohort)?	Were the groups comparable at baseline?	Did the study use accurate methods for ascertaining exposures, potential confounders, and outcomes?	Were outcome assessors and/or data analysts blinded to treatment?	Did the article report attrition?	Did the study perform appropriate statistical analyses on potential confounders?	Is there important differential loss to follow-up or overall high loss to follow-up?	Were outcomes prespecified, defined, and ascertained using accurate methods?	Quality
Beil et al., 2012[46] *Effect of early preventive dental visits on subsequent dental treatment and expenditures*	Yes	Yes	Unclear	Unclear	Yes	Yes	No	Yes	Fair

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Type of study	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed
Topical fluoride					
Chu et al., 2002[69] *Effectiveness of silver diamine flouride and sodium flouride varnish in arresting dentin caries in Chinese pre-school children*	Controlled clinical trial	A: Removal of carious tissue plus 38% silver diamine fluoride solution every 12 months B: 38% silver diamine fluoride solution every 12 months C: Removal of carious tissue plus 5% sodium fluoride every 3 months D: 5% sodium fluoride varnish every 3 months E: Placebo (water)	Age, mean: 4.0 years Female: 44% Race: NR (study conducted in China) dmfs score: 3.92 Used fluoridated toothpaste: 73%	Children from 8 kindergartens with caries in upper primary anterior teeth	Number approached: NR Number eligible: NR Number enrolled: 375 (76 vs. 77 vs. 76 vs. 73 vs. 73) Number analyzed: 308 (61 vs. 62 vs. 62 vs. 61 vs. 62)
Jiang et al., 2005[70] *The effect of a bi-annual professional application of APF foam on dental caries increment in primary teet: 24-month clinical trial*	Cluster RCT (15 clusters)	A: 0.6-0.8 g of 1.23% acidulated phosphate flouride foam applied every 6 months, max 4 applications B: Placebo foam	Age, mean: 3.5 vs. 3.6 yrs Female: 46% vs. 46% Non-white: 100% Chinese dmft, mean: 1.6 vs. 1.7 dmfs, mean: 2.4 vs. 2.8 Use of fluoride toothpaste: 23% vs. 20% Toothbrushing at least once a day: 42% vs. 50%	Children from 4 kindergartens	Number approached: NR Number eligible: NR Number enrolled: 392 (209 vs. 183) Number analyzed: 318 (167 vs. 151)
Lawrence et al., 2008[47] *A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children*	Cluster RCT (20 clusters)	A: 0.3-0.5 ml 5% sodium fluoride varnish applied to full primary dentition every 6 months B: No fluoride varnish	A vs. B Age, mean: 2.5 years overall Female: 50% vs. 52% Race: 100% aboriginal dmft, mean: 7.2 vs. 6.5 (p=0.80) Caries experience: 73% vs. 69% (p=0.50)	Children aged 6 month to 5 years, with ≥1 primary tooth, residing in First Nations community in study region, with signed consent from primary caregiver. Excluded children with no teeth, stainless steel crowns only, ulcerative gingivitis, stomatitis or allergy to colophony component.	Number approached: 1,793 Number eligible: 1,275 Number enrolled: 1,275 Number analyzed: 1,146 (818 vs. 328)
Slade et al., 2011[48] *Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial*	Cluster RCT (30 clusters)	A: 0.25 ml of 5% sodium fluoride varnish to maxillary anterior teeth/molars, mandibular molars/ incisors every 6 months, education/ advice to caregiver with toothbrush/ paste provided, community oral health promotion program B: No interventions	A vs. B Age, mean: 34 vs. 33 months Female: 50% vs. 48% Race: All aboriginal dmfs >0: 64% vs. 65% d3mfs (mean): 4.9 vs. 4.6 Fluoride concentration in drinking water <0.6 ppm F: 92% vs. 81%	Aboriginal identity, permanent residency in community, 18 to 48 months old, no history of asthma, signed informed consent of caregivers	Number approached: 685 Number eligible: 666 Number enrolled: 666 Number analyzed: 666 (344 vs. 322)

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Type of study	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed
Weinstein et al., 2001[71] *Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years*	RCT with 3 treatment groups	A: One application of 5% fluoride varnish at baseline and 6 months B: Three applications of 5% fluoride varnish within 2 weeks of baseline C: Three applications of 5% fluoride varnish within 2 weeks of baseline and 6 months	Age: NR Female: 46% Race: 90% Hispanic, 10% Caucasion or Native American Clinical dmfs, mean: 11 vs. 13 vs. 10 Radiographic dmfs, mean: 3.5 vs. 3.1 vs. 3.4 Mean dmft for entire population: 6.0	Children aged 3 to 5 years, with ≥1 carious lesion in primary molars and no fluoride treatment in the previous 6 months	Number approached: NR Number eligible: 156 Number enrolled: 156 (51 vs. 52 vs. 53) Number analyzed: 111 (32 vs. 36 vs. 43)
Weinstein et al., 2009[72] *Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition*	RCT with 2 treatment groups	A: One 5% fluoride varnish treatment and two placebo treatments every 6 months B: One set of three 5% fluoride varnish treatments over 2 weeks once per year and three placebo treatments over 2 weeks 6 months later	A vs. B Age, mean: 55 vs.56 months Female: 48% vs. 51% Race: All Hispanic >7 dmfs at baseline: 22% vs. 33% dmfs, mean (SD): 5.3 (9.8) vs. 7.2 (9.3)	Hispanic children aged 36 to 71 months, living in study county, with at least one sound primary tooth surface present. Children were excluded if they were developmentally unable to participate in the study.	Number approached: 787 Number eligible: 600 Number enrolled: 600 (306 vs. 294) Number analyzed: 515 (264 vs. 251)
Weintraub et al., 2006[49] *Fluoride varnish efficacy in preventing early childhood caries*	RCT	A: 0.1 mL of 5% sodium fluoride varnish per arch applied twice per year with four intended applications B: 0.1 mL of 5% sodium fluoride varnish per arch applied once per year with two intended applications C: No fluoride varnish	Age, mean: 1.8 years Female: 53% Race: 47% Hispanic, 46% Asian, 7% other race or ethnicity All caries free at baseline, see eligibility criteria	Children age 6 to 44 months with 4 erupted maxillary incisors, all primary teeth caries-free without demineralized, white spots, born in San Francisco or fluoridated community in the Bay Area, planning to reside in San Francisco for at least 2 years, parent providing informed consent. Excluded children with medical problems or medications affecting oral health (cleft lip/palate)	Number approached: NR Number eligible: NR Number enrolled: 376 Number analyzed: 280 (87 vs. 93 vs. 100)

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Type of study	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed
Xylitol					
Alamoudi et al., 2012[74] *Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs*	RCT	A: Xylitol chewable tablets (1.2 grams, 84% xylitol) chewed for 5 minutes three times daily B: Fluoride varnish, every 6 months throughout study	Age: 2 to 5 years Female: NR Race: NR (conducted in Saudi Arabia) High mutans streptococci (>=10^5 CFU): 100% vs. 100% Baseline dmft score: 8.37 vs. 10.27 (p=0.191)	Mothers and children with high count of salivary MS (≥105), presence of ≥1 decayed or filled primary teeth in mothers. Excluded children with systemic disorders such as iabetes,hyperglycemia, or sleeping disorders; irregular medications; removable dental prosthesis, or prone to TMJ complaints; and children attending clinics without mothers, or reared by a nanny	Number approached: 62 Number eligible: 60 Number enrolled: 60 (30 vs. 30) Number analyzed: 34 (21 vs. 13)
Kovari et al., 2003[51] *Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland*	Cluster RCT (11 clusters)	A: 65% Xylitol gum three times per day, chewed for 3-5 minutes, for total of 2.5 g/day B: Toothbrushing with Aquafresh with 0.05% NaF after lunch	Age: 3 to 6 years Female: 46.9% (184/392) vs. 46.7% (247/529) Non-white: NR Risk level: NR	Children in the town of Savolinna, Finland, aged 3-6 years attending daycare centers	Number approached: NR Number eligible: NR Number enrolled: 921 Number analyzed: 786 (392 vs. 529)
Milgrom et al., 2009[73] *Xylitol pediatric topical oral syrup to prevent dental caries*	RCT	A: Xylitol 8 gram per day syrup, divided into 2 doses (4 gram per dose) B: Xylitol 8 gram per day syrup, divided into 3 doses (2.67 gram per dose)C: Xylitol 2.67 gram dose syrup, one dose per day	Age: 15.9 vs. 13.7 vs. 15.6 months Female: 58% vs. 56% vs. 48% Non-white: NR Risk level: NR	Children aged 9 to 15 months. Excluded for history of esophageal or digestive disease, congenital craniofacial malformations or history of adenoidectomy, or <10th percentile of U.S. standard weight and height	Number approached: 110 Number eligible: 108 Number enrolled: 100 Number analyzed: 94 (33 vs. 32 vs. 29)

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Type of study	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed
Oscarson et al., 2006[52] *Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children*	RCT	A: One 0.48 g xylitol tablet at bedtime after brushing for 6 months then one tablet twice daily to age 3 years and 6 months B: No tablets	Age: 25 vs. 25 months Female: 49% vs. 46% (p>0.05) Non-white: NR Seldom/irregular tooth-brushing: 7% vs. 3% (p>0.05) High (>100 CFU) mutans streptococci counts: 11% vs. 6% (p>0.05) Daily sugary soft drinks: 17% vs. 27% (p>0.05) Daily sugars sweets: 0% vs. 2% (p>0.05)	Healthy 2 year olds. Excluded children with severe disabilities or uncooperative for oral exam	Number approached: NR Number eligible: NR Number enrolled: 132 (66 vs. 66) Number analyzed: 115 (55 vs. 63)
Seki et al., 2011[53] *Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomized trial*	Cluster, nonrandomized controlled clinical trial (3 clusters)	A: Xylitol chewing gum (100% xylitol); one pellet chewed 5 minutes four times daily B: No intervention	Baseline data only reported by group for children who completed follow-up Age 4 years old: 66% vs. 72% Female: 46% vs. 48% Race: NR (conducted in Japan) dfs index (mean): 2.5 vs. 4.2 (p=0.07) Individual plaque mutans streptococci score: 0.5 vs. 0.7 Salivary mutans streptococci score >0: 25% vs. 42%	Attending preschool in one region in Tokyo	Number approached: NR Number eligible: 432 Number enrolled: 248 (142 vs. 106) Number analyzed: 161(76 vs. 85)
Zhan et al., 2012[50] *Effects of xylitol wipes on cariogenic bacteria and caries in young children*	RCT	A: Xylitol wipes, two at a time, three times per day (estimated daily dosage 4.2 g) every 3 months B: Placebo wipes	Age: 6 to 35 months vs. 6 to 35 months Female: 36% vs. 40% Non-white: 90% vs. 95% Brush teeth daily: 68% vs. 68% Use fluoride toothpaste: 36% vs. 27%	Mothers with healthy children aged 6 to 35 months; mothers were primary care givers (>8 hrs daily) and with ≥1 active caries lesion within a year; no children with oral or systemic diseases; no mothers or children who took antibiotics or other medication affecting oral flora in previous 3 months	Number approached: 82 Number eligible: 57 Number enrolled: 44 (22 vs. 22) Number analyzed: 37 (20 vs. 17)

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Type of study	Interventions	Population characteristics	Eligiblity criteria	Number approached, eligible, enrolled, analyzed
Other intervention					
Du et al., 2006[54] *A 2-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children*	Cluster RCT (14 clusters)	A: 40% w/w chlorhexidine acetate varnish every 6 months B: Placebo varnish	Age: NR Female: NR Race: NR (study conducted in China) dmfs-molar, mean: 2.8 vs. 2.6, p=0.39	All children aged 4 to 5 years old, attending one of four kindergartens in study district.	Number approached: NR Number eligible: NR Number enrolled: 334 Number analyzed: 290 (155 vs. 135)
Lopez et al., 2002[55] *Topical antimicrobial therapy in the prevention of early childhood caries: a followup report*	RCT	A: 0.2 ml of 10% povidone iodine solution applied every 2 months B: Placebo solution	Age, mean (range): 16 (12-19) months Female: 48% Non-white: NR All children high risk (used bottle at bedtime containing cariogenic liquid, 2 consecutive positive streptococcus mutans cultures)	Infants attending one clinic with unremarkable medical history, 4 maxillary primary incisors with no visible defects and were caries free, who used a bottle at naptime/ bedtime containing cariogenic liquid, and had two consecutive positive streptococcus mutans cultures from pooled maxillary incisor plaque	Number approached: NR Number eligible: NR Number enrolled: 83 (39 vs. 44) Number analyzed: 83 (39 vs. 44)

Author, year, title	Country Setting	Sponsor	Duration of followup	Outcomes	Adverse events/harms	Attrition	Quality rating
Topical fluoride							
Chu et al., 2002[69] *Effectiveness of silver diamine flouride and sodium flouride varnish in arresting dentin caries in Chinese pre-school children*	China Recruitment setting: Kindergarten Water fluoridation status: <0.2 ppm	University of Hong Kong	2.5 years	A vs. B vs. C vs. D vs. E New caries surfaces: 0.26 vs. 0.47 vs. 0.89 vs. 0.70 vs. 1.58, p for ANOVA <0.001 (E vs. others) Arrested caries surfaces: 2.49 vs 2.82 vs. 1.45 vs. 1.54 vs. 1.27; p for ANOVA <0.001 (E vs. others) Absolute reduction in caries increment: 1.32 vs. 1.11 vs. 0.69 vs. 0.88 vs. E as comparator (vs. others) Reduction in caries increment: 84% vs. 70% vs. 44% vs. 56% vs. E as comparator (vs. others)	No adverse events detected	Overall 18%; 20% vs. 19% vs. 18% vs. 16% vs. 15%	Poor

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Country Setting	Sponsor	Duration of followup	Outcomes	Adverse events/harms	Attrition	Quality rating
Jiang et al., 2005[70] *The effect of a bi-annual professional application of APF foam on dental caries increment in primary teeth: 24-month clinical trial*	China Recruitment setting: Kindergarten Water fluoridation status: 0.1-0.3 ppm	National Key Technologies R&D Program of the Tenth-five Year Plan, Ministry of Science and Technology China	2 years	A vs. B No increase in dmfs: 38% (64/167) vs. 26% (40/151) dmfs increase of 1 to 5: 34% (56/167) vs. 38% (58/151) dmfs increase of 6 to 10: 17% (28/167) vs. 18% (27/151) dmfs increase of >10: 11% (19/167) vs. 17% (26/151) Net dmfs increment (all surfaces): 3.8 vs. 5.0; p=0.03 Absolute reduction in caries increment: 1.2 Reduction in caries increment: 24%	No adverse events detected	A vs. B: 20% (42/209) vs. 17% (32/183)	Good
Lawrence et al., 2008[47] *A 2-year community randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children*	Canada Recruitment setting: Rural Aboriginal communities Water fluoridation status: No fluoridation	Institute of Aboriginal Peoples' Health/Canadian Insititutes of Health Research; Toronto Hospital for Sick Children Foundation	2 years	A vs. B Dental caries in aboriginal cohort: 72% (595/832) vs. 75% (247/328), adjusted OR 0.72 (95% CI 0.42 to 1.25); NNT 26 Dental caries in those caries free at baseline: 44% (157/354) vs. 58% (73/126); adjusted OR 0.63 (95% CI 0.33 to 1.1); NNT 7.4 Net dmfs increment in aboriginal cohort, mean: 11 vs. 13.4; adjusted difference, mean (SE) 2.4 (2.0), p=0.24; prevented fraction 18% Net dmfs increment in those caries free at baseline, mean (SE): 4.3 (0.5) vs. 6.1 (0.8); adjusted difference, mean (SE): 1.8 (1.3); p=0.18; prevented fraction 29% Absolute reduction in caries increment: 2.4 (1.8) Reduction in caries increment: 18% (29%)	One child allergic to lanolin experienced an adverse event	11% (96/915) vs. 9% (32/360)	Good

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Country Setting	Sponsor	Duration of followup	Outcomes	Adverse events/harms	Attrition	Quality rating
Slade et al., 2011[48] *Effect of health promotion and fluoride varnish on dental caries among Australian Aborigina children: results from a community-randomized controlled trial*	Australia Recruitment setting: Rural Aboriginal communities Water fluoridation status: See population characteristics	Australian National Health and Medical Research Council	2 years	A vs. B Net dmfs increment per child, (mean) Adjusted for cluster effects: 6.9 vs. 9.9, difference 3.0 (95% CI 1.2 to 4.9), prevented fraction 31% Adjusted for cluster effects plus fluoride concentration in water: 6.2 vs. 9.7, difference 3.5 (95% CI 1.9 to 5.1), prevented fraction 36% Adjusted for cluster effects plus child's age and baseline dmfs: 7.0 vs. 9.4, 2.4 (0.6 to 4.3), prevented fraction 26% Adjusted for cluster effects plus loss to followup: 7.3 vs. 9.6, difference 2.3 (0.8 to 3.7), prevented fraction 24% Absolute reduction in caries increment: 2.3 Reduction in caries increment: 24%	No adverse events detected	A vs. B: 19% (60/322) vs. 18% (63/344)	Good
Weinstein et al., 2001[71] *Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years*	U.S. Recruitment setting: Head Start programs Water fluoridation status: NR (Yakima voters approved fluoridation in 1999)	NIDCR/NIH grants	1 year	A vs. B vs. C Radiographic dmfs increment, mean: 0.9 vs. 0.5 vs. 0.1, p=0.28 Clinical dmfs increment, mean: 4.6 vs. 3.2 vs. 4.7, p=0.65 Absolute reduction in caries increment: Not calculated Reduction in caries increment: Not calculated	Study states no loss to followup from adverse events	A vs. B vs. C: 33% (17/51) vs. 27% (14/52) vs. 13% (7/53) Note: Study states that 119 subjects examined at 1 year visit, but analysis shows 111	Fair
Weinstein et al., 2009[72] *Randomized equivalence trial of intensive and semi-annual applications of fluoride varnish in the primary dentition*	U.S. Recruitment setting: Head Start programs Water fluoridation status: NR (Yakima voters approved fluoridation in 1999)	NIDCR, NIH grants	3 years	A vs. B New tooth decay in primary surfaces (number of surfaces per child): 7.4 vs. 9.8, p=0.001; adjusted rate ratio 1.13 (95% CI 0.94 to 1.37) Absolute reduction in caries increment: 2.4 Reduction in caries increment: 24%	No adverse events detected	A vs. B: 27% (84/306) vs. 29% (86/294); 38% (230/600 not followed entire 3 years	Fair

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Country Setting	Sponsor	Duration of followup	Outcomes	Adverse events/harms	Attrition	Quality rating
Weintraub et al., 2006[49] *Fluoride varnish efficacy in preventing early childhood caries*	U.S. Recruitment setting: Family dental center and public health center serving primarily low-income, underserved Hispanic and Chinese populations Water fluoridation status: ~1 ppm	National Institute of Dental and Craniofacial Research; the National Center for Minority Health and Health Disparities; UCSF Department of Preventive and Restorative Dental Sciences	2 years	A vs. B vs. C Caries lesions at 12 months: 11/83 vs. 13/86 vs. 27/92; RR 0.45 (95% CI 0.24 to 0.83); NNT 7 for A vs. C and 0.52 (95% CI 0.28 to 0.93); NNT 8 for B vs. C Caries lesions at 24 months: 3/70 vs. 10/69 vs. 15/63; RR 0.18 (95% CI 0.06 to 0.59); NNT 6 for A vs. C and 0.61 (95% CI 0.30 to 1.26); NNT 11 for B vs. C dmfs, mean: 0.7 vs. 0.7 vs. 1.7; p<0.01 for A vs. C and B vs. C dmfs + pre-cavitated lesions, mean: 1.4 vs. 1.3 vs. 2.7; p<0.01 for A vs. C and B vs. C Absolute reduction in caries increment: 1.0 Reduction in caries increment: 59% (A + B vs. C)	No adverse events detected	A vs. B vs. C: 31% (39/126) vs. 25% (31/124) vs. 21% (26/126)	Fair
Xylitol							
Alamoudi et al., 2012[74] *Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs*	Saudi Arabia Recruitment setting: Well baby clinics and dental clinics Water fluoridation status: Not reported	Deanship of Scientific Research, King Abdulaziz University, Jeddah, Saidi Arabia	18 months	A vs. B dmft score at 6 months (mean): 8.95 vs. 13.00, p=0.024 dmft score at 12 months (mean): 9.64 vs. 13.12, p=0.041 dmft score at 18 months (mean): 9.19 vs. 14.69, p=0.001 dmft, mean: 0.8 vs. 4.4; p=NR Absolute reduction in caries increment: 3.6 Reduction in caries increment: 82%	NR	A vs. B 30% (9/30) vs. 57% (17/30)	Poor
Kovari et al., 2003[51] *Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland*	Finland Recruitment setting: Daycare centers Water fluoridation status: Not reported	NR	3 to 6 years (assessed at up to age 9 years)	A vs. B Caries-free at 7 years old: 69% (218/316) vs. 65% (278/427), RR 1.06 (95% CI 0.96 to 1.17) Caries-free at 9 years old: 57% (177/310) vs. 49% (213/434), RR 1.16 (95% CI 1.02 to 1.33) Decayed/missing/filled teeth: 1.1 vs. 1.0 at 7 years, 1.2 vs. 1.6 at 9 years dmft, mean: NR Absolute reduction in caries increment: NR Reduction in caries increment: NR	NR	A vs. B: 16.3% (64/392) vs. 13.4% (71/529) at age 9 years follow-up	Fair

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Country Setting	Sponsor	Duration of followup	Outcomes	Adverse events/harms	Attrition	Quality rating
Milgrom et al., 2009[73] *Xylitol pediatric topical oral syrup to prevent dental caries*	Marshall Islands Recruitment setting: Community based Water fluoridation status: Drinking water not fluoridated (supplemental and topical fluoride not available)	The Health Resources and Services Administration Maternal and Child Health Bureau and the National Institute of Dental and Craniofacial Research	1 year	A vs. B vs. C Tooth decay: 24.2% (8/33) vs. 40.6% (13/32) vs. 51.7% (15/29), RR 0.47 (95% CI 0.23 to 0.94) for A vs. C and 0.79 (95% CI 0.45 to 0.1.4) for B vs. C Mean decayed teeth: 0.6 vs. 1.0 vs. 1.9; p<0.05 for A or B vs. C; incidence rate ratio 0.30 (95% CI 0.13 to 0.66) for A vs. C and 0.50 (95% CI 0.26 to 0.96) for B vs. C Decayed primary teeth per year: 0.66 vs. 1.10 vs. 2.20 Absolute reduction in caries increment: 1.3 vs. 0.9 vs. C as comparator (vs. others) Reduction in caries increment: 68% vs. 47% vs. C as comparator (vs. others)	A vs. B vs. C Withdrawals due to adverse events: not reported Loose stool or diarrhea: 11.7% vs. 10.6% vs. 11.4% (p>0.05)	A vs. B vs. C: 17.1% (6/35) vs. 15.2% (5/33) vs. 15.6% (5/32)	Fair
Oscarson et al., 2006[52] *Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children*	Sweden Recruitment setting: Public dental clinic Water fluoridation status: Not reported	County of Vasterbotten, The Patent Revenue Fund for Dental Prophylaxis and Swedish Dental Society	2 years	A vs. B Dental caries: 18% (10/55) vs. 25% (16/63), OR 0.65 (95% CI 0.27 to 1.59) dmfs, mean: 0.38 vs. 0.80 (p>0.05) Absolute reduction in caries increment: 0.42 Reduction in caries increment: 52%	A vs. B Withdrawals due to adverse events: NR	A vs. B: 16.7% (11/66) vs. 4.5% (3/66)	Fair
Seki et al., 2011[53] *Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomized trial*	Japan Recruitment setting: preschool Water fluoridation status: NR (states fluoridation "limited" in Japan)	Uemura Fund, Nihon University School of Dentistr from the Ministry of Education, Science, Sports, Culture and Technology, Japan	1 year	A vs. B Development of caries from baseline to 6 months: 1.7 vs. 1.6 (p>0.05) Development of caries from 6 months to 1 year: 1.6 vs. 1.8 (p>0.05) Mean development of caries: 3.3 vs. 3.4; p>0.05 Absolute reduction in caries increment: 0.1 Reduction in caries increment: 3%	Diarrhea in 11% (8/76) in xylitol group	A vs. B 46% (66/142) vs. 20% (21/106)	Poor
Zhan et al., 2012[50] *Effects of xylitol wipes on cariogenic bacteria and caries in young children*	U.S. Recruitment setting: University pediatric clinic Water fluoridation status: Not reported	California Society of Pediatric Dentistry Foundation, a Graduate Scientific Research Award from American Academy of Pediatric Dentistry	1 year	A vs. B Mean new decayed surfaces: 0.05 vs. 0.53 (p=0.01) New caries lesions at 1 year: 5% vs. 40% (p=0.03); NNT 3 ITT analysis of new caries lesions at 1 year: 5% vs. 32%; RR 0.14 (95% CI 0.02 to 1.07); NNT 4 Absolute reduction in caries increment: 0.48	None	A vs. B 9% (2/22) vs. 23% (5/22)	Fair

Appendix B7. Trials of Preventive Treatments for the Prevention of Dental Caries

Author, year, title	Country Setting	Sponsor	Duration of followup	Outcomes	Adverse events/harms	Attrition	Quality rating
		and NIH/NIDCR grant U54 DEO19285		Reduction in caries increment: 91%			
Other intervention							
Du et al., 2006[54] *A 2-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children*	China Recruitment setting: Kindergartens in rural communities Water fluoridation status: 0.1-0.3 ppm	National Key Technologies R&D Program of the tenth Five-Year Plan; Ministry of Science and Technology; National Committee for Oral Health; People's Republic of China	2 years	A vs. B dmfs-molar increment, mean: 1.0 vs. 1.6, mean difference 0.6, 37% reduction in caries molar increment, p = 0.036 Absolute reduction in caries increment: 0.6 Reduction in caries increment: 37%	No adverse events detected	13% (44/334) overall	Fair
Lopez et al., 2002[55] *Topical antimicrobial therapy in the prevention of early childhood caries: a followup report*	U.S. Recruitment setting: women, infant and child clinic in Puerto Rico Water fluoridation status: NR	National Institute of Health Grants; University of Puerto Rico	1 year	A vs. B White spot lesions on maxillary primary incisors at 1 year: 8% (3/39) vs. 32% (14/44); RR 0.24 (95% CI 0.1 to 0.8) Mean white spot lesions: NR Absolute reduction in caries increment: NR Reduction in caries increment: NR	NR	A vs. B: 44% (17/39) vs. 34% (15/44)	Fair

Abbreviations: ANOVA = Analysis of Variance; CI = confidence interval; CFU = colony forming unit; dmfs = decayed, missing, filled surfaces; dmft = decayed, missing, filled teeth; g = gram; ITT = intention to treat; mL = milliliter; MS = mutans streptococcus; NaF = sodium fluoride; NIDCR = National Institute of Dental and Craniofacial Research; NIH = National Institutes of Health; NNT = number needed to treat; NR = not reported;OR = odds ratio; ppm = parts per million; RCT = randomized controlled trial; RR = relative risk; SE = standard error; TMJ = temporomandibular joint disorder; UCSF = University of California San Francisco; U.S. = United States.

Appendix B8. Systematic Review of Fluorosis Due to Fluoride Supplements

Author, year, title	Databases searched, date of last search	Number and type of studies	Methods for rating methodological quality of primary studies	Methods for synthesizing results of primary studies	Number of patients (treatment and control)	Adverse events	Quality rating
Ismail and Hasson, 2008[38] *Fluoride supplements, dental caries, and fluorosis: a systematic review*	MEDLINE: 1966-June 2006 Cochrane: up to 2nd quarter 2006 EMBASE: 1974-2006	5 observational studies	Cochrane Handbook of Systematic Reviews	Qualitative analyses only, due to high heterogeneity of subjects, outcomes, and duration of followup	Not reported	5 observational studies reported fluorosis outcomes associated with early childhood use of fluoride supplementation - All studies found an association between fluoride supplementation in early childhood and risk of fluorosis - 1 study (n=383) found OR increased by 84% per year of use of fluoride supplements (95% CI 1.4 to 2.5) - 1 study (n=188) found OR 10.3 in children started on fluoride supplements within the first 2 years of life (95% CI 1.9 to 61.6) - Largest study (n=3978) found slightly increased risk that ranged	Good

Abbreviations: CI = confidence interval; OR = odds ratio

Appendix B9. Quality Rating of Systematic Review

Author, year, title	Study design pre-determined?	Dual review of studies and data abstraction?	Comprehensive literature search?	Publication status used as inclusion criteria?	List of included and excluded studies provided?	Characteristics of included studies provided?	Included studies quality assessed?	Quality of included studies considered in formulating conclusions?	Appropriate methods used to combine studies?	Publication bias assessed?	Conflict of interest stated?	Quality rating
Ismail and Hasson, 2008[38] *Fluoride supplements, dental caries, and fluorosis: a systematic review*	Yes	Not reported	Yes	No	No	Yes	Yes	No	Yes	No	Yes	Good

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Effectiveness of Preventive Dental Treatments by Physicians for Young Medicaid Enrollees

Bhavna T. Pahel, R. Gary Rozier, Sally C. Stearns and Rocio B. Quiñonez

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Effectiveness of Preventive Dental Treatments by Physicians for Young Medicaid Enrollees

WHAT'S KNOWN ON THIS SUBJECT: Mixed evidence exists regarding the effectiveness of preventive dental services in medical settings. Physicians and nurses are willing to provide preventive dental services, parents are satisfied with the services their children receive, and programs that encourage physician participation increase access.

WHAT THIS STUDY ADDS: Despite declines in effectiveness since fluoride treatment and referrals to dentists to treat existing disease, this study reports that oral health services by non-dental health care providers for Medicaid preschool-aged children lead to reductions in caries-related treatments.

abstract

OBJECTIVE: To estimate the effectiveness of a medical office–based preventive dental program (Into the Mouths of Babes [IMB]), which included fluoride varnish application, in reducing treatments related to dental caries.

METHODS: We used longitudinal claims and enrollment data for all children aged 72 months or younger enrolled in North Carolina Medicaid from 2000 through 2006. Regression analyses compared subgroups of children who received up to 6 IMB visits at ages 6 to 35 months with children who received no IMB visits. Analyses were adjusted for child and area characteristics.

RESULTS: Children enrolled in North Carolina Medicaid with ≥4 IMB visits experienced, on average, a 17% reduction in dental-caries–related treatments up to 6 years of age compared with children with no IMB visits.When we simulated data for initial IMB visits at 12 and 15 months of age, there was a cumulative 49% reduction in caries-related treatments at 17 months of age. The cumulative effectiveness declined because of an increase in treatments from 24 to 36 months, an increase in referrals for dental caries occurred with increasing time since fluoride application, and emergence of teeth not initially treated with fluoride.

CONCLUSIONS: North Carolina's IMB program was effective in reducing caries-related treatments for children with ≥4 IMB visits. Multiple applications of fluoride at the time of primary tooth emergence seem to be most beneficial. Referrals to dentists for treatment of existing disease detected by physicians during IMB implementation limited the cumulative reductions in caries-related treatments, but also contributed to improved oral health. *Pediatrics* 2011;127:e682–e689

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KEY WORDS

dental caries, Medicaid, fluoride varnish, dental treatment, preschool children, physicians

ABBREVIATIONS

ECC—early childhood caries
IMB—Into the Mouths of Babes

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ARTICLE

COMPARATIVE EFFECTIVENESS RESEARCH

Cost-effectiveness of Preventive Oral Health Care in Medical Offices for Young Medicaid Enrollees

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Objective: To estimate the cost-effectiveness of a medical office–based preventive oral health program in North Carolina called Into the Mouths of Babes (IMB).

Design: Observational study using Medicaid claims data (2000-2006).

Setting: Medical staff delivered IMB services in medical offices, and dentists provided dental services in offices or hospitals.

Participants: A total of 209 285 children enrolled in Medicaid at age 6 months.

Interventions: Into the Mouths of Babes visits included screening, parental counseling, topical fluoride application, and referral to dentists, if needed. The cost-effectiveness analysis used the Medicaid program perspective and a propensity score–matched sample with regression analysis to compare children with 4 or more vs 0 IMB visits.

Main Outcome Measures: Dental treatments and Medicaid payments for children up to age 6 years enabled assessment of the likelihood of whether IMB was cost-saving and, if not, the additional payments per hospital episode avoided.

Results: Into the Mouths of Babes is 32% likely to be cost-saving, with discounting of benefits and payments. On average, IMB visits cost $11 more than reduced dental treatment payments per person. The program almost breaks even if future benefits from prevention are not discounted, and it would be cost-saving with certainty if IMB services could be provided at $34 instead of $55 per visit. The program is cost-effective with 95% certainty if Medicaid is willing to pay $2331 per hospital episode avoided.

Conclusions: Into the Mouths of Babes improves dental health for additional payments that can be weighed against unmeasured hospitalization costs.

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VARIOUS STUDIES HAVE documented high and increasing rates of dental caries among children younger than 5 years of age[1,2] as well as related negative health consequences.[3,4] Most children with dental caries are in low-income families and use dental care infrequently, despite eligibility for services through public insurance.[2] The limited dentist supply and dentists' low rate of participation in Medicaid further preclude access, motivating many communities to examine alternate approaches to this pressing public health problem.[5]

For editorial comment see page 965

The pediatric primary care setting provides an alternative site to deliver preventive oral health interventions for preschool-aged children before they develop poor oral health.[6,7] Although very young children are unlikely to visit dentist offices, they frequently make well-child visits to primary care physicians.[8] Preventive oral health care programs in medical offices include screening and risk assessment, parental counseling, topical fluoride application, and referral to dentists for further assessment or treatment, if needed.[7] Topical fluoride varnish is viewed as a cost-effective component of oral health care for low-income children, with recommendations for use every 3 to 6 months in high-risk children younger than 6 years of age.[9-11] Studies have shown that intervention in preschool-aged children with fluoride varnish improves dental health and defrays costs but is not cost-saving.[12,13]

Evidence of the effectiveness of oral health care in medical settings is limited.[14] A program called Into the Mouths of Babes (IMB) was initiated in North Carolina (NC) in 2000 in which physicians are reimbursed by Medicaid to conduct dental screenings of children 3 years of age or younger, apply fluoride varnish, and counsel parents. Into the Mouths of Babes im-

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Guideline on Infant Oral Health Care

Originating Committee
Clinical Affairs Committee – Infant Oral Health Subcommittee

Review Council
Council on Clinical Affairs

Adopted
1986

Revised
1989, 1994, 2001, 2004, 2009, 2011, 2012

Purpose
The American Academy of Pediatric Dentistry (**AAPD**) recognizes that infant oral health is one of the foundations upon which preventive education and dental care must be built to enhance the opportunity for a lifetime free from preventable oral disease. The AAPD proposes recommendations for preventive strategies, oral health risk assessment, anticipatory guidance, and therapeutic interventions to be followed by dental, medical, nursing, and allied health professional programs.

