Health Evidence Review Commission's Value-based Benefits Subcommittee

March 10, 2016

8:30 AM

Clackamas Community College
Wilsonville Training Center, Room 111-112
29373 SW Town Center Loop E, Wilsonville, Oregon, 97070

Section 1.0

Call to Order

AGENDA
VALUE-BASED BENEFITS SUBCOMMITTEE
March 10, 2016
8:30am - 1:00pm
Clackamas Community College
Wilsonville Training Center, Rooms 111-112
Wilsonville, Oregon
A working lunch will be served at approximately 12:00 PM
All times are approximate

I. Call to Order, Roll Call, Approval of Minutes – Susan Williams **8:30 AM**

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

III. Straightforward/Consent agenda – Ariel Smits **8:40 AM**
- **A.** Straightforward table
- **B.** Rosacea
- **C.** Vitamin A deficiencies

IV. 2018 Biennial Review – Ariel Smits **8:45 AM**
- **A.** Merging newborn lines

V. Previous discussion topics – Ariel Smits **9:00 AM**
- **A.** Diaphragmatic hernia
- **B.** Intracranial stenting and angioplasty for atherosclerosis
- **C.** Balloon dilation of intracranial vasospasm

VI. Guidelines – Ariel Smits **9:30 AM**
- **A.** Hormone requirements for chest surgery in the gender dysphoria guideline/other gender dysphoria issues
- **B.** Acupuncture for tobacco cessation—Erica Pettigrew
- **C.** Hyperbaric oxygen

VII. New discussion topics – staff **10:15 AM**
- **A.** Pectus excavatum and pectus caravatum—with Dr. Kim Ruscher
- **B.** Retractile testicles
- **C.** Remote imaging for screening and management of retinopathy of prematurity
- **D.** Implantable cardiac loop recorders
- **E.** Electric tumor treatment fields for initial treatment of glioblastoma
- **F.** Introduction to issues regarding services for autism and dementia

VIII.	**Coverage guidances – Cat Livingston** **A.** Skin substitutes for chronic skin ulcers (EGBS) **B.** Metabolic and bariatric surgery (HTAS)	**11:30 AM**
IX.	**Public comment**	**12:55 PM**
X.	**Adjournment – Susan Williams**	**1:00 PM**

Value-based Benefits Subcommittee Recommendations Summary
For Presentation to:
Health Evidence Review Commission on January 14, 2016

For specific coding recommendations and guideline wording, please see the text of the 1-14-2016 VbBS minutes.

RECOMMENDED CODE MOVEMENT (effective with the next set of interim modifications, no later than 10/1/16, unless otherwise indicated)

- Move the diagnosis code for Barrett's esophagus without dysplasia from an uncovered line to a covered line with a guideline change allowing long term proton pump inhibitor therapy
- Move the diagnosis codes for Barrett's esophagus with dysplasia from an uncovered line to the covered esophageal cancer line, a line title was changed to reflect this inclusion
- Move the eosinophilic esophagitis diagnosis code from one covered line to another
- Move several conditions of the mouth with no treatment from a covered line to an uncovered line
- Add procedure codes for acupuncture and chiropractic/osteopathic manipulation to the scoliosis line *(implemented along with delayed changes related to conditions of the back and spine)*
- Move the procedure code for placement of artificial discs from the scoliosis line to the covered back surgery line
- Delete the procedure codes for epidural steroid injections from the back conditions line and add to the Services Recommended For Non-Coverage Table
- Delete the procedure codes for maintenance of intrathecal pumps from the back condition lines
- Add procedure codes for proton beam therapy to nine lines for pediatric malignancies and remove from one benign tumor line
- Various straightforward coding changes

ITEMS CONSIDERED BUT NO RECOMMENDATIONS FOR CHANGES MADE

- A guideline on smoking cessation prior to elective surgical procedures was discussed in detail and staff was directed to complete more research and bring the topic back in March

RECOMMENDED GUIDELINE CHANGES (effective with the next set of interim modifications, no later than 10/1/16, unless otherwise indicated)

- Edit the wording of the guideline regarding disease of the lips to clarify the included ICD-10 codes
- Edit the surgical back guideline to remove the requirement for 6 months of conservative therapy prior to a patient being eligible for surgery on the uncovered back surgery line; add epidural steroid injections to the list of uncovered procedures *(implemented along with delayed changes related to conditions of the back and spine)*
- Edit the guideline for advanced imaging for low back conditions to specify that repeat imaging is only covered for significant changes in a patient's condition, and to return to

the old definition of radiculopathy as neurologic changes rather than just radiating pain *(implemented along with delayed changes related to conditions of the back and spine)*

- The epidural steroid injection guideline and the intrathecal pump maintenance guideline were deleted
- Add a new guideline on proton beam therapy
- Add a new guideline on nitrous oxide for labor pain management

VALUE-BASED BENEFITS SUBCOMMITTEE
Clackamas Community College
Wilsonville Training Center, Rooms 111-112
Wilsonville, Oregon
January 14, 2016
9:00 AM – 1:00 PM

Members Present: Kevin Olson, MD, Chair; David Pollack, MD; Susan Williams, MD (via phone until 10:30, then in person); Mark Gibson; Irene Croswell, RPh; Holly Jo Hodges, MD; Gary Allen, DMD (at 9:30 AM)

Members Absent: None

Staff Present: Darren Coffman; Ariel Smits, MD, MPH; Cat Livingston, MD, MPH; Jason Gingerich; Denise Taray, RN; Daphne Peck.

Also Attending: Jesse Little and Kim Wentz, MD, MPH (Oregon Health Authority); Valerie King, MD, MPH, Adam Obley, MD, MPH, and Craig Mosbaek (OHSU Center for Evidence-based Policy); Erica Pettigrew, MD, JD (OHSU); Nancy Noe (Johnson & Johnson); Reb Huggins (Oregon Affiliate, American College of Nurse Midwives).

- **Roll Call/Minutes Approval/Staff Report**

  The meeting was called to order at 9:10 am and roll was called. Minutes from the November 12, 2015 VbBS meeting were reviewed and approved.

  Coffman reported that Vern Saboe, DC will be joining VbBS as the complementary and alternative medicine representative. Kevin Olson, MD will be joining the HERC as well as maintaining his role as VbBS chair. Coffman also reported that there is not yet an implementation date for the back line changes.

  Smits reported on several issues:

  1) Staff will be changing the ICD-10 codes in all guidelines to remove terminal "x's" which are there to indicated that all further digit "children" codes are included. These entries will be changed to simply have the ICD-10 code terminated at the digit that includes all children codes. Staff will be eliminating ICD-9 codes from guidelines, and will be eliminating ICD-10 codes from guidelines unless they are absolutely necessary. These changes will not be routinely brought to VbBS for approved.
  2) The 2018 biennial review is starting. Smits requested suggestions for topics. Topics proposed to date include obesity (subject of a new taskforce), merging the two low birth weight lines into a single prematurity line, and review of coverage for uncomplicated inguinal hernia. A provider has also requested review of treatment of allergic rhinitis, but staff feels that this topic was recently reviewed and will only do a scan to see if

significant new evidence has been found. Gibson suggested reviewing shorter course radiation therapy for breast cancer in situ. Pollack suggested reviewing personalized medicine/gene tests for targeted drug therapy. Staff reported that many of these types of tests are going to be reviewed through the coverage guidance process, and therefore this topic does not need to be part of the biennial review.

3) The publication of errata continues, and the most recent errata was summarized in the packet.
4) The statewide back pain guidelines will be retired with HERC approval. The coverage guidances resulting from these guidelines will continued to be maintained and updated.
5) Staff has identified that diaphragmatic hernia with obstruction or gangrene diagnosis codes have been separated from their treatment CPT codes. Staff will move the ICD-10 diagnosis codes for these conditions to the upper GERD line where the CPT codes reside as an errata, and bring back the issue for more definitive discussion in March. The subcommittee agreed with this plan.

- **Topic: Straightforward/Consent Agenda**

Discussion: There was no discussion about the consent agenda items.

Recommended Actions:

1) Add 50948 (Laparoscopy, surgical; ureteroneocystostomy without cystoscopy and ureteral stent placement) to line 184 URETERAL STRICTURE OR OBSTRUCTION; HYDRONEPHROSIS; HYDROURETER
2) Add 47535 (Conversion of external biliary drainage catheter to internal-external biliary drainage catheter, percutaneous, including diagnostic cholangiography when performed, imaging guidance (eg, fluoroscopy), and all associated radiological supervision and interpretation) to line 320 CANCER OF LIVER
3) Add 47534-47536 (Placement/conversion/ exchange of biliary drainage catheter, percutaneous) to line 84 INJURY TO INTERNAL ORGANS
4) Add 27130 (Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty), with or without autograft or allograft) to line 205 CANCER OF BONES
5) Modify guideline note 65 as shown in Appendix A
6) Delete guideline note 16 as shown in Appendix C

MOTION: To approve the recommendations stated in the consent agenda. CARRIES 6-0. ***(Absent: Allen)***

- **Topic: Barrett's esophagus**

Discussion: Smits reviewed the summary document. Two separate options for code and guideline changes were reviewed. The subcommittee agree with the changes in "option A" as they felt that Barrett's with dysplasia should have a higher priority for treatment than GERD.

Recommended Actions:

1) Add K20.0 (Eosinophilic esophagitis) to line 383 ESOPHAGEAL STRICTURE; ACHALASIA and remove from lines 385 ESOPHAGITIS; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS and 516 ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM; ASYMPTOMATIC DIAPHRAGMATIC HERNIA
2) Affirm addition of K22.70 (Barrett's esophagus) to line 385 ESOPHAGITIS; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS (done as an errata) and remove from line 516 ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM; ASYMPTOMATIC DIAPHRAGMATIC HERNIA
3) Affirm addition of K22.711 (Barrett's esophagus with high grade dysplasia) to line 319 CANCER OF ESOPHAGUS (done as an errata) and remove from line 516 ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM; ASYMPTOMATIC DIAPHRAGMATIC HERNIA
4) Affirm addition of K22.710 (Barrett's esophagus with low grade dysplasia) and K22.719 (Barrett's esophagus with unspecified dysplasia) to line 319 CANCER OF ESOPHAGUS (done as an errata) and remove from line 516 ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM; ASYMPTOMATIC DIAPHRAGMATIC HERNIA
5) Change the title of line 319 CANCER OF ESOPHAGUS; BARRETT'S ESOPHAGUS WITH DYSPLASIA
6) Modify GN 144 as shown in Appendix A

MOTION: To recommend the code and guideline note changes as presented as "option A." CARRIES 7-0.

- **Topic: Other diseases of the lips and oral mucosa**

Discussion: Smits reviewed the summary document. Gary Allen, DMD agreed with the dental changes. There was no other discussion.

Recommended Actions:

1) Affirm the change in line title for line 168 ~~LEUKOPLAKIA AND~~ CARCINOMA IN SITU OF UPPER AIRWAY, INCLUDING ORAL CAVITY (done as an errata)
2) Add K13.2 (Minimal keratinized residual ridge mucosa) to line 579 STOMATITIS AND OTHER DISEASES OF ORAL SOFT and remove from line 623 BENIGN LESIONS OF TONGUE
3) Add K13.23 (Excessive keratinized residual ridge mucosa) to line 579 STOMATITIS AND OTHER DISEASES OF ORAL SOFT and remove from line 168 ~~LEUKOPLAKIA AND~~ CARCINOMA IN SITU OF UPPER AIRWAY, INCLUDING ORAL CAVITY

4) Add K13.24 (Leukokeratosis nicotina palati) to line 579 STOMATITIS AND OTHER DISEASES OF ORAL SOFT and remove from line 168 ~~LEUKOPLAKIA AND~~ CARCINOMA IN SITU OF UPPER AIRWAY, INCLUDING ORAL CAVITY
5) Modify GN113 as shown in Appendix A

MOTION: To recommend the code and guideline note changes as presented. CARRIES 7-0.

- **Topic: Straightforward back line items**

Discussion: Smits reviewed the summary document. There was no discussion of these items. Note that these changes will be implemented along with the currently delayed changes related to treatments of conditions of the back and spine.

Recommended Actions:

1) Add M96.5 (Postradiation scoliosis) to line 366 SCOLIOSIS and remove from lines 407 CONDITIONS OF THE BACK AND SPINE and 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS.
2) Add Q06.0 (Amyelia), Q06.1 (Hypoplasia and dysplasia of spinal cord), Q06.3 (Other congenital cauda equina malformations) and Q06.8 (Other specified congenital malformations of spinal cord) to line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
3) Add Q67.5 (Congenital deformity of spine) and Q76.3 (Congenital scoliosis due to congenital bony malformation) to line 366 SCOLIOSIS and delete from the applicable lines in the set of lines including 407 CONDITIONS OF THE BACK AND SPINE and 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS and 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
4) Add S23.101, S23.111, S23.121, S23.123, S23.131, S23.133, S23.141, S23.143, S23.151, S23.153, S23.161, S23.163, S23.171 (Dislocation of thoracic vertebra), and S33.101, S33.111, S33.121, S33.131, S33.141 (Dislocation of lumbar vertebra) to line 482 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY and remove from any of the following lines on which they appear: 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS and/or 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
5) Remove M46.1 (Sacroiliitis, not elsewhere classified) from line 532.
6) Add S33.8XXA (Sprain of other parts of lumbar spine and pelvis, initial encounter) to line 407 CONDITIONS OF THE BACK AND SPINE and remove from line 611 SPRAINS AND STRAINS OF ADJACENT MUSCLES AND JOINTS, MINOR

7) Remove M42.1 (Adult osteochondrosis of spine) and M42.9 (Spinal osteochondrosis, unspecified) from line 530 DEFORMITIES OF UPPER BODY AND ALL LIMBS and add to line 407
8) Remove M43.3 (Recurrent atlantoaxial dislocation with myelopathy), M43.4 (Other recurrent atlantoaxial dislocation), M43.5x2 (Other recurrent vertebral dislocation, cervical region) and M43.5x3 (Other recurrent vertebral dislocation, cervicothoracic region) from any of the following lines on which they currently appear: line 364 DEFORMITY/CLOSED DISLOCATION OF MAJOR JOINT AND RECURRENT JOINT DISLOCATIONS, and/or line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS. Add these codes to line 154 CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR UNSTABLE; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF VERTEBRAL INJURY
9) Remove M43.5X3, M43.5x4, M43.5X5, M43.5X6, M43.5X7, M43.5X8, M43.5X9, (Other recurrent vertebral dislocation, non cervical) from lines 364 DEFORMITY/CLOSED DISLOCATION OF MAJOR JOINT AND RECURRENT JOINT DISLOCATIONS, and line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS. Add these codes to line 482 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY
10) Remove M45 (Ankylosing spondylitis) from line 50 RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES
11) Add M45.9 (Ankylosing spondylitis of unspecified sites in spine) to line 407 CONDITIONS OF THE BACK AND SPINE
12) Remove M46.0 (Spinal enthesopathy) form line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
13) Remove M46.2x (Osteomyelitis of vertebra) from line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS. This condition is on the osteomyelitis line with appropriate surgeries.
14) Remove M46.3 (Infection of intervertebral disc (pyogenic)) from line 259 CHRONIC OSTEOMYELITIS and line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS and add to line 51 DEEP ABSCESSES, INCLUDING APPENDICITIS AND PERIORBITAL ABSCESS
15) Remove M46.5 (Other infective spondylopathies) from line 50 RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES and add to line 407 CONDITIONS OF THE BACK AND SPINE
16) Remove M46.80 (Other specified inflammatory spondylopathies, site unspecified) and M46.90 (Unspecified inflammatory spondylopathy, site unspecified) from line 50 RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES and add to line 407 CONDITIONS OF THE BACK AND SPINE
17) Remove M46.81-M46.89 (Other specified inflammatory spondylopathies) and M46.91-M46.99 (Unspecified inflammatory spondylopathy) from line 50

18) Remove M48.8X (Other specified spondylopathies) from line 467 OSTEOARTHRITIS AND ALLIED DISORDERS and add to line 407 CONDITIONS OF THE BACK AND SPINE
19) Remove M53.2X9 (Spinal instabilities, site unspecified) from line 663 MUSCULOSKELETAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY and add to line 407 CONDITIONS OF THE BACK AND SPINE
20) Remove M99.80 (Other biomechanical lesions of head region) from line 261 DEFORMITIES OF HEAD and line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS and add to line 543 TENSION HEADACHES
21) Remove M99.81-M99.85 (Other biomechanical lesions of spine) from line 663 MUSCULOSKELETAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY and add to line 407 CONDITIONS OF THE BACK AND SPINE
22) Remove M99.86-M99-.89 (Other biomechanical lesions of extremity or trunk) from line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
23) Add Q06.2 (Diastematomyelia) and Q06.9 (Congenital malformation of spinal cord, unspecified) to line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
24) Remove S13.0XXA (Traumatic rupture of cervical intervertebral disc, initial encounter) from line 520 and add to line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS.
25) Add S34.3XXA (Injury of cauda equina, initial encounter) to line 532 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
26) Add Z47.82 (Encounter for orthopedic aftercare following scoliosis surgery) to line 366 SCOLIOSIS and remove from lines 351 CONDITIONS OF THE BACK AND SPINE WITH URGENT SURGICAL INDICATIONS and 407 CONDITIONS OF THE BACK AND SPINE
27) Add acupuncture and chiropractic CPT codes (97810-97814, 98925- 98929, 98940-98942) to line 366 SCOLIOSIS

MOTION: To recommend the code changes as presented. CARRIES 7-0.

- **Topic: Artificial discs**

Discussion: Smits reviewed the summary document. The question was raised about whether artificial discs should be an included procedure on the upper back surgical line, as the conditions on this line are all urgent indications for surgery and the artificial disc guideline requires 6 months of conservative care. Livingston noted that artificial discs have equivalent efficacy as fusion, and as fusion is on this line, she felt that artificial discs should be included as an option which might avoid fusion. This led to a discussion about whether spinal fusion should be included on the upper surgical back line. Smits noted that the surgical back guideline does have some restrictions for fusion. The decision was to approve the recommended changes as presented. These changes will be implemented with the other changes to the treatment of conditions of the back and spine once their delay is lifted.

Recommended Actions:

1) Add CPT 22586-22865 (placement, revision and removal of total disc arthroplasty (artificial disc), anterior approach, cervical and lumbar) to line 351 CONDITIONS OF THE BACK AND SPINE WITH URGENT SURGICAL INDICATIONS
2) Remove CPT 22586-22865 from line 366 SCOLIOSIS

MOTION: To recommend the code changes as presented. CARRIES 7-0.

- **Topic: Surgical back guideline revisions**

Discussion: Smits reviewed the summary document. The concern was raised that not requiring conservative care prior to surgery on the lower priority back surgical line would be an issue if the funding line dropped below this line number. A member also pointed out that the current back surgery guideline may actually prevent surgery on the lower line as the patient must have neurologic deficits to qualify for surgery and it is doubtful that any diagnoses on the lower line would meet these guideline note requirements.

The decision was to delete the problematic phrase from the guideline note without adding any alternative wording. This change will be implemented with the other changes to the treatment of conditions of the back and spine once their delay is lifted.

Recommended Actions:

1) Modify GN 37 as shown in Appendix A

MOTION: To recommend the guideline note changes as presented. CARRIES 7-0.

- **Topic: Advanced imaging for low back conditions guidelines**

Discussion: Smits reviewed the summary document. Williams raised concerns about the fact that much of the evidence included in this summary was reviewed at VbBS previously, with different conclusions. Gingerich answered that the evidence reviewed previously included the coverage guidance for percutaneous interventions for low back pain, which included two Chou reviews, but not the AHRQ report, and likely not the Cochrane review. Smits answered that the AHRQ report was presented to the VbBS during the previous discussion, but that the only substantive discussion of the report centered on the definition of radiculopathy used in that review. Livingston noted that the coverage guidance on which the decision to include epidural steroid injections (ESIs) was based upon will be revised shortly, using the AHRQ report and its negative findings.

Pollack then shared his personal, very positive experience with ESI. He was concerned about not allowing OHP patients access to such a possibly beneficial therapy. He felt that

ESI is essential to get immediate pain relief, and get patients into PT or other active therapy. He was concerned that not covering ESI would increase opioid use.

Olson and Gibson responded that VbBS decisions need to focus on the population studies rather than personal anecdote. Williams raised a concern that the larger population studies have conflicting results and that VbBS should not pick and choose what evidence to consider. Smits noted that most studies found poor evidence of effectiveness for the general population. Livingston pointed out that the AHRQ report noted that there were few patients included with acute or subacute symptoms in the studies reviewed, and therefore the AHRQ report may not reflect the population response for patients with acute/subacute pain.

Hodges noted that ESI could be covered as an exception, but that she could not recall a request for an exception for ESI from a patient with acute, incapacitating back pain. Her exceptions normally involve patients with chronic back pain.

Pollack requested that when the coverage guidance goes back through re-review, that HTAS or EGBS attempt to identify what subpopulations could benefit from ESI. Staff replied that this was part of the re-review process.

Note: As the placement of epidural steroid injections were prioritized on the list based on the coverage guidance prior to the biennial review resulting in the "package" of changes to related to the treatment of conditions of the back and spine that are currently delayed, changes involving the placement of ESI will occur at the time of the next set of interim modifications to the list. The changes to the diagnostic guideline on advanced imaging of the back were a part of the "package" of back changes, and therefore will only go into effect once the implementation of those changes is lifted.

Recommended Actions:

1) Remove CPT 64483 (Injection(s), anesthetic agent and/or steroid, transforaminal epidural, with imaging guidance (fluoroscopy or CT); lumbar or sacral, single level) and 64484 (each additional level) from line 407 CONDITIONS OF THE BACK AND SPINE
2) Modify GN37 as shown in Appendix A
3) Remove 64484 (Injection(s), anesthetic agent and/or steroid, transforaminal epidural, with imaging guidance (fluoroscopy or CT); lumbar or sacral, additional levels) from line 159 HERPES ZOSTER; HERPES SIMPLEX AND WITH NEUROLOGICAL AND OPHTHALMOLOGICAL COMPLICATIONS
4) Place 64483 and 64484 ((Injection(s), anesthetic agent and/or steroid, transforaminal epidural, with imaging guidance (fluoroscopy or CT); lumbar or sacral) on the Services Recommended for Non-Coverage table
5) Delete guideline note 105 EPIDURAL STEROID INJECTIONS FOR LOW BACK PAIN as shown in Appendix C

6) Modify DIAGNOSTIC GUIDELINE D4, ADVANCED IMAGING FOR LOW BACK PAIN as shown in Appendix A

MOTION: To recommend the code and guideline note changes as presented. CARRIES 5-0. ***(Abstained: Pollack and Williams)***

- **Topic: Intrathecal pump guideline deletion**

Discussion: Smits reviewed the evidence summary. Gibson was concerned that adding the maintenance codes for these pumps to the complications line would allow use of an intervention that the Commission has previously determined was not effective. Hodges agreed, noting that OHP does not generally pay for complications directly related to uncovered procedures. Hodges felt that OHP should pay for pump removal for back pain indications, but not maintenance. Wentz noted that it was relatively common to have patients have pumps placed for back pain prior to coming on an OHP plan, and they need maintenance. It was noted that maintenance of these pumps could be covered as an exception if it was placed for a non-pairing condition if the patient was doing well. It was also noted that intrathecal pumps are not benign, but rather have some rather serious complications including CNS infections. The decision was to remove the pump maintenance codes from the back condition lines and delete the guideline note that applied to these lines. The subcommittee voted to not place the maintenance CPT codes or the maintenance ICD-10 Z code on the complications line. This leave coverage for maintenance only for indications on the dysfunction or cancer lines. A patient may appeal for continued coverage through the exception process. This change will be implemented with the other changes to the treatment of conditions of the back and spine once their delay is lifted.

Recommended Actions:

1) Delete GN72 as shown in Appendix C
2) Remove 62367 (Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); without reprogramming or refill), 62368 (with reprogramming), 62369 (with reprogramming and refill), and 62370 (with reprogramming and refill (requiring skill of a physician or other qualified health care professional)) from lines 351* CONDITIONS OF THE BACK AND SPINE WITH URGENT SURGICAL INDICATIONS, 366* SCOLIOSIS, and 532* CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS, and 607 DISORDERS OF SOFT TISSUE
    a. *implementation of these lines is delayed

MOTION: To recommend the code and guideline note changes as amended. CARRIES 7-0.

- **Topic: Tobacco cessation and elective surgical procedures**

Discussion:

Livingston presented an update on feedback from the QHOC Medical Directors. There was a debate about whether cessation support or requiring cessation was the most appropriate requirement. There was general agreement that implementing cessation support would be difficult, and most members favored moving forward with requiring cessation.

There was a proposal to have cessation counseling be offered in the first year, and then a smoking requirement in the second year of implementation, but this was felt to be too confusing to providers. A proposal to leave certain types of surgeries out was made (e.g. dental). King shared that there is an updated MED report that looks at procedures in detail. Livingston said she would bring this back to the group.

Additionally, there were concerns raised about the acceptability of other nicotine replacement strategies and appropriate testing of smoking abstinence, what the definition of elective entails, the possibility of a severe comorbid psychiatric disorder interfering with cessation, and which specific surgeries might be included or excluded. Members asked HERC staff to return with further details that would assist with implementation.

Recommended Actions:

1) Staff to perform further review and return with additional information and modifications to the proposed guideline note

- **Topic: Coverage Guidance—Proton beam therapy**

Discussion:

Obley reviewed the evidence. Livingston reviewed the Coverage Guidance box language and the proposed application to the Prioritized List. Staff recommended some additional amendments for clarification purposes in the guideline note.

Questions were raised about the availability of proton beam therapy (PBT) in Oregon. It was clarified that there is no proton beam therapy centers in Oregon. OHP would have to cover travel, lodging, and transportation expenses, as well as an attendant. There was clarification about the duration of treatment with protons. Dr. Rengan clarified that PBT intensity and duration is similar to other radiation regimens and may need daily radiation for several weeks. There are trials underway to examine more intense treatments of shorter duration.

Dr. Rengan addressed a question about how to decide which gliomas need proton beam therapy compared to x-ray radiation therapy. He explained that low-grade glioma patients with excellent prognosis would benefit from protons as opposed to those with high-grade gliomas in which prevention of secondary malignancies may be less relevant.

Dr. Rengan wanted to clarify the intent to cover benign brain and spinal cord tumors. It was clarified that those lines for which there is no additional guideline note language (eye

tumor, benign brain and malignant brain tumor lines) there are no specific restrictions and PBT is to be covered for these conditions. For all other listed tumors, PBT is only covered for malignancy. Members asked for the condition descriptions of the lines with no restrictions be added for clarity.

Recommended Actions:

1) Add proton beam therapy codes (77520, 77522, 77523,77525) to the following lines:
   a. 97 CHILDHOOD LEUKEMIAS
   b. 133 GRANULOMATOSIS WITH POLYANGIITIS
   c. 195 CANCER OF BREAST; AT HIGH RISK OF BREAST CANCER
   d. 205 CANCER OF BONES
   e. 242 ACUTE PROMYELOCYTIC LEUKEMIA
   f. 280 CANCER OF SKIN, EXCLUDING MALIGNANT MELANOMA
   g. 292 CANCER OF ORAL CAVITY, PHARYNX, NOSE AND LARYNX
   h. 402 ACUTE MYELOID LEUKEMIA
   i. 403 MYELOID DISORDERS
2) Remove proton beam therapy codes from Line 377 BENIGN NEOPLASM OF RESPIRATORY AND INTRATHORACIC ORGANS
3) Add a new guideline note as show in Appendix B

MOTION: To approve the recommended changes to the Prioritized List based on the draft Indications for Proton Beam Therapy Coverage Guidance scheduled for review by HERC immediately following the VbBS meeting. CARRIES 7-0.

- **Topic: Coverage Guidance—Nitrous oxide for labor pain management**

Discussion:

Dr. Valerie King reviewed the evidence and coverage guidance process. Livingston reviewed the box language and application to the Prioritized List.

There was discussion about the challenge implementation will present with no specific code for nitrous oxide, the costs associated with this service, women's preferences when compared to an epidural, and about the safety of nitrous oxide in out-of-hospital birth settings. No changes were proposed.

Recommended Actions:

1) Advise HSD to consider reimbursement options for the use of nitrous oxide
2) Adopt a new guideline note indicating inclusion of nitrous oxide for labor pain on Line 1 as shown in Appendix B

MOTION: To approve the recommended changes to the Prioritized List based on the draft Nitrous Oxide for Labor Pain Coverage Guidance scheduled for review by HERC immediately following the VbBS meeting. CARRIES 7-0.

- **Public Comment:**

  No additional public comment was received.

- **Issues for next meeting:**
  - 2018 Biennial review
    - Merging the two low birth weight lines
  - Inguinal hernias
  - Intracranial stenting and angioplasty
  - Pectus excavatum and pectus caravatum
  - Diaphragmatic hernias
  - Retractile testicles
  - Remote imaging for screening and management of retinopathy of prematurity
  - Tobacco cessation and elective surgery
  - Hyperbaric oxygen
  - Rehabiliation guideline for mental health disorders
  - Bariatric surgery coverage guidance
  - Electronic tumor treatment fields
  - Gender dysphoria
  - Acupuncture for smoking cessation
  - Nasal steroids for obstructive sleep apnea

- **Next meeting:**

  March 10. 2016 at Clackamas Community College, Wilsonville Training Center, Wilsonville Oregon, Rooms 111-112.

- **Adjournment:**

  The meeting adjourned at 1:10 PM.

Appendix A
Revised Guideline Notes

DIAGNOSTIC GUIDELINE D4, ADVANCED IMAGING FOR LOW BACK PAIN

In patients with non-specific low back pain and no "red flag" conditions [see Table D4], imaging is not a covered service; otherwise work up is covered as shown in the table. Repeat imaging is only covered when there is a substantial clinical change (e.g. progressive neurological deficit) or new clinical indication for imaging (i.e. development of a new red flag condition). Repeat imaging for acute exacerbations of chronic radiculopathic pain is not covered.

Electromyelography (CPT 96002-4) is not covered for non-specific low back pain.

Table D4
Low Back Pain - Potentially Serious Conditions ("Red Flags") and Recommendations for Initial Diagnostic Work-up

Possible cause	Key features on history or physical examination	Imaging[1]	Additional studies[1]
Cancer	• History of cancer with new onset of LBP	MRI	ESR
	• Unexplained weight loss • Failure to improve after 1 month • Age >50 years • Symptoms such as painless neurologic deficit, night pain or pain increased in supine position	Lumbosacral plain radiography	
	• Multiple risk factors for cancer present	Plain radiography or MRI	
Spinal column infection	• Fever • Intravenous drug use • Recent infection	MRI	ESR and/or CRP
Cauda equina syndrome	• Urinary retention • Motor deficits at multiple levels • Fecal incontinence • Saddle anesthesia	MRI	None
Vertebral compression fracture	• History of osteoporosis • Use of corticosteroids • Older age	Lumbosacral plain radiography	None
Ankylosing spondylitis	• Morning stiffness • Improvement with exercise • Alternating buttock pain • Awakening due to back pain during the second part of the night • Younger age	Anterior-posterior pelvis plain radiography	ESR and/or CRP, HLA-B27
Nerve compression/ disorders (e.g. herniated disc with radiculopathy)	• Back pain with leg pain in an L4, L5, or S1 nerve root distribution present < 1 month • Positive straight-leg-raise test or crossed straight-leg-raise test	None	None
	• Radiculopathic [CDD1] signs [CDD2] present >1 month • Severe/progressive neurologic deficits (such as foot drop), progressive motor weakness	MRI[3]	Consider EMG/NCV
Spinal stenosis	• Radiating leg pain • Older age • Pain usually relieved with sitting (Pseudoclaudication a weak predictor)	None	None
	• Spinal stenosis symptoms present >1 month	MRI[3]	Consider EMG/NCV

Appendix A
Revised Guideline Notes

[1] Level of evidence for diagnostic evaluation is variable

[2] Radiculopathic signs are defined for the purposes of this guideline as ~~pain, weakness, or sensory deficits, in a nerve root distribution~~ the presence of any of the following:

A. Markedly abnormal reflexes
B. Segmental muscle weakness
C. Segmental sensory loss
D. EMG or NCV evidence of nerve root impingement
E. Cauda equina syndrome,
F. Neurogenic bowel or bladder
G. Long tract abnormalities

[3] Only if patient is a potential candidate for surgery ~~or, if indicated, lumbar epidural steroid injection (see guideline note 105)~~

~~[4] Only if patient is a potential candidate for surgery~~

Red Flag: Red flags are findings from the history and physical examination that may be associated with a higher risk of serious disorders. CRP = C-reactive protein; EMG = electromyography; ESR = erythrocyte sedimentation rate; MRI = magnetic resonance imaging; NCV = nerve conduction velocity.

Extracted and modified from Chou R, Qaseem A, Snow V, et al: Diagnosis and Treatment of Low Back Pain: A Joint Clinical Practice Guideline from the American College of Physicians and the American Pain Society. Ann Intern Med. 2007; 147:478-491.

The development of this guideline note was informed by a HERC coverage guidance. See http://www.oregon.gov/oha/herc/Pages/blog-adv-imaging-low-back.aspx

GUIDELINE NOTE 37, SURGICAL INTERVENTIONS FOR CONDITIONS OF THE BACK AND SPINE OTHER THAN SCOLIOSIS

Lines 351, 532

Surgical consultation/consideration for surgical intervention are included on these lines only for patients with neurological complications, defined as showing objective evidence of one or more of the following:

A) Markedly abnormal reflexes
B) Segmental muscle weakness
C) Segmental sensory loss
D) EMG or NCV evidence of nerve root impingement
E) Cauda equina syndrome
F) Neurogenic bowel or bladder
G) Long tract abnormalities

Spondylolithesis (ICD-9 738.4, 756.11-756.12 / ICD-10 M43.1~~x~~, Q76.2) is included on line 351 only when it results in spinal stenosis with signs and symptoms of neurogenic claudication. Otherwise, these diagnoses are included on line 532.

Appendix A
Revised Guideline Notes

Surgical correction of spinal stenosis (ICD-9 ~~721.1,~~ 723.0, 724.0x / ICD-10 M48.0~~x~~) is only included on line 351 for patients with:

1. MRI evidence of moderate to severe central or foraminal spinal stenosis AND
2. A history of neurogenic claudication, or objective evidence of neurologic impairment consistent with MRI findings.

Only decompression surgery is covered for spinal stenosis; spinal fusion procedures are not covered for this diagnosis. Otherwise, these diagnoses are included on line 532.

~~For conditions on line 532, surgical interventions may only be considered after the patient has completed at least 6 months of conservative treatment, provided according to Guideline Note 56, NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.~~

The following interventions are not covered due to lack of evidence of effectiveness for back pain, with or without radiculopathy:

- facet joint corticosteroid injection
- prolotherapy
- intradiscal corticosteroid injection
- local injections
- botulinum toxin injection
- intradiscal electrothermal therapy
- therapeutic medial branch block
- radiofrequency denervation
- radiofrequency denervation
- sacroiliac joint steroid injection
- coblation nucleoplasty
- percutaneous intradiscal radiofrequency thermocoagulation
- epidural steroid injections

GUIDELINE NOTE 65, TELEPHONE AND EMAIL CONSULTATIONS

Included on all lines with evaluation & management (E&M) codes

Telephone and email consultations (CPT 98966-98969) must meet the following criteria:

1) Patient must have a pre-existing relationship with the provider as demonstrated by at least one prior office visit within the past 12 months.
2) E-visits must be provided by a physician or licensed provider within their scope of practice.
3) Documentation should model SOAP charting; must include patient history, provider assessment, and treatment plan; follow up instructions; be adequate so that the information provided supports the assessment and plan; must be retained in the patient's medical record and be retrievable.
4) Telephone and email consultations must involve permanent storage (electronic or hard copy) of the encounter.

5) Telephone and email consultations must meet HIPAA standards for privacy.
6) There needs to be a patient-clinician agreement of informed consent for E-visits by email. This should be discussed with and signed by the patient and documented in the medical record.

Examples of reimbursable telephone and email consultations include but are not limited to:

1) Extended counseling when person-to-person contact would involve an unwise delay.
2) Treatment of relapses that require significant investment of provider time and judgment.
3) Counseling and education for patients with complex chronic conditions.

Examples of non-reimbursable telephone and email consultations include but are not limited to:

1) Prescription renewal.
2) Scheduling a test.
3) Scheduling an appointment.
4) Reporting normal test results.
5) Requesting a referral.
6) Follow up of medical procedure to confirm stable condition, without indication of complication or new condition.
7) Brief discussion to confirm stability of chronic problem and continuity of present management.

GUIDELINE NOTE 113, DISEASES OF LIPS

Lines 210,585

ICD-10-CM code K13.0 (Diseases of lips) is included on Line 210 only for treatment of abscess or cellulitis of the lips. All other ~~subdiagnoses~~ diagnoses coded using K13.0 ~~under this code~~ are included on Line 585.

GUIDELINE NOTE 144, PROTON PUMP INHIBITOR THERAPY FOR GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Lines 385,516

Short term treatment (up to 8 weeks) of GERD without Barrett's (ICD-10 K20.8, K20.9, K21.0, K21.9) with proton pump inhibitor therapy is included on Line 385. Long term treatment is included on Line 516.

Long term proton pump inhibitor therapy is included on line 385 for Barrett's esophagus (ICD-10 K22.70).

Appendix B
New Guideline Notes

GUIDELINE NOTE XXX, PROTON BEAM THERAPY FOR CANCER

Lines 97, 117, 130, 133, 195, 205, 242, 280, 292, 299, 377, 402, 403

Proton beam therapy is included on lines 117 CANCER OF EYE AND ORBIT, 130 BENIGN NEOPLASM OF THE BRAIN AND SPINAL CORD and 299 CANCER OF BRAIN AND NERVOUS SYSTEM.

Proton beam therapy is included on lines 133, 205, and 292 only for: malignant skull base, paranasal sinus (including lethal midline granuloma), spinal, and juxtaspinal tumors .

Proton beam therapy is additionally included on lines 97, 195, 242, 280, 402, and 403 only for pediatric malignant tumors (incident cancer under age 21.)

GUIDELINE NOTE XXX, NITROUS OXIDE FOR LABOR PAIN

Line 1

Nitrous oxide for labor pain is included on this line.

Appendix C
Deleted Guideline Notes

~~GUIDELINE NOTE 16, CYSTIC FIBROSIS CARRIER SCREENING~~

~~Lines 1,625~~

~~Cystic fibrosis carrier testing is covered for 1) non-pregnant adults if indicated in the genetic testing algorithm or 2) pregnant women.~~

~~GUIDELINE NOTE 72, ELECTRONIC ANALYSIS OF INTRATHECAL PUMPS~~

~~Lines 351, 366, 532, 612~~

~~Electronic analysis of intrathecal pumps, with or without programming (CPT codes 62367-62370), is included on these lines only for pumps implanted prior to April 1, 2009.~~

~~GUIDELINE NOTE 105, EPIDURAL STEROID INJECTIONS FOR LOW BACK PAIN~~

~~Line 407~~

~~Epidural lumbar steroid injections (CPT 62311, 64483, 64484) are included on this line for patients with persistent radiculopathy due to herniated lumbar disc, where radiculopathy is defined as lower extremity pain in a nerve root distribution, with or without weakness or sensory deficits.~~

~~One epidural steroid injection is included on this line; a second epidural steroid injection may be provided after 3-6 months only if objective evidence of 3 months of sustained pain relief was provided by the first injection. It is recommended that shared decision-making regarding epidural steroid injection include a specific discussion about inconsistent evidence showing moderate short-term benefits, and lack of long-term benefits. Epidural lumbar steroid injections are not included on this line for spinal stenosis or for patients with low back pain without radiculopathy. Epidural steroid injections are only included on this line when the patient is also participating in an active therapy such as physical therapy or home exercise therapy.~~

~~The development of this guideline note was informed by a HERC coverage guidance. See http://www.oregon.gov/oha/herc/Pages/blog_percutaneous-low-back.aspx~~

Section 2.0

Staff Report

Prioritized List Errata for March 2016

1) Added L20.9 (Atopic dermatitis, unspecified) to line 535 ATOPIC DERMATITIS
2) Added P07.30 (Preterm newborn, unspecified weeks of gestation) and P07.32 (Preterm newborn, gestational age 29 completed weeks) to line 17 VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS). All other preterm newborn P17.3 family codes are already on line 17
3) Moved K44.0 (Diaphragmatic hernia with obstruction, without gangrene) and K44.1 (Diaphragmatic hernia with gangrene) from line 172 COMPLICATED HERNIAS; UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER; PERSISTENT HYDROCELE to line 385 ESOPHAGITIS; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS
    a. Line 385 contains the CPT codes for diaphragmatic hernia repair
    b. The ICD-9 code equivalent is on line 385
4) Moved E51.2 (Wernicke's encephalopathy) from line 122 NUTRITIONAL DEFICIENCIES to line 205 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS to pair with hospitalization CPT codes
5) The following neonatal conditions were moved
    a. Moved P78.89 (Other specified perinatal digestive system disorders) from line 2 to line 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION
    b. Moved the following codes from line 2 BIRTH OF NEWBORN to line 186 SEPTICEMIA
        i. P36 Sepsis of newborn
            1. ECMO codes on 186 needed to pair with ECMO codes
6) Added Q30.0 Choanal atresia to line 124 CHOANAL ATRESIA and removed from line 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
7) M79.7 (fibromyalgia) was removed from line 607 DISORDERS OF SOFT TISSUES and left on the fibromyalgia line
8) Z51.0 (Encounter for antineoplastic radiation therapy) was added to all the cancer lines with radiation therapy codes and HSD was advised to remove it from the Informational List
9) Z51.12 (Encounter for antineoplastic immunotherapy) was added to all the cancer lines with chemotherapy and HSD was advised to remove it from the Informational List
10) The nerve block codes were moved to the Ancillary Procedures File effective January 1, 2015, but several of these codes were mistakenly not moved. CPT 64505-64530 were removed from all lines on the Prioritized List and HSD was advised to add them to the Ancillary Procedures File.
11) Added ICD-10 M93.0 (Acute/chronic slipped upper femoral epiphysis) to line 360 CLOSED FRACTURE OF EXTREMITIES (EXCEPT MINOR TOES) where the CPT code series 27175-27181 (Repair of femoral slipped epiphysis) will pair. Removed M93.0 from line 85 FRACTURE OF HIP

12) Removed G0458 (Low dose rate (ldr) prostate brachytherapy services, composite rate) from all current lines and added to line 334 CANCER OF PROSTATE GLAND. This code was moved from 334 to 8 other lines in 2015 as some type of data input error.
13) GN 42 was corrected. These changes were adopted at the October, 2015 VBBS/HERC meetings but were not included in the January 1, 2016 PL in error.

GUIDELINE NOTE 42, CHEMODENERVATION FOR CHRONIC MIGRAINE

Line 414

Chemodenervation for treatment of chronic migraine (CPT 64615) is included on this line for prophylactic treatment of adults who meet all of the following criteria:

1) have chronic migraine defined as headaches on at least 15 days per month of which at least 8 days are with migraine
2) has not responded to or have contraindications to at least three prior pharmacological prophylaxis therapies (beta-blocker, calcium channel blocker, anticonvulsant or tricyclic antidepressant)
3) treatment is administered in consultation with a neurologist or headache specialist.

Treatment is limited to two ~~injections~~ treatments given 3 months apart. Additional treatment requires documented positive response to therapy. Positive response to therapy is defined as a reduction of at least ~~6~~ 7 headache days per month compared to baseline headache frequency.

Section 3.0

Consent Agenda-

Straightforward Items

Straightforward Issues—March, 2016

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
20924	Tendon graft, from a distance (eg, palmaris, toe extensor, plantaris)	436 INTERNAL DERANGEMENT OF KNEE AND LIGAMENTOUS DISRUPTIONS OF THE KNEE, RESULTING IN SIGNIFICANT INJURY/IMPAIRMENT	Alison Little, MD requested that 20924 be added to the knee line for use in ACL reconstruction. 20924 appears on 7 other lines.	Add 20924 to line 436
D62	Acute posthemorrhagic anemia	122 NUTRITIONAL DEFICIENCIES 152 ACQUIRED HEMOLYTIC ANEMIAS	D62 is currently on line 122, which does not have hospitalization codes, and this condition may require inpatient treatment. Line 152 has inpatient CPT codes	Add D62 to line 152 Remove D62 from line 122
96150-96155	Health and behavior assessment	3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS	Line 3 needs to have screening procedure codes which are not currently there. This code series is on approximately 170 other lines.	Add 96150-96155 to line 3
64505 64508 64510 64517 64520 64530	Injection, anesthetic agent	3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS	Several anesthetic injections are found on line 3 and there is no diagnoses on this line that need to pair with these codes.	Remove 64505, 64508, 64510, 64517, 64520, and 64530 from line 3
L66.2 L66.3 L66.8 L66.9	Folliculitis decalvans Perifolliculitis capitis abscedens Other cicatricial alopecia Cicatricial alopecia, unspecified	517 HIDRADENITIS SUPPURATIVA; DISSECTING CELLULITIS OF THE SCALP 588 DISEASE OF NAILS, HAIR AND HAIR FOLLICLES	Folliculitis decalvans and cicatricial alopecia are conditions very similar to dissecting cellulitis of the scalp, and are treated in similar ways. L66.3 is the most commonly used code for dissecting cellulitis of the scalp.	Add L66.2, L66.8 and L66.9 to line 517 Remove L66.2, L66.3, L66.8 and L66.9 from line 588

Straightforward Issues—March, 2016

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
92507-92508 92526 92607-92609 92633 Inpatient and ICU codes	Speech therapy services	501 CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD) AND HYDROXYAPETITE DEPOSITION DISEASE	A series of CPT codes for speech therapy appear on line 501 with no diagnosis which is appropriate to pair. Inpatient and ICU and similar codes appear on this line and are not appropriate.	Remove 92507-92508, 92526, 92607-92609, and 92633 from line 501 Remove all CPT codes for inpatient care.
E11.49 E11.59 E11.628	Type 2 diabetes mellitus with other diabetic neurological complication Type 2 diabetes mellitus with other circulatory complications Type 2 diabetes mellitus with other skin complications	169 PREVENTIVE FOOT CARE IN HIGH RISK PATIENTS	HSD requested that E11.49 and E11.59 and E11.628 pair with CPT 11721 (Debridement of nail(s) by any method(s); 6 or more) which appears on line 169. Similar diagnosis codes appear on line 169	Add E11.49 and E11.59 and E11.628 to line 169
27175-27185	Treatment of slipped femoral epiphysis	431 ACUTE PERIPHERAL MOTOR AND DIGITAL NERVE INJURY 360 CLOSED FRACTURE OF EXTREMITIES (EXCEPT MINOR TOES) 508 PERIPHERAL ENTHESOPATHIES	27175-27185 pair with slipped femoral epiphysis diagnosis codes on line 360; no appropriate diagnoses appear on lines 431 or 508	Remove 27175-27185 from lines 431 and 508

Straightforward Issues—March, 2016

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
96904	Whole body integumentary photography, for monitoring of high risk patients with dysplastic nevus syndrome or a history of dysplastic nevi, or patients with a personal or familial history of melanoma	234 MALIGNANT MELANOMA OF SKIN 280 CANCER OF SKIN, EXCLUDING MALIGNANT MELANOMA 631 BENIGN NEOPLASMS OF SKIN AND OTHER SOFT TISSUES	HSD requested review of the placement of 96904. This code appears on a large number of lines that do not contain relevant diagnoses. It needs to be added to line 234 to pair with melanoma, line 280 to pair with D48.5 which codes for dysplastic nevus syndrome, and line 631 to pair with various melanocytic nevi codes.	Add 96904 to lines 234, 280 and 631 Remove 96904 from lines 60,217,363,378,413,430,493,525, 535,536,544 and 548

Rosacea

Issue: Multiple rosacea ICD-10 codes were identified on lines other than line 525 ROSACEA; ACNE. No rosacea diagnosis codes are currently on line 525. Additionally, several CPT codes for treatment of hidradenitis are found on line 525 when this diagnosis (with appropriate CPT codes) is found on line 517 HIDRADENITIS SUPPURATIVA; DISSECTING CELLULITIS OF THE SCALP.

HERC staff recommendations:

1) Add roseacea ICD-10 diagnosis codes to line 525 ROSACEA; ACNE and remove from line 507 ERYTHEMATOUS CONDITIONS
    a. L71.1 Rhinophyma
    b. L71.8 Other rosacea
    c. L71.9 Rosacea, unspecified
2) Remove hidradenitis treatment CPT codes from lines 378 ACNE CONGLOBATA (SEVERE CYSTIC ACNE), 525 ROSACEA; ACNE and 631 BENIGN NEOPLASMS OF SKIN AND OTHER SOFT TISSUES
    a. CPT 11450-11471 (Excision of skin and subcutaneous tissue for hidradenitis)
    b. Already on appropriate other lines (517 HIDRADENITIS SUPPURATIVA; DISSECTING CELLULITIS OF THE SCALP, 520 DISORDERS OF SWEAT GLANDS)

Vitamin A Deficiencies

Issue: several diagnoses related to Vitamin A deficiency are on the incorrect lines. Vitamin A deficiency can cause ulceration of the conjunctiva or cornea and night blindness. The main treatment is high dose vitamin A supplementation. Ophthalmology evaluation may be necessary, although there is no surgical treatment or other ophthalmology intervention for these conditions. Xerosis is dry eyes, and does not need ophthalmology treatment. Corneal ulcers due to vitamin A supplementation may require treatment, as might keratomalacia.

These diagnoses should be placed on the vitamin deficiency line. The diagnostic ophthalmology visit should be covered as a diagnostic visit, but further ophthalmology visits would not pair.

ICD-10 Code	**Code Description**	**Current Placement**
E50.0	Vitamin A deficiency with conjunctival xerosis	456 EXOPHTHALMOS AND CYSTS OF THE EYE AND ORBIT
E50.1	Vitamin A deficiency with Bitot's spot and conjunctival xerosis	456
E50.2	Vitamin A deficiency with corneal xerosis	456
E50.3	Vitamin A deficiency with corneal ulceration and xerosis	456
E50.4	Vitamin A deficiency with keratomalacia	122 NUTRITIONAL DEFICIENCIES 315 CORNEAL OPACITY AND OTHER DISORDERS OF CORNEA
E50.5	Vitamin A deficiency with night blindness	122 455 DISORDERS OF REFRACTION AND ACCOMMODATION
E50.6	Vitamin A deficiency with xerophthalmic scars of cornea	122
E50.7	Other ocular manifestations of vitamin A deficiency	122
E50.8	Other manifestations of vitamin A deficiency	122
E50.9	Vitamin A deficiency, unspecified	122

HERC staff recommendations:

1) Add E50.0-E50.3 to line 122 NUTRITIONAL DEFICIENCIES and remove from line 456 EXOPHTHALMOS AND CYSTS OF THE EYE AND ORBIT
2) Add E50.3 to line 249 CORNEAL ULCER; SUPERFICIAL INJURY OF EYE AND ADNEXA
3) Remove E50.5 from line 455 DISORDERS OF REFRACTION AND ACCOMMODATION

Section 4.0

Biennial Review

2018 Biennial Review

Merging Selected Neonatal Lines

Issue: There are multiple lines on the Prioritized List which related to the birth of an infant or to newborn medical conditions. Many of these lines contain basically the same treatment CPT codes—hospitalization codes, NICU codes, and pediatric intensive care codes. Each also contains diagnosis codes for possibly serious newborn conditions which might require nursery or NICU care. These lines are generally all in the highest priority area of the Prioritized List.

These lines were reviewed by the ICD-10 neonatology reviewers, who made few suggestions for change. However, HERC staff feel that many of these lines should be merged together due to very similar diagnoses, having only one or a few diagnoses, or having diagnoses that are equally important to treat compared to another line.

The following 26 lines contain newborn conditions. Lines for conditions which require specific surgical interventions, such as congenital heart disease or cleft palate, are not included in this list and are not recommended by staff for merging at this time.

2 BIRTH OF INFANT—contains ICD-10 codes for newborns affected by various maternal conditions/infections/exposures, multiple gestation, possible birth defects, observation for suspected conditions in newborns, infants with serious infections such as sepsis, as well as normal newborns with no suspected conditions

11 RESPIRATORY CONDITIONS OF FETUS AND NEWBORN—contains ECMO codes

15 CONGENITAL INFECTIOUS DISEASES—contains diagnoses that might be used for an extended period

16 CONGENITAL SYPHILIS— contains diagnoses that might be used for an extended period

17 VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS)—contains ICD-10 codes for premature infants, as well as a subset of brain injury and bleeding codes (intraventricular hemorrhage and hypoxic ischemic encephalopathy).

18 NEONATAL MYASTHENIA GRAVIS

19 FEEDING PROBLEMS IN NEWBORNS

21 SYNDROME OF "INFANT OF A DIABETIC MOTHER" AND NEONATAL HYPOGLYCEMIA

22 OMPHALITIS OF THE NEWBORN AND NEONATAL INFECTIVE MASTITIS

23 LOW BIRTH WEIGHT (1500-2500 GRAMS)—contains ICD-10 codes for premature infants, mostly overlapping with line 17

27 INTRACRANIAL HEMORRHAGES; CEREBRAL CONVULSIONS, DEPRESSION, COMA, AND OTHER ABNORMAL CERERAL SIGNS OF THE NEWBORN

31 DRUG WITHDRAWAL SYNDROME IN NEWBORN

34 SEVERE BIRTH TRAUMA FOR BABY—contains mostly intracranial hemorrhage diagnoses, which are missing from line 27

35 NEONATAL THYROTOXICOSIS

36 HEMATOLOGICAL DISORDERS OF FETUS AND NEWBORN

43 DISORDERS RELATING TO LONG GESTATION AND HIGH BIRTHWEIGHT—contain ICD-10 codes for large for gestational age and post-term infants

45 HYPOCALCEMIA, HYPOMAGNESEMIA AND OTHER ENDOCRINE AND METABOLIC DISTURBANCES SPECIFIC TO THE FETUS AND NEWBORN
77 POLYCYTHEMIA NEONATORUM, SYMPTOMATIC
92 NECROTIZING ENTEROCOLITIS IN FETUS OR NEWBORN—contains multiple surgical codes for intestinal procedures
106 HEMOLYTIC DISEASE DUE TO ISOIMMUNIZATION, ANEMIA DUE TO TRANSPLACENTAL HEMORRHAGE, AND FETAL AND NEONATAL JAUNDICE—contains light therapy codes
146 CONDITIONS INVOLVING THE TEMPERATURE REGULATION OF NEWBORNS
149 ANEMIA OF PREMATURITY OR TRANSIENT NEONATAL NEUTROPENIA
283 HYDROPS FETALIS
296 ADRENAL OR CUTANEOUS HEMORRHAGE OF FETUS OR NEONATE
353 MILD/MODERATE BIRTH TRAUMA FOR BABY
648 EDEMA AND OTHER CONDITIONS INVOLVING THE SKIN OF THE FETUS AND NEWBORN—contains conditions that require no treatment

Additionally, staff have identified multiple neonatal diagnoses on the dysfunction lines which are not included on current neonatal disease specific lines. Line 2 BIRTH OF INFANT contains many diagnoses that could be moved to disease specific lines as well.

Staff feel that some or many of these 26 lines can be merged together. There are several ways to do this. There could be a merging of conditions of the same organ system together as larger lines such as "NEONATAL ENDOCRINE AND METABOLIC DISORDERS," "HEMATOLOGICAL DISORDERS OF FETUS AND NEWBORN," and "PREMATURITY." Many of the conditions currently on line 2 BIRTH OF INFANT would be moved onto one of these new lines, leaving mainly normal newborn codes and observation for suspected condition codes on line 2. Lines considered for merging would need to contain diagnoses that are only seen in the neonatal period, and that have no disease specific sequelae (other than conditions included on the dysfunction lines). This type of lumping would result in approximately 10 lines rather than 26. The advantage of this strategy is that is reduces arbitrary differences between similar lines and makes the Prioritized List somewhat less confusing and arbitrary.

There could also be more extensive merging, with most lines merged into an expanded line 2 BIRTH OF INFANT. All diagnoses for this line would conditions of the newborn which do not persist much past the neonatal period (other than sequelae which are on the dysfunction lines) and which do not require specialized treatments represented by CPT codes other than hospital/NICU/pediatric intensive care codes (i.e. surgery, light therapy, ECMO, etc.). Conditions of similar seriousness already appear on line 2. Thirteen lines would be merged into line 2 in this scenario. Two additional lines would be created, one for neonatal hemorrhages and similar diagnoses, and one for jaundice and neonatal hemolytic disease. This scenario would merge the 26 lines into approximately 5 lines. The advantage of this scenario is that it reflects the reality of care. A newborn who does not appear healthy or normal is evaluated and receives nursery or NICU care in much the same way regardless of the eventual diagnosis. These conditions are all identified and treated in similar ways (i.e. have the same CPT codes),

have similar prioritization (i.e. are all important to treat), and generally have similar prognoses. Separating these conditions into so many lines seems arbitrary.

A third scenario would have minimal line merging. This could consist of merging a few lines, such as the two low birth weight lines, that have no real reason to be separated, but would leave the majority of current lines as is. This scenario would reduce the number of lines to approximately 20. The advantage of this strategy is that it reflects how these conditions have been prioritized for the past 25 years and is consistent with the recommendations of the Neonatology ICD-10 reviewers.

In all scenarios, staff would move certain diagnoses as they are identified as being on incorrect lines, and try to place diagnoses only found on the dysfunction lines onto specific disease lines. Staff have identified many diagnoses that would fall into this category.

<u>HERC staff recommendation</u>:

1) Discuss merging strategies for the neonatal lines and give staff guidance on which merging scenario is preferred by the Commission
    a. Minimal line merging
    b. Merge lines into organ system groups
    c. Merge lines into a few large lines
    d. In all cases, incorrectly placed codes will be identified and more appropriate placement recommended

Neonatal Line Scoring (does not include congenital heart disease or other congenital anomaly lines)

Line	Score	Comments
2 BIRTH OF INFANT	5000	Hand moved to line position
10 GALACTOSEMIA	5625	Affects for extended period
11 RESPIRATORY CONDITIONS OF FETUS AND NEWBORN	5600	Do not merge—has unique treatment CPTs
13 CONGENITAL HYPOTHYROIDISM	4875	Affects for extended period
14 PHENYLKETONURIA (PKU)	4875	Affects for extended period
15 CONGENITAL INFECTIOUS DISEASES	4800	Affects for extended period
16 CONGENITAL SYPHILIS	4800	Affects for extended period
17 VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS)	4800	
18 NEONATAL MYASTHENIA GRAVIS	4400	
19 FEEDING PROBLEMS IN NEWBORNS	4400	
21 SYNDROME OF "INFANT OF A DIABETIC MOTHER" AND NEONATAL HYPOGLYCEMIA	4000	
22 OMPHALITIS OF THE NEWBORN AND NEONATAL INFECTIVE MASTITIS	4000	
23 LOW BIRTH WEIGHT (1500-2500 GRAMS)	4000	
27 INTRACRANIAL HEMORRHAGES; CEREBRAL CONVULSIONS, DEPRESSION, COMA, AND OTHER ABNORMAL CERERAL SIGNS OF THE NEWBORN	3600	
31 DRUG WITHDRAWAL SYNDROME IN NEWBORN	3300	
34 SEVERE BIRTH TRAUMA FOR BABY	3300	Diagnoses overlap with line 27
35 NEONATAL THYROTOXICOSIS	3200	
36 HEMATOLOGICAL DISORDERS OF FETUS AND NEBORN	3200	
43 DISORDERS RELATING TO LONG GESTATION AND HIGH BIRTHWEIGHT	3000	
45 HYPOCALCEMIA, HYPOMAGNESEMIA AND OTHER ENDOCRINE AND METABOLIC DISTURBANCES SPECIFIC TO THE FETUS AND NEWBORN	3000	
77 POLYCYTHEMIA NEONATORUM, SYMPTOMATIC	2500	
92 NECROTIZING ENTEROCOLITIS IN FETUS OR NEWBORN	2400	Do not merge—has unique treatment CPTs
106 HEMOLYTIC DISEASE DUE TO ISOIMMUNIZATION, ANEMIA DUE TO TRANSPLACENTAL HEMORRHAGE, AND FETAL AND NEONATAL JAUNDICE	2240	Do not merge—has unique treatment CPTs
146 CONDITIONS INVOLVING THE TEMPERATURE REGULATION OF NEWBORNS	2000	
149 ANEMIA OF PREMATURITY OR TRANSIENT NEONATAL NEUTROPENIA	2000	
283 HYDROPS FETALIS	1200	

296 ADRENAL OR CUTANEOUS HEMORRHAGE OF FETUS OR NEONATE	1120	
353 MILD/MODERATE BIRTH TRAUMA FOR BABY	750	
648 EDEMA AND OTHER CONDITIONS INVOLVING THE SKIN OF THE FETUS AND NEWBORN	0	No treatment necessary

Line merging – fewer line merges proposal

1) Merge line 15 CONGENITAL INFECTIOUS DISEASES and 16 CONGENITAL SYPHILIS
    a. Same score, syphilis is an infectious disease
2) Merge line 17 VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS) and line 23 LOW BIRTH WEIGHT (1500-2500 GRAMS)
    a. Similar scoring, mostly overlapping diagnosis codes
3) Merge line 21 SYNDROME OF "INFANT OF A DIABETIC MOTHER" AND NEONATAL HYPOGLYCEMIA, 35 NEONATAL THYROTOXICOSIS, and line 45 HYPOCALCEMIA, HYPOMAGNESEMIA AND OTHER ENDOCRINE AND METABOLIC DISTURBANCES SPECIFIC TO THE FETUS AND NEWBORN
    a. All are endocrine issues for neonates
    b. Scoring varies between 3000 and 4000
4) Merge lines 36 HEMATOLOGICAL DISORDERS OF FETUS AND NEBORN, 77 POLYCYTHEMIA NEONATORUM, SYMPTOMATIC, 149 ANEMIA OF PREMATURITY OR TRANSIENT NEONATAL NEUTROPENIA
    a. All are hematologic issues for neonates
    b. Scoring varies between 2000 and 3200
5) Merge lines 27 INTRACRANIAL HEMORRHAGES; CEREBRAL CONVULSIONS, DEPRESSION, COMA, AND OTHER ABNORMAL CERERAL SIGNS OF THE NEWBORN and 34 SEVERE BIRTH TRAUMA FOR BABY
    a. Line 34 contains nearly all diagnosis codes for intracranial hemorrhages. Other diagnoses include other CNS injuries
    b. Scoring is nearly identical

Section 5.0

Previously Discussed Items

Diaphragmatic Hernia

Question: Where should obstructed or gangrenous diaphragmatic hernia be prioritized?

Question source: HERC staff

Issue: ICD-10 K44.0 (Diaphragmatic hernia with obstruction, without gangrene) and K44.1 (Diaphragmatic hernia with gangrene) were moved from line 172 COMPLICATED HERNIAS; UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER; PERSISTENT HYDROCELE to line 385 ESOPHAGITIS; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS as an errata in January 2016. Line 385 contains the CPT codes for diaphragmatic hernia repair that need to pair with these diagnoses and the ICD-9 code equivalent for these diagnoses was on line 385. This errata was done to allow pairing of these diagnoses with appropriate treatment. Uncomplicated diaphragmatic hernia (K44.9 Diaphragmatic hernia without obstruction or gangrene) is on line 516 ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM; ASYMPTOMATIC DIAPHRAGMATIC HERNIA, which is appropriate as the major issue with this diagnosis is GERD type symptoms and complications.

The ICD-10 Gastroenterology reviewers had intentionally moved the diaphragmatic hernia codes to the upper line as they felt that any obstructed or gangrenous hernia should be prioritized together and relatively high on the Prioritized List.

Expert Input

Dr. Kimberly Ruscher, pediatric surgeon

> If you need to pair the K44 codes with treatment, I would keep them under the complicated hernia line…gangrenous or complicated hernias are just as dangerous as other complicated hernias. The reason I say this is that whether the hernia is in the diaphragm, the abdominal wall, inguinal region, or an internal hernia, if there is an obstruction we have to treat it by treating the hernia, and if gangrene is present the patient's life will be threatened. Thus, I think that the most straightforward thing is to pair gangrenous/obstructed diaphragmatic hernia and treatment on the line for complicated hernias.

HERC staff recommendations:

1) Add ICD-10 K44.0 (Diaphragmatic hernia with obstruction, without gangrene) and K44.1 (Diaphragmatic hernia with gangrene) to line 172 COMPLICATED HERNIAS; UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER; PERSISTENT HYDROCELE and remove from line 385 ESOPHAGITIS; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS
2) Add the CPT codes for repair of complicated diaphragmatic hernia to line 172 and remove from line 385
    a. 39503 Repair, neonatal diaphragmatic hernia, with or without chest tube insertion and with or without creation of ventral hernia
    b. 39540 Repair, diaphragmatic hernia (other than neonatal), traumatic; acute
    c. 39541 Repair, diaphragmatic hernia (other than neonatal), traumatic; chronic
    d. 39560 Resection, diaphragm; with simple repair (eg, primary suture)
    e. 39561 Resection, diaphragm; with complex repair (eg, prosthetic material, local muscle flap)
3) Change the line title for line 385
    a. Condition: ESOPHAGITIS; GERD~~; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS~~

Balloon angioplasty and Intravascular Stenting

Issue: During the 2016 CPT code review of intra-arterial mechanical thrombectomy, similar procedures were identified that are currently being covered and which appear to have limited evidence of effectiveness. 61630 (Balloon angioplasty, intracranial (eg, atherosclerotic stenosis), percutaneous) and 61635 (Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed) were new CPT codes for 2006 and do not appear to have been reviewed extensively at the time of their placement on the Prioritized List. At some point between 2006 and present, 61635 was placed on the non-covered list.

Current Placement

61630 Balloon angioplasty, intracranial (eg, atherosclerotic stenosis), percutaneous: line 200 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN.

61635 Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed: Services Recommended for Non-Coverage Table

Evidence

1) **NICE 2012** Endovascular stent insertion for intracranial atherosclerotic disease
    a. Current evidence on the efficacy of endovascular stent insertion for intracranial atherosclerotic disease shows no substantial differences in clinical outcomes compared with medical treatment after 1–2 years. Evidence on its safety shows that there is a significant risk of periprocedural stroke and death. Therefore, this procedure should only be used in the context of research.
2) **VISSIT**; RCT of balloon angioplasty/stent vs medical management for intracranial stenosis http://jama.jamanetwork.com/article.aspx?articleid=2208809
    a. **Zaidat 2015**, VISSIT
        i. N=112 patients randomized to medical management alone vs medical management plus balloon-expandable stent placement
            1. Enrollment stopped early due to early analysis finding negative outcomes
        ii. RESULTS The 30-day primary safety end point occurred in more patients in the stent group (14/58; 24.1%[95%CI, 13.9%-37.2%]) vs the medical group (5/53; 9.4%[95%CI, 3.1%-20.7%]) (*P* = .05). Intracranial hemorrhage within 30 days occurred in more patients in the stent group (5/58; 8.6%[95%CI, 2.9%-19.0%]) vs none in the medical group (95%CI, 0%-5.5%) (*P* = .06). The 1-year primary outcome of stroke or hard TIA occurred in more patients in the stent group (21/58; 36.2%[95%CI, 24.0-49.9]) vs the medical group (8/53; 15.1% [95%CI, 6.7-27.6]) (*P* = .02).Worsening of baseline disability score (modified Rankin Scale) occurred in more patients in the stent group (14/58; 24.1%[95%CI, 13.9%-37.2%]) vs the medical group (6/53; 11.3%[95%CI, 4.3%-23.0%]) (*P* = .09).The EuroQol-

5D showed no difference in any of the 5 dimensions between groups at 12-month follow-up.

iii. CONCLUSIONS Among patients with symptomatic intracranial arterial stenosis, the use of a balloon-expandable stent compared with medical therapy resulted in an increased 12-month risk of added stroke or TIA in the same territory, and increased 30-day risk of any stroke or TIA. These findings do not support the use of a balloon-expandable stent for patients with symptomatic intracranial arterial stenosis.

3) **SAMMPRIS**; RCT of stenting vs aggressive medical management for acute stroke and intracranial artery stenosis
    a. **Chimowitz 2011**, SAMMPRIS RCT early outcomes
        i. N=451 patients (enrolment stopped early due to serious negative outcomes) randomized to either aggressive medical management alone or aggressive medical management plus stenting
        ii. The primary endpoint was any of the following: stroke or death within 30 days after enrolment, ischemic stroke in the territory of the qualifying artery beyond 30 days of enrolment, or stroke or death within 30 days after a revascularization procedure of the qualifying lesion during follow-up
        i. Results: 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non–stroke-related death, 0.4%) (P = 0.002). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups (P = 0.009), with 1-year rates of the primary end point of 20.0% in the PTAS group and 12.2% in the medical-management group.
        ii. Conclusions: In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected.
    b. **Derdeyn 2014**, SAMMPRIS RCT later outcomes
        i. N=451 patients (follow up of Chimowitz paper)
        ii. Findings During a median follow-up of 32·4 months, 34 (15%) of 227 patients in the medical group and 52 (23%) of 224 patients in the stenting group had a primary endpoint event. The cumulative probability of the primary endpoints was smaller in the medical group versus the percutaneous transluminal angioplasty and stenting (PTAS) group (p=0·0252). Beyond 30 days, 21 (10%) of 210 patients in the medical group and 19 (10%) of 191 patients in the stenting group had a primary endpoint. The absolute differences in the primary endpoint rates between the two groups were 7·1% at year 1 (95% CI 0·2 to 13·8%;

p=0·0428), 6·5% at year 2 (−0·5 to 13·5%; p=0·07) and 9·0% at year 3 (1·5 to 16·5%; p=0·0193). The occurrence of the following adverse events was higher in the PTAS group than in the medical group: any stroke (59 [26%] of 224 patients *vs* 42 [19%] of 227 patients; p=0·0468) and major haemorrhage (29 [13%] of 224 patients *vs* 10 [4%] of 227 patients; p=0·0009).

iii. Conclusions: The early benefit of aggressive medical management over stenting with the Wingspan stent for highrisk patients with intracranial stenosis persists over extended follow-up. Our findings lend support to the use of aggressive medical management rather than PTAS with the Wingspan system in high-risk patients with atherosclerotic intracranial arterial stenosis.

4) **Teleb 2014**, review of endovascular management for intracranial atherosclerotic disease
   a. Early studies of angioplasty for intracranial atherosclerotic disease found very high rates of complications
      i. Complication rates as high as 50%, including dissections, emboli and rupture
      ii. Newer studies with new technology have found better outcomes
         1. "Some studies have suggested that restenosis and outcomes in balloon angioplasty without stenting are similar to those with stenting"
         2. These studies defined success as being a reduction in stenosis to less than 50%; outcomes such as stroke and death not used
5) **Cruz-Flores 2008**, Cochrane review of angioplasty for intracranial atherosclerosis
   a. N=79 articles (case series)
   b. The safety profile of the procedure showed an overall perioperative rate of stroke of 7.9% (95% confidence intervals (CI) 5.5% to 10.4%), perioperative death of 3.4% (95% CI 2.0% to 4.8%), and perioperative stroke or death of 9.5% (95% CI 7.0% to 12.0%).
   c. No comments can be made on the effectiveness of the procedure
      1. At present there is insufficient evidence to recommend angioplasty with or without stent placement in routine practice for the prevention of stroke in patients with intracranial artery stenosis. The descriptive studies show that the procedure is feasible although carries a significant morbidity and mortality risk

<u>Other expert guidelines</u>

1) **Jauch 2013** AHA/ASA guidelines for the treatment of acute stroke http://stroke.ahajournals.org/content/44/3/870 (study not included in packet due to length)
   a. The usefulness of emergent intracranial angioplasty and/or stenting is not well established. These procedures should be used in the setting of clinical trials *(Class IIb; Level of Evidence C)*. (New recommendation)

b. The usefulness of emergent angioplasty and/or stenting of the extracranial carotid or vertebral arteries in unselected patients is not well established *(Class IIb; Level of Evidence C)*. Use of these techniques may be considered in certain circumstances, such as in the treatment of acute ischemic stroke resulting from cervical atherosclerosis or dissection *(Class IIb; Leve of Evidence C)*. Additional randomized trial data are needed.

HERC staff summary

Good evidence finds that intracranial vascular stenting results in significantly worse outcomes that medical management of intracranial vascular stenosis. Intracranial balloon angioplasty appears to be much less studied, but has similar or worse outcomes than stenting in the studies identified.

HERC staff recommendations:

1) Remove 61630 (Balloon angioplasty, intracranial (eg, atherosclerotic stenosis), percutaneous) from line 200 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN and place on the Services Recommended for Non-Coverage List
    a. No evidence of effectiveness and evidence of harm
2) Affirm placement of 61635 (Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed) on the Services Recommended for Non-Coverage Table

NICE guidance

Endovascular stent insertion for intracranial atherosclerotic disease

Interventional procedure guidance
Published: 23 July 2012
nice.org.uk/guidance/ipg429

This guidance replaces IPG233.

1 Guidance

This document replaces previous guidance on endovascular stent insertion for intracranial atherosclerotic disease (interventional procedure guidance 233).

1.1 Current evidence on the efficacy of endovascular stent insertion for intracranial atherosclerotic disease shows no substantial differences in clinical outcomes compared with medical treatment after 1–2 years. Evidence on its safety shows that there is a significant risk of periprocedural stroke and death. Therefore, this procedure should only be used in the context of research. Research should clearly define patient selection and be designed to provide outcome data based on follow-up of at least 2 years.

2 The procedure

2.1 Indications and current treatments

2.1.1 Intracranial atherosclerotic disease is the narrowing or obstruction of arteries within the skull that supply blood to the brain. It is caused by atheromatous

plaques, which can reduce blood flow and may be associated with thrombosis or embolism, leading to transient ischaemic attacks (TIA), stroke or death. Intracranial atherosclerotic disease is usually diagnosed only after a patient has presented with a TIA or stroke.

2.1.2 Symptomatic intracranial atherosclerotic disease is usually treated with antiplatelet medication together with a statin and attention to risk factors for atherosclerosis such as smoking, hypertension and diabetes.

2.1.3 Direct intervention to treat intracranial atherosclerotic disease is not commonly used. It involves balloon angioplasty to dilate diseased arteries, which may then be followed by stent insertion, with the aim of improving patency compared with balloon angioplasty alone.

2.2 Outline of the procedure

2.2.1 The procedure is carried out with the patient under general or local anaesthesia. Under fluoroscopic control, a catheter is introduced percutaneously through an artery in the arm or leg and guided into the affected intracranial artery. Balloon angioplasty of the target lesion is normally done to dilate it before inserting a stent. It is possible to insert more than 1 stent or to treat more than 1 lesion in a treatment session.

2.2.2 Two main types of stent have been used – balloon expandable and self-expanding. Some studies have also used drug-eluting stents. The technology has evolved over the past decade and continues to do so.

> Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview.

2.3 Efficacy

2.3.1 The efficacy outcomes described below include stroke or death occurring more than 30 days after the procedure (unless specified otherwise). Stroke or death occurring on or before 30 days is considered to be a safety outcome.

2.3.2 A randomised controlled trial of 451 patients treated by angioplasty and stent insertion or medical management alone reported ischaemic stroke in the area of the brain supplied by the artery with the index lesion more than 30 days after enrolment in 6% of patients in both groups (13/224 and 13/227, respectively, p value not stated) at a mean follow-up of 12 months. A case series of 213 patients reported lesion-related ischaemic stroke more than 30 days after the procedure in 3% (7/213) of patients, at a mean follow-up of 27 months. A case series of 158 patients reported that 20% (22/110) of patients had a stroke or TIA between 30 days and 12 months after the procedure.

2.3.3 The randomised controlled trial of 451 patients treated by angioplasty and stent insertion or medical management alone reported a death rate of 3% in both groups (7/224 and 7/227, respectively, p=0.95) at a mean follow-up of 12 months.

2.3.4 A systematic review comparing 36 studies of angioplasty and endovascular stent insertion with 33 studies of angioplasty alone reported stroke and/or death in 12% (123/1070) and 17% (125/731) of patients respectively at 1-year follow-up (p=0.0002).

2.3.5 The case series of 213 patients reported an overall restenosis rate of 19% (19/99) identified on follow-up angiography at a mean follow-up of 9 months. A case series of 189 patients reported recurrent stenosis in 25% (43/174) of lesions identified on angiography at a mean follow-up of 4 months. A case series of 113 patients reported an overall restenosis rate of 18% (16/89; identified by transcranial doppler ultrasound or angiography) at a mean follow-up of 29 months.

2.3.6 The Specialist Advisers listed key efficacy outcomes as reduction in TIA or stroke frequency.

2.4 Safety

2.4.1 The randomised controlled trial of 451 patients treated by angioplasty and stent insertion or by medical management alone reported stroke or death within 30 days of enrolment in 15% (33/224) and 6% (13/227) of patients, respectively (p=0.002). There were 5 stroke-related deaths in the stent group and 1 non-stroke-related death in the medical management group. The systematic review

comparing 36 studies of angioplasty and endovascular stent insertion with 33 studies of angioplasty alone reported stroke and/or death in 8% (104/1291) and 9% (91/1027) of patients respectively at 1-month follow-up (p=0.49).

2.4.2 Stent occlusion occurred in 4% (2/53) of patients treated by endovascular stent insertion in a non-randomised comparative study. One occlusion occurred 2 days after stent insertion and the patient had extracranial-intracranial bypass surgery because of recurrent TIAs. The second occlusion occurred 9 days after stent insertion in a patient who was not receiving antiplatelet medication because of a gastrointestinal haemorrhage; the patient had a stroke and died.

2.4.3 Vessel rupture during stent navigation was reported in 2% (2/113) of patients in the case series of 113 patients; 1 patient died of massive subarachnoid haemorrhage, and the other was treated by emergency craniotomy and surgical clipping of the middle cerebral artery. One patient died after vessel rupture during the procedure in the case series of 189 patients.

2.4.4 Fatal intracerebral haemorrhage was reported in 1 patient in the case series of 189 patients (timing not reported). There were haemorrhages in 3 other patients; 1 intracerebral haemorrhage 6 days after the procedure (resolved within 30 days) and 2 subarachnoid haemorrhages (1 resolved without treatment and the other was successfully treated by coil occlusion). Bilateral intracerebral haemorrhage was reported in 1 patient in the case series of 113 patients, 2 weeks after the procedure (no other details provided). Symptomatic subarachnoid haemorrhage (not otherwise described) was reported in 1% (2/213) of patients and symptomatic brain haemorrhage (not otherwise described) was reported in 1 patient, within 30 days of the procedure, in the case series of 213 patients.

2.4.5 Specialist Advisers listed anecdotal adverse events as basilar artery rupture resulting in death, disabling thalamic infarction, and reperfusion haemorrhage. They stated that theoretical adverse events included vessel dissection, embolisation, myocardial infarction, groin haematoma and contrast reactions.

2.5 Other comments

2.5.1 The Committee noted that a number of different devices have been used for endovascular stent insertion for intracranial atherosclerotic disease and that technical evolution of devices is continuing.

2.5.2 The Committee also noted that medical management is variable and continues to evolve. This complicates interpretation of studies that compare the procedure with medical treatment.

3 Further information

3.1 For related NICE guidance see www.nice.org.uk.

Information for patients

NICE has produced information on this procedure for patients and carers ('Understanding NICE guidance'). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

4 About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE interventional procedures guidance process.

It updates and replaces NICE interventional procedure guidance 233.

We have produced a summary of this guidance for patients and carers. Tools to help you put the guidance into practice and information about the evidence it is based on are also available.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the

available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Original Investigation

Effect of a Balloon-Expandable Intracranial Stent vs Medical Therapy on Risk of Stroke in Patients With Symptomatic Intracranial Stenosis
The VISSIT Randomized Clinical Trial

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IMPORTANCE Intracranial stenosis is one of the most common etiologies of stroke. To our knowledge, no randomized clinical trials have compared balloon-expandable stent treatment with medical therapy in symptomatic intracranial arterial stenosis.

OBJECTIVE To evaluate the efficacy and safety of the balloon-expandable stent plus medical therapy vs medical therapy alone in patients with symptomatic intracranial stenosis (≥70%).

DESIGN, SETTING, AND PATIENTS VISSIT (the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy) trial is an international, multicenter, 1:1 randomized, parallel group trial that enrolled patients from 27 sites (January 2009-June 2012) with last follow-up in May 2013.

INTERVENTIONS Patients (N = 112) were randomized to receive balloon-expandable stent plus medical therapy (stent group; n = 59) or medical therapy alone (medical group; n = 53).

MAIN OUTCOMES AND MEASURES Primary outcome measure: a composite of stroke in the same territory within 12 months of randomization or hard transient ischemic attack (TIA) in the same territory day 2 through month 12 postrandomization. A hard TIA was defined as a transient episode of neurological dysfunction caused by focal brain or retinal ischemia lasting at least 10 minutes but resolving within 24 hours. Primary safety measure: a composite of any stroke, death, or intracranial hemorrhage within 30 days of randomization and any hard TIA between days 2 and 30 of randomization. Disability was measured with the modified Rankin Scale and general health status with the EuroQol-5D, both through month 12.

RESULTS Enrollment was halted by the sponsor after negative results from another trial prompted an early analysis of outcomes, which suggested futility after 112 patients of a planned sample size of 250 were enrolled. The 30-day primary safety end point occurred in more patients in the stent group (14/58; 24.1% [95% CI, 13.9%-37.2%]) vs the medical group (5/53; 9.4% [95% CI, 3.1%-20.7%]) (*P* = .05). Intracranial hemorrhage within 30 days occurred in more patients in the stent group (5/58; 8.6% [95% CI, 2.9%-19.0%]) vs none in the medical group (95% CI, 0%-5.5%) (*P* = .06). The 1-year primary outcome of stroke or hard TIA occurred in more patients in the stent group (21/58; 36.2% [95% CI, 24.0-49.9]) vs the medical group (8/53; 15.1% [95% CI, 6.7-27.6]) (*P* = .02). Worsening of baseline disability score (modified Rankin Scale) occurred in more patients in the stent group (14/58; 24.1% [95% CI, 13.9%-37.2%]) vs the medical group (6/53; 11.3% [95% CI, 4.3%-23.0%]) (*P* = .09).The EuroQol-5D showed no difference in any of the 5 dimensions between groups at 12-month follow-up.

CONCLUSIONS AND RELEVANCE Among patients with symptomatic intracranial arterial stenosis, the use of a balloon-expandable stent compared with medical therapy resulted in an increased 12-month risk of added stroke or TIA in the same territory, and increased 30-day risk of any stroke or TIA. These findings do not support the use of a balloon-expandable stent for patients with symptomatic intracranial arterial stenosis.

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Supplemental content at jama.com

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ORIGINAL ARTICLE

Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis

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ABSTRACT

BACKGROUND

Atherosclerotic intracranial arterial stenosis is an important cause of stroke that is increasingly being treated with percutaneous transluminal angioplasty and stenting (PTAS) to prevent recurrent stroke. However, PTAS has not been compared with medical management in a randomized trial.

METHODS

We randomly assigned patients who had a recent transient ischemic attack or stroke attributed to stenosis of 70 to 99% of the diameter of a major intracranial artery to aggressive medical management alone or aggressive medical management plus PTAS with the use of the Wingspan stent system. The primary end point was stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days.

RESULTS

Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non–stroke-related death, 0.4%) ($P=0.002$). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. Currently, the mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups ($P=0.009$), with 1-year rates of the primary end point of 20.0% in the PTAS group and 12.2% in the medical-management group.

CONCLUSIONS

In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected. (Funded by the National Institute of Neurological Disorders and Stroke and others; SAMMPRIS ClinicalTrials.gov number, NCT00576693.)

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*The investigators in the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial are listed in the Supplementary Appendix, available at NEJM.org.

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Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial

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Summary

Background Early results of the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis trial showed that, by 30 days, 33 (14·7%) of 224 patients in the stenting group and 13 (5·8%) of 227 patients in the medical group had died or had a stroke (percentages are product limit estimates), but provided insufficient data to establish whether stenting offered any longer-term benefit. Here we report the long-term outcome of patients in this trial.

Methods We randomly assigned (1:1, stratified by centre with randomly permuted block sizes) 451 patients with recent transient ischaemic attack or stroke related to 70–99% stenosis of a major intracranial artery to aggressive medical management (antiplatelet therapy, intensive management of vascular risk factors, and a lifestyle-modification programme) or aggressive medical management plus stenting with the Wingspan stent. The primary endpoint was any of the following: stroke or death within 30 days after enrolment, ischaemic stroke in the territory of the qualifying artery beyond 30 days of enrolment, or stroke or death within 30 days after a revascularisation procedure of the qualifying lesion during follow-up. Primary endpoint analysis of between-group differences with log-rank test was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT 00576693.

Findings During a median follow-up of 32·4 months, 34 (15%) of 227 patients in the medical group and 52 (23%) of 224 patients in the stenting group had a primary endpoint event. The cumulative probability of the primary endpoints was smaller in the medical group versus the percutaneous transluminal angioplasty and stenting (PTAS) group (p=0·0252). Beyond 30 days, 21 (10%) of 210 patients in the medical group and 19 (10%) of 191 patients in the stenting group had a primary endpoint. The absolute differences in the primary endpoint rates between the two groups were 7·1% at year 1 (95% CI 0·2 to 13·8%; p=0·0428), 6·5% at year 2 (–0·5 to 13·5%; p=0·07) and 9·0% at year 3 (1·5 to 16·5%; p=0·0193). The occurrence of the following adverse events was higher in the PTAS group than in the medical group: any stroke (59 [26%] of 224 patients *vs* 42 [19%] of 227 patients; p=0·0468) and major haemorrhage (29 [13%] of 224 patients *vs* 10 [4%] of 227 patients; p=0·0009).

Interpretation The early benefit of aggressive medical management over stenting with the Wingspan stent for high-risk patients with intracranial stenosis persists over extended follow-up. Our findings lend support to the use of aggressive medical management rather than PTAS with the Wingspan system in high-risk patients with atherosclerotic intracranial arterial stenosis.

Funding National Institute of Neurological Disorders and Stroke (NINDS) and others.

Introduction

Intracranial atherosclerosis is a common cause of stroke and is associated with a high risk of recurrent stroke, especially in patients with a recent stroke or transient ischaemic attack and severe arterial stenosis.[1–4] The Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial was designed to assess whether percutaneous transluminal angioplasty and stenting (PTAS) plus aggressive medical treatment is more effective than aggressive medical treatment alone in high-risk patients with this disease.[5] Enrolment in SAMMPRIS began on Nov 25, 2008, but was stopped for safety concerns on April 5, 2011, because the 30-day rate of stroke and death was higher in the PTAS group.[6]

When enrolment was stopped, fewer than half the 451 patients had been followed up for longer than 1 year.[6] Since then, patients in both treatment groups have been followed up for 2 more years to establish whether the early benefit in the medical group would persist over longer follow-up, or whether the medical group would have a high incidence of late strokes that would eliminate the early efficacy gap between the two groups. In this Article, we report the final results of the SAMMPRIS trial.

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See **Comment** page 290

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Endovascular Management of Intracranial Atherosclerosis

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KEYWORDS

• Intracranial atherosclerotic disease • Endovascular • Stroke • Stenosis • Angioplasty • Stenting
• Percutaneous transluminal angioplasty and stenting

KEY POINTS

- Intracranial atherosclerotic disease (ICAD) is responsible for a considerable proportion of ischemic strokes worldwide.
- The clinical presentation of ICAD is heterogeneous and may involve more than 1 mechanism.
- Delineating the mechanism of ischemia requires careful clinical analysis, and usually necessitates multimodal imaging.
- Conservative medical management is the appropriate first step in the treatment of ICAD.
- An endovascular treatment approach based on the mechanism of stroke may be beneficial for select patients.
- Patient selection will be a critical factor in the design of future ICAD clinical trials.

INTRODUCTION

Epidemiology and Natural History

A common cause of stroke worldwide, intracranial atherosclerotic disease (ICAD) is most prevalent in Black, Asian, and Hispanic populations.[1] In the United States, ICAD was found in an estimated 10% of stroke patients, whereas in Asia ICAD accounts for approximately 30% to 50% of all strokes.[2] Risk factors for ICAD include age, hypertension, smoking, diabetes mellitus, hypercholesterolemia, and metabolic syndrome.[3] Although the high rate of certain uncontrolled risk factors, such as diabetes mellitus, hypertension, and hyperlipidemia, may partially account for the increased incidence of ICAD in African Americans,[4,5] the rates of these risk factors do not differ significantly in the Chinese population in comparison with Caucasians, and thus do not account for the significant burden of ICAD in this population.[6]

Data from the randomized, double-blind, controlled trial Warfarin versus Aspirin for Symptomatic Intracranial Disease (WASID) revealed that patients with symptomatic ICAD carry a high risk of subsequent stroke.[7] Despite the use of aspirin and management of risk factors, patients with a recent transient ischemic attack (TIA) or stroke and a stenosis of 70% or greater had a 23% risk of stroke at 1 year.[7,8]

Clinical Manifestations

Intracranial atherosclerotic disease presents with ischemic stroke or TIA, which may be single or recurrent.[9] Depending on the stroke location, there

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1042-3680/14/$ – see front matter

Angioplasty for intracranial artery stenosis (Review)

Cruz-Flores S, Diamond AL

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2008, Issue 4

http://www.thecochranelibrary.com

Balloon Dilation of Intracranial Vasospasm

Question: Should balloon dilation of intracranial vasospasm be removed from the Prioritized List?