Methods
This guideline is an update of the previous Guideline on Infant Oral Health Care, revised in 2009. This revision included a hand search of literature as well as a new search of the MEDLINE/PubMed® electronic database using the following parameters: Terms: "infant oral health", "infant oral health care", and "early childhood caries"; Fields: all; Limits: within the last 10 years, humans, English, and clinical trials. Papers for review were chosen from the resultant list of 449 articles and from references within selected articles. When data did not appear sufficient or were inconclusive, recommendations were based upon expert and/or consensus opinion by experienced researchers and clinicians.

Background
The Centers for Disease Control and Prevention reports that caries is the most prevalent infectious disease in our nation's children.[1] More than 40 percent of children have caries by the time they reach kindergarten.[2] In contrast to declining prevalence of dental caries among children in older age groups, the prevalence of caries in poor US children under the age of five is increasing.[3] Early childhood caries (**ECC**) and the more severe form of ECC (**S-ECC**) can be particularly virulent forms of caries, beginning soon after tooth eruption, developing on smooth surfaces, progressing rapidly, and having a lasting detrimental impact onthe dentition.[4-9] This disease affects the general population but is 32 times more likely to occur in infants who are of low socioeconomic status, who consume a diet high in sugar, and whose mothers have a low education level.[10,11] Caries in primary teeth can affect children's growth, result in significant pain and potentially life-threatening infection, and diminish overall quality of life.[12-21] Since medical health care professionals are far more likely to see new mothers and infants than are dentists, it is essential that they be aware of the infectious etiology and associated risk factors of ECC, make appropriate decisions regarding timely and effective intervention, and facilitate the establishment of the dental home.[4,22-25]

Dental caries
Dental caries is a common chronic infectious transmissible disease resulting from tooth-adherent specific bacteria, primarily mutans streptococci (**MS**), that metabolize sugars to produce acid which, over time, demineralizes tooth structure.[26] MS generally is considered to be the principal group of bacterial organisms responsible for the initiation of dental caries.[27] MS colonization of an infant may occur from the time of birth.[28-34] Significant colonization occurs after dental eruption as teeth provide non-shedding surfaces for adherence. Other surfaces also may harbor MS.[32,35,36] For example, the furrows of the tongue appear to be an important ecological niche in harboring the bacteria in predentate infants.[33,35]

Vertical transmission of MS from mother to infant is well documented.[37-39] Genotypes of MS in infants appear identical to those present in mothers in 17 reports, ranging from 24 to 100 percent.[39] The higher the levels of maternal salivary MS, the greater the risk of the infant being colonized.[40,41] Along with salivary levels of MS, mother's oral hygiene, periodontal disease, snack frequency, and socioeconomic status also are associated with infant colonization.[36] Reports indicate that horizontal transmission (ie, transmission between members of a group such as siblings of a similar age or children in a daycare center) also may be of concern.[42-45] Dental caries is a disease that generally is preventable. Early risk assessment allows for identification of parent-infant groups who are at risk for ECC and would benefit from early preventive intervention. The ultimate goal of early assessment is the timely delivery of educational information to populations at high risk for developing caries in order to prevent the need for later surgical intervention.

Anticipatory guidance

Caries-risk assessment for infants allows for the institution of appropriate strategies as the primary dentition begins to erupt. Even the most judiciously designed and implemented caries-risk assessment, however, can fail to identify all infants at risk for developing ECC. In these cases, the mother may not be the colonization source of the infant's oral flora, the dietary intake of simple carbohydrates may be extremely high, or other uncontrollable factors may combine to place the infant at risk for developing dental caries. Therefore, screening for risk of caries in the parent and infant, coupled with oral health counseling, is not a substitute for the early establishment of the dental home.[41] The early establishment of a dental home, including ECC prevention and management, is the ideal approach to infant oral health care.[25,37] The inclusion of education regarding the infectious and transmissible nature of bacteria that cause ECC, as well as methods of oral health risk assessment, anticipatory guidance, and early intervention, into the curriculum of medical, nursing, and allied health professional programs has shown to be effective in increasing the establishment of a dental home.[47,48] Recent studies, noting that a majority of pediatricians and general dentists were not advising patients to see a dentist by one year of age, point to the need for increased infant oral health care education in the medical and dental communities.[49,50]

Recommendations

Recommendations for parental oral health[51]

Oral health education: All primary health care professionals who serve parents and infants should provide education on the etiology and prevention of ECC. Educating the parent on avoiding saliva-sharing behaviors (eg, sharing spoons and other utensils, sharing cups, cleaning a dropped pacifier or toy with their mouth) can help prevent early colonization of MS in infants.

Comprehensive oral examination: Referral for a comprehensive oral examination and treatment during pregnancy is especially important for the mother.

Professional oral health care: Routine professional dental care for the parent can help optimize oral health. Removal of active caries, with subsequent restoration of remaining tooth structure, in the parents suppresses the MS reservoir and minimizes the transfer of MS to the infant, thereby decreasing the infant's risk of developing ECC.[52]

Oral hygiene: Brushing with fluoridated toothpaste and flossing by the parent are important to help dislodge food and reduce bacterial plaque levels.

Diet: Dietary education for the parents includes the cariogenicity of certain foods and beverages, role of frequency of consumption of these substances, and the demineralization/remineralization process.

Fluoride: Using a fluoridated toothpaste and rinsing with an alcohol-free, over-the-counter mouth rinse containing 0.05 percent sodium fluoride once a day or 0.02 percent sodium fluoride rinse twice a day have been suggested to help reduce plaque levels and promote enamel remineralization.[22]

Xylitol chewing gum: Evidence suggests that the use of xylitol chewing gum (at least two to three times a day by the mother) has a significant impact on mother-child transmission of MS and decreasing the child's caries rate.[53-55]

Recommendations for the infant's oral health

Oral health risk assessment: Every infant should receive an oral health risk assessment from his/her primary health care provider or qualified health care professional by six months of age. This initial assessment should evaluate the patient's risk of developing oral diseases of soft and hard tissues, including caries-risk assessment, provide education on infant oral health, and evaluate and optimize fluoride exposure.

Establishment of a dental home: Parents should establish a dental home for infants by 12 months of age.[56] The initial visit should include thorough medical (infant) and dental (parent and infant) histories, a thorough oral examination, performance of an age-appropriate tooth brushing demonstration, and prophylaxis and fluoride varnish treatment if indicated. In addition, assessing the infant's risk of developing caries and determining a prevention plan and interval for periodic re-evaluation should be done. Infants should be referred to the appropriate health professional if specialized intervention is necessary. Providing anticipatory guidance regarding dental and oral development, fluoride status, non-nutritive sucking habits, teething, injury prevention, oral hygiene instruction, and the effects of diet on the dentition are also important components of the initial visit.

Teething: Teething can lead to intermittent localized discomfort in the area of erupting primary teeth, irritability, and excessive salivation; however, many children have no apparent difficulties. Treatment of symptoms includes oral analgesics and chilled rings for the child to "gum".[57] Use of topical anesthetics, including over-the-counter teething gels, to relieve discomfort are discouraged due to potential toxicity of these products in infants.[58-60]

Oral hygiene: Oral hygiene measures should be implemented no later than the time of eruption of the first primary tooth. Cleansing the infant's teeth as soon as they erupt with a soft toothbrush will help reduce bacterial colonization. Toothbrushing should be performed for children by a parent twice daily, using a soft toothbrush of age-appropriate size. Flossing should be initiated when adjacent tooth surfaces can not be cleansed with a toothbrush.[40]

Diet: Epidemiological research shows that human milk and breast-feeding of infants provide general health, nutritional, developmental, psychological, social, economic, and environmental advantages while significantly decreasing risk for a large number of acute and chronic diseases.[61] Human breast milk is uniquely superior in providing the best possible nutrition to infants and has not been epidemiologically associated with caries.[62-64] Frequent night time bottle feeding with milk is associated with, but not consistently implicated in, ECC.[63] Breastfeeding greater than seven times daily after 12 months of age is associated with increased risk for ECC.[66] Night time bottle feeding with juice, repeated use of a sippy or no-spill cup, and frequent in between meal consumption of sugar-containing

snacks or drinks (eg, juice, formula, soda) increase the risk of caries.[67-68] High-sugar dietary practices appear to be established early, by 12 months of age, and are maintained throughout early childhood.[69,70] The American Academy of Pediatrics has recommended children one through six years of age consume no more than four to six ounces of fruit juice per day, from a cup (ie, not a bottle or covered cup) and as part of a meal or snack.[71]

Fluoride: Optimal exposure to fluoride is important to all dentate infants and children.[72] Decisions concerning the administration of fluoride are based on the unique needs of each patient.[73-75] The use of fluoride for the prevention and control of caries is documented to be both safe and effective.[76-80] When determining the risk-benefit of fluoride, the key issue is mild fluorosis versus preventing devastating dental disease. In children considered at moderate or high caries risk under the age of two, a 'smear' of fluoridated toothpaste should be used. In all children ages two to five, a 'pea-size' amount should be used.[81-83] Professionally-applied topical fluoride, such as fluoride varnish, should be considered for children at risk for caries.[76,79,80,84,85] Systemically-administered fluoride should be considered for all children at caries risk who drink fluoride deficient water (less than 0.6 ppm) after determining all other dietary sources of fluoride exposure.[86] Careful monitoring of fluoride is indicated in the use of fluoride-containing products. Fluor-osis has been associated with cumulative fluoride intake during enamel development.

Injury prevention: Practitioners should provide age-appropriate injury prevention counseling for orofacial trauma. Initially, discussions would include play objects, pacifiers, car seats, and electric cords.[56]

Non-nutritive habits: Non-nutritive oral habits (eg, digit or paci-fier sucking, bruxism, abnormal tongue thrust) may apply forces to teeth and dentoalveolar structures. It is important to discuss the need for early sucking and the need to wean infants from these habits before malocclusion or skeletal dysplasias occur.[56]

Additional recommendations

Health care professionals and all other stakeholders in children's oral health should support the identification of a dental home for all infants by 12 months of age. Legislators, policy makers, and third party payors should be educated regarding the importance of early interventions to prevent ECC.

References

1. US Dept of Health and Human Services. Oral health in America: A report of the Surgeon General. Rockville, Md: US Dept of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health; 2000.
2. Pierce KM, Rozier RG, Vann WF Jr. Accuracy of pediatric primary care providers' screening and referral for early childhood caries. Pediatrics 2002;109(5):E82-2.
3. Dye BA, Tan S, Smith V, et al. Trends in oral health status: United States, 1988-1994 and 1999-2004. National Center for Health Statistics. Vital Health Stat 2007;11(248).
4. Nowak AJ, Warren JJ. Infant oral health and oral habits. Pediatr Clin North Am 2000;47(5):1043-66.
5. Gray MM, Marchment MD, Anderson RJ. The relationship between caries experience in deciduous molars at 5 years and in first permanent molars of the same child at 7 years. Community Dent Health 1991;8(1):3-7.
6. Grindefjord M, Dahllöf G, Modéer T. Caries development in children from 2.5 to 3.5 years of age: A longitudinal study. Caries Res 1995;29(6):449-54.
7. O'Sullivan DM, Tinanoff N. The association of early dental caries patterns with caries incidence in preschool children. J Public Health Dent 1996;56(2):81-3.
8. Johnsen DC, Gerstenmaier JH, DiSantis TA, Berkowitz RJ. Susceptibility of nursing-caries children to future approximal molar decay. Pediatr Dent 1997;19(1):37-41.
9. Heller KE, Eklund SA, Pittman J, Ismail AA. Associations between dental treatment in the primary and permanent dentitions using insurance claims data. Pediatr Dent 2000;22(6):469-74.
10. Drury TF, Horowitz AM, Ismail AA, et al. Diagnosing and reporting early childhood caries for research purposes. J Public Health Dent 1999;59(3):192-7.
11. Mobley C, Marshall TA, Milgrom P, Coldwell SE. The contribution of dietary factors to dental caries and disparities in caries. Acad Pediatr 2009;9(6):410-4.
12. Acs G, Lodolini G, Kaminsky S, Cisneros GJ. Effect of nursing caries on body weight in a pediatric population. Pediatr Dent 1992;14(5):302-5.
13. Ayhan H, Suskan E, Yildirim S. The effect of nursing or rampant caries on height, body weight, and head circumference. J Clin Pediatr Dent 1996;20(3):209-12.
14. Fleming P, Gregg TA, Saunders ID. Analysis of an emergency dental service provided at a children's hospital. Int J Paediatr Dent 1991;1(1):25-30.
15. Schwartz S. A one-year statistical analysis of dental emergencies in a pediatric hospital. J Can Dent Assoc 1994; 60(11):959-62, 966-8.
16. Sheller B, Williams BJ, Lombardi SM. Diagnosis and treatment of dental caries-related emergencies in a children's hospital. Pediatr Dent 1997;19(8):470-5.
17. Low W, Tan S, Schwartz S. The effect of severe caries on the quality of life in young children. Pediatr Dent 1999; 21(6):325-6.
18. Acs G, Pretzer S, Foley M, Ng MW. Perceived outcomes and parental satisfaction following dental rehabilitation under general anesthesia. Pediatr Dent 2001;23(5): 419-23.
19. Thomas CW, Primosch RE. Changes in incremental weight and well-being of children with rampant caries following complete dental rehabilitation. Pediatr Dent 2002;24(2):109-13.
20. Cunnion DT, Spiro A III, Jones JA, et al. Pediatric oral health-related quality of life improvement after treatment of early childhood caries: A prospective multi-site study. J Dent Child 2010;77(1):4-11.
21. Sheller B, Churchill SS, Williams BJ, Davidson B. Body mass index of children with severe early childhood caries. Pediatr Dent 2009;31(3):216-21.

22. American Academy of Pediatrics. Policy on oral health risk assessment timing and establishment of the dental home. Pediatrics 2003;111(5Pt1):1113-6.
23. Lewis CW, Grossman DC, Domoto PK, et al. The role of the pediatrician in the oral health of children: A national survey. Pediatrics 2000;106(6):E84.
24. Harrison R. Oral health promotion for high-risk children: Case studies from British Columbia. J Can Dent Assoc 2003;69(5):292-6.
25. American Academy of Pediatrics, Section on Pediatric Dentistry and Oral Health. A policy statement: Preventive intervention for pediatricians. Pediatrics 2008;122(6): 1387-94.
26. Loesche WJ. Role of *Streptococcus mutans* in human dental decay. Microbiol Rev 1986;50(4):353-80.
27. Ge Y, Caufield PW, Fisch GS, Li Y. *Streptococcus mutans* and *Streptococcus sanguis* colonization correlated with caries experience in children. Caries Res 2008;42(6): 444-8. Epub October 3, 2008.
28. Berkowitz RJ, Jordan HV, White G. The early establishment of *Streptococcus mutans* in the mouths of infants. Arch Oral Biol 1975;20(3):171-4.
29. Stiles HM, Meyers R, Brunnelle JA, Wittig AB. Occurrence of *Streptococcus mutans* and *Streptococcus sanguis* in the oral cavity and feces of young children. In: Stiles M, Loesch WJ, O'Brien T, eds. Microbial Aspects of Dental Caries. Washington, DC: Information Retrieval; 1976:187.
30. Loesche WJ. Microbial adhesion and plaque. In: Dental Caries: A Treatable Infection. 2nd ed. Grand Haven, Mich; Automated Diagnostic Documentation, Inc; 1993: 81-116.
31. Wan AK, Seow WK, Purdie DM, Bird PS, Walsh LJ, Tudehope DI. A longitudinal study of *Streptococcus mutans* colonization in infants after tooth eruption. J Dent Res 2003;82(7):504-8.
32. Wan AK, Seow WK, Walsh LJ, Bird P, Tudehope DI, Purdie DM. Association of *Streptococcus mutans* infection and oral developmental nodules in predentate infants. J Dent Res 2001;80(10):1945-8.
33. Berkowitz RJ. Mutans streptococci: Acquisition and transmission. Pediatr Dent 2006;28(2):106-9, discussion 192-8.
34. Law V, Seow WK, Townsend G. Factors influencing oral colonization of mutans streptococci in young children. Aust Dent J 2007;52(2):93-100, quiz 159.
35. Tanner ACR, Milgrom PK, Kent R Jr, et al. The microbiotia of young children from tooth and tongue samples. J Dent Res 2002;81(1):53-7.
36. Wan AK, Seow WK, Purdie DM, Bird PS, Walsh LJ, Tudehope DI. Oral colonization of *Streptococcus mutans* in six-month-old predentate infants. J Dent Res 2001; 80(12):2060-5.
37. Davey AL, Rogers AH. Multiple types of the bacterium *Streptococcus mutans* in the human mouth and their intrafamily transmission. Arch Oral Biol 1984;29(6):453-60.
38. Berkowitz R, Jones P. Mouth-to-mouth transmission of the bacterium *Streptococcus mutans* between mother and child. Arch Oral Biol 1985;30(4):377-9.
39. Douglass JM, Li Y, Tinanoff N. Association of mutans streptococci between caregivers and their children. Pediatr Dent 2008;29(5):375-87.
40. American Academy of Pediatric Dentistry. Policy on early childhood caries (ECC): Classifications, consequences, and preventive strategies. Pediatr Dent 2011;33(special issue):47-9.
41. Parisotto TM, Steiner-Oliveira C, Silva CM, Rodrigues LK, Nobre-dos-Santos M. Early childhood caries and mutans streptococci: A systematic review. Oral Health Prev Dent 2010;8(1):59-70.
42. Mattos-Graner RO, Li Y, Caufield PW, Duncan M, Smith DJ. Genotypic diversity of Mutans streptococci in Brazilian nursery children suggests horizontal transmission. J Clin Microbiol 2001:39(6):2313-6.
43. Van Loveren C, Bujis JF, ten Cate JM. Similarity of bacteriocin activity profiles of Mutans streptococci within the family when the children acquire strains after the age of 5. Caries Res 2000;34(6):481-5.
44. Emanuelsson L, Wang X. Demonstration of identical strains of Mutans streptococci within Chinese families by genotyping. Eur J Oral Sci 1998;106(3):778-94.
45. Mitchell SC, Ruby JD, Moser S, et al. Maternal transmission of Mutans streptococci in severe-early childhood caries. Pediatr Dent 2009;31(3):193-201.
46. American Academy of Pediatric Dentistry. Policy on the dental home. Pediatr Dent 2011;33(special issue):24-5.
47. Douglass JM, Douglass AB, Silk HJ. Infant oral health education for pediatric and family practice residents. Pediatr Dent 2005;27(4):284-91.
48. Fein JE, Quiñonez RB, Phillips C. Introducing infant oral health into dental curricula: A clinical intervention. J Dent Educ 2009;73(10);1171-7.
49. Brickhouse TH, Unkel JH, Kancitis I, Best AM, Davis RD. Infant oral health care: A survey of general dentists, pediatric dentists, and pediatricians in Virginia. Pediatr Dent 2008;30(2):147-53.
50. Malcheff S, Pink TC, Sohn W, Inglehart MR, Briskie D. Infant oral health examinations: Pediatric dentists' professional behavior and attitudes. Pediatr Dent 2009;31(3): 202-9.
51. Nowak AJ, Casamassimo PS. Using anticipatory guidance to provide early dental intervention. J Am Dent Assoc 1995;126(8):1156-63.
52. New York State Department of Health. Oral health care during pregnancy and early childhood: Practice guidelines. Aug, 2006. Available at: "http://www.nyhealth.gov/publications/0824.pdf". Accessed September 6, 2012.
53. Isokangas P, Söderling E, Pienihäkkinen K, Alanen P. Occurrence of dental decay in children after maternal consumption of xylitol chewing gum: A follow-up from 0 to 5 years of age. J Dent Res 2000;79(11):1885-9.
54. Söderling E, Isokangas P, Pienihäkkinen K, Tenovou J. Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants. J Dent Res 2000;79 (3):882-7.

55. Thorild I, Lindau B, Twetman S. Caries in 4-year-old children after maternal chewing of gums containing combinations of xylitol, sorbitol, chlorhexidine, and fluoride. Eur Arch Paediatr Dent 2006;7(4):241-5.
56. American Academy of Pediatric Dentistry. Guideline on periodicity of examination, preventive dental services, anticipatory guidance/counseling, and oral treatment for infants, children, and adolescents. Pediatr Dent 2010;32 (special issue):93-100.
57. Tinanoff NT. The oral cavity. In: Kliegman RM, Stanton BF, St Geme J, Schor N, Behrman RE eds. Nelson Textbook of Pediatrics, 19th ed. Philadelphia, Pa: Elsevier (Saunders); 2011:1257.
58. Balicer RD, Kitai E. Methemoglobinemia caused by topical teething preparation: A case report. Scientific World J 2004;15(4):517-20.
59. Bong CL, Hilliard J, Seefelder C. Severe methemoglobinemia from topical benzocaine 7.5% (baby Orajel) use for teething pain in a toddler. Clin Pediatr 2009;48(2): 201-11.
60. US Food and Drug Administration. FDA drug safety communication: Reports of a rare, but serious and potentially fatal adverse effect with the use of over-the-counter (OTC) benzocaine gels and liquids applies to the gums or mouth. Available at: "http:www.fda.gov/Drugs/DrugSafety/ucm250024.htm". Accessed September 6, 2012.
61. American Academy of Pediatrics. Policy statement: Breastfeeding and the use of human milk. Pediatrics 2012;129 (3):e827-41.
62. Erickson PR, Mazhari E. Investigation of the role of human breast milk in caries development. Pediatr Dent 1999;21(2):86-90.
63. Iida H, Auinger P, Billings RJ, Weitzman M. Association between infant breastfeeding and early childhood caries in the United States. Pediatrics 2007;120(4):e944-52.
64. Mohebbi SZ, Virtanen JI, Vahid-Golpayegani M, Vehkalahti MM. Feeding habits as determinants of early childhood caries in a population where prolonged breastfeeding is the norm. Community Dent Oral Epidemiol 2008;36(4):363-9.
65. Reisine S, Douglass JM. Psychosocial and behavioral issues in early childhood caries. Commun Dent Oral Epidem 1998;26(suppl):32-44.
66. Feldens CA, Giugliani ERJ, Vigo Á, Vítolo MR. Early feeding practices and severe early childhood caries in four-year-old children from southern Brazil: A birth cohort study. Caries Res 2010;44(5):445-52.
67. Tinanoff NT, Kanellis MJ, Vargas CM. Current understanding of the epidemiology, mechanism, and prevention of dental caries in preschool children. Pediatr Dent 2002;24(6):543-51.
68. Tinanoff N, Palmer C. Dietary determinants of dental caries in preschool children and dietary recommendation for preschool children. J Pub Health Dent 2000;60(3): 197-206.
69. Douglass JM. Response to Tinanoff and Palmer: Dietary determinants of dental caries and dietary recommendations for pre-school children. J Public Health Dent 2000; 60(3):207-9.
70. Kranz S, Smiciklas-Wright H, Francis LA. Diet quality, added sugar, and dietary fiber intake in American preschoolers. Pediatr Dent 2006;28(2):164-71.
71. American Academy of Pediatrics Committee on Nutrition. Policy statement: The use and misuse of fruit juices in pediatrics. Pediatrics 2001;107(5):1210-3. Reaffirmed October, 2006.
72. Milgrom PM, Huebner CE, Ly KA. Fluoridated toothpaste and the prevention of early childhood caries: A failure to meet the needs of our young. J Am Dent Assoc 2009;140(6):628, 630-1.
73. American Academy of Pediatric Dentistry. Policy on use of fluoride. Pediatr Dent 2012;34(special issue):43-4.
74. Hale K, Heller K. Fluorides: Getting the benefits, avoiding the risks. Contemp Pediatr 2000;2:121.
75. American Dental Association. Caries diagnosis and risk assessment: A review of preventive strategies and management. J Am Dent Assoc 1995;126(suppl):1S-24S.
76. Adair SM. Evidence-based use of fluoride in contemporary pediatric dental practice. Pediatr Dent 2006;28(2): 133-42.
77. Whitford GM. The physiological and toxicological characteristics of fluoride. J Dent Res 1990;69(special issue): 539-49, discussion 556-7.
78. Workshop Reports I, II, III from "A symposium on changing patterns of fluoride intake" held at UNC-Chapel Hill, April 23-25, 1991. J Dent Res 1992;71(5):1214-27.
79. CDC. Recommendations for using fluoride to prevent and control dental caries in the United States. MMWR Recomm Rep 2001;50(RR-14):1-42.
80. Facts about fluoride. CDS Rev 2006;99(1):44.
81. Pang DT, Vann WF Jr. The use of fluoride-containing toothpastes in young children: The scientific evidence for recommending a small amount. Pediatr Dent 1992;14 (6):384-7.
82. Ramos-Gomez FJ, Crall JJ, Gansky SA, Slayton RL, Featherstone JD. Caries risk assessment appropriate for the age 1 visit (infants and toddlers). J Calif Dent Assoc 2007;35(10):687-702.
83. Scottish Intercollegiate Guideline Network. Prevention and management of dental decay in the pre-school child. A national guideline. Available at: "http://www.sign.ac.uk/pdf/qrg83.pdf". Accessed September 6, 2012.
84. American Dental Association, Council on Scientific Affairs. Professionally-applied topical fluoride: Evidence-based clinical recommendations. J Amer Dent Assoc 2006;137(8):1151-9.
85. American Academy of Pediatric Dentistry. Guideline on caries-risk assessment and management for infants, children, and adolescents. Pediatr Dent 2011;33(special issue):110-7.
86. American Academy of Pediatric Dentistry. Guideline on fluoride therapy. Pediatr Dent 2012;34(special issue): 162-5.

Promoting Oral Health

Theme 7

Introduction

Oral health is critically important to the overall health and well-being of children and adolescents. It covers a range of health promotion and disease prevention concerns, including dental caries (tooth decay); periodontal health; proper development and alignment of facial bones, jaws, and teeth; oral diseases and conditions; and trauma or injury to the mouth and teeth. Oral health is an important and continuing health supervision issue for the health care professional.

Childhood caries (tooth decay) is a preventable and transmissible infectious disease, caused by bacteria (eg, *Streptococcus mutans or Streptococcus sobrinus*) that form plaque on the surface of teeth. The bacteria interact with sugar in foods and beverages, turning it into acids that dissolve tooth enamel, causing caries.

Caries is the most common chronic disease in children—5 times more common than asthma.[1] Left untreated, pain and infection caused by tooth decay can lead to problems in eating, speaking, and learning.[1] Forty percent of children have caries by the time they reach kindergarten,[2] and many school hours are lost each year due to dental problems related to caries.[1-3]

Several population groups are particularly vulnerable to caries. For example, children and youth with special health care needs are at increased risk. National surveys also have demonstrated that children in low-income and moderate-income households are more likely to have caries and more decayed or filled teeth than children who are from more affluent households. Even within income levels, children of color are more likely to have caries than white children.[4] Thus, sociodemographic status should be viewed as an initial indicator of risk that can be offset by the absence of other risk indicators.

Health care professionals can teach children, adolescents, and their families about oral hygiene, healthy diet and feeding practices, optimal exposure to fluoride, and timely referral to a dentist. Health care professionals also often make the initial response for oral trauma. They should keep in mind that the differential diagnosis for oral trauma includes intentional injury.[5]

Bright Futures in Practice: Oral Health Pocket Guide (2004) provides a structured and comprehensive approach to this anticipatory guidance for the health care professional.[6] The Health Resources and Services Administration's (HRSA's) National Maternal and Child Oral Health Resource Center (www.mchoralhealth.org) also provides many valuable tools and resources for health care professionals.[7] Additional information is available at the American Academy of Pediatrics (AAP) Web site (www.aap.org).

The Importance of a Dental Home

The dental home is the "ongoing relationship between the dentist and the patient, inclusive of all aspects of oral health delivered in a comprehensive, continuously accessible coordinated and family-centered way."[8]

Box 1 describes the services that should be provided within a dental home.

The dental community (the American Dental Association, the Academy of General Dentistry, and the American Academy of Pediatric Dentistry [AAPD]) is united in encouraging families to establish a dental home by the time their child is 1 year old.[9] Having a dental home is the ideal deterrence to the development of caries, from infancy through adolescence. Early preventive dental

The dental community (the American Dental Association, the Academy of General Dentistry, and the American Academy of Pediatric Dentistry) is united in encouraging families to establish a dental home by the time their child is 1 year old.

BOX 1
Dental Home

According to the American Academy of Pediatric Dentistry (AAPD), the dental home should provide the following:

- Comprehensive oral health care, including acute care and preventive services, in accordance with AAPD periodicity schedules.
- Comprehensive assessment for oral diseases and conditions.
- An individualized preventive dental health program based on a caries risk assessment and a periodontal disease risk assessment.
- Anticipatory guidance about growth and development issues (ie, teething, thumb or finger or pacifier habits).
- A plan for acute dental trauma.
- Information about proper care of the child's teeth and gingivae. This would include prevention, diagnosis, and treatment of disease of the supporting and surrounding tissues and the maintenance of health, function, and esthetics of those structures and tissues.
- Dietary counseling.
- Referrals to specialists when care cannot directly be provided within the dental home.
- Education regarding future referral to a dentist knowledgeable and comfortable with adult oral health issues for continuing oral health care; referral at an age determined by patient, parent, and pediatric dentist.

Adopted from: American Academy of Pediatric Dentistry. *Policy on the Dental Home*. American Academy of Pediatric Dentistry; revised 2004.[9]

visits have been shown to reduce dental disease and reduce costs. For example, Savage et al[10] showed that dental costs for Medicaid-eligible children who began dental visits between the ages of 1 and 2 years were approximately 60% of the cost for children who began dental visits between the ages of 4 and 5 years.

As children and adolescents mature into adulthood, a dental home also can ensure that they receive oral health education/counseling, preventive and early intervention measures, and treatment, including treatment for periodontal care, orthodontic services, trauma, and other conditions.

Efforts to establish a dental home offer an opportunity for partnerships and foster a connection with the community. A partnership among health care professionals in primary care, dental health, public health, child care, and school settings can help ensure access to a dental home for each child during the early childhood, middle childhood, and adolescent years. (For more information on this topic, see the Promoting Community Relationships and Resources theme.)

Supplemental Fluoride

Fluoride plays a key role in preventing and controlling caries. Fluoride helps reduce loss of minerals from tooth enamel (demineralization) and promotes replacement of minerals (remineralization) in dental enamel that has been damaged by acids produced by bacteria in plaque. Regular and frequent exposure to small amounts of fluoride is the best way to protect the teeth against caries. This exposure can be readily accomplished through drinking water that has been optimally fluoridated and brushing with fluoride toothpaste twice daily.[11]

Fluoride supplementation typically is not needed in the first 6 months of life. Beginning at the age of 6 months, children should drink fluoridated community drinking water or take prescribed supplements (ie, drops or chewable tablets).[11-13] As an alternative to fluoride supplements, parents can purchase bottled water that contains fluoride.

Additional types of fluoride may be used as a primary preventive measure and, generally, are recommended for infants, children, and adolescents who are deemed to be at high risk of caries. Research has shown that the primary caries prevention effects of fluoride result from its topical contact with enamel and through its antibacterial actions. Therefore, topical agents (eg, concentrated fluoride gels, foams, and varnishes) may be used as a strategy for children who are deemed to be at elevated risk of tooth decay.[11,14]

Even if indicated, additional fluoride should be used judiciously in children 6 years and younger to minimize the risk of fluorosis (ie, overexposure to fluoride).[11] Fluorosis can come from using too much toothpaste that contains fluoride, drinking water with higher than recommended fluoride levels, and taking fluoride supplements when other sources of fluoride are available.[15] To prevent fluorosis, the primary water source(s) must be tested before parents are advised to supplement with fluoride.[16]

For adolescents, optimal fluoride levels in drinking water, combined with fluoride-containing preparations, such as toothpastes, gels, varnishes, and rinses, have significantly reduced dental decay, but caries risk remains high during this age period.[17,18] Adolescents at high risk of caries should be evaluated for topical fluoride beyond that provided by water supply and a fluoridated toothpaste.

Children and Youth With Special Health Care Needs

Children with special health care needs (eg, infants at risk of enamel demineralization and hypoplasia because of poor mineralization or osteopenia, nutritional deficiencies, or medication usage) present a unique set of concerns for oral health because they are

Fluoride helps reduce loss of minerals from tooth enamel (demineralization) and promotes replacement of minerals (remineralization) in dental enamel that has been damaged by acids produced by bacteria in plaque.

particularly prone to the development of caries. Because dental care for these children is often difficult and sometimes risky, the health care professional should refer the child to a dentist as early as possible for vigilant preventive dental care, which may alleviate the need for future surgical intervention.

Oral diseases also may have a direct and devastating impact on the general health of children with certain systemic or developmental problems or conditions. Children with compromised immunity or certain cardiac, kidney, or liver conditions may be especially vulnerable to the effects of oral diseases. Children with cognitive disabilities or developmental or neuromuscular conditions who do not have the ability to understand and assume responsibility for, or cooperate with, preventive oral health practices may be at higher risk for complications or systemic infections from oral diseases.[19]

The child with special needs should begin dental care in the first year and visit the dentist every 6 months or more frequently as needed.

Children and youth with special health care needs may require more help with their oral self-care routines (ie, brushing and flossing) than other children. Health care professionals should advise parents or caregivers to supervise and intervene as needed to help their children with brushing and flossing if their special needs prevent them from doing a thorough job. The child with special needs should begin dental care in the first year and visit the dentist every 6 months or more frequently as needed.

Adolescents with special health care needs may face difficulties because of their physical condition, malformations, medicines, or nutrition. They should receive regular dental care and be encouraged to take as much responsibility as possible for their own oral hygiene.

Promoting Oral Health: Infancy—Birth to 11 Months

Even though a child's teeth do not begin to appear until the middle of this developmental period, oral health is still a concern because of the potential that caries can develop during the first year of life.

Oral Hygiene and Feeding Practices That Promote Oral Health

Even before the baby's birth, parents and other caregivers should make sure their own mouths are as healthy as possible to reduce transmission of caries-causing harmful bacteria from their saliva to the newborn baby's mouth. Health care professionals should educate family members or caregivers in the following ways to prevent transmission of these bacteria from themselves to the infant:

- Practice good oral hygiene and seek dental care.
- Do not share utensils, cups, spoons, or toothbrushes with the infant.
- Do not clean a pacifier in their own mouths before giving it to the infant.
- Consult with an oral health professional about the use of xylitol gum (if the adult's oral health is a concern). This gum can have a positive impact on oral health by decreasing the bacterial load in an adult's mouth.[20]

The primary teeth begin to erupt at different ages during the first year of life. An infant is susceptible to tooth decay as soon as her first teeth erupt if she has a sufficient bacterial load already present in her mouth and prolonged exposure to carbohydrates. Chalky white areas on the teeth are the first sign of dental decay. Both inadequate oral hygiene and inappropriate feeding practices that expose teeth to natural or refined sugars for prolonged periods contribute to the development of early childhood caries. Health care professionals should educate parents in the

following ways to keep teeth clean and remove plaque:

- Minimize exposure to natural or refined sugars in the infant's mouth.
  - Avoid frequent exposure to foods that can lead to early childhood caries.
  - Hold the infant while feeding. Never prop a bottle (ie, use pillows or any other object to hold a bottle in the infant's mouth).
  - Do not allow the infant to fall asleep with a bottle that contains milk, formula, juice, or other sweetened liquid.
  - Avoid dipping pacifiers in any sweetened liquid, sugars, or syrups.[16]
- Use a toothbrush twice daily as soon as teeth erupt. In children younger than 2 years, the teeth should be brushed with plain water twice a day (after breakfast and before bed),[6] unless advised by a dentist to use fluoridated toothpaste based on a child's elevated dental caries risk.