Question source: HERC staff

Issue: New CPT codes 61650 and 61651 (Endovascular intracranial prolonged administration of pharmacologic agent(s) other than for thrombolysis, arterial, including catheter placement diagnostic angiography, and imaging guidance) were reviewed at the November, 2015 VBBS/HERC meeting and were added to the Services Recommended for Non-Coverage Table due to lack of evidence of effectiveness for this therapy. During this review, HERC staff noted that the level and type of evidence for intracranial vasodilator therapy was similar to the evidence for intracranial balloon dilation for intracranial vasospasm. Currently, balloon dilation (CPT 61640-61642 Balloon dilation of intracranial vasospasm, percutaneous) appears on line 200 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN Treatment: BURR HOLES, CRANIECTOMY/CRANIOTOMY.

Both Intracranial vasodilator therapy and balloon dilation are used for treatment of cerebral vasospasm after intracranial hemorrhage. The major treatment of cerebral vasospasm appears to be administration of medications via peripheral or central IV.

In 2012, the use of balloon dilation of intracranial vasospasm for treatment of transient cerebral ischemia (TIA) was reviewed by HERC and found to be experimental.

Evidence

1) **Abruzzo 2012**, review of the safety and efficacy of transluminal balloon angioplasty (TBA) and intra-arterial vasodilator infusion therapy (IAVT) for management of posthemorrhagic cerebral vasospasm (PHCV)
    a. N=12 studies for balloon angioplasty (361 patients)
        i. All studies case series, most retrospective
    b. N=7 studies for IAVT (109 patients)
        i. 6 retrospective case series, 1 prospective case series
    c. Major risks for balloon angioplasty identified, including cerebral artery rupture (reported to be 1-5% in large case series), thromboembolic complications (4-5% of cases), ischemic stroke, arterial dissection
    d. The technical efficacy of TBA reversing cerebral vasoconstriction in patients with PHCV is in the 80-100% range. Clinical series have reported improvements in TCD velocities, luminal caliber assessed by DSA and cerebral blood flow. More importantly, it has been demonstrated that TBA reduces neurological deficits in patients with PHCV and that early treatment (<2 h from symptom onset) significantly increases the probability of sustained clinical improvement. Technically successful restoration of normal or near normal luminal caliber is achieved in the majority of TBA procedures. Case series report angiographic

improvement in 82-100% of patients. On the other hand, clinical success varies widely, with reversal of DCI in 31-77% of patients.

e. There is no significant evidence that the intervention results in better long term clinical outcomes relative to medical management.
f. TBA may be beneficial and may be considered for flow limiting PHCV involving the proximal intradural cerebral arteries (ICA, M1, VA, basilar artery, A1, P1) symptomatic with cerebral ischemia and refractory to maximal medical therapy.
g. The assessment shows that for the indications described above, TBA and IAVT are classified as Class IIb, Level B interventions according to the American Heart Association guidelines, and Level 4, Grade C interventions according to the University of Oxford Centre for Evidence Based Medicine guidelines.

2) Velat 2011, review and meta-analysis of therapies for intracranial vasospasm
   a. Identified 1 RCT on prophylactic balloon angioplasty vs no treatment
      i. N=85 patients with balloon angioplasty vs 94 control
   b. Patients undergoing prophylactic TBA experienced a non-significant reduction in DIND incidence (*P*=0.30). A significant decrease in therapeutic angioplasty (*P* = 0.03) was observed, however, for patients who had prophylactic TBA compared to controls. A high rate of vessel perforation was observed during the trial, resulting in three iatrogenic deaths.
   c. Although anecdotal reports suggest that TBA provides durable relief of vasospasm, no RCTs using therapeutic angioplasty alone have been published to date.
   d. Nimodipine is the only treatment that provided a significant benefit across multiple studies.

3) Kimball 2011, review of endovascular management of cerebral vasospasm
   a. N=27 studies (1028 patients) for balloon angioplasty
      i. 26 retrospective case series, 1 RCT
      ii. Included prophylactic studies excluded from Abruzzo 2012. Concluded that "prophylactic treatment, however, has been associated with potential risks, and the data have not shown an improvement in clinical outcome after prophylactic treatment."
   b. Improvements in vessel diameters as well as neurological deficits were observed in most studies following balloon angioplasty
   c. Complications of balloon angioplasty including vessel perforation, hemorrhage and death
   d. In summary, endovascular intervention for clinically identified vasospasm may be indicated as when medical management has failed or when there is a concern for complications from medical management.

Expert guidelines

1) **Conolly 2012**, AHA/ASA guidelines for management of subarachnoid hemorrhage (link to pdf included in November, 2015 packet)

   a. Oral nimodipine should be administered to all patients with aSAH *(Class I; Level of Evidence A*
   b. Maintenance of euvolemia and normal circulating blood volume is recommended to prevent DCI *(Class I; Level of Evidence B).*
   c. Prophylactic hypervolemia or balloon angioplasty before the development of angiographic spasm is not recommended *(Class III; Level of Evidence B).*
   d. Induction of hypertension is recommended for patients with DCI unless blood pressure is elevated at baseline or cardiac status precludes it *(Class I; Level of Evidence B).*
   e. Cerebral angioplasty and/or selective intra-arterial vasodilator therapy is reasonable in patients with symptomatic cerebral vasospasm, particularly those who are not rapidly responding to hypertensive therapy *(Class IIa; Level of Evidence B*).

2) **Deringer 2011**, Neurocritical Care Society consensus statement (link to pdf included in November, 2015 packet)
   a. There was wide international variation in the use of endovascular therapies with some groups strongly recommending their use and other not utilizing them at all
   b. Recommendation: Endovascular treatment using intra-arterial vasodilators and/or angioplasty may be considered for vasospasm related DCI (moderate quality evidence-strong recommendation).
   c. Recommendation: The timing and triggers of endovascular treatment of vasospasm remains unclear, but generally rescue therapy for ischemic symptoms that remain refractory to medical treatment should be considered. The exact timing is a complex decision which should consider the aggressiveness of the hemodynamic intervention, the patients' ability to tolerate it, prior evidence of large artery narrowing, and the availability of and the willingness to perform angioplasty or infusion of intra-arterial agents (moderate quality evidence—strong recommendation).
3) **Steiner 2013**, European Stroke Organization guideline of treatment of subarachnoid hemorrhage (link to pdf included in November, 2015 packet)
   a. no recommendations for balloon angioplasty or intra-arterial vasodilators

Summary:
Some preliminary evidence from retrospective case series finds that balloon angioplasty may be useful for treatment of intracranial vasospasm following aneurysmal subarachnoid hemorrhage, but its effectiveness needs to be verified by prospective RCTs. This procedure is recommended as a possible therapy after failure of optimal medical management by expert guidelines which rate the underlying evidence to be of low to moderate strength. There is risk of serious adverse events including arterial rupture and death from this procedure. The best available evidence does not find improvement in long term outcomes with balloon angioplasty vs optimal medical management.

HERC staff recommendation:

1) Option 1: Remove CPT 61640-61642 Balloon dilation of intracranial vasospasm, percutaneous) from line 200 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN and place on the Services Recommended for Non-Coverage Table
    a. Evidence shows efficacy at best similar to optimal medical management
    b. Evidence of harm from treatment not seen with optimal medical management
2) Option 2: leave CPT 61640-61642 on line 200 and adopt the following new guideline note
    a. There is good evidence that prophylactic use is not effective and is harmful
    b. Expert guidelines recommend use only with failure of optimal medical management

GUIDELINE NOTE XXX BALLOON DILATION OF INTRACRANIAL VASOSPASM

Line 200

Balloon dilation of intracranial vasospasm is included on this line only for patients with flow limiting posthemorrhagic cerebral vasospasm involving the proximal intradural cerebral arteries symptomatic with cerebral ischemia and refractory to maximal medical therapy.

Invasive interventional management of post-hemorrhagic cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage

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► Additional tables are published online only. To view these files please visit the journal online (http://jnis.bmj.com/content/4/3.toc).

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ABSTRACT

Current clinical practice standards are addressed for the invasive interventional management of post-hemorrhagic cerebral vasospasm (PHCV) in patients with aneurysmal subarachnoid hemorrhage. The conclusions, based on an assessment by the Standards Committee of the Society of Neurointerventional Surgery, included a critical review of the literature using guidelines for evidence based medicine proposed by the Stroke Council of the American Heart Association and the University of Oxford, Centre for Evidence Based Medicine. Specifically examined were the safety and efficacy of established invasive interventional therapies, including transluminal balloon angioplasty (TBA) and intra-arterial vasodilator infusion therapy (IAVT). The assessment shows that these invasive interventional therapies may be beneficial and may be considered for PHCV—that is, symptomatic with cerebral ischemia and refractory to maximal medical management. As outlined in this document, IAVT may be beneficial for the management of PHCV involving the proximal and/or distal intradural cerebral circulation. TBA may be beneficial for the management of PHCV that involves the proximal intradural cerebral circulation. The assessment shows that for the indications described above, TBA and IAVT are classified as Class IIb, Level B interventions according to the American Heart Association guidelines, and Level 4, Grade C interventions according to the University of Oxford Centre for Evidence Based Medicine guidelines.

INTRODUCTORY REMARKS

Post-hemorrhagic cerebral vasospasm (PHCV), a well known complication of aneurysmal subarachnoid hemorrhage (SAH), is responsible for significant morbidity and mortality among SAH patients.[1 2] Morbidity and mortality are related to the development of cerebral ischemia and infarction in affected vascular territories.[3] Recent studies have suggested that other undefined factors also contribute to the resulting neurological damage.[4] Nevertheless, angiographically demonstrable vasoconstriction is the most important modifiable risk factor for neurological deterioration and poor outcome.

The precise events that lead to cerebral arterial narrowing in PHCV remain unknown. Numerous inciting factors have been implicated, including erythrocyte degradation products, serum derived lipids and hematogenic proteins. Presumably, the inciting factors trigger a cascade of biochemical and immunoinflammatory reactions that ultimately lead to unopposed activation of the contractile apparatus within cerebrovascular smooth muscle cells. Although loss of luminal caliber is initially reversible, if the process is sustained, vessel wall fibrosis can lead to irreversible stenosis.[5]

There is wide variability in the frequency, intensity and clinical significance of PHCV after aneurysmal SAH. The likelihood of developing PHCV and its severity most strongly correlates with the amount of blood entering the subarachnoid space.[6 7]

Although large focal subarachnoid hematomas will affect adjacent pial arteries most severely, PHCV is often multifocal and may involve remote vascular territories. PHCV has a predictably delayed onset after cerebral aneurysm rupture. It generally does not begin until 3–5 days after the ictus but earlier onset is observed. The PHCV process is characteristically monophasic with an initial period of worsening vasoconstriction, peaking in approximately 10–14 days followed by a gradual return to normal arterial caliber by 2–4 weeks. Delayed cerebral ischemia (DCI) secondary to PHCV may result in severe permanent disability or death. DCI may be partially or completely reversible when effective treatment is administered. Although reversible constriction of the cerebral arteries can be shown angiographically in up to 70% of patients with aneurysmal SAH, DCI only develops in 20–30% of cases.[8–10] DCI and infarction strongly correlate with the angiographic severity of vasospasm and nearly half of patients who experience severe vasospasm will develop territory specific cerebral infarctions.[3]

LITERATURE REVIEW

The National Library of Medicine database (PubMed 1966–2011) was searched electronically: (1) to identify relevant peer reviewed publications containing outcome data for the procedures under examination to be used as benchmarks for quality assessment; (2) to assess the collective experience with a view to identifying potential risk adjustment variables; and (3) to identify data that can be used to develop monitoring protocols to track the efficacy and appropriateness of endovascular treatment of cerebral vasospasm after SAH.

Searches were performed using broad keyword phrases relating to the disease (cerebral vasospasm, delayed neurological deficit) and the procedure of

Vasospasm After Aneurysmal Subarachnoid Hemorrhage: Review of Randomized Controlled Trials and Meta-Analyses in the Literature

Gregory J. Velat, Matthew M. Kimball, J D. Mocco, Brian L. Hoh

Key words
- Aneurysm
- Cerebral vasospasm
- Delayed ischemic neurologic deficit
- Subarachnoid hemorrhage

Abbreviations and Acronyms
A1: First segment of the anterior cerebral artery
CCB: Calcium channel blocker(s)
DCI: Delayed cerebral infarction
DIND: Delayed ischemic neurological deficit(s)
GOS: Glasgow Outcome Scale
IV: Intravenous
M1: First segment of the middle cerebral artery
P1: First segment of the posterior cerebral artery
RCT: Randomized controlled trial
SAH: Subarachnoid hemorrhage
TCD: Transcranial Doppler

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*Available online: **www.sciencedirect.com***

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OBJECTIVE: **Cerebral vasospasm is a major source of morbidity and mortality following aneurysmal subarachnoid hemorrhage (SAH). A variety of therapies have been utilized to prevent or treat vasospasm. Despite the large number of clinical trials, few randomized controlled trials (RCTs) of sufficient quality have been published. We review the RCTs and meta-analyses in the literature regarding the treatment and prevention of cerebral vasospasm following aneurysmal SAH.**

METHODS: **A literature search of MEDLINE, the Cochrane Controlled Trials Registry, and the National Institutes of Health/National Library of Medicine clinical trials registry was performed in January 2010 using predefined search terms. These trials were critically reviewed and categorized based on therapeutic modality.**

RESULTS: **Forty-four RCTs and 9 meta-analyses met the search criteria. Significant findings from these trials were analyzed. The results of this study were as follows: nimodipine demonstrated benefit following aneurysmal SAH; other calcium channel blockers, including nicardipine, do not provide unequivocal benefit; triple-H therapy, fasudil, transluminal balloon angioplasty, thrombolytics, endothelin receptor antagonists, magnesium, statins, and miscellaneous therapies such as free radical scavengers and antifibrinolytics require additional study. Tirilazad is ineffective.**

CONCLUSIONS: **There are many possible successful treatment options for preventing vasospasm, delayed ischemic neurologic deficits, and poor neurologic outcome following aneurysmal subarachnoid hemorrhage; however, further multicenter RCTs need to be performed to determine if there is a significant benefit from their use. Nimodipine is the only treatment that provided a significant benefit across multiple studies.**

INTRODUCTION

Aneurysmal subarachnoid hemorrhage (SAH) occurs in approximately 30,000 Americans each year (24). Mortality is estimated to be as high as two-thirds (19), although recent data suggest improved mortality rates (48). Other than rebleeding, cerebral vasospasm is the leading cause of morbidity and mortality following aneurysmal SAH. Angiographic vasospasm may occur in up to 70% of patients, which is typically observed between 5 and 14 days after the onset of SAH (13, 18); however, symptomatic vasospasm may only occur in about 30% of patients. Delayed ischemic neurologic deficits (DINDs) occur in about 50% of patients with angiographic vasospasm, which may lead to stroke or death despite maximal therapy (15, 28).

There are a large number of studies in the literature reporting on multiple experimental therapies for cerebral vasospasm; however, very few prospectiverandomized controlled trials (RCTs) are available. For the practicing neurosurgeon, making management and protocol decisions in the prevention and treatment of cerebral vasospasm for patients can be difficult given the variable results in the literature. Our goal was to identify the RCTs and meta-analyses in the literature regarding cerebral vasospasm prevention and treatment to summarize their results and provide readers with a simple, concise information source (**Table 1**).

METHODS

A literature search of MEDLINE, the Cochrane Controlled Trials Registry, and the National Institutes of Health/National Library of Medicine clinical trials registry was performed in January 2010. The following search terms were used: cerebral vasospasm, or delayed cerebral ischemia, or delayed ischemic neurological deficit, with aneurysm and subarachnoid hemorrhage. No limitation for publication date was used.

neurocritical care society Neurocrit Care (2011) 15:336–341
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REVIEW

Critical Care Guidelines on the Endovascular Management of Cerebral Vasospasm

Matthew M. Kimball · Gregory J. Velat · Brian L. Hoh · The Participants in the International Multi-disciplinary Consensus Conference on the Critical Care Management of Subarachnoid Hemorrhage

Published online: 15 July 2011

Abstract Cerebral vasospasm and delayed cerebral ischemia account for significant morbidity and mortality after aneurysmal subarachnoid hemorrhage. While most patients are managed with triple-H therapy, endovascular treatments have been used when triple-H treatment cannot be used or is ineffective. An electronic literature search was conducted to identify English language articles published through October 2010 that addressed endovascular management of vasospasm. A total of 49 articles were identified, addressing endovascular treatment timing, intra-arterial treatments, and balloon angioplasty. Most of the available studies investigated intra-arterial papaverine or balloon angioplasty. Both have generally been shown to successfully treat vasospasm and improve neurological condition, with no clear benefit from one treatment compared with another. There are reports of complications with both therapies including vessel rupture during angioplasty, intracranial hypertension, and possible neurotoxicity associated with papaverine. Limited data are available evaluating nicardipine or verapamil, with positive benefits reported with nicardipine and inconsistent benefits with verapamil.

Keywords Balloon angioplasty · Intra-arterial · Nicardipine · Papaverine · Verapamil

Introduction

Cerebral vasospasm and delayed cerebral ischemia (DCI) account for the majority of morbidity and mortality for patients who survive to undergo treatment following aneurysmal subarachnoid hemorrhage (SAH). Angiographic vasospasm is observed in 30–70% of patients between days 5 and 14 following the initial aneurysmal bleed [1, 2]. Approximately 50% of patients with angiographic vasospasm will develop DCI, with 15–20% of these patients suffering stroke or death despite maximal therapy [3, 4].

Medical management of vasospasm primarily consists of hemodynamic augmentation that is associated with significant risks of complications, such as heart failure and pulmonary edema [5]. Endovascular therapies, such as intra-arterial vasodilator administration or transluminal balloon angioplasty, might benefit patients with cerebral vasospasm when hemodynamic therapy has failed or when there is concern for complications of hemodynamic therapy.

Despite the potential benefit from endovascular therapy, clear guidelines directing use of these treatments for vasospasm after SAH are not available. The decision of when to intervene endovascularly is not clear and certain across all patients. A review of the medical literature was conducted to determine the role of endovascular treatment in the management of cerebral vasospasm.

Methods

A search was performed of the English language literature published through October 2010 using MEDLINE, the

The Participants in the International Multi-disciplinary Consensus Conference: Michael N. Diringer, Thomas P. Bleck, Nicolas Bruder, E. Sander Connolly Jr, Giuseppe Citerio, Daryl Gress, Daniel Hanggi, J. Claude Hemphill III MAS, Brian Hoh, Giuseppe Lanzino, Peter Le Roux, David Menon, Alejandro Rabinstein, Erich Schmutzhard, Lori Shutter, Nino Stocchetti, Jose Suarez, Miriam Treggiari, MY Tseng, Mervyn Vergouwen, Paul Vespa, Stephan Wolf, Gregory J. Zipfel.

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NICE guidance

Endovascular stent insertion for intracranial atherosclerotic disease

Interventional procedure guidance
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nice.org.uk/guidance/ipg429

This guidance replaces IPG233.

1 Guidance

This document replaces previous guidance on endovascular stent insertion for intracranial atherosclerotic disease (interventional procedure guidance 233).

1.1 Current evidence on the efficacy of endovascular stent insertion for intracranial atherosclerotic disease shows no substantial differences in clinical outcomes compared with medical treatment after 1–2 years. Evidence on its safety shows that there is a significant risk of periprocedural stroke and death. Therefore, this procedure should only be used in the context of research. Research should clearly define patient selection and be designed to provide outcome data based on follow-up of at least 2 years.

2 The procedure

2.1 Indications and current treatments

2.1.1 Intracranial atherosclerotic disease is the narrowing or obstruction of arteries within the skull that supply blood to the brain. It is caused by atheromatous

plaques, which can reduce blood flow and may be associated with thrombosis or embolism, leading to transient ischaemic attacks (TIA), stroke or death. Intracranial atherosclerotic disease is usually diagnosed only after a patient has presented with a TIA or stroke.

2.1.2 Symptomatic intracranial atherosclerotic disease is usually treated with antiplatelet medication together with a statin and attention to risk factors for atherosclerosis such as smoking, hypertension and diabetes.

2.1.3 Direct intervention to treat intracranial atherosclerotic disease is not commonly used. It involves balloon angioplasty to dilate diseased arteries, which may then be followed by stent insertion, with the aim of improving patency compared with balloon angioplasty alone.

2.2 Outline of the procedure

2.2.1 The procedure is carried out with the patient under general or local anaesthesia. Under fluoroscopic control, a catheter is introduced percutaneously through an artery in the arm or leg and guided into the affected intracranial artery. Balloon angioplasty of the target lesion is normally done to dilate it before inserting a stent. It is possible to insert more than 1 stent or to treat more than 1 lesion in a treatment session.

2.2.2 Two main types of stent have been used – balloon expandable and self-expanding. Some studies have also used drug-eluting stents. The technology has evolved over the past decade and continues to do so.

> Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview.

2.3 Efficacy

2.3.1 The efficacy outcomes described below include stroke or death occurring more than 30 days after the procedure (unless specified otherwise). Stroke or death occurring on or before 30 days is considered to be a safety outcome.

2.3.2 A randomised controlled trial of 451 patients treated by angioplasty and stent insertion or medical management alone reported ischaemic stroke in the area of the brain supplied by the artery with the index lesion more than 30 days after enrolment in 6% of patients in both groups (13/224 and 13/227, respectively, p value not stated) at a mean follow-up of 12 months. A case series of 213 patients reported lesion-related ischaemic stroke more than 30 days after the procedure in 3% (7/213) of patients, at a mean follow-up of 27 months. A case series of 158 patients reported that 20% (22/110) of patients had a stroke or TIA between 30 days and 12 months after the procedure.

2.3.3 The randomised controlled trial of 451 patients treated by angioplasty and stent insertion or medical management alone reported a death rate of 3% in both groups (7/224 and 7/227, respectively, p=0.95) at a mean follow-up of 12 months.

2.3.4 A systematic review comparing 36 studies of angioplasty and endovascular stent insertion with 33 studies of angioplasty alone reported stroke and/or death in 12% (123/1070) and 17% (125/731) of patients respectively at 1-year follow-up (p=0.0002).

2.3.5 The case series of 213 patients reported an overall restenosis rate of 19% (19/99) identified on follow-up angiography at a mean follow-up of 9 months. A case series of 189 patients reported recurrent stenosis in 25% (43/174) of lesions identified on angiography at a mean follow-up of 4 months. A case series of 113 patients reported an overall restenosis rate of 18% (16/89; identified by transcranial doppler ultrasound or angiography) at a mean follow-up of 29 months.

2.3.6 The Specialist Advisers listed key efficacy outcomes as reduction in TIA or stroke frequency.

2.4 Safety

2.4.1 The randomised controlled trial of 451 patients treated by angioplasty and stent insertion or by medical management alone reported stroke or death within 30 days of enrolment in 15% (33/224) and 6% (13/227) of patients, respectively (p=0.002). There were 5 stroke-related deaths in the stent group and 1 non-stroke-related death in the medical management group. The systematic review

comparing 36 studies of angioplasty and endovascular stent insertion with 33 studies of angioplasty alone reported stroke and/or death in 8% (104/1291) and 9% (91/1027) of patients respectively at 1-month follow-up (p=0.49).

2.4.2 Stent occlusion occurred in 4% (2/53) of patients treated by endovascular stent insertion in a non-randomised comparative study. One occlusion occurred 2 days after stent insertion and the patient had extracranial-intracranial bypass surgery because of recurrent TIAs. The second occlusion occurred 9 days after stent insertion in a patient who was not receiving antiplatelet medication because of a gastrointestinal haemorrhage; the patient had a stroke and died.

2.4.3 Vessel rupture during stent navigation was reported in 2% (2/113) of patients in the case series of 113 patients; 1 patient died of massive subarachnoid haemorrhage, and the other was treated by emergency craniotomy and surgical clipping of the middle cerebral artery. One patient died after vessel rupture during the procedure in the case series of 189 patients.

2.4.4 Fatal intracerebral haemorrhage was reported in 1 patient in the case series of 189 patients (timing not reported). There were haemorrhages in 3 other patients; 1 intracerebral haemorrhage 6 days after the procedure (resolved within 30 days) and 2 subarachnoid haemorrhages (1 resolved without treatment and the other was successfully treated by coil occlusion). Bilateral intracerebral haemorrhage was reported in 1 patient in the case series of 113 patients, 2 weeks after the procedure (no other details provided). Symptomatic subarachnoid haemorrhage (not otherwise described) was reported in 1% (2/213) of patients and symptomatic brain haemorrhage (not otherwise described) was reported in 1 patient, within 30 days of the procedure, in the case series of 213 patients.

2.4.5 Specialist Advisers listed anecdotal adverse events as basilar artery rupture resulting in death, disabling thalamic infarction, and reperfusion haemorrhage. They stated that theoretical adverse events included vessel dissection, embolisation, myocardial infarction, groin haematoma and contrast reactions.

2.5 Other comments

2.5.1 The Committee noted that a number of different devices have been used for endovascular stent insertion for intracranial atherosclerotic disease and that technical evolution of devices is continuing.

2.5.2 The Committee also noted that medical management is variable and continues to evolve. This complicates interpretation of studies that compare the procedure with medical treatment.

3 Further information

3.1 For related NICE guidance see www.nice.org.uk.

Information for patients

NICE has produced information on this procedure for patients and carers ('Understanding NICE guidance'). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

4 About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE interventional procedures guidance process.

It updates and replaces NICE interventional procedure guidance 233.

We have produced a summary of this guidance for patients and carers. Tools to help you put the guidance into practice and information about the evidence it is based on are also available.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the

available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

[Intervention Review]

Angioplasty for intracranial artery stenosis

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ABSTRACT

Background

Intracranial artery stenosis causes up to 10% of all ischaemic strokes. The rate of recurrent vascular ischaemic events is very high. Angioplasty with or without stent placement is a feasible procedure to dilate the vessel affected. However, its safety and efficacy have not been systematically studied.

Objectives

To determine the efficacy and safety of angioplasty combined with best medical treatment compared with best medical treatment alone in patients with acute ischaemic stroke or transient ischaemic attack (TIA) resulting from intracranial artery stenosis for preventing recurrent ischaemic strokes, death, and vascular events.

Search strategy

We searched the Cochrane Stroke Group Trials Register (last searched March 2006). In addition we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 1, 2006), MEDLINE (1966 to March 2006), EMBASE (1980 to February 2006) and Science Citation Index (1945 to March 2006). To identify further published, unpublished and ongoing trials we searched reference lists of relevant articles and contacted authors and experts in the field.

Selection criteria

Randomised or otherwise controlled studies comparing best medical care plus angioplasty of the intracranial cerebral arteries, with or without stent placement, with best medical care alone. Studies were only included if data for clinical significant endpoints such as recurrent ischaemic stroke, haemorrhagic stroke and death were available.

Data collection and analysis

Two review authors selected trials for inclusion, and independently assessed trial quality and extracted data. Calculation of relative treatment effects with subgroup analysis was done if possible.

Main results

No randomised controlled trials were found. There were 79 articles of interest consisting of open-label case series with three or more cases. The safety profile of the procedure showed an overall perioperative rate of stroke of 7.9% (95% confidence intervals (CI) 5.5% to 10.4%), perioperative death of 3.4% (95% CI 2.0% to 4.8%), and perioperative stroke or death of 9.5% (95% CI 7.0% to 12.0%). No comments can be made on the effectiveness of the procedure.

Authors' conclusions

At present there is insufficient evidence to recommend angioplasty with or without stent placement in routine practice for the prevention of stroke in patients with intracranial artery stenosis. The descriptive studies show that the procedure is feasible although carries a significant morbidity and mortality risk. Evidence from randomised controlled trials is needed to assess the safety of angioplasty and its effectiveness in preventing recurrent stroke.

PLAIN LANGUAGE SUMMARY

Angioplasty for intracranial artery stenosis

There is insufficient evidence to support the use of angioplasty for intracranial artery stenosis. Narrowing of the arteries inside the skull is a significant cause of stroke. Medical treatment for prevention consists of the control of risk factors such as high blood pressure, diabetes, and high cholesterol. Blood thinners are also used, but none has been demonstrated to be superior to another. Angioplasty, a procedure for opening narrowed arteries by means of a balloon or stent, is feasible but its safety and efficacy is not known. This review found no randomised controlled trials and no evidence to support the use of this procedure in routine practice. More research is needed to establish the role of this procedure in the treatment of this disease.

BACKGROUND

Intracranial artery stenosis secondary to atherosclerosis is a significant cause of ischaemic stroke, accounting for 5% to 10% of all ischaemic strokes (Gorelick 1993; Hass 1968; Sacco 1995; Wityk 1996). Although the annual risk of stroke in patients with intracranial artery stenosis was estimated at 3% to 15% (Bogousslavsky 1986; Chimowitz 1995; Corston 1984; Craig 1982; EC/IC Bypass 1985; Hinton 1979; Marzewski 1982; Moufarrij 1986; Pessin 1987; WASID 1998; Wechsler 1986) a recent clinical trial showed a risk of recurrent vascular events at 15% to 17% (Chimowitz 2005; Kasner 2006). Patients with severe stenosis of the vertebral artery, the basilar artery, or both, are at particularly high risk of recurrent stroke despite antithrombotic therapy (Chimowitz 1995; Chimowitz 2005; Thijs 2000; WASID 1998). Retrospective studies suggested that chronic anticoagulation with warfarin was the best therapeutic alternative (Benesch 2000; Chimowitz 1995; WASID 1998); however, a randomised trial showed no benefit of warfarin over aspirin for the prevention of stroke or vascular events. Moreover, its use was associated with higher rates of adverse events such as bleeding (Chimowitz 2005). Despite claims of ballon angioplasty low complication rate associated with improved experience and technology (Gomez 2001), the reported rate of stroke or death during or after angioplasty ranges from 3% to 40%. Even fewer data exist on the evaluation of cerebral artery stenting. Although there have been several large series undertaken, these have included rather heterogeneous groups of patients with variable follow up (Abou-Chebl 2005; Alazzaz 2000; Barakate 2001; Boulos 2005; Callahan 1997; Chow 2005; Connors 1999; Ferguson 1993; Gomez 2000b;Gomez 2000a; Mori 2000; Qureshi 2000; Rasmussen 2000). In this systematic review of all randomised or otherwise controlled studies, we aimed to compare the effectiveness of angioplasty with or without stent placement and medical care with medical care alone in patients with symptomatic or asymptomatic intracranial artery stenosis.

OBJECTIVES

The objective of this review was to determine the safety and effectiveness of percutaneous transluminal angioplasty with or without stent placement combined with best medical care compared to best medical care alone in preventing recurrent stroke in patients with either symptomatic or asymptomatic intracranial artery stenosis.

METHODS

Criteria for considering studies for this review

Types of studies

Section 6.0

Guidelines

Breast/Chest Surgery Requirements for Gender Dysphoria
Other Coverage Concerns for Gender Dysphoria

Questions:

1) Should the gender dysphoria guideline be modified to remove the requirement for 1 year of cross sex hormone therapy prior to breast/chest surgery?
2) Should laser hair removal be a covered treatment for pre-operative site preparation?
3) What is the HERC policy regarding revisions to previous gender dysphoria related surgeries?
4) Should smoking cessation be required prior to genital surgery for gender dysphoria?
5) Do we need to add PT procedure codes to the gender dysphoria line to allow pre- and post-procedure therapy for vaginoplasty?
6) Should other procedures requested by patients be considered for addition to the gender dysphoria line?

Question sources:

1) Stephanie Detlefsen, MD, and Heather M. Leffler, MSW, LCSW, Kaiser Permanente Gender Pathways Clinic/Transgender Care Team
2) CCO medical director; OHSU transgender surgical team
3) Joyce Liu, MD, Medicaid medical director for Kaiser Permanente NW
4) HERC staff
5) HERC staff
6) Patients

Issues:

Issue 1: The current gender dysphoria guideline requires 1 year of cross-sex hormone therapy prior to bilateral mastectomy for female-to-male transgender patients or breast augmentation surgeries for male-to-female transgender patients. The Kaiser medical team caring for their transgender population is requesting that this requirement be removed. It is not consistent with WPATH guidelines and is not a requirement for various private insurers, and so is causing confusion and denials of service for the Kaiser program.

The issue raised by the Kaiser clinicians appears to specifically concern female-to-male transitioning persons. When patients are not able to tolerate the side effects of testosterone, they are being denied chest/breast surgery.

An OHP CCO medical director also raised a question about whether requiring 1 year of living as the desired gender is required by WPATH prior to breast/chest surgery. The current HERC guideline requires this step prior to surgery for both breast/chest surgery and for genital surgery.

From Dr. Detlefsen

I want to remind HERC that WPATH creates their guidelines as a world standard on how to treat these patients. Gender is a spectrum and everyone's gender identity is very personal and the choice of hormones, surgery, etc is very individualized. Gender is a spectrum hence treatment is a spectrum. Testosterone has a fair amount of side effects... WPATH writes the guidelines we all follow and more and more patients are obtaining surgical benefits. I'm not sure if you know, but as of January 1st ALL Kaiser members have surgical benefits (with rare exception) and we are following the WPATH guidelines for all of them except OHP members due to the HERC language around the 1 year testosterone requirement prior to top surgery.

I cannot speak for other organizations, but Heather has informally outreached to "other" organizations and they too (mostly due to strict UM interpretation) are not performing top surgery based on HERC language. UM committees often have complex goals that reach beyond clinical care goals. It is not common that patients don't want testosterone but it happens and again I think this is a moot point. Gender is spectrum and everyone's gender identity is different whether cis-gendered, trans-tendered or other. I have included WPATH's language below. I think their wording is quite blunt. I know evidence based scientists hate to hear we don't have a lot of data but we don't have good demographic data on the transgender population due to numerous barriers but that should not prevent us from caring for these patients humanely…Heather and I would be happy to discuss this further with HERC because ultimately, the issue is this: is it ethical to force patients to take medications they do not want to take, which has side effects they want to avoid, when there are clear guidelines from WPATH that says it is not necessary and there is no clinical literature that shows hormones increases the "success" for chest masculinization surgery?

From Dr. Jens Urs Berli, OHSU Plastic and Reconstructive Surgery

Not every patient qualifies for testosterone based on their preexisting conditions (i.e. coronary artery disease, polycythemia vera, exacerbation of psychiatric comorbidities)…Although hormonal treatment for 12 months in the male to female patient is strongly encouraged, there may also here be patients that do not qualify for estrogen treatment (i.e. previous deep venous thrombosis/pulmonary embolus).

Breast construction/reconstruction guidance should be modified to remove that term “medical” from the contra-indication exemption to allow for a broader application. There may be patients for whom hormone therapy is not desirable due to being of an older generation, may have cancer risks or other medical or psychiatric issues and that don’t meet strict contra-indication but may have associate undesirable risks.

Issue 2: Another issue raised by a provider was the question of whether we cover laser hair removal for surgical site preparation, or only electrolysis. HERC added electrolysis (CPT 17380) to the gender dysphoria line with a limitation to surgical site preparation last fall, but did not

add laser hair removal due to the nonspecific nature of the CPT code (CPT 17999 Unlisted procedure, skin, mucous membrane and subcutaneous tissue). CPT 17999 is currently listed as Ancillary.

The CCOs are finding considerable difficulty in identifying providers for electrolysis who have Medicaid billing numbers and who are willing to contract with them. The CCOs have questions about what is actually required for surgical site preparation.

Expert Input: Dr. Daniel Dugi, OHSU urology, gender affirming surgery provider
From materials he gives to prospective patients:

> **Permanent hair removal:** As the skin of the penis and scrotum is used to make the new vagina, it is important to permanently remove hair from this area before surgery. This is to avoid having hair within the vagina. Options for hair removal include electrolysis and laser hair removal. Electrolysis is the most permanent form of hair removal. Laser hair removal may not be as effective in the long-term or in individuals with lighter hair color. I recommend electrolysis. We will provide you with a letter of medical necessity and a diagram showing the pattern for hair removal (see Dr. Dugi's handout in packet). Hair removal is the biggest delay in moving forward with surgery! Not all hair grows at the same time, and it takes at least three cycles of hair growth to achieve adequate hair removal. This may take anywhere between 3-12 months depending on how stubborn your hair is. The earlier you can start with this process, the better.

From Dr. Dugi's letter to the Commission:

> Laser hair removal should be added as an option for pre-surgical site hair removal. While not all patient will be good candidates for laser hair removal (vs electrolysis) prior to gender-affirming surgery, some people will be good candidates for this less expensive, less painful, and more efficient method of hair reduction should be an option, consistent with best medical practices and patient autonomy.
>
> As a urologist and genital reconstructive surgeon, it is my professional opinion that these treatments are medically necessary. I have seen firsthand the impact these procedures have on the quality of life and safely of the transgender patient I work with.

Expert input: Heather Onoday, NP, OHSU Dermatology

> From our perspective, when doing billing for hair laser that is medically necessary, the typical code that we utilize is 17110 or 17111. It is based on number of follicles treated, so most of the time the 17111 is used.
>
> The laser is very effective for permanent hair reduction. Essentially, a patient typically requires approximately 5 to 6 treatments to remove approximately 90% of their hair. Over the course of many months to years they may get a small percentage of the hair back, but generally speaking there is a very large quantity of hair permanently removed (10-25% may recur over a varied time period of months to years). This is comparable to electrolysis

which also offers permanent hair reduction. There's not yet an actual method of complete permanent removal available.

Laser Treatments are spaced approximately 4 to 6 weeks apart, to accommodate the changes in hair growth cycles. The advantages of hair laser over electrolysis are that it is a smaller number of overall treatments required and pain is reduced due to the very short time of treatment required, typically the groin area or chest area is an approximately 10 to 15 minute procedure. Electrolysis allows for very blonde or white hair to be treated, whereas hair laser does require that there is at least some pigmentation to the hair. This accounts for the majority of patients-it is a very rare patient who does not have some pigment within their hair follicles.

From Dr. Jens Urs Berli, OHSU Plastic and Reconstructive Surgery

Laser hair removal should be added as an option for pre-surgical site hair removal. A combined approach of electrolysis and laser hair removal may at times be more effective. Pre-genital surgery: last hair removal is an integral part of the preoperative preparation. Hair that grows within the neourethra can lead to urinary obstruction and infection. Growth of intravaginal hair is stigmatizing and undesired. I therefore strongly support presurgical laser hair removal as an alternative for those who cannot tolerate electrolysis.

From Megan Bird, MD and Amy Penkin, submitted testimony

The advantages of hair laser over electrolysis are that it requires a small number of overall treatments and pain is reduced due to the reduction in treatments. A typical groin or chest area is approximately 10 to 15 min procedure with laser treatments, compared to electrolysis, which can require 16-20 hours of treatments. Electrolysis, however, can be more effective for treatment very blonder or white hair.

We also support adding a code or modifying guidance to allow for expanding the length of time for a single daily electrolysis session from 30 minutes to up to two hours for patients who can't use laser removal and have sufficient pain management. This will reduce the overall number of sessions needed, which is critical for patients who must travel for treatments.

Issue 3: Kaiser Permanente has contacted HERC staff for guidance on policy for coverage of revisions to previous sex reassignment surgery. Dr. Megan Bird also contacted HERC for clarification of coverage for revisions and repairs.

From Dr. Liu:

We have a request from a 55 yo transgender women (M-> F) who had surgery 30 years ago. She had full SRS including a vaginoplasty in 1986. Her vagina was very small from the beginning and she would like to have a functional vagina and there is newer technology available.

Based on your interpretation of the relatively new transgender benefit do you think this revision should be covered? She meets the other HERC requirements for the surgery but this is the first revision we have been asked to cover. Thanks so much for your help on this.

From: Dr. Megan Bird

I have had a couple of patients who have had surgery out of state or out of country now living in Oregon. They have either chronic pain or a surgical complication of the procedure (fistula, erosion) and needed revision but were denied. I know one gave up and did not pursue appeal as they should have. I would suggest something on the order of revisions of covered service may be done in cases of chronic pain or surgical complication. There is no guidance in WPATH as you said. There is no real literature on the subject but it makes sense that if the original surgery would have been covered and they had a complication to cover the revision. I would like to avoid revisions for cosmetic reasons (for example the labia are uneven on a vaginoplasty) as I don't think that is a good use of resources.

From: Dr. Daniel Dugi, OHSU reconstructive urologist

Guidance for revision surgery should be clarified for pain complications or other medical complications. As we endeavor to treat care for gender dysphoria as any other medical condition that has surgery as a possible therapy, we will need to deal with and care for the inevitable complications. Research shows that complications of genital surgery are very distressing to all patients and especially transgender patients. Complications can be related to urinary or sexual function in addition to pain, and we must be able to effectively treat complications of gender-affirming surgery.

From Dr. Jens Urs Berli, OHSU Plastic and Reconstructive Surgery

Revision surgery may include: vaginal strictures, urethral strictures, extrusion of phallic prosthesis, testicular prosthesis, implant associated problems (i.e. capsular contracture), pain from nerve entrapment, excess scar formation (hypertrophic scars, keloids). All patients should be able to access revisions to manage above mentioned complications, many of which are associated with pain, medical risk and continued dysphoria.

From Megan Bird, MD and Amy Penkin, submitted testimony

Fistulas [lines 234 and 303] and urethral strictures of stenosis [line 184] are covered, but others are not currently covered (surgical wound breakdown, abscess). For patients with chronic pain or surgical complications it is appropriate to provide for revision of the original surgery to obtain the outcome necessary.

Note: abscess and necrosis of surgical wound is covered on line 230

There is no guidance in the current WPATH version regarding revisions to surgeries, other than obvious need to treat surgical complications.

Issue 4: Dr. Dugi (the only surgeon performing genital gender dysphoria surgery in Oregon) strongly feels that smoking cessation is required prior to vaginoplasty surgery.

From Dr. Dugi's surgical information packet:

> **Smoking** I require that people not smoke or use any nicotine or tobacco products for at least 6 weeks before surgery and at least 6 weeks after surgery - and it is best for your overall health to never start again!. This includes e-cigarettes, nicotine gum, and nicotine patches. Nicotine is a very powerful drug that decreases blood flow to the tissues that need this nutrition after surgery. Research shows that people who smoke even 1 cigarette a day have a **10-time increased risk of surgery failure**. Second hand smoke exposure should be avoided as well for all of the above reasons. Your primary care provider and tobacco cessation groups can be very helpful in this process. Vaginoplasty is an affirming procedure, and we do not want you to have wound healing complications that lead to a less than desired result. This is so important, that as a policy for all my patients, a urine nicotine test will be performed as part of your pre-surgery lab tests, and we will reschedule if you have not been able to quit.
>
> He uses a urine cotinine test 2 weeks prior to surgery to confirm smoking cessation**.**

Issue 5: Dr. Dugi requires pelvic physical therapy pre- and post-operatively for vaginoplasty. There are currently no PT CPT codes on the current gender dysphoria line.

From Dr. Dugi's surgical materials:

> **Physical therapy** Creating the vagina requires making a space between the pelvic muscles. These muscles normally work to support your organs and help with control of urination and bowel movements... You will need to learn what it feels like to contract and relax these muscles, as being good at relaxing these muscles will make dilation of the vaginal later on much more comfortable. You will meet with a physical therapist who specializes in pelvic muscle function before and after surgery to help teach you these techniques.

<u>Pelvic physical therapy CPT codes</u>:
97001 Physical therapy evaluation
97002 Physical therapy re-evaluation
97110 Therapeutic procedure, 1 or more areas, each 15 minutes; therapeutic exercises to develop strength and endurance, range of motion and flexibility
97140 Manual therapy techniques (eg, mobilization/ manipulation, manual lymphatic drainage, manual traction), 1 or more regions, each 15 minutes
97530 Therapeutic activities, direct (one-on-one) patient contact (use of dynamic activities to improve functional performance), each 15 minutes

Issue 6: A patient has contacted the HERC to request consideration of the addition of facial feminization and chest liposuction (CPT 15877) to the gender dysphoria line. Other patient testimony was received regarding the need to cover facial feminization. For more information about these requests, please see the submitted testimony available on the HERC secure website.

Current Prioritized List Guideline

GUIDELINE NOTE 127, GENDER DYSPHORIA

Line 317

Hormone treatment with GnRH analogues for delaying the onset of puberty and/or continued pubertal development is included on this line for gender questioning children and adolescents. This therapy should be initiated at the first physical changes of puberty, confirmed by pubertal 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.

Cross-sex hormone therapy is included on this line for treatment of adolescents and adults with gender dysphoria who meet appropriate eligibility and readiness criteria. To qualify for cross-sex hormone therapy, the patient must:

1. have persistent, well-documented gender dysphoria
2. have the capacity to make a fully informed decision and to give consent for treatment
3. have any significant medical or mental health concerns reasonably well controlled
4. have a comprehensive mental health evaluation provided in accordance with Version 7 of the World Professional Association for Transgender Health (WPATH) Standards of Care (www.wpath.org).

Sex reassignment surgery is included for patients who are sufficiently physically fit and meet eligibility criteria. To qualify for surgery, the patient must:

1. have persistent, well documented gender dysphoria
2. have completed twelve months of continuous hormone therapy as appropriate to the member's gender goals unless hormones are not clinically indicated for the individual
3. have completed twelve months of living in a gender role that is congruent with their gender identity unless a medical and a mental health professional both determine that this requirement is not safe for the patient
4. have the capacity to make a fully informed decision and to give consent for treatment
5. have any significant medical or mental health concerns reasonably well controlled
6. for breast/chest surgeries, have one referral from a mental health professional provided in accordance with version 7 of the WPATH Standards of Care.
7. For genital surgeries, have two referrals from mental health professionals provided in accordance with version 7 of the WPATH Standards of Care.

Electrolysis (CPT 17380) is only included on this line for surgical site electrolysis as part of pre-surgical preparation for chest or genital surgical procedures also included on this line. It is not included on this line for facial or other cosmetic procedures or as pre-surgical preparation for a procedure not included on this line.

Mammoplasty (CPT 19316, 19324-19325, 19340, 19342, 19350, 19357-19380) is only included on this line when 12 continuous months of hormonal (estrogen) therapy has failed to result in breast tissue growth of Tanner Stage 5 on the puberty scale OR there is a medical contraindication to hormonal therapy.

From WPATH 7.0 (not included in the packet due to length)

Criteria for mastectomy and creation of a male chest in FtM patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Hormone therapy is not a prerequisite.

Criteria for breast augmentation (implants/lipofilling) in MtF patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the *SOC* for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Although not an explicit criterion, it is recommended that MtF patients undergo feminizing hormone therapy (minimum 12 months) prior to breast augmentation surgery. The purpose is to maximize breast growth in order to obtain better surgical (aesthetic) results.

Other policies

1) **Cigna 2015**
    a. Has no hormone requirement prior to female to male chest surgery
    b. Does not appear that mammoplasty is a covered service
2) **Aetna 2015**
    a. Note: mammoplasty is not a covered services
    b. Aetna considers gender reassignment surgery medically necessary when all of the following criteria are met:
        i. Requirements for mastectomy for female-to-male patients:
            1. Single letter of referral from a qualified mental health professional (see Appendix); and
            2. Persistent, well-documented gender dysphoria (see Appendix); and
            3. Capacity to make a fully informed decision and to consent for treatment; and
            4. Age of majority (18 years of age or older); and

5. If significant medical or mental health concerns are present, they must be reasonably well controlled.
6. Note that a trial of hormone therapy is not a pre-requisite to qualifying for a mastectomy.

HERC staff recommendations:

1) Modify the gender dysphoria guideline as shown below
    a. Removes hormone requirement prior to female-to-male type chest/breast surgeries
        i. Consistent with other insurance carriers and WPATH guidelines
    b. Modifies the requirement for hormone (estrogen) therapy prior to mammoplasty, allowing for "any contraindication" which could include intolerance of the medication or medical conditions which preclude use
        i. Alternate: remove any requirement for estrogen therapy prior to mammoplasty
    c. Removes the requirement for a year of living as the desired gender prior to breast/chest surgery
        i. Consistent with other insurance carriers and WPATH guidelines
    d. Clarifies when surgical revisions are a covered service
    e. Add requirement for smoking cessation prior to genital surgeries
        i. Evidence of improved outcomes; agrees with Dr. Dugi's recommendations
2) Add laser hair removal for surgical site preparation (CPT 17110, 17111) to line 317 GENDER DYSPHORIA
    a. 17110: Destruction (eg, laser surgery, electrosurgery, cryosurgery, chemosurgery, surgical curettement), of benign lesions other than skin tags or cutaneous vascular proliferative lesions; up to 14 lesions
    b. 17111: 15 or more lesions
    c. Modify the guideline note as shown below regarding hair removal
3) Add pelvic physical therapy to line 317 GENDER DYSPHORIA
    a. 97001 Physical therapy evaluation
    b. 97002 Physical therapy re-evaluation
    c. 97110 Therapeutic procedure, 1 or more areas, each 15 minutes; therapeutic exercises to develop strength and endurance, range of motion and flexibility
    d. 97140 Manual therapy techniques (eg, mobilization/ manipulation, manual lymphatic drainage, manual traction), 1 or more regions, each 15 minutes
    e. 97530 Therapeutic activities, direct (one-on-one) patient contact (use of dynamic activities to improve functional performance), each 15 minutes
    f. Modify the guideline note as shown below to specify use only for pre- and post-operative therapy for included genital surgery.

GUIDELINE NOTE 127, GENDER DYSPHORIA

Line 317

Hormone treatment with GnRH analogues for delaying the onset of puberty and/or continued pubertal development is included on this line for gender questioning children and adolescents. This therapy should be initiated at the first physical changes of puberty, confirmed by pubertal 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.

Cross-sex hormone therapy is included on this line for treatment of adolescents and adults with gender dysphoria who meet appropriate eligibility and readiness criteria. To qualify for cross-sex hormone therapy, the patient must:

1. have persistent, well-documented gender dysphoria
2. have the capacity to make a fully informed decision and to give consent for treatment
3. have any significant medical or mental health concerns reasonably well controlled
4. have a comprehensive mental health evaluation provided in accordance with Version 7 of the World Professional Association for Transgender Health (WPATH) Standards of Care (www.wpath.org).

Sex reassignment surgery is included for patients who are sufficiently physically fit and meet eligibility criteria. To qualify for surgery, the patient must:

1. have persistent, well documented gender dysphoria
2. for genital surgeries, have completed twelve months of continuous hormone therapy as appropriate to the member's gender goals unless hormones are not clinically indicated for the individual
3. for genital surgeries, have completed twelve months of living in a gender role that is congruent with their gender identity unless a medical and a mental health professional both determine that this requirement is not safe for the patient
4. have the capacity to make a fully informed decision and to give consent for treatment
5. have any significant medical or mental health concerns reasonably well controlled
6. for breast/chest surgeries, have one referral from a mental health professional provided in accordance with version 7 of the WPATH Standards of Care.
7. For genital surgeries, have two referrals from mental health professionals provided in accordance with version 7 of the WPATH Standards of Care.
8. For genital surgeries, be abstinent from tobacco products for 6 weeks prior to surgery, to be confirmed by urine cotinine testing.

Electrolysis (CPT 17380) and laser hair removal (CPT 17110, 17111) are ~~is~~ only included on this line ~~for surgical site electrolysis~~ as part of pre-surgical preparation for chest or genital surgical procedures also included on this line. ~~It is~~ These procedures are not included on this line for facial or other cosmetic procedures or as pre-surgical preparation for a procedure not included on this line.

Mammoplasty (CPT 19316, 19324-19325, 19340, 19342, 19350, 19357-19380) is only included on this line when 12 continuous months of hormonal (estrogen) therapy has failed to result in breast tissue growth of Tanner Stage 5 on the puberty scale OR there is any ~~a medical~~ contraindication to hormonal therapy.

Revisions to surgeries for the treatment of gender dysphoria are only covered in cases where the revision is required to address complications of the surgery (wound dehiscence, fistula, chronic pain, etc.). Revisions are not covered solely for cosmetic issues.

Pelvic physical therapy (CPT 97001, 97001, 97110, 97140, and 97530) is included on this line only for pre- and post-operative therapy related to genital surgeries also included on this line.

Thank you for your interest in gender-affirming surgery at OHSU. Included here is a document that Dr Dugi wrote that covers some information he thinks is important to know about vaginoplasty surgery preparation, etc.

During your visit, Dr Dugi will ask you about your transition, what is important to you about having gender-affirming surgery, about your support system when recovering from surgery, and you will have plenty of time to ask questions. Please come with all your questions ready and written down! As part of your visit, there will be a very brief and painless genital examination.

Dr Dugi asks that anyone planning to undergo gender-affirming vaginoplasty have permanent hair removal of the areas of skin that will be used to make the vagina. There is a diagram included in this document that shows what areas should be treated. You may start on this as soon as you like; this is usually what keeps people from having surgery as soon as they would like, because it takes several months. You will be able to discuss this with Dr Dugi at your appointment. For most people, electrolysis is preferred over laser hair removal. If you like, we can send you a letter of medical necessity for this hair removal even before your appointment (or give this to you at the time of your appointment), as some insurance companies will cover this service before vaginoplasty.

Before scheduling your surgery (vaginoplasty, but also orchiectomy if you choose to do that by itself), we will need to receive two letters in support of your gender-affirming surgery from mental health providers (as per World Professional Association for Transgender Health Standards of Care). Included here is information to give to your letter writers so that the letters include the necessary information.

Please know that we follow WPATH guidelines for performing surgery only after a person has been socially transitioned and taking hormone therapy for at least 1 year, although we do make exceptions in limited circumstances.

Gender-affirming Vaginoplasty

Daniel Dugi, MD FACS
Assistant Professor
Department of Urology
Oregon Health & Science University

Who I am, Why I do this

I am a Board-certified urologist, a specialist surgeon of the genitals and urinary system. After finishing medical school and then five years of training to specialize in urology, I completed an additional year of fellowship training in Reconstructive Urology. This is a subspecialty of Urology which focuses on surgery for complex issues of the genitals and urinary tract such as urethral narrowing or strictures, genital trauma or birth defects of the genitals. I do complex genital surgery every week, and my colleagues and consulting physicians refer to me the most difficult reconstructive genital and urinary problems.

I am not trans, but I am an ally. I feel strongly about providing access to trans* surgical procedures in Oregon and feel it is an honor to be trusted by my patients during such important part of transition. I first began treating trans* patients when I joined OHSU in 2009. These were generally people who had had complications after gender-affirming surgery performed elsewhere. I learned a lot from my early patients, and this prompted me to co-found the OHSU Transgender Health Program in 2012. After this, I responded to a challenge from one of my patients to begin offering these surgeries in Oregon. In preparation to start offering gender-affirming bottom surgery at OHSU, I have spent the past two years studying and learning techniques at several world-renown transgender surgery centers.

You may notice as you read below the word “we” a lot. This refers to me operating with my surgical team at times, but even more importantly, **you** and us. For success, this will be a partnership.

Overview— Our goal is to create natural-appearing and functional female genitalia, the vagina and external parts. Initially, as a baby develops before birth, all the genital parts are the same. Through the influence of hormones, the genitalia then develop differently for males and females. Wherever possible, we will use the tissue that *would have* been the female part to make the new female part. For instance, the basic structures of the penis and clitoris are the same. The glans, or head, of the penis with its nerves and blood supply is used to make the clitoris. Likewise, the scrotal skin is used to make the larger, outer labia. Skin from the penis and the urethra will be used to make the vagina and the area around the clitoris, the smaller or inner labia, and vagina. Some skin from the scrotum is also used for the vagina. Occasionally, some women may need to have additional skin used from the lower belly or groin to help in creating the vagina.

I offer what most surgeons refer to as a “one stage” operation, meaning all the important structures are created at the main operation. For reasons of safety, some things cannot be done in this surgery. For instance, the large, outer lips (labia majora) will be more separated above the clitoris after this surgery than they are in genetic women. A second surgery at least 3 months after the main surgery can fix this. The delay in time is necessary for reasons of tissue blood supply and safety. Not everyone will chose this 2nd operation, but it will also allow for a

time to touch up areas that didn't heal as well as expected, are uneven/asymmetric, etc. We will submit to insurance that we plan a 2-stage operation so that if you choose the 2nd operation, this should not be difficult to get insurance to cover.

Preparation for Surgery

Letters of Support We follow The World Professional Association for Transgender Health (WPATH) "Standards of Care" guidelines. This requires that you have two letters in support of your transition surgery prior to scheduling the surgery (insurance providers also require this). One of these letters should be written by a mental health profession who knows you well. Letters should include specifically that you are being recommended for bottom surgery (see additional form describing what should be included in a letter of support).

Permanent hair removal As the skin of the penis and scrotum is used to make the new vagina, it is important to permanently remove hair from this area before surgery. This is to avoid having hair within the vagina. Options for hair removal include electrolysis and laser hair removal. Electrolysis is the most permanent form of hair removal. Laser hair removal may not be as effective in the long-term or in individuals with lighter hair color. I recommend electrolysis. We will provide you with a letter of medical necessity and a diagram showing the pattern for hair removal. Hair removal is the biggest delay in moving forward with surgery! Not all hair grows at the same time, and it takes at least three cycles of hair growth to achieve adequate hair removal. This may take anywhere between 3-12 months depending on how stubborn your hair is. The earlier you can start with this process, the better. (See additional form showing the areas to be cleared of hair before surgery)

Health Before Surgery

Any surgery is a challenge to your body, and you will want to be as healthy before surgery as possible. For a successful surgery, our first chance will be our best chance! Be as healthy as possible at the time of surgery.

Smoking I require that people not smoke or use any nicotine or tobacco products for at least 6 weeks before surgery and at least 6 weeks after surgery - and it is best for your overall health to never start again!. This includes e-cigarettes, nicotine gum, and nicotine patches. Nicotine is a very powerful drug that decreases blood flow to the tissues that need this nutrition after surgery. Research shows that people who smoke even 1 cigarette a day have a **10-time increased risk of surgery failure**. Second hand smoke exposure should be avoided as well for all of the above reasons. Your primary care provider and tobacco cessation groups can be very helpful in this process. Vaginoplasty is an affirming procedure, and we do not want you to have wound healing complications that lead to a less than desired result. This is so important, that as a policy for all my patients, a urine nicotine test will be performed as part of your pre-surgery lab tests, and we will reschedule if you have not been able to quit. For people who use marijuana, please do not SMOKE for at least 4 weeks before surgery—use edibles, etc to avoid the carbon monoxide poisoning that comes from inhaling any type of smoke. I am much more concerned about nicotine than marijuana, however.

Weight You will have the best result if you are as close as possible to your ideal body weight. Structures like the clitoris, urethra, and vagina have to be placed near the pelvic bones, and if you are obese, they will be more buried by the extra tissue, just like in genetic women. But more importantly, it will be more difficult to make the vagina, and you may not have as good a result.

Also, being severely overweight increased your chances of having problems after surgery, such as problems with breathing, infections at the surgery area, and blood clots to the legs and lungs. We may discuss losing weight before surgery.

Diabetes People with diabetes may have greater risk of poor healing and infections. If you have diabetes, you should work with your primary care provider to make sure your diabetes is under good control before surgery.

Physical therapy Creating the vagina requires making a space between the pelvic muscles. These muscles normally work to support your organs and help with control of urination and bowel movements. Prior to surgery, you may not have thought much about these muscles, but the pelvic muscles are very important as you recover from vaginoplasty. You will need to learn what it feels like to contract and relax these muscles, as being good at relaxing these muscles will make dilation of the vaginal later on much more comfortable. You will meet with a physical therapist who specializes in pelvic muscle function before and after surgery to help teach you these techniques.

Before Surgery

About two weeks before surgery, you will have a preoperative appointment for lab work (including a nicotine test) and a general check on your health for surgery. We will also review details regarding surgery again. You will be given instructions regarding a bowel prep prior to surgery. Our anesthesia team will give you instructions on what medications you should take or not take leading up to surgery.

You will be instructed to stop taking estrogen for two weeks before surgery. This can be stressful and unpleasant, but it is important to reduce your risk of having dangerous blood clots after surgery. You will be able to restart about 1 week after surgery. You do not need to stop taking spironolactone before surgery.

Day of Surgery

You will be given instructions on when to arrive for surgery. This will likely be very early in the morning. You may not be a “morning person” but the operating room runs like a British train schedule—on time! Make sure to arrange a ride to the hospital well in advance and be there when instructed. Surgeries are often cancelled if people are late for their surgeries. Some people may have a party or celebration the night before surgery—make it an early night and do not drink alcohol or use recreational drugs. You want to be in good shape for surgery.

Please do not wear make-up, jewelry, or nail polish the day of surgery.

Do not eat or drink anything after midnight the night before surgery!!! This is for your safety and the anesthesiologist will cancel surgery if this rule is not followed! Exceptions are only for medications that you have been given instructions to take with a small sip of water.

We will meet on the morning of your surgery, but this is not the time to have critical questions answered—let’s do that ahead of time! I will have an assistant during surgery who will likely have you sign some paperwork before surgery. I need an assistant for surgery, but I am in charge of your surgery, I will be performing your surgery, and I will be there the entire time.

Your surgery will last several hours. Family or friends may wait in the OHSU waiting room or elsewhere, and our staff will give updates by phone during the surgery. I will speak with them after surgery.

After Surgery

You will be in the hospital for about 6 days after surgery. You will have a dressing on the surgical area that will stay in place until the 5th day after surgery. You will have a tube or a catheter in the bladder to drain your urine, and a stent to keep the new vaginal skin pressed against the surrounding tissue while it starts to "take" or heal. There will also be a tube called a drain that helps prevent blood and fluid from collecting.. During this time, you will be on strict bed rest. This is critical for proper healing of the vagina! Getting up and moving around early after surgery can cause the skin graft to fail. You will have pain medication available, but this will still be uncomfortable. Bring books, movies, or other entertaining things to help you during this boring time.

Because the vaginal stent/packing is pressing on both the bladder and the rectum, you may feel like you need to have a bowel movement even if you really don't. You may also feel like you need to urinate even though the bladder catheter is already draining your bladder. This will improve once the dressing is removed and the vaginal stent is removed.

People often feel as though they need to urinate when a bladder catheter is in place. This catheter will be removed after your surgical dressing and the vaginal stent is removed. About 1 out of 5 people are temporarily unable to urinate on their own after the catheter comes out or do not empty the bladder well enough. In that case, we will need to put a catheter back in for another week.

Before or at the time the vaginal stent is removed, you be given your set of vaginal dilators, supplies, and instructions. We will show you how do dilate the vagina, and we will help you begin to do this. You will need to do this three times. You will have specific, detailed instructions before you leave the hospital.

After You Leave the Hospital

You will be given specific instructions on taking care of your incisions and vagina when you leave the hospital. You should shower and use a mild soap externally every day. You will have a set of dilators to use for the vagina. You will also have instructions for cleaning the vagina. Dilation will be uncomfortable, but keep with it! This is very important for your healing!

You will have a lot of swelling and bruising after surgery. It will take weeks, even up to 3 months, for all the swelling to go away. Be patient—you won't know what the final appearance will be for a good while. You will have some drainage or small amount of old blood that drains for a while after surgery. You may have to use large maxi pads as needed at first after surgery, and having this snug against you with underwear that puts a little pressure on the skin is a good thing, but things should not be too tight. You can change to small pads as the drainage slows down.

You have just had a major operation. Don't make any big plans for when you get home. You should plan on mostly resting and recovering your strength for the first couple of weeks. You may gradually increase your activity level, but take it easy. It can be uncomfortable to sit since

most of the surgery was in this area. You might find that sitting on a foam donut, hemorrhoid pillow, U-shaped neck pillow, or "portable gel seat" may be more comfortable. You may find these at a pharmacy, Amazon.com, or other sites on the internet.

No working out, running, bicycling, strenuous yard work, heavy lifting, etc for 6 weeks after surgery. Then start slowly and let your body be your guide. You are still healing, but in different ways, for months after surgery, even up to a year after surgery. Also, the area of surgery tends to be pulled on during normal walking. This can be sore when walking, especially as you become more active, even for several months after surgery.

There may be areas of the skin that feel numb at first—this will likely improve over several months. Some areas, especially the clitoris, may be overly sensitive. The nerves are healing. Repetitive touch to sensitive areas can help signal your brain and body to be less sensitive. If you were able to achieve orgasm before surgery, you should be able to do so after surgery. But you will likely have to "re-learn" what feels good after you begin to heal. You may begin penetrating sexual activity starting three months after surgery.

After Surgery Results Vaginal depth and width depends on your anatomy, your healing, and your dedication to dilation. Some slight difference in size of the labia is normal and normal in genetic women, too. If these things are very bothersome, or if you desire cosmetic "touch up" after surgery, this is best done several months after surgery when things settle down.

We intentionally make the clitoris large at the time of surgery because it tends to shrink as you heal. I have extensive experience and success in safely moving the nerves to the new clitoris off the penile tissue beneath in my other surgical procedures. If you can reach orgasm before surgery, you should be able to reach orgasm after surgery, although it can take months for nerves to heal after surgery. Also, you will have to learn for yourself what feels good and works for you after surgery.

There is no surgery without scars, but we will try to keep them small. You can help with this by taking good care of your body after surgery—keeping the incisions and surgery area clean and dry, showing daily as you recover from surgery, NOT SMOKING, etc. Using medical silicone sheeting on top of your incisions after surgery can help the scars be less visible sooner, although we don't know exactly why this works.

The opening to the vagina and the space around the urethra and clitoris will be moist, but you should expect to need to use additional lubrication for sexual intercourse. I believe this is important to prevent trauma to the vagina by pulling it outwards too much during sex without enough lubrication. Genetic women frequently need additional lubrication too—there is a reason there are so many different brands of lubrication available!

Complications Complications are unfortunately a risk of surgery. I tend to be a conservative surgeon, meaning I tend to avoid things that are risky for you. I will never win a prize for being the fastest surgeon, but I take the time needed to do a good job. You may do everything right, I may do everything right, but nevertheless, sometimes things do not go as planned. Things like hematomas (blood clots that form in the surgery area) and infections of wound are not extremely common but do happen. Rarely, small areas of skin may fail after surgery, or a part of the skin graft may not survive, or the sutures may separate in a small area. Although troubling and scary, these are rarely major problems. Because we are creating a space on top of the rectum, injury to the rectum is a rare possibility. Most of these heal on their own after we repair

them. Very rarely, a “fistula” may form, an abnormal connection between the vagina and the rectum. This would likely require major surgery to fix.

Because the space for the vagina is made between the rectum and the bladder, as well as the urethra and the muscles that control urination, there is a small chance of a change in bladder and urinary function after surgery. What we call “urinary urgency”, or a feeling of needing to go to the bathroom suddenly, is common soon after surgery due to bladder irritation. Some people have difficulty emptying their bladders right after surgery and may need a bladder catheter longer than originally planned. Sometimes people notice that it can be harder prevent urine leakage after surgery. If this is a problem, exercises for the pelvic muscles can help quite a bit—another reason to see the physical therapist after surgery!

Follow-up I will want to see you in follow-up to see how you are feeling, how you are healing, and how you feel about your surgery. I will ask you to allow me to take pictures, both for my own learning about how you heal (I have done this since I started my career for most surgeries) but also, with your permission, to potentially share privately in the office with other people thinking about surgery to show how I do this surgery. If you allow this, there will be nothing that identifies who you are.

It is important to know that the prostate is not removed during surgery. It is thought that the risk of prostate cancer after vaginoplasty and for people who have estrogen is low, but the risk is not zero. There are no proven rules for how to continue to check the prostate in follow-up.

Last Thoughts

The easiest way to get in touch with me before surgery is email: dugi@ohsu.edu Please let me know how your hair removal is going as this is what slows down being able to schedule surgery.

This is obviously an extremely important event in your life. It is natural to have intense emotions before and after surgery, and these emotions may change quickly! It is scary to have surgery, and then afterwards it hurts, then it is frustrating as you wait for healing. You may feel extremely excited, nervous, happy, exhausted, or even disappointed. People have talked about feeling after surgery something like post-partum depression. These are real and natural feelings. Share your feelings with the people who are good for you in your life.

Letters of Support for Gender-affirming Genital Surgery

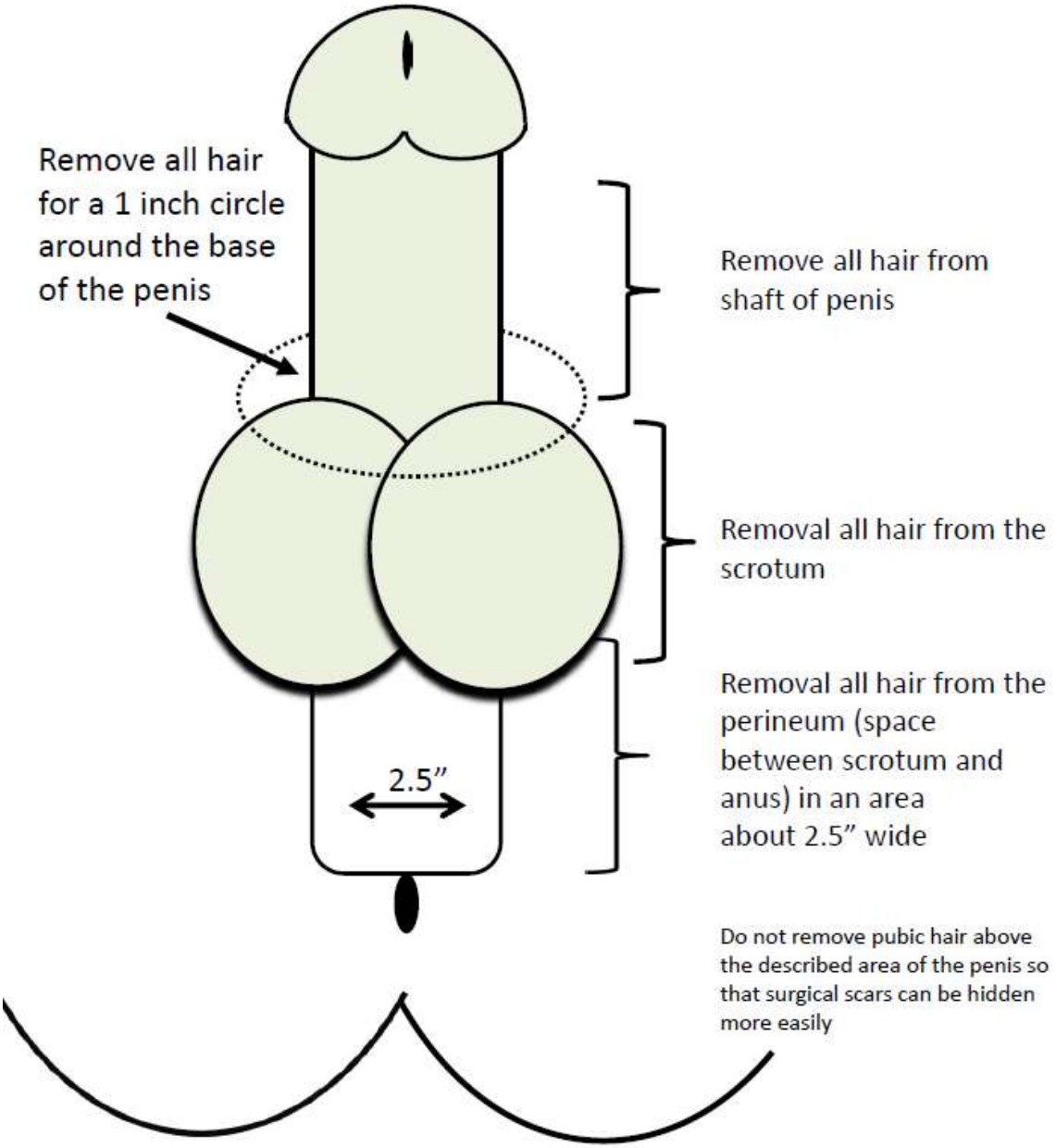
We follow the World Professional Association for Transgender Health (WPATH) Standards of Care. These guidelines, as well as most insurance companies, require that a person have two letters in support of gender-affirming genital surgery (orchiectomy, vaginoplasty, metoidioplasty, or phalloplasty).

These letters should come from mental health professionals with experience with transgender care. The mental health professional's documentation letter for surgery should succinctly specify:

1. The patient's general identifying characteristics;
2. The initial and evolving gender, sexual, and other psychiatric diagnoses;
3. The duration of their professional relationship including the type of psychotherapy or evaluation that the patient underwent;
4. The eligibility criteria that have been met (persistent well-documented gender dysphoria, a capacity make a fully informed decision and to consent to treatment, age of majority in a given country, and if significant medical or mental health concerns are present that they must be reasonably well-controlled) and the mental health professional's rationale for surgery – ***the letter must clearly state that the patient is a candidate for gender-affirming genital surgery.***
5. The degree to which the patient has followed the Standards of Care to date and the likelihood of future compliance;
6. Whether the author of the report is part of a gender team;
7. That the sender welcomes a phone call to verify the fact that the mental health professional actually wrote the letter as described in this document.

The organization and completeness of these letters provide the surgeon an important degree of assurance that mental health professional is knowledgeable and competent concerning gender identity disorders.

Permanent Hair Removal
Prior to Vaginoplasty



Cigna Medical Coverage Policy

Effective Date **1/15/2015**
Next Review Date **1/15/2016**
Coverage Policy Number **0266**

Subject **Gender Reassignment Surgery**

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Hyperlink to Related Coverage Policies

Panniculectomy and Abdominoplasty
Blepharoplasty, Reconstructive Eyelid Surgery, and Brow Lift
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Redundant Skin Surgery
Speech Therapy

INSTRUCTIONS FOR USE

*The following Coverage Policy applies to health benefit plans administered by Cigna companies. Coverage Policies are intended to provide guidance in interpreting certain **standard** Cigna benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supersedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2015 Cigna*

Coverage Policy

Coverage for gender reassignment surgery and related services, including pre and post-surgical hormonal therapy is specifically addressed under many health benefit plans. In addition, procedures associated with gender reassignment surgery that are performed solely for the purpose of improving or altering appearance or self-esteem related to one's appearance, are considered cosmetic in nature and not medically necessary. Please refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage.

If coverage for gender reassignment surgery is available, the following conditions of coverage apply.

Cigna covers the following gender reassignment surgery, including pre- and post-surgical hormone therapy, as medically necessary when the individual is age 18 or older, has confirmed gender dysphoria, and is an active participant in a recognized gender identity treatment program:

- Female-to-male gender reassignment
  - breast surgery (i.e., initial mastectomy, breast reduction) when there is one letter of support from a qualified mental health professional
  - hysterectomy and salpingo-oophorectomy when BOTH of the following additional criteria are met:
    - documentation of at least 12 months of continuous hormonal* sex reassignment therapy
    - recommendation for sex reassignment surgery (i.e., genital surgery) by two qualified mental health professionals with written documentation submitted to the physician performing the genital surgery (At least one letter should be a comprehensive report. Two separate letters

or one letter with two signatures is acceptable. One letter from a Master's degree mental health professional is acceptable if the second letter is from a psychiatrist or Ph.D. clinical psychologist)

- vaginectomy (including colpectomy, metoidioplasty with initial phalloplasty, urethroplasty, urethromeatoplasty) when ALL of the following criteria are met:
  - documentation of at least 12 months of continuous hormonal* sex reassignment therapy (May be simultaneous with real life experience.)
  - the individual has lived within the desired gender role for at least 12 continuous months and which includes a wide range of life experiences and events (e.g., family events, holidays, vacations, season-specific work or school experiences), including notification to partners, family, friends, and community members (e.g., at school, work, other settings) of their identified gender
  - recommendation for sex reassignment surgery (i.e., genital surgery) by two qualified mental health professionals with written documentation submitted to the physician performing the genital surgery (At least one letter should be a comprehensive report. Two separate letters or one letter with two signatures is acceptable. One letter from a Master's degree mental health professional is acceptable if the second letter is from a psychiatrist or Ph.D. clinical psychologist.)

- Male-to-female gender reassignment

  - orchiectomy when BOTH of the following additional criteria are met:
    - documentation of at least 12 months of continuous hormonal* sex reassignment therapy
    - recommendation for sex reassignment surgery (i.e., genital surgery) by two qualified mental health professionals with written documentation submitted to the physician performing the genital surgery (At least one letter should be a comprehensive report. Two separate letters or one letter with two signatures is acceptable. One letter from a Master's degree mental health professional is acceptable if the second letter is from a psychiatrist or Ph.D. clinical psychologist.)

  - vaginoplasty (including colovaginoplasty, penectomy, labiaplasty, clitoroplasty, vulvoplasty, penile skin inversion, repair of introitus, construction of vagina with graft, coloproctostomy), when ALL of the following criteria are met:
    - documentation of at least 12 months of continuous hormonal* sex reassignment therapy,(May be simultaneous with real life experience.)
    - the individual has lived within the desired gender role for at least 12 continuous months, and which includes a wide range of life experiences and events (e.g., family events, holidays, vacations, season-specific work or school experiences), including notification to partners, family, friends, and community members (e.g., at school, work, other settings) of their identified gender
    - recommendation for sex reassignment surgery (i.e., genital surgery) by two qualified mental health professionals with written documentation submitted to the physician performing the genital surgery (At least one letter should be a comprehensive report. Two separate letters or one letter with two signatures is acceptable. One letter from a Master's degree mental health professional is acceptable if the second letter is from a psychiatrist or Ph.D. clinical psychologist.)

<u>*Note</u>: For individuals considering hysterectomy/salpingo-oophorectomy, orchiectomy, vaginectomy or vaginoplasty procedures a total of 12 months continuous hormonal sex reassignment therapy is required. An additional 12 months of hormone therapy is not required for vaginectomy or vaginoplasty procedures.

Cigna does not cover procurement, cryopreservation or storage of ANY of the following as part of gender reassignment for the preservation of fertility because it is excluded under many benefit plans and considered not medically necessary:

- embryo
- sperm

- oocytes

Cigna does not cover cryopreservation, storage, and thawing of reproductive tissue (i.e., ovaries, testicular tissue) because each is considered experimental, investigational, or unproven.

Cigna considers the following cosmetic in nature and not medically necessary when performed as a component of a gender reassignment, even when there is a benefit for gender reassignment surgery (this list may not be all-inclusive):

- abdominoplasty
- blepharoplasty
- breast enlargement procedures, including augmentation mammoplasty, implants, and silicone injections of the breast
- calf implants
- cheek/malar implants
- chin/nose implants
- collagen injections
- electrolysis
- face/forehead lift
- brow lift
- hair removal/hair transplantation
- penile prosthesis (noninflatable /inflatable)
- testicular expanders
- jaw shortening/sculpturing/facial bone reduction
- laryngoplasty
- lip reduction/enhancement
- liposuction
- mastopexy
- neck tightening
- nipple/areola reconstruction
- pectoral implants
- removal of redundant skin
- replacement of tissue expander with permanent prosthesis testicular insertion
- rhinoplasty
- scrotoplasty
- second stage phalloplasty
- skin resurfacing (e.g., dermabrasion, chemical peels)
- surgical correction of hydraulic abnormality of inflatable (multi-component) prosthesis including pump and/or cylinders and/or reservoir
- testicular prostheses
- trachea shave/reduction thyroid chondroplasty
- voice modification surgery
- voice therapy/voice lessons

General Background

Gender reassignment therapy is an umbrella term for all medical procedures relating to gender reassignment of both transgender (i.e., internal gender identity is incongruent with genetic sex) and people with disorders of sexual development (DSD) (formerly known as “intersex”). The term "gender reassignment surgery," also known as sexual reassignment surgery, may be used to mean either the reconstruction of male or female genitals, specifically, or the reshaping, by any surgical procedure, of a male body into a body with female appearance, or vice versa. Gender reassignment surgery is part of a treatment plan for gender dysphoria. The causes of gender dysphoria and the developmental factors associated with them are not well-understood. The individual who is genetically male but whose gender identity is female, and who assumes a female gender presentation and role

is known as a transwoman; and the individual who is genetically female but whose gender identity is male, and who assumes a male gender presentation and role is known as a transman.
Individuals that are transsexual, transgender, or gender nonconforming (i.e., gender identity differs from the cultural norm) may experience gender dysphoria. Gender dysphoria is defined as discomfort or distress that is caused by a discrepancy between a person's gender identity and the person's assigned sex at birth (World Professional Association for Transgender Health [WPATH], 2012), including the associated gender role and/or primary and secondary sex characteristics. Gender dysphoria can be alleviated through various treatments, some of which involve a change in gender expression or body modifications, such as hormones and/or surgery. The term "transsexual" refers to an individual whose gender identity is not congruent with their genetic and/or assigned sex and usually seeks hormone replacement therapy (HRT) and possibly gender-affirmation surgery to feminize or masculinize the body and who may live full-time in the crossgender role. Transsexualism is a form of gender dysphoria. Other differential diagnoses include, but are not limited to, partial or temporary disorders as seen in adolescent crisis, transvestitism, refusal to accept a homosexual orientation, psychotic misjudgments of gender identity and severe personality disorders (Becker, et al., 1998).

Gender reassignment surgery is intended to be a permanent change, establishing congruency between an individual's gender identity and physical appearance and is not easily reversible. Therefore, a careful and accurate diagnosis is essential for treatment and can be made only as part of a long-term diagnostic process involving a multidisciplinary specialty approach that includes an extensive case history; gynecological, endocrine and urological examination, and a clinical psychiatric/psychological examination. A patient's self-assessment and desire for sex reassignment cannot be viewed as reliable indicators of gender dysphoria.

Mental health professionals play a strong role in working with individuals with gender dysphoria as they need to diagnose the gender disorder and any co-morbid psychiatric conditions accurately, counsel the individual regarding treatment options, and provide psychotherapy (as needed) and assess eligibility and readiness for hormone and surgical therapy. Once the individual is evaluated, the mental health professional provides documentation and formal recommendations to medical and surgical specialists. Documentation recommending hormonal or surgical treatment should be comprehensive and include all of the following:

- individual's general identifying characteristics
- the initial and evolving gender, sexual and psychiatric diagnoses
- details regarding the type and duration of psychotherapy or evaluation the individual recieved
- documentation of the extent to which eligibility criteria have been met
- the mental health professional's rationale for hormone therapy or surgery
- the degree to which the individual has followed the standards of care and likelihood of continued compliance
- whether or not the mental health professional is a part of a gender team

Psychiatric care may need to continue for several years after gender reassignment surgery, as major psychological adjustments may continue to be necessary. Other providers of care may include a family physician or internist, endocrinologist, urologist, plastic surgeon, general surgeon and gynecologist. The overall success of the surgery is highly dependent on psychological adjustment and continued support.

After diagnosis, the therapeutic approach is individualized but generally includes three elements: sex hormone therapy of the identified gender, real life experience in the desired role, and surgery to change the genitalia and other sex characteristics.

Prior to gender reassignment surgery, patients usually undergo hormone replacement therapy, which plays an important role in the gender transition process. Biological males are often treated with estrogens and anti-androgens to increase breast size, redistribute body fat, soften skin, decrease body hair, and decrease testicular size and erections. Biological females are treated with testosterone to deepen voice, increase muscle and bone mass, decrease breast size, increase clitoris size, and increase facial and body hair. In both sexes HRT may be effective in reducing the adverse psychologic impact of gender dysphoria. Hormone therapy must be administered by a physician and requires ongoing medical management, including physical examination and laboratory evaluation studies to manage dosage, side effects, etc. Lifelong maintenance is usually required. Hormone therapy also limits fertility, and individuals should be informed of sperm preservation options and cryopreservation of fertilized embryos prior to starting hormone therapy.

The individual identified with gender dysphoria also undergoes what is referred to as a “real life experience,” prior to irreversible genital surgery, in which he/she adopts the new or evolving gender role and lives in that role as part of the transition pathway. This process assists in confirming the person’s desire for gender role change, ability to function in this role long-term, as well as the adequacy of his/her support system. During this time, a person would be expected to maintain their baseline functional lifestyle, participate in community activities, and provide an indication that others are aware of the change in gender role.

Surgery for Disorders of Sexual Development
Surgery for disorders of sexual development consists of a series of staged procedures where the physician removes portions of the genitalia and creates either male genitalia or female genitalia.

Female-to-Male Transsexuals: Gender reassignment surgery from female to male (FTM) transsexual people includes genital surgical procedures that reshape a female body into the appearance of a male body.

Breast or chest surgery, which may include subcutaneous mastectomy and/or creation of a male chest may also be perfomed. Other nongenital nonbreast related surgeries include voice surgery, liposuction, lipoprofiling, pectoral implants and other masculinizing procedures.

Male-to-Female Transsexuals: Gender reassignment surgery from male-to-female (MTF) transsexuals includes genital procedures that shape a male body into the appearance of and, to the maximum extent possible, the function of a female body.

Breast augmentation may be considered when 12 months of hormone treatment fails to result in breast enlargement that is sufficient for the individual’s comfort in the female gender role. Breast surgery, which includes augmentation mammoplasty (implants/lipofilling) is a surgical procedure that may also be performed. In addition, other nongenital, nonbreast related surgeries, often considered feminization procedures, may be performed.

Other Associated Surgical Procedures
Preservation of Fertility: Procedures aimed at preservation of fertility (e.g., procurement, cryopreservation, and storage of sperm, oocytes and/or embryos) performed prior to gender reassignment surgery are considered not medically necessary.

Cosmetic Procedures: Various other surgical procedures may be performed as part of gender reassignment surgery. When performed as part of gender reassignment surgery these associated procedures, aimed primarily at improving personal appearance, are performed to assist with improving culturally appropriate male or female appearance characteristics and hence are considered cosmetic and are not medically necessary. Procedures that are considered cosmetic and not medically necessary include, but are not limited to, the following:

- abdominoplasty
- blepharoplasty
- breast enlargement procedures, including augmentation mammoplasty, implants, and silicone injections of the breast
- brow lift
- calf implants
- cheek/malar implants
- chin/nose implants
- collagen injections
- electrolysis
- face/forehead lift
- gamete preservation in anticipation of future infertility
- hair removal/hair transplantation
- insertion of penile prosthesis (noninflatable /inflatable)
- insertion of testicular expanders
- jaw shortening/sculpturing/facial bone reduction
- laryngoplasty
- lip reduction/enhancement

- liposuction
- mastopexy
- nipple/areola reconstruction
- pectoral implants
- removal of redundant skin
- replacement of tissue expander with permanent prosthesis testicular insertion
- rhinoplasty
- scrotoplasty
- second stage phalloplasty
- skin resurfacing (e.g., dermabrasion, chemical peels)
- surgical correction of hydraulic abnormality of inflatable (multi-component) prosthesis including pump and/or cylinders and/or reservoir
- testicular prostheses
- trachea shave/reduction thyroid chondroplasty
- voice modification surgery
- voice therapy/voice lessons

Professional Society/Organization
WPATH Guidelines: The World Professional Association for Transgender Health (WPATH) promotes standards of health care for individuals through the articulation of "Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People" (WPATH, 2012). WPATH recommendations for standards of care are based on scientific evidence and expert consensus and are commonly utilized as guidelines for individuals seeking treatment of gender disorders. In addition to breast surgeries (e.g., augmentation mammoplasty, mastectomy), according to the guidelines the following genital surgeries are considered procedures that may be performed for the treatment of gender dysphoria:

- hysterectomy
- salpingo-oophorectomy (ovariectomy)
- vaginectomy (i.e., removal of the vagina)
- metoidioplasty (i.e., clitoral tissue is released and moved forward to approximate the position of a penis, skin from the labia minora is used to create a penis)
- urethroplasty
- scrotoplasty
- insertion of erection and/or testicular prosthesis (i.e., the labia majora is dissected forming cavities allowing for placement of testicular implants)
- phalloplasty (i.e., skin tissue graft is used to form a penis, the objective for which is standing micturation, improved sexual sensation, function and/or appearance).
- penectomy
- orchiectomy
- vaginoplasty/colovaginoplasty (the objective for which is improved sexual sensation, function and appearance)
- clitoroplasty
- vulvoplasty
- colovaginoplasty (penile inversion to create a vagina and clitoris, or creation of a vagina from the sigmoid colon)

Endocrine Society Guidelines: In 2009 the Endocrine Society published a clinical practice guideline for endocrine treatment of transsexual persons (Hembree, et al., 2009). As part of this guideline, the endocrine society recommends that transsexual persons consider genital sex reassignment surgery only after both the physician responsible for endocrine transition therapy and the mental health professional find surgery advisable; that surgery be recommended only after completion of at least one year of consistent and compliant hormone treatment; and that the physician responsible for endocrine treatment medically clear the individual for sex reassignment surgery and collaborate with the surgeon regarding hormone use during and after surgery.