To help prevent early childhood caries, parents also should take advantage of this developmental stage to establish lifelong nutritious eating patterns for the family that emphasize consumption of fruits, vegetables, whole grains, lean meats, and dairy products, and that minimize consumptions of foods and liquids high in sugars. (For more information on this topic, see the Promoting Healthy Nutrition theme.)

Oral Health Risk Assessment

In 2003, the AAP developed a policy statement, Oral Health Risk Assessment Timing and Establishment of the Dental Home, that recommended that primary care child health care professionals conduct an oral health risk assessment when a child is 6 months of age (Box 2).[21] This assessment consists of asking parents about their, and the child's, oral hygiene and looking at the child's mouth to assess the risk of caries.

The AAP recognizes that, even today, some children live in communities that lack pediatric dentists or general dentists who are able to see infants and young children. Therefore, primary care child health care professionals who care for these children may have to continue to perform periodic oral health risk assessments even after the first 6 to 12 months of age. These assessments allow health care professionals to identify children at the highest risk of oral health problems so that they can be referred to whatever limited resources are available. Some child health care professionals also may provide enhanced oral health counseling or apply fluoride varnish to help with caries prevention in

BOX 2
Pediatric Oral Health Risk Assessment

Adopted from the AAP policy statement that states that all children should undergo an oral health risk assessment beginning at 6 months of age by a qualified pediatric health care professional:

"If an infant is assessed to be in one of the following risk groups, the care requirements could be significant and surgically invasive. Therefore, these infants should be referred to a dentist as early as 6 months of age and no later than 6 months after the first tooth erupts or 12 months of age (whichever comes first) for establishment of a dental home:

- Children with special health care needs
- Children of mothers with a high caries rates
- Children with demonstrable caries, plaque, demineralization, and/or staining
- Children who sleep with a bottle or breastfeed throughout the night
- Children in families of low socioeconomic status"

In 2003, the American Academy of Pediatrics… recommended that primary care child health care professionals conduct an oral health risk assessment when a child is 6 months of age.

high-risk children.[22,23] In addition, public health professionals often assist health care professionals and families to link to a dental home.

Promoting Oral Health: Early Childhood—1 to 4 Years

The key oral health priorities of this developmental stage are the same as those of infancy, namely preventing caries and developing healthy oral hygiene habits. Early childhood also is a good time for parents, caregivers, and health care professionals to build positive dietary habits as they introduce new foods and the child establishes taste preferences. Parents may have questions during this period about pacifiers and thumb-sucking and finger-sucking behaviors that are related to teeth and jaw alignment.

Oral Hygiene, Fluoride, and Feeding Practices That Promote Oral Health

Parents and caregivers can do much to prevent the development of caries and promote overall oral health during this period. As noted earlier, caries is an infectious disease, and parents should make sure their oral hygiene and diet meet the standards outlined here. Health care professionals should educate the family and caregivers in the following ways to reduce transmission of bacteria from themselves to the child:

- Practice good oral hygiene and seek dental care.
- Do not share utensils, cups, spoons, or toothbrushes with the child.
- Do not put the child's pacifiers in their own mouths. Clean pacifiers with mild soap and water.
- Consult with their oral health care professional about the use of gum containing xylitol (if the adult's oral health is a concern).

Health care professionals also should educate parents about ways to keep their child's teeth clean and ensure sufficient fluoride intake.

- Brush the child's teeth twice daily as soon as teeth erupt. Because young children do not have the manual dexterity to properly clean their own teeth, an adult usually must brush the teeth of preschool-aged children. When parents feel their child is doing a thorough job, they should allow the child more independence and freedom.
  - For children younger than 2 years, brush the teeth with plain water twice a day (after breakfast and before bed) unless advised by a dentist to use fluoridated toothpaste based on a child's elevated dental caries risk.
  - For children 2 years and older, brush the teeth with no more than a pea-sized amount (small smear) of fluoride toothpaste twice a day (after breakfast and before bed). The child should spit out the toothpaste after brushing, but not rinse his mouth with water. The small amount of toothpaste that remains in his mouth helps prevent tooth decay.[6] Children can be taught to floss if recommended by the dental professional.
- Make sure the child drinks fluoridated water or takes prescribed fluoride supplements.

Early childhood is a time in which children are exposed to new tastes, textures, and eating experiences. It is an important opportunity for parents and caregivers to firmly establish healthful eating patterns for the child and her family. These patterns should emphasize consumption of fruits, vegetables, whole grains, lean meats, and dairy products, and minimize consumptions of foods and liquids high in sugars. (For more information on this topic, see the Promoting Healthy Nutrition theme.)

Early childhood is a time in which children are exposed to new tastes, textures, and eating experiences. It is an important opportunity for parents and caregivers to firmly establish healthful eating patterns for the child and her family.

Oral Health Risk Assessment

The AAPD recommends that, after 12 months of age, a child should be seen by a dentist every 6 months or according to a schedule recommended by the dentist, based on the child's individual needs and susceptibility to disease.[24] The AAP notes that, in the absence of a dental home program that is able to see the 1- to 4-year-old child, the primary care child health care professional should continue to perform oral health risk assessments in the 1- to 4-year-old child.

The AAPD also recommends that health care professionals use the Caries-Risk Assessment Tool (CAT) beginning at age 1 year (Table 1) as part of the oral risk assessment.[25]

Other Oral Health Issues

The health care professional should be prepared to discuss the use of pacifiers and finger sucking or thumb sucking. Finger sucking often fills an emotional need, but it can lead to malocclusion, including anterior open bite (top teeth do not overlap the bottom teeth) and excess overjet (top teeth protrude relative to the bottom teeth). The intensity, duration, and nature of the sucking habit can be used to predict the amount of harm that can occur. Positive reinforcement, including a reward system or reminder system, is the most effective way to discourage finger sucking.

Promoting Oral Health: Middle Childhood—5 to 10 Years

During the early part of middle childhood, a child loses his first tooth and the first permanent teeth (maxillary and mandibular incisors and first molars) start to erupt. By the end of middle childhood, most of the permanent teeth have erupted. For the child, these are exciting signs of getting older. Middle childhood also is a good time for parents and caregivers to reinforce oral hygiene, optimal fluoride exposure, and positive diet habits they pursued in early childhood.

The history and physical examination performed by the health care professional should include oral health. The child also should see the dentist every 6 months or according to a schedule recommended by the dentist, based on the child's individual needs and susceptibility to disease. When the permanent molars erupt, the child's dentist should evaluate his teeth to determine the need for sealants that protect the teeth from caries.

The key oral health issues for this developmental stage are preventing caries and gingivitis, and ensuring proper development of the mouth and jaw. Reducing the risk of injury or trauma to the mouth and teeth and avoiding risk behaviors that negatively affect oral health also are important.

Oral Hygiene, Fluoride, and Nutrition Practices That Promote Oral Health

Health care professionals should educate parents in the following ways to help their child keep his teeth clean and remove plaque:

- Helping with, and supervising, the brushing of their child's teeth at least twice a day and flossing if recommended by the dental professional.
- Using only a pea-sized amount of fluoridated toothpaste to clean the child's teeth. The child should spit out the toothpaste after brushing, but not rinse his mouth with water. The small amount

The American Academy of Pediatric Dentistry recommends that, after 12 months of age, a child should be seen by a dentist every 6 months or according to a schedule recommended by the dentist, based on the child's individual needs and susceptibility to disease.

TABLE 1

American Academy of Pediatric Dentistry Caries-Risk Assessment Tool (CAT)

Risk Factors to Consider	**Risk Indicators**		
(For each item below, circle the most accurate response found to the right under "Risk Indicators")	High	Moderate	Low
Part 1 – History (determined by interviewing the parent/primary caregiver)			
Child has special health care needs, especially any that impact motor coordination or cooperation[A]	Yes		No
Child has condition that impairs saliva (dry mouth)[B]	Yes		No
Child's use of dental home (frequency of routine dental visits)	None	Irregular	Regular
Child has decay	Yes		No
Time lapsed since child's last cavity	<12 months	12 to 24 months	>24 months
Child wears braces or orthodontic/oral appliances[C]	Yes		No
Child's parent and/or sibling(s) have decay	Yes		No
Socioeconomic status of child's parents[D]	Low	Mid-level	High
Daily between-meal exposures to sugars/cavity producing foods (includes on demand use of bottle/sippy cup containing liquid other than water; consumption of juice, carbonated beverages, or sports drinks; use of sweetened medications)[E]	>3	1 to 2	Mealtime only
Child's exposure to fluoride[F,G]	Does not use fluoridated toothpaste; drinking water is not fluoridated and is not taking fluoride supplements	Uses fluoridated toothpaste; usually does not drink fluoridated water and does not take fluoride supplements	Uses fluoridated toothpaste; drinks fluoridated water or takes fluoride supplements
Times per day that child's teeth/gums are brushed	<1	1	2-3
Part 2 – Clinical evaluation (determined by examining the child's mouth)			
Visible plaque (white, sticky buildup)	Present		Absent
Gingivitis (red, puffy gums)[H]	Present		Absent
Areas of enamel demineralization (chalky white-spots on teeth)	More than 1	1	None
Enamel defects, deep pits/fissures[I]	Present		Absent
Part 3 – Supplemental professional assessment (Optional)[J]			
Radiographic enamel caries	Present		Absent
Levels of mutans streptococci or lactobacilli	High	Moderate	Low

Each child's overall assessed risk for developing decay is based on the highest level of risk indicator circled above (ie, single risk indicator in any area of the "high risk" category classifies a child as being "high risk").

A Children with special health care needs are those who have a physical, developmental, mental, sensory, behavioral, cognitive, or emotional impairment or limiting condition that requires medical management, health care intervention, and/or use of specialized services. The condition may be developmental or acquired and may cause limitations in performing daily self-maintenance activities or substantial limitations in a major life activity. Health care for special needs patients is beyond that considered routine and requires specialized knowledge, increased awareness and attention, and accommodation.

B Alteration in salivary flow can be the result of congenital or acquired conditions, surgery, radiation, medication, or age-related changes in salivary function. Any condition, treatment, or process known or reported to alter saliva flow should be considered an indication of risk unless proven otherwise.

C Orthodontic appliances include both fixed and removable appliances, space maintainers, and other devices that remain in the mouth continuously or for prolonged time intervals and which may trap food and plaque, prevent oral hygiene, compromise access of tooth surfaces to fluoride, or otherwise create an environment supporting caries initiation.

D National surveys have demonstrated that children in low-income and moderate-income households are more likely to have caries and more decayed or filled primary teeth than children from more affluent households. Also, within income levels, minority children are more likely to have caries. Thus, socioeconomic status should be viewed as an initial indicator of risk that may be offset by the absence of other risk indicators.

E Examples of sources of simple sugars include carbonated beverages, cookies, cake, candy, cereal, potato chips, French fries, corn chips, pretzels, breads, juices, and fruits. Clinicians using caries-risk assessment should investigate individual exposures to sugars known to be involved in caries initiation.

F Optimal systemic and topical fluoride exposure is based on use of a fluoride dentifrice and American Dental Association/American Academy of Pediatrics guidelines for exposure from fluoride drinking water and/or supplementation.

G Unsupervised use of toothpaste and at-home topical fluoride products are not recommended for children unable to expectorate predictably.

H Although microbial organisms responsible for gingivitis may be different than those primarily implicated in caries, the presence of gingivitis is an indicator of poor or infrequent oral hygiene practices and has been associated with caries progression.

I Tooth anatomy and hypoplastic defects (eg, poorly formed enamel, developmental pits) may predispose a child to develop caries.

J Advanced technologies such as radiographic assessment and microbiologic testing are not essential for using this tool.

of toothpaste that remains in his mouth helps prevent tooth decay.[6]

- Make sure the child drinks fluoridated water or takes prescribed fluoride supplements.

As children begin school and expand their horizons beyond the immediate circle of home and family, they are increasingly exposed to eating habits and foods that put them at increased risk of caries. Media, especially television, likely play a role in this increasing risk. Studies of the content of television programming show that advertisements directed at children are heavily weighted toward foods that are high in sugar, such as sweetened breakfast cereals, soft drinks, snacks, and candy.[26-28]

Parents continue to have the most influence on their children's eating behaviors and attitudes toward food. To the extent possible, parents should make sure that nutritious foods are available to their children, and they should continue to emphasize the healthful eating patterns and limitations of snacks that were established in infancy and early childhood. (For more information on this topic, see the Promoting Healthy Nutrition theme.)

Other Oral Health Issues

Finger or other sucking habits sometimes continue into middle childhood. These habits should be stopped when the permanent teeth begin to erupt. As the child begins to grow, the mouth grows, and the child should be evaluated by a dentist if malocclusion is seen.

Some children begin using tobacco during middle childhood. Therefore, the child should be encouraged not to smoke or use smokeless tobacco because it increases the risk of periodontal disease and oral cancer and poses substantial risks to overall health.

As children mature and begin to play with increased strength and vigor, both in free play

As children begin school and expand their horizons beyond the immediate circle of home and family, they are increasingly exposed to eating habits and foods that put them at increased risk of caries.

and organized sports, the risk of injury to the mouth increases. The child and parent or caregiver should know what to do in the event of an emergency, especially if a tooth is visibly broken (chipped or fractured), displaced (luxated), or knocked completely out of the socket (avulsed). In these cases, the patient should be referred to a dentist immediately. An avulsed permanent tooth needs to be reimplanted as quickly as possible, but an avulsed primary tooth should not be reimplanted, because it likely would cause damage to developing permanent teeth.

Mouth guards worn during sports and other athletics greatly reduce the severity of accidental trauma to individual teeth by distributing the forces of impact to all of the teeth and jaws. Custom adaptations range from softening a generic plastic mouth guard in boiling water and biting into it to register a custom bite, to fabricating a guard on a custom mold. Both types work well to prevent oral trauma and differ only in cost and comfort. The protection afforded by any type of guard mandates use in both organized and leisure-time sports activity.

Mouth guards worn during sports and other athletics greatly reduce the severity of accidental trauma to individual teeth by distributing the forces of impact to all of the teeth and jaws.

Promoting Oral Health: Adolescence—11 to 21 Years

Adolescence is characterized by the loss of the remaining primary teeth and complete eruption of all the permanent teeth, including the third molars or wisdom teeth in late adolescence. Growth spurts of the facial bones occur early and then taper off as adolescence progresses. The end result is a fully established bite.

Several oral health issues from earlier developmental stages continue to be important in adolescence. For example, vigilant oral hygiene and positive dietary habits can strengthen a sound foundation for adult oral health by preventing destructive periodontal disease and dental decay. Avoiding traumatic injury to the mouth is another continuing priority. Other issues are new. For example, adolescence brings increased susceptibility to irreversible periodontal or gum disease that may be related to hormonal and immunologic changes. A comprehensive oral hygiene regimen of brushing and flossing, combined with regular professional care, can manage this response.

Oral Hygiene, Fluoride, and Nutrition Practices That Promote Oral Health

The adolescent should be responsible for her own preventive oral health care and should have an established dental home. She should see the dentist every 6 months or according to a schedule recommended by the dentist, based on individual needs and susceptibility to disease. The dental professional also may consider diet analysis, topical fluoride applications, antimicrobial regimens, and dental sealants for high-risk patients or those with significant dental disease.

Although preventive therapy has resulted in increased numbers of adolescents with healthy teeth, caries is still common in teens and growing evidence suggests that a small percentage of adolescents account for the most severe caries.[4,17,18]

Adolescents' risk of caries may be increased by the following:

- Susceptible tooth surfaces as a result of immature enamel in newly erupted permanent teeth.
- Indifference to oral hygiene, which allows plaque to accumulate and mature.
- Frequent and unregulated exposure to high quantities of natural and refined sugars, a feature of many adolescent diets, which provides the perfect medium for caries to develop.[29,30]
- Eating disorders, such as bulimia, which can result in a characteristic erosion of the dental enamel by repeated exposure of the teeth to gastric acids.

- Use of certain drugs, specifically methamphetamine, which has a detrimental effect on oral health. Methamphetamine abuse is associated with rampant decay that is attributed to some combination of the acidic nature of the drug, decreased saliva, tooth grinding and clenching, poor oral hygiene, and cravings for high-calorie beverages.[31]
- Frequent consumption of acidic drinks, which can directly erode the enamel.[32]

Health care professionals should educate adolescents to keep their teeth clean and remove plaque by following a comprehensive, daily home care regimen, including a minimum of twice-daily brushing with fluoride toothpaste and once-daily flossing. It is recommended that the adolescent spit out the toothpaste but not rinse with water. This regimen should be customized to each patient based on risk factors. Adolescents also should follow nutritious eating patterns that include only modest consumption of high-sugar foods (for more information on this topic, see the Promoting Healthy Nutrition theme) and should drink fluoridated water. If necessary, prescribed fluoride supplements until the age of 16 years are appropriate.[33]

Other Oral Health Issues

Adolescence is a period of experimentation and making choices. Added freedom and extension of boundaries are characteristic of appropriate supervision, but certain behaviors can lead to oral health problems. Substance use, including tobacco and drugs, can affect soft and hard tissues of the oral cavity and is linked to oral cancer.[34] Oral piercing can cause local and systemic infection, tooth fracture, and hemorrhage. Sexual behaviors can lead to infectious and traumatic consequences to the mouth. The health care professional should continue to counsel the adolescent about these nondietary behavioral factors that affect oral health.

Substance use, including tobacco and drugs, can affect soft and hard tissues of the oral cavity and is linked to oral cancer.

PERIODONTAL CONDITIONS

Evidence suggests that irreversible tissue damage from periodontal disease begins in late adolescence and early adulthood. Early diagnosis, prevention, and minor treatment can, in most cases, prevent irreversible damage to the periodontal structures in adulthood.[33,35] Preventing this damage obviates the need for dental restorations, which require lifelong care and monitoring.

TRAUMATIC INJURY TO THE MOUTH

Adolescents' risk of traumatic injury to the mouth may be increased by the following:

- High-risk behaviors that may involve trauma to the head and neck
- Driving crashes
- Injuries that occur as a result of participating in organized and leisure-time sports
- Unrecognized psychiatric and behavioral problems, such as bulimia or substance use
- Family or peer violence

Health care professionals should make sure that parents and adolescents know what to do and who to call if an injury occurs and a tooth is fractured or avulsed.

ORTHODONTIA

Genetically related abnormal development, premature primary tooth loss or extraction, or thumb sucking or finger sucking all can result in significant crowding and malalignment of the teeth, which can adversely affect oral health, function, and esthetics. Most orthodontic problems are not debilitating and can be resolved with appropriate treatment.[36] Preventing premature tooth loss early in life has a significant impact on minimizing space loss and the resultant crowding in adolescence.

References

1. National Institute of Dental and Craniofacial Research. *Oral Health in America: A Report of the Surgeon General*. Rockville, MD: US Department of Health and Human Services; 2000. NIH publication 00-4713
2. Pierce KM, Rozier RG, Vann WF, Jr. Accuracy of pediatric primary care providers' screening and referral for early childhood caries. *Pediatrics*. 2002;109:e82. Available at: www.pediatrics.org/cgi/content/full/109/5/e82. Accessed April 17, 2007
3. Gift HC, Reisine ST, Larach DC. The social impact of dental problems and visits. *Am J Public Health*. 1992;82:1163-1668
4. Vargas CM, Crall JJ, Schneider DA. Sociodemographic distribution of pediatric dental caries: NHANES III, 1988-1994. *J Am Dent Assoc*. 1998;129:1229-1238
5. American Academy of Pediatrics, Committee on Child Abuse and Neglect. Oral and dental aspects of child abuse and neglect. *Pediatrics*. 1999;104:348-350
6. Casamassimo PS, Holt KA, eds. *Bright Futures in Practice: Oral Health Pocket Guide*. Washington, DC: National Maternal and Child Oral Health Resource Center; 2004
7. National Maternal and Child Oral Health Resource Center Web site. http://www.mchoralhealth.org/. Accessed June 29, 2006
8. American Academy of Pediatric Dentistry. Definition of Dental Home. Chicago, IL: American Academy of Pediatric Dentistry; 2006 Available at: http://www.aapd.org/media/Policies_Guidelines/D_DentalHome.pdf. Accessed April 17, 2007
9. American Academy of Pediatric Dentistry. Policy on the Dental Home. Chicago, IL: American Academy of Pediatric Dentistry; 2004. Available at: http://www.aapd.org/media/Policies_Guidelines/P_DentalHome.pdf. Accessed April 17, 2007
10. Savage MF, Lee JY, Kotch JB, Vann WF, Jr. Early preventive dental visits: effects on subsequent utilization and costs. *Pediatrics*. 2004;114(4):e418-e423. Available at: www.pediatrics.org/cgi/content/full/114/4/e418. Accessed April 17, 2007
11. Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. *MMWR Recomm Rep*. 2001; 50(RR-14):1-42
12. American Academy of Pediatric Dentistry. Policy on the Use of Fluoride. Available at: http://www.aapd.org/media/Policies_Guidelines/P_FluorideUse.pdf. Accessed April 17, 2007
13. US Preventive Services Task Force Prevention of Dental Caries in Preschool Children. In: *Guide to Clinical Preventive Services, 2006: Recommendations of the US Preventive Services Task Force*. Rockville, MD: Agency for Healthcare Research and Quality; 2006. AHRQ publication 06-0588
14. American Dental Association, Council on Scientific Affairs. Professionally applied topical fluoride: evidence-based clinical recommendations. *J Am Dent Assoc*. 2006;137:1151-1159
15. Centers for Disease Control and Prevention. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis—United States, 1988-1994 and 1999-2002. *MMWR Surveill Summ*. 2005;54:1-43
16. American Academy of Pediatrics, Committee on Nutrition. Nutrition and oral health. In: Kleinman RE, ed. *Pediatric Nutrition Handbook*. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2004:789-800
17. Kaste LM, Selwitz RH, Oldakowski RJ, Brunelle JA, Winn DM, Brown LJ. Coronal caries in the primary and permanent dentition of children and adolescents 1-17 years of age: United States, 1988-1991. *J Dent Res*. 1996;75 (spec No):631-641
18. Allukian M Jr. The neglected epidemic and the surgeon general's report: a call to action for better oral health. *Am J Public Health*. 2000;90:843-845
19. American Academy of Pediatric Dentistry. Guideline on Management of Persons with Special Health Care Needs. Chicago, IL: American Academy of Pediatric Dentistry; 2004. Available at: http://www.aapd.org/media/Policies_Guidelines/G_SHCN.pdf. Accessed April 17, 2007
20. American Academy of Pediatric Dentistry. Clinical Guideline on Infant Oral Health Care. Chicago, IL: American Academy of Pediatric Dentistry; 2004
21. Hale KS, American Academy of Pediatrics. Section on Pediatric Dentistry. Oral health risk assessment timing and establishment of the dental home. *Pediatrics*. 2003;111(5):1113-1116
22. Rozier RG. Primary care physicians enlisted to provide preventative dental services. *AAP News*. 2006;27:18
23. Rozier RG, Slade GD, Zeldin LP, Wang H. Parents' satisfaction with preventive dental care for young children provided by nondental primary care providers. *Pediatr Dent*. 2005;27:313-322
24. American Academy of Pediatric Dentistry. *Guideline on Periodicity of Examination, Preventive Dental Services, Anticipatory Guidance Counseling, and Oral Treatment for Infants, Children and Adolescents*. Chicago, IL: American Academy of Pediatric Dentistry; 2007
25. American Academy of Pediatric Dentistry. Policy on Use of a Caries-risk Assessment Tool (CAT) for Infants, Children, and Adolescents. Chicago, IL: American Academy of Pediatric Dentistry; 2006. Available at: http://www.aapd.org/media/Policies_Guidelines/P_CariesRiskAssess.pdf. Accessed April 17, 2007
26. Byrd-Bredbenner C. Saturday morning children's television advertising: a longitudinal content analysis. *Fam Consum Sci Res J*. 2002;30:382-403
27. Harrison K, Marske AL. Nutritional content of foods advertised during the television programs children watch most. *Am J Public Health*. 2005;95:1568-1574
28. Kotz K, Story M. Food advertisements during children's Saturday morning television programming: are they consistent with dietary recommendations? *J Am Diet Assoc*. 1994;94:1296-1300
29. Majewski RF. Dental caries in adolescents associated with caffeinated carbonated beverages. *Pediatr Dent*. 2001;23:198-203
30. Freeman R, Sheiham A. Understanding decision-making processes for sugar consumption in adolescence. *Community Dent Oral Epidemiol*. 1997;25:228-232

31. American Dental Association. For the dental patient ... methamphetamine use and oral health. *J Am Dent Assoc*. 2005;136:1491
32. American Academy of Pediatric Dentistry. Policy on Dietary Recommendations for Infants, Children, and Adolescents. Chicago, IL: American Academy of Pediatric Dentistry; 2006. Available at: http://www.aapd.org/media/Policies_Guidelines/P_DietaryRec.pdf. Accessed April 17, 2007
33. American Academy of Pediatric Dentistry. *Guideline on Adolescent Oral Health Care*. Chicago, IL: American Academy of Pediatric Dentistry; 2005
34. American Cancer Society. *Detailed Guide: Oral Cavity and Oropharyngeal Cancer*. Atlanta, GA: American Cancer Society; 2004
35. American Academy of Periodontology, Research, Science and Therapy Committee. Periodontal diseases of children and adolescents. *J Periodontal.* 2003;74:1696-1704
36. Proffit WR, Fields HW, Moray LJ. Prevalence of malocclusion and orthodontic treatment need in the United States: estimates from the NHANES III survey. *Int J Adult Orthodon Orthognath Surg*. 1998;13:97-106

Oral Health Risk Assessment Tool

The American Academy of Pediatrics (AAP) has developed this tool to aid in the implementation of oral health risk assessment during health supervision visits. This tool has been subsequently reviewed and endorsed by the National Interprofessional Initiative on Oral Health.

Instructions for Use

This tool is intended for documenting caries risk of the child, however, two risk factors are based on the mother or primary caregiver's oral health. All other factors and findings should be documented based on the child.

The child is at an absolute high risk for caries if any risk factors or clinical findings, marked with a ⚠ sign, are documented yes. In the absence of ⚠ risk factors or clinical findings, the clinician may determine the child is at high risk of caries based on one or more positive responses to other risk factors or clinical findings. Answering yes to protective factors should be taken into account with risk factors/clinical findings in determining low versus high risk.

Patient Name:_____ Date of Birth:_____ Date:_____

Visit: ☐ 6 month ☐ 9 month ☐ 12 month ☐ 15 month ☐ 18 month ☐ 24 month ☐ 30 month ☐ 3 years ☐ 4 years ☐ 5 years ☐ 6 years ☐ Other_____

RISK FACTORS

⚠ Mother or primary caregiver had active decay in the past 12 months
☐ Yes ☐ No

- Mother or primary caregiver does not have a dentist
  ☐ Yes ☐ No
- Continual bottle/sippy cup use with fluid other than water
  ☐ Yes ☐ No
- Frequent snacking
  ☐ Yes ☐ No
- Special health care needs
  ☐ Yes ☐ No
- Medicaid eligible
  ☐ Yes ☐ No

PROTECTIVE FACTORS

- Existing dental home
  ☐ Yes ☐ No
- Drinks fluoridated water or takes fluoride supplements
  ☐ Yes ☐ No
- Fluoride varnish in the last 6 months
  ☐ Yes ☐ No
- Has teeth brushed twice daily
  ☐ Yes ☐ No

CLINICAL FINDINGS

⚠ White spots or visible decalcifications in the past 12 months
☐ Yes ☐ No

⚠ Obvious decay
☐ Yes ☐ No

⚠ Restorations (fillings) present
☐ Yes ☐ No

- Visible plaque accumulation
  ☐ Yes ☐ No
- Gingivitis (swollen/bleeding gums)
  ☐ Yes ☐ No
- Teeth present
  ☐ Yes ☐ No
- Healthy teeth
  ☐ Yes ☐ No

ASSESSMENT/PLAN

Caries Risk:
☐ Low ☐ High

Completed:
☐ Anticipatory Guidance
☐ Fluoride Varnish
☐ Dental Referral

Self Management Goals:

☐ Regular dental visits	☐ Wean off bottle	☐ Healthy snacks
☐ Dental treatment for parents	☐ Less/No juice	☐ Less/No junk food or candy
☐ Brush twice daily	☐ Only water in sippy cup	☐ No soda
☐ Use fluoride toothpaste	☐ Drink tap water	☐ Xylitol

Treatment of High Risk Children

If appropriate, high-risk children should receive professionally applied fluoride varnish and have their teeth brushed twice daily with an age-appropriate amount of fluoridated toothpaste. Referral to a pediatric dentist or a dentist comfortable caring for children should be made with follow-up to ensure that the child is being cared for in the dental home.

Adapted from Ramos-Gomez FJ, Crystal YO, Ng MW, Crall JJ, Featherstone JD. Pediatric dental care: prevention and management protocols based on caries risk assessment. *J Calif Dent Assoc.* 2010;38(10):746–761; American Academy of Pediatrics Section on Pediatric Dentistry and Oral Health. Preventive oral health intervention for pediatricians. *Pediatrics.* 2003; 122(6):1387–1394; and American Academy of Pediatrics Section of Pediatric Dentistry. Oral health risk assessment timing and establishment of the dental home. *Pediatrics.* 2003;111(5):1113–1116.

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Bright Futures™
prevention and health promotion for infants, children, adolescents, and their families™

National Interprofessional Initiative on Oral Health
engaging clinicians eradicating dental disease

Oral Health Risk Assessment Tool Guidance

Timing of Risk Assessment

The Bright Futures/AAP "Recommendations for Preventive Pediatric Health Care," (ie, Periodicity Schedule) recommends all children receive a risk assessment at the 6- and 9-month visits. For the 12-, 18-, 24-, 30-month, and the 3- and 6-year visits, risk assessment should continue if a dental home has not been established. View the Bright Futures/AAP Periodicity Schedule—http://brightfutures.aap.org/clinical_practice.html.

Risk Factors

⚠ Maternal Oral Health

Studies have shown that children with mothers or primary caregivers who have had active decay in the past 12 months are at greater risk to develop caries. **This child is high risk.**

Maternal Access to Dental Care

Studies have shown that children with mothers or primary caregivers who do not have a regular source of dental care are at a greater risk to develop caries. A follow-up question may be if the child has a dentist.

Continual Bottle/Sippy Cup Use

Children who drink juice, soda, and other liquids that are not water, from a bottle or sippy cup continually throughout the day or at night are at an increased risk of caries. The frequent intake of sugar does not allow for the acid it produces to be neutralized or washed away by saliva. Parents of children with this risk factor need to be counseled on how to reduce the frequency of sugar-containing beverages in the child's diet.

Frequent Snacking

Children who snack frequently are at an increased risk of caries. The frequent intake of sugar/refined carbohydrates does not allow for the acid it produces to be neutralized or washed away by saliva. Parents of children with this risk factor need to be counseled on how to reduce frequent snacking and choose healthy snacks such as cheese, vegetables, and fruit.

Special Health Care Needs

Children with special health care needs are at an increased risk for caries due to their diet, xerostomia (dryness of the mouth, sometimes due to asthma or allergy medication use), difficulty performing oral hygiene, seizures, gastroesophageal reflux disease and vomiting, attention deficit hyperactivity disorder, and gingival hyperplasia or overcrowding of teeth. Premature babies also may experience enamel hypoplasia.

Protective Factors

Dental Home

According to the American Academy of Pediatric Dentistry (AAPD), the dental home is oral health care for the child that is delivered in a comprehensive, continuously accessible, coordinated and family-centered way by a licensed dentist. The AAP and the AAPD recommend that a dental home be established by age 1. Communication between the dental and medical homes should be ongoing to appropriately coordinate care for the child. If a dental home is not available, the primary care clinician should continue to do oral health risk assessment at every well-child visit.

Fluoridated Water/Supplements

Drinking fluoridated water provides a child with systemic and topical fluoride exposure, a proven caries reduction intervention. Fluoride supplements may be prescribed by the primary care clinician or dentist if needed. View fluoride resources on the Oral Health Practice Tools Web Page http://aap.org/oralhealth/PracticeTools.html.

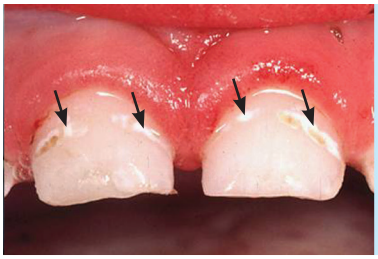
Fluoride Varnish in the Last 6 Months

Applying fluoride varnish provides a child with highly concentrated fluoride to protect against caries. Fluoride varnish may be professionally applied. For online fluoride varnish training, access the Child Oral Health and Fluoride Varnish Modules in the Smiles for Life National Oral Health Curriculum, www.smilesforlifeoralhealth.org.

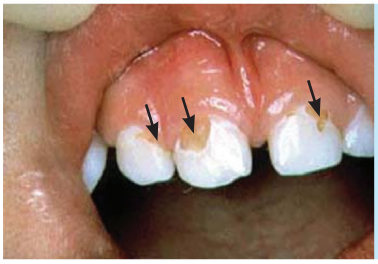
Tooth Brushing and Oral Hygiene

Primary care clinicians can reinforce good oral hygiene by teaching parents and children simple practices. Infants should have their mouths cleaned after feedings with a wet soft washcloth. Once teeth erupt it is recommended that children have their teeth brushed twice a day. For children under the age of 2 determined to be at moderate or high risk for caries, it is appropriate to recommend a smear of fluoridated toothpast twice per day. Children older than 2 years old should use a pea-sized amount of fluoridated toothpaste twice a day. View fluoride resources in the AAP Protecting All Children's Teeth Curriculum Fluoride Module http://www.aap.org/oralhealth//pact/ppt/Fluoride.ppt.

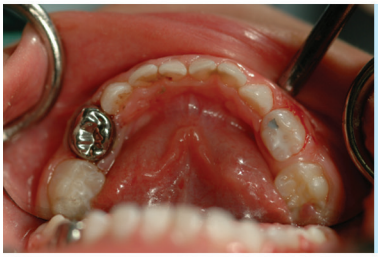
Clinical Findings



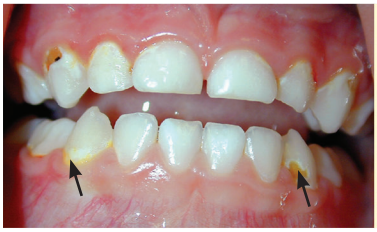
⚠ **White Spots/Decalcifications**
This child is high risk.
White spot decalcifications present—immediately place the child in the high-risk category.



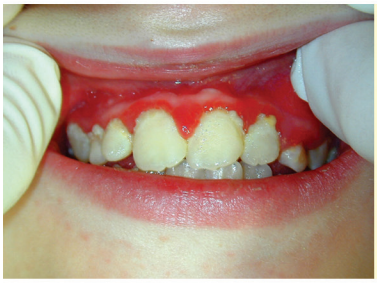
⚠ **Obvious Decay**
This child is high risk.
Obvious decay present—immediately place the child in the high-risk category.



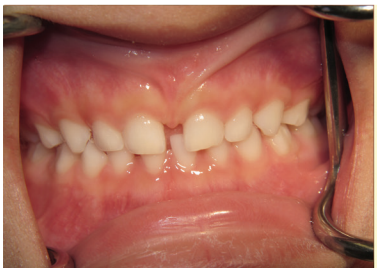
⚠ **Restorations (Fillings) Present**
This child is high risk.
Restorations (Fillings) present—immediately place the child in the high-risk category.



Visible Plaque Accumulation
Plaque is the soft and sticky substance that accumulates on the teeth from food debris and bacteria. Primary care clinicians can teach parents how to remove plaque from the child's teeth by brushing and flossing.



Gingivitis
Gingivitis is the inflamation of the gums. Primary care clinicians can teach parents good oral hygiene skills to reduce the inflammation.



Healthy Teeth
Children with healthy teeth have no signs of early childhood caries and no other clinical findings. They are also experiencing normal tooth and mouth development and spacing.

For more information about the AAP's oral health activities email oralhealth@aap.org or visit www.aap.org/oralhealth.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Bright Futures™
prevention and health promotion for infants, children, adolescents, and their families™

National Interprofessional Initiative on Oral Health
engaging clinicians eradicating dental disease

Rehabilitation Guideline

Question: Should the rehabilitation guideline note be revised to remove differing visit allotments based on age?

Question source: HERC staff

Issue: The current rehabilitation guideline has different numbers of visits allowed based on age. The ACA prohibits differential treatment based on age without medical justification.

The current rehabilitative therapies guideline was created in 2004/2005 with input from the PT community, the CDRC, a physiatrist, and the available literature. It was acknowledged that the literature was sparse on the effectiveness of PT/OT, the optimal number of visits for certain conditions, etc. Various limits on PT/OT services were discussed, including limits based on diagnoses, limiting certain modalities, and limiting number of visits based on age. There was great concern about limiting young children's visits, based on developmental issues. There was also great concern about limiting visits for persons with disabilities. The current visit limits were created from this discussion. See Appendix A for excerpts from HOSC/HSC meeting minutes regarding the rehabilitation guideline.

Evidence review

No general guidance on PT/OT/speech therapy was found with NICE, SIGN or Cochrane

The literature reviews PT/OT by condition that it is treating, and number/intensity of visits is rarely addressed.

Current guideline:

GUIDELINE NOTE 6, REHABILITATIVE THERAPIES

Lines 37,50-52,64,74-76,78,80,85,89,90,94,95,98-101,108,109,115,116,122,129,139,141-143,145,146,158,161,167,179,184,185,189,190,192,194,195,201,202,208,209,216,226,237,239,270,271,273,274,279,288,289,293,297,302,304,307-309,318,336,342,349,350,363,367,369,375,376,378,382,384,385,387,400,406, 407,434,441,443,448,455,467,478,489,493,507,516,535,549,562,580,597,619,638

Physical, occupational and speech therapy, and cardiac and vascular rehabilitation, are covered for diagnoses paired with the respective CPT codes, depending on medical appropriateness, for up to 3 months immediately following stabilization from an acute event.

Following the 3 month stabilization after an acute event, or, in the absence of an acute event, the following number of combined physical and occupational therapy visits are allowed per year, depending on medical appropriateness:

- Age < 8: 24
- Age 8-12: 12
- Age > 12: 2

And the following number of speech therapy visits are allowed per year, depending on medical appropriateness (with the exception of swallowing disorders, for which limits do not apply):

- Age < 8: 24
- Age 8-12: 12
- Age > 12: 2

Whenever there is a change in status, regardless of age, such as surgery, botox injection, rapid growth, an acute exacerbation or for
evaluation/training for an assistive communication device, the following additional visits are allowed:

- 6 visits of speech therapy and/or
- 6 visits of physical or occupational therapy

No limits apply while in a skilled nursing facility for the primary purpose of rehabilitation, an inpatient hospital or an inpatient
rehabilitation unit.

Other PT/OT guidelines/coverage

CMS

Annual limitations on per beneficiary incurred expenses for outpatient therapy services under Medicare Part B are commonly referred to as "therapy caps." All beneficiaries began a new cap year on January 1, 2014 since the therapy caps are determined on a calendar year basis. For physical therapy (PT) and speech-language pathology services (SLP) combined, the limit on incurred expenses is $1,920 in 2014. For occupational therapy (OT) services, the limit is $1,920 in 2014. Deductible and coinsurance amounts paid by the beneficiary for therapy services count toward the amount applied to the limit.

DMAP

Does not cover "maintenance" PT/OT

410-131-0100 Maintenance

(1) Determination of when maintenance therapy is reached is made through comparison of written documentation of evaluation of the last several functional evaluations related to initial baseline measurements.

(2) Therapy becomes maintenance when any one of the following occur:

(a) The therapy plan of care goals and objectives are reached; or

(b) There is no progress toward the therapy plan of care goals and objectives; or

(c) The therapy plan of care does not require the skills of a therapist; or

(d) The client, family, foster parents, and/or caregiver have been taught and can carry out the therapy regimen and are responsible for the maintenance therapy.

(3) Maintenance therapy is not a reimbursable service.

(4) Re-evaluation to change the therapy plan of care and up to two treatments for brief retraining of the client, family, foster parents or caregiver are not considered maintenance therapy and are reimbursable.

(5) Providers must maintain adequate documentation as outlined in OAR 410-120-1360, Requirements for Financial, Clinical and Other Records.

Oregon Essential Health Benefits (PacificSource Codeduct plan):

30 visits per year for OP therapy services provided by a licensed physical therapist, occupational therapist, speech language pathologist, physician, or other practitioner licensed to provide physical, occupational, or speech therapy. Only treatment of neurologic conditions (e.g. stroke, spinal cord injury, head injury, pediatric neurodevelopmental problems, and other problems associated with pervasive developmental disorders for which rehabilitative services would be appropriate for children under 18 years of age) may be considered for additional benefits, not to exceed 30 visits per condition, when criteria for supplemental services are met. Services for speech therapy will only be allowed when needed to correct stuttering, hearing loss, peripheral speech mechanism problems, and deficits due to neurological disease or injury.

PEBB Providence Statewide 2014

(from member handbook)

5.10.11 Outpatient Rehabilitation Services

Benefits are included for short-term outpatient physical, occupational and speech therapy Covered Services provided by a physician or licensed/registered therapist to restore or improve lost function following illness or injury. Rehabilitative services also include

neurodevelopmental therapy for children up to age 18 when such services are for maintenance of a child whose condition would otherwise significantly deteriorate without the services. Benefits are limited to Covered Services that can be expected to result in measurable improvement of a Member's condition. Benefits are subject to the visit limit and coverage listed in your Benefit Summary.
Covered Services under this benefit do not include: Adjustments and manipulations of any spinal or bodily area (spinal manipulation is covered under section 5.10.14);
❑ Exercise programs;
❑ Rolfing, polarity therapy and similar therapies;
❑ Growth and cognitive therapies, including sensory integration; and
❑ Rehabilitation Services provided under an authorized home health care plan as specified in section 5.10.6.

OEBB (Moda):

30 days per plan year, 60 for spinal/head injury

Coverage for neurodevelopmental therapy is limited to services for insureds through age 17. Coverage is limited to 30 inpatient days each for rehabilitation and habilitation services / year. Coverage is limited to 30 outpatient visits each for rehabilitation and habilitation services / year.

PEBB Kaiser Oregon PEBB Full time

Limited to 20 outpatient visits per year. Therapy Services (physical, occupational and speech) are covered to the treatment of acute conditions or acute exacerbations of chronic conditions which, in the judgment of the Participating Physician, will show sustainable, objective, measurable improvement as a result of the prescribed therapy.

Physical, Occupational and Speech Therapy Limitations

- Physical therapy Services and occupational therapy Services are limited to those necessary to restore or improve functional abilities when physical and/or sensory perceptual impairment exists due to injury, illness, stroke or surgery
- Speech therapy Services are covered for speech impairments of specific organic origin such as cleft palate or when speech, language, or the swallowing function is lost due to injury, illness, stroke or surgery
- This limitation does not apply to hospital inpatient Services.

HERC staff recommendation:

1) Discuss options to revise the current rehabilitation guideline
    a. Option 1: Delete guideline. Not supported by the plans/DMAP
    b. Option 2: place limitation on visit numbers
        i. 30 visits per year appears to be standard for most PEBB/OEBB plans
    c. Option 3: place limitations on the type of coverage/require documented improvement
    d. Option 4: some combination of the above

GUIDELINE NOTE 6, REHABILITATIVE THERAPIES

Lines 37,50-52,64,74-76,78,80,85,89,90,94,95,98-101, 108, 109, 115, 116, 122, 129, 139, 141-143,145,146,158,161,167,179,184,185,189, 190, 192, 194, 195, 201, 202, 208, 209,216,226,237,239,270,271,273,274,279,288,289,293,297,302,304,307-309, 318, 336,342,349, 350, 363, 367, 369, 375,376,378, 382,384,385,387, 400,406, 407, 434, 441,443,448,455,467,478,489,493,507,516,535,549,562, 580, 597,619,638

Physical, occupational and speech therapy, and cardiac and vascular rehabilitation, are covered for diagnoses paired with the respective CPT codes, depending on medical appropriateness, for up to 3 months immediately following stabilization from an acute event.

Following the 3 month stabilization after an acute event, or, in the absence of an acute event, therapy is covered when the following criteria are met:

1) therapy is provided by a licensed physical therapist, occupational therapist, speech language pathologist, physician, or other practitioner licensed to provide physical, occupational, or speech therapy
2) there is objective, measurable documentation of progress toward the therapy plan of care goals and objectives
3) the therapy plan of care requires the skills of a therapist, and
4) the client and/or caregiver cannot be taught to carry out the therapy regimen independently.

~~t~~The number of combined ~~physical and occupational~~ therapy visits ~~are~~ allowed per year, depending on medical appropriateness, is not to exceed 30 visits. The initial 3 month period of coverage after an acute event is not included in this 30 visit maximum. An additional 30 visits may be authorized only for treatment of neurologic conditions (e.g. stroke, spinal cord injury, head injury, pediatric neurodevelopmental problems, and other problems associated with pervasive developmental disorders for which rehabilitative services would be appropriate for children under 18 years of age), when medically appropriate.

~~• Age < 8: 24~~
~~• Age 8-12: 12~~
~~• Age > 12: 2~~

~~And the following number of speech therapy visits are allowed per year, depending on medical appropriateness (with the exception of swallowing disorders, for which limits do not apply):~~

~~• Age < 8: 24~~
~~• Age 8-12: 12~~
~~• Age > 12: 2~~

~~Whenever there is a change in status, regardless of age, such as surgery, botox injection, rapid growth, an acute exacerbation or forevaluation/training for an assistive communication device, the following additional visits are allowed:~~

~~• 6 visits of speech therapy and/or~~
~~• 6 visits of physical or occupational therapy~~

No limits apply while in a skilled nursing facility for the primary purpose of rehabilitation, an inpatient hospital or an inpatient rehabilitation unit.

Appendix A
HOSC/HSC Minutes Concerning Creation of the Rehabilitation Guideline

HOSC minutes March 2004
Dr. Little directed the members to two summaries of the literature included in their packets, titled "Summary of Therapy Evidence" and "Summary of Physical Therapy Literature Provided by PT Association." She presented a number of possible options for limiting therapy, including limiting it based on type of care (e.g., post-operative), limiting the number of visits allowed, or elimination of certain types of therapy, such as ultrasound. It was recommended to continue therapy post-operatively and for stroke. Dr. Kitchen encouraged the members to continue to cover maintenance visits for the disabled, which are done every 6 to 12 months. These represent essentially management of a home PT program. It was recommended to limit therapy on the dysfunction lines to 2 visits per year. Dr. Kitchen expressed concern about limiting therapy for children. Dr. Little noted that the lack of limits on therapy for disabled children is one of the biggest complaints of the medical directors. Dr. Kitchen suggested querying the disability subcommittee of the Oregon Pediatric Society (or CDRC), who at one point had developed some guidelines for therapy. Ultimately *it was agreed to suggest limitation of therapy on the dysfunction lines for chronic conditions to 24 visits up to age 3, 12 visits per year up to age 12, 2 visits a year there after, and 3 months with unlimited visits post acute event. Dr. Little will propose these to the medical directors at their next meeting and solicit feedback, as well as contact CDRC about therapy guidelines. It was also recommended to combine PT and OT, but keep speech therapy separate when applying visit limits.* Specific modalities were discussed, and given the poor evidence surrounding some of these, Dr. Saha recommended eliminating ultrasound, UV light, microwave, vasopneumatic device, paraffin baths, diathermy and infrared. Dr. Mangum also felt that electrical stimulation should be limited. *Dr. Walsh was concerned about making sweeping changes that eliminate therapy modalities without input from the disability community and recommended that no action be taken at this time.*

HSC minutes May 2004
Physical Therapy Guidelines
Dr. Little informed the Commission that draft guidelines for limiting the number of physical therapy visits had been reviewed at the last meeting of the Health Outcomes Subcommittee. These were circulated to the OMAP Medical Directors, and she incorporated one change that they had recommended (see Attachment B). The goals for the current meeting are to determine if the visit limits are appropriate for the dysfunction lines, if the acute diagnoses listed are appropriate for unlimited acute therapy for up to 3 months, and to decide if limits should be placed on speech therapy. Dr. Kitchen stated that she feels there are two categories of patients, those with general developmental delay, and those with specific speech impediments, with the latter being more susceptible to therapy. Chris Barber clarified that currently there are no limits on speech therapy for fee-for-service patients, as long as they are showing progress. Dr. Kitchen recommended a combined limit for physical, occupational and speech therapy, especially in very young children. Ms. Lowe questioned the age breakdown, suggesting that 4 – 12 years of age was overly broad, and that children at the lower end of that age range may have more needs than those at the upper end. Dr. Kitchen expressed concern that the discussion was moving too quickly and without adequate input from

specialists. Dr. Walsh reminded her that this discussion began in September, and that the physical therapy community had testified in January. It was also clarified that this decision needed to be made now in order to be incorporated into the biennial review. Dr. Kitchen didn't feel that the physical therapists response had been very helpful. Ms. Lowe asked if staff had consulted CDRC. It was noted that an attempt had been made to get the guidelines from CDRC, but it was not thus far successful. Ms. McGough recommended starting with a conservative limit number that could be adjusted in the future, as it was likely an emotional issue. Dr. Kitchen recommended a combined total of 45 visits per year for 0-3 and 52 visits for speech therapy from 4-8. Dr. Glass felt most of the therapy should be aimed at the pre-school age. Dr. Kitchen was concerned that children with speech impediments will not get appropriate therapy. Dr. Sohl stated that he did not feel that any of the commissioners had adequate information to make a decision. Ms. McGough expressed concern that even with input from specialists, the Commission will still not have any data on outcomes or effectiveness. Other commissioners felt that it would be preferable to at least have professional opinion and an estimate of the standard of care. Dr. Walsh stated that the problem with professional judgment is that it tends to be self-serving. Dr. Saha stated that there was a danger in becoming too data-driven. Dr. Kitchen stated that there is some data showing effectiveness, but that it was soft, and that effectiveness tended to decrease over time. *It was ultimately agreed to defer the decision until input is received from CDRC. A conference call meeting will be arranged within the next two weeks.*

Dr. Walsh recommended at least making a determination about the therapies for acute conditions. Dr. Sohl felt that the guideline was too broad, and would allow wide variability in the number of visits allowed. Dr. Little clarified that the intent is to start generously, due to lack of time and expertise. Therapies would be limited based on diagnosis initially, and refinements can be made later. Dr. Glass asked if a visit limit could be administered by OMAP. Dr. Turek replied that they could, and that a dollar limit would be more difficult. There was discussion about whether or not 3 months was sufficient for acute conditions.

MOTION: Adopt the portion of the guidelines in Attachment B that list the acute conditions for which physical therapy will be an indicated treatment. Change the introductory sentence that begins with "Diagnoses on the following lines….." and ends with "Other Complications Of A Procedure", with the revision to insert the word "physical" in the first sentence between "of" and "therapy".
MOTION CARRIES: 5-1, Ayes: Walsh, Glass, Saha, McGough, Williams. Nays: Sohl. Abstentions: Dodson, Lowe.

Next discussed was the latter portion of the guideline pertaining to modalities. Dr. Little reminded the Commission that the literature had been reviewed, and no effectiveness identified. Ms. Dodson asked about the use of massage. Dr. Turek noted that paraffin baths are standard therapy for patients with burns.

MOTION: Delete all physical therapy modalities listed in the last section of Attachment B from the Prioritized List.
MOTION CARRIES: 8-0.

*Attachment **B***
PHYSICAL THERAPY GUIDELINES
The following number of combined physical and occupational therapy visits are allowed

per year for any combination of diagnoses on Lines 219, 336, 455 and 456:
Ages 0-3: 24
Ages 4-12: 12
Age > 12: 2

Diagnoses on the following lines are allowed visits not subject to the above limits but depending on medical necessity, for up to 3 months after the initiation of therapy:

SEVERE/MODERATE HEAD INJURY: HEMATOMA/EDEMA WITH LOSS OF CONSCIOUSNESS
ACUTE BACTERIAL MENINGITIS
SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; COMPRESSION OF BRAIN
ACUTE OSTEOMYELITIS
PYOGENIC ARTHRITIS
BURN, PARTIAL THICKNESS GREATER THAN 30% OF BODY SURFACE
BURN, PARTIAL THICKNESS WITH VITAL SITE; FULL THICKNESS WITH VITAL SITE, LESS THAN
10% OF BODY SURFACE
DEFORMITIES OF HEAD AND COMPOUND/DEPRESSED FRACTURES OF SKULL
CONGENITAL DISLOCATION OF HIP; COXA VARA & VALGA
CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL
DISLOCATIONS/FRACTURES, OPEN; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF
VERTEBRAL INJURY
FRACTURE OF PELVIS, OPEN AND CLOSED
FRACTURE OF JOINT, OPEN
FRACTURE OF SHAFT OF BONE, OPEN
OPEN FRACTURE OF EPIPHYSIS OF LOWER EXTREMITIES
DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT
CRUSH INJURIES: TRUNK, UPPER LIMBS, LOWER LIMB INCLUDING BLOOD VESSELS
BURN FULL THICKNESS GREATER THAN 10% OF BODY SURFACE
FRACTURE OF HIP, CLOSED
BURN, PARTIAL THICKNESS WITHOUT VITAL SITE, 10-30% OF BODY SURFACE
TRAUMATIC AMPUTATION OF LEG(S) (COMPLETE)(PARTIAL) W/ & W/O COMPLICATION
TRAUMATIC AMPUTATION OF ARM(S), HAND(S) THUMB(S) AND FINGER(S) (COMPLETE)(PARTIAL) WITH AND WITHOUT COMPLICATION
ACUTE POLIOMYELITIS
INTRACEREBRAL HEMORRHAGE
STROKE
DISLOCATION KNEE & HIP, OPEN
DISLOCATION OF ELBOW, HAND, ANKLE, FOOT, CLAVICLE AND SHOULDER, OPEN
TRAUMATIC AMPUTATION OF FOOT/FEET (COMPLETE)(PARTIAL) W/ & W/O COMPLICATION
RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC
NECROSIS OF BONE
RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES
RHEUMATIC FEVER
GUILLAIN-BARRE SYNDROME

LYME DISEASE AND OTHER ARTHROPOD BORNE DISEASES
FRACTURE OF SHAFT OF BONE, CLOSED
CLOSED FRACTURE OF PHYSIS OF LOWER EXTREMITIES
CLOSED FRACTURE OF PHYSIS OF UPPER EXTREMITIES
DISLOCATION / DEFORMITY KNEE & HIP
DISLOCATION/DEFORMITY OF ELBOW, HAND, ANKLE, FOOT, JAW, CLAVICLE AND SHOULDER
CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT
SPINAL CORD INJURY
DISRUPTIONS OF THE LIGAMENTS AND TENDONS OF THE ARMS AND LEGS, EXCLUDING THE
KNEE, GRADE II AND III
PERIPHERAL NERVE INJURY WITH OPEN WOUND
GOUT AND CRYSTAL ARTHROPATHIES
FRACTURE OF JOINT, CLOSED (EXCEPT HIP)
DISORDERS OF SHOULDER
MALUNION & NONUNION OF FRACTURE
OSTEOARTHRITIS AND ALLIED DISORDERS
INTERNAL DERANGEMENT OF KNEE AND LIGAMENTOUS DISRUPTIONS OF THE KNEE, GRADE
II AND III
CHONDROMALACIA
INTERNAL DERANGEMENT OF JOINT OTHER THAN KNEE
PERIPHERAL ENTHESOPATHIES
ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT
SPRAINS OF JOINTS AND ADJACENT MUSCLES, GRADE I
SYNOVITIS AND TENOSYNOVITIS
COMPLICATIONS OF A PROCEDURE ALWAYS REQUIRING TREATMENT
COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT
OTHER COMPLICATIONS OF A PROCEDURE

The Commission is also considering eliminating coverage for some modalities. Possible deletions include the following:
Vasopneumatic devices
Paraffin baths
Microwave
Diathermy
Infrared
Ultraviolet
Iontophoresis
Contrast baths
Ultrasound
Massage

HSC minutes June 2004
III. Physical Therapy Guidelines
Dr. Little informed the HSC she had sent out three documents on the topic of physical

therapy: 1) a revision to the previously reviewed guidelines (See Attachment A, Draft Physical Therapy Guidelines for Patients with Chronic Disease), 2) guidelines from William Curran at the Child Development & Rehabilitation Center (CDRC), and 3) an article from the American Academy of Pediatrics about prescribing physical therapy for disabled children (which she indicated includes a good review of the literature on the second page). Dr. Little had also contacted a pediatric physiatrist from Central Oregon to receive her input on the general guidelines. The revisions came from her suggestions. The physiatrist was hesitant about putting any limits on the guidelines. However, if she had to, she felt that therapy is most needed up until children get established in elementary school. That is why the visit limit was pushed from age 0-3 with 24 visits/yr to age 0-7 with 24 visits/yr. Likewise with speech therapy, she felt that therapy would be needed from the time that the child was learning to talk (basically age three) until the time the child is well into elementary school (age 3-7 with 24 visits/yr).

Dr. Walsh commented that the CDRC article had so much variation and so many exceptions, he wondered if the guideline for the Prioritized List could be as simple as the draft indicates. He thought the draft would be fine if the appeals process could handle problems that are not anticipated.

Dr. Glass said that he felt that the paper from the American Academy of Pediatrics puts the therapy programs in a more sober context, where they questioned how beneficial therapy programs are due to poor evidence and lack of research. Dr. Glass further mentioned that he receives many requests for sensory integration and is unsure of what it is.

Dr. Tina Kitchin spoke about her concerns with the draft guidelines, especially how speech therapy would not be covered after the age of 12. She feels that it does not address chronic conditions. Feeding/swallowing studies for dysphasia and assessment/training for assistive communicative devices are examples of necessary services that wouldn't be covered. Individuals with cerebral palsy and muscular dystrophy would be examples where ongoing evaluation and training would be required as the disease progressed. She requested that the HSC exempt these two aspects of speech therapy from the guideline. Mr. Coffman indicated that there are separate codes for evaluation and treatment of swallowing function and assistive communicative devices, so guideline limits could be handled differently for those codes.

Dr. Daniel Mangum asked Dr. Kitchen whether a limit on the number of these types of visits (e.g., 2 visits per year) would be appropriate since this would be consistent with the visit limitations for other services in this guideline. Dr. Kitchen said that two per year for people that are stable is sufficient; however, those whose condition is unstable will likely need intense services for a short period of time, almost like an acute event, then go into a stable phase where 2 visits per year would be adequate.

Ms. Savicki stated she was reluctant to apply visit limits because of the individualized nature of these complex conditions. She would much rather have the visits be preauthorized by the health plan, OMAP or by physician discretion.

Dr. Tom Turek added that it is the concern of the plans that therapies are being asked for without any evidence that there has been progress. Dr. Glass agreed and added that if one reads the physical therapy notes, patients are always described as making progress; however, and after looking back at the chart from the year before it doesn't

seem like the patient had made progress at all. He thought that this was truer with the disabled population because the acute population does not keep asking for more therapy. Dr. Dan Mangum said he thought there were tendencies in chronic cases where the doctor, family/patient, and even the therapist develop a relationship and there is a push for the maximum number of visits with very little documentation showing longterm benefits. Dr. Walsh thinks the HSC needs to accept the lack of evidence as a given in this case and try to figure out what is meant by progress, whether that would include a lack of decline or a slower grade of decline. At the same time, if there are limits with an appeals process. Dr. Kitchin explained that the appeals process is for seeing if the rules or guidelines are fairly applied and the exception process is for seeing which way is less costly or if there is a comorbid condition involved.

Dr. Kitchin suggested a guideline for those over 12 years old whereby they should not be covered unless there is a need due to an acute event, assistive communicated devices, or a swallowing disorder, with a maximum of six therapy visits a year in those cases. Dr. Kitchen wanted to go on record that she was not an activist for limits, but she understood that limits were better than not having benefits available.

Dr. Walsh clarified that that these guidelines only apply to chronic conditions residing on the dysfunction lines. He confirmed that the language “after an acute event” in these cases refers to an exacerbation of the patient’s chronic condition. Dr. Little said that the modifications being discussed would also apply if the patient had surgery or a contracture release. Dr. Saha felt that physical and occupation therapies should be thought in the same context. Dr. Walsh and Ms. Dodson agreed. Therefore the motion is stated as “up to six visits per year for speech, physical and occupational therapies.”

MOTION: Regarding physical and occupational therapy, for age > 12, allow up to six visits per year for an acute exacerbation of an underlying chronic condition. Regarding speech therapy, for age > 12, allow two visits per year for maintenance therapy and up to six additional visits per year for an acute exacerbation of an underlying chronic condition, a progressive swallowing disorder and/or evaluation/training for speech aids. VOTES: Ayes, 9; Abstained, 1-Sohl. MOTION CARRIES 9-0.

Dr. Glass felt these were good modifications but his concern was for the big numbers of speech therapy visits for the 3 years to 7 years range. Dr. Turek indicated that prior authorization is required by both the fully capitated health plans and OMAP individual health plans do prior authorize, as well as, the Oregon Health Plan.

Dr. Glass further mentioned his concern that there are patients within the 3 - 7 age range that are not physically disabled but are mentally retarded and have desperate parents who throw their children into speech therapy in the hopes of improvement of the retardation. He does not think that is appropriate therapy and wonders how other health plans deal with these cases. Dr. Turek said it would be unusual for these visits to be denied under OHP.

Dr. Saha wanted to know what was meant by “consideration should be given to an increased number of visits after a procedure, such as botox or baclofen pump placement.” Dr. Little replied that was her comment for what the physiatrist had told her. However she thought is was essentially the same as the acute exacerbation. Dr. Walsh asked if the phrase should be deleted from the guideline. Dr. Little answered with a yes and the “acute event” language would replace it. Therefore Dr. Walsh asked

for a motion. Dr. Saha moved to delete the phrase, since the “acute event” language had already been voted upon. Ellen Lowe seconded.

MOTION: Remove, “…after a procedure, …” and replace with “after an acute event “.
VOTES: Ayes, 9, Abstained, 1- Sohl. MOTION CARRIES 9-0.

Mr. Coffman asked if there was any public comment. No further changes or comments were made.

The final guideline will read as follows:
ADD THE FOLLOWING GUIDELINE TO LINES 219,336,455,45
The following number of combined physical and occupational therapy visits are allowed per year for any combination of diagnoses on these lines:
• Ages 0-7: 24*
• Ages 8-12: 12*
• Age > 12: 2*
The following numbers of speech therapy visits are allowed per year for any combination of diagnoses on these lines:
• Age 0-2: 0*
• Age 3-7: 24*
• Age 8-12: 12*
• Age > 12: 2*
*An additional 6 visits of speech, physical or occupational therapy are allowed whenever there is a change in status, such as surgery, injection, or an acute exacerbation, OR for evaluation and treatment of swallowing.

HSC minutes January 2005
II. Therapy Guidelines
Dr. Alison Little referred the HSC to the documentation within the Therapy Guidelines section of the packet. Dr. Little proposed that the guidelines for the chronic and acute therapies be combined into one guideline and exclude limits on swallowing disorders. Dr. Little explained that she had combined the chronic and acute therapies into one because otherwise a limit of two therapy visits for a stroke patient would apply as soon as they were discharged from the hospital.

There was discussion about connecting the guideline to a diagnosis. Dr. Glass brought up that fact that many times there is no diagnosis given by the therapist. Usually it is a description of the speech and articulation problems, a description of school behavior, or how the individual is functioning at home. Kathy Savicki expressed the concern about the need to have the guideline be able to distinguish where the impairment is small, but broad enough for those with a real disability.

Dr. Walsh wondered why the acute stage of treatment extended to six months, with the potential for a huge number of visits should the patient be seen everyday. An example of a young child with a severe head injury was given, where even more than six months of visits may be needed after leaving the hospital. Dr. Walsh explained to the therapists that the HSC is looking to manage a perceived over-utilization of visits. He challenged the therapists to go through the articles they sent and find where it states that a certain number of visits are better than another number. Also he explained that the HSC is

looking for specificity, and the articles only had antidotal evidence. The HSC needs to see evidence of the utility of different types of treatment and the appropriate frequency of that treatment. Furthermore, Dr. Walsh requested that the therapists establish a gradation of severity for specific diagnoses to which guidelines can be attached. The therapists said they do not have evidence that a certain number of visits gives a better outcome than another amount, but they do have evidence that children improve on standard scores or on functional outcomes after treatment. The concerns are not for the children with mild articulation issues but rather to provide for the children under the age of two that have autism, cerebral palsy and other severe disabilities. They said there is a critical learning period for communication skills for children under age two (e.g. reciprocity).

It was noted that inpatient stays were considered acute with an unlimited number of visits available, but they wanted patients seen in a skilled nursing facility (SNF) to be exempt from the limits as well. Dr. Little clarified that they are acute facilities, but as it is being implemented now, SNF patients are subjected to limits. That was a decision that OMAP said they made because there was not a clear direction from the HSC.

Dr. Saha mentioned that it would be useful to the HSC to have a list of diagnoses, with a recommended approach supported by evidence for the acute phase and the chronic phase of each disease. The therapists replied that there is a need for standard outcome measures across all fields of therapy so that they could measure progress. Dr. Janice Cockrell pointed out that there is difficulty in using such measurements in children due to their natural development. There are good adult outcomes available; however for children there does not appear to be a minimum “dose”. In pediatrics, much of the treatment involves educating the family so that they can follow through with a home treatment program. Dr. Cockrell’s concern is cutting back on treatment visits when there are periods of rapid development that should be occurring in childhood -- below the age of three and at puberty. Dr. Cockrell recognizes that the diagnosis of developmental delay is a problem as the etiology of the delay needs to be known before the patient’s management can be determined.

Ms. Savicki asked if stringent guidelines could be crafted for children with minor problems because they would be the easiest to manage. Upon discussion the HSC concluded that the diagnostic system does not delineate disease severity. Upon review of the literature, however, it was pointed out that there are some qualification schemes, including a seven-level language skill qualification. The Commission asked if they could provide a list of important diagnostic codes that should be exempt from the guidelines and a grading system to be used for follow-up visits to determine when a patient’s progress becomes stationary. Again the HSC urged the therapists to present the best evidence-based approaches. The therapists replied that they understood there was a need for management of these services and they would be happy to supply the requested information. Furthermore, they would promote good treatment notes and charts that show whether or not the patient is making progress, whether there is follow through on the treatment plan, and whether the patient can act independently. Ms. Savicki said she thought it would be best to look at simple things that would allow the managed care systems to manage these services, such as the level of disability and the level of progress.

The therapists asked if the HSC could modify the guideline for age two and under that would provide speech pathologists some visits for evaluation. Dr. Little mentioned that

she was still struggling with importance of visits for children from age 0-2 years because the one study dealing with the treatment of young children had an average age of 3-1/2 years and it showed no significance between treatment and control groups. A separate commentary on services for this age group was unclear as to whether the children received hearing aids and/or speech therapy.

Marcia Becker-Mehr, from OMAP, informed the HSC that evaluations are not prior authorized. OMAP would not know the age of the individual as claims get processed, therefore evaluations are currently covered for children of any age.

Ms Savicki was concerned about the cost impact of restoring services. Mr. Coffman explained the changes that went into effect in October 2004 were a reduction in service and they were felt to be within the allowable boundaries of fiscal impact because the restoration of services would still be at a lower level than what they were prior to October 1, 2004.

The subject of dysphagia was brought up and whether there should be a limit of visits attached. Dr. Little explained that she felt the results of not treating it are costly, and it appears that it is not being abused in the same way as speech therapy.

There was a motion to accept Dr. Little's draft to remove swallowing disorders from the current set of visit limits while the HSC continues to work on the other aspects of the guideline.

Prior to a second to the motion, Dr. Mangum said he was concerned about the teenagers with head injuries having enough visits. Three months seemed too short in a nursing home setting because recovery time from a head injury can be significant. He further stated that 6 months could even be relatively short in that situation. He did not want to withhold care by sticking with the guideline as it is. Ms. Savicki suggested adding a clause to the guideline stating that it does not apply to an individual in a skilled nursing facility for rehabilitation purposes. Dr. Mangum agreed with the concept, however noted that it would also allow for individuals that have less acute problems to receive ongoing therapy.

MOTION: Remove limits on visits for the evaluation and treatment of swallowing disorders from the current guideline. MOTION CARRIES: 9-0, Ayes: Walsh, Mangum, Glass, Saha, Dodson, Savicki, Williams, Lowe, Sohl. Abstention: McGough.

MOTION: Have no limits apply to therapies in a setting of inpatient hospital care, inpatient rehabilitation units, and skilled nursing facilities with the primary purpose of rehabilitation. MOTION CARRIES: 10-0.

After some discussion, Dr. Walsh clarified that the HSC still has concerns with therapy visits for 0-2 year olds, the current distribution of limits by age, and the fact that the current guideline covers all severity levels with one set of limits. Dr. Walsh asked the therapists to work with the HSC to set sensible limits with specific guidelines.
The therapists mentioned that the federal government does not mandate services for children under 36 months. Therefore these children rely on the state for these services and given Oregon's financial situation, these services are being decimated.