Use Outside of the US: No relevant information found.

Summary

Sex reassignment surgical procedures, including pre and post-surgery hormone therapy, for diagnosed cases of gender dysphoria should be recommended only after a comprehensive evaluation by a qualified mental health professional. The surgeon should have a demonstrated competency and extensive training in sexual reconstructive surgery. Long-term follow-up is highly recommended for the enduringly successful outcome of surgery.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Intersex Surgery: Male to Female

Covered when medically necessary:

CPT®* Codes	**Description**
55970†	Intersex surgery; male to female
	†Includes only the following procedures:
54125	Amputation of penis; complete
54520	Orchiectomy, simple (including subcapsular), with or without testicular prosthesis, scrotal or inguinal approach
54690	Laparoscopy, surgical; orchiectomy
56800	Plastic repair of introitus
56805	Clitoroplasty for intersex state
57291	Construction of artificial vagina; without graft
57292	Construction of artificial vagina; with graft
57335	Vaginoplasty for intersex state

Intersex Surgery: Female to Male

Covered when medically necessary:

CPT®* Codes	**Description**
55980†	Intersex surgery, female to male
	†Includes only the following procedures:
19303	Mastectomy, simple, complete
19304	Mastectomy, subcutaneous
53430	Urethroplasty, reconstruction of female urethra
56625	Vulvectomy simple; complete
57110	Vaginectomy, complete removal of vaginal wall
58150	Total abdominal hysterectomy (corpus and cervix), with or without removal of tube(s), with or without removal of ovary(s);
58262	Vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s), and/or ovary(s)
58291	Vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58552	Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58554	Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58571	Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)

58573	Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58661	Laparoscopy, surgical; with removal of adnexal structures (partial or total oophorectomy and/or salpingectomy)
58999[††]	Unlisted procedure, female genital system (nonobstetrical)

[††]**NOTE: Covered when medically necessary when used to report metoidioplasty with initial phalloplasty.**

Not Covered

Generally Excluded/Not Medically Necessary/Not Covered:

CPT®* Codes	Description
89258	Cryopreservation; embryo(s)
89259	Cryopreservation; sperm
89337	Cryopreservation, mature oocyte(s)(Code effective 01/01/2015)
89342	Storage (per year); embryo(s)
89343	Storage (per year); sperm/semen
89346	Storage (per year); oocyte(s)
0059T	Cryopreservation; oocyte(s) (Code deleted 12/31/2014)
0357T	Cryopreservation; immature oocyte(s) (Code effective 07/01/2014)
S4027	Storage of previously frozen embryos
S4030	Sperm procurement and cryopreservation services; initial visit
S4031	Sperm procurement and cryopreservation services; subsequent visit
S4040	Monitoring and storage of cryopreserved embryos, per 30 days

Experimental/Investigational/Unproven/Not Covered:

CPT®* Codes	Description
89335	Cryopreservation, reproductive tissue, testicular
89344	Storage (per year); reproductive tissue, testicular/ovarian
89354	Thawing of cryopreserved; reproductive tissue, testicular/ovarian
0058T	Cryopreservation; reproductive tissue, ovarian

Cosmetic/Not Covered when performed as a component of gender reassignment, even when coverage for gender reassignment surgery exists:

CPT®* Codes	Description
11950	Subcutaneous injection of filling material (eg, collagen); 1 cc or less
11951	Subcutaneous injection of filling material (eg, collagen); 1.1 to 5.0 cc
11952	Subcutaneous injection of filling material (eg, collagen); 5.1 to 10.0 cc
11954	Subcutaneous injection of filling material (eg, collagen); over 10.0 cc
11960	Insertion of tissue expander(s) for other than breast, including subsequent expansion
11970	Replacement of tissue expander with permanent prosthesis
11971	Removal of tissue expander(s) without insertion of prosthesis
15775	Punch graft for hair transplant; 1 to 15 punch grafts
15776	Punch graft for hair transplant; more than 15 punch grafts
15780	Dermabrasion; total face (eg, for acne scarring, fine wrinkling, rhytids, general keratosis)

15781	Dermabrasion; segmental, face
15782	Dermabrasion; regional, other than face
15783	Dermabrasion; superficial, any site (eg, tattoo removal)
15786	Abrasion; single lesion (eg, keratosis, scar)
15787	Abrasion; each additional 4 lesions or less (List separately in addition to code for primary procedure)
15788	Chemical peel, facial; epidermal
15789	Chemical peel, facial; dermal
15792	Chemical peel, nonfacial; epidermal
15793	Chemical peel, nonfacial; dermal
15820	Blepharoplasty, lower eyelid;
15821	Blepharoplasty, lower eyelid with extensive herniated fat pad
15822	Blepharoplasty, upper eyelid
15823	Blepharoplasty, upper eyelid; with extensive skin weighting down lid
15824	Rhytidectomy, forehead
15825	Rhytidectomy; neck with platysmal tightening (platysmal flap, P-flap)
15826	Rhytidectomy; glabellar frown lines
15828	Rhytidectomy; cheek, chin, and neck
15829	Rhytidectomy; superficial musculoaponeurotic system (SMAS) flap
15830	Excision, excessive skin and subcutaneous tissue (includes lipectomy); abdomen, infraumbilical panniculectomy
15832	Excision, excessive skin and subcutaneous tissue (includes lipectomy); thigh
15833	Excision, excessive skin and subcutaneous tissue (includes lipectomy); leg
15834	Excision, excessive skin and subcutaneous tissue (includes lipectomy); hip
15835	Excision, excessive skin and subcutaneous tissue (includes lipectomy); buttock
15836	Excision, excessive skin and subcutaneous tissue (includes lipectomy); arm
15837	Excision, excessive skin and subcutaneous tissue (includes lipectomy); forearm or hand
15838	Excision, excessive skin and subcutaneous tissue (includes lipectomy); submental fat pad
15839	Excision, excessive skin and subcutaneous tissue (includes lipectomy); other area
15847	Excision, excessive skin and subcutaneous tissue (includes lipectomy); abdomen (eg, abdominoplasty) (includes umbilical transposition and fascial plication) (List separately in addition to code for primary procedure)
15876	Suction assisted lipectomy; head and neck
15877	Suction assisted lipectomy; trunk
15878	Suction assisted lipectomy; upper extremity
15879	Suction assisted lipectomy; lower extremity
17380	Electrolysis epilation, each 30 minutes
17999†	Unlisted procedure, skin, mucous membrane and subcutaneous tissue
19316	Mastopexy
19324	Mammaplasty, augmentation; without prosthetic implant
19325	Mammaplasty, augmentation; with prosthetic implant
19340	Immediate insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19342	Delayed insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19350	Nipple/areola reconstruction
21120	Genioplasty; augmentation (autograft, allograft, prosthetic material)
21121	Genioplasty; sliding osteotomy, single piece
21122	Genioplasty; sliding osteotomies, 2 or more osteotomies (eg, wedge excision or bone wedge reversal for asymmetrical chin)
21123	Genioplasty; sliding, augmentation with interpositional bone grafts (includes obtaining autografts)
21125	Augmentation, mandibular body or angle; prosthetic material

21127	Augmentation, mandibular body or angle; with bone graft, onlay or interpositional (includes obtaining autograft)
21137	Reduction forehead; contouring only
21210	Graft, bone; nasal, maxillary or malar areas (includes obtaining graft)
21270	Malar augmentation, prosthetic material
30400	Rhinoplasty, primary; lateral and alar cartilages and/or elevation of nasal tip
30410	Rhinoplasty, primary; complete, external parts including bony pyramid, lateral and alar cartilages, and/or elevation of nasal tip
30420	Rhinoplasty, primary; including major septal repair
30430	Rhinoplasty, secondary; minor revision (small amount of nasal tip work)
30435	Rhinoplasty, secondary; intermediate revision (bony work with osteotomies)
30450	Rhinoplasty, secondary; major revision (nasal tip work and osteotomies)
31599††	Unlisted procedure, larynx
40799†††	Unlisted procedure, loips
54400	Insertion of penile prosthesis; noninflatable (semi-rigid)
54401	Insertion of penile prosthesis; inflatable (self-contained)
54405	Insertion of multi-component inflatable penile prosthesis, including placement of pump, cylinders and reservoir
54660	Insertion of testicular prosthesis (separate procedure)
55175	Scrotoplasty; simple
55180	Scrotoplasty; complicated
92507	Treatment of speech, language, voice, communication, and/or auditory processing disorder; individual

HCPCS Codes	**Description**
C1789	Prosthesis, breast (implantable)
C1813	Prosthesis, penile, inflatable
C2622	Prosthesis, penile, noninflatable
L8600	Implantable breast prosthesis, silicone or equal

†**NOTE: Cosmetic/Not covered when used to report calf, cheek, malar or pectoral implants or fat transfers performed in conjunction with gender reassignment surgery, even when coverage for gender reassignment surgery exists.**

††**NOTE: Cosmetic/Not covered when used to report laryngoplasty performed in conjunction with gender reassignment surgery, even when coverage for gender reassignment surgery exists.**

†††**NOTE: Cosmetic/Not covered when used to report lip reduction/enhancement performed in conjunction with gender reassignment surgery, even when coverage for gender reassignment surgery exists.**

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Close

Gender Reassignment Surgery

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Policy

Aetna considers gender reassignment surgery medically necessary when all of the following criteria are met:

I. Requirements for mastectomy for female-to-male patients:

A. Single letter of referral from a qualified mental health professional (see Appendix); *and*
B. Persistent, well-documented gender dysphoria (see Appendix); *and*
C. Capacity to make a fully informed decision and to consent for treatment; *and*
D. Age of majority (18 years of age or older); *and*
E. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Note that a trial of hormone therapy is not a pre-requisite to qualifying for a mastectomy.

II. Requirements for gonadectomy (hysterectomy and oophorectomy in female-to-male and orchiectomy in male-to-female):

A. Two referral letters from qualified mental health professionals, one in a purely evaluative role (see appendix); *and*
B. Persistent, well-documented gender dysphoria (see Appendix); *and*
C. Capacity to make a fully informed decision and to consent for treatment; *and*
D. Age of majority (18 years or older); *and*
E. If significant medical or mental health concerns are present, they must be reasonably well controlled; *and*
F. Twelve months of continuous hormone therapy as appropriate to the member's gender goals (unless the member has a medical contraindication or is otherwise unable or unwilling to take hormones)

III. Requirements for genital reconstructive surgery (i.e., vaginectomy, urethroplasty, metoidioplasty, phalloplasty, scrotoplasty, and placement of a testicular prosthesis and erectile prosthesis in female to male; penectomy, vaginoplasty, labiaplasty, and clitoroplasty in male to female)

A. Two referral letters from qualified mental health professionals, one in a purely evaluative role (see appendix); *and*
B. Persistent, well-documented gender dysphoria (see Appendix); *and*
C. Capacity to make a fully informed decision and to consent for treatment; *and*

D. Age of majority (age 18 years and older); *and*
E. If significant medical or mental health concerns are present, they must be reasonably well controlled; *and*
F. Twelve months of continuous hormone therapy as appropriate to the member's gender goals (unless the member has a medical contraindication or is otherwise unable or unwilling to take hormones); *and*
G. Twelve months of living in a gender role that is congruent with their gender identity (real life experience).

Note: Rhinoplasty, face-lifting, lip enhancement, facial bone reduction, blepharoplasty, breast augmentation, liposuction of the waist (body contouring), reduction thyroid chondroplasty, hair removal, voice modification surgery (laryngoplasty or shortening of the vocal cords), and skin resurfacing, which have been used in feminization, are considered cosmetic. Similarly, chin implants, nose implants, and lip reduction, which have been used to assist masculinization, are considered cosmetic.

Note on gender specific services for the transgender community:

Gender-specific services may be medically necessary for transgender persons appropriate to their anatomy. Examples include:

1. Breast cancer screening may be medically necessary for female to male trans identified persons who have not undergone a mastectomy;
2. Prostate cancer screening may be medically necessary for male to female trans identified persons who have retained their prostate.

Aetna considers gonadotropin-releasing hormone medically necessary to suppress puberty in trans identified adolescents if they meet World Professional Association for Transgender Health (WPATH) criteria (see CPB 501 - Gonadotropin-Releasing Hormone Analogs and Antagonists).

Aetna considers the following procedures that may be performed as a component of a gender reassignment as cosmetic (not an all-inclusive list) (see also CPB 0031 - Cosmetic Surgery):

- Abdominoplasty
- Blepharoplasty
- Brow lift
- Calf implants
- Cheek/malar implants
- Chin/nose implants
- Collagen injections
- Construction of a clitoral hood
- Drugs for hair loss or growth
- Forehead lift
- Hair removal
- Hair transplantation
- Lip reduction
- Liposuction
- Mastopexy
- Neck tightening
- Pectoral implants
- Removal of redundant skin
- Rhinoplasty
- Voice therapy/voice lessons.

Background

Transsexualism is a gender identity condition "in which the person manifests, with constant and persistent conviction, the desire to live as a member of the opposite sex and progressively take steps to live in the opposite sex role full-time." People who wish to change their sex may be referred to as "Transsexuals" or as people suffering from "gender dysphoria" (meaning unhappiness with one's gender).

For male to female trans identified individuals selected for surgery, procedures may include genital reconstruction (vaginoplasty, penectomy, orchidectomy, clitoroplasty), breast augmentation and cosmetic surgery (facial reshaping, rhinoplasty, abdominoplasty, laryngeal shaving, vocal cord shortening, hair transplants) (Day, 2002). For female to male trans identified individuals, surgical procedures may include genital reconstruction (phalloplasty, genitoplasty, hysterectomy, bilateral oophorectomy), mastectomy, chest wall contouring and cosmetic surgery (Day, 2002).

The criterion noted above for some types of genital surgeries – i.e., that patients engage in 12 continuous months of living in a gender role that is congruent with their gender identity – is based on expert clinical consensus that this experience provides ample opportunity for patients to experience and socially adjust in their desired gender role, before undergoing irreversible surgery (Coleman, et al., 2011).

In addition to hormone therapy and gender reassignment surgery, psychological adjustments are necessary in affirming sex. Treatment should focus on psychological adjustment, with hormone therapy and gender reassignment surgery being viewed as confirmatory procedures dependent on adequate psychological adjustment. Mental health care may need to be continued after gender reassignment surgery. The overall success of treatment depends partly on the technical success of the surgery, but more crucially on the psychological adjustment of the trans identified person and the support from family, friends, employers and the medical profession.

Nakatsuka (2012) noted that the 3rd versions of the guideline for treatment of people with gender dysphoria (GD) of the Japanese Society of Psychiatry and Neurology recommends that feminizing/masculinizing hormone therapy and genital surgery should not be carried out until 18 years old and 20 years old, respectively. On the other hand, the 6th (2001) and the 7th (2011) versions of the standards of care for the health of transsexual, transgender, and gender non-conforming people of World Professional Association for Transgender Health (WPATH) recommend that transgender adolescents (Tanner stage 2, [mainly 12 to 13 years of age]) are treated by the endocrinologists to suppress puberty with gonadotropin-releasing hormone (GnRH) agonists until age 16 years old, after which cross-sex hormones may be given. A questionnaire on 181 people with GID diagnosed in the Okayama University Hospital (Japan) showed that female to male (FTM) trans identified individuals hoped to begin masculinizing hormone therapy at age of 15.6 +/- 4.0 (mean +/- S.D.) whereas male to female (MTF) trans identified individuals hoped to begin feminizing hormone therapy as early as age 12.5 +/- 4.0, before presenting secondary sex characters. After confirmation of strong and persistent trans gender identification, adolescents with GD should be treated with cross-gender hormone or puberty-delaying hormone to prevent developing undesired sex characters. These treatments may prevent transgender adolescents from attempting suicide, suffering from depression, and refusing to attend school.

Spack (2013) stated that GD is poorly understood from both mechanistic and clinical standpoints. Awareness of the condition appears to be increasing, probably because of greater societal acceptance and available hormonal treatment. Therapeutic options include hormone and surgical treatments but may be limited by insurance coverage because costs are high. For patients seeking MTF affirmation, hormone treatment includes estrogens, finasteride, spironolactone, and GnRH analogs. Surgical options include feminizing genital and facial surgery, breast augmentation, and various fat transplantations. For patients seeking a FTM gender affirmation, medical therapy includes testosterone and GnRH analogs and surgical therapy includes mammoplasty and phalloplasty. Medical therapy for both FTM and MTF can be started in early puberty, although long-term effects are not known. All patients considering treatment need counseling and medical monitoring.

Leinung and colleagues (2013) noted that the Endocrine Society's recently published clinical practice guidelines for the treatment of transgender persons acknowledged the need for further information on transgender health. These investigators reported the experience of one provider with the endocrine treatment of transgender persons over the past 2 decades. Data on demographics, clinical response to treatment, and psychosocial status were collected on all transgender persons receiving cross-sex hormone therapy since 1991 at the endocrinology clinic at Albany Medical Center, a tertiary care referral center serving upstate New York. Through 2009, a total 192 MTF and 50 FTM transgender persons were seen. These patients had a high prevalence of mental health and psychiatric problems (over 50 %), with low rates of employment and high levels of disability. Mental health and psychiatric problems were inversely correlated with age at presentation. The prevalence of gender reassignment surgery was low (31 % for MTF). The

number of persons seeking treatment has increased substantially in recent years. Cross-sex hormone therapy achieves very good results in FTM persons and is most successful in MTF persons when initiated at younger ages. The authors concluded that transgender persons seeking hormonal therapy are being seen with increasing frequency. The dysphoria present in many transgender persons is associated with significant mood disorders that interfere with successful careers. They stated that starting therapy at an earlier age may lessen the negative impact on mental health and lead to improved social outcomes.

Meyer-Bahlburg (2013) summarized for the practicing endocrinologist the current literature on the psychobiology of the development of gender identity and its variants in individuals with disorders of sex development or with transgenderism. Gender reassignment remains the treatment of choice for strong and persistent gender dysphoria in both categories, but more research is needed on the short-term and long-term effects of puberty-suppressing medications and cross-sex hormones on brain and behavior.

Appendix

Table 1: DSM 5 Criteria for Gender Dysphoria in Adults and Adolecents:.

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by two or more of the following:

I. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or, in young adolescents, the anticipated secondary sex characteristics)
II. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or, in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
III. A strong desire for the primary and/or secondary sex characteristics of the other gender
IV. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender)
V. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender)
VI. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender)

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Table 2: Format for referral letters from Qualified Health Professional: (From SOC-7)

I. Client's general identifying characteristics; *and*
II. Results of the client's psychosocial assessment, including any diagnoses; *and*
III. The duration of the mental health professional's relationship with the client, including the type of evaluation and therapy or counseling to date; *and*
IV. An explanation that the WPATH criteria for surgery have been met, and a brief description of the clinical rationale for supporting the patient's request for surgery; *and*
V. A statement about the fact that informed consent has been obtained from the patient; *and*
VI. A statement that the mental health professional is available for coordination of care and welcomes a phone call to establish this.

Note: There is no minimum duration of relationship required with mental health professional. It is the professional's judgment as to the appropriate length of time before a referral letter can appropriately be written. A common period of time is three months, but there is significant variation in both directions. When two letters are required, the second referral is intended to be an evaluative consultation, not a representation of an ongoing long-term therapeutic relationship, and can be written by a medical practitioner of sufficient experience with gender dysphoria.

Note: Evaluation of candidacy for sex reassignment surgery by a mental health professional is covered under the member's medical benefit, unless the services of a mental health professional are necessary to evaluate and treat a mental health problem, in which case the mental health professional's services are covered under the member's behavioral health benefit. Please check benefit plan descriptions.

Table 3: Characteristics of a Qualified Mental Health Professional: (From SOC-7):

I. Master's degree or equivalent in a clinical behavioral science field granted by an institution accredited by the appropriate national accrediting board. The professional should also have documented credentials from the relevant licensing board or equivalent; *and*
II. Competence in using the Diagnostic Statistical Manual of Mental Disorders and/or the International Classification of Disease for diagnostic purposes; *and*
III. Ability to recognize and diagnose co-existing mental health concerns and to distinguish these from gender dysphoria; *and*
IV. Knowledgeable about gender nonconforming identities and expressions, and the assessment and treatment of gender dysphoria; *and*
V. Continuing education in the assessment and treatment of gender dysphoria. This may include attending relevant professional meetings, workshops, or seminars; obtaining supervision from a mental health professional with relevant experience; or participating in research related to gender nonconformity and gender dysphoria.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

19301, 19303 - 19304	Mastectomy
53430	Urethroplasty, reconstruction of female urethra
54125	Amputation of penis; complete
54400 - 54417	Penile prosthesis
54520	Orchiectomy, simple (including subcapsular), with or without testicular prosthesis, scrotal or inguinal approach
54660	Insertion of testicular prosthesis (separate procedure)
54690	Laparoscopic, surgical; orchiectomy
55175	Scrotoplasty; simple
55180	complicated
55970	Intersex surgery; male to female [a series of staged procedures that includes male genitalia removal, penile dissection, urethral transposition, creation of vagina and labia with stent placement]
55980	female to male [a series of staged procedures that include penis and scrotum formation by graft, and prostheses placement]
56625	Vulvectomy simple; complete
56800	Plastic repair of introitus
56805	Clitoroplasty for intersex state
56810	Perineoplasty, repair of perineum, nonobstetrical (separate procedure)
57106 - 57107, 57110 - 57111	Vaginectomy
57291 - 57292	Construction of artificial vagina
57335	Vaginoplasty for intersex state
58150, 58180, 58260 - 58262, 58275 - 58291, 58541 - 58544, 58550 - 58554	Hysterectomy
58570 - 58573	Laparoscopy, surgical, with total hysterectomy
58661	Laparoscopy, surgical; with removal of adnexal structures (partial or total oophorectomy and/or salpingectomy)
58720	Salpingo-oophorectomy, complete or partial, unilateral or bilateral

CPT codes not covered for indications listed in the CPB [considered cosmetic]:

11950 - 11954	Subcutaneous injection of filling material (e.g., collagen)

15775	Punch graft for hair transplant; 1 to 15 punch grafts
15776	Punch graft for hair transplant; more than 15 punch grafts
15780 - 15787	Dermabrasion
15788 - 15793	Chemical peel
15820 - 15823	Blepharoplasty
15824 - 15828	Rhytidectomy [face-lifting]
15830 - 15839	Excision, excessive skin and subcutaneous tissue (includes lipectomy); abdomen, infraumbilical panniculectomy
15876 - 15879	Suction assisted lipectomy
17380	Electrolysis epilation, each 30 minutes
19316	Mastopexy
19318	Reduction mammaplasty
19324 - 19325	Mammaplasty, augmentation
19340	Immediate insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19342	Delayed insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19350	Nipple/areola reconstruction
21120 - 21123	Genioplasty
21125 - 21127	Augmentation, mandibular body or angle; prosthetic material or with bone graft, onlay or interpositional (includes obtaining autograft)
21208	Osteoplasty, facial bones; augmentation (autograft, allograft, or prosthetic implant)
21210	Graft, bone; nasal, maxillary or malar areas (includes obtaining graft)
21270	Graft, bone; nasal, maxillary or malar areas (includes obtaining graft)
30400 - 30420	Rhinoplasty; primary
30430 - 30450	Rhinoplasty; secondary
67900	Repair of brow ptosis (supraciliary, mid-forehead or coronal approach)
92507	Treatment of speech, language, voice, communication, and/or auditory processing disorder; individual
92508	Treatment of speech, language, voice, communication, and/or auditory processing disorder; group, two or more individuals

Other CPT codes related to the CPB:

11980	Subcutaneous hormone pellet implantation (implantation of estradiol and/or testosterone pellets beneath the skin)
90785	Interactive complexity (List separately in addition to the code for primary procedure)
90832 - 90838	Psychotherapy
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance of drug); subcutaneous or intramuscular

HCPCS codes covered if selection criteria are met:

J1950	Injection, leuprolide acetate (for depot suspension), per 3.75 mg
J9217	Leuprolide acetate (for depot suspension), 7.5 mg
J9218	Leuprolide acetate, per 1 mg
J9219	Leuprolide acetate implant, 65 mg

HCPCS codes not covered for indications listed in the CPB :

G0153	Services performed by a qualified speech-language pathologist in the home health or hospice setting, each 15 minutes
S9128	Speech therapy, in the home, per diem

ICD-9 codes covered if selection criteria are met:

302.50 - 302.53	Trans-sexualism
302.85	Gender identity disorder in adolescents or adults

ICD-9 codes not covered for indications listed in the CPB:

293.0 - 302.4, 302.6 - 302.84, 302.89 - 319	Mental disorders [other than transexualism and gender identity disorder]
752.7	Indeterminate sex and pseudohermaphroditism
758.0 - 758.9	Chromosomal anomalies

The above policy is based on the following references:

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Policy History

- Last Review 09/19/2014
  Effective: 05/14/2002
  Next Review: 07/09/2015
- Review History
- Definitions

Additional Information

- Clinical Policy Bulletin Notes

Acupuncture for Tobacco Cessation

Question: Should limits be placed on the use of acupuncture for tobacco cessation?

Question source: HERC staff

Issue: Acupuncture (CPT 97810-97814) is included on line 5 TOBACCO DEPENDENCE but currently has no mention/limits in the acupuncture guideline. The ACA does not require coverage for acupuncture treatment for smoking cessation.

Line: 5
Condition: TOBACCO DEPENDENCE (See Guideline Notes 4,64,65)
Treatment: MEDICAL THERAPY/BEHAVIORAL COUNSELING
ICD-10: F17.200-F17.228,F17.290-F17.299,Z71.6
CPT: 96150-96154,97810-97814,98966-98969,99078,99201-99215,99224,99324-99350, 99366,99406,99407,99415,99416,99441-99449,99487-99498,99605-99607
HCPCS: D1320,G0425-G0427,G0436,G0437,G0459,G0463,G0466,G0467,G0469,G0470, G9016,H0038,S9453

Current guideline

GUIDELINE NOTE 92, ACUPUNCTURE (ADAPTED FROM THE OCT. 1, 2015 PRIORITIZED LIST†)
Lines 1,208,351,415,467,532,543 (Lines 351 and 532 represent lines 374 and 545 from the Oct. 1, 2015 Prioritized List†)
Inclusion of acupuncture (CPT 97810-97814) on the Prioritized List has the following limitations:
Line 1 PREGNANCY
Acupuncture pairs on Line 1 for the following conditions.

Hyperemesis gravidarum

ICD-10-CM: O21.0, O21.1

Acupuncture pairs with hyperemesis gravidarum when a diagnosis is made by the maternity care provider and referred for acupuncture treatment for up to 12 sessions of acupressure/acupuncture.

Breech presentation

ICD-10-CM: O32.1

Acupuncture (and moxibustion) is paired with breech presentation when a referral with a diagnosis of breech presentation is made by the maternity care provider, the patient is between 33 and 38 weeks gestation, for up to 6 visits.

Back and pelvic pain of pregnancy

ICD-10-CM: O99.89

Acupuncture is paired with back and pelvic pain of pregnancy when referred by maternity care provider/primary care provider for up to 12 sessions.

Line 208 DEPRESSION AND OTHER MOOD DISORDERS, MILD OR MODERATE

Acupuncture is paired with the treatment of post-stroke depression only. Treatments may be billed to a maximum of 30 minutes face-to-face time and limited to 12 total sessions, with documentation of meaningful improvement.

Line 351 DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT (Line 374 from the Oct. 1, 2015 Prioritized List†)

Acupuncture is included on Line 351 (Line 374 from the Oct. 1, 2015 Prioritized List†) only for pairing with disorders of the spine with myelopathy and/or radiculopathy represented by ICD-10-CM G83.4, M47.2, M50.0, M50.1, M51.0, M51.1, M54.1), for up to 12 sessions.

Line 415 MIGRAINE HEADACHES

Acupuncture pairs on Line 415 for migraine (ICD-10-CM G43.0, G43.1, G43.5, G43.7, G43.8, G43.9), for up to 12 sessions.

Line 467 OSTEOARTHRITIS AND ALLIED DISORDERS

Acupuncture pairs on Line 467 for osteoarthritis of the knee only (ICD-10-CM M17), for up to 12 sessions.

*Line 532 ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT (Line 545 from the Oct. 1, 2015 Prioritized List†)

Acupuncture pairs on Line 532 (Line 545 from the Oct. 1, 2015 Prioritized List†) with the low back diagnoses appearing on this line (ICD-10-CM M51.36, M51.86, M54.5, M99.03, S33.5, S33.9, S39.092, S39.82, S39.92). Acupuncture pairs with chronic (>90 days) neck pain diagnoses on this line (ICD-10-CM M53.82, M54.2, S13.4, S13.8), for up to 12 sessions.

*Line 543 TENSION HEADACHES

Acupuncture is included on Line 543 for treatment of tension headaches (ICD-10-CM G44.2), for up to 12 sessions.

The development of this guideline note was informed by a HERC evidence-based guideline. See http://www.oregon.gov/oha/herc/Pages/blog-low-back-non-pharmacologic-intervention.aspx

Evidence:

1) **White 2014**[i]**,** Cochrane review of acupuncture for smoking cessation
    a. N=38 studies
        i. N=3 studies (393 patients) comparing acupuncture to waiting list control
        ii. N=19 studies (1,588 patients) comparing active acupuncture to sham acupuncture
    a. Based on three studies, acupuncture was not shown to be more effective than a waiting list control for long-term abstinence, with wide confidence intervals and evidence of heterogeneity (n = 393, risk ratio [RR] 1.79, 95% confidence interval [CI] 0.98 to 3.28, I^2 = 57%). Compared with sham acupuncture, the RR for the short-term effect of acupuncture was 1.22 (95% CI 1.08 to 1.38), and for the long-term effect was 1.10 (95% CI 0.86 to 1.40). Acupuncture was less effective than nicotine replacement therapy (NRT). There was no evidence that acupuncture is superior to psychological interventions in the short- or long-term.
    b. Moderate quality of evidence of no long term benefit for acupuncture on smoking cessation, although evidence of short term effect
    c. Wide variety of acupuncture protocols. Details of included studies' intervention frequency/duration as well as adjunct therapy, if any (studies only listed here if full articles were available):
    i. Bier 2002: 20 sessions over 4 wks. Three arms: true acupuncture, true acupuncture + intensive ed program, sham acupuncture + intensive ed program
    ii. Clavel 1985: single session. *Adjunct therapy: 3 one-hour sessions of group therapy in first month
    iii. Clavel 1992: 3 sessions over one month
    iv. Cottraux 1983: 3 weekly sessions
    v. Fritz 2013: 5 weekly 20 min sessions of b/l auriculotherapy
    vi. He 1997: Both groups received combination of body electroacupuncture, ear acupuncture and ear acupressure (genuine vs sham points), 6 treatments over 3 wks + 6 plant seeds taped to "correct" or "incorrect" points on the ear and subjects instructed to press on each seed 100x on 4 occasions daily
    vii. Lagrue 1980: facial acupuncture vs sham acupuncture, day 0 and day 7. *Adjunct therapy: "standardised advice"
    viii. Waite 1998: lung point in ear vs control patella point. *Both groups received one 20-minute session of acupuncture w electrical stimulation followed by placement of seed on needle site. Instructed to press seed with desire to smoke.ix. White 1998: acupuncture with electrical stim to lung points in both ears vs sham acupuncture to mastoid bone. Days 1,3, 7. *Adjunct therapy: counseling by a nurse
    x. Wu 2007: indwelling auricular needles in active vs sham points, 4 points retained for one week, then replaced. 8 wk tx period. *Adjunct therapy: counseling from nurse
    d. **Authors' conclusions** Although pooled estimates suggest possible short-term effects there is no consistent, bias-free evidence that acupuncture, acupressure, or laser therapy have a sustained benefit on smoking cessation for six months or

more. However, lack of evidence and methodological problemsmean that no firm conclusions can be drawn.

2) **Patnode 2015[ii]: USPSTF Review of Reviews.** (article not included in meeting materials due to length)

a. Includes all types of behavioral and pharmacotherapy interventions. In total, reviewed 638 abstracts and 114 full-text reviews for possible inclusion, narrowing down to 54 systematic reviews which met eligibility criteria. Identifies 2 reviews on acupuncture (White 2014 and Di 2014) and classifies them both as "good." Additionally, it evaluates Cheng 2012's review of acupoint stimulation as "fair." No other reviews regarding acupuncture or acupressure identified.

b. Authors' conclusions: Concluded that "evidence on the use of...complementary and alternative therapies was limited and not definitive."

3) **McRobbie 2007[iii]: NICE Rapid Review of Non NHS Treatments for Smoking Cessation** (Study not included in meeting materials due to length)

a. 19 reviews narrowed to 9 reviews after further exclusion based on poor quality, no systematic method, or review of reviews. Included White's Cochrane review from 2006. Additionally, 21 studies were narrowed to 14 studies after exclusion for not being an RCT. Further, of those 14 studies, 13 were included in the Cochrane Review. Only one new RCT (Docherty 2003) was included, but it was examining laser therapy and thus is not relevant to this lit review.

b. Since this NICE Review relied heavily on an old Cochrane review, this is less relevant to HERC's current lit review.

c. **Authors' conclusion**: Marginal effect compared to placebo in short-term but no evidence of efficacy in long-term abstinence rates. Level 1+ evidence "well-conducted meta-analyses, systematic reviews of RCTs, or RCTs (including cluster RCTs) with a low risk of bias."

4) **Cheng 2012[iv]** Systematic Review and Meta-Analysis in American Journal of Chinese Medicine.

a. n = 20 studies total
n = 9 studies evaluating smoking cessation rate at 3,6 months
n = 3 studies evaluating daily cigarette consumption

b. Includes 13 of same acupuncture studies as White 2014 Cochrane.

c. Combined all types of acupoint stimulation (acupuncture, acupressure, laser therapy) and all types of controls into single analysis. White 2014 comments that this likely explains the differences in the reviews.

d. Smoking cessation RR 1.24 (95% CI 1.07,1.43) immediately after tx, 1.70 (1.17,2.46) at 3 months, 1.79 (1.13,2.82) at 6 months compared to control or sham interventions.

d. Authors' conclusions: "Acupoint stimulation increases smoking cessation rate and reduces daily cigarette consumption. Multi-modality treatment,

especially acupuncture combined with smoking cessation education..., can help."

5) **Di 2014**[v] (Drug and Alcohol Dependence Journal) "A Meta-Analysis of Ear-Acupuncture, Ear-Acupressure and Auriculotherapy for Cigarette Smoking Cessation"
   a. Did not take body acupuncture or laser therapy into account.
   b. n = 25 RCTs, two pools: 1) comparing to inactive control and 2) comparing to other smoking cessation specific treatment.
   c. Pool 1) immediate RR = 1.77 (1.39, 2.25), 3 months RR = 1.54 (1.14, 2.08), 6 months RR = 2.01 (1.23, 3.28), insufficient data for 12 months. Pool 2) "no superiority or inferiority...[immediately] or at 3 and 6 month follow-ups." Small trials.
   d. Authors' conclusions: Ear acupuncture, ear acupressure and auriculotherapy is superior to inactive controls for smoking cessation immediately and at 3 months and 6 months.
6) **Tahiri 2012**[vi] Meta-analysis in American Journal of Medicine
   a. n = 6 acupuncture trials (823 patients). All 6 were included in Di 2014 meta-analysis and 5 of them included in White 2014. The sixth RCT (Kerr 2008) was classified as laser therapy and excluded from White 2014.
   b. OR = 3.53 (1.03,12.07)
   c. Very wide confidence interval.
   d. Authors' conclusions: "acupuncture...may help smokers quit."

<u>Expert input</u>:
From Laura Ocker, Lac

February 18 2016

I think 12 acupuncture treatments is a good starting point for pain / chronic pain conditions. For smoking cessation, more treatment would be warranted (assuming the patient is truly making progress). For smoking cessation, my recommendation to patients is 2-3 visits per week the first two or three weeks and then 1-2 times per week for several weeks following. Then I am available for a few follow-up appointments throughout the year when stressors trigger the urge to start smoking again. **So, I'd say 18 treatments would be better.** For the person who is truly making progress. If I treat them 3-5 times and they show no signs of cutting down or quitting, I suggest they pursue other options or come back when they feel more ready.

Would be great to combine acupuncture with CBT or other therapies, but I wouldn't necessarily make it a requirement. If someone is doing really well with acupuncture alone, they may not need the additional support. Or vice versa. Also, there are times when medications are not appropriate, such as pregnancy or for patients who are medication-adverse, and this is another good area for acupuncture.

I'd say 18 treatments is a good number for private practice. Although in community health center / community acupuncture settings where a patient can come in more easily and more often for a drop-in treatment (and where you're more likely to be seeing Medicaid patients and people with multiple chronic health conditions and other significant life stressors) up to 24-30 treatments (IF MAKING PROGRESS) would be completely reasonable.

I would recommend 18. I would expect my colleagues to be ethical enough to not treat past the first couple of weeks if the patient has not quit or substantially reduced the number of cigarettes per day.

March 2015

I think that smoking cessation may be one of those conditions, like so many others, for which we see a high degree of efficacy in clinical practice, but for which there may not adequate evidence to support the use of acupuncture as a treatment option from a coverage standpoint. My colleagues and I find that acupuncture and Oriental medicine is a helpful therapy for smoking cessation - in that it reduces cravings and withdrawal symptoms and reduces associated symptoms such as anxiety, rage, nervousness, frustration, etc. Acupuncture alone, or often combined with other therapies, such as CBT or use of nicotine products gradually weaned under a physician's guidance, is very helpful to people who would like to quit smoking. I would like to see acupuncture remain an option for smoking cessation.

HERC staff summary

Four meta-analyses (White 2014, Di 2014, Cheng 2012, and Tahiri 2012) came to varying conclusions, either finding superiority of acupuncture over control/sham at 0-6 months or inconclusive. The differences between the meta-analyses was most attributable to differing methods of pooling. In general, the widely varying acupuncture techniques and protocols used in RCTs let to the inability to draw firm conclusions on effectiveness.

The general staff conclusion is that acupuncture may be helpful for smoking cessation, and is definitely not harmful. The number of visits used in study protocols ranged from 3-20, but were generally fewer than recommended by experts. There is insufficient evidence about the need to pair acupuncture with other therapies for smoking cessation.

HERC staff recommendations:

1) Modify GN92 Acupuncture as shown below
    a. 18 visits maximum

GUIDELINE NOTE 92, ACUPUNCTURE (ADAPTED FROM THE OCT. 1, 2015 PRIORITIZED LIST†)

Lines 1,208,351,415,467,532,543 (Lines 351 and 532 represent lines 374 and 545 from the Oct. 1, 2015 Prioritized List†)

Inclusion of acupuncture (CPT 97810-97814) on the Prioritized List has the following limitations:

Line 1 PREGNANCY

Acupuncture pairs on Line 1 for the following conditions.

Hyperemesis gravidarum

ICD-10-CM: O21.0, O21.1

Acupuncture pairs with hyperemesis gravidarum when a diagnosis is made by the maternity care provider and referred for acupuncture treatment for up to 12 sessions of acupressure/acupuncture.

Breech presentation

ICD-10-CM: O32.1

Acupuncture (and moxibustion) is paired with breech presentation when a referral with a diagnosis of breech presentation is made by the maternity care provider, the patient is between 33 and 38 weeks gestation, for up to 6 visits.

Back and pelvic pain of pregnancy

ICD-10-CM: O99.89

Acupuncture is paired with back and pelvic pain of pregnancy when referred by maternity care provider/primary care provider for up to 12 sessions.

Line 5 TOBACCO DEPENDENCE

Acupuncture is included on this line for a maximum of 18 sessions.

Line 208 DEPRESSION AND OTHER MOOD DISORDERS, MILD OR MODERATE

Acupuncture is paired with the treatment of post-stroke depression only. Treatments may be billed to a maximum of 30 minutes face-to-face time and limited to 12 total sessions, with documentation of meaningful improvement.

Line 351 DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT (Line 374 from the Oct. 1, 2015 Prioritized List†)

Acupuncture is included on Line 351 (Line 374 from the Oct. 1, 2015 Prioritized List†) only for pairing with disorders of the spine with myelopathy and/or radiculopathy represented by ICD-10-CM G83.4, M47.2, M50.0, M50.1, M51.0, M51.1, M54.1), for up to 12 sessions.

Line 415 MIGRAINE HEADACHES

Acupuncture pairs on Line 415 for migraine (ICD-10-CM G43.0, G43.1, G43.5, G43.7, G43.8, G43.9), for up to 12 sessions.

Line 467 OSTEOARTHRITIS AND ALLIED DISORDERS

Acupuncture pairs on Line 467 for osteoarthritis of the knee only (ICD-10-CM M17), for up to 12 sessions.

*Line 532 ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT (Line 545 from the Oct. 1, 2015 Prioritized List†)

Acupuncture pairs on Line 532 (Line 545 from the Oct. 1, 2015 Prioritized List†) with the low back diagnoses appearing on this line (ICD-10-CM M51.36, M51.86, M54.5, M99.03, S33.5, S33.9, S39.092, S39.82, S39.92). Acupuncture pairs with chronic (>90 days) neck pain diagnoses on this line (ICD-10-CM M53.82, M54.2, S13.4, S13.8), for up to 12 sessions.

*Line 543 TENSION HEADACHES

Acupuncture is included on Line 543 for treatment of tension headaches (ICD-10-CM G44.2), for up to 12 sessions.

The development of this guideline note was informed by a HERC evidence-based guideline. See http://www.oregon.gov/oha/herc/Pages/blog-low-back-non-pharmacologic-intervention.aspx

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[i] White, Adrian R., et al. "Acupuncture and related interventions for smoking cessation." *Cochrane Database Syst Rev* 1 (2014).

[ii] Patnode, Carrie D., et al. "Behavioral Counseling and Pharmacotherapy Interventions for Tobacco Cessation in Adults, Including Pregnant Women: A Review of Reviews for the US Preventive Services Task Force." *Annals of internal medicine* 163.8 (2015): 608-621.

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[iv] Cheng, Hsiao-Min, et al. "Systematic review and meta-analysis of the effects of acupoint stimulation on smoking cessation." *The American journal of Chinese medicine* 40.03 (2012): 429-442.

[v] Di, Yuan Ming, et al. "A meta-analysis of ear-acupuncture, ear-acupressure and auriculotherapy for cigarette smoking cessation." *Drug and alcohol dependence* 142 (2014): 14-23.

[vi] Tahiri, Mehdi, et al. "Alternative smoking cessation aids: a meta-analysis of randomized controlled trials." *The American journal of medicine* 125.6 (2012): 576-584.

Acupuncture and related interventions for smoking cessation (Review)

White AR, Rampes H, Liu JP, Stead LF, Campbell J

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2014, Issue 1

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WILEY

[Intervention Review]

Acupuncture and related interventions for smoking cessation

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ABSTRACT

Background

Acupuncture and related techniques are promoted as a treatment for smoking cessation in the belief that they may reduce nicotine withdrawal symptoms.

Objectives

The objectives of this review are to determine the effectiveness of acupuncture and the related interventions of acupressure, laser therapy and electrostimulation in smoking cessation, in comparison with no intervention, sham treatment, or other interventions.

Search methods

We searched the Cochrane Tobacco Addiction Group Specialized Register (which includes trials of smoking cessation interventions identified from the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO) and AMED in October 2013. We also searched four Chinese databases in September 2013: Sino-Med, China National Knowledge Infrastructure, Wanfang Data and VIP.

Selection criteria

Randomized trials comparing a form of acupuncture, acupressure, laser therapy or electrostimulation with either no intervention, sham treatment or another intervention for smoking cessation.

Data collection and analysis

We extracted data in duplicate on the type of smokers recruited, the nature of the intervention and control procedures, the outcome measures, method of randomization, and completeness of follow-up.

We assessed abstinence from smoking at the earliest time-point (before six weeks) and at the last measurement point between six months and one year. We used the most rigorous definition of abstinence for each trial, and biochemically validated rates if available. Those lost to follow-up were counted as continuing smokers. Where appropriate, we performed meta-analysis pooling risk ratios using a fixed-effect model.