MOTION: Give four visits for speech therapy to those less than 3 years of age.

MOTION CARRIES: 9-0, Ayes: Walsh, Mangum, Glass, Saha, Dodson, Savicki, Williams, Lowe, Sohl. Abstention: McGough.
See Attachment A

ATTACHMENT A
Revised Guideline for Rehabilitative Therapies
GUIDELINE NOTE 1, SPEECH, OCCUPATIONAL, AND PHYSICAL THERAPY
On Lines 1, 19, 21, 24, 26, 29, 31, 35, 37, 38, 40, 42, 52, 89, 95, 96, 97, 98, 101, 102, 103, 104, 105, 106, 112, 113, 114, 115, 132, 133, 134, 136, 143, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 165, 168, 175, 177, 180, 191, 198, 199, 209, 215, 219, 216, 240, 241, 248, 261, 264, 286, 287, 288, 289, 290, 294, 299, 313, 318, 319, 323, 324, 325, 330, 336, 371, 374, 375, 382, 383, 384, 388, 441, 454, 455, 456, 469, 470, 471, 483, 484, 485, 486, 498, 516, 517, 518, 519, 522, 568, 584, 589, 594, 645, 646, 685
Physical, occupational and speech therapy, and cardiac and vascular rehabilitation, are covered for these diagnoses when paired with the respective CPT codes, depending on medical necessity, for up to 3 months after the initiation of the therapies. Thereafter, the following number of combined physical and occupational therapy visits are allowed per year, depending on medical necessity:
• Ages < 8: 24
• Ages 8-12: 12
• Age > 12: 2
Following 3 months of acute therapy, the following number of speech therapy visits are allowed per year, depending on medical necessity (with the exception of swallowing disorders, for which limits do not apply):
• Age < 3: 4
• Age 3-7: 24
• Age 8-12: 12
• Age > 12: 2
An additional 6 visits of speech, and/or an additional 6 visits of physical or occupational therapy are allowed, regardless of age, whenever there is a change in status, such as surgery, botox injection, or an acute exacerbation OR for evaluation/training for an assistive communication device.
No limits apply while in a skilled nursing facility for the primary purpose of rehabilitation, an inpatient hospital, or an inpatient rehabilitation unit.

Section 6.0

New Discussion Items

Hormone Therapy for Transgender People

Question: Should hormone therapy for transgender people be a covered service on the Prioritized List?

Question Source: HERC staff, OHA

Issue:
The October 1, 2014 Prioritized List includes Gender Dysphoria as a new, covered line (413). Currently, the only treatments on this line are office visits, psychotherapy and puberty suppression medication for transgender and gender questioning youth.

Hormone therapy is covered for women with menopausal symptoms, men in need of testosterone, and for similar hormone replacement needs. Transgender cross-sex hormone therapy is not a covered benefit. Cross-sex hormone treatment is an off-label use of estrogens and androgens.

Background:
Hormone therapy in transgender individuals is cross-sex hormone therapy (rather than "replacement therapy") with the goal of reducing endogenous hormones and replacing those with cross-sex hormones. This would alter secondary sexual characteristics and psychological characteristics with the goal of relieving gender dysphoria.

Endocrine Society 2009

> Transsexual persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will 1) suppress endogenous hormone secretion determined by the person's genetic/biologic sex and 2) maintain sex hormone levels within the normal range for the person's desired gender. A mental health professional (MHP) must recommend endocrine treatment and participate in ongoing care throughout the endocrine transition and decision for surgical sex reassignment. The endocrinologist must confirm the diagnostic criteria the MHP used to make these recommendations. Because a diagnosis of transsexualism in a prepubertal child cannot be made with certainty, we do not recommend endocrine treatment of prepubertal children. We recommend treating transsexual adolescents (Tanner stage 2) by suppressing puberty with GnRH analogues until age 16 years old, after which cross-sex hormones may be given. We suggest suppressing endogenous sex hormones, maintaining physiologic levels of gender-appropriate sex hormones and monitoring for known risks in adult transsexual persons.

Herbst, 2007 – systematic review
Transgender people have high rates of risky behaviors. Male to female transgender persons have an HIV prevalence rate of 28%, FTM 0-3%. This is a group with higher rates of illicit drug use, engagement in risky sexual behaviors, social isolation, physical abuse and economic marginalization.

Evidence Summary
No evidence from NICE, SIGN, or Cochrane available

Murad, 2010

1. Systematic review and metanalysis of impact of hormonal therapy and sex reassignment on health outcomes

2. Included 28 observational studies, N = 1833 participants with GID (1093 male-to-female, 801 female-to male) who underwent sex reassignment that included hormonal therapies.
3. Results: after sex reassignment, 80% of individuals with GID reported significant improvement in gender dysphoria (95% CI = 68–89%; 8 studies; I2 = 82%); 78% reported significant improvement in psychological symptoms (95% CI = 56–94%; 7 studies; I2 = 86%); 80% reported significant improvement in quality of life (95% CI = 72–88%; 16 studies; I2 = 78%); and 72% reported significant improvement in sexual function (95% CI = 60–81%; 15 studies; I2 = 78%).
4. Conclusions: Very low quality evidence suggests that sex reassignment that includes hormonal interventions in individuals with GID likely improves gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life.

Elamin, 2010

1) Systematic review of harms of hormone therapy in transgender persons
2) N = 16 uncontrolled studies (very low quality)
3) Conclusions: cross-sex hormone therapies increase serum triglycerides in MF and FM and have a trivial effect on HDL-cholesterol and systolic blood pressure in FM. Data about patient important outcomes are sparse and inconclusive.

Summary

Cross-sex hormone therapy, in conjunction with psychotherapy, may offer some benefit in self-reported outcomes for persons with gender dysphoria based on very poor quality evidence.

HSC Staff Recommendations

1) Change the guideline note for line 413 GENDER DYSPHORIA as shown below to allow cross-sex hormone therapy for adults
2) Discuss possible coverage of sex reassignment surgery
    a. New line as part of biennial review?
    b. Add to line 413?
    c. Keep as Excluded?

GUIDELINE XXX GENDER DYSPHORIA

Line 413

Hormone treatment is included on this line for cross-sex hormone treatment of adults with gender dysphoria. Hormone treatment is also included for use in delaying the onset of puberty and/or continued pubertal development with GnRH analogues for gender questioning children and adolescents. This therapy should be initiated at the first physical changes of puberty, confirmed by purbertal levels of estradiol or testosterone, but no earlier than Tanner stages 2-3. Prior to initiation of puberty suppression therapy, adolescents must fulfill eligibility and readiness criteria, and must have a comprehensive mental health evaluation. Ongoing psychological care is strongly encouraged for continued puberty suppression therapy.

The Endocrine Society's
CLINICAL GUIDELINES

Endocrine Treatment of Transsexual Persons:

An Endocrine Society Clinical Practice Guideline

The Endocrine Society®

The Journal of Clinical Endocrinology & Metabolism

Authors: Wylie C. Hembree, Peggy Cohen-Kettenis, Henriette A. Delemarre-van de Waal, Louis J. Gooren, Walter J. Meyer III, Norman P. Spack, Vin Tangpricha, and Victor M. Montori

Co-Sponsoring Associations: European Society of Endocrinology, European Society for Paediatric Endocrinology, Lawson Wilkins Pediatric Endocrine Society, and World Professional Association for Transgender Health

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Evidence-based reviews for this guideline were prepared under contract with The Endocrine Society.

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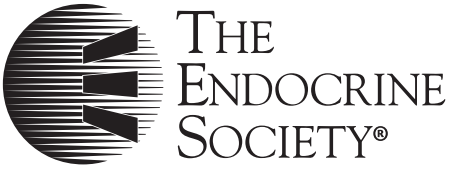

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The Endocrine Society's
CLINICAL GUIDELINES

Endocrine Treatment of Transsexual Persons:

An Endocrine Society Clinical Practice Guideline

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Table of Contents

Abstract

Objective: The aim was to formulate practice guidelines for endocrine treatment of transsexual persons.

Participants: An Endocrine Society-appointed Task Force of experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe the strength of recommendations and the quality of evidence, which was low or very low.

Consensus Process: Committees and members of The Endocrine Society, European Society of Endocrinology, European Society for Paediatric Endocrinology, Lawson Wilkins Pediatric Endocrine Society, and World Professional Association for Transgender Health commented on preliminary drafts of these guidelines.

Conclusions: Transsexual persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will 1) suppress endogenous hormone secretion determined by the person's genetic/biologic sex and 2) maintain sex hormone levels within the normal range for the person's desired gender. A mental health professional (MHP) must recommend endocrine treatment and participate in ongoing care throughout the endocrine transition and decision for surgical sex reassignment. The endocrinologist must confirm the diagnostic criteria the MHP used to make these recommendations. Because a diagnosis of transsexualism in a prepubertal child cannot be made with certainty, we do not recommend endocrine treatment of prepubertal children. We recommend treating transsexual adolescents (Tanner stage 2) by suppressing puberty with GnRH analogues until age 16 years old, after which cross-sex hormones may be given. We suggest suppressing endogenous sex hormones, maintaining physiologic levels of gender-appropriate sex hormones and monitoring for known risks in adult transsexual persons.

(J Clin Endocrinol Metab 94: 3132–3154, 2009)

Abbreviations: BMD, Bone mineral density; FTM, female-to-male; GID, gender identity disorder; MHP, mental health professional; MTF, male-to-female; RLE, real-life experience.

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ORIGINAL ARTICLE

Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes

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Summary

Objective To assess the prognosis of individuals with gender identity disorder (GID) receiving hormonal therapy as a part of sex reassignment in terms of quality of life and other self-reported psychosocial outcomes.

Methods We searched electronic databases, bibliography of included studies and expert files. All study designs were included with no language restrictions. Reviewers working independently and in pairs selected studies using predetermined inclusion and exclusion criteria, extracted outcome and quality data. We used a random-effects meta-analysis to pool proportions and estimate the 95% confidence intervals (CIs). We estimated the proportion of between-study heterogeneity not attributable to chance using the I^2 statistic.

Results We identified 28 eligible studies. These studies enrolled 1833 participants with GID (1093 male-to-female, 801 female-to-male) who underwent sex reassignment that included hormonal therapies. All the studies were observational and most lacked controls. Pooling across studies shows that after sex reassignment, 80% of individuals with GID reported significant improvement in gender dysphoria (95% CI = 68–89%; 8 studies; I^2 = 82%); 78% reported significant improvement in psychological symptoms (95% CI = 56–94%; 7 studies; I^2 = 86%); 80% reported significant improvement in quality of life (95% CI = 72–88%; 16 studies; I^2 = 78%); and 72% reported significant improvement in sexual function (95% CI = 60–81%; 15 studies; I^2 = 78%).

Conclusions Very low quality evidence suggests that sex reassignment that includes hormonal interventions in individuals with GID likely improves gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life.

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Introduction

Therapy with cross-sex hormones is used as a primary sex reassignment intervention or as an adjunct to sex reassignment surgery in individuals with gender identity disorder (GID). Hormonal therapies clearly exert a rapid and direct effect on gender specific behaviours such as aggressiveness, arousal, verbal fluency and visuospatial abilities.[1] Several studies have reported sex reassignment to be associated with favourable changes in family, psychological and social life, sexual relationships and gender dysphoria, defined as the distress that originates from the difference between one's biological sex and one's basic sense of being a male or a female.[2–4]

Despite these putative benefits, individuals with GID who undergo this transition continue to have high prevalence of psychiatric comorbidities such as depression and anxiety disorders, as well as a suicide rate that is higher than that of the general population.[2,5] Hormonal therapies may also be associated with adverse effects that should be considered in addition to other costs and burdens of treatments. These adverse events have improved with the use of newer transdermal preparations and the routine administration of lower doses,[6,7] but may continue to be of concern to patients and providers.

We sought to systematically review the literature for the best available evidence regarding the benefits and risks of hormonal therapy administered in this context. In this manuscript, we summarize the available evidence about benefits in terms of self-reported outcomes such as the resolution of gender dysphoria and the effects on sexual function, psychiatric comorbidities and quality of life.

Methods

The report of this protocol-driven systematic review adheres to the standards for reporting Meta-analysis Of Observational Studies in Epidemiology (MOOSE).[8]

Eligibility criteria

We considered studies to be eligible for this review if they enrolled male-to-female (MF) or female-to-male (FM) individuals

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REVIEW ARTICLE

Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analyses

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Summary

Objective To summarize the available evidence on the cardiovascular effects of cross-sex steroid use in transsexuals.

Methods We searched relevant electronic databases and sought additional references from experts. Eligible studies reported on cardiovascular events, venous thromboembolism, blood pressure and fasting serum lipids. Data were extracted in duplicate. We used the random-effects model to estimate the pooled weighted mean difference (WMD) and 95% confidence intervals (CIs).

Results We found 16 eligible studies, mostly uncontrolled cohorts of varied follow-up durations (1471 male-to-female (MF) and 651 female-to-male (FM) individuals). In the MF individuals, cross-sex hormone use was associated with a statistically significant increase in fasting serum triglycerides without changes in the other parameters (WMD = 23·39 mg/dl; 95% CI = 4·82–41·95). In the FM individuals, there was a similar increase of triglycerides (WMD = 31·35 mg/dl; 95% CI = 7·53–55·17) and a reduction of high density lipoprotein (HDL)-cholesterol (WMD = −6·09 mg/dl; 95% CI = −11·44 to −0·73). There was a statistically significant but clinically trivial increase in systolic blood pressure (WMD = 1·74 mmHg; 95% CI = 0·21–3·27). Analyses were associated with significant heterogeneity across studies. There were very few reported cardiovascular events (deaths, strokes, myocardial infarctions or venous thromboembolism), more commonly among MF individuals.

Conclusions Very low quality evidence, downgraded due to methodological limitations of included studies, imprecision and heterogeneity, suggests that cross-sex hormone therapies increase serum triglycerides in MF and FM and have a trivial effect on HDL-cholesterol and systolic blood pressure in FM. Data about patient important outcomes are sparse and inconclusive.

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Introduction

Gender identity disorder (GID) affects individuals preoccupied with their wish to live as members of the opposite sex. Such individuals intensely desire to adopt the social role of the other sex or to acquire the physical appearance of the other sex through hormonal or surgical manipulation.[1] Sex reassignment therapy seeks to achieve this transition using a multi-modality approach that often includes psychological, hormonal and surgical interventions.[2] Men seeking transition to the female sex (MF) generally use oestrogen, antiandrogens (cyproterone acetate, spironolactone) or a gonadotropin-releasing hormone agonist (GnRH agonists). Women seeking transition to the male sex (FM) generally use testosterone.[3]

It is plausible that sex steroid use may be associated with potential adverse effects such as acne, venous thromboembolism, atherosclerosis, hypertension, hyperlipidemia, prostate hyperplasia; and may cause or exacerbate neoplasia of the prostate, breast and ovaries.[3,4] Two large randomized trials characterized the effect of oestrogen-containing hormonal use on cardiovascular risk in women,[5,6] and the Coronary Drug Project evaluated this therapy in men post-myocardial infarction.[7] A recent review reported on the weak available evidence linking testosterone use with cardiovascular risk in hypogonadal and eugonadal men,[8] a finding that was echoed in the recently published Endocrine Society guidelines for androgen use in women, in which the panel described limited evidence regarding the cardiovascular safety of low-dose testosterone use in women with presumed androgen deficiency.[9] The different characteristics of the patients and of the hormone schedule in these trials mean these studies apply only indirectly to sexual steroid use in transsexual individuals.

In this systematic review, we sought to summarize the available evidence of the effects of cross-sex hormone use on the cardiovascular risk of transsexual individuals. Outcomes of interest were cardiovascular events, venous thromboembolism, fasting serum lipid fractions and blood pressure.

Methods

This report adheres to the standards of reporting of Meta-analysis Of Observational Studies in Epidemiology.[10]

Eligibility criteria

We sought to include both randomized trials and observational studies of transsexual individuals who used cross-sex steroids regardless of whether they had sex reassignment surgery or not. Eligible studies exposed MF to oestrogen, antiandrogens (cyproterone acetate, spironolactone) or GnRH agonists and FM to testosterone. Studies must have clearly stated that individuals used sex steroids for at least 3 months and those participants were followed up for at least 3 months. In order to avoid selection bias and ascertain a well-documented exposure, eligible studies excluded individuals who had received sex steroids, even if self-prescribed, before the initiation of the study. In the case of a study having two transsexual groups, one of them previously exposed to sex steroids, we included data only from the group not previously exposed.

Outcomes of interest were cardiovascular events, e.g. death, stroke, myocardial infarction, venous thromboembolism. We were also interested in levels of blood pressure and lipid fractions. Eligible studies provided comparison between intervention and controls groups or a pre–post intervention comparison. We included studies regardless of their publication status, language or size. Review articles, commentaries and letters that did not contain original data were excluded.

Study identification

An expert reference librarian designed and conducted the electronic search strategy with input from study investigators with expertise in conducting systematic reviews. To identify eligible studies, we searched electronic databases (Ovid MEDLINE, Ovid Embase, Ovid PsycInfo, Thomson Scientific Web of Science and Elsevier Scopus) and bibliographies of eligible studies through February 2008 and sought additional references from the experts. The detailed search strategy is available upon request.

Reviewers, working independently and in duplicate, reviewed all abstracts and titles and, upon retrieval of potentially eligible studies, the full text publications for eligibility. Disagreements were resolved by consensus (the two reviewers discussed the discrepancy and reached a decision) or arbitration (if disagreement was not resolved by the two reviewers, a third reviewer adjudicated the difference). We estimated chance-adjusted agreement among reviewers using the kappa statistic.

Quality assessment

Reviewers, working independently and in duplicate, analysed the eligible articles to assess the reported quality of each study, i.e. the confidence in the accuracy of the estimates. For each study, we assessed whether investigators were able to ensure that participants had started with similar prognosis (through randomization with allocation concealment or through careful matching among individuals free of the outcome at baseline, or through adjustment for confounders at baseline), and maintained such similarity during the study (by blinding of participants and investigators, and by careful accounting and adjusting for co-interventions), and through the end (by minimizing loss to follow-up, and similar assessment of outcome measures in an intention-to-treat manner). In addition, we looked at length and adequacy of follow-up and how the outcome was assessed (self-report and interview *vs.* medical records). We assessed our chance-adjusted agreement on study quality using the kappa statistic with disagreements resolved by consensus or arbitration.

Data extraction

Reviewers, working independently and in pairs, used a standardized form to extract full description of study participants, including age, whether MF or FM, type, dose and duration of hormonal therapy, and data related to blood lipid fractions and blood pressure levels. We also noted the number of venous thromboembolic events, myocardial infarctions, strokes or deaths reported.

Author contact

We sent letters to the corresponding authors (or any other author if we were not able to reach the corresponding author) of each of the eligible studies by electronic mail. We asked these authors to verify the data we extracted and to complete data missing from the published record. In case of no response, we repeated the request three weeks later.

Statistical analysis

Analysis was conducted using StatsDirect version 2.6.7 (StatsDirect Ltd., UK, 2005). Using DerSimonian-Laird random effects meta-analyses,[11] we pooled the weighted mean differences (WMD) for continuous outcomes and their associated 95% confidence interval (CI). When measures of variability were not reported, we estimated standard errors from P and t values.[12] Longitudinal and cross-sectional studies were pooled separately. We measured inconsistency across studies that cannot be explained by chance alone, but rather by differences in participants, interventions, outcomes or design, using the I^2 statistic.[13] We also planned to estimate the pooled cumulative incidence of cardiovascular events; however, the varied follow-up duration across studies and the limited number of events precluded pooling.

Subgroup and sensitivity analyses

A priori hypotheses to explore potential causes of heterogeneity included possible differences in: population age, e.g. adolescents (who have brief exposure to sex hormones prior to transition) *vs.* adults; different treatment regimens (e.g. oestrogens alone, *vs.* oestrogen + GnRH agonists *vs.* oestrogen + antiandrogens), oral *vs.* transdermal oestrogen, high *vs.* physiological dose, agonist alone *vs.* agonist alone + pituitary suppression (e.g. oestrogen alone *vs.* oestrogen + goserelin); outcome characteristics, e.g. symptomatic *vs.* all events; study design, e.g. controlled study *vs.* single cohort; and study quality, e.g. blinded *vs.* open outcome assessment, patients lost to follow-up and follow-up duration (arbitrarily chosen durations of 1 year or shorter *vs.* longer). We also sought to

explore how results of the meta-analyses would change when borderline eligible articles are excluded.

Results

Study identification

Initial search of the literature yielded 341 publications, of which 64 were potentially relevant to this review based on titles and abstracts (Fig. 1). After full-text review, we found 15 eligible studies,[14–28] selected with near-perfect agreement across reviewers (kappa statistic = 0·9; 95% CI = 0·8–1·0). Data from an unpublished study was kindly offered by one of the primary authors contacted (Schneiders *et al*., unpub. obs.) Four studies, fulfilling our inclusion criteria, had overlapping patient populations with other included studies,[29–32] which was confirmed by author contact, and were not included to avoid duplicating individuals. We also excluded studies in which participants used sex steroids for less than 3 months or measured cardiovascular risk factors of unclear significance, e.g. leptin, homocysteine and vascular reactivity.

Study characteristics

Table 1 summarizes the characteristics of eligible studies. Twelve studies included groups of MF and 10 studies had FM groups; overall, the literature reviewed included 1471 MF and 651 FM individuals. Patients averaged 31 years of age. MF individuals used various regimens that mainly included oral, intramuscular or transdermal oestrogens with less frequent use of cyproterone acetate, goserelin acetate or spironolactone. FM individuals used various regimens of testosterone that were mainly administered intramuscularly with infrequent use of oral preparations. No transdermal testosterone was used. Progestins were added if menses did not cease.

Author contact

We successfully contacted all of the corresponding authors (another author in two studies) by electronic mail. All authors either contributed missing data (where these data had been collected but not reported in the format we needed for analyses) or confirmed study characteristics, quality assessments and data as collected.

Study quality

Table 2 summarizes the methodological quality of the 16 included studies. Studies were uncontrolled or self-controlled observational studies, one of which included a nested trial (randomizing MF individuals to oral or transdermal oestrogen preparations). Medical records were the most frequent method of ascertaining exposure to hormonal therapy and assessing outcomes.

Meta-analyses

Patient important outcomes. There were very few reported cardiovascular events across the trials, with varied length of follow-up. Figure 2 shows the proportion of participants in each eligible study who had reported cardiovascular events.

Serum lipids and blood pressure. Tables 3 and 4 represent pooled data for the lipid parameters and blood pressure measurements in MF and FM individuals after sex steroid use, respectively.

Subgroup and sensitivity analyses

All feasible subgroup interaction analyses are shown in Tables 5 and 6. In MF individuals, significant interaction existed in HDL level-route of hormonal administration, showing a higher serum level after oral administration than the transdermal route. The same was observed with triglycerides levels. In FM individuals, we found insufficient data to compare the route of administration of hormonal therapy (intramuscularly *vs*. orally). Subgroups defined by individuals followed up for more than 1 year *vs*. less than 1 year, showed significant increase in cholesterol and triglycerides in studies with follow-up period of more than 1 year. All other subgroup analyses were nonsignificant.

In terms of sensitivity analyses, pooling studies with a cross-over study design separately did not show any significant change in measured lipid fractions. The exclusion of unpublished data decreased between study heterogeneity and drove the statistically significant decrease in HDL and increase in systolic blood pressure towards

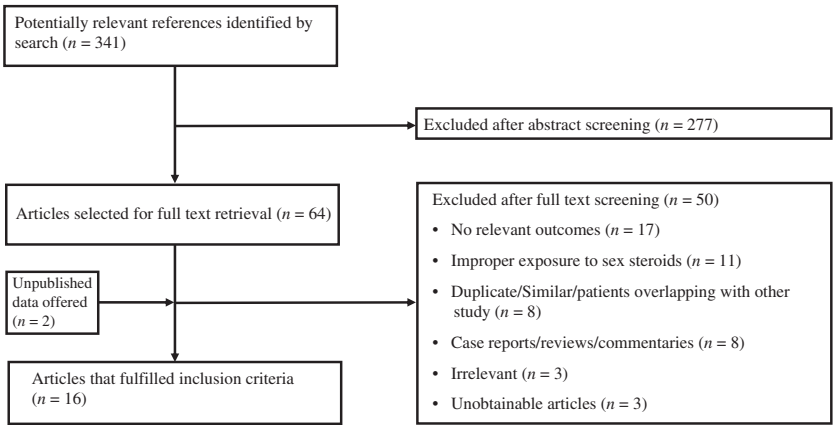

Fig. 1 The process of study selection.

Table 1. Baseline characteristics of included studies

Author, yr	Mean age, yr	Patients	No. intervention group	Description of intervention	Duration of exposure	Control group	Presence of CV risk factors
Asscheman, 1989[14]	32	MF	303	100 mg cyproterone acetate and 100 μg ethinylestradiol qd (n = 258). Until 1980, diethylstillbestrol (5–15 mg/day) was prescribed for a few patients. Some patients insisted on IM oestrogen. They procured the oestrogen outside the clinic and these were self-administered in doses of 200–800 mg oestradiol17-undecanoate/ IM / mo (n = 45). Recommended dose in post-menopausal women was 20–100 mg/mo	53 mo	NA	No
	25·4	FM	122	Long-acting testosterone esters 250 mg IM/2 weeks (n = 69), or testosterone undecanoate 120–160 mg/day/PO (n = 19), or both, but not simultaneously (n = 34). If menstrual activity did not cease within 3 mo after start of the hormone administration, lynestrol 5 mg/PO/day was added (n = 3)	43 mo	NA	Smoking, HTN and family history of heart disease
Berra, 2006[15]	30	FM	16	Testosterone depot (100 mg testosterone enanthate + 25 mg testosterone propionate)/IM/q 10 day	6 mo	NA	No
Damewood, 1989[16]	NR	MF	18	Premarin (oestrone sulphate 48%, equilin sulphate 26%, 17alpha dehydroequilin sulphate 15%), PO, 1·25–2·5 mg/day	> 3 yrs	28healthy volunteers, No Rx	Smoking
De Cuypere, 2005[17]	42	MF	32	Multiple regimens	Unclear	NA	More smokers, older
	33	FM	23	Multiple regimens	Unclear	NA	No
Dittrich, 2005[18]	38	MF	60	3·8 goserelin acetate, SQ/ q 4 weeks + 6 mg oestradiol-17b valerate, PO/qd	24 mo	NA	3 patients had thrombophilia
Elbers, 2003[19]	26	MF	20	Ethinyl oestradiol 100 μg/day + cyproterone acetate 100 mg/day	12 mo	NA	No
	23	FM	17	Testosterone esters 250 mg/IM/2 weeks	12 mo	NA	No
Giltay, 2003[20]	32	MF	15	Oral ethinyl oestradiol 100 μg/day + CA 100 mg/day	4 mo	NA	Smoking
	32	MF	15	Transdermal 17b-oestradiol 100 μg 2 × /week + CA 100 mg/day	4 mo	NA	Smoking
Jacobeit, 2007[21]	33	FM	12	Testosterone undecanoate 1,000 mg/IM at weeks 0, 6 and q 12–14	12 mo	NA	No
Mueller, 2006[22]	37	MF	40	3·8 mg goserelin acetate/4 weeks + 6 mg PO 17 Boestradiol valerate qd	12 mo	NA	No
Mueller, 2007[23]	30	FM	37	Testosterone undecanoate 1000 mg/IM/q 12 weeks	12 mo	NA	Smoking
Prior, 1989[24]	31	MF	23	Spironolactone (less than 100 up to 200 mg qd) and conjugated oestrogens (PO, 0·625–2·5 mg qd) and progesterone (PO, 10 mg qd)	12 mo	NA	5 of 23 had HTN
Schlatterer, 1998[25]	NR	MF	46	Cyproterone acetate 50–100 mg/ PO/qd + depot oestrogens IM at varying intervals	Variable	NA	NR
	NR	FM	42	Depot testosterone 250 mg IM every 2–4 weeks	Variable	NA	NR
Toorians, 2003[26]	35	MF	8	Cyproterone acetate 50 mg/PO/bid	4 mo	NA	No

Table 1. *Continued*

Author, yr	Mean age, yr	Patients	No. intervention group	Description of intervention	Duration of exposure	Control group	Presence of CV risk factors
	32	MF	14	Ethinyl oestradiol 50 mg/PO/bid + cyproterone acetate 50 mg/PO/bid	4 mo	NA	No
	30	MF	20	E2-valerate 2 mg/PO/bid + cyproterone acetate 50 mg/PO/bid	4 mo	NA	No
	26	FM	14	Testosterone esters 250 mg/IM/q 2 weeks	4 mo	NA	No
	30	MF	14	17-b-oestradiol 100 µg E2/TD/qd + cyproterone acetate 50 mg/PO/bid	4 mo	NA	No
Van Kesteren, 1997[27]	41	MF	816	Cyproterone acetate 100 mg + ethinyl oestradiol 100 µg/PO/qd	2 mo–41 yrs	NA	1 had a previous VTE
	34	FM	293	Testosterone esters 250 mg IM/2 weeks or testosterone undecanoate/ PO/qd	2 mo–41 yrs	NA	No
Wilson, 2006[28]	38	MF	25	Oestrogen 1·5 to 5·0 mg/PO/qd	18 mo	13 MF, No Rx	No
Schneiders, unpub. obs.	51	FM	75	Testosterone esters 250 mg/IM/q 2 weeks (n = 46) or testosterone undecanoate 160–240 mg/PO/qd (n = 29), depending on the patient's preference.	13 yrs	NA	NR

No, number; NA, not applicable; NR, not reported; FM, female-to-male; MF, male-to-female; Rx, treatment; VTE, venous thromboembolism; mo, month; yr, year; PO, orally; IM, intramuscularly; SQ, subcutaneous; TD, transdermal; qd, daily; bid, twice daily; HTN, hypertension.

the null, although a strong trend continued to exist (P = 0·05 and 0·06; respectively).

Discussion

Summary of findings

We conducted a systematic review and meta-analyses of studies that enrolled transsexual individuals who used sex steroids as part of a sex reassignment programme. Overall, we found no significant effect of hormones on cardiovascular outcomes. As expected, HDL-cholesterol decreased in FM receiving androgens and increased in MF receiving oestrogens, although these changes were statistically significant in FM only. Reciprocal increase of serum triglycerides was noted in both FM and MF. The effects of cross-sex steroids on other lipid fractions and on blood pressure were imprecisely measured and thus remain uncertain. Data were insufficient to allow meaningful assessment of patient important outcomes like death, stroke, MI or venous thromboembolism, although Fig. 2 suggests a higher incidence of these events among MF individuals. Of note, most of the individuals in these studies are from one centre and received a fairly high dose of oestrogens. Therefore, the only identifiable effects of cross-sex hormones appear to be on surrogate outcomes of less importance to patients.[33] The quality of evidence is very low. This is due to the uncontrolled and observational nature of included studies, small number of events leading to wide CIs and imprecision of estimates, brief and varied duration of follow-up, heterogeneity of treatment regimens, and inconsistency of results across studies that was unexplained by subgroup analyses.[34,35]

Comparison with published literature

To our knowledge, this is the first meta-analysis evaluating cardiovascular outcomes in transsexual individuals using sex steroids. Several randomized trials of sex steroid use in different populations can be considered in the light of the paucity of direct evidence in transsexual individuals. In the Coronary Drug Programme, men 30–64 years of age who had experienced a myocardial infarction were randomly allocated to either 2·5 mg or 5 mg of conjugated oestrogens. The 5-mg arm was stopped earlier than planned because it was associated with increased cardiovascular mortality. The 2·5-mg arm did not affect cardiovascular risk but was associated with a trend towards increased risk of thromboembolism (4·7% in the oestrogen group *vs.* 2·9% in the placebo group).[7] How these results apply to MF individuals, who are usually at lower cardiovascular risk than the coronary patients participating in this trial and who may use higher doses of oestrogen with different administration route, remains unclear. Nonetheless this evidence, along with randomized trial evidence of the cardiovascular effects of oestrogen use in postmenopausal women,[5,6] raises concern about the extent to which oestrogen preparations could cause harmful cardiovascular events. Uncertainty also affects the applicability of the findings of studies of androgens in women with low libido or presumed androgen deficiency, who use smaller doses of androgens, to the care of FM individuals.[9]

Table 2. Quality assessment of included studies

Author	Study design	Only for randomized trials		Selection of control group	Ascertainment of exposure	Ascertainment of outcome status at baseline	Factors controlled for	Assessment of outcome	Length of follow-up	% lost to follow-up
		Allocation concealment	Blinding							
Asscheman, 1989[14]	Single cohort, retrospective, compared with age-adjusted data	NA	NA	Different source	Medical records	No	Age, sex, Sex-steroid, exposure time	Medical records	1–17 yrs	15%
Berra, 2006[15]	Single cohort, prospective, before and after comparison	NA	NA	NA	Medical records	Yes	None	Medical records	6 mo	Unclear
Damewood, 1989[16]	Cross-sectional	NA	NA	Different source	Unclear	Unclear	Age, Smoking status, Alcohol intake, exercise, dietary habits	Interview	NA	0%
De Cuypere, 2005[17]	Cross-sectional	NA	NA	NA	Interview/Questionnaire	No	None	Blinded assessment	Unclear	51·3%
Dittrich, 2005[18]	Single cohort, prospective, before and after comparison	NA	NA	NA	Medical records	Yes	None	Medical records	24 mo	0%
Elbers, 2003[19]	Prospective cohorts, before and after comparison	NA	NA	NA	Interview/Questionnaire	Yes	NA	Interview	12 mo	Unclear
Giltay, 2003[20]	RCT	No	No	No	Interview/Questionnaire	Yes	NA	Interview	4 mo	0%
Jacobeit, 2007[21]	Single cohort, retrospective, before and after comparison	NA	NA	NA	Medical records	Yes	None	Medical records	12 mo	Unclear
Mueller, 2006[22]	Single cohort, prospective, before and after comparison	NA	NA	NA	Interview/Questionnaire	No	NA	Interview	24 mo	NR
Mueller, 2007[23]	Single cohort, prospective, before and after comparison	NA	NA	NA	Unclear	No	None	Medical records	12 mo	0%
Prior, 1989[24]	Prospective cohorts, before and after comparison	NA	NA	NA	Investigator	No	None	Investigator	12 mo	0%
Schlatterer, 1998[25]	Cross-sectional	NA	NA	NA	Medical records	No	None	Medical records	Variable	0%
Toorians, 2003[26]	5 arms; 2 were randomized, all exposed	No	No	NA	Investigator	Yes	NA	Investigator	4 mo	10%
Van Kesteren, 1997[27]	Single cohort, retrospective	NA	NA	NA	Medical records	No	Age, gender, period of time on sex-steroid	Medical records	2–19 yrs	11%
Wilson, 2006[28]	Cross-sectional	NA	NA	Same community	Unclear	No	None	Medical records	NA	Unclear
Schneiders, unpub. obs.	Single cohort, retrospective, before and after comparison	NA	NA	NA	Medical records	No	None	Medical records	13 yrs	31%

NA, not applicable; NR, not reported; mo, month; yr, year.

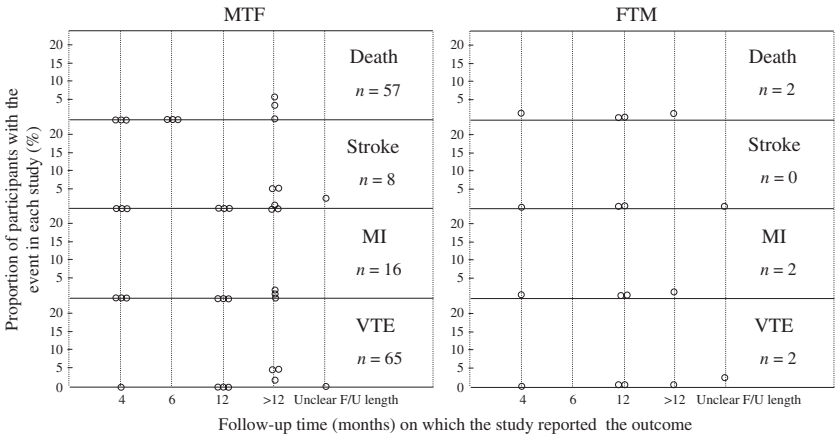

Fig. 2 Proportions of cardiovascular outcomes in included studies. Each study is represented by a circle. F/U, follow-up; FM, female-to-male individuals; MF, male-to-female individuals; MI, myocardial infarction; VTE, venous thromboembolism.

Table 3. Meta-analysis of serum lipids and blood pressure measurements after hormonal therapy in male-to-female individuals

	Pooled weighted mean difference* (95% CI)	*P*-value	Heterogeneity across studies (I^2)
Lipids (mg/dl)			
Cholesterol[18,19,22,24]	−1·31 (−13·42 to 10·79)	0·83	84%
Triglycerides[18–20,22,24]	23·39 (4·82 to 41·95)	0·01	84%
Low-density lipoproteins[19]	–	–	NA
High-density lipoproteins[19,20,24]	3·70 (−2·3 to 9·69)	0·23	93%
Blood pressure (mmHg)			
Systolic[19,24]	0·16 (−14·04 to 14·37)	0·98	NA
Diastolic[19,24]	1·42 (−6·71 to 9·55)	0·73	NA

Results expressed as post–pre intervention difference. Positive values indicate an increase of the tested parameter after sexual steroid use.
CI, confidence interval; NA, I^2 incalculable when pooling fewer than three studies.
*Random-effect meta-analyses.

Table 4. Meta-analysis of serum lipids and blood pressure measurements after hormonal therapy in female-to-male individuals

	Pooled weighted mean difference* (95% CI)	*P*-value	Heterogeneity across studies (I^2) (%)
Lipids (mg/dl)			
Total cholesterol[15,19,21,23] unpub. obs.	1·19 (−10·92 to 13·31)	0·85	69
Triglycerides[15,19,23] unpub. obs.	31·35 (7·53 to 55·17)	0·01	85
Low-density lipoproteins[15,19,21,23] unpub. obs.	2·07 (−8·49 to 12·63)	0·70	81
High-density lipoproteins[15,19,21,23] unpub. obs.	−6·09 (−11·44 to −0·73)	0·03	95
Blood pressure (mmHg)			
Systolic[15,19,23] unpub. obs.	1·74 (0·21 to 3·27)	0·03	27
Diastolic[15,19,23] unpub. obs.	1·45 (−0·57 to 3·48)	0·16	73

Results expressed as post–pre intervention difference. Positive values indicate an increase of the tested parameter after hormonal therapy.
CI, confidence interval.
*Random-effect meta-analyses.

Limitations and strengths

The main limitation of this review stems from the limited methodological quality of the primary studies identified and summarized here and the potential for biased reporting of these cohorts. Data were sparse and total sample size is limited. In addition, study-level analysis did not allow proper evaluation of the effect of some important patient-level characteristics that impact cardiovascular risk, e.g. smoking.

The strengths stem from the focussed review question, the comprehensive literature search that included multiple databases without language restrictions, the explicit eligibility criteria, the rigorous protocol-driven methodology of executing the review with protection against bias (e.g. use of

Table 5. Male-to-female subgroup analyses for lipid and blood pressure parameters

Subgroup	Subgroup description	Difference from baseline (95% CI)	*P*-value
Cholesterol: Hormonal preparation used	Oestrogen+antiandrogen[19,24]	−3·62 (−17·51 to 10·27)	0·41
	Oestrogen + GnRH agonists[18,22]	7·90 (−15·75 to 31·54)	
Cholesterol: Patients follow-up time	1 yr or less[19,24]	−3·62 (−17·51 to 10·27)	0·41
	More than 1 yr[18,22]	7·90 (−15·75 to 31·54)	
HDL: Route of hormonal administration	TD[20]	−4·68 (−2·01 to −7·35)	0·00
	PO[19,20,24]	6·45 (2·68 to 10·23)	
Triglycerides: Hormonal preparation used	Oestrogen+antiandrogen[19,20,24]	23·76 (1·97 to 45·55)	0·83
	Oestrogen + GnRH agonists[18,22]	19·36 (−13·72 to 52·45)	
Triglycerides: Route of hormonal administration	TD[20]	−9·79, (6·56 to −26·14)	0·00
	PO[18–20,22,24]	31·98 (12·79 to 51·16)	
Triglycerides: Patients follow-up time	1 yr or less[19,20,24]	23·76 (1·97 to 45·55)	0·83
	More than 1 yr[18,22]	19·36 (−13·72 to 52·45)	

Subgroup analyses of outcomes not reported in this table were unfeasible due to sparse data.
CI, confidence interval; TD, transdermal; PO, oral.

Table 6. Female-to-male subgroup analyses for lipid and blood pressure parameters

Outcome/subgroup	Subgroup description	Mean difference from baseline (95% CI), SE	*P*-value
Cholesterol: Route of hormonal administration	IM[15,19,21,23]	−3·25 (−15·19 to 8·70)	0·02
	Mixed routes/Oral unpub. obs.	15·60 (4·92 to 26·28)	
Cholesterol: Individuals follow-up time	1 yr or less[15,19,21,23]	−3·25 (−15·19 to 8·70)	0·02
	More than 1 yr unpub. obs.	15·60 (4·92 to 26·28)	
Cholesterol: Individuals lost to follow-up	None reported[23]	3·74 (−7·80 to 15·28)	0·14
	Any loss of patients unpub. obs.	15·60 (4·92 to 26·28)	
LDL: Route of hormonal administration	IM[15,19,21,23]	0·51 (−13·01 to 14·04)	0·38
	Mixed routes unpub. obs.	7·80 (−1·33 to 16·93)	
LDL: Individuals follow-up time	1 yr or less[15,19,21,23]	0·51 (−13·01 to 14·04)	0·38
	More than 1 yr unpub. obs.	7·80 (−1·33 to 16·93)	
LDL: Individuals lost to follow-up	None reported[23]	6·89 (−3·91 to 17·69)	0·90
	Any loss of patients unpub. obs.	7·80 (−1·33 to 16·93)	
HDL: Route of hormonal administration	IM[15,19,21,23]	−6·67 (13·38 to 0·04)	0·47
	Mixed routes unpub. obs.	−3·90 (−0·35 to −7·45)	
HDL: Individuals follow-up time	1 yr or less[15,19,21,23]	−6·67 (13·38 to 0·04)	0·47
	More than 1 yr unpub. obs.	−3·90 (−0·35 to −7·45)	
HDL: Individuals lost to follow-up	None reported[23]	−10·70 (−5·98 to −15·42)	0·02
	Any loss of patients unpub. obs.	−3·90 (−0·35 to −7·45)	
Triglycerides: Route of hormonal administration	IM[15,19,23]	14·40 (4·51 to 24·30)	0·00
	Mixed routes unpub. obs.	97·90 (57·01 to 138·79)	
Triglycerides: Individuals follow-up time	1 yr or less[15,19,23]	14·40 (4·51 to 24·30)	0·00
	More than 1 yr unpub. obs.	97·90 (57·01 to 138·79)	
Triglycerides: Individuals lost to follow-up	None reported[23]	30·29 (5·97 to 54·61)	0·01
	Any loss of patients unpub. obs.	97·90 (57·01 to 138·79)	
SBP: Route of hormonal administration	IM[15,19,23]	1·39 (−0·04 to 2·82)	0·26
	Mixed routes unpub. obs.	4·00 (−0·33 to 8·33)	
SBP: Individuals follow-up time	1 yr or less[15,19,23]	1·39 (−0·04 to 2·82)	0·26
	More than 1 yr unpub. obs.	4·00 (−0·33 to 8·33)	
SBP: Individuals lost to follow-up	None reported[23]	4·28 (0·36 to 8·20)	0·93
	Any loss of patients unpub. obs.	4·00 (−0·33 to 8·33)	
DBP: Route of hormonal administration	IM[15,19,23]	1·73 (−1·04 to 4·51)	0·75
	Mixed routes unpub. obs.	1·10 (−1·59 to 3·79)	
DBP: Individuals follow-up time	1 yr or less[15,19,23]	1·73 (−1·04 to 4·51)	0·75
	More than 1 yr unpub. obs.	1·10 (−1·59 to 3·79)	
DBP: Individuals lost to follow-up	None reported[23]	2·86 (0·57 to 5·15)	0·33
	Any loss of patients unpub. obs.	1·10 (−1·59 to 3·79)	

Subgroup analyses of outcomes not reported in this table were unfeasible due to sparse data
CI, confidence interval; IM, intramuscular.

independent reviewer pairs) and the parsimonious analysis plan.

Implications for research and practice

The uncertainty in relation to cardiovascular events bears on the recommendations for using sex steroids to achieve the desired sex. Future research is needed to ascertain harms of hormonal therapies in this context. It is possible to conduct randomized trials nested within these cohorts to test the relative efficacy and safety of different sex steroid administration approaches. It is also possible to use registries of transsexual individuals to characterize individuals with and without cardiovascular events at a given point in time (sufficiently long after sex steroid use starts) and to identify what risk factors contributed to this situation. High-quality observational studies in which baseline risk of cardiovascular disease is assessed and balanced between study arms and proper ascertainment of exposure and outcome are also feasible and desirable. For clinicians involved in prescribing cross-sex hormones, this review highlights the very low quality of evidence and encourages them to convey this uncertainty to their patients. Treatment decisions in the light of low-quality evidence should be made based on patients' values, preferences, resources, cultural and social factors.[34,35]

Conclusions

Very low-quality evidence, downgraded due to methodological limitations of included studies, imprecision and heterogeneity, suggests that cross-sex hormone therapies increase serum triglycerides in MF and FM and have a trivial effect on HDL-cholesterol and systolic blood pressure in FM. Data about patient important outcomes are sparse and inconclusive.

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Competing interests/financial disclosure

MBE, MZG, MHM, PJE and VMM have nothing to declare.

References

1 American Psychiatric Association. (2000) *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn, Text Revision. American Psychiatric Association, Washington, DC, pp. 576–582.
2 Benjamin, H. (1967) Transvestism and transsexualism in the male and female. *Journal of Sex Research*, **3**, 107–127.
3 Gooren, L. (2005) Hormone treatment of the adult transsexual patient. *Hormone Research*, **64**(Suppl. 2), 31–36.
4 Gooren, L.J. & Giltay, E.J. (2008) Review of studies of androgen treatment of female-to-male transsexuals: effects and risks of administration of androgens to females. *Journal of Sexual Medicine*, **5**, 765–776.
5 Hulley, S., Grady, D., Bush, T. *et al.* (1998) Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. *Journal of the American Medical Association*, **280**, 605–613.
6 Rossouw, J.E., Anderson, G.L., Prentice, R.L. *et al.* (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *Journal of the American Medical Association*, **288**, 321–333.
7 [No authors listed] (1973) The Coronary Drug Project. Findings leading to discontinuation of the 2·5-mg day estrogen group. The coronary Drug Project Research Group. *Journal of the American Medical Association*, **226**, 652–657.
8 Haddad, R.M., Kennedy, C.C., Caples, S.M. *et al.* (2007) Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clinic Proceedings*, **82**, 29–39.
9 Wierman, M.E., Basson, R., Davis, S.R. *et al.* (2006) Androgen therapy in women: an endocrine society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism*, **91**, 3697–3710.
10 Stroup, D.F., Berlin, J.A., Morton, S.C. *et al.* (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *Journal of the American Medical Association*, **283**, 2008–2012.
11 DerSimonian, R. & Laird, N. (1986) Meta-analysis in clinical trials. *Controlled Clinical Trials*, **7**, 177–188.
12 Wiebe, N., Vandermeer, B., Platt, R.W. *et al.* (2006) A systematic review identifies a lack of standardization in methods for handling missing variance data. *Journal of Clinical Epidemiology*, **59**, 342–353.
13 Higgins, J.P., Thompson, S.G., Deeks, J.J. *et al.* (2003) Measuring inconsistency in meta-analyses. *British Medical Journal*, **327**, 557–560.
14 Asscheman, H., Gooren, L.J. & Eklund, P.L. (1989) Mortality and morbidity in transsexual patients with cross-gender hormone treatment. *Metabolism: Clinical and Experimental*, **38**, 869–873.
15 Berra, M., Armillotta, F., D'Emidio, L. *et al.* (2006) Testosterone decreases adiponectin levels in female to male transsexuals. *Asian Journal of Andrology*, **8**, 725–729.
16 Damewood, M.D., Bellantoni, J.J., Bachorik, P.S. *et al.* (1989) Exogenous estrogen effect on lipid/lipoprotein cholesterol in transsexual males. *Journal of Endocrinological Investigation*, **12**, 449–454.
17 De Cuypere, G., T'Sjoen, G., Beerten, R. *et al.* (2005) Sexual and physical health after sex reassignment surgery. *Archives of Sexual Behavior*, **34**, 679–690.
18 Dittrich, R., Binder, H., Cupisti, S. *et al.* (2005) Endocrine treatment of male-to-female transsexuals using gonadotropin-releasing hormone agonist. *Experimental and Clinical Endocrinology and Diabetes*, **113**, 586–592.
19 Elbers, J.M.H., Giltay, E.J., Teerlink, T. *et al.* (2003) Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. *Clinical Endocrinology*, **58**, 562–571.
20 Giltay, E.J., Verhoef, P., Gooren, L.J. *et al.* (2003) Oral and transdermal estrogens both lower plasma total homocysteine in male-to-female transsexuals. *Atherosclerosis*, **168**, 139–146.

21 Jacobeit, J.W., Gooren, L.J. & Schulte, H.M. (2007) Long-acting intramuscular testosterone undecanoate for treatment of female-to-male transgender individuals. *Journal of Sexual Medicine*, **4**, 1479–1484.
22 Mueller, A., Binder, H., Cupisti, S. *et al.* (2006) Effects on the male endocrine system of long-term treatment with gonadotropin-releasing hormone agonists and estrogens in male-to-female transsexuals. *Hormone Metabolic Research*, **38**, 183–187.
23 Mueller, A., Kiesewetter, F., Binder, H. *et al.* (2007) Long-term administration of testosterone undecanoate every 3 months for testosterone supplementation in female-to-male transsexuals. *Journal of Clinical Endocrinology and Metabolism*, **92**, 3470–3475.
24 Prior, J.C., Vigna, Y.M. & Watson, D. (1989) Spironolactone with physiological female steroids for presurgical therapy of male-to-female transsexualism. *Archives of Sexual Behavior*, **18**, 49–57.
25 Schlatterer, K., Yassouridis, A., von Werder, K. *et al.* (1998) A follow-up study for estimating the effectiveness of a cross-gender hormone substitution therapy on transsexual patients. *Archives of Sexual Behavior*, **27**, 475–492.
26 Toorians, A.W.F.T., Thomassen, M.C.L.G.D., Zweegman, S. *et al.* (2003) Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. *Journal of Clinical Endocrinology and Metabolism*, **88**, 5723–5729.
27 van Kesteren, P.J., Asscheman, H., Megens, J.A. *et al.* (1997) Mortality and morbidity in transsexual subjects treated with cross-sex hormones. *Clinical Endocrinology*, **47**, 337–342.
28 Wilson, R., Jenkins, C., Miller, H. *et al.* (2006) The effect of oestrogen on cytokine and antioxidant levels in male to female transsexual patients. *Maturitas*, **55**, 14–18.
29 Giltay, E.J., Elbers, J.M.H., Gooren, L.J.G. *et al.* (1998) Visceral fat accumulation is an important determinant of PAI-1 levels in young, nonobese men and women: modulation by cross-sex hormone administration. *Arteriosclerosis, Thrombosis, and Vascular Biology*, **18**, 1716–1722.
30 Giltay, E.J., Gooren, L.J., Emeis, J.J. *et al.* (2000) Oral, but not transdermal, administration of estrogens lowers tissue-type plasminogen activator levels in humans without affecting endothelial synthesis. *Arteriosclerosis, Thrombosis, and Vascular Biology*, **20**, 1396–1403.
31 Giltay, E.J., Hoogeveen, E.K., Elbers, J.M. *et al.* (1998) Effects of sex steroids on plasma total homocysteine levels: a study in transsexual males and females. *Journal of Clinical Endocrinology and Metabolism*, **83**, 550–553.
32 Giltay, E.J., Lambert, J. & Gooren, L.J. (1999) Sex steroids, insulin, and arterial stiffness in women and men. *Hypertension*, **34**, 590–597.
33 Gandhi, G.Y., Murad, M.H., Fujiyoshi, A. *et al.* (2008) Patient-important outcomes in registered diabetes trials. *Journal of the American Medical Association*, **299**, 2543–2549.
34 Murad, M.H., Swiglo, B.A., Sidawy, A.N. *et al.* (2008) Methodology for clinical practice guidelines for the management of arteriovenous access. *Journal of Vascular Surgery*, **48**, 26S–30S.
35 Swiglo, B.A., Murad, M.H., Schunemann, H.J. *et al.* (2008) A case for clarity, consistency, and helpfulness: state-of-the-art clinical practice guidelines in endocrinology using the grading of recommendations, assessment, development, and evaluation system. *Journal of Clinical Endocrinology and Metabolism*, **93**, 666–673.

EVALUATION OF EVIDENCE: APPLIED BEHAVIOR ANALYSIS FOR AUTISM SPECTRUM DISORDERS

What are we trying to do? Oregon Senate Bill 365 was passed in 2013. This bill directs the Health Evidence Review Commission (HERC) to evaluate the evidence related to applied behavior analysis (ABA) for the treatment of autism spectrum disorder (ASD) in children that receive services as determined by the Prioritized List of Health Services under the Oregon Health Plan (OHP).

The history of coverage of treatment for ASD by OHP

1) This issue was last examined in 2008 by the Oregon Health Resources Commission. Currently, applied behavior analysis is not covered by OHP. Individuals may receive up to eight hours of treatment per month for the behaviors associated with ASD.
2) ASD often exists with other conditions, and these conditions have their own considerations for treatment, most of which are covered. Short-term rehabilitation and certain medicines are also covered.

What has been done so far?

1) HERC met August 8, 2013, discussed the process for completion of this evaluation of evidence, and referred the issue to the Evidence-Based Guidelines Subcommittee (EBGS) for further discussion. On September 12, 2013, the EbGS reviewed the initial draft evaluation of evidence, heard public testimony and requested additional research by staff.
2) EbGS continued discussions at the November 7, 2013 meeting where it approved a draft evaluation of the evidence and preliminary conclusions that were released for public comment.
3) During a 30-day written public comment period that ended on December 16, 2013, 28 individuals submitted comments along with 356 citations for consideration.
4) Three ad hoc experts have been appointed to assist the subcommittee with its review of the evidence.
    a. Eric Fombonne, MD (Professor, OHSU Dept. of Psychiatry)
    b. Eric Larsson, PhD, LP, BCBA-D (Lovaas Institute for Early Intervention, Midwest Headquarters)
    c. Katharine Elizabeth Zuckerman, MD, MPH, FAAP (Assistant Professor, OHSU Division of General Pediatrics and Child and Adolescent Health Measurement Initiative)
5) The Evidence-based Guidelines Subcommittee had planned to continue discussions at its February 7 meeting, but the meeting was cancelled due to a snowstorm, and additional meetings for this topic have been scheduled for March 20, 2014 and April 24, 2014.

EVALUATION OF EVIDENCE: APPLIED BEHAVIOR ANALYSIS FOR AUTISM SPECTRUM DISORDERS

What are the initial conclusions based on the evidence?

1) The evaluation will not be final until after the consideration of the public comments. In the initial review of the evidence, EbGS determined that evidence indicates benefit for certain types of ABA in children with ASD between the ages of 2-12.
2) Based on the initial review of the evidence, EbGS has so far found insufficient evidence that ABA is effective in children with ASD who are over the age of 12.

What happens now?

1) On March 13, 2014 the VbBS will discuss implementation considerations, to provide guidance to staff in developing coverage parameters for this service.
2) Once finalized after considering the written public comment, the EbGS evaluation and conclusions will then go to the Value-Based Benefits Subcommittee (VbBS). VbBS will use the EbGS conclusions to determine what changes may be needed to the Prioritized List of Health Services and if there are any issues that would be involved in implementing these changes in OHP.
3) The evidence evaluation and any changes to the Prioritized List will eventually need final approval by the full HERC, which has members from many areas of health care (doctors, nurses, chiropractic, patients, health plan administrators, and more).
4) Any changes to the Prioritized List affecting OHP coverage of ABA would go into effect sometime between October 1, 2014 and April 1, 2015.

How can you participate?

1) You can subscribe to the HERC website at www.oregon.gov/OHA/OHPR/Pages/HERC/ to receive notifications of future meetings and look at materials being discussed.
2) You can attend the meetings, which are open to the public, and provide verbal testimony during time set aside for public comment.

Applied Behavior Analysis for Autism

Question: If coverage for applied behavior analysis (ABA) treatment for autism is adopted, what limits should be in place for intensity and duration of treatment?

Question source: EbGS, HERC staff

Issue: The EbGS has been reviewing ABA treatment for autism and will likely have their evidence review ready for presentation to the HERC in May, 2014. The draft EbGS report recommends coverage of ABA treatments for younger children ages 2-12. However, the EbGS review is not expected to include recommendations regarding any limitations for ABA (number of visits, frequency, duration etc.).

This VbBS conversation will be begin discussions of potential intensity and duration limits while EbGS completes its process. They have completed the public comment period and will have follow up meetings to potentially finalize the draft evidence review in March and possibly April. They have chosen to remain silent on issues of intensity and duration of treatment because of the dearth of evidence to address this issue. Recommendations on specific draft language for a Guideline Note based on EbGS Draft evidence review will be presented at the following VbBS meeting once they have approved final language.

Senate Bill 365 (see attached for complete bill)
Oregon Senate Bill 365 was passed by the Oregon legislature in the 2013 regular session. That bill establishes requirements for state-regulated commercial health plans to approve and manage autism treatment, including ABA therapy and any other medical or mental health services identified in an individualized treatment plan. The law applies to patients who seek care before age nine, covering up to 25 hours of ABA per week, and continuing as long as medically necessary. Health plans that provide coverage to OEBB and PEBB are required to begin coverage in 2015, and all other health plans are required to begin coverage in 2016. The bill required HERC to evaluate the evidence for ABA and make a prioritization decision that will determine coverage for OHP.

Applied behavior analysis is defined in the bill as the following:

> The design, implementation and evaluation of environmental modifications, using behavioral stimuli and consequences, to produce significant improvement in human social behavior, including the use of direct observation, measurement and functional analysis of the relationship between environment and behavior and that is provided by:
>
> > (i) A licensed health care professional registered under section 3 of this 2013 Act;
> > (ii) A behavior analyst or an assistant behavior analyst licensed under section 3 of this 2013 Act; or
> > (iii) A behavior analysis interventionist registered under section 3 of this 2013 Act.
>
> "Applied behavior analysis" excludes psychological testing, neuropsychology, psychotherapy, cognitive therapy, sex therapy, psychoanalysis, hypnotherapy and long-term counseling as treatment modalities.

Current Prioritized List information:
Line: 313
Condition: AUTISM SPECTRUM DISORDERS (See Guideline Notes 64,65,75)
Treatment: CONSULTATION/MEDICATION MANAGEMENT/LIMITED BEHAVIORAL MODIFICATION

ICD-10: F84.0,F84.3,F84.5,F84.8,F84.9
CPT: 90785,90832-90840,90846-90849,90882,90887,96101,96118,98966-98969, 99051,99060,99070,99078,99201-99215,99281-99285,99354-99378,99381-99404,99408-99412,99429,99441-99444,99487-99496,99605-99607
HCPCS: G0176,G0177,G0396,G0397,G0459,G0463,H0023,H0032,H0034,H0038, H2010,H2011,H2014,H2027,H2032,S9484,T1016

Current guideline
GUIDELINE NOTE 75, AUTISM SPECTRUM DISORDERS
Line 334
There is limited evidence of the effectiveness of treatment (e.g., Applied Behavioral Analysis) for Autism Spectrum Disorders (ASD). However, effective treatments may be available for co-morbid conditions such as mood disorders. When treating co-morbid conditions, that condition, not an ASD diagnosis, should be the primary diagnosis for billing purposes. The treatment of co-morbid mental health conditions should be consistent with the treatment methods, frequency, and duration normally applied to those diagnoses. Treatment of neurologic dysfunctions that may be seen in individuals with an ASD diagnosis are prioritized according to the four dysfunction lines found on the Prioritized List (Lines 78, 318, 375 and 407). Treatment for associated behaviors, such as agitation, that do not meet the criteria for co-morbid mental health diagnoses should be limited in frequency to a maximum of 8 hours of behavioral health service per month, subject to utilization management review by the mental health organization (MHO) or other relevant payer.

<u>New CPT codes for ABA therapy</u>

1) New category III CPT codes have been published by the AMA effective July 1, 2014
    a. 0359T-0363T (adaptive behavior assessments)
    b. See attached AMA document for information on definition of these codes

Of note, DMAP has a rule that excludes the use of temporary codes. This rule would need to be deleted. As a result, there is a good likelihood of a number of temporary codes being brought to VBBS/HERC for review.

Draft EGBS evidence review:

SUMMARY CONCLUSIONS

Applied behavior analysis (ABA), including early intensive behavioral intervention (EIBI), is recommended for coverage for treatment of autism spectrum disorder in children ages 2-12 (*strong recommendation*).

> Rationale: This strength of recommendation was based on sufficient (moderate quality) evidence and expert input, including testimony on parent/caregiver values and preferences.

Parent/caregiver involvement and training is recommended to be a component of treatment *(strong recommendation).*

> Rationale: Evidence and expert input indicated that parental involvement in ABA is a key part of effective treatment.

Initial coverage should be provided for up to six months. Ongoing coverage should be based on demonstrated progress towards meaningful predefined objectives (objectives should be achieved as a result of the intervention(s) under scrutiny, over and beyond gains that would be expected to arise from maturation alone) using a standardized, multimodal assessment, no more frequently than every six months *(strong recommendation).*

> Rationale: Ensuring that patients are making meaningful progress is important to ensure quality outcomes and effective use of resources. The six month assessment was chosen based on expert input to allow for sufficient time for progress while not being burdensome to providers and plans.

In studies showing benefit, interventions ranged from less than two to 40 hours per week and had a duration of 10 weeks to three years. No specific minimum duration or intensity has been determined to be required for efficacy.

ABA is not recommended for coverage for treatment of autism spectrum disorder in persons over the age of 12 (*weak recommendation*).

> Rationale: There is insufficient evidence to support ABA treatment at older ages.

Note: The evidence for the treatment of conditions comorbid with autism spectrum disorder is beyond the scope of this evidence summary.

ABA/EIBI intensity information in EGBS report

1) RCTs of EIBI found improvement in autism symptoms in children treated with EIBI vs controls (4 out of 5 studies). Intensity ranged from a mean of 13 to 26 hours per week. Interventions lasted from 6 months to 2 years
2) The 2014 AHRQ report on ABA treatment found that
    a. Young children receiving high intensity applied behavior analysis-based early intervention over extended time frames commonly displayed substantial improvement in cognitive functioning and language skills relative to community controls.
    b. The AHRQ report included 27 studies which addressed ABA, parent training, or similar treatments. With regard to the impact of intensity or duration on treatment effectiveness, treatment duration ranged from 6 weeks to 2 years, and intensity ranged from 1 to 30 hours per week.
    c. In a retrospective cohort study, treatment duration was not determined to be a significant predictor of outcome after controlling for other variables.
    d. In one parent training RCT evaluating ESDM, total intervention hours were associated with reduced restrictive and repetitive behavior and nonsocial orienting and improved developmental quotient and vocabulary comprehension.
    e. In a prospective cohort study, hours of intervention did not correlate with outcomes.
    f. Summary: A growing evidence base suggests that children receiving early intensive behavioral and developmental interventions (e.g., many hours of intervention a week over the course of 1-2 years) show substantial improvements in cognitive and language skills over time compared with children receiving low-intensity interventions, community controls, and eclectic non-ABA based intervention approaches.

Applied Behavior Analysis for Autism

Items needing consideration

1) Comprehensive versus focused ABA. Should these be distinguished? With different requirements for evaluation and demonstrated progress?
2) Do you want to include duration and intensity in the guideline for both comprehensive and focused ABA? If yes, is there specific information you wish for additionally?
3) Current coverage of 8 hours of behavioral health coverage a month. How does this relate to new possible coverage?
4) The law says that therapy must be started before age 9. Much more evidence exists for younger, rather than older ages.
5) If a child fails to demonstrate progress with comprehensive ABA, should they have access to focused, more short term interventions?
6) What about self-injury and intellectual disability?

HERC staff recommendations:

1) Plan to delete current guideline note 75
2) Add CPT 0359T-0363T (adaptive behavior assessments) to line 313 AUTISM SPECTRUM DISORDERS
    a. More details in guideline?
3) Discuss desired components of a new guideline for ABA/EIBI for autism spectrum disorders
    a. Age(s) of children to be included in guideline
        i. Likely will be better defined in final EGBS report.
    b. Hours of comprehensive ABA/EIBI to be covered per week
        i. SB365 requires commercial plans to cover up to 25 hours per week
        ii. Studies range from 1 to 40 hours per week
        iii. No relationship has been shown with intensity and outcomes within comprehensive ABA/EIBI
    c. Should focused ABA interventions for specific behavior areas be covered if child does not qualify for ongoing comprehensive ABA treatment?
        i. How does this relate to current coverage of 8 hours per month?
        ii. What about maintenance of previously effective interventions?
    d. Requirements for additional treatment periods
        i. How specific? Define the tests needed to be conducted (i.e. specific assessment tools) or simply have a statement that objective evidence of demonstrated progress towards predefined goals (that surpasses gains based on maturation) is required?
        ii. Note: assessments cannot be more frequent than every 6 months per SB365

    e. How to include PT/OT/speech services
        i. Consider adopting language such as: ABA services are provided in addition to any rehabilitative services (physical therapy, occupational therapy, speech therapy) included in Guideline Note 6, REHABILITATIVE THERAPIES that are otherwise indicated for a different qualifying diagnosis.

Enrolled
Senate Bill 365

Sponsored by Senators BATES, EDWARDS; Senators DEVLIN, HASS, JOHNSON, Representatives CONGER, MCLANE, PARRISH (Presession filed.)

CHAPTER .....

AN ACT

Relating to treatment for autism spectrum disorders; creating new provisions; amending ORS 676.610, 676.612, 676.613, 676.622, 676.625, 676.992, 743A.190 and 750.055; and declaring an emergency.

Be It Enacted by the People of the State of Oregon:

SECTION 1. Section 2 of this 2013 Act is added to and made a part of the Insurance Code.

SECTION 2. (1) As used in this section and sections 3 and 3a of this 2013 Act:

(a)(A) "Applied behavior analysis" means the design, implementation and evaluation of environmental modifications, using behavioral stimuli and consequences, to produce significant improvement in human social behavior, including the use of direct observation, measurement and functional analysis of the relationship between environment and behavior and that is provided by:

(i) A licensed health care professional registered under section 3 of this 2013 Act;

(ii) A behavior analyst or an assistant behavior analyst licensed under section 3 of this 2013 Act; or

(iii) A behavior analysis interventionist registered under section 3 of this 2013 Act.

(B) "Applied behavior analysis" excludes psychological testing, neuropsychology, psychotherapy, cognitive therapy, sex therapy, psychoanalysis, hypnotherapy and long-term counseling as treatment modalities.

(b) "Autism spectrum disorder" has the meaning given that term in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) published by the American Psychiatric Association.

(c) "Diagnosis" means medically necessary assessment, evaluation or testing.

(d) "Health benefit plan" has the meaning given that term in ORS 743.730.

(e) "Medically necessary" means in accordance with the definition of medical necessity that is specified in the policy or certificate for the health benefit plan and that applies to all covered services under the plan.

(f) "Treatment for autism spectrum disorder" includes applied behavior analysis for up to 25 hours per week and any other mental health or medical services identified in the individualized treatment plan, as described in subsection (6) of this section.

(2) A health benefit plan shall provide coverage of:

(a) The screening for and diagnosis of autism spectrum disorder by a licensed neurologist, pediatric neurologist, developmental pediatrician, psychiatrist or psychologist, who has experience or training in the diagnosis of autism spectrum disorder; and

(b) Medically necessary treatment for autism spectrum disorder and the management of care, for an individual who begins treatment before nine years of age, subject to the requirements of this section.

(3) This section does not require coverage for:

(a) Services provided by a family or household member;

(b) Services that are custodial in nature or that constitute marital, family, educational or training services;

(c) Custodial or respite care, equine assisted therapy, creative arts therapy, wilderness or adventure camps, social counseling, telemedicine, music therapy, neurofeedback, chelation or hyperbaric chambers;

(d) Services provided under an individual education plan in accordance with the Individuals with Disabilities Education Act, 20 U.S.C. 1400 et seq.;

(e) Services provided through community or social programs; or

(f) Services provided by the Department of Human Services or the Oregon Health Authority, other than employee benefit plans offered by the department and the authority.

(4) An insurer may not terminate coverage or refuse to issue or renew coverage for an individual solely because the individual has received a diagnosis of autism spectrum disorder or has received treatment for autism spectrum disorder.

(5) Coverage under this section may be subject to utilization controls that are reasonable in the context of individual determinations of medical necessity. An insurer may require:

(a) An autism spectrum disorder diagnosis by a professional described in subsection (2)(a) of this section if the original diagnosis was not made by a professional described in subsection (2)(a) of this section.

(b) Prior authorization for coverage of a maximum of 25 hours per week of applied behavior analysis recommended in an individualized treatment plan approved by a professional described in subsection (2)(a) of this section for an individual with autism spectrum disorder, as long as the insurer makes a prior authorization determination no later than 30 calendar days after receiving the request for prior authorization.