Main results

We included 38 studies. Based on three studies, acupuncture was not shown to be more effective than a waiting list control for long-term abstinence, with wide confidence intervals and evidence of heterogeneity (n = 393, risk ratio [RR] 1.79, 95% confidence interval [CI] 0.98 to 3.28, I^2 = 57%). Compared with sham acupuncture, the RR for the short-term effect of acupuncture was 1.22 (95% CI 1.08 to 1.38), and for the long-term effect was 1.10 (95% CI 0.86 to 1.40). The studies were not judged to be free from bias, and there was evidence of funnel plot asymmetry with larger studies showing smaller effects. The heterogeneity between studies was not explained by the technique used. Acupuncture was less effective than nicotine replacement therapy (NRT). There was no evidence that acupuncture is superior to psychological interventions in the short- or long-term. There is limited evidence that acupressure is superior to sham acupressure for short-term outcomes (3 trials, n = 325, RR 2.54, 95% CI 1.27 to 5.08), but no trials reported long-term effects, The pooled estimate for studies testing an intervention that included continuous auricular stimulation suggested a short-term benefit compared to sham stimulation (14 trials, n = 1155, RR 1.69, 95% CI 1.32 to 2.16); subgroup analysis showed an effect for continuous acupressure (7 studies, n = 496, RR 2.73, 95% CI 1.78 to 4.18) but not acupuncture with indwelling needles (6 studies, n = 659, RR 1.24, 95% CI 0.91 to 1.69). At longer follow-up the CIs did not exclude no effect (5 trials, n = 570, RR 1.47, 95% CI 0.79 to 2.74). The evidence from two trials using laser stimulation was inconsistent and could not be combined. The combined evidence on electrostimulation suggests it is not superior to sham electrostimulation (short-term abstinence: 6 trials, n = 634, RR 1.13, 95% CI 0.87 to 1.46; long-term abstinence: 2 trials, n = 405, RR 0.87, 95% CI 0.61 to 1.23).

Authors' conclusions

Although pooled estimates suggest possible short-term effects there is no consistent, bias-free evidence that acupuncture, acupressure, or laser therapy have a sustained benefit on smoking cessation for six months or more. However, lack of evidence and methodological problems mean that no firm conclusions can be drawn. Electrostimulation is not effective for smoking cessation. Well-designed research into acupuncture, acupressure and laser stimulation is justified since these are popular interventions and safe when correctly applied, though these interventions alone are likely to be less effective than evidence-based interventions.

PLAIN LANGUAGE SUMMARY

Do acupuncture and related therapies help smokers who are trying to quit

We reviewed the evidence that acupuncture, acupressure, laser therapy or electrical stimulation help people who are trying to stop smoking.

Background

Acupuncture is a traditional Chinese therapy, generally using fine needles inserted through the skin at specific points in the body. Needles may be stimulated by hand or using an electric current (electroacupuncture). Related therapies, in which points are stimulated without the use of needles, include acupressure, laser therapy and electrical stimulation. Needles and acupressure may be used just during treatment sessions, or continuous stimulation may be provided by using indwelling needles or beads or seeds taped to to acupressure points. The aim of these therapies is to reduce the withdrawal symptoms that people experience when they try to quit smoking. The review looked at trials comparing active treatments with sham treatments or other control conditions including advice alone, or an effective treatment such as nicotine replacement therapy (NRT) or counselling. Sham treatment involves inserting needles or applying pressure to other points of the body not believed to have an active effect, or using dummy needles that do not go through the skin, or inactive laser or electrical stimulation devices. Using this type of control means that the patients should not know whether they are receiving active treatment or not.

To assess whether there was a sustained benefit in helping people to stop smoking we looked at the proportion of people who were abstinent at least six months after quit date. We also looked at short term outcomes, up to six weeks after quit date. Evidence of benefit after six months is regarded as necessary to show that a treatment could help people stop smoking permanently.

Study characteristics

We included 38 randomised studies published up to October 2013. Trials tested a variety of different interventions and controls. The specific points used, the number of sessions and whether there was continuous stimulation varied. Three studies (393 people) compared acupuncture to a waiting list control. Nineteen studies (1,588 people) compared active acupuncture to sham acupuncture, but only 11 of these studies included long-term follow-up of six months or more. Three studies (253 people) compared acupressure to sham

acupressure but none had long-term follow-up. Two trials used laser stimulation and six (634 people) used electrostimulation. The overall quality of the evidence was moderate.

Key findings

Three studies comparing acupuncture to a waiting list control and reporting long-term abstinence did not show clear evidence of benefit. For acupuncture compared with sham acupuncture, there was weak evidence of a small short-term benefit but not of any long-term benefit. Acupuncture was less effective than nicotine replacement therapy (NRT) and not shown to be better than counselling. There was limited evidence that acupressure is superior to sham acupressure in the short term but no evidence about long-term effects. In an analysis of the subgroup of trials where the treatment included continuous stimulation, those trials which used continuous acupressure to points on the ear had the largest short-term effect. The evidence from two trials using laser stimulation was inconsistent. The seven trials of electrostimulation do not suggest evidence of benefit compared to sham electrostimulation.

The review did not find consistent evidence that active acupuncture or related techniques increased the number of people who could successfully quit smoking. However, some techniques may be better than doing nothing, at least in the short term, and there is not enough evidence to dismiss the possibility that they might have an effect greater than placebo. They are likely to be less effective than current evidence-based interventions. They are safe when correctly applied.

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Systematic Review and Meta-Analysis of the Effects of Acupoint Stimulation on Smoking Cessation

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Abstract: Smoking represents a serious worldwide public health problem because of its close association with the development of chronic disease and cancer. Acupoint stimulation has been used as treatment mode for smoking cessation but its efficacy remains controversial. This systematic review and meta-analysis aimed to determine the effects of acupoint stimulation on smoking cessation rate and daily cigarette consumption. Electronic literature searches in eight electronic databases up to March 2011 were performed to identify acupoint stimulation for smoking cessation. The outcomes assessed were smoking cessation rate and cigarette consumption. We assessed abstinence from smoking at the earliest and last measured time points, and at the 3- and 6-month follow-ups. Meta-analysis was performed using CMA software. A total of 20 RCTs were included in the meta-analysis. A significant effect of acupoint stimulation was found in smoking cessation rates and cigarette consumption at immediate, 3- and 6-month follow-ups, with effect sizes 1.24 (95%CI = $1.07 \sim 1.43$, $p = 0.003$), -2.49 (95%CI = $-4.65 \sim -0.34$, $p = 0.02$), 1.70 (95%CI = $1.17 \sim 2.46$, $p = 0.01$), and 1.79 (95%CI = $1.13 \sim 2.82$, $p = 0.01$), respectively. Multi-modality treatments, especially acupuncture combined with smoking cessation education or other interventions, can help smokers to eschew smoking during treatment, and to avoid relapse after treatment.

Keywords: Acupoint Stimulation; Smoking Cessation; Meta-Analysis; Acupuncture; Acupressure; Electroacupuncture.

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Review

A meta-analysis of ear-acupuncture, ear-acupressure and auriculotherapy for cigarette smoking cessation

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ABSTRACT

Background: This systematic review evaluated the effects of ear acupuncture, ear acupressure and auriculotherapy for cigarette smoking cessation (SC) at end-of-treatment (EoT), three, six and 12 months follow-up.
Methods: Searches of six English and Chinese databases located 25 randomized controlled trials (3735 participants). Methodological quality was assessed using Cochrane Risk of Bias. Meta-analyses were conducted in two pools: 1. SC-specific ear acupuncture/acupressure or auriculotherapy (EAP/R) vs. non-specific/inactive control; and 2. SC-specific EAP/R vs. other SC-specific treatment. Sensitivity analyses were conducted based on the validity of interventions as SC-specific treatments or non-specific/inactive interventions; and the use of biochemical SC confirmation.
Results: Pool 1: the 12 valid SC-specific EAP/R interventions were superior to inactive EAP/R controls at EoT (RR = 1.77 [1.39, 2.25]), three months follow-up (RR = 1.54 [1.14, 2.08]), and six months follow-up (RR = 2.01, [1.23, 3.28]) but data were insufficient at 12 months. In Pool 2: there was no superiority or inferiority for EAP/R at EoT or at 3 and 6 month follow-ups compared to SC-specific behavioural therapy or SC-specific body acupuncture.
Conclusions: Pool 1 data appeared most consistent for studies of ear acupressure (EAPR) vs. non-specific EAPR controls, with confirmed SC rates at 3 months post-treatment of 20.0% for test groups vs. 7.5% for controls. In Pool 2 the EAP/R interventions appeared neither inferior nor superior to the behavioural interventions at 3 and 6 month follow-ups. However, meta-analysis results derived from relatively small-sized trials with no biochemical validation of SC in Pool 2. Larger, well-controlled studies using biochemical confirmation of SC are needed.

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CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Alternative Smoking Cessation Aids: A Meta-analysis of Randomized Controlled Trials

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ABSTRACT

BACKGROUND: Acupuncture, hypnotherapy, and aversive smoking are the most frequently studied alternative smoking cessation aids. These aids are often used as alternatives to pharmacotherapies for smoking cessation; however, their efficacy is unclear.

METHODS: We carried out a random effect meta-analysis of randomized controlled trials to determine the efficacy of alternative smoking cessation aids. We systematically searched the Cochrane Library, EMBASE, Medline, and PsycINFO databases through December 2010. We only included trials that reported cessation outcomes as point prevalence or continuous abstinence at 6 or 12 months.

RESULTS: Fourteen trials were identified; 6 investigated acupuncture (823 patients); 4 investigated hypnotherapy (273 patients); and 4 investigated aversive smoking (99 patients). The estimated mean treatment effects were acupuncture (odds ratio [OR], 3.53; 95% confidence interval [CI], 1.03-12.07), hypnotherapy (OR, 4.55; 95% CI, 0.98-21.01), and aversive smoking (OR, 4.26; 95% CI, 1.26-14.38).

CONCLUSION: Our results suggest that acupuncture and hypnotherapy may help smokers quit. Aversive smoking also may help smokers quit; however, there are no recent trials investigating this intervention. More evidence is needed to determine whether alternative interventions are as efficacious as pharmacotherapies.

 • *The American Journal of Medicine (2012) 125, 576-584*

KEYWORDS: Acupuncture; Alternative smoking cessation aid; Aversive smoking; Hypnotherapy; Meta-analysis; Smoking cessation

Smoking is the most preventable cause of morbidity and mortality in North America and costs the economy $210 billion each year in the United States alone.[1-3] Annually, approximately half of the 51 million smokers in North America try to quit for at least 1 day.[4-6] Of these smokers attempting cessation, less than half use pharmacologic cessation aids (nicotine replacement therapy, bupropion, or varenicline) because of concerns about potential side effects and limited efficacy.[7]

Many smokers have turned to alternative smoking cessation aids as a substitute for pharmacotherapies, of which the most studied include acupuncture, hypnotherapy, and aversive smoking. Acupuncture for smoking cessation consists of stimulating specific acupoints on the ear.[8] Hypnotherapy consists of inducing an altered state of conscious-

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Conflict of Interest: None.

Authorship: All authors had access to the data and played a role in writing this manuscript.

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Hyperbaric Oxygen Guideline

Question: Should the hyperbaric oxygen guideline be clarified/simplified?

Question source: HERC staff, CCO medical directors

Issue: The current hyperbaric oxygen guideline is confusing to many readers. HERC staff has worked to clarify language for this guideline.

Dr. Carl Stevens, a medical director with CareOregon, has suggested modifications to the guideline to clarify language. One specific request was to apply the requirement for re-evaluation of the wound healing to all conditions listed in the guideline, as all may or may not respond to hyperbaric oxygen therapy

Further staff suggested clarifications are:

1) Clarifying that there are many conditions included in this line (such as carbon monoxide poisoning, air embolism, etc.) which are not included in the guideline as the guideline is just a list of limitations for certain ICD-10 codes or restrictions on certain conditions
2) Applying the same restrictions as now apply to diabetic gangrenous wounds regarding need for reassessment at 30 days, etc. to all conditions that this restriction applied to in the CMS coverage determination, as the original intent was to mirror this. CMS applies restrictions to diabetic wounds of the lower extremities, peripheral ischemia, crush injuries, compromised skin grafts, osteoradionecrosis, and soft tissue radionecrosis.

Other issues found on review:

1) The ICD-10 code for osteoradionecrosis of the jaw is incorrect. Currently M27.8 (Other specified diseases of jaws) is included on this line, while the correct code is M27.2 (Inflammatory conditions of jaws) which is only on a dental line.

Guideline history

1) 2011, reviewed osteomyelitis and determined no evidence to support coverage
2) 2013, modified guideline wording to improve readibility
3) 2014, coverage guidance on hyperbaric oxygen was adopted and a modified guideline was adopted to reflect the coverage guidance recommendations. The diabetic wound portions of the guideline note were adopted with exact wording from the coverage guidance, except the addition of the requirement for re-evaluation every 30 days. This requirement was added to address medical director concerns and was based on the CMS coverage determination.
    a. Note: the CMS coverage determination actually applied the requirement for 30 day re-evaluation to ALL conditions treated with hyperbaric oxygen, not just diabetic wounds

Current guideline note:

GUIDELINE NOTE 107, HYPERBARIC OXYGEN

Line 337

Hyperbaric oxygen is a covered service only under the following circumstances:

- when paired with ICD-10-CM codes E11.5x and E11.621, E11.622 and E11.623 for diabetic wounds with gangrene OR diabetic wounds of the lower extremities in patients who meet the all of the following criteria:
    - Patient has Type 1 or Type 2 diabetes and has a lower extremity wound that is due to diabetes, AND
    - Patient has a wound classified as Wagner grade III or higher, AND
    - Patient has failed an adequate course of standard wound therapy including arterial assessment, with no measurable signs of healing after at least thirty days, AND
    - Wounds must be evaluated at least every 30 days during administration of hyperbaric oxygen therapy. Continued treatment with hyperbaric oxygen therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.
- when paired with ICD-10-CM codes M27.8 for osteoradionecrosis of the jaw only
- when paired with ICD-10-CM codes O08.0, M60.000-M60.09 only if the infection is a necrotizing soft-tissue infection
- when paired with ICD-10 CM codes S07.xxx,S17.xxx,S38.xxx,S47.1xxA-S47.1xxD,S47.2xxA-S47.2xxD,S47.9xxA-S47.9xxD, S57.xxx,S67.xxx, S77.xxx,S87.xxx,S97.xxx, T79.Axx only for posttraumatic crush injury of Gustilo type III B and C
- when paired with ICD-10--CM codes T66.xxxA only for osteoradionecrosis and soft tissue radiation injury
- when paired with ICD-10-CM codes T86.820-T86.829,T82.898A/T82.898D, T82.9xxA/T82.9xxD, T83.89xA/T83.89xD, T83.9xxA/T83.9xxD, T84.89xA/T84.89xD, T84.9xxA/T84.9xxD, T85.89xA/T85.89xD, T859xxA/T859xxD only for compromised myocutaneous flaps

HERC staff recommendations:

1) Remove M27.8 (Other specified diseases of jaws) from line 337 and add M27.2 (Inflammatory conditions of jaws) to line 337
    a. M27.2 is the correct ICD-10 code for osteoradionecrosis of the jaw
2) Modify GN107 as shown below

[easier to read format]

GUIDELINE NOTE 107, HYPERBARIC OXYGEN

Line 337

Hyperbaric oxygen therapy is included on this line, subject to the following limitations:

1. Courses of treatment for wounds or ulcers are limited to 30 days after the initial treatment; additional 30 day treatment courses are only covered for patients with incomplete wound/infection resolution AND measurable signs of healing
2. For the diagnoses specified below, inclusion on this line is subject to the following additional limitations:
    a. Codes appearing on this line from ICD-10-CM E08-E13 are included only when they are diabetic wound ulcers of the lower extremities which are Wagner grade 3 or higher (that is, involving bone or gangrenous) and show no measurable signs of healing after 30 days of adequate standard wound therapies including arterial assessment
    b. ICD-10-CM M27.2 is included on this line for osteoradionecrosis of the jaw only
    c. ICD-10-CM O08.0 and M60.0 are included on this line only if the infection is a necrotizing soft-tissue infection
    d. ICD-10-CM S07, S17, S38, S47.1, S47.2, S47.9, S57, S67, S77, S87, S97, T79.A are included on this line only for posttraumatic crush injury of Gustilo type III B and C
    e. ICD-10-CM T66.XXXA-T66.XXXD are included on this line only for osteoradionecrosis and soft tissue radiation injury
    f. ICD-10-CM T86.82, T82.898, T82.9, T83.89, T83.9, T84.89, T84.9, T85.89, T85.9 are included on this line only for compromised myocutaneous flaps

[edited guideline format]

GUIDELINE NOTE 107, HYPERBARIC OXYGEN

Line 337

A course of ~~H~~hyperbaric oxygen treatment is included on this line ~~a covered service~~ subject to the following limitations:~~ only under the following circumstances~~:

1. Courses of treatment for wounds or ulcers are limited to 30 days after the initial treatment; additional 30 day treatment courses are only covered for patients with incomplete wound/infection resolution AND measurable signs of healing
    ~~when paired with ICD-10-CM codes E11.5x and E11.621, E11.622 and E11.623 for diabetic wounds with gangrene OR diabetic wounds of the lower extremities in patients who meet the all of the following criteria:~~
        ~~a. Patient has Type 1 or Type 2 diabetes and has a lower extremity wound that is due to diabetes, AND~~

~~b. Patient has a wound classified as Wagner grade III or higher, AND~~
~~c. Patient has failed an adequate course of standard wound therapy including arterial assessment, with no measurable signs of healing after at least thirty days, AND~~
~~d. Wounds must be evaluated at least every 30 days during administration of hyperbaric oxygen therapy. Continued treatment with hyperbaric oxygen therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.~~

2. For the diagnoses specified below, inclusion on this line is subject to the following additional limitations:
    a. Codes appearing on this line from ICD-10-CM E08-E13 are included only when they are diabetic wound ulcers of the lower extremities which are Wagner grade 3 or higher (that is, involving bone or gangrenous) and show no measurable signs of healing after 30 days of adequate standard wound therapies including arterial assessment
    b. ~~when paired with~~ ICD-10-CM ~~M27.8~~ M27.2 is included on this line for osteoradionecrosis of the jaw only
    c. ~~when paired with~~ ICD-10-CM O08.0 and M60.0 are included on this line only if the infection is a necrotizing soft-tissue infection
    d. ~~when paired with diagnosis codes included on this line from~~ ICD-10-CM S07, S17, S38, S47.1, S47.2, S47.9, S57, S67, S77, S87, S97, T79.A are included on this line only for posttraumatic crush injury of Gustilo type III B and C
    e. ~~when paired with~~ ICD-10-CM T66.XXXA-T66.XXXD are included on this line only for osteoradionecrosis and soft tissue radiation injury
    f. ~~when paired with~~ ICD-10-CM T86.82, T82.898, T82.9, T83.89, T83.9, T84.89, T84.9, T85.89, T85.9 are included on this line only for compromised myocutaneous flaps

Tracking Information

Publication Number

100-3 Manual Section Number

20.29 Manual Section Title

Hyperbaric Oxygen Therapy

Version Number

3 Effective Date of this Version

6/19/2006 Implementation Date

6/19/2006

Description Information

Benefit Category

Incident to a physician's professional Service
Outpatient Hospital Services Incident to a Physician's Service
Physicians' Services

Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

Item/Service Description

CIM 35-10
For purposes of coverage under Medicare, hyperbaric oxygen (HBO) therapy is a modality in which the entire body is exposed to oxygen under increased atmospheric pressure.

Indications and Limitations of Coverage

A. Covered Conditions
Program reimbursement for HBO therapy will be limited to that which is administered in a chamber (including the one man unit) and is limited to the following conditions:

- Acute carbon monoxide intoxication,
- Decompression illness,
- Gas embolism,
- Gas gangrene,
- Acute traumatic peripheral ischemia. HBO therapy is a valuable adjunctive

treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened.
Crush injuries and suturing of severed limbs. As in the previous conditions, HBO therapy would be an adjunctive treatment when loss of function, limb, or life is threatened.
Progressive necrotizing infections (necrotizing fasciitis),
Acute peripheral arterial insufficiency,
Preparation and preservation of compromised skin grafts (not for primary management of wounds),
Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management,
Osteoradionecrosis as an adjunct to conventional treatment,
Soft tissue radionecrosis as an adjunct to conventional treatment,
Cyanide poisoning,
Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment,
Diabetic wounds of the lower extremities in patients who meet the following three criteria:
Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes;
Patient has a wound classified as Wagner grade III or higher; and
Patient has failed an adequate course of standard wound therapy.

The use of HBO therapy is covered as adjunctive therapy only after there are no measurable signs of healing for at least 30 –days of treatment with standard wound therapy and must be used in addition to standard wound care. Standard wound care in patients with diabetic wounds includes: assessment of a patient's vascular status and correction of any vascular problems in the affected limb if possible, optimization of nutritional status, optimization of glucose control, debridement by any means to remove devitalized tissue, maintenance of a clean, moist bed of granulation tissue with appropriate moist dressings, appropriate off-loading, and necessary treatment to resolve any infection that might be present. Failure to respond to standard wound care occurs when there are no measurable signs of healing for at least 30 consecutive days. Wounds must be evaluated at least every 30 days during administration of HBO therapy. Continued treatment with HBO therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.

B. Noncovered Conditions
All other indications not specified under §270.4(A) are not covered under the Medicare program. No program payment may be made for any conditions other than those listed in §270.4(A).
No program payment may be made for HBO in the treatment of the following conditions:
Cutaneous, decubitus, and stasis ulcers.
Chronic peripheral vascular insufficiency.
Anaerobic septicemia and infection other than clostridial.
Skin burns (thermal).
Senility.

Myocardial infarction.
Cardiogenic shock.
Sickle cell anemia.
Acute thermal and chemical pulmonary damage, i.e., smoke inhalation with pulmonary insufficiency.
Acute or chronic cerebral vascular insufficiency.
Hepatic necrosis.
Aerobic septicemia.
Nonvascular causes of chronic brain syndrome (Pick's disease, Alzheimer's disease, Korsakoff's disease).
Tetanus.
Systemic aerobic infection.
Organ transplantation.
Organ storage.
Pulmonary emphysema.
Exceptional blood loss anemia.
Multiple Sclerosis.
Arthritic Diseases.
Acute cerebral edema.

C. Topical Application of Oxygen
This method of administering oxygen does not meet the definition of HBO therapy as stated above. Also, its clinical efficacy has not been established. Therefore, no Medicare reimbursement may be made for the topical application of oxygen.

Cross Reference
§270.5 of this manual.

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Transmittal Information
Transmittal Number

48
Coverage Transmittal Link

http://www.cms.gov/transmittals/downloads/R48NCD.pdf
Revision History

07/01/1997 - Clarified coverage limited to conditions listed under §35-10.A. Effective date 08/11/1997. (TN 102)
04/01/1999 - Clarified covered conditions and physician supervision requirement. Effective date 05/01/1999. (TN 112)
10/19/2000 - Manualized program memorandum AB-00-15 (dated 4/1/2000) and clarified that "preparation and preservation of compromised skin graft" in section 35-10A.9 is not for primary management of wounds. Effective date NA. (TN 129) (CR 1138)
12/27/2002 - Expanded coverage for treatment of diabetic wounds of the lower

extremities in patients that meet three criteria. Effective date 04/01/2003. (TN 164) (CR 2388)
03/2006 - Technical corrections to the NCD Manual. Effective date 06/19/2006. (TN48) (CR4278)
01/2013 - CMS translated the information for this policy from ICD-9-CM/PCS to ICD-10-CM/PCS according to HIPAA standard medical data code set requirements and updated any necessary and related coding infrastructure. These updates do not expand, restrict, or alter existing coverage policy. Implementation date: 04/01/2013 Effective date: 10/1/2015. (TN 1165) (CR 8109)
05/2014 - CMS translated the information for this policy from ICD-9-CM/PCS to ICD-10-CM/PCS according to HIPAA standard medical data code set requirements and updated any necessary and related coding infrastructure. These updates do not expand, restrict, or alter existing coverage policy. Implementation date: 10/06/2014 Effective date: 10/1/2015. (TN 1388) (TN 1388) (CR 8691)

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National Coverage Analyses (NCAs)
National Coverage Analyses (NCAs)

This NCD has been or is currently being reviewed under the National Coverage Determination process. The following are existing associations with NCAs, from the National Coverage Analyses database.
Original consideration for Hyperbaric Oxygen Therapy for Hypoxic Wounds and Diabetic Wounds of the Lower Extremities (CAG-00060N) opens in new window
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Additional Information
Other Versions

Hyperbaric Oxygen Therapy - Version 2, Effective between 4/1/2003 - 6/19/2006

Hyperbaric Oxygen Therapy - Version 1, Effective between 10/19/2000 - 4/1/2003

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Section 7.0

New Discussion Items

Pectus Excavatum and Pectus Carinatum

Question: Should pectus excavatum and pectus carinatum be moved to a higher priority line on the Prioritized List?

Question source: Kimberly Ruscher, MD, pediatric surgeon, through coverage guidance topic nomination process and direct contact with HERC; Garret Zallen from PeaceHealth through coverage guidance topic nomination process.

Issue: Currently, pectus excavatum (ICD-10 Q67.6) and pectus carinatum (Q67.7) are on line 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY. There are no surgical repair codes on line 665. These conditions are generally considered cosmetic.

Pectus excavatum is the most common congenital deformity of the anterior wall of the chest, in which several ribs and the sternum grow abnormally. This produces a caved-in or sunken appearance of the chest. It can either be present at birth or not develop until puberty. Pectus excavatum is sometimes considered to be cosmetic; however, depending on the severity, it can impair cardiac and respiratory function and cause pain in the chest and back. People with the condition may experience negative psychosocial effects. Pectus excavatum is sometimes referred to as cobbler's chest, sunken chest, the crevasse, or funnel chest. The severity of pectus excavatum is determined by the Haller index. The patient's Haller is calculated by obtaining the ratio of the transverse diameter (the horizontal distance of the inside of the ribcage) and the anteroposterior diameter (the shortest distance between the vertebrae and sternum) from a chest CT scan. A Haller Index of greater than 3.25 is generally considered severe, while normal chest has an index of 2.5. Surgical correction is done with implants (cosmetic results only) or a more extensive surgical correction, generally with the Nuss procedure in which a metal bar is placed to push the sternum outward; this procedure allows correction of cardiopulmonary issues as well as the cosmetic chest defect. Magnetic mini-movers and vacuum bells are also used, which are non-surgical attempts at correction.

Pectus carinatum, also called pigeon chest, is a deformity of the chest characterized by a protrusion of the sternum and ribs. It is normally treated with bracing. Surgical correction is done for very severe cases.

Poland syndrome (ICD-10 Q79.8), a more severe form of chest wall deformity, is coded with the generic ICD-10 code Q79.8 (Other congenital malformations of musculoskeletal system) which is currently on line 530 DEFORMITIES OF UPPER BODY AND ALL LIMBS. Poland syndrome is a rare birth defect characterized by underdevelopment or absence of the pectoralis chest muscle on one side of the body, and usually has finger and hand abnormalities on the same side. Additional muscles in the chest wall and adjacent areas can be missing or underdeveloped. There may also be rib cage abnormalities, such as shortened ribs. In most cases, the abnormalities in the chest area do not cause health problems or affect movement.

From Dr. Ruscher

I am a Pediatric Surgeon here in Oregon, currently working at Sacred Heart Medical Center at Riverbend in Springfield and at Shriner's Hospital in Portland. One of my areas of interest is caring for children and young adults with chest wall deformities. This email is to ask that you review two conditions, Pectus Carinatum, Q67.7 and Pectus excavatum, Q67.6, to include treatment. I would like to present public comment during the January meeting, and will provide written testimony and reference materials ahead of that time. Regarding this matter, I have no conflicts of interest; specifically, I am a salaried employee of PeaceHealth, and am not compensated for my work at Shriners. I would not benefit in any way from a change in coverage for these conditions.

Pectus carinatum (incidence 1 in 1000) and pectus excavatum (incidence 1 in 500) are common chest wall deformities affecting children. Until the early 20th century, there were no treatments available. Nearly 100 years ago, surgeons developed procedures for these conditions. The surgery was quite invasive and for some children had devastating complications. In many cases, the treatment was worse than the disease. After this time, chest wall deformities were treated as cosmetic and only the worst patients were sent for surgery. Further, little was known in the medical literature about the long term effects of untreated chest wall deformities.

The teaching that chest wall deformities are cosmetic has persisted, though the knowledge about and therapy for these conditions has improved greatly. Research has clearly demonstrated that there are long-term physiological effects especially of having pectus excavatum, and that modern therapies are safe and effective. Pectus carinatum can be completely treated in 90-95% of children with a simple bracing protocol, and pectus excavatum can be diagnosed with little work-up and treated with a minimally invasive surgery.

From Dr. Ruscher's coverage guidance review request

Q5: What is the specific intervention that requires an evidence review?
Bracing for pectus carinatum; Surgery for pectus excavatum
Q6: What patients or group(s) of patients does your question involve?
Any patient with pectus carinatum; Patients with pectus excavatum with moderate defect, Haller index of 3.25 or higher, or co-morbidities (cardiac compression, shortness of breath, chest pain, cardiac rhythm abnormalities)
Q7: What treatment alternatives are relevant to your question?
Pectus carinatum- bracing is 90-95% effective; failure of bracing would require surgery for treatment. Pectus excavatum- other treatments (magnet mini-mover or vacuum bell) are under trial but have not demonstrated long term efficacy.
Q8: Describe any health-related outcomes (benefits or harms) of interest.
Pectus carinatum - bracing could fail, especially if started too late in life. Pectus excavatum - complications of surgery or from the implant could occur.

Q9: Why are you suggesting this topic? How would a HERC coverage guidance be useful to patients, providers or policy makers? Check all that apply

- Intervention is more effective
- Intervention has fewer harms
- Other (please specify) These defects were formerly considered cosmetic or to have no good treatments. New research is available.

Q10: Why did you decide to bring this topic to the HERC's attention? Why should the HERC spend its time on this over other topics?

These are common conditions (for example, pectus excavatum affects at least 1 in 500) that cause physical and emotional problems in the short and long term, with good treatment options. Bracing for pectus carinatum is especially cost -effective compared to surgery.

From Mr. Zallen's coverage guidance review request

Q5: What is the specific intervention that requires an evidence review?

Thoracoscopic assisted Pectus Excavatum repair

Q6: What patients or group(s) of patients does your question involve?

Pectus Excavatum

Q7: What treatment alternatives are relevant to your question?

There is no effective non-surgical treatment

Q8: Describe any health-related outcomes (benefits or harms) of interest.

Improved cardiac function and improved lifestyle

Q9: Why are you suggesting this topic? How would a HERC coverage guidance be useful to patients, providers or policy makers? Check all that apply

- Intervention is more effective
- Intervention has fewer harms

Q10: Why did you decide to bring this topic to the HERC's attention? Why should the HERC spend its time on this over other topics?

One in 500 people suffer from chest wall deformities and Pectus Excavatum is the most common. It has physiological consequences as well as significant body image issues in those who have PE.

Current Prioritized List status

Q67.6 (pectus excavatum) is on line 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY

Q67.7 (pectus carinatum) is on line 665

Q76.6-Q76.9 (congential malformation of ribs/sternum/bony thorax) are on line 530 DEFORMITIES OF UPPER BODY AND ALL LIMBS

21740 Reconstructive repair of pectus excavatum or carinatum; open

21742 minimally invasive approach (Nuss procedure), without thoracoscopy

21743 minimally invasive approach (Nuss procedure), with thoracoscopy

All appear on line 530 DEFORMITIES OF UPPER BODY AND ALL LIMBS

Evidence—pectus excavatum

1) **de Oliveira Carvalho 2014**, Cochrane review of surgical interventions for pectus excavatum
    a. No RCT or quasi-RCTs found that met inclusion criteria
2) **Johnson 2008**, review of cardiopulmonary outcomes of pectus excavatum repair
    a. N=11 studies (387 patients), various surgical methods
    b. Postoperative total lung capacity for patients who had Ravitch repair was significantly lower (SMD, 0.71 [CI -1.06, -0.36]; I2 =19.6%) than preoperative. Based on 2 studies after removal of the Nuss bar, FEV1 was significantly increased from preoperative values (SMD, 0.39 [CI, 0.03, 0.74]; I2 = 0%). Stroke volume increased after surgery (SMD, 0.40 [CI, 0.10, 0.70]; I2 = 0%) after Ravitch repair. There was a trend toward improved exercise tolerance, but it was not statistically significant.
    c. Conclusions: Total lung capacity was decreased after Ravitch repair, and FEV1 was increased after Nuss bar removal. Stroke volume may be increased after Ravitch repair. Exercise tolerance was not improved after either type of surgical repair.
3) **Guntheroth 2007**, review of studies on cardiac function outcomes of pectus excavatum surgery
    a. N=5 studies (118 patients, 82 controls)
    b. No improvements were found in left ventricular size, stroke volume, and cardiac output after surgery in 4 of 5 studies, using radionuclides, 2-dimensional echocardiography, radiographic planimetry, and cardiac output by the Fick method. Only a single study, with volumes calculated by squaring the diameter of the left ventricle from M-mode echocardiography, reported an increase (22%) in left ventricular stroke volume after operation, but that increased (17%) in the investigators' unoperated controls.
    c. In conclusion, there is no reliable documentation of improved cardiac function from thoracic surgery for pectus excavatum.
4) **Malek 2006,** review and meta-analysis of cardiac outcomes of surgical repair of pectus excavatum
    a. N=8 studies (169 patients)
    b. Random-effects modeling yielded a mean weighted effect size (ES) for cardiovascular function that was statistically significant (ES, 0.59; 95% confidence interval, 0.25 to 0.92; $p < 0.0006$).
    c. *Conclusions:* The findings of the present study indicated that surgical repair of the pectus excavatum significantly improves cardiovascular function and contradicts arguments that surgical repair is primarily cosmetic yielding minimal physiologic improvement.
5) **Malek 2006,** review and meta-analysis of pulmonary outcomes of surgical repair of pectus excavatum
    a. N=12 studies (313 patients)

b. Random-effects modeling yielded a mean weighted effect size (ES) for pulmonary function which was statistically nonsignificant (ES = 0.08, 95% CI = -0.20 to 0.35; P = 0.58). The findings of the present study indicated that surgical repair of pectus excavatum does not significantly improve pulmonary function. These findings, however, may be a result of testing pulmonary function under conditions in which pectus excavatum does not manifest itself.

Submitted evidence—pectus excavatum

1) **Jayaramakrishnan 2013**, systematic review
    a. N=22 papers, studies grouped by type of repair
    b. Nuss repair (N=4 studies)
        i. Pulmonary function and exercise tolerance 3-6 months post-op decreased
        ii. Studies after 6 months found improvement in pulmonary and cardiac function
        iii. The majority of the studies performed post-bar removal demonstrated a small but significant improvement in pulmonary function
    c. Ravich procedure
        i. Early post op to 8 months post-op, studies found no improvement in or reduced pulmonary function. Late post-op (1 study) found modest improvement in pulmonary function only in a subgroup with severely reduced pulmonary function (FEV1 < 75% predicted) preoperatively.
        ii. Significant improvements in cardiac function including right ventricular diastolic volume indexes were noted.
    d. Other procedures:
        i. Reduced pulmonary function found short and long term
    e. Conclusions: Pectus repair using minimally invasive Nuss technique and Ravitch procedure cause an early decrease in the pulmonary function. However, a small, but significant, return of function does occur during the late postoperative period. Cardiac function increases during the early postoperative period, an improvement that is sustained [improvement noted to be modest]. In contrast, pectus repair using other techniques has not shown similar improvements.

2) Chao 2015
    a. Retrospective case series of 168 adults undergoing modified Nuss repair
    b. There was an increase in right atrium (15.1%), tricuspid annulus (10.9%), and right ventricular outflow tract (6.1%) size after surgery (all P<0001). Right ventricular cardiac output measured in a subset of 42 patients improved by 38%.
    c. No change in chamber size or cardiac output occurred before and after bar removal surgery in the control group.
        i. Note: control group had previously had surgery and were undergoing bar removal. N=17 pts, average time after initial Nuss surgery 3 years

d. Exercise capacity or other patient centered outcomes not studied
e. ECHO readers not blinded to type of surgery
f. CONCLUSIONS: Surgical correction of PE deformity caused a significant improvement in right heart chamber size and cardiac output.

3) O'Keefe 2013

a. Case series, N=67 patients (excluded patients with connective tissue disorders or other co-morbidities)
b. Cardiopulmonary outcomes, standardized for height and weight, showed significant improvements in FEV-1 as (pre) 81.1±17.0 vs post 89.8±20.5*, FVC: 91.2±18.6 vs 98.9±22.9*, O2 pulse: 75.8±14.4 vs 80.5±18.3* (each as % predicted). Both the self-ratings of appearance (2.5±0.8 vs 4.4±0.5) and ability to exercise (3.3±0.7 vs 4.3±0.6, scale 1–5) increased significantly.
c. No improvements seen in cardiac dynamics at rest
d. Conclusions: the results of this study show a modest improvement in pulmonary function and exercise testing in moderate to severe pectus defects when repaired with the Nuss procedure. However, it is the impact on appearance and the perceived exercise tolerance that show the greatest improved with pectus repair.

4) **Maagaard 2013/Tang 2012** (appear to be reporting on same patient group)

a. Prospective case series of 75 patients (49 with PE, 26 controls)
    i. Haller index of PE patients 5.3 +/- 2.3 pre-operatively (i.e. more severely affected patients)
b. PE patients underwent Nuss procedure
c. Preoperatively, PE patients had lower maximum cardiac index. Cardiac index increased significantly 1 year after surgery, and there was no difference between PE patients and controls at 3 years post-op
d. Forced expiratory volume (FEV1) was significantly lower in PE patients prior to surgery; there was no significant difference found between groups post-operatively
e. Before operation, the patients exercised less than the controls, and there was no difference in training level one year after the operation, although this was mainly due to less activity in the control group.

5) **Krueger 2010**

a. Prospective case series of 17 patients studied with intraoperative ECHO during PE repair with Ravitch-Shamberger technique
b. End diastolic RV diameter, area, and volume all significant increased after surgery. LV ejection fraction also significantly increased after surgery
c. No correlation found in degree of RV function improvement and degree of pre-op degree of chest wall deformity
d. No report regarding clinical impact, exercise tolerance change, or other outcomes

6) Kelly 2005

a. Autopsy series of 62 patients
    i. 35 died of other causes

ii. 21 found to have co-existing conditions or syndromes
iii. 1 died of complications of pectus repair in 1947
iv. 5 children cause of death not mentioned
v. No data on severity of pectus deformity
vi. Pectus excavatum patients tended to die earlier (P = .0001). However, pectus excavatum patients who survived past the age of 56 years tended to survive longer than their matched controls (P = .0001).

Evidence—Pectus carinatum

1) **Kravarusic 2006,** case series of chest bracing for pectus carinatum
    a. N=24 patients
    b. Nineteen (79.2%) patients have completed initial treatment (mean CP time, 4.3 F 2.1 months). There were 3 patients (12.5%) who were noncompliant, and 2 (8.3%) are still in the initial CP phase of therapy. Fourteen (58.3%) patients are presently in maintenance phase, nocturnally braced, and 2 (8.3%) have completed therapy. In patients completing initial treatment, the pectus carinatum protrusion (pre 22 F 6 vs post 6.0 F 6.2) and subjective appearance (change + 1.8F0.4) showed a significant improvement (P > .001 for both) with no change in exercise tolerance.
    c. Conclusion: Compressive bracing results in a significant subjective and objective improvement in PC appearance in skeletally immature patients. However, patient compliance and diligent follow up appear to be paramount for the success of this method of treatment. Further studies are required to show the durability of this method of treatment.
2) **Desmarais 2013**, review of pectus carinatum
    a. Recent evidence confirms that children with pectus carinatum have a disturbed body image and a reduced quality of life. Treatment has been shown to improve the psychosocial outcome of these patients.
    b. A growing body of literature, however, now supports the use of orthotic bracing as a nonoperative alternative in select patients.

Submitted evidence—pectus carinatum

1) Knudsen 2015
    a. Prospective case series (N=28 patients)
    b. Disease-specific health-related quality of life was improved by 33% (95% CI: 23; 44%)—the instrument used included all questions about perceived appearance and how this affected life
    c. The improvement for generic mental health-related quality of life was 7% (95% CI: 3; 12%). The improvement in self-esteem was 9% (95% CI: 2; 17%)
    d. No significant improvement in depression or anxiety
    e. Conclusion: This study confirms positive effects of surgical correction of pectus carinatumon health-related quality of life and self-esteem.

Other policies

1) **NICE 2009**
    a. Current evidence on the safety and efficacy of placement of pectus bar for pectus excavatum (also known as MIRPE [minimally invasive repair of pectus excavatum] or the Nuss procedure) is adequate to support its use
    b. Key efficacy outcomes in the review were cosmetic appearance and patient satisfaction
        i. Outcomes listed in review were improved quality of life, self-esteem and cosmetic appearance scores
2) **Cigna 2009**
    a. Under many benefit plans, surgery for chest wall deformities is not covered when performed solely for the purpose of improving or altering appearance or self-esteem or to treat psychological symptomatology or psychosocial complaints related to one's appearance.
    b. If coverage for surgical repair of chest wall deformities is available, the following conditions of coverage apply.
        i. CIGNA covers surgical repair of severe pectus excavatum as medically necessary when imaging studies (e.g., computerized tomography [CT] scans, radiographs) confirm a pectus index (i.e., Haller index) greater than 3.25 and EITHER of the following criteria is met:
            1. Pulmonary function studies demonstrate at least a moderately severe restrictive lung defect.
            2. Cardiac imaging (e.g., echocardiography, stress echocardiography, magnetic resonance imaging [MRI]) demonstrates findings consistent with external compression.
    c. CIGNA covers surgical repair of pectus carinatum as medically necessary when there is documented evidence of significant physical functional impairment (e.g., cardiac or respiratory insufficiency), and the procedure is expected to correct the impairment
    d. CIGNA covers the surgical repair of a chest deformity associated with Poland syndrome as medically necessary when rib formation is absent.
3) **Aetna 2015** Aetna considers surgical repair of severe pectus excavatum deformities that cause functional deficit medically necessary when done for medical reasons in members who meet all of the following criteria:
    a. Well-documented evidence of complications arising from the sternal deformity. Complications include but may not be limited to:
        i. Asthma
        ii. Atypical chest pain
        iii. Cardiopulmonary impairment documented by respiratory and/or cardiac function tests
        iv. Exercise limitation
        v. Frequent lower respiratory tract infections; *and*

b. An electrocardiogram or echocardiogram has been done if a heart murmur or known heart disease is present to define the relationship of the cardiac problem to the sternal deformity; a*nd*
c. A CT scan of the chest demonstrates a pectus index, derived from dividing the transverse diameter of the chest by the anterior-posterior diameter, greater than 3.25.
d. Aetna considers surgical repair of pectus excavatum cosmetic when criteria are not met.
e. Aetna considers the following interventions for the treatment of pectus excavatum experimental and investigational because their effectiveness has not been established;
    i. The magnetic mini-mover procedure
    ii. The vacuum bell
    iii. Dynamic Compression System
f. Aetna considers surgical reconstruction of musculo-skeletal chest wall deformities associated with Poland's syndrome that cause functional deficit medically necessary
g. Aetna considers bracing and surgical procedures to correct pectus carinatum cosmetic because this deformity does not cause physiologic disturbances from compression of the heart or lungs.

4) **<u>United Indications for Coverage</u>**
    a. Surgical repair of pectus excavatum is considered reconstructive and medically necessary when the following criteria has been met:
        i. Pectus Excavatum
            1. Imaging studies confirm Haller index greater than 3.25; and
            2. The functional impairment is defined by one or more of the following:
                a. For restrictive lung capacity the total lung capacity is documented in the physician current office notes as <80% of the predicted value; or
                b. There is cardiac compromise as demonstrated by decreased cardiac output on the echocardiogram; or
                c. There is objective evidence of exercise intolerance as documented by:
                    i. Cardiopulmonary exercise testing that is below the predicted values; or
                    ii. Exercise pulmonary function tests that are below the predicted values and show restrictive lung disease
        ii. Pectus Carinatum
            1. It is extremely uncommon that pectus carinatum will cause a functional/physiological deficit. Pectus carinatum is not a congenital anomaly; it is a developmental condition of the cartilage that generally occurs during an adolescents growth

spurt. (Goretsky, 2004) Requests for coverage of repair of pectus carinatum will be reviewed by a UHC Medical Director on a case by case basis.