(6) If an individual is receiving applied behavior analysis, an insurer may require submission of an individualized treatment plan, which shall include all elements necessary for the insurer to appropriately determine coverage under the health benefit plan. The individualized treatment plan must be based on evidence-based screening criteria. An insurer may require an updated individualized treatment plan, not more than once every six months, that includes observed progress as of the date the updated plan was prepared, for the purpose of performing utilization review and medical management. The insurer may require the individualized treatment plan to be approved by a professional described in subsection (2)(a) of this section, and to include the:

(a) Diagnosis;

(b) Proposed treatment by type;

(c) Frequency and anticipated duration of treatment;

(d) Anticipated outcomes stated as goals, including specific cognitive, social, communicative, self-care and behavioral goals that are clearly stated, directly observed and continually measured and that address the characteristics of the autism spectrum disorder; and

(e) Signature of the treating provider.

(7)(a) Once coverage for applied behavior analysis has been approved, the coverage continues as long as:

(A) The individual continues to make progress toward the majority of the goals of the individualized treatment plan; and

(B) Applied behavior analysis is medically necessary.

(b) An insurer may require periodic review of an individualized treatment plan, as described in subsection (6) of this section, and modification of the individualized treatment plan

if the review shows that the individual receiving the treatment is not making substantial clinical progress toward the goals of the individualized treatment plan.

(8) Coverage under this section may be subject to requirements and limitations no more restrictive than those imposed on coverage or reimbursement of expenses arising from the treatment of other medical conditions under the policy or certificate, including but not limited to:

(a) Requirements and limitations regarding in-network providers; and

(b) Provisions relating to deductibles, copayments and coinsurance.

(9) This section applies to coverage for up to 25 hours per week of applied behavior analysis for an individual if the coverage is first requested when the individual is under nine years of age. This section does not limit coverage for any services that are otherwise available to an individual under ORS 743A.168 or 743A.190, including but not limited to:

(a) Treatment for autism spectrum disorder other than applied behavior analysis or the services described in subsection (3) of this section.

(b) Applied behavior analysis for more than 25 hours per week; or

(c) Applied behavior analysis for an individual if the coverage is first requested when the individual is nine years of age or older.

(10) Coverage under this section includes treatment for autism spectrum disorder provided in the individual's home or a licensed health care facility or, for treatment provided by a licensed health care professional registered with the Behavior Analysis Regulatory Board or a behavior analyst or assistant behavior analyst licensed under section 3 of this 2013 Act, in a setting approved by the health care professional, behavior analyst or assistant behavior analyst.

(11) An insurer that provides coverage of applied behavior analysis in accordance with a decision of an independent review organization that was made prior to January 1, 2016, shall continue to provide coverage, subject to modifications made in accordance with subsection (7) of this section.

(12) ORS 743A.001 does not apply to this section.

SECTION 3. (1) There is created, within the Oregon Health Licensing Agency, the Behavior Analysis Regulatory Board consisting of seven members appointed by the Governor, including:

(a) Three members who are licensed by the board;

(b) One member who is a licensed psychiatrist or developmental pediatrician, with experience or training in treating autism spectrum disorder;

(c) One member who is a licensed psychologist registered with the board;

(d) One member who is a licensed speech-language pathologist registered with the board; and

(e) One member of the general public who does not have a financial interest in the provision of applied behavior analysis and does not have a ward or family member who has been diagnosed with autism spectrum disorder.

(2) Not more than one member of the Behavior Analysis Regulatory Board may be an employee of an insurer.

(3) The term of office of each member is four years, but a member serves at the pleasure of the Governor. Before the expiration of the term of a member, the Governor shall appoint a successor whose term begins on November 1 next following. A member is eligible for reappointment. If there is a vacancy for any cause, the Governor shall make an appointment to become immediately effective for the unexpired term.

(4) A member of the Behavior Analysis Regulatory Board is entitled to compensation and expenses as provided in ORS 292.495.

(5) The Behavior Analysis Regulatory Board shall select one of its members as chairperson and another as vice chairperson, for such terms and with duties and powers necessary for the performance of the functions of such offices as the board determines.

(6) A majority of the members of the Behavior Analysis Regulatory Board constitutes a quorum for the transaction of business.

(7) The Behavior Analysis Regulatory Board shall meet at least once every three months at a place, day and hour determined by the board. The board may also meet at other times and places specified by the call of the chairperson or of a majority of the members of the board.

(8) In accordance with ORS chapter 183, the Behavior Analysis Regulatory Board shall establish by rule criteria for the:

(a) Licensing of:

(A) Behavior analysts; and

(B) Assistant behavior analysts; and

(b) Registration of:

(A) Licensed health care professionals; and

(B) Behavior analysis interventionists.

(9) The criteria for the licensing of a behavior analyst must include, but are not limited to, the requirement that the applicant:

(a) Be certified by the Behavior Analyst Certification Board, Incorporated, as a Board Certified Behavior Analyst; and

(b) Have successfully completed a criminal records check.

(10) The criteria for the licensing of an assistant behavior analyst must include, but are not limited to, the requirement that the applicant:

(a) Be certified by the Behavior Analyst Certification Board, Incorporated, as a Board Certified Assistant Behavior Analyst;

(b) Be supervised by a behavior analyst who is licensed by the Behavior Analysis Regulatory Board; and

(c) Have successfully completed a criminal records check.

(11) The criteria for the registration of a behavior analysis interventionist must include, but are not limited to, the requirement that the applicant:

(a) Have completed coursework and training prescribed by the Behavior Analysis Regulatory Board by rule;

(b) Receive ongoing oversight by a licensed behavior analyst or a licensed assistant behavior analyst, or by another licensed health care professional approved by the board; and

(c) Have successfully completed a criminal records check.

(12) In accordance with applicable provisions of ORS chapter 183, the Behavior Analysis Regulatory Board shall adopt rules:

(a) Establishing standards and procedures for the licensing of behavior analysts and assistant behavior analysts and for the registration of licensed health care professionals and behavior analysis interventionists in accordance with this section;

(b) Establishing guidelines for the professional methods and procedures to be used by individuals licensed and registered under this section;

(c) Governing the examination of applicants for licenses and registrations under this section and the renewal, suspension and revocation of the licenses and registrations; and

(d) Establishing fees sufficient to cover the costs of administering the licensing and registration procedures under this section.

(13) The Behavior Analysis Regulatory Board shall issue a license to an applicant who:

(a) Files an application in the form prescribed by the board;

(b) Pays fees established by the board; and

(c) Demonstrates to the satisfaction of the board that the applicant meets the criteria adopted under this section.

(14) The Behavior Analysis Regulatory Board shall establish the procedures for the registration of licensed health care professionals and behavior analysis interventionists.

(15) All moneys received by the Behavior Analysis Regulatory Board under subsection (13) of this section shall be paid into the General Fund of the State Treasury and credited to the Oregon Health Licensing Agency Account.

(16) An individual who has not been licensed or registered by the Behavior Analysis Regulatory Board in accordance with criteria and standards adopted under this section may not claim reimbursement for services described in section 2 of this 2013 Act under a health benefit plan or under a self-insured health plan offered by the Public Employees' Benefit Board or the Oregon Educators Benefit Board.

SECTION 3a. (1) Notwithstanding the composition of the Behavior Analysis Regulatory Board specified in section 3 of this 2013 Act, for the period beginning on the operative date of section 3 of this 2013 Act and ending on October 31, 2015, the board shall consist of seven members appointed by the Governor, including:

(a) Three members who are certified by the Behavior Analyst Certification Board, Incorporated, as Board Certified Behavior Analysts;

(b) One member who is a licensed psychiatrist or developmental pediatrician and who has experience or training in applied behavior analysis;

(c) One member who is a licensed psychologist and who has experience in the diagnosis or treatment of autism spectrum disorders;

(d) One member who is a licensed speech-language pathologist and who has experience or training in applied behavior analysis; and

(e) One member of the general public who does not have a financial interest in the provision of applied behavior analysis and does not have a ward or family member who has been diagnosed with autism spectrum disorder.

(2) Notwithstanding the term of office specified by section 3 of this 2013 Act, if members first appointed to the Behavior Analysis Regulatory Board under this section continue to serve after October 31, 2015, the board shall adopt a method for establishing the terms of office of board members so that the terms of office do not all expire on the same date.

SECTION 4. Notwithstanding section 3 (16) of this 2013 Act, an individual actively practicing applied behavior analysis on the effective date of this 2013 Act may continue to claim reimbursement from a health benefit plan, the Public Employees' Benefit Board or the Oregon Educators Board for services provided without a license before January 1, 2016.

SECTION 5. The Oregon Health Licensing Agency may take any action before November 1, 2013, that is necessary for the agency to implement the provisions of sections 3 and 3a of this 2013 Act on and after November 1, 2013.

SECTION 6. Not later than August 30, 2013, the Health Evidence Review Commission shall begin the process of evaluating applied behavior analysis, as defined in section 2 of this 2013 Act, as a treatment for autism spectrum disorder, as defined in section 2 of this 2013 Act, for the purpose of updating the list of health services recommended under ORS 414.690. Any adjustments to the list of health services that result from the evaluation process must be implemented not later than:

(1) October 1, 2014, if the adjustments do not require the development of new medical coding; and

(2) April 1, 2015, if the adjustments require the development or adoption of new medical coding.

SECTION 7. ORS 743A.190 is amended to read:

743A.190. (1) A health benefit plan, as defined in ORS 743.730, must cover for a child enrolled in the plan who is under 18 years of age and who has been diagnosed with a pervasive developmental disorder all medical services, including rehabilitation services, that are medically necessary and are otherwise covered under the plan.

(2) The coverage required under subsection (1) of this section, including rehabilitation services, may be made subject to other provisions of the health benefit plan that apply to covered services, including but not limited to:

(a) Deductibles, copayments or coinsurance;

(b) Prior authorization or utilization review requirements; or

(c) Treatment limitations regarding the number of visits or the duration of treatment.

(3) As used in this section:

(a) "Medically necessary" means in accordance with the definition of medical necessity that is specified in the policy, certificate or contract for the health benefit plan and that applies uniformly to all covered services under the health benefit plan.

(b) "Pervasive developmental disorder" means a neurological condition that includes [*Asperger's syndrome,*] autism **spectrum disorder**, developmental delay, developmental disability or mental retardation.

(c) "Rehabilitation services" means physical therapy, occupational therapy or speech therapy services to restore or improve function.

(4) The provisions of ORS 743A.001 do not apply to this section.

(5) The definition of "pervasive developmental disorder" is not intended to apply to coverage required under ORS 743A.168 **or section 2 of this 2013 Act**.

SECTION 8. ORS 750.055, as amended by section 3, chapter 21, Oregon Laws 2012, is amended to read:

750.055. (1) The following provisions of the Insurance Code apply to health care service contractors to the extent not inconsistent with the express provisions of ORS 750.005 to 750.095:

(a) ORS 705.137, 705.139, 731.004 to 731.150, 731.162, 731.216 to 731.362, 731.382, 731.385, 731.386, 731.390, 731.398 to 731.430, 731.428, 731.450, 731.454, 731.488, 731.504, 731.508, 731.509, 731.510, 731.511, 731.512, 731.574 to 731.620, 731.592, 731.594, 731.640 to 731.652, 731.730, 731.731, 731.735, 731.737, 731.750, 731.752, 731.804, 731.844 to 731.992, 731.870 and 743.061.

(b) ORS 732.215, 732.220, 732.230, 732.245, 732.250, 732.320, 732.325 and 732.517 to 732.592, not including ORS 732.582.

(c) ORS 733.010 to 733.050, 733.080, 733.140 to 733.170, 733.210, 733.510 to 733.680 and 733.695 to 733.780.

(d) ORS chapter 734.

(e) ORS 742.001 to 742.009, 742.013, 742.061, 742.065, 742.150 to 742.162, 742.400, 742.520 to 742.540, 743.010, 743.013, 743.018 to 743.030, 743.050, 743.100 to 743.109, 743.402, 743.472, 743.492, 743.495, 743.498, 743.499, 743.522, 743.523, 743.524, 743.526, 743.527, 743.528, 743.529, 743.549 to 743.552, 743.560, 743.600 to 743.610, 743.650 to 743.656, 743.764, 743.804, 743.807, 743.808, 743.814 to 743.839, 743.842, 743.845, 743.847, 743.854, 743.856, 743.857, 743.858, 743.859, 743.861, 743.862, 743.863, 743.864, 743.894, 743.911, 743.912, 743.913, 743.917, 743A.010, 743A.012, 743A.020, 743A.034, 743A.036, 743A.048, 743A.058, 743A.062, 743A.064, 743A.065, 743A.066, 743A.068, 743A.070, 743A.080, 743A.084, 743A.088, 743A.090, 743A.100, 743A.104, 743A.105, 743A.110, 743A.140, 743A.141, 743A.144, 743A.148, 743A.160, 743A.164, 743A.168, 743A.170, 743A.175, 743A.184, 743A.185, 743A.188, 743A.190 and 743A.192 and section 2, chapter 21, Oregon Laws 2012**, and section 2 of this 2013 Act**.

(f) The provisions of ORS chapter 744 relating to the regulation of insurance producers.

(g) ORS 746.005 to 746.140, 746.160, 746.220 to 746.370, 746.600, 746.605, 746.607, 746.608, 746.610, 746.615, 746.625, 746.635, 746.650, 746.655, 746.660, 746.668, 746.670, 746.675, 746.680 and 746.690.

(h) ORS 743A.024, except in the case of group practice health maintenance organizations that are federally qualified pursuant to Title XIII of the Public Health Service Act unless the patient is referred by a physician associated with a group practice health maintenance organization.

(i) ORS 735.600 to 735.650.

(j) ORS 743.680 to 743.689.

(k) ORS 744.700 to 744.740.

(L) ORS 743.730 to 743.773.

(m) ORS 731.485, except in the case of a group practice health maintenance organization that is federally qualified pursuant to Title XIII of the Public Health Service Act and that wholly owns and operates an in-house drug outlet.

(2) For the purposes of this section, health care service contractors shall be deemed insurers.

(3) Any for-profit health care service contractor organized under the laws of any other state that is not governed by the insurance laws of the other state is subject to all requirements of ORS chapter 732.

(4) The Director of the Department of Consumer and Business Services may, after notice and hearing, adopt reasonable rules not inconsistent with this section and ORS 750.003, 750.005, 750.025 and 750.045 that are deemed necessary for the proper administration of these provisions.

SECTION 9. Section 10 of this 2013 Act is added to and made a part of ORS chapter 343.

SECTION 10. (1) Section 2 of this 2013 Act does not limit, replace or affect any obligation of a school district to provide services under an individualized education program to a child with a disability in accordance with the Individuals with Disabilities Education Act, 20 U.S.C. 1400 et seq., or other publicly funded programs to assist individuals with autism spectrum disorder.

(2) Any governmental or educational entity providing services as required under the Individuals with Disabilities Education Act, 20 U.S.C. 1400 et seq., as amended, or other state or federal law requiring the provision of services to individuals with disabilities, is prohibited from reducing, eliminating or shifting required services to coverage provided under section 2 of this 2013 Act.

SECTION 11. In the manner prescribed in ORS chapter 183 for contested cases, the Oregon Health Licensing Agency may impose a form of discipline listed in ORS 676.612 against any person licensed or registered under section 3 of this 2013 Act for any of the prohibited acts listed in ORS 676.612 and for any violation of a rule adopted under section 3 of this 2013 Act.

SECTION 12. ORS 676.610 is amended to read:

676.610. (1)(a) The Oregon Health Licensing Agency is under the supervision and control of a director, who is responsible for the performance of the duties, functions and powers and for the organization of the agency.

(b) The Director of the Oregon Department of Administrative Services shall establish the qualifications for and appoint the Director of the Oregon Health Licensing Agency, who holds office at the pleasure of the Director of the Oregon Department of Administrative Services.

(c) The Director of the Oregon Health Licensing Agency shall receive a salary as provided by law or, if not so provided, as prescribed by the Director of the Oregon Department of Administrative Services.

(d) The Director of the Oregon Health Licensing Agency is in the unclassified service.

(2) The Director of the Oregon Health Licensing Agency shall provide the boards, councils and programs administered by the agency with such services and employees as the agency requires to carry out the agency's duties. Subject to any applicable provisions of the State Personnel Relations Law, the Director of the Oregon Health Licensing Agency shall appoint all subordinate officers and employees of the agency, prescribe their duties and fix their compensation.

(3) The Director of the Oregon Health Licensing Agency is responsible for carrying out the duties, functions and powers under ORS 675.360 to 675.410, 676.605 to 676.625, 676.992, 678.710 to 678.820, 680.500 to 680.565, 687.405 to 687.495, 687.895, 688.701 to 688.734, 688.800 to 688.840, 690.005 to 690.235, 690.350 to 690.415, 691.405 to 691.485 and 694.015 to 694.185 **and sections 3 and 11 of this 2013 Act** and ORS chapter 700.

(4) The enumeration of duties, functions and powers in subsection (3) of this section is not intended to be exclusive or to limit the duties, functions and powers imposed on or vested in the Oregon Health Licensing Agency by other statutes.

SECTION 13. ORS 676.612 is amended to read:

676.612. (1) In the manner prescribed in ORS chapter 183 for contested cases and as specified in ORS 675.385, 678.780, 680.535, 687.445, 688.734, 688.836, 690.167, 690.407, 691.477, 694.147 and 700.111 **and section 11 of this 2013 Act**, the Oregon Health Licensing Agency may refuse to issue or renew, may suspend or revoke or may otherwise condition or limit a certificate, license, permit or registration to practice issued by the agency or may discipline or place on probation a holder

of a certificate, license, permit or registration for commission of the prohibited acts listed in subsection (2) of this section.

(2) A person subject to the authority of a board, council or program listed in ORS 676.606 commits a prohibited act if the person engages in:

(a) Fraud, misrepresentation, concealment of material facts or deception in applying for or obtaining an authorization to practice in this state, or in any written or oral communication to the agency concerning the issuance or retention of the authorization.

(b) Using, causing or promoting the use of any advertising matter, promotional literature, testimonial, guarantee, warranty, label, insignia or any other representation, however disseminated or published, that is false, misleading or deceptive.

(c) Making a representation that the certificate, license, permit or registration holder knew or should have known is false or misleading regarding skill or the efficacy or value of treatment or remedy administered by the holder.

(d) Practicing under a false, misleading or deceptive name, or impersonating another certificate, license, permit or registration holder.

(e) Permitting a person other than the certificate, license, permit or registration holder to use the certificate, license, permit or registration.

(f) Practicing with a physical or mental condition that presents an unreasonable risk of harm to the holder of a certificate, license, permit or registration or to the person or property of others in the course of performing the holder's duties.

(g) Practicing while under the influence of alcohol, controlled substances or other skill-impairing substances, or engaging in the illegal use of controlled substances or other skill-impairing substances so as to create a risk of harm to the person or property of others in the course of performing the duties of a holder of a certificate, license, permit or registration.

(h) Failing to properly and reasonably accept responsibility for the actions of employees.

(i) Employing, directly or indirectly, any suspended, uncertified, unlicensed or unregistered person to practice a regulated occupation or profession subject to the authority of the boards, councils and programs listed in ORS 676.606.

(j) Unprofessional conduct, negligence, incompetence, repeated violations or any departure from or failure to conform to standards of practice in performing services or practicing in a regulated occupation or profession subject to the authority of the boards, councils and programs listed under ORS 676.606.

(k) Conviction of any criminal offense, subject to ORS 670.280. A copy of the record of conviction, certified by the clerk of the court entering the conviction, is conclusive evidence of the conviction. A plea of no contest or an admission of guilt shall be considered a conviction for purposes of this paragraph.

(L) Failing to report any adverse action, as required by statute or rule, taken against the certificate, license, permit or registration holder by another regulatory jurisdiction or any peer review body, health care institution, professional association, governmental agency, law enforcement agency or court for acts or conduct similar to acts or conduct that would constitute grounds for disciplinary action as described in this section.

(m) Violation of a statute regulating an occupation or profession subject to the authority of the boards, councils and programs listed in ORS 676.606.

(n) Violation of any rule regulating an occupation or profession subject to the authority of the boards, councils and programs listed in ORS 676.606.

(o) Failing to cooperate with the agency in any investigation, inspection or request for information.

(p) Selling or fraudulently obtaining or furnishing any certificate, license, permit or registration to practice in a regulated occupation or profession subject to the authority of the boards, councils and programs listed in ORS 676.606, or aiding or abetting such an act.

(q) Selling or fraudulently obtaining or furnishing any record related to practice in a regulated occupation or profession subject to the authority of the boards, councils and programs listed in ORS 676.606, or aiding or abetting such an act.

(r) Failing to pay an outstanding civil penalty or fee that is due or failing to meet the terms of any order issued by the agency that has become final.

(3) For the purpose of requesting a state or nationwide criminal records check under ORS 181.534, the agency may require the fingerprints of a person who is:

(a) Applying for a certificate, license, permit or registration that is issued by the agency;

(b) Applying for renewal of a certificate, license, permit or registration that is issued by the agency; or

(c) Under investigation by the agency.

(4) If the agency places a holder of a certificate, license, permit or registration on probation under subsection (1) of this section, the agency, in consultation with the appropriate board, council or program, may determine and at any time modify the conditions of the probation.

(5) If a certificate, license, permit or registration is suspended, the holder may not practice during the term of suspension. Upon the expiration of the term of suspension, the certificate, license, permit or registration may be reinstated by the agency if the conditions of suspension no longer exist and the holder has satisfied all requirements in the relevant statutes or administrative rules for issuance, renewal or reinstatement.

SECTION 14. ORS 676.613 is amended to read:

676.613. (1) In addition to all other remedies, when it appears to the Oregon Health Licensing Agency that a person is engaged in, has engaged in or is about to engage in any act, practice or transaction that violates any provision of ORS 675.360 to 675.410, 676.617, 678.710 to 678.820, 680.500 to 680.565, 687.405 to 687.495, 688.701 to 688.734, 688.800 to 688.840, 690.005 to 690.235, 690.350 to 690.415, 691.405 to 691.485 or 694.015 to 694.185 **or section 3 of this 2013 Act** or ORS chapter 700, the agency may, through the Attorney General or the district attorney of the county in which the act, practice or transaction occurs or will occur, apply to the court for an injunction restraining the person from the act, practice or transaction.

(2) A court may issue an injunction under this section without proof of actual damages. An injunction issued under this section does not relieve a person from any other prosecution or enforcement action taken for violation of statutes listed in subsection (1) of this section.

SECTION 15. ORS 676.622 is amended to read:

676.622. (1) A transaction conducted through a state or local system or network that provides electronic access to the Oregon Health Licensing Agency information and services is exempt from any requirement under ORS 675.360 to 675.410, 676.605 to 676.625, 676.992, 680.500 to 680.565, 687.405 to 687.495, 688.701 to 688.734, 688.800 to 688.840, 690.005 to 690.235, 690.350 to 690.415, 691.405 to 691.485 and 694.015 to 694.185 **and section 3 of this 2013 Act** and ORS chapter 700, and rules adopted thereunder, requiring an original signature or the submission of handwritten materials.

(2) Electronic signatures subject to ORS 84.001 to 84.061 and facsimile signatures are acceptable and have the same force as original signatures.

SECTION 16. ORS 676.625 is amended to read:

676.625. (1) The Oregon Health Licensing Agency shall establish by rule and shall collect fees and charges to carry out the agency's responsibilities under ORS 676.605 to 676.625 and 676.992 and any responsibility imposed on the agency pertaining to the boards, councils and programs administered and regulated by the agency pursuant to ORS 676.606.

(2) The Oregon Health Licensing Agency Account is established in the General Fund of the State Treasury. The account shall consist of the moneys credited to the account by the Legislative Assembly. All moneys in the account are appropriated continuously to and shall be used by the Oregon Health Licensing Agency for payment of expenses of the agency in carrying out the duties, functions and obligations of the agency, and for payment of the expenses of the boards, councils and programs administered and regulated by the agency pursuant to ORS 676.606. The agency shall keep

a record of all moneys credited to the account and report the source from which the moneys are derived and the activity of each board, council or program that generated the moneys.

(3) Subject to prior approval of the Oregon Department of Administrative Services and a report to the Emergency Board prior to adopting fees and charges credited to the account, the fees and charges may not exceed the cost of administering the agency and the boards, councils and programs within the agency, as authorized by the Legislative Assembly within the agency's budget, as the budget may be modified by the Emergency Board.

(4) All moneys credited to the account pursuant to ORS 675.405, 676.617, 680.525, 687.435, 688.728, 688.834, 690.235, 690.415, 691.479, 694.185 and 700.080 **and section 3 of this 2013 Act**, and moneys credited to the account from other agency and program fees established by the agency by rule, are continuously appropriated to the agency for carrying out the duties, functions and powers of the agency under ORS 676.605 to 676.625 and 676.992 **and section 3 of this 2013 Act**.

(5) The moneys received from civil penalties assessed under ORS 676.992 shall be deposited and accounted for as are other moneys received by the agency and shall be for the administration and enforcement of the statutes governing the boards, councils and programs administered by the agency.

SECTION 17. ORS 676.992 is amended to read:

676.992. (1) Except as provided in subsection (3) of this section, and in addition to any other penalty or remedy provided by law, the Oregon Health Licensing Agency may impose a civil penalty not to exceed $5,000 for each violation of the following statutes and any rule adopted thereunder:

(a) ORS 688.701 to 688.734 (athletic training);

(b) ORS 690.005 to 690.235 (cosmetology);

(c) ORS 680.500 to 680.565 (denture technology);

(d) ORS 687.405 to 687.495 (direct entry midwifery);

(e) ORS 690.350 to 690.415 (tattooing, electrolysis, body piercing, dermal implanting and scarification);

(f) ORS 694.015 to 694.185 (dealing in hearing aids);

(g) ORS 688.800 to 688.840 (respiratory therapy and polysomnography);

(h) ORS chapter 700 (environmental sanitation);

(i) ORS 676.617 (single facility licensure);

(j) ORS 675.360 to 675.410 (sex offender treatment);

(k) ORS 678.710 to 678.820 (nursing home administrators);

(L) ORS 691.405 to 691.485 (dietitians); [*and*]

(m) ORS 676.612 (prohibited acts)**; and**

(n) Section 3 of this 2013 Act (applied behavior analysis).

(2) The agency may take any other disciplinary action that it finds proper, including but not limited to assessment of costs of disciplinary proceedings, not to exceed $5,000, for violation of any statute listed in subsection (1) of this section or any rule adopted under any statute listed in subsection (1) of this section.

(3) Subsection (1) of this section does not limit the amount of the civil penalty resulting from a violation of ORS 694.042.

(4) In imposing a civil penalty pursuant to this section, the agency shall consider the following factors:

(a) The immediacy and extent to which the violation threatens the public health or safety;

(b) Any prior violations of statutes, rules or orders;

(c) The history of the person incurring a penalty in taking all feasible steps to correct any violation; and

(d) Any other aggravating or mitigating factors.

(5) Civil penalties under this section shall be imposed as provided in ORS 183.745.

(6) The moneys received by the agency from civil penalties under this section shall be paid into the General Fund of the State Treasury and credited to the Oregon Health Licensing Agency Account established under ORS 676.625. Such moneys are continuously appropriated to the agency for

the administration and enforcement of the laws the agency is charged with administering and enforcing that govern the person against whom the penalty was imposed.

SECTION 18. Section 3 of this 2013 Act and the amendments to ORS 676.610, 676.612, 676.613, 676.622, 676.625 and 676.992 by sections 12 to 17 of this 2013 Act become operative November 1, 2013.

SECTION 19. Section 3 of this 2013 Act is amended to read:

Sec. 3. (1) There is created, within the Oregon Health Licensing Agency, the Behavior Analysis Regulatory Board consisting of seven members appointed by the Governor, including:

(a) Three members who are licensed by the board;

(b) One member who is a licensed psychiatrist or developmental pediatrician, with experience or training in treating autism spectrum disorder;

(c) One member who is a licensed psychologist registered with the board;

(d) One member who is a licensed speech-language pathologist registered with the board; and

(e) One member of the general public who does not have a financial interest in the provision of applied behavior analysis and does not have a ward or family member who has been diagnosed with autism spectrum disorder.

(2) Not more than one member of the Behavior Analysis Regulatory Board may be an employee of an insurer.

(3) The term of office of each member is four years, but a member serves at the pleasure of the Governor. Before the expiration of the term of a member, the Governor shall appoint a successor whose term begins on November 1 next following. A member is eligible for reappointment. If there is a vacancy for any cause, the Governor shall make an appointment to become immediately effective for the unexpired term.

(4) A member of the Behavior Analysis Regulatory Board is entitled to compensation and expenses as provided in ORS 292.495.

(5) The Behavior Analysis Regulatory Board shall select one of its members as chairperson and another as vice chairperson, for such terms and with duties and powers necessary for the performance of the functions of such offices as the board determines.

(6) A majority of the members of the Behavior Analysis Regulatory Board constitutes a quorum for the transaction of business.

(7) The Behavior Analysis Regulatory Board shall meet at least once every three months at a place, day and hour determined by the board. The board may also meet at other times and places specified by the call of the chairperson or of a majority of the members of the board.

(8) In accordance with ORS chapter 183, the Behavior Analysis Regulatory Board shall establish by rule criteria for the:

(a) Licensing of:

(A) Behavior analysts; and

(B) Assistant behavior analysts; and

(b) Registration of:

(A) Licensed health care professionals; and

(B) Behavior analysis interventionists.

(9) The criteria for the licensing of a behavior analyst must include, but are not limited to, the requirement that the applicant:

(a) Be certified by the Behavior Analyst Certification Board, Incorporated, as a Board Certified Behavior Analyst; and

(b) Have successfully completed a criminal records check.

(10) The criteria for the licensing of an assistant behavior analyst must include, but are not limited to, the requirement that the applicant:

(a) Be certified by the Behavior Analyst Certification Board, Incorporated, as a Board Certified Assistant Behavior Analyst;

(b) Be supervised by a behavior analyst who is licensed by the Behavior Analysis Regulatory Board; and

(c) Have successfully completed a criminal records check.

(11) The criteria for the registration of a behavior analysis interventionist must include, but are not limited to, the requirement that the applicant:

(a) Have completed coursework and training prescribed by the Behavior Analysis Regulatory Board by rule;

(b) Receive ongoing oversight by a licensed behavior analyst or a licensed assistant behavior analyst, or by another licensed health care professional approved by the board; and

(c) Have successfully completed a criminal records check.

(12) In accordance with applicable provisions of ORS chapter 183, the Behavior Analysis Regulatory Board shall adopt rules:

(a) Establishing standards and procedures for the licensing of behavior analysts and assistant behavior analysts and for the registration of licensed health care professionals and behavior analysis interventionists in accordance with this section;

(b) Establishing guidelines for the professional methods and procedures to be used by individuals licensed and registered under this section;

(c) Governing the examination of applicants for licenses and registrations under this section and the renewal, suspension and revocation of the licenses and registrations; and

(d) Establishing fees sufficient to cover the costs of administering the licensing and registration procedures under this section.

(13) The Behavior Analysis Regulatory Board shall issue a license to an applicant who:

(a) Files an application in the form prescribed by the board;

(b) Pays fees established by the board; and

(c) Demonstrates to the satisfaction of the board that the applicant meets the criteria adopted under this section.

(14) The Behavior Analysis Regulatory Board shall establish the procedures for the registration of licensed health care professionals and behavior analysis interventionists.

(15) All moneys received by the Behavior Analysis Regulatory Board under subsection (13) of this section shall be paid into the General Fund of the State Treasury and credited to the Oregon Health Licensing Agency Account.

[*(16) An individual who has not been licensed or registered by the Behavior Analysis Regulatory Board in accordance with criteria and standards adopted under this section may not claim reimbursement for services described in section 2 of this 2013 Act under a health benefit plan or under a self-insured health plan offered by the Public Employees' Benefit Board or the Oregon Educators Benefit Board.*]

SECTION 20. ORS 743A.190, as amended by section 7 of this 2013 Act, is amended to read:

743A.190. (1) A health benefit plan, as defined in ORS 743.730, must cover for a child enrolled in the plan who is under 18 years of age and who has been diagnosed with a pervasive developmental disorder all medical services, including rehabilitation services, that are medically necessary and are otherwise covered under the plan.

(2) The coverage required under subsection (1) of this section, including rehabilitation services, may be made subject to other provisions of the health benefit plan that apply to covered services, including but not limited to:

(a) Deductibles, copayments or coinsurance;

(b) Prior authorization or utilization review requirements; or

(c) Treatment limitations regarding the number of visits or the duration of treatment.

(3) As used in this section:

(a) "Medically necessary" means in accordance with the definition of medical necessity that is specified in the policy, certificate or contract for the health benefit plan and that applies uniformly to all covered services under the health benefit plan.

(b) "Pervasive developmental disorder" means a neurological condition that includes autism spectrum disorder, developmental delay, developmental disability or mental retardation.

(c) "Rehabilitation services" means physical therapy, occupational therapy or speech therapy services to restore or improve function.

(4) The provisions of ORS 743A.001 do not apply to this section.

(5) The definition of "pervasive developmental disorder" is not intended to apply to coverage required under ORS 743A.168 [*or section 2 of this 2013 Act*].

SECTION 21. ORS 750.055, as amended by section 3, chapter 21, Oregon Laws 2012, and section 8 of this 2013 Act, is amended to read:

750.055. (1) The following provisions of the Insurance Code apply to health care service contractors to the extent not inconsistent with the express provisions of ORS 750.005 to 750.095:

(a) ORS 705.137, 705.139, 731.004 to 731.150, 731.162, 731.216 to 731.362, 731.382, 731.385, 731.386, 731.390, 731.398 to 731.430, 731.428, 731.450, 731.454, 731.488, 731.504, 731.508, 731.509, 731.510, 731.511, 731.512, 731.574 to 731.620, 731.592, 731.594, 731.640 to 731.652, 731.730, 731.731, 731.735, 731.737, 731.750, 731.752, 731.804, 731.844 to 731.992, 731.870 and 743.061.

(b) ORS 732.215, 732.220, 732.230, 732.245, 732.250, 732.320, 732.325 and 732.517 to 732.592, not including ORS 732.582.

(c) ORS 733.010 to 733.050, 733.080, 733.140 to 733.170, 733.210, 733.510 to 733.680 and 733.695 to 733.780.

(d) ORS chapter 734.

(e) ORS 742.001 to 742.009, 742.013, 742.061, 742.065, 742.150 to 742.162, 742.400, 742.520 to 742.540, 743.010, 743.013, 743.018 to 743.030, 743.050, 743.100 to 743.109, 743.402, 743.472, 743.492, 743.495, 743.498, 743.499, 743.522, 743.523, 743.524, 743.526, 743.527, 743.528, 743.529, 743.549 to 743.552, 743.560, 743.600 to 743.610, 743.650 to 743.656, 743.764, 743.804, 743.807, 743.808, 743.814 to 743.839, 743.842, 743.845, 743.847, 743.854, 743.856, 743.857, 743.858, 743.859, 743.861, 743.862, 743.863, 743.864, 743.894, 743.911, 743.912, 743.913, 743.917, 743A.010, 743A.012, 743A.020, 743A.034, 743A.036, 743A.048, 743A.058, 743A.062, 743A.064, 743A.065, 743A.066, 743A.068, 743A.070, 743A.080, 743A.084, 743A.088, 743A.090, 743A.100, 743A.104, 743A.105, 743A.110, 743A.140, 743A.141, 743A.144, 743A.148, 743A.160, 743A.164, 743A.168, 743A.170, 743A.175, 743A.184, 743A.185, 743A.188, 743A.190 and 743A.192 and section 2, chapter 21, Oregon Laws 2012[*, and section 2 of this 2013 Act*].