5) **HealthPartners Indications for Coverage**
    a. Pectus Excavatum:
        i. All of the following criteria must be met for coverage of repair of pectus excavatum:
            1. A Pectus/ Haller Index greater than 3.25 (calculated by using chest measurements from a CT scan of the area of the chest with the greatest depression.)
            2. Exercise limitation with symptoms OR chest pain related to pectus excavatum present for more than six months and unresponsive to more conservative treatment. Documentation of either of these is required.
            3. Diminished cardiopulmonary function during exercise, documented by lung/cardiac function tests (i.e. 20% depression of cardiopulmonary function.); and
            4. Cardiologist/pulmonologist concurs with need for surgical correction.
        ii. Pectus Carinatum repair is not covered unless there is documentation in the medical record of related functional problems.
        iii. Repairs for cosmetic reasons are not covered.

HERC staff summary:

Pectus excavatum: The literature is conflicting regarding whether surgical repair of pectus excavatum improves cardiac or pulmonary function or exercise tolerance, based on large case series and case-control studies. At best, there is a modest improvement in cardiopulmonary function long term, with short term decreases in pulmonary function after surgery. The vast majority of the literature reports on intermediate outcomes such as cardiac ejection fraction or forced expiratory volume, rather than patient oriented outcomes such as exercise tolerance. Cases with severe deformities causing measurable cardiac or pulmonary impairment or patients with certain co-morbidities may benefit more from surgical intervention than less impacted individuals.

Pectus carinatum: There is no evidence that surgical correction or bracing of this condition improves cardiac or pulmonary outcomes or improves other health outcomes. Correction of this condition appears to be solely cosmetic.

HERC staff recommendations:

1) Keep Q67.7 (pectus carinatum) on line 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
    a. Treatment is cosmetic
2) Move Q67.6 (pectus excavatum) from line 665 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY to line 530 DEFORMITIES OF UPPER BODY AND ALL LIMBS
    a. CPT codes for Nuss procedures and other repair procedures (CPT 21740-21743) are on line 530 and would pair with this diagnosis
    b. Similar conditions Q76.6-Q76.9 (congential malformation of ribs/sternum/bony thorax) are on line 530
    c. Movement would continue non-coverage for this condition due to the prioritization of line 530 below the current funding line
    d. Very severe cases could be reviewed for surgical repair through the exceptions process. The CCO medical directors report approving cases through the co-morbidity rule when cardiac or pulmonary dysfunction has been present.
    b. Alternative:
        i. Add Q67.6 to line 406 BENIGN CONDITIONS OF BONE AND JOINTS AT HIGH RISK FOR COMPLICATIONS in addition to adding to line 530 and removing from line 665.
        ii. Add Q79.8 (Other congenital malformations of musculoskeletal system) to line 406 and keep on line 530.
        iii. Add a new guideline note shown as the first entry below

HERC staff recommended wording:

GUIDELINE NOTE XXX PECTUS EXCAVATUM

Lines 406, 530

Pectus excavatum (ICD-10 Q67.6) is included on line 406 only for patients with all of the following

1) severe deformity (Haller index >3.25) AND
2) exercise limitation with symptoms related to pectus excavatum present for more than six months and unresponsive to more conservative treatment AND
3) Documented pulmonary or cardiac dysfunction demonstrated by either
    a. pulmonary function studies demonstrating at least a moderately severe restrictive lung defect OR
    b. Cardiac effects to include cardiac compression or displacement, bundle branch block or other cardiac pathology secondary to compression of the heart AND
4) cardiologist/pulmonologist concurs with need for surgical correction AND
5) these conditions are reasonably expected to be relieved with surgery.

Otherwise, this condition is included on line 530.

ICD-10 Q79.8 is included on line 406 only for Poland syndrome. Other diagnoses using this code are on line 530. Surgical reconstruction of musculo-skeletal chest wall deformities associated with Poland's syndrome are only included on line 406 when causing functional deficit(s).

Dr. Ruscher suggested guideline wording:

GUIDELINE NOTE XXX PECTUS EXCAVATUM

Lines 406, 530

Pectus excavatum (ICD-10 Q67.6) is included on line 406 only for patients with

1) severe deformity (Haller index >3.25), history of failed repair, progression of deformity AND one of either
    a. Cardiac effects to include cardiac compression or displacement, mitral valve prolapse, bundle branch block or other cardiac pathology secondary to compression of the heart, OR
    b. Pulmonary function studies demonstrating at least a moderately severe restrictive lung defect, OR
    c. Exercise limitation with symptoms, OR
    d. Atypical chest pain, OR
    e. Poland syndrome or connective tissue disorder, OR
    f. Paradoxical movement of the chest wall with deep inspiration, OR
    g. Significant body image disturbance
2) AND these conditions are reasonably expected to be relieved with surgery.

Otherwise, this condition is included on line 530.

Disposition of submitted literature

1) Li 2015
    a. Case study; higher level of evidence found
2) Kinuya 2005
    a. Case series of 3 patients; higher level of evidence found
3) Tardy 2015
    a. Prospective case control series; PE patients had decreased maximal exercise tolerance compared to controls
    b. Report was a letter with little data provided; unclear if peer reviewed
4) Sigalet 2003
    a. Included in Jayaramakrishnan 2013
5) Lawson 2005
    a. Included in Jayaramakrishnan 2013
6) Coln 2006
    a. Included in Jayaramakrishnan 2013
7) Redlinger 2010
    a. Examined outcomes in Marfan patients with PE; did not directly address question for this review
8) St Peter 2011
    a. Study regarding new measure for PE severity; Did not directly address question for this review
9) Koumbourlis 2015
    a. General review of condition; no specific evidence supporting treatment included
10) Castellani 2010
    a. Included in Jayaramakrishnan 2013
11) Sigalet 2007
    a. Included in Jayaramakrishnan 2013
12) Jaroszewski 2009
    a. Case study; higher level of evidence available
13) Poston 2014
    a. Involved index used to measure severity of disease; did not address the question at hand
14) Kaguraoka 1992
    a. Older study; newer studies available

[Intervention Review]

Surgical interventions for treating pectus excavatum

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ABSTRACT

Background

Pectus excavatum is characterized by a depression of the anterior chest wall (sternum and lower costal cartilages) and is the most frequently occurring chest wall deformity. The prevalence ranges from 6.28 to 12 cases per 1000 around the world. Generally pectus excavatum is present at birth or is identified after a few weeks or months; however, sometimes it becomes evident only at puberty. The consequence of the condition on a individual's life is variable, some live a normal life and others have physical and psychological symptoms such as: precordial pain after exercises; impairments of pulmonary and cardiac function; shyness and social isolation. For many years, sub-perichondrial resection of the costal cartilages, with or without transverse cuneiform osteotomy of the sternum and placement of a substernal support, called conventional surgery, was the most accepted option for surgical repair of these patients. From 1997 a new surgical repair called, minimally invasive surgery, became available. This less invasive surgical option consists of the retrosternal placement of a curved metal bar, without resections of the costal cartilages or sternum osteotomy, and is performed by videothoracoscopy. However, many aspects that relate to the benefits and harms of both techniques have not been defined.

Objectives

To evaluate the effectiveness and safety of the conventional surgery compared with minimally invasive surgery for treating people with pectus excavatum.

Search methods

With the aim of increasing the sensitivity of the search strategy we used only terms related to the individual's condition (pectus excavatum); terms related to the interventions, outcomes and types of studies were not included. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Embase, LILACS, and ICTPR. Additionally we searched yet reference lists of articles and conference proceedings. All searches were done without language restriction.

Date of the most recent searches: 14 January 2014.

Selection criteria

We considered randomized or quasi-randomized controlled trials that compared traditional surgery with minimally invasive surgery for treating pectus excavatum.

Data collection and analysis

Two review authors independently assessed the eligibility of the trials identified and agreed trial eligibility after a consensus meeting. The authors also assessed the risk of bias of the eligible trials.

Main results

Initially we located 4111 trials from the electronic searches and two further trials from other resources. All trials were added into reference management software and the duplicates were excluded, leaving 2517 studies. The titles and abstracts of these 2517 studies were independently analyzed by two authors and finally eight trials were selected for full text analysis, after which they were all excluded, as they did not fulfil the inclusion criteria.

Authors' conclusions

There is no evidence from randomized controlled trials to conclude what is the best surgical option to treat people with pectus excavatum.

PLAIN LANGUAGE SUMMARY

Surgical treatments for pectus excavatum

Pectus excavatum is characterized by a depression (sunken appearance) of the anterior (front) chest wall (sternum and lower costal cartilages); it is the most common chest wall defect. The frequency ranges from 6.28 to 12 cases per 1000 around the world. It is generally regarded as a genetic condition, based on the fact that it is usually present in several members of the same family and is often associated with other genetic diseases; however, its causes remain in debate. To what degree the disorder affects the individual's life is variable, some will live a normal life and others can have physical and psychological symptoms such as: precordial pain after exercises; problems with pulmonary and cardiac function; shyness and social isolation.

Many types of non-surgical treatments have been tried, among them there are physical and respiratory exercises and different methods or devices to put pressure on the elevated parts of the chest wall or do traction in the depressed parts. Despite these different options of conservative treatment, the widespread treatment is that of surgical correction. For many years the surgical correction was based on the resections of the deformed costal cartilages (which aim to extend the ribs forward and contribute to the elasticity of the walls of the thorax (area between abdomen and neck)) and the placement of a support behind of the externum to move it forward. Since 1997 a new surgical technique became available, the externum is displaced forward by the placement of a metal bar behind it, the bar is placed by video-assisted throat surgery and the costal cartilage is resected. However, there is a debate if one surgery is better (reach a better result with less complications) than the other. To clarify this question we performed a systematic review, but, no trials were eligible for inclusion. We conclude that, there is no evidence to decide what is the best surgical procedure to treat pectus excavatum.

BACKGROUND

Description of the condition

Pectus excavatum or funnel chest, is characterized by a depression of the sternum and the lower costal cartilages, the depression starts at the manubriosternal articulation and increases toward the xiphoid which is angulated forward and depressed until very close to the spine resulting in a funnel-shaped thorax (Head 1950). Often pectus excavatum has an asymmetric shape with the right side deeper than the left side, in such cases the sternum is rotated counter-clockwise (Ravitch 1977). The grade of depression can vary from small and almost imperceptible, to very large, which is the typical case. Many different indexes have been proposed for grading the depression, generally these indexes consider the distance between the sternum and the spine (Haller 1987; von der Oelsnitz 1981; Welch 1980). Despite many attempts to classify pectus excavatum in an objective manner, there are no universally accepted classifications (Welch 1989). Recently Lawson proposed a new classification based on the cross-sectional area of the thorax determined by computed tomography scans (Lawson 2006). The diagnosis of pectus excavatum is done by physical examination,

Cardiorespiratory Function after Operation for Pectus Excavatum

Jonathan N. Johnson, MD, Tyler K. Hartman, MD, Paul T. Pianosi, MD, and David J. Driscoll, MD

Objective We performed a review of current data to determine the effect that operation has on pulmonary function, aerobic capacity, and stroke volume in patients with pectus excavatum.

Study design Two reviewers independently assessed clinical trials and collected data on interventions and outcomes. To qualify for inclusion, a study had to include preoperative and postoperative assessment, provide outcomes in either a published percentile or qualified matched control form to control for interval growth, and include only original patient groups.

Results Postoperative total lung capacity for patients who had Ravitch repair was significantly lower (SMD, 0.71 [CI −1.06, −0.36]; $I^2 = 19.6\%$) than preoperative. Based on 2 studies after removal of the Nuss bar, FEV_1 was significantly increased from preoperative values (SMD, 0.39 [CI, 0.03, 0.74]; $I^2 = 0\%$). Stroke volume increased after surgery (SMD, 0.40 [CI, 0.10, 0.70]; $I^2 = 0\%$) after Ravitch repair. There was a trend toward improved exercise tolerance, but it was not statistically significant.

Conclusions Total lung capacity was decreased after Ravitch repair, and FEV_1 was increased after Nuss bar removal. Stroke volume may be increased after Ravitch repair. Exercise tolerance was not improved after either type of surgical repair. *(J Pediatr 2008;153:359-64)*

Pectus excavatum, a common major congenital anomaly, occurs in approximately 1 of 300 to 400 births.[1,2] Most experts agree that there is a cosmetic role for operation in this condition and that patients usually report subjective improvement in exercise tolerance after surgical correction. However, it remains unclear if surgery improves cardiorespiratory function or exercise capacity. Cardiopulmonary function after these procedures (most often the Ravitch or the Nuss repair) has been investigated, with conflicting results. Some investigators have reported improved cardiorespiratory function after surgical correction and others have found no change or deterioration.[3-6]

The Ravitch repair involves a midline thoracic incision, cauterization and reflection of the pectoralis major, and a resection of costal cartilages. A transverse sternal osteotomy is then performed. This releases the inferior portion of the sternum to be brought forward to flatten the chest wall.[7] More recent versions of the Ravitch repair also use a steel bar behind the sternum to help it keep its new shape.[8] In contrast, the Nuss repair does not involve a sternotomy. Instead, using thoracoscopy, a vascular clamp or pectus introducer is inserted into an intercostal space and brought through to the opposite side. The Nuss bar is then inserted along the tract of the introducer, in opposite concavity orientation to the chest wall. A bar rotator is used to rotate the bar 180°, which forces the sternum out from its original depressed location.[9]

The purpose of this study was to perform a systematic and critical review to determine the effect that surgical correction of pectus excavatum has on pulmonary function, cardiac, and exercise data, with quality control of included studies.

METHODS

A search strategy was designed using the MEDLINE, EMBASE, ERIC, CINAHLL, Cochrane Database of Systematic Reviews, and Current Contents databases from inception until November 2006 to find eligible studies. Reviews of reference lists from published reviews and content expert advice provided further potentially eligible studies.

Two reviewers extracted the following data from each eligible article: year and journal of publication, age and sex of patients, type of surgery performed, type of outcome measures reported, presence of ancillary diagnoses in patients, time of follow-up for postoperative studies, adjustment for weight and height changes of patients, and presence of a control group. When authors reported both end-of-study results and change-from-baseline results, we used the end-of-study results in our meta-analysis. When necessary,

FVC	Functional vital capacity	TLC	Total lung capacity

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Cardiac Function Before and After Surgery for Pectus Excavatum

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A 2006 meta-analysis concluded that thoracic surgery for pectus excavatum (PE) significantly improves cardiovascular function. However, that analysis was flawed by a high level of heterogeneity in the outcomes and inappropriate methods in 5 of the 8 publications analyzed. Therefore, a search of the published research from 1965 to the present was conducted, and only 5 publications were found that reported studies of cardiac function before and after operation, including 118 patients and 82 unoperated controls. Cardiac function was studied most frequently by echocardiography, despite the limitations imposed by the abnormal anatomy of pectus excavatum, but only studies that did not report cardiac or left ventricular dimensions or output were excluded. Studies using indirect estimates on the basis of oxygen pulse, which depends on several other variables, were not included. No improvements were found in left ventricular size, stroke volume, and cardiac output after surgery in 4 of 5 studies, using radionuclides, 2-dimensional echocardiography, radiographic planimetry, and cardiac output by the Fick method. Only a single study, with volumes calculated by squaring the diameter of the left ventricle from M-mode echocardiography, reported an increase (22%) in left ventricular stroke volume after operation, but that increased (17%) in the investigators' unoperated controls. This and 2 other studies used in this meta-analysis were also included in a meta-analysis conducted by Malek et al. In a fourth study, Malek et al included only the first study that found an improvement, but the final study reported no improvement. In conclusion, there is no reliable documentation of improved cardiac function from thoracic surgery for pectus excavatum. **(Am J Cardiol 2007;99:1762–1764)**

In 1963, Polgar and Koop[1] expressed concern over the number of operations for pectus excavatum (PE) that were being performed and whether they were justified by objective measures of improvement. Forty-three years later, we find 2 published meta-analyses by Malek et al[2,3] of functional outcomes for PE after thoracic surgery that found no improvement in pulmonary data[2] but significant improvement in cardiovascular function.[3] The pulmonary analysis was based on 12 studies with a total of 313 patients, and the tests used were relatively homogenous, satisfying the criteria for a meta-analysis.[4] In contrast, Malek et al's[3] meta-analysis of cardiovascular function included only 8 publications, and the tests were heterogenous and sometimes inappropriate. We performed our own review of the published research and critiqued the citations of Malek et al,[2,3] concentrating on direct cardiac performance rather than derivatives of exercise performance.

Methods

Methods were inadequate in 3 studies[5–7] included by Malek et al,[2,3] because they were derived from only exercise performance. Specifically, oxygen pulse is derived from 2 variables, maximal oxygen consumption and maximal heart rate. Although heart rate may certainly be affected by cardiac status, even at rest, it is not a stand-alone indicator of cardiac performance. Morshuis et al[6] found a dissociation between oxygen consumption and maximal work accomplished. Maximal heart rate and maximum oxygen uptake can be changed independently by motivation and pulmonary function, as well as fitness, and do not provide a specific statement on cardiac status.

Three studies[8–10] of of cardiovascular testing included by Malek et al[2,3] were based on echocardiographic studies. Feigenbaum et al's[11] 2004 textbook on echocardiography warns that the accuracy of left ventricular dimensions and function is subject to anatomic limitations, specifically PE, imposed on conventional echocardiographic windows, a problem that is obvious to any sonographer when attempting a study on a patient with a funnel-shaped precordium. Although we included 2 studies based on echocardiography,[8,9] we excluded 1 of the echocardiographic reports[10] in our synthesis that inferred cardiovascular function from only the right ventricular shape and function and lacked any data on left ventricular stroke volume or cardiac indexes. In short, we challenge the statistical conclusion in Malek et al's[3] report on the improvement of cardiac function because 5 of their 8 studies[5–7,10,11] used inappropriate methods.

Another citation by Malek et al[2,3] that we found inappropriate was a study by Sigalet et al,[9] insofar as a subsequent publication from that group[12] containing more subjects reached the opposite conclusion. All in all, only 3 of the studies cited by Malek et al[2,3] seem to have been appropriate,[8,13,14] and 1 of those[8] was based on only M-mode echocardiography, based on squaring the diameter for volume. However, we have included that study.

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Cardiovascular Function Following Surgical Repair of Pectus Excavatum*

A Metaanalysis

Moh H. Malek, MS; Dale E. Berger, PhD; Terry J. Housh, PhD; William D. Marelich, PhD; Jared W. Coburn, PhD; and Travis W. Beck, MPE

Background: **Despite numerous published reports, there is no consensus in the literature as to whether the surgical repair of the pectus excavatum improves cardiovascular function. As a result, it has been suggested that correction should be considered a cosmetic procedure, and therefore, many health insurance companies have questioned whether the repair of the pectus excavatum improves cardiovascular function and thus are reluctant to authorize the procedure. The purpose of this study was to apply metaanalysis methodology to generate a quantitative synthesis of the effects of surgical repair on cardiovascular function and to test the hypothesis that surgical repair of the pectus excavatum results in significant improvements in cardiovascular function.**

Methods: **Studies were retrieved via computerized literature searches, cross-referencing from original and review articles, and a review of the reference list by a recognized authority in the area of pectus excavatum repair. The inclusion criteria were as follows: (1) reporting quantitative measures of preoperative and postoperative cardiovascular function; (2) published in the English language; (3) indexed between January 1960 and May 2005; (4) reporting the duration between which preoperative and postoperative assessments were conducted; and (5) describing the cardiovascular assessment procedures.**

Results: **A comprehensive search of the literature identified eight studies that met all of the inclusion criteria. These studies, representing 169 pectus excavatum patients, were used for the metaanalysis. Random-effects modeling yielded a mean weighted effect size (ES) for cardiovascular function that was statistically significant (ES, 0.59; 95% confidence interval, 0.25 to 0.92; p = 0.0006).**

Conclusions: **The findings of the present study indicated that surgical repair of the pectus excavatum significantly improves cardiovascular function and contradicts arguments that surgical repair is primarily cosmetic yielding minimal physiologic improvement.**

(CHEST 2006; 130:506–516)

Key words: cardiac anatomy; cardiopulmonary function; chest wall deformity; oxygen uptake; physiology; surgery

Abbreviations: CI = confidence interval; ES = effect size; $\dot{V}O_2max$ = maximal oxygen uptake; τ-$\dot{V}O_2$ = oxygen uptake kinetics

Pectus excavatum (Fig 1) is a relatively common congenital deformity of the chest wall with an incidence of approximately 1 in every 300 to 400 white male births.[1] Although the pathogenesis of pectus excavatum remains unclear, investigators have hypothesized that the deformity results from unbalanced overgrowth in the costochondral regions. As a result, the chest appears concave, and a displaced heart is often palpable on the left mid-axillary line slightly below the armpit. Pectus excavatum occurs more often in male patients than female patients (6:1) and accounts for 90% of congenital chest wall deformities.[2,3] Approximately 40% of pectus excavatum patients are aware of one or more members of their family who have pectus deformities; however, a genetic link has not been established.[3] Despite numerous published reports, there is no consensus in the literature as to whether surgical repair improves cardiovascular function.[1,4–11]

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Review

Pulmonary function following surgical repair of pectus excavatum: a meta-analysis

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Summary

The purpose of this study was to use a meta-analytical technique to examine the efficacy of surgical repair of pectus excavatum on pulmonary function. Studies were retrieved via computerized literature searches, cross-referencing from original and review articles. Inclusion criteria were as follows: (1) reporting quantitative measures of preoperative and postoperative pulmonary function; (2) published in the English language; (3) indexed between January 1960 and September 2005; (4) reporting the duration between which preoperative and postoperative assessments were conducted; and (5) describing the pulmonary assessment procedures. The titles and abstracts of potentially relevant articles were reviewed to determine whether they met the criteria for inclusion. Twelve studies representing 313 pectus excavatum patients met the inclusion criteria and were used for the meta-analysis. Random-effects modeling yielded a mean weighted effect size (ES) for pulmonary function which was statistically nonsignificant (ES = 0.08, 95% CI = −0.20 to 0.35; $P = 0.58$). The findings of the present study indicated that surgical repair of pectus excavatum does not significantly improve pulmonary function. These findings, however, may be a result of testing pulmonary function under conditions in which pectus excavatum does not manifest itself.

Keywords: Chest wall deformity; Lung function; Respiratory physiology; Surgery; Ventilation

1. Introduction

Pectus excavatum is a congenital deformity of the chest wall with an incidence of approximately one in every 300—400 Caucasian male births [1]. This condition is more common than Down syndrome which occurs one in every 600—1000 births [2]. Although the pathogenesis of pectus excavatum remains unclear, investigators have hypothesized that the deformity results from unbalanced overgrowth in the costochondral regions. As a result, the chest appears concave and a displaced heart is often palpable on the left mid-axillary line slightly below the axilla. Pectus excavatum occurs more often in males than females (6:1) and accounts for 90% of congenital chest wall deformities [3,4]. Approximately 40% of pectus excavatum patients are aware of one or more members of their family who have pectus deformities; however, a genetic link has not been established [4]. Despite numerous published reports, there is no consensus in the literature as to whether surgical repair improves pulmonary function [5—12]. Thus, it has been suggested by some researchers that correction of pectus excavatum should be considered a cosmetic procedure [13—15].

Although there have been a number of review articles discussing the effects of surgical repair of pectus excavatum on pulmonary function [16—19], they provide only narrative summaries which rely on statistical significance to differentiate between studies. This approach is potentially misleading because statistical significance in any individual study is influenced by multiple factors including sample size and variance [20—23]. Consequently, narrative summaries do not make optimal use of all available quantitative information. Meta-analysis is a statistical technique for literature synthesis in which quantifiable results from individual studies addressing a common problem are statistically analyzed to arrive at conclusions about a body of research [24]. In the present study, meta-analysis was used to (1) aggregate and compare findings on the effectiveness of surgical repair of pectus excavatum on pulmonary function; (2) summarize and

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Does repair of pectus excavatum improve cardiopulmonary function?

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Abstract

A best evidence topic was written according to a structured protocol. The question addressed was 'Does repair of pectus excavatum (PE) improve cardiopulmonary function?' One hundred and sixty-eight papers were found using the reported search, 19 level III evidence papers and three meta-analyses were relevant. Studies were divided into four groups based on the surgical technique applied and pulmonary and cardiac functions in these groups were analysed. The meta-analyses show conflicting results for improvements in pulmonary and cardiac functions when comparing surgical techniques, while four more recent studies show improved long-term results using the Nuss technique. The best evidence of papers studying the PE repair using the minimally invasive Nuss technique demonstrates a decrease in pulmonary function during the early postoperative period, however, there is a small but significant improvement during the late postoperative period and after bar removal. The best evidence for cardiac function in this group suggests an early improvement that is sustained during further follow-up. The best evidence of papers studying the PE repair using the Ravitch technique shows that pulmonary function decreased during the early postoperative period, however, there is a small but significant improvement during the late postoperative period. The best evidence for cardiac function in this group suggests an early improvement that is sustained during further follow-up. The best evidence of papers studying the PE repair using other techniques (modified Daniel's technique, modified Baronofsky's technique, sterno-costal turn-over technique and sterno-costal elevation technique) or where surgical techniques used were not described (preceding year 1985) suggests that there is no improvement in pulmonary function after surgery. There is some evidence that certain aspects of cardiac function improved after surgery in this group.

Keywords: Pectus excavatum • Nuss • Ravitch • Pectus repair • Cardiac function • Pulmonary function

INTRODUCTION

A best evidence topic was constructed according to a structured protocol as described in *ICVTS* [1].

THREE-PART QUESTION

Does [repair] of [pectus excavatum] improve [cardiopulmonary function]? Search strings were used as below.

[Pectus excavatum] OR [Pectus] and [repair] OR [Surgery] and [cardiopulmonary] OR [cardio respiratory] OR [cardiac function and pulmonary function].

CLINICAL SCENARIO

A 23-year old Caucasian man was referred by his general practitioner with a history of 'funnel chest' since birth. He describes symptoms of increasing breathlessness on exertion. How does pectus excavatum (PE) affect cardiopulmonary function? Does his symptom improve after surgery?

SEARCH STRATEGY

MEDLINE 1948 to present, OLD MEDLINE(R) 1946–1965, HMIC 1979-November 2011, EMBASE 1980–2012 Week 8 were searched via the OVID interface.

SEARCH OUTCOME

Of the 168 results found, studies with quantitative measures of, and including duration between, preoperative and postoperative cardiopulmonary function, published in the English language, indexed from January 1948 till February 2012 and describing the cardiopulmonary assessment procedures were considered. Pulmonary function including any of forced vital capacity, forced expiratory volume measured over 1 s (FEV_1), total lung capacity, vital capacity, residual volume (RV) or maximal oxygen uptake (VO_2 max) and cardiac function assessed using echocardiography, radionuclide assays, cardiac output and cardiac index studies were used as common criteria. Studies not matching all of the above criteria, narrative reviews and expert opinions not including statistical data analysis were excluded.

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Surgical repair of pectus excavatum relieves right heart chamber compression and improves cardiac output in adult patients—an intraoperative transesophageal echocardiographic study

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KEYWORDS:
Pectus excavatum;
Nuss surgery;
Right heart;
Cardiac output;
Transesophageal echocardiography;
Doppler ultrasound

Abstract

BACKGROUND: Cardiac compression in pectus excavatum (PE) deformity and effect of PE surgery on cardiac function in adults have been debated. We examined the effect of PE correction on right heart size and cardiac output.

METHODS: A retrospective evaluation was performed of 168 adult patients who underwent a modified Nuss PE repair with intraoperative transesophageal echocardiography from 2011 to 2014. Seventeen patients with prior PE repair undergoing bar removal acted as controls.

RESULTS: Mean age was 33.0 years (range, 18 to 71 years). There was an increase in right atrium (15.1%), tricuspid annulus (10.9%), and right ventricular outflow tract (6.1%) size after surgery (all $P < .0001$). Right ventricular cardiac output measured in a subset of 42 patients improved by 38%. No change in chamber size or cardiac output occurred before and after bar removal surgery in the control group.

CONCLUSIONS: Surgical correction of PE deformity caused a significant improvement in right heart chamber size and cardiac output.

Pectus excavatum (PE) is a common malformation of the chest wall with posterior depression of the sternum and adjacent costal cartilages. PE may cause physiologic symptoms and impairment by compression of the right heart chambers and limitation of diastolic filling.[1] The cardiac benefits of surgical correction on PE deformity have been debated.[2–15] Most studies report cardiopulmonary functional performance after surgical repair of PE.[2–14]

The authors declare no conflicts of interest.

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Longer term effects of closed repair of pectus excavatum on cardiopulmonary status

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Key words:
VO_2 max;
Exercise stress testing;
Stroke volume;
FEV-1;
Nuss repair

Abstract

Background: The "Nuss" repair is done for correction of moderate to severe pectus excavatum (PE). The long term cardiopulmonary and psychosocial effects of repair are uncertain. The objective of this study was to compare cardiopulmonary function and subjective evaluation of appearance and exercise tolerance pre-bar insertion with post-bar removal.

Methods: All patients underwent preoperative and post-bar (3 month) removal evaluation with complete pulmonary function tests, exercise stress testing, echocardiogram, and self-rated appearance and exercise tolerance scoring. The protocol was approved by the regional ethics board, and all families gave informed consent.

Results: Sixty-seven patients underwent pre and post testing. Preoperative CT index was 4.4±1.3. Cardiopulmonary outcomes, standardized for height and weight, showed significant improvements in FEV-1 as (pre) 81.1±17.0 vs post 89.8±20.5*, FVC: 91.2±18.6 vs 98.9±22.9*, O_2 pulse: 75.8±14.4 vs 80.5±18.3* (each as % predicted). Both the self-ratings of appearance (2.5±0.8 vs 4.4±0.5) and ability to exercise (3.3±0.7 vs 4.3±0.6, scale 1–5) increased significantly. (All data: mean±St Dev, *$p<0.05$)

Conclusions: Closed repair of PE results in improvements in pulmonary and aerobic exercise function and perceived appearance and exercise tolerance. Our data suggest that the impact on appearance and self-perceived well being is greater than the physical effect.

Pectus excavatum is the most common chest wall deformity in children representing >90% of all congenital chest wall deformities [1]. It has an incidence of approximately 1:300 to 1:400 in white males. In sporadic cases, although approximately 40% of patients have a relative with the deformity, no specific genetic link has been established. The pathogenesis is unclear, however it is postulated that the deformity results from an unbalanced overgrowth in the costochondral regions with the lower ribs being more affected [2].

Patients with pectus excavatum frequently complain of psychosocial consequences with a poor self image as well as physical limitations, typically dyspnea on exertion and decreased ability to perform prolonged rigorous activity compared to their classmates [3,4]. These same patients subjectively find an increase in exercise tolerance and improved self image post repair [4–8]. However, despite

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PubMed

Abstract

Full text links

ELSEVIER FULL-TEXT ARTICLE

Ann Thorac Surg. 2013 Jul;96(1):272-8. doi: 10.1016/j.athoracsur.2013.03.034. Epub 2013 May 14.

Normalized cardiopulmonary exercise function in patients with pectus excavatum three years after operation.

Maagaard M[1], Tang M, Ringgaard S, Nielsen HH, Frøkiær J, Haubuf M, Pilegaard HK, Hjortdal VE.

Author information

Abstract

BACKGROUND: During exercise cardiac function is often limited in patients with pectus excavatum. Therefore, we hypothesized that cardiopulmonary exercise function would improve after the Nuss procedure.

METHODS: Seventy-five teenagers (49 patients, 26 controls) were investigated at rest and during bicycle exercise before surgery, and 1 year and 3 years postoperatively (after pectus-bar removal). Echocardiography and lung spirometry were performed at rest. Cardiac output, heart rate, and aerobic exercise capacity were measured using a photoacoustic gas-rebreathing technique during rest and exercise.

RESULTS: Forty-four patients and 26 controls completed 3 years follow-up. Preoperatively, patients had lower maximum cardiac index, mean ± SD, 6.6 ± 1.2 l·min(-1)·m(-2) compared with controls 8.1 ± 1.0 l·min(-1)·m(-2) during exercise (p = 0.0001). One year and 3 years postoperatively, patients' maximum cardiac index had increased significantly and after 3 years there was no difference between patients and controls (8.1 ± 1.2 l·min(-1)·m(-2) and 8.3 ± 1.6 l·min(-1)·m(-2), respectively [p = 0.572]). The maximum oxygen consumption was unchanged. Left ventricular dimensions increased in patients over 3 years; however, no difference was seen between the 2 groups. Preoperatively, patients had lower forced expiratory volume in the first second of expiration (FEV1; 86% ± 13%) as compared with controls (94% ± 10%), p = 0.009. Postoperatively, no difference was found in FEV1 between the 2 groups.

CONCLUSIONS: Before operation, FEV1 and maximum cardiac index were lower in patients compared with healthy, age-matched controls. One year after, both parameters had increased, although only FEV1 had normalized. After 3 years and bar removal, cardiopulmonary function in patients during exercise had normalized.

Comment in

Evidence of normalized cardiopulmonary function after pectus excavatum repair. [Ann Thorac Surg. 2014]
Invited commentary. [Ann Thorac Surg. 2013]

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ORIGINAL ARTICLE

Improved cardiopulmonary exercise function after modified Nuss operation for pectus excavatum

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Abstract

OBJECTIVES: Patients with pectus excavatum have compromised cardiac function during exercise. We hypothesized that the Nuss technique would improve cardiopulmonary function during exercise.

METHODS: We investigated 75 teenagers (49 patients and 26 controls) at rest and during bicycle exercise prior to surgery and 1 year postoperative.

RESULTS: Prior to surgery, patients had a lower cardiac index 6.6 ± 1.1 l/min/m^2 when compared with controls 8.1 ± 1.0 l/min/m^2 during submaximal exercise, $P = 0.0001$. There was no difference in heart rate or increase in heart rate between the two groups. One year after surgery, cardiac index had significantly increased in the pectus group, $P = 0.0054$ although cardiac index was still significantly lower 7.2 ± 1.0 l/min/m^2 when compared with the control subjects (8.5 ± 1.6 l/min/m^2, $P = 0.0008$). Both the patients and the controls increased their VO_2 max during the one-year study period although the controls increased most. Right ventricular diastolic dimension increased in both groups over the one-year study period and left ventricular dimensions increased in the patients. Before operation, the patients had lower forced expiratory capacity FEV_1 86 ± 13% when compared with controls 94 ± 10%, $P = 0.009$. Patients increased FEV_1/forced vital capacity over the one-year long study course although there were no differences between groups.

CONCLUSION: Patients with pectus excavatum have lower cardiac index at submaximal exercise when compared with healthy age-matched controls. Their cardiac index and FEV_1 are increased one year after the modified Nuss operation.

Keywords: Cardiopulmonary exercise • Pectus excavatum • Musculoskeletal disease • Lung function • Stroke index

THORACIC

INTRODUCTION

Pectus excavatum is known to cause symptoms such as fatigue, tachypnoea, discomfort and dyspnoea [1, 2]. Objective signs of compromised cardiopulmonary function are, however, not easily found and despite a vast amount of studies the conclusions are not consistent. Nevertheless, it is generally agreed that the influence of pectus excavatum on cardiorespiratory function is trivial at rest.

During exercise, the situation is different. We have, in a previous paper, found that cardiac index during bicycle exercise is decreased in children with pectus excavatum when compared with age-matched controls [3]. Our study confirmed the findings from the other two studies investigating teenagers with pectus excavatum and control subjects during exercise [4, 5]. The inability to increase stroke volume at higher cardiac output may be due to the shallow thoracic cavity.

The next question is whether surgical correction of pectus excavatum will relieve the symptoms, and whether the observed limitations in cardiopulmonary function during exercise can be reverted. With respect to the resting state, several studies have looked at changes in cardiac [2, 6–10] and pulmonary functions [2, 7–13] after operation for pectus excavatum. Results have shown no change in cardiac function [6, 7] and pulmonary function has varied from no change [11, 12] to slightly decreased [8] function.

Some of the studies also investigated the exercise capacity [2, 7, 8, 11] but they did not measure cardiac function during the exercise. The only study looking at cardiac function during exercise after pectus repair is the one by Peterson *et al*. [14], who investigated 13 patients with pectus excavatum before and 6 months after operation. Using radionuclide measurements of cardiac output and dimensions of the cardiac chambers, they found no change in cardiac output but increased chamber dimensions. The increased chamber dimension could however be explained by the growth of the teenagers between the baseline and the follow-up study.

The technique for surgical correction of pectus excavatum has changed to more minimally invasive techniques since Peterson did his study in the mid 1980's and it is relevant to investigate children who have undergone a less invasive surgical procedure

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Pectus excavatum in a 112-year autopsy series: anatomic findings and the effect on survival

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Index words:
Pectus excavatum;
Autopsy;
Survival;
Comorbid conditions

Abstract

Background/Purpose: The purpose of this study was to determine the frequency of pectus excavatum and associated conditions in a large autopsy series. It also sought to determine whether there were different survival patterns for pectus excavatum patients than for patients without pectus excavatum.

Methods: A computer-assisted search of autopsy files maintained by Johns Hopkins University was conducted, dating from 1889 to 2001. Each patient's Autopsy Pathology Information System report was reviewed for diagnosis and comorbid conditions. To determine whether there were differences in survival patterns, we tested whether pectus excavatum patients survived longer than controls, using a standard epidemiological method. Each patient in the autopsy series was compared with the 2 patients entered in the autopsy database chronologically immediately before and the 2 patients immediately after the case. A Kaplan-Meier survival analysis was conducted.

Results: Pectus excavatum was identified at autopsy in 62 of 50,496 cases. Of these 62 patients, 17 were 65 years or older and appeared to have died of causes unrelated to pectus excavatum, the oldest being 91 years. Twenty-one were between the ages of 14 and 65 years and were found to have coexisting conditions or syndromes. Six were between the ages of 1 and 4 years. One of the 6 died in 1947 because of complications from pectus repair. No autopsied patient with pectus excavatum died between the ages of 5 and 14 years. Eighteen were infants younger than 1 year, and all 18 died because of conditions unrelated to pectus excavatum. There were no reported cases of pectus excavatum before 1947, and the severity of deformity could not be determined from the autopsy data. Survival analysis indicated that pectus excavatum patients had a different survival than the controls. Pectus excavatum patients tended to die earlier ($P = .0001$). However, pectus excavatum patients who survived past the age of 56 years tended to survive longer than their matched controls ($P = .0001$).

Conclusion: Although there were no histological abnormalities noted in the cartilage of the pectus excavatum patient's conditions, pectus excavatum was associated with several connective tissue abnormalities. Analysis is consistent with the theory that this condition can impact survival.

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PubMed

Abstract

Full text links

ELSEVIER FULL-TEXT ARTICLE

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Cardiac function assessed by transesophageal echocardiography during pectus excavatum repair.

Krueger T[1], Chassot PG, Christodoulou M, Cheng C, Ris HB, Magnusson L.

Author information

Abstract

BACKGROUND: We assessed end-diastolic right ventricular (RV) dimensions and left ventricular (LV) ejection fraction by use of intraoperative transesophageal echocardiography before and after surgical correction of pectus excavatum in adults.

METHODS: A prospective study was conducted including 17 patients undergoing surgical correction of pectus excavatum according to the technique of Ravitch-Shamberger between 1999 and 2004. Intraoperative transesophageal echocardiography was performed under general anesthesia before and after surgery to assess end-diastolic RV dimensions and LV ejection fraction. The end-diastolic RV diameter and area were measured in four-chamber and RV inflow-outflow view, and the RV volume was calculated from these data. The LV was assessed by transgastric short-axis view, and its ejection fraction was calculated by use of the Teichholz formula.

RESULTS: The end-diastolic RV diameter, area, and volume all significantly increased after surgery (mean values +/- SD, respectively: 2.4 +/- 0.8 cm versus 3.0 +/- 0.9 cm, $p < 0.001$; 12.5 +/- 5.2 cm(2) versus 18.4 +/- 7.5 cm(2), $p < 0.001$; and 21.7 +/- 11.7 mL versus 40.8 +/- 23 mL, $p < 0.001$). The LV ejection fraction also significantly increased after surgery (58.4% +/- 15% versus 66.2% +/- 6%, $p < 0.001$).

CONCLUSIONS: Surgical correction of pectus excavatum according to Ravitch-Shamberger technique results in a significant increase in end-diastolic RV dimensions and a significantly increased LV ejection fraction.

Comment in

Invited commentary. [Ann Thorac Surg. 2010]

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Publication Types, MeSH Terms

LinkOut - more resources

Pectus carinatum

Thomas J. Desmarais[a,b] *and Martin S. Keller*[a]

Purpose of review
Pectus carinatum has been termed the undertreated chest wall deformity. Recent advances in patient evaluation and management, including the development of nonoperative bracing protocols, have improved the care of children with this condition.

Recent findings
Recent evidence confirms that children with pectus carinatum have a disturbed body image and a reduced quality of life. Treatment has been shown to improve the psychosocial outcome of these patients.

Summary
Patients with pectus carinatum are at risk for a disturbed body image and reduced quality of life. Until recently, treatment required surgical reconstruction. A growing body of literature, however, now supports the use of orthotic bracing as a nonoperative alternative in select patients. This article reviews the current literature and describes the evaluation and management of children with pectus carinatum deformity.

Keywords
chondrogladiolar, chondromanubrial, orthotic bracing, pectus carinatum

INTRODUCTION

Pectus carinatum is the second most common chest wall deformity observed in children. Whereas the more common pectus excavatum deformity has received a great deal of recent attention in the literature due to the associated cardiac and pulmonary dysfunction and alternative surgical options, recent evidence affirms the long held belief that pectus carinatum can lead to significant psychological distress and thus warrants an equally aggressive management approach. Numerous studies have demonstrated the efficacy of both operative repair and nonoperative bracing for correction of pectus carinatum. The authors' current approach to evaluation and management of children with pectus carinatum will be reviewed.

DEFINITIONS

Pectus carinatum is a term used to characterize a range of chest wall deformities defined by anterior protrusion of the sternum and adjacent costal cartilages, and is in distinction to the more common pectus excavatum, which describes chest wall depression deformities. Pectus carinatum deformities can be subclassified into two distinct entities depending on the component of the sternum involved. The chondrogladiolar variant describes protrusion of the gladiolus, or body of the sternum (Figs 1a and 2a). This deformity has also been referred to as 'keel chest'. The chondromanubrial variant describes protrusion of the manubrium, or superior component of the sternum, and has been termed the 'pouter pigeon breast', 'Currarino–Silverman syndrome', 'horseshoe chest', and 'horns of steer'. This deformity can present as either an isolated manubrial protrusion or 'mixed' defect with manubrial protrusion and gladiolar depression (Fig. 3a).

EPIDEMIOLOGY

Pectus carinatum is a relatively common chest wall deformity occurring with a male to female ratio of approximately 4 : 1 [1,2▪]. Two groups have investigated the overall prevalence of both pectus deformities in children. Westphal *et al.* [3], in a cohort of 1332 children aged 11–14 years of age,

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The Calgary protocol for bracing of pectus carinatum: a preliminary report

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Index words:
Pectus carinatum;
External bracing;
Adjustable device

Abstract

Background: The optimal treatment of pectus carinatum (PC) deformities is unclear. We propose a nonoperative approach using a lightweight, patient-controlled dynamic chest-bracing device.

Material and Methods: With ethical approval, 24 patients with PC were treated at the Alberta Children's Hospital between January 1998 and April 2005. There were 6 (25%) females and 18 (75%) males, with a mean age of 12.9 years at the onset of treatment. Treatment involved fitting of a lightweight, patient-controlled chest brace, worn for 23 hours per day (correction phase [CP]) until the convex deformity was corrected. Following correction of the deformity, bracing was reduced to 8 hours per day (maintenance phase) until axial skeletal maturation ceased. Monitoring was done by measurement of the external pectus carinatum protrusion as well as subjective patient and surgeon appraisal of appearance and exercise tolerance.

Results: Nineteen (79.2%) patients have completed initial treatment (mean CP time, 4.3 $\pm$ 2.1 months). There were 3 patients (12.5%) who were noncompliant, and 2 (8.3%) are still in the initial CP phase of therapy. Fourteen (58.3%) patients are presently in maintenance phase, nocturnally braced, and 2 (8.3%) have completed therapy. In patients completing initial treatment, the protrusion pectus carinatum protrusion (pre 22 $\pm$ 6 vs post 6.0 $\pm$ 6.2) and subjective appearance (change + 1.8$\pm$0.4) showed a significant improvement ($P < .001$ for both) with no change in exercise tolerance.