(f) The provisions of ORS chapter 744 relating to the regulation of insurance producers.

(g) ORS 746.005 to 746.140, 746.160, 746.220 to 746.370, 746.600, 746.605, 746.607, 746.608, 746.610, 746.615, 746.625, 746.635, 746.650, 746.655, 746.660, 746.668, 746.670, 746.675, 746.680 and 746.690.

(h) ORS 743A.024, except in the case of group practice health maintenance organizations that are federally qualified pursuant to Title XIII of the Public Health Service Act unless the patient is referred by a physician associated with a group practice health maintenance organization.

(i) ORS 735.600 to 735.650.

(j) ORS 743.680 to 743.689.

(k) ORS 744.700 to 744.740.

(L) ORS 743.730 to 743.773.

(m) ORS 731.485, except in the case of a group practice health maintenance organization that is federally qualified pursuant to Title XIII of the Public Health Service Act and that wholly owns and operates an in-house drug outlet.

(2) For the purposes of this section, health care service contractors shall be deemed insurers.

(3) Any for-profit health care service contractor organized under the laws of any other state that is not governed by the insurance laws of the other state is subject to all requirements of ORS chapter 732.

(4) The Director of the Department of Consumer and Business Services may, after notice and hearing, adopt reasonable rules not inconsistent with this section and ORS 750.003, 750.005, 750.025 and 750.045 that are deemed necessary for the proper administration of these provisions.

SECTION 22. Section 2 of this 2013 Act is repealed January 2, 2022.

SECTION 23. Sections 2 and 10 of this 2013 Act and the amendments to ORS 743A.190 and 750.055 by sections 7 and 8 of this 2013 Act apply to health benefit plan policies and certificates:

(1) Offered by the Public Employees' Benefit Board or the Oregon Educators Benefit Board for coverage beginning on or after January 1, 2015; and

(2) Other than for plans offered by the Public Employees' Benefit Board or the Oregon Educators Benefit Board, for coverage beginning on or after January 1, 2016.

SECTION 24. The amendments to section 3 of this 2013 Act by section 19 of this 2013 Act and the amendments to ORS 743A.190 and 750.055 by sections 20 and 21 of this 2013 Act become operative January 2, 2022.

SECTION 25. This 2013 Act being necessary for the immediate preservation of the public peace, health and safety, an emergency is declared to exist, and this 2013 Act takes effect on its passage.

Passed by Senate June 29, 2013

.....
Robert Taylor, Secretary of Senate

.....
Peter Courtney, President of Senate

Passed by House July 1, 2013

.....
Tina Kotek, Speaker of House

Received by Governor:

.....M.,....., 2013

Approved:

.....M.,....., 2013

.....
John Kitzhaber, Governor

Filed in Office of Secretary of State:

.....M.,....., 2013

.....
Kate Brown, Secretary of State

CPT® Category III Codes
January 1, 2014

The following CPT codes are an excerpt of the CPT Category III code set, a temporary set of codes for emerging technologies, services, and procedures.

For more information on the criteria for CPT Category I, II and III codes, see Applying for Codes.

To assist users in reporting the most recently approved Category III codes, the AMA's CPT Web site features updates of the CPT Editorial Panel actions and early release of the Category III codes in July and January in a given CPT cycle. This was approved by the CPT Editorial Panel as a part of the 1998-2000 CPT-5 projects. These dates for early release correspond with the three annual CPT Editorial Panel meetings for each CPT cycle (June, October, and February). Although publication of Category III codes through early release to the CPT web site allows for expedient dispersal of the code and descriptor, early availability does not imply that these codes are immediately reportable before the posted implementation date.

Publication of the Category III codes to this Web site takes place on a semiannual basis when the codes have been approved by the CPT Editorial Panel. The full set of temporary Category III codes for emerging technology, procedures and services are published annually in the code set for each CPT publication cycle.

As with CPT Category I codes, inclusion of a descriptor and its associated code number does not represent endorsement by the AMA of any particular diagnostic or therapeutic procedure or service. Inclusion or exclusion of a procedure or service does not imply any health insurance coverage or reimbursement policy.

Background information for Category III codes
CPT Category III codes are a set of temporary codes that allow data collection for emerging technology, services, and procedures. These codes are intended to be used for data collection to substantiate widespread usage or to provide documentation for the Food and Drug Administration (FDA) approval process. The CPT Category III codes may not conform to the following CPT Category I code requirements:

- All devices and drugs necessary for performance of the procedure or service have received FDA clearance or approval when such is required for performance of the procedure or service.
- The procedure or service is performed by many physicians or other qualified health care professionals across the United States.
- The procedure or service is performed with frequency consistent with the intended clinical use (ie, a service for a common condition should have high volume, whereas a service commonly performed for a rare condition may have low volume).
- The procedure or service is consistent with current medical practice.
- The clinical efficacy of the procedure or service is documented ~~in literature~~ that meets the requirements set forth in the CPT code change application.

These codes have an alpha character as the 5th character in the string preceded by four digits (e.g., 1234T) and are located in a separate section of the CPT codebook, following the Medicine section. The introductory language for this code section explains the purpose of these codes.

CPT Category III codes are intended to be used for data collection purposes to substantiate widespread usage or to provide documentation for the FDA approval process. Category III codes are not developed as a result of Panel review of an incomplete proposal, the need for more information, or a lack of CPT Advisory Committee support of a code change application.

CPT Category III codes are not referred to the AMA-Specialty RVS Update Committee (RUC) for valuation because no relative value units (RVUs) are assigned to these codes. Payment for these services or procedures is based on the policies of payers and not on a yearly fee schedule.

In general, a given Category III code will be archived five years from the date of initial publication or extension unless a modification of the archival date is specifically noted at the time of a revision or change to a code (eg, addition of parenthetical instructions, reinstatement).

Category III codes for CPT 2015

It is important to note that, because future CPT Editorial Panel or Executive Committee actions may affect these items, codes and descriptor language may differ at the time of publication. Also, future Panel actions may result in gaps in code number sequencing. A cross-reference will appear in the Category III section of the CPT codebook to direct users to the newly established CPT Category I code.

Unless otherwise indicated, the symbol ● indicates new procedure codes that will be added to the CPT codebook in 2015.

Category III codes

The following section contains a set of temporary codes for emerging technology, services, and procedures. Category III codes allow data collection for these services or procedures. Use of unlisted codes does not offer the opportunity for the collection of specific data. If a Category III code is available, this code must be reported instead of a Category I unlisted code. This is an activity that is critically important in the evaluation of health care delivery and the formation of public and private policy. The use of the codes in this section allows physicians and other qualified health care professionals, insurers, health services researchers, and health policy experts to identify emerging technology, services, and procedures for clinical efficacy, utilization, and outcomes.

The inclusion of a service or procedure in this section neither implies nor endorses clinical efficacy, safety, or the applicability to clinical practice. The codes in this section may not conform to the usual requirements for CPT Category I codes established by the Editorial Panel. The nature of emerging technology, services, and procedures is such that the requirements for the Category I criteria may not be met. For these reasons, temporary codes for emerging technology, services, and procedures have been placed in a separate section of the CPT codebook, and the codes are differentiated from CPT Category I codes by the use of the alphanumeric characters.

Services/procedures described in this section make use of alphanumeric characters. These codes have an alpha character as the 5th character in the string (ie, four digits followed by the letter T). The digits are not intended to reflect the placement of the code in the Category I section of CPT nomenclature. Codes in this section may or may not eventually receive a Category I CPT code. In either case, in general, a given Category III code will be archived five years from the date of initial publication or extension unless a modification of the archival date is specifically noted at the time of a revision or change to a code (eg, addition of parenthetical instructions, reinstatement). Services/procedures described by Category III codes which have been archived after five years, without conversion, must be reported using the Category I unlisted code unless another specific cross reference is established at the time of archiving. New codes or revised codes are released semi-annually via the AMA/CPT internet site, to expedite dissemination for reporting. The full set of temporary codes for emerging technology, services, and procedures are published annually in the CPT codebook. Go to www.ama-assn.org/go/cpt for the most current listing.

Category III codes 0340T-0346T were accepted at the May 2013 CPT Editorial Panel meeting for the 2015 CPT production cycle. Therefore, these codes do not appear in the 2014 CPT codebook. However, due to the Category III code early release policy, these codes are effective on January 1, 2014, following the six-month implementation period which began on July 1, 2013. Shaded text refers to additional refinements accepted at the October 2013 CPT Editorial Panel meeting for the 2015 CPT production cycle.			
⊙●0340T	Ablation, pulmonary tumor(s), including pleura or chest wall when involved by tumor extension, percutaneous, cryoablation, unilateral, includes imaging guidance	Released July 1, 2013 Implemented January 1, 2014 Moderate Sedation symbol ⊙ added October 2013	***CPT 2015***
	(Do not report code 0340T in conjunction with 76940, 77013, 77022)		
●0341T	Quantitative pupillometry with interpretation and report, unilateral or bilateral	Released July 1, 2013 Implemented January 1, 2014	***CPT 2015***
●0342T	Therapeutic apheresis with selective HDL delipidation and plasma reinfusion	Released July 1, 2013 Implemented January 1, 2014	***CPT 2015***
●0343T	Transcatheter mitral valve repair percutaneous approach including transseptal puncture when performed; initial prosthesis	Released July 1, 2013 Implemented January 1, 2014	***CPT 2015***
●0344T	additional prosthesis (es) during same session (List separately in addition to code for primary procedure)	Released July 1, 2013 Implemented January 1, 2014	***CPT 2015***
	(Use 0343T in conjunction with 0344T)		
●0345T	Transcatheter mitral valve repair percutaneous approach via the coronary sinus	Released July 1, 2013 Implemented January 1, 2014	***CPT 2015***
	(0343T is applicable for initial prosthesis placed during a session even when patient has an existing mitral valve prosthesis in place)		

	(Do not report 0343T, 0344T, 0345T in conjunction with 93451, 93452, 93453, 93456, 93457, 93458, 93459, 93460, 93461for diagnostic left and right heart catheterization procedures intrinsic to the valve repair procedure)		
	(Do not report 0345T in conjunction with 93453, 93454 for coronary angiography intrinsic to the valve repair procedure)		
●0346T	Ultrasound, elastography (List separately in addition to code for primary procedure)	Released July 1, 2013 Implemented January 1, 2014	***CPT 2015***
	(Use 0346T in conjunction with 76536, 76604, 76645, 76700, 76705, 76770, 76775, 76830, 76856, 76857, 76870, 76872, 76881, 76882)		
	(For elastography without ultrasound imaging, use an unlisted code)	Refinement approved October 2013	
Category III codes were accepted at the October 2013 CPT Editorial Panel meeting for the 2015 CPT production cycle. However, due to the Category III code early release policy, these codes are effective on July 1, 2014, following the six-month implementation period which begins January 1, 2014.			
●0347T	Placement of interstitial device(s) in bone for radiostereometric analysis (RSA)	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
●0348T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed)	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
●0349T	upper extremity(ies), (includes shoulder, elbow and wrist, when performed)	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
●0350T	lower extremity(ies), (includes hip, proximal femur, knee and ankle, when performed)	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***

●0351T	Optical coherence tomography of breast or axillary lymph node, excised tissue, each specimen; real time intraoperative	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
●0352T	interpretation and report, real time or referred	Released January 1, 2014 Implemented July 1, 2014	
	(Do not report 0352T in conjunction with 0351T when performed by the same physician)		
●0353T	Optical coherence tomography of breast, surgical cavity; real time intraoperative	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
	(Report 0353T once per session)		
●0354T	interpretation and report, real time or referred	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
	(Do not report 0354T in conjunction with 0353T when performed by the same physician)		
●0355T	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), colon, with interpretation and report	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
	(Use 0355T for imaging of distal ileum, when performed)		
	(Do not report 0355T in conjunction with 91110, 91111)		
●0356T	Insertion of drug-eluting implant (including punctal dilation and implant removal when performed) into lacrimal canaliculus, each	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***

●0358T	Bioelectrical impedance analysis whole body composition assessment, supine position, with interpretation and report	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
Adaptive Behavior Assessments ***Behavior identification assessment (0359T)*** conducted by the physician or other qualified health care professional, includes a detailed behavioral history, patient observation, administration of standardized and non-standardized tests and structured guardian/caregiver interview to identify and describe deficient adaptive or maladaptive behaviors (eg, impaired social skills and communication deficits, destructive behaviors, and additional functional limitations secondary to maladaptive behaviors). 0359T also includes the physician's or other qualified health care professional's interpretation of results and development of plan of care, which may include further observational or exposure behavioral follow-up assessment(s) (0360T, 0361T, 0362T, 0363T), discussion of findings and recommendations with the primary guardian(s)/caregiver(s), and preparation of report. ***Observational behavioral follow-up assessment (0360T, 0361T)*** is administered by a technician under the direction of a physician or other qualified health care professional. The physician or other qualified health care professional may or may not be on-site during the face-to-face assessment process. Codes 0360T, 0361T include the physician's or other qualified health care professional's interpretation of results, discussion of findings and recommendations with the primary caregiver(s), and preparation of report. Codes 0360T, 0361T describe services provided to patients who present with specific destructive behavior(s) (eg, self-injurious behavior, aggression, property destruction) or behavioral problems secondary to repetitive behaviors or deficits in communication or social relatedness. These assessments include use of structured observation and/or standardized and non-standardized tests to determine levels of adaptive behavior. Areas assessed may include cooperation, motivation, visual understanding, receptive and expressive language, imitation, requests, labeling, play and leisure and social		

interactions. Specific destructive behavior(s) assessments include structured observational testing to examine events, cues, responses, and consequences associated with the behavior(s). ***Exposure behavioral follow-up assessment (0362T, 0363T)*** is administered by the physician or other qualified health care professional with the assistance of one or more technicians. Codes 0362T, 0363T include the physician's or other qualified health care professional's interpretation of results, discussion of findings and recommendations with the primary caregiver(s), and preparation of report. The typical patients for 0362T, 0363T include patients with one or more specific severe destructive behavior(s) (eg, self-injurious behavior, aggression, property destruction). Specific severe destructive behavior(s) are assessed using structured testing to examine events, cues, responses, and consequences associated with the behavior(s).		
Codes 0362T, 0363T include exposing the patient to a series of social and environmental conditions associated with the destructive behavior(s). Assessment methods include using testing methods designed to examine triggers, events, cues, responses, and consequences, associated with the before mentioned maladaptive behavior(s). This assessment is completed in a structured, safe environment. Codes 0360T, 0361T, 0362T, 0363T are reported following 0359T based on the time that the patient is face-to-face with one or more technician(s). Only count the time of one technician when two or more are present. Codes 0360T, 0361T, 0362T, 0363T are reported per the CPT Time Rule (eg, a unit of time is attained when the mid-point is passed). See Table 1. The time reported with 0360T, 0361T, 0362T, 0363T is over a single day and is not cumulative over a longer period. Do not report 0359T, 0360T, 0361T, 0362T, 0363T in conjunction with 90785-90899, 96101-96125, 96150, 96151, 96152, 96153, 96154, 96155 on the same date. (For psychiatric diagnostic evaluation, see 90791, 90792) (For speech evaluations, use 92506) (For occupational therapy evaluation, see 97003, 97004) (For medical team conference, see 99366, 99367, 99368) (For health and behavior assessment/intervention, see 96150, 96151, 96152, 96153, 96154, 96155) (For neurobehavioral status exam, use 96116) (For neuropsychological testing, use 96118)		

Table 1

Reporting of 0360T, 0361T, 0362T, 0363T per CPT Time Rule

Utilizing Face-to-Face Technician Time

Less than 16 min	Not reportable
16-45 min	0360T or 0362T
46-75 min	0360T and 0361T; or 0362T and 0363T
Each additional increment up to 30 min	Additional 0361T or 0363T

●0359T	Behavior identification assessment, by the physician or other qualified health care professional, face-to-face with patient and caregiver(s), includes administration of standardized and non-standardized tests, detailed behavioral history, patient observation and caregiver interview, interpretation of test results, discussion of findings and recommendations with the primary guardian(s)/caregiver(s), and preparation of report	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
●0360T	Observational behavioral follow-up assessment, includes physician or other qualified health care professional direction with interpretation and report, administered by one technician; first 30 minutes of technician time, face-to-face with the patient	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
+●0361T	each additional 30 minutes of technician time, face-to-face with the patient (List separately in addition to code for primary service)	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
	(Use 0361T in conjunction with 0360T)		

●0362T	Exposure behavioral follow-up assessment, includes physician or other qualified health care professional direction with interpretation and report, administered by physician or other qualified health care professional with the assistance of one or more technicians; first 30 minutes of technician(s) time, face-to-face with the patient	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
+●0363T	each additional 30 minutes of technician(s) time, face-to-face with the patient (List separately in addition to code for primary procedure)	Released January 1, 2014 Implemented July 1, 2014	***CPT 2015***
	(Use 0363T in conjunction with 0362T)		
	(0362T, 0363T are reported based on a single technician's face-to-face time with the patient and not the combined time of multiple technicians)		
	Do not report 0359T, 0360T, 0361T, 0362T, 0363T in conjunction with 90785-90899, 96101-96125, 96150, 96151, 96152, 96153, 96154, 96155)		
Coding Tip If the physician or other qualified health care professional personally performs the technician activities, his or her time engaged in these activities may be included as part of the required technician time to meet the elements of the code.			

Section 7.0

Previously Discussed Items

Oral health risk assessment codes revision

Question: Oral health risk assessment codes revision

Question source: DMAP Staff

Issue: At the January 9, 2014 VBBS meeting, the codes for providing oral health risk assessments in medical settings were discussed. OHAP had made recommendations to have D0145 only on the dental lines (as the CDT book specifies this is by a dentist) and between the OHAP meeting and the VBBS meeting staff had found evidence that 8 other states were using D0145 for medical providers (7 of which requiring additional training). Based on this, and the coding description also being more applicable, a recommendation was made to place this code on the medical prevention line.

Since then DMAP, and Dr. Tyack, and input from Deborah Loy (Capital Dental Care) have supported the withdrawal of D0145 as a potential code due to the CDT limitation of this being for the exclusive use of dentists, the D0191 code to be used by medical providers instead.

Additionally, DMAP has again requested holding off on implementing the move of D0191 and the oral health risk assessment codes to the medical lines (Line 1 and 3) in order for them to complete the rules process. The guideline was added to ensure that there would be criteria that had to be met for a provider to be eligible for the additional payment. The rules are currently undergoing development but have not yet been established. Simultaneously, there is input from some other CCOs and subcommittee members that moving forward with this is important and do not wish to delay.

Codes in question

Code	Code Description	Lines
D0601	Caries risk assessment and documentation with a finding of low risk	1,57
D0602	Caries risk assessment and documentation with a finding of moderate risk	1,57
D0603	Caries risk assessment and documentation with a finding of high risk	1,57

Code	Code Description	Lines
D0191	Assessment of a patient - a limited clinical inspection that is performed to identify possible signs of oral or systemic disease malformation or injury and the potential need for referral for diagnosis and treatment.	1,57

Code	Code Description	Lines
D0145	Oral evaluation for a patient under three years of age and counseling with primary caregiver	57 preventive dental services

1/9/14 VBBS meeting minutes

> **Discussion:** Livingston presented an issue summary. The question was raised as to whether this would diminish patients seeking dental services if preventive services were provided in primary care offices. Members agreed that barriers to dental evaluations and services were significant and that risk of not having these

services is greater than a potential risk of relocation of services. Shaffer raised the concern that there are some implementation issues that may take longer to resolve than by the April 1, 2014 List. The specific concerns are about what would qualify as a training program and which standardized risk assessment tools would be appropriate. There was concern that if risk assessment and counseling codes were added to medical lines prior to establishment of criteria that there would be confusion. There was clarification that DMAP administrative rules would have authority over training and tools. Additionally, there was a question about the choice of 21 as a cutoff for children and it was clarified that was chosen because of the ACA requirements of dental services for up to age 21. After discussion, a guideline was proposed that would enable these codes to be placed on the April 1, 2014 List, and DMAP will go through its administrative rules process to address the implementation issues that may take longer than April 1 to fully define. There was a discussion about the D0191 code which is currently only open for payment for dentists. The decision was made to add this code to Line 3 and Line 1 with a guideline as well. D0145 was discussed and DMAP would need to determine how this may be opened up to non-dentists given other states have done this, although the coding definition appears specific to dentists.

Dodson suggested OMA, OAFP, AAP society, and OHAP all work together to determine implementation considerations.

Actions:

1) Place D0601-0603 and D0191 on Lines 1,3, and 58
2) Adopt a new guideline:

   Guideline Note XXX Oral Health Risk Assessment

   Line 1,3, 58

   CDT codes D0601-D0603 and D0191 coverage is restricted on these lines as follows:

   Line 1: pregnant women only
   Line 3: children under the age of 6 only
   Line 58: children under the age of 21 only

   These services are included only when performed using approved tools and when performed by a provider who has completed an approved program.
3) Place D0145 on Lines 3 and 58
4) DMAP will address through its rules process:
   a. Appropriate standardized tools that would be required to receive reimbursement for risk assessment
   b. Necessary training for medical providers to bill using these codes
5) Dodson and Tyack to work together with staff on coordinating logistics of a stakeholder workgroup.

<u>HERC Staff Recommendations:</u>

1) Remove D0145 from Line 3. Keep only on Line 58.
2) Discuss whether to delay implementation of D0601-D0603 and D0191 being placed on Lines 1 and 3.

Policy Issue Paper

Issue: Dental Examinations in Medical Settings

Date: 1/7/2014

1. What is the policy question?

Should OHP cover D0145 dental evaluations provided by non-dentists in medical settings?

2. Describe the issue background.

- Preventing onset of early childhood caries is one of the best ways to improve oral health and reduce cost: fewer E.R. visits, fewer extensive restorations, less anesthesia, fewer school absences, etc.
- One strategy is to increase oral health services for young children in primary care offices.
    - Receptivity: Parents of infants and toddlers are especially receptive to guidance.
    - Frequency: Pediatricians have frequent contact with young clients; they often see children up to six times before age two.
    - Access: It is often easier to find a pediatrician than a pediatric dentist.
- The HERC recently recommended adding coverage of D0145 in medical settings for the April 2014 Prioritized List.
- OHP currently separately covers topical fluoride varnish in medical settings. Medical providers may also include an oral health assessment during well child visits. However, the provider does not bill separately for the assessment, unless required to do so by a CCO.

Coding Concerns

- D0145 provided by non-dentists is contrary to the CDT. Per the American Dental Association (ADA), dental evaluations include diagnosis and treatment planning, which cannot be delegated and are a dentist's responsibility.
- A survey from the American Academy of Pediatrics (AAP) identified eight states that cover robust oral health services in medical settings.
- All eight cover D0145 (oral evaluation for a patient under three) and D1206 (topical fluoride varnish).
- However, all eight started before there was a code for D0191 (assessment of a patient).
- If these states had it to do over again, some would likely rely on D0191 instead.
    - Example: The dental policy director for Alaska says they might have instead reimbursed for D0191 if the code had been available when they started their program.

- The purpose of CDT codes is to provide "uniformity, consistency and specificity in accurately reporting/documenting dental treatment."

- OHP currently covers D0145 (at $23.66) evaluations in dental settings. An evaluation conducted by a dentist is far different than what a physician, PA or NP can provide in a well-child visit.

- D0191 became available in 2013. The HERC previously concluded D0191 was intended for mid-level providers, hygienists, physicians, physician assistants, and nurses.

- Currently, CCOs are free to voluntarily choose to separately cover D0191 in medical settings.

Timing Concerns

- All but one of the programs identified by AAP requires medical practitioners to complete specialized oral health training before billing for oral health services.

- A majority also have a risk assessment form for providers to complete. The forms play a role in educating caregivers and streamlining urgent referrals. They also give assurance that the provider is providing oral health services as intended and beyond what is typically included in a well child visit.

- Reimbursement rates for evaluation/varnish run from $25/$15 to $40.38/$23.41.

- Most, if not all, of the programs grew out of broad coalition efforts. They often include major education components with training materials for providers and education materials for parents and caregivers.

3. Recommendation.

OHP should not reimburse medical providers for D0145 (or D0191) at this time.

> If done thoughtfully, opening D0145 or D0191 for medical practitioners is a step toward better health and better care at a lower cost. Opening the codes would also allow us to better capture the full extent of oral health services in the OHP program. However, reimbursement should not begin until there is a proper framework for a viable program.

OHP should not reimburse medical providers for D0145 until decision makers consider and reject the possibility of opening D0191 instead, and make a determination on delegation.

4. Analysis and Assumptions

I assume CCOs are currently free to separately reimburse their providers for D0191 in medical settings, despite the fact that D0191 is only included on line 58 for preventative dentistry. This is based in part on a conversation with a representative of Trillium.

5. What will be the impact of this change on: no impact; recommendation preserves the status quo

a. Clients

b. Providers

c. Other stakeholders and community members

d. **DHS/OHA staff**

6. Will new rules, contracts or protocols be required to implement this change?
No.

7. Is federal approval required for this change/modification? (If yes explain).
No.

8. What is the planned effective date for this change?
n/a

9. **What is the economic impact of this change? Describe any economic impact or cost you anticipate, Depending on the issue, detailed fiscal documentation may be required.**

no impact; recommendation preserves the status quo

Loy Letter

February 11, 2014

Oregon Health Policy & Research
Health Evidence Review Commission
1225 Ferry Street
Suite C
Salem, Oregon 97301

RE: Dental Procedure Codes D01206, D0145, and D0191

Dear Darren Coffman:

The Health Evidence Review Commission (HERC) has made some recent decisions regarding dental procedure coverage and line placement. I do not feel these decisions have necessarily included input from the Oral Health Advisory Panel (OHAP) and/or if they were discussed the subjects were not well vetted before HERC made a decision. There is a great deal of broad based oral health expertise on the advisory panel to not use it to full advantage.

A decision was made by the HERC to expand coverage in a medical setting of fluoride varnish D1206 up through age 18. As an oral health advisory panel member I do not dispute the evidence and value of fluoride varnish in a medical setting for younger children. It is questionable on its impact for older school age children. This HERC decision was made without input from the OHAP. Having a dental home is a key factor in a child's oral health. It is for this reason that the American Academy of Pediatrics 'Oral Health Risk Assessment Tool' lists 'existing dental home' first on its 'protective factors'. Oregon Health Plan (OHP) utilization shows low penetration rates for young children however, penetration numbers rise significantly for school aged children.

Families covered under OHP struggle with environmental barriers (i.e. transportation, time off from work/school, arranging child care for children not scheduled to be seen etc.). It is for these reasons that medical-dental collaboration surrounding the young child is seen as a best practice. Young children during the first years of life are seeing medical providers for well child checks and immunizations. Incorporating oral health assessment, anticipatory guidance and fluoride varnish during these visits makes good practical sense. It makes less sense to do so with older children and potential confuse parents or through the convenience of not having to seek services from yet one more provider (a dentist) negatively impact either an established dental home or motivation to acquire one. If I am a stressed out mom and my medical provider looks into my child's mouth, gives some hygiene instructions and applies fluoride varnish I am going to think why do I have to make that 'extra visit' to see the dentist.

A medical provider should need to do an oral health risk assessment in order to bill D01206. If a child has an existing dental home (at age?? to be determined in conjunction with input from the OHAP) the OHP member should be found low risk and fluoride varnish in a medical setting after that age would not be covered. If the child does not have an existing dental home vanish would be covered. However, in addition to applying varnish the medical provider would need to make a referral to the coordinated care organization (CCO) for a dental home to be established. One of the CCO metrics being proposed is dental service penetration. Services delivered by a medical provider are not per Medicaid counted as dental services they are oral health services. The CCO has a wonderful opportunity to coordinate care across delivery systems. The HERC's decision to cover fluoride varnish in a medical setting for the older age child seems counter intuitive to Triple Aim goals of better care, services and lower costs. Tearing down delivery system silos versus building new ones is a vision of transformation.

Another decision by the HERC was to place D0145 (oral evaluation for a patient under three years of age) on a medical line to cover this procedure being done by medical providers. I wholeheartedly disagree with this decision. With the Health Insurance Portability and Accountability Act (HIPPA) it not only included privacy rules but also mandated use of national coding standards. For dental that would be the American Dental Association (ADA) Current Dental Terminology (CDT) coding manual. In the CDT under the 'Diagnostic' section are found the clinical evaluation codes. The evaluation codes descriptors state 'the codes in this section recognize the cognitive skills necessary for **patient evaluation**. The collection and recording of some data and components of the dental examination may be delegated, however, the **evaluation, which includes diagnosis and treatment planning, is the responsibility of the dentist…**

The CDT is a copy-write manual. No other procedure code descriptors other than the evaluation codes so clearly calls out the dentist and him/her not delegating this diagnostic component. These evaluation codes are not simply an assessment and/or screening they encompasses the full breadth of dental diagnosing, and treatment planning including development of a preventive oral health regimen. Although I have the utmost respect for the cognitive skills of medical providers the ADA code descriptor requirements of D0145 cannot be met by a medical provider.

Under the OHP and any other Medicaid program requirements a provider must bill the '**most accurate code**' that describes the service delivered. ADA recognized the importance of non-dentists in conducting oral health pre-diagnostic services such as screening and/or assessment. Unlike the evaluation codes the new screening and assessment codes can be done by non-dentists (i.e. medical and/or mid-level dental providers). My recommendation is that HERC remove D0145 from a medical line and instead D0191 (assessment of a patient) described as 'a limited clinical inspection that is performed to identify possible signs of oral or systemic disease, malformation, or injury, and the potential need for referral for diagnosis and treatment should be added to a medical line in its place.

Although Oregon does allow physicians to do dental services it does not relieve a medical provider from being held to the cognitive skills and standard of care expected to do the service as described. It also does not relieve a provider from billing the most accurate code that describes the service. It makes dill or beans to me if some states are allowing medical providers to bill D0145. Many states made this well intentioned but ill resulted decision trying to fill a void of not having any other dental screening and/or assessment codes to choose from. That is not the case today with D0190 and D0191 added to the CDT coding manual. I feel medical providers should be paid in addition to a well child check for doing D0191.

In closing, many in dental have anxiously awaited risk assessment codes. The new risk assessment codes are D0601 (low), D0602 (moderate) and D0603 (high) risk come with a flurry of expectations. The risk assessment that will take place in a medical setting will look very different than those in a dental setting. The average medical encounter has a lot to squeeze in a limited duration of time. Dental will be working out what we hope to see done in utilizing risk assessment codes. Some of those decisions will need additional evidence and debate. Medical on the other hand has an acceptable tool in the oral health risk assessment proposed by the American Academy of Pediatrics. This is the same tool recommended by 'Smiles for Life' a training program with wide support from the medical community. I would recommend its use for medical providers.

I have recommended to the Division of Medical Assistance Programs that medical provider has oral health training available to them similar to what is done in other states. Oregon's 'First Tooth' program or 'Smiles for Life' could be the training curriculum for medical providers. A medical provider who wishes to receive higher reimbursement for oral prevention codes would in states like Washington and North Carolina be required to complete training. Ones who do not want to complete training still may bill the codes but will not be reimbursed at the higher level.

I sincerely hope the HERC reconsiders recent decisions and reconvenes the OHAP for further discussion and vetting.

Sincerely,

Deborah Loy
Capitol Dental Care

Botulinum Toxin for Chronic Migraine

Question: How should botulinum toxin as a treatment for chronic migraine be placed on the Prioritized List?

Question source: P&T, HERC staff, DMAP, Allergan

Issue: A unique CPT code for botulinum toxin injection for treatment of chronic migraine (CPT 64615) was reviewed at the December, 2012 VBBS meeting as part of the 2013 CPT code review. Based on a 2012 MED review finding that botulinum toxin is ineffective for the treatment of chronic migraine, the VBBS/HERC recommended that this CPT code be placed on the Excluded List.

In the interim, HERC staff, DMAP, and P&T have become aware that all pharmaceutical treatments require a "pathway to coverage" under federal Medicaid drug rebate law.

P&T will be reviewing the use of botulinum toxin for all indications at their May, 2014 meeting. It is expected that P&T will recommend certain requirements that a patient must meet to qualify for botulinum toxin therapy for chronic migraine.

HERC staff recommendation:

1) Add CPT 64615 (Chemodenervation for migraine) to line 414 MIGRAINE HEADACHES to the October 1, 2014 list.
2) Staff to bring back a new guideline note to the August, 2014 VBBS/HERC meeting in the format below that is based on P&T's recommended Prior Authorization criteria from their May 2014 review, which will then be incorporated into the October 1, 2014 Prioritized List of health services.

Model guideline note language for Line 435

Chemodenervation for treatment of chronic migraine (CPT 64615) is included on this line for prophylactic treatment of adults with chronic migraine (defined as headaches on at least 15 days per month of which at least 8 days are with migraine) only when the patient meets [insert here the criteria for use as defined by the Pharmacy and Therapeutics Committee at its May, 2014 meeting].

Section 8.0

ICD-10 Mapping

Summary of Work to Date Correct Errors on the ICD-10 Prioritized List

The HERC staff have been working with DMAP and outside stakeholders and have been conducting internal data analyses to ensure that the October 1, 2014 Prioritized List is published with as few errors as possible. To this end, staff completed the following tasks:

1) DMAP provided a list of approximately 1000 ICD-10 codes which appeared on various DMAP lists (Ancillary, Diagnostic, Excluded) which were more appropriate for placement on the Prioritized List. HERC staff reviewed this list and placed codes on appropriate lines on the PL/gave suggestions to DMAP for placement on their lists.
2) HERC staff have noted various errors in code placement as topics are reviewed and have moved codes to more appropriate line(s) as deemed necessary. In many cases these errors were administrative errors; in some cases they were based on further review by HERC staff, but in all cases the changes were made to better align the codes with the intended prioritization of the HERC, based on input from the VbBS as well as the experts who assisted with the ICD-10 conversion.
    a. Many leukemia and lymphoma codes were on incorrect lines, and have been adjusted.
    b. Fracture lines had various code errors resulting in incorrect codes on the extremity lines, hip and pelvic fracture lines. Also some codes needed to be moved to different lines based on whether they were an open or closed fracture, or a fracture with delayed healing, malunion or nonunion.
    c. Viral codes on various incorrect lines.
    d. Anemia codes on incorrect lines.
    e. Influenza line with various incorrect codes.
3) HERC staff have run various data analyses and tabulated, analyzed and corrected various errors.
    a. Assigned codes appearing only on deleted lines to appropriate lines.
4) HERC staff have reviewed the guideline notes for correct inclusion of ICD10 codes.
5) Administrative corrections to typographical and similar errors.