Conclusion: Compressive bracing results in a significant subjective and objective improvement in PC appearance in skeletally immature patients. However, patient compliance and diligent follow up appear to be paramount for the success of this method of treatment. Further studies are required to show the durability of this method of treatment.

Pectus carinatum (PC) is a common pediatric condition, characterized by an idiopathic overgrowth of the costal cartilages resulting in protrusion of the sternum. The severity of this abnormality generally worsens during the growth spurt of adolescence. The overall prevalence of PC is 0.6%; it is more common in boys [1,2]. The cause of PC is unknown;

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Surgical correction of pectus carinatum improves perceived body image, mental health and self-esteem☆

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Pectus carinatum
Body image
Quality of life
Self concept

ABSTRACT

Purpose: The purpose of this study was to assess the effects of surgical correction of pectus carinatum on health-related quality of life and self-esteem.
Methods: Between May 2012 and May 2013, a prospective observational single-center cohort study was conducted on consecutive patients undergoing surgical correction of pectus carinatum at our institution. Patients filled in questionnaires on health-related quality of life and self-esteem before and six months after surgery.
Results: Disease-specific health-related quality of life was improved by 33% (95% CI: 23; 44%) according to responses to the Nuss Questionnaire modified for Adults. The improvement for generic mental health-related quality of life was 7% (95% CI: 3; 12%) in responses to the Short Form-36 Questionnaire. The improvement in self-esteem was 9% (95% CI: 2; 17%) as assessed with the Rosenberg Self-Esteem Scale. A Single Step Questionnaire supported the improvements in health-related quality of life and self-esteem six months postsurgery.
Conclusion: This study confirms positive effects of surgical correction of pectus carinatum on health-related quality of life and self-esteem. Patients were to a greater extent self-satisfied about chest appearance following surgery, indicating this to be a step in the right direction toward improved body image, mental health and self-esteem.

Pectus carinatum (PC) is an anterior chest wall deformity caused by an outward displacement of the sternum and/or an abnormal protrusion of the ribs [1,2]. The deformity becomes often more apparent during early puberty, a period characterized by great physical, social and emotional changes [2,3]. The psychological effects of the disfigurement can be severe and may influence patients' physical, mental and social function [1,2]; also termed Health-Related Quality of Life (HRQoL) [4]. Patients often express body image concerns about the unusual chest contour, and they experience low self-esteem with embarrassment and shame because of their physical appearance [1–3,5]. Defensive camouflaging with poor posture and folded arms and an unwillingness to be seen without a shirt or to participate in sports or social activities is common [3,5]. In the literature, the deformity has shown a tendency to affect cosmetic appearance and impact negatively on patients' HRQoL and self-esteem. Steinmann *et al.* found a significantly impaired body image, reduced mental HRQoL and low self-esteem in 19 patients with PC compared to healthy age-matched subjects [3]. However, the study was only based on preoperative data. To the best of our knowledge, only a single study has previously evaluated patient-reported outcome of surgical correction of PC [6]. Bostanci *et al.* found evaluation of body image and physical appearance significantly improved in 30 patients with PC six months after surgery [6]. Thus, the mental and physical health consequences of surgical correction of PC remain poorly characterized. The purpose of this study was to assess the effects of surgical correction of PC on body image, HRQoL and self-esteem.

1. Materials and methods

1.1. Study design

A prospective observational single-center cohort study was conducted on consecutive patients undergoing surgical correction of PC between May 2012 and May 2013 with six months follow-up.

1.2. Participants

All patients undergoing the modified Ravitch procedure of PC from May 2012 to May 2013 at the Department of Cardiothoracic and Vascular Surgery, Aarhus University Hospital in Denmark were invited to participate [7]. Exclusion criterion was inability to speak and understand Danish.

☆ Preliminary results presented at the 5th Joint Scandinavian Conference in Cardiothoracic Surgery, Aarhus, Denmark, August 22, 2013.

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NICE guidance

Placement of pectus bar for pectus excavatum (also known as MIRPE or the Nuss procedure)

Interventional procedure guidance
Published: 26 August 2009
nice.org.uk/guidance/ipg310

This guidance replaces IPG3.

1 Guidance

This document replaces previous guidance on minimally invasive placement of pectus bar (interventional procedure guidance 3).

1.1 Current evidence on the safety and efficacy of placement of pectus bar for pectus excavatum (also known as MIRPE [minimally invasive repair of pectus excavatum] or the Nuss procedure) is adequate to support its use provided that normal arrangements are in place for clinical governance, consent and audit.

1.2 Placement of pectus bar for pectus excavatum should be carried out only by surgeons with cardiac and thoracic training and experience, who are capable of managing cardiac or liver injury, and where there are facilities for this.

1.3 This procedure should be carried out only by surgeons with specific training in inserting the device, and they should perform their initial procedures with an experienced mentor.

2 The procedure

2.1 Indications and current treatments

2.1.1 Pectus excavatum is the most common congenital deformity of the sternum and anterior chest wall. The cosmetic disfigurement of pectus excavatum may sometimes be accompanied by impaired cardiac or respiratory function.

2.1.2 Surgery may be carried out in mid-to-late childhood, and includes open surgical repair involving subperichondrial resection of abnormal costal cartilages, transverse osteotomy and internal fixation of the sternum (the Ravitch procedure).

2.2 Outline of the procedure

2.2.1 Placement of pectus bar for pectus excavatum is carried out with the patient under general anaesthesia. The procedure is performed through several small incisions on either side of the chest, and is usually carried out under visualisation by thoracoscopy.

2.2.2 After subcutaneous tunnelling, a curved steel (pectus) bar is inserted behind the ribs and sternum with its concavity facing anteriorly. The bar is then rotated through 180° using a 'flipper' device, so that its convexity faces anteriorly, pushing out the sternum and correcting the deformity. Sometimes two bars are used.

2.2.3 Various fixation techniques are used to keep the bars in place, including lateral stabilisers attached to the bars and ribs using wires and/or sutures.

> Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview.

2.3 Efficacy

2.3.1 Data from a UK register for 260 patients recorded cosmetic appearance scores preoperatively (on a scale from 1 [dislike] to 10 [like]) and postoperatively (from 1 [no change] to 10 [perfect]). Of 109 patients with preoperative scores and 119

patients with postoperative scores, the mean scores were 3.1 and 8.4, respectively (mean follow-up 369 days). A case series of 947 patients reported that of 521 patients who had the bar removed and had a follow-up of 2 years, 83% had an 'excellent' cosmetic result, 12% had a 'good' result, 2% had a 'fair' result (method of assessment not stated) and 2% had recurrence of pectus excavatum (absolute figures not stated) (follow-up 1–15 years).

2.3.2 In a survey of 45 patients, the mean patient satisfaction score for postoperative appearance was 4.1 (±0.8) (on a scale from 1 [very dissatisfied] to 5 [extremely satisfied]) at 54-month follow-up. The patients rated their self-esteem preoperatively as 6.3 (±1.2). This score improved to 7.9 (±0.8) after the procedure (on a scale from 1 [very dissatisfied] to 10 [extremely satisfied]) (mean follow-up 54 months). When asked if they would have the operation again, the mean patient score was 9.1 (on a scale from 0 [no] to 10 [yes]).

2.3.3 In a survey of 43 patients who had either the Nuss procedure or the Ravitch procedure, there were no reported differences in health-related quality of life (assessed using the Child Health Questionnaire) or in physical and psychosocial quality of life (assessed using the Pectus Excavatum Evaluation Questionnaire) between the groups (mean follow-up 16 months).

2.3.4 The Specialist Advisers listed the key efficacy outcomes as cosmetic appearance and patient satisfaction.

2.4 Safety

2.4.1 In 2 case series of 167 and 172 patients, each reported 1 case of intraoperative liver perforation. In 2 case series of 167 and 322 patients, each reported 1 case of intraoperative cardiac perforation. A case report described cardiac injury during surgery in all 4 patients resulting in 1 death.

2.4.2 The case series of 167 patients reported 15 cases of intraoperative rupture of the intercostal muscles (in older patients), 10 cases of haemothorax or haematopneumothorax and 7 cases of minor pericardial tears (follow-up not stated).

2.4.3 Data from the UK register reported perioperative adverse events in 9% (24/260) of patients and postoperative adverse events in 19% (49/260) of patients (follow-up 4–2477 days).

2.4.4 In 3 case series, bar displacements required surgical revision in 7% (50/668), 3% (11/322) and 2% (3/167) of patients, respectively (follow-up not stated).

2.4.5 In 4 case series and the UK register, pneumothorax occurred in 55% (369/668), 7% (24/322), 3% (5/172), 9% (15/167) and 2% (6/260) of patients, respectively.

2.4.6 The studies of 668, 322 and 172 patients reported pneumonia in 7, 3 and 3 patients; and pleural effusion in 5, 8 and 3 patients, respectively (follow-up not stated). The studies of 322 and 172 patients and the UK register data for 260 patients reported pericardial effusion in 8, 1 and 1 patients, respectively (timing of events not stated). In the study of 668 patients pericarditis was reported in 6 patients (timing of event not stated). The UK register reported 1 case of perioperative lower lobe collapse and 1 case of persistent air leak.

2.4.7 The retrospective case series of 863 patients reported metal allergies in 2% (19/863) of patients.

2.4.8 The Specialist Advisers listed adverse events as injury to the lungs, heart, mammary artery and liver; pericarditis; pericardial effusion; bar migration; pleural effusion; pneumothorax; haemothorax; infection; osteochondrodystrophy; pain; metal allergy; and anaesthetic complications.

3 Further information

Information for patients

NICE has produced information on this procedure for patients and carers ('Understanding NICE guidance'). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

4 About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions

are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE interventional procedure guidance process.

It updates and replaces NICE interventional procedure guidance 3.

We have produced a summary of this guidance for patients and carers. Information about the evidence it is based on is also available.

Changes since publication

6 January 2012: minor maintenance.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Accreditation

CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject **Surgical Treatment for Chest Wall Deformities (Pectus Excavatum/Carinatum and Poland Syndrome)**

Effective Date 3/15/2009
Next Review Date 3/15/2010
Coverage Policy Number 0309

Table of Contents

Hyperlink to Related Coverage Policies

Breast Reconstruction Following Mastectomy or Lumpectomy
Cardiopulmonary Exercise Testing (CPET)

INSTRUCTIONS FOR USE

*Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2009 CIGNA*

Coverage Policy

Coverage for surgical repair of chest wall deformities is dependent upon benefit plan language and may be subject to the provisions of a cosmetic and/or reconstructive surgery benefit and may be governed by state and/or federal mandates. Under many benefit plans, surgery for chest wall deformities is not covered when performed solely for the purpose of improving or altering appearance or self-esteem or to treat psychological symptomatology or psychosocial complaints related to one's appearance. Please refer to the applicable benefit plan document to determine benefit availability and the terms, conditions and limitations of coverage.

If coverage for surgical repair of chest wall deformities is available, the following conditions of coverage apply.

CIGNA covers surgical repair of severe pectus excavatum as medically necessary when imaging studies (e.g., computerized tomography [CT] scans, radiographs) confirm a pectus index (i.e., Haller index) greater than 3.25 and EITHER of the following criteria is met:

- Pulmonary function studies demonstrate at least a moderately severe restrictive lung defect.
- Cardiac imaging (e.g., echocardiography, stress echocardiography, magnetic resonance imaging [MRI]) demonstrates findings consistent with external compression.

CIGNA covers surgical repair of pectus carinatum as medically necessary when there is documented evidence of significant physical functional impairment (e.g., cardiac or respiratory insufficiency), and the procedure is expected to correct the impairment.

CIGNA covers the surgical repair of a chest deformity associated with Poland syndrome as medically necessary when rib formation is absent.

Under many benefit plans, CIGNA does not cover breast reconstruction procedures performed in association with surgical repair of a chest wall deformity for Poland syndrome because they are considered cosmetic in nature and not medically necessary. Such reconstruction procedures include, but are not limited to the following:

- breast reconstruction with latissimus dorsi flap or other technique
- mastopexy
- mammoplasty with or without prosthetic implant
- nipple/areolar reconstruction
- breast reconstruction with tissue expander
- revision of reconstructed breast
- insertion of breast prosthesis
- reconstructive surgery to produce a symmetrical appearance

General Background

The thorax (i.e., chest cavity) is a rigid structure that protects the thoracic organs and supports the upper extremities. Abnormalities of the chest wall can lead to restrictive pulmonary disease, impaired respiratory muscle strength, and decreased ventilatory performance in response to physical stress (Boas, 2004). In many cases however, cosmetic complaints are associated with chest wall abnormalities. Generally, severe chest wall deformities result in physiologic impairment and associated functional limitations, such as activity intolerance related to cardiac or respiratory impairment. Symptoms resulting from the abnormality may include mild to moderate exercise limitation, respiratory infections, and asthmatic symptoms. Moreover, the deformity may place physiological restrictions on the patient and result in decreased stamina and endurance.

Commonly reported chest wall deformities include pectus excavatum (PE), pectus carinatum (PC) and Poland syndrome. While pectus excavatum and carinatum may occur as isolated abnormalities, they may be associated with Marfan syndrome, congenital heart disease and scoliosis.

Pectus Excavatum
PE, also referred to as a sunken chest or funnel chest, is the most common congenital chest wall deformity, occurring in approximately one in 400 births. The deformity may be deeper on the right side than on the left and result in a rotation of the sternum. It is usually diagnosed within the first year of life, with wide variations in the degree of sternal depression. During periods of rapid bone growth (e.g., puberty), the appearance of the chest may worsen and symptoms may develop. Moderate to severe deformities may displace the heart into the left chest, decreasing stroke volume and cardiac output. Chest deformities may also depress the sternal volume, adversely affecting the flow of air in and out of the lungs. Symptoms may include fatigue, dyspnea, chest discomfort and palpitations with mild exercise. The body generally compensates by increasing the heart rate with activity to overcome the decreased cardiac output and by more rapid, shallow breathing to compensate for the respiratory deficit. Scoliosis, congenital heart disease and functional heart murmurs can also be associated with PE.

Pectus Carinatum
PC (i.e., pigeon breast or chicken breast) is a congenital chest deformity characterized by an anterior protrusion deformity of the sternum and costal cartilages. Although this condition also affects males more frequently than females (4:1), it occurs less frequently than PE. PC is typically not confirmed until after the growth spurts of early adolescence. This deformity produces a rigid chest and, while symptoms are uncommon, it may result in inefficient respiration as a result of the restrictive chest formation. Three types of PC-related defects have been identified in the literature:

- anterior displacement of the body of the sternum and symmetrical concavity of the costal cartilages
- lateral depression of the ribs on one or both sides of the sternum
- the pouter pigeon breast (the least common of the three): a defect that consists of an upper or chondromalacial prominence with protrusion of the manubrium and depression of the sternal body

The degree of physiological impairment is related to the degree of chest deformity. Patients with PC may develop symptoms as a result of restricted air exchange; complete expiration of air from the lungs may not occur. In addition, pain may result from the secondary pressures that develop from the overgrowth of cartilage. Other conditions that may be associated with PC include frequent respiratory infections, asthma, rickets and cardiac changes.

Poland Syndrome
Poland syndrome (i.e., Poland's anomaly, Poland's syndactyly), a rare congenital disorder, is associated with lateral depression of the ribs on one or both sides of the sternum. The right side of the body is affected twice as often as the left, .When the anomaly occurs on the left side of the body, the heart and lungs are vulnerable, because they may be covered only by skin, fascia and pleura (Rush, Ginsberg, 1999). Although the anomaly is associated with a wide range of malformations, the condition is characterized by absence or hypoplasia of the pectoralis major muscle, absence or hypoplasia of the pectoralis minor muscle, absence of costal cartilages, hypoplasia of the breast and subcutaneous tissue, and a variety of hand and upper-extremity anomalies. In cases of severe cartilage deficiency, patients may develop lung hernia and paradoxical respiratory motion. In less severe cases, patients may develop a simple flattening of the anterior chest wall.

Diagnosis and Evaluation
There is controversy regarding whether there is abnormal cardiopulmonary function in patients with chest wall deformities, particularly PE. When testing, various factors may affect cardiopulmonary function including the severity of the deformity, the patient's age, and associated conditions, whether the tests are done supine or erect, and whether the tests are done at rest or during exercise (Goretsky, et al., 2004). Cardiac effects associated with PE generally include decreased cardiac output, mitral valve prolapse and arrhythmias; pulmonary effects associated with PE generally include restrictive lung disease, atelectasis, and paradoxical respiration. Patients with PC are usually asymptomatic; however the deformity may be associated with other conditions such as mitral valve disease, Marfan's syndrome, and scoliosis.

The severity of the chest wall abnormality is dependent upon the depth, symmetry and width of the deformity. Chest radiographs are commonly used to determine the degree of chest wall deformity. Plain anteroposterior and lateral radiographs may be used to determine the Haller index. In addition, cross-sectional imaging such as computerized tomography (CT) scans and magnetic resonance imaging (MRI) are used to evaluate the degree of cardiac compression, pulmonary compression, and cardiac displacement. CT scan ratios that reveal transverse to AP diameter of greater than 3.25 are considered significant for pectus excavatum. A normal chest has an index of 2.5 (Malek, et al., 2003; Fonkalsrud, 2004). Echocardiography and/or electrocardiography may also be used to evaluate cardiac status. Respiratory status can be determined with the use of pulmonary function studies. In some cases, pulmonary function studies may reveal a restrictive pattern (incomplete lung expansion) and a subsequent decrease in pulmonary volume and reserve. The forced expiratory volume (in one second) (FEV_1), forced vital capacity (FVC), and total lung capacity (TLC) are reduced while the ratio of FEV_1/FVC may be normal or increased in the presence of restrictive airway disease.

The diagnosis of Poland syndrome is usually obtained by clinical exam. Chest wall abnormalities and determining the presence of latissimus dorsi muscles may require CT scans; chest radiographs may be utilized to evaluate rib formation.

Surgical Treatment
Indications for surgical correction are controversial and vary widely. Surgical repair is offered primarily as a method of improving cosmesis and psychological factors but may be necessary to improve cardiopulmonary function in some patients, as the disfigurement may be accompanied by physiologic impairment.

Pectus Excavatum/Pectus Carinatum: If patients with severe deformities do not undergo surgical repair in childhood, their symptoms will likely worsen in adulthood. If surgical repair is performed at an early age, it has been reported there is a high recurrence rate due to periods of rapid bone growth (Fonkalsrud, 2004). While the

optimal age for surgical repair is generally between the ages of 11 and 18 years, each case must be reviewed individually for the presence of impaired cardiopulmonary symptoms. In some cases, surgery may be performed in adults to correct pectus deformities. Adults who have uncorrected PE deformity and experience symptoms of activity limitation may undergo surgical repair with low morbidity, short-term limitation of activities and improvement of symptoms (Fonkalsrud, 2003).

Surgery for PE may be performed using any of several techniques, including a sternal osteotomy (i.e., a modified osteotomy that involves supporting, removing and repositioning the sternum) or implantation of a Silastic mold in the subcutaneous space to fill the defect without altering the thoracic cage. Surgical correction often employs a metal bar behind the sternum; the bar may be removed in one to two years, after remolding has occurred. The standard surgical procedure is the open Ravitch procedure, which involves extensive dissection, cartilage resection and sternal osteotomy. More recently, minimally invasive techniques, such as the Nuss procedure (i.e., a minimally invasive repair of pectus excavatum [MIRPE]), have been utilized that involve the insertion of a convex steel bar beneath the sternum through small thoracic incisions. These recently developed minimally invasive methods do not require cartilage resection or osteotomy. Another method of correction currently being investigated involves placing a magnet on the sternum (breastbone) and then applying an external magnetic force that will pull the sternum outward gradually. This method has been referred to as Magnetic Mini-Mover Procedure. Theoretically, this method applies constant outward force on the deformed cartilage with the use of magnetic forces in order to produce biologic reformation of cartilage and correction of the chest wall deformity. A magnet is implanted on the sternum in an outpatient procedure and is pulled outward by way of an external device molded to the patient's anterior chest wall (National Institutes of Health, [NIH], NCT00466206).

Goretsky et al. (2004) reported on their experience with surgical correction of chest wall deformities and identified criteria used to demonstrate severe PE and the need for surgical repair, which requires two or more of the following:

- a Haller CT index greater than 3.25
- pulmonary function studies that indicate restrictive or obstructive airway disease
- a cardiology evaluation, where the compression is causing murmurs, mitral valve prolapse, cardiac displacement, or conduction abnormalities on the echocardiogram or EKG
- documentation of progression of the deformity with associated physical symptoms other than isolated concerns of body image
- a failed Ravitch procedure
- a failed minimally invasive procedure

For correction or improvement of PC, authors recommend bracing to exert pressure on the anteroposterior direction. More specifically, bracing may be utilized for skeletally immature children with mild deformities; however, the candidate must be motivated to wear the brace (Goretsky, et al., 2004). If unsuccessful, bracing does not preclude surgery. The initial surgical repair for PC involves removing the affected cartilages and mobilizing the skin and pectoralis muscle flaps. To straighten the sternum, any one of the following surgeries may be performed:

- an osteotomy
- a subperichondrial resection of the involved costal cartilages
- a wedge-shaped osteotomy in the anterior sternal plate

Poland Syndrome: Patients with Poland syndrome typically present for surgical reconstruction to improve physical appearance and correct breast asymmetry. Surgical procedures involving the breast and muscles to achieve symmetry are considered cosmetic since there is no significant impairment being corrected. Patients who present with absent ribs are also considered candidates for surgical repair (Townsend, 2004). In such cases, operative reconstruction may eliminate paradoxical motion, improving respiratory impairment. For more severe conditions, reconstructive surgery also provides protection of the underlying heart and lung structures. While there are a variety of surgical techniques to correct the deformity, a common approach is to use the latissimus dorsi muscle with autologous rib grafts to reconstruct the chest wall.

Surgical treatment of Poland Syndrome often consists of reconstruction of the breast and nipple on the affected side by a plastic surgeon, in addition to surgical repair of the chest wall muscles and hypoplastic bone. Surgery is performed early (approximately age 13) in males, however, in females, reconstructive surgery is often deferred until breast development is complete. If there are rib abnormalities and paradoxical motion, the rib grafts or other chest wall stabilization may occur before breast development is complete. Generally, reconstruction of the breast involves tissue expansion, placement of permanent breast implants and may involve myocutaneous or latissimus dorsi flaps if there is an associated anomaly of the pectoral muscle. Nipple-areolar reconstruction is generally performed at a later stage. Consequently, for patients with Poland syndrome, treatment provided before complete breast development may involve the use of tissue expanders in the affected side which can be inflated periodically to match development of the unaffected breast. Expanders allow for tissue expansion and accommodation of a permanent implant and latissimus muscle upon completion of breast development. Once breast development is complete, the expander is removed and a permanent prosthesis is inserted and breast reconstruction is performed.

Surgical repair of the chest wall includes the reconstruction of the pectoral muscles and resection of deformed cartilages. This repair typically involves muscle transfers and/or flaps to match normal development of the unaffected side, reconstruction of the axillary line, and correction of infraclavicular flattening. If necessary, reconstruction of the rib cage may be performed at this time with autologous rib grafts.

Literature Review
Several studies have been published in the peer-reviewed scientific literature evaluating surgical repair of chest wall deformities. Many studies evaluate and report on the methods of surgical repair, improved cosmetic outcome, and the impact of PE or PC on cardiopulmonary function. Evidence primarily consists of meta-analyses, retrospective reviews, case series, cross- comparison studies and prospective trials. Data suggesting improvement in cardiovascular and/or pulmonary function and activity tolerance after surgical repair has been reported in some of the studies (Jaroszewski, Fonkalsrud, 2007; Kubiak, et al., 2007; Lawson, et al., 2005; Bawazir, et al., 2005; Fonkalsrud and Anselmo, 2004; Haller and Loughlin, 2000; Fonkalsrud, et al., 1994). Outcome measures of these studies generally include total lung capacity (TLC), functional residual capacity (FRC), vital capacity,(VC), expiratory flow rate (EFR), and maximum expiratory flow rate (MEFR), exercise tolerance and endurance typically measured prior to surgery, immediately following surgery and three to six months postoperatively.

Recently, Johnson and colleagues (2008) conducted a meta-analysis to determine the effect surgical correction of pectus excavatum had on pulmonary function, cardiac output and exercise data. The authors analyzed 19 studies and concluded there was substantial evidence to support total lung capacity decreases after the Ravitch procedure; there was evidence supporting a modest increase in forced expiratory volume after bar removal (Nuss procedure); and there was evidence to suggest stroke volume increased after the Ravitch procedure (although it was not conclusive).There was no evidence repair of PE improved exercise capacity. A meta-analysis published by Guntheroth and Spiers (2007) assessed whether or not thoracic surgery for PE significantly improved cardiovascular function and reported that the studies they reviewed were flawed by inadequate methods and failed to show improvement in cardiac function after thoracic surgery for PE. Nonetheless, Malek et al. (August 2006) published the results of a meta-analysis (some of the studies overlapped with the Guntheroth publication) suggesting surgical repair of pectus excavatum significantly improved cardiovascular function. Additionally, this same group of authors (Malek, et al., 2006b) reported the results of a meta-analysis assessing the efficacy of pectus excavatum repair on pulmonary function, using similar methods, and concluded surgical repair does not significantly improve pulmonary function. Overall, the results of the meta-analysis lend some support that surgical correction improves cardiovascular function.

There is no consensus among authors regarding the degree of cardiopulmonary impairment, if any, that is associated with these anomalies. Although the effects of surgery on exercise tolerance are not clearly established —some of the published results are variable and may be considered controversial — authors have reported improvement in cardiopulmonary functioning postoperatively for treatment of PE and PC. Improvement is generally seen only with increased periods of exercise and not with routine pulmonary function testing at rest. Patient selection criteria are dependent upon the degree of deformity and degree of activity intolerance demonstrated through cardiopulmonary testing. Overall, the reported outcomes may be considered controversial; differences among studies may be related to patient selection criteria, the degree of severity of the deformity, the surgical technique utilized, and future growth effects.

Professional Societies/Organizations
A review of current professional society recommendations and policy statements from the American Thoracic Society and the American Academy of Pediatrics does not confirm existence of established guidelines for the treatment of congenital chest wall deformities.

Regarding breast augmentation in teenagers, the American Society of Plastic Surgeons (ASPS) has a policy statement that supports breast augmentation for reconstructive purposes related to congenital defects (ASPS, 2004).

Regarding cardiopulmonary exercise testing (CPET) with ventilatory gas analysis, the American College of Cardiology/American Heart Association (ACC/AHA) (Gibbons, et al., 2002), and the American Thoracic Society/American College of Chest Physicians (ATS/ACCP) (ATS/ACCP, 2002) have established indications and guidelines for exercise testing; however, these recommendations do not address the utility of CPET for chest deformities such as PE, PC or those associated with Poland syndrome.

Summary
Congenital chest wall deformities may result in functional limitations such as activity intolerance related to cardiac or respiratory impairment. Some patients report symptoms which include mild to moderate exercise limitation, respiratory infections, and asthmatic conditions. In many cases, the deformity does not lead to a functional impairment, and treatment is focused on improving appearance. Some of the evidence in the published, peer-reviewed scientific literature indicates that surgical repair for PE or PC does improve postoperative cardiopulmonary functioning and exercise tolerance and is therefore considered a viable treatment option for selected candidates with severe deformity and functional impairment.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT®* Codes	Description
21740	Reconstructive repair of pectus excavatum or carinatum; open
21742	Reconstructive repair of pectus excavatum or carinatum; minimally invasive approach (Nuss procedure), without thoracoscopy
21743	Reconstructive repair of pectus excavatum or carinatum; minimally invasive approach (Nuss procedure), with thoracoscopy

ICD-9-CM Diagnosis Codes	Description
738.3	Acquired deformity of chest and rib
754.81	Pectus excavatum
754.82	Pectus carinatum
754.89	Other specified nonteratogenic anomalies

Not Medically Necessary/Cosmetic/Not Covered:

CPT®* Codes	Description
19316†	Mastopexy
19324†	Mammaplasty, augmentation; without prosthetic implant
19325†	Mammaplasty, augmentation; with prosthetic implant
19340†	Immediate insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19342†	Delayed insertion of breast prosthesis following mastopexy, mastectomy or in

	reconstruction
19350†	Nipple/areola reconstruction
19357†	Breast reconstruction, immediate or delayed, with tissue expander, including subsequent expansion
19361†	Breast reconstruction with latissimus dorsi flap, without prosthetic implant
19364†	Breast reconstruction with free flap
19366†	Breast reconstruction with other technique
19367†	Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM), single pedicle, including closure of donor site;
19368†	Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM), single pedicle, including closure of donor site; with microvascular anastomosis (supercharging)
19369†	Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM), double pedicle, including closure of donor site
19380†	Revision of reconstructed breast

HCPCS Codes	**Description**
L8600†	Implantable breast prosthesis, silicone or equal
S2066†	Breast reconstruction with gluteal artery perforator (GAP) flap, including harvesting of the flap, microvascular transfer, closure of donor site and shaping the flap into a breast, unilateral
S2067†	Breast reconstruction of a single breast with "stacked" deep inferior epigastric perforator (DIEP) flap(s) and/or gluteal artery perforator (GAP) flap(s), including harvesting of the flap(s), microvascular transfer, closure of donor site(s) and shaping the flap into a breast, unilateral
S2068†	Breast reconstruction with deep inferior epigastric perforator (DIEP) flap or superficial inferior epigastric artery (SIEA) flap, including harvesting of the flap, microvascular transfer, closure of donor site and shaping the flap into a breast, unilateral

†Note: Cosmetic in nature and not medically necessary when performed in association with surgical repair of chest wall deformity for Poland syndrome.

ICD-9-CM Diagnosis Codes	**Description**
	Multiple/Varied

References

1. American Society of Plastic Surgeons (ASPS). Breast augmentation in teenagers. Policy statement. Approved 2004 Dec. Accessed January 25, 2008. Available at URL address: http://www.plasticsurgery.org/medical_professionals/health_policy/Policy-Statements.cfm

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3. American Society of Plastic Surgeons (ASPS). Breast reconstruction for deformities unrelated to cancer treatment. Recommended insurance coverage criteria. September 2004. Accessed January 29, 2008. Available at URL address:

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	3/15/2008	0309	Surgical Treatment for Chest Wall Deformities (Pectus Excavatum/Carinatum and Poland Syndrome)

Close

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Pectus Excavatum and Poland's Syndrome: Surgical Correction

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Number: 0272

Policy

I. Aetna considers surgical repair of severe pectus excavatum deformities that cause functional deficit medically necessary when done for medical reasons in members who meet all of the following criteria:

A. Well-documented evidence of complications arising from the sternal deformity. Complications include but may not be limited to:

- Asthma
- Atypical chest pain
- Cardiopulmonary impairment documented by respiratory and/or cardiac function tests
- Exercise limitation
- Frequent lower respiratory tract infections; *and*

B. An electrocardiogram or echocardiogram has been done if a heart murmur or known heart disease is present to define the relationship of the cardiac problem to the sternal deformity; a*nd*

C. A CT scan of the chest demonstrates a pectus index, derived from dividing the transverse diameter of the chest by the anterior-posterior diameter, greater than 3.25.

Aetna considers surgical repair of pectus excavatum cosmetic when criteria are not met.

II. Aetna considers surgical reconstruction of musculo-skeletal chest wall deformities associated with Poland's syndrome that cause functional deficit medically necessary (also see CPB 0185 - Breast Reconstructive Surgery).

III. Aetna considers bracing and surgical procedures to correct pectus carinatum cosmetic because this deformity does not cause physiologic disturbances from compression of the heart or lungs.

IV. Aetna considers the following interventions for the treatment of pectus excavatum experimental and investigational because their effectiveness has not been established;

- The magnetic mini-mover procedure
- The vacuum bell
- Dynamic Compression System

Background

Pectus excavatum (PE) is often a cosmetic defect, but it may have varied anatomic and symptomatic presentations. There is no conclusive evidence supporting the existence of a functional component whose physiological basis can be consistently defined. Until recently, the indications for surgery in patients with PE were based solely on clinical judgment because the extensive literature on PE demonstrates that there is a discordance between patients' subjective assessment of shortness of breath and objective measures of cardiorespiratory function. In more recent years, the judgment of when to proceed with surgery has been made more objective by following the pectus index criteria advocated by Haller for surgical intervention. Computed tomography (CT) scans used in patients being evaluated for surgery document more clearly the severity of the fore-shortening of the antero-posterior diameter of the chest, the degree of cardiac compression and displacement, the degree of lung compression and other unexpected problems. It clarifies the need for operation by showing the dramatic internal morbidity of what is often portrayed as a "cosmetic" deformity.

As originally described by Sir Alfred Poland, Poland's syndrome consists of absence or hypoplasia of the pectoralis major and minor muscles, hypoplasia or absence of nipple and breast, hypoplasia of subcutaneous fat, absence of axillary hair, and partial absence of the upper costal cartilages and portions of ribs, usually the 2nd, 3rd, and 4th. The absence of the sternal head of the pectoralis major muscle is considered the minimal expression of this syndrome (Wilhelmi and Cornette, 2002). Brachysyndactyly, ectrodactyly, and ectromelia are frequently described associations.

In children with very severe deformity, staged procedures involving split rib grafts from the contralateral side combined with Teflon felt or Marlex mesh have been advocated. This results in a stable chest wall, abolition of paradoxical movement, and protection of the subjacent viscera. In the absence of the pectoralis major and with deficient breast and subcutaneous tissue, the chest is still visibly asymmetric. As soon as the asymmetry becomes a problem for the adolescent female patient, a round tissue expander can be placed beneath the pectoralis muscle and hypoplastic breast through a transaxillary incision, to avoid scars on the breast itself. The prosthesis is then inflated at appropriate intervals to maintain symmetry until development of the opposite breast stabilizes, at which time the expander can be replaced with a prosthetic mammary implant or an autologous soft-tissue transfer using pedicled myocutaneous flaps.

Schier et al (2005) described their experience in using a vacuum to pull the abnormal chest wall outward in patients with PE. A suction cup was used to create a vacuum at the chest wall. A patient-activated hand pump was used to reduce pressure up to 15 % below atmospheric pressure (atm). The device was used by 60 patients (56 males and 4 females), aged 6.1 to 34.9 years (median of 14.8 years), for a minimum of 30 mins, twice-daily, up to 5 hours per day (median of 90 mins). Patient progress was documented using photography, radiography, and plaster casts of the defect. In 14 children this method was used during the Nuss procedure to enlarge the retrosternal space for safer passage of the introducer. Follow-up occurred between 2 and 18 months (median of 10 months). Computed tomographic scans

showed that the device lifted the sternum and ribs within 1 to 2 mins; this was confirmed thoracoscopically during the Nuss procedure. The suction cup enlarged the retrosternal space for safer passage of the introducer. Initially, the sternum sank back after few minutes. After 1 month, an elevation of 1 cm was noted in 85 % of the patients. After 5 months, the sternum was lifted to a normal level in 12 patients (20 %) when evaluated immediately after using the suction cup. All patients exhibited moderate subcutaneous hematoma, although the skin was not injured. One patient suffered from transient paresthesis in the right arm and leg; 2 patients experienced orthostatic disturbances during the first application of the suction cup. There were no other complications. In patients with PE, application of a vacuum effectively pulled the depressed anterior chest wall forward. The initial results proved dramatic, although it is not yet known how much time is required for long-term correction. The authors concluded that this vacuum method holds promise as a valuable adjunct treatment in both surgical and non-surgical correction of PE.

Haecker and Mayr (2006) examined the benefits of conservative treatment of patients with PE by means of the vacuum bell. A suction cup is used to create a vacuum at the anterior chest wall. A patient-activated hand pump is used to reduce the pressure up to 15 % below atm. Three different sizes of vacuum bell exist that were selected according to the individual patient's age. When creating the vacuum, the lift of the sternum was obvious and remained for a different time period. The device should be used for a minimum of 30 mins (twice-daily), and may be used up to a maximum of several hours daily. Presently, a 12- to 15-month course of treatment is recommended. In addition, the device was used intra-operatively during the minimally invasive repair (MIRPE) procedure to enlarge the retrosternal space to ensure safer passage of the introducer in a few patients. A total of 34 patients (31 males and 3 females), aged 6 to 52 years (median of 17.8 years) used the vacuum bell for 1 to maximum 18 months (median of 10.4 months). Follow-up included photography and clinical examination every 3 months. Computed tomographic scans showed that the device lifted the sternum and ribs immediately. In addition, this was confirmed thoracoscopically during the MIRPE procedure. After 3 months, an elevation of more than 1.5 cm was documented in 27 patients (79 %). After 12 months, the sternum was lifted to a normal level in 5 patients (14.7 %). Relevant side effects were not noted. The authors concluded that the vacuum bell has proved to be an alternative therapeutic option in selected patients with PE. Moreover, they stated that while the initial results proved to be dramatic, long-term results are so far lacking, and further evaluation and follow-up studies are necessary.

Haecker (2011) provided additional data on the 2006 trial by Haecker and Mayr; but the conclusion remained unchanged. A total of 133 patients (110 males and 23 females) aged from 3 to 61 years (median of 16.21 years) used the vacuum bell for 1 to a maximum of 36 months. Computed tomographic scans showed that the device lifted the sternum and ribs immediately. In addition, this was confirmed thoracoscopically during the MIRPE procedure. A total of 105 patients showed a permanent lift of the sternum for more than 1 cm after 3 months of daily application; 13 patients stopped the application and underwent MIRPE. Relevant side effects were not noted. The authors concluded that the vacuum bell has proved to be an alternative therapeutic option in selected patients suffering from PE. The initial results proved to be dramatic, but long-term results are so far lacking, and further evaluation and follow-up studies are necessary.

Harrison et al (2007) noted that correction of PE results in measurable improvement in lung capacity and cardiac performance as well as improved appearance and self-image. The Nuss and modified Ravitch approaches attempt to correct the chest wall deformity by forcing the sternum forward in 1-step and holding it in place using a metal strut. The initial operation requires extensive manipulation under general anesthesia and results in post-operative pain, requiring hospitalization and regional anesthesia. Pain and disability may last for weeks. Both procedures are expensive. A better principle would be a gradual bit-by-bit repair via small increments of pressure applied over many months. These researchers

developed the magnetic mini-mover procedure (3MP) and applied this strategy to correct PE. The procedure uses magnetic force to pull the sternum forward. An internal magnet implanted on the sternum and an external magnet in a non-obtrusive custom-fitted anterior chest wall orthosis produce an adjustable outward force on the sternum. Outward force is maintained until the abnormal costal cartilages are remodeled and the pectus deformity is corrected. These investigators implanted a magnet in human skeletons and measured the force applied to the sternum when the distance between the internal and external magnets was varied in increments. With the 2 magnets 1 cm apart, the outward force was adequate to move the sternum at least 1 cm. They also mapped the magnetic field in the 2-magnet configuration and found that maximum field strengths at the surface of the heart and at the outer surface of the orthosis were at safe levels. The authors concluded that the 3MP allows correction of PE by applying magnetic force over a period of months. Crucial questions raised during the design, re-design, and simulation testing have been satisfactorily answered, and the authors have received a Food and Drug Administration (FDA) Investigation Device Exemption (G050196/A002) to proceed with a phase I to II clinical trial.

Harrison et al (2012) performed a pilot study of safety, probable efficacy, and cost-effectiveness of 3MP. A total of 10 otherwise healthy patients, aged 8 to 14 years, with severe pectus excavatum (pectus severity index [PSI] greater than 3.5) underwent 3MP treatment (mean of 18.8 +/- 2.5 months). Safety was assessed by post-implant and post-explant electrocardiograms and monthly chest x-rays. Efficacy was assessed by change in pectus severity index as measured using pre-treatment and post-treatment computed tomographic scan. Cost of 3MP was compared with that of standard procedures. The 3MP device had no detectable ill effect. Device weld failure or mal-positioning required revision in 5 patients. Average wear time was 16 hrs/day. Pectus severity index improved in patients in the early or mid-puberty but not in patients with non-compliant chest walls. Average cost for 3MP was $46,859, compared with $81,206 and $81,022 for Nuss and Ravitch, respectively. The authors concluded that the 3MP is a safe, cost-effective, outpatient alternative treatment for pectus excavatum that achieves good results for patients in early and mid-puberty stages.

Ji and Luan (2012) reviewed the current development in therapy of congenital funnel chest. The main therapies for congenital funnel chest are thoracoplasty (Ravitch sternum elevation procedure and minimal invasive Nuss procedure) and prosthesis implantation. The magnetic mini-mover procedure and the vacuum bell are still in the research phase.

An UpToDate review on “Pectus excavatum: Treatment” (Mayer, 2013) states that “Currently, surgical correction for PE is done with either the modified Ravitch procedure (open resection of the subperichondrial cartilage and sternal osteotomy, with placement of an internal stabilizing device), or the Nuss procedure (minimally invasive technique in which a curved bar is inserted to lift the sternum; the bar is removed about two years later)”.

An UpToDate review on “Pectus carinatum” (Nuchtern and Mayer, 2014) states that “In more than 90 percent of patients, pectus carinatum deformity is first noted during early adolescence, and it often worsens dramatically during the adolescent growth spurt. The defect does not resolve spontaneously. The vast majority of patients have no physiologic symptoms, and cosmetic appearance is the primary concern …. The decision of whether to treat depends on the severity of the defect, and the patient and family's level of concern”.

Johnson et al (2014) compared outcome measures of current PE treatments, namely the Nuss and Ravitch procedures, in pediatric and adult patients. Original investigations that stratified PE patients based on current treatment and age (pediatric = 0 to 21 years; adult 17 to 99 years) were considered for inclusion. Outcome measures were: operation duration, analgesia duration, blood loss, length of stay (LOS), outcome ratings, complications, and percentage requiring reoperations. Adult implant patients

(18.8 %) had higher re-operation rates than adult Nuss or Ravitch patients (5.3 % and 3.3 %, respectively). Adult Nuss patients had longer LOS (7.3 days), more strut/bar displacement (6.1 %), and more epidural analgesia (3 days) than adult Ravitch patients (2.9 days, 0 %, 0 days). Excluding pectus bar and strut displacements, pediatric and adult Nuss patients tended to have higher complication rates (pediatric -- 38 %; adult -- 21 %) compared to pediatric and adult Ravitch patients (12.5 %; 8 %). Pediatric Ravitch patients clearly had more strut displacements than adult Ravitch patients (0 % and 6.4 %, respectively). These results suggested significantly better results in common PE surgical repair techniques (i.e., Nuss and Ravitch) than uncommon techniques (i.e., Implants and Robicsek). The authors concluded that these results suggested slightly better outcomes in pediatric Nuss procedure patients as compared with all other groups. They recommended that symptomatic pediatric patients with uncomplicated PE receive the Nuss procedure. They suggested that adult patients receive the Nuss or Ravitch procedure, even though the long-term complication rates of the adult Nuss procedure require more investigation.

Ina Cochrane review, de Oliveira Carvalho (2014) evaluated the safety and effectiveness of the conventional surgery compared with minimally invasive surgery for treating people with PE. With the aim of increasing the sensitivity of the search strategy, these researchers used only terms related to the individual's condition (pectus excavatum); terms related to the interventions, outcomes and types of studies were not included. They searched the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Embase, LILACS, and ICTPR. Additionally they searched yet reference lists of articles and conference proceedings. All searches were done without language restriction. Date of the most recent searches was January 14, 2014. These investigators considered randomized or quasi-randomized controlled trials that compared traditional surgery with minimally invasive surgery for treating PE. Two review authors independently assessed the eligibility of the trials identified and agreed trial eligibility after a consensus meeting. The authors also assessed the risk of bias of the eligible trials. Initially the authors located 4,111 trials from the electronic searches and 2 further trials from other resources. All trials were added into reference management software and the duplicates were excluded, leaving 2,517 studies. The titles and abstracts of these 2,517 studies were independently analyzed by 2 authors and finally 8 trials were selected for full text analysis, after which they were all excluded, as they did not fulfil the inclusion criteria. The authors concluded that there is no evidence from randomized controlled trials to conclude what is the best surgical option to treat people with PE.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

ICD-10 codes will become effective as of October 1, 2015 :

Pectus excavatum:

CPT codes covered if selection criteria are met:

21740	Reconstructive repair of pectus excavatum or carinatum; open
21742	minimally invasive approach (Nuss procedure), without thoracoscopy
21743	minimally invasive approach (Nuss procedure), with thoracoscopy

Other experimental and investigational interventions:

No specific codes:

Dynamic Compression System, Vacuum bell

ICD-10 codes covered if selection criteria are met:

Q67.6	Pectus excavatum [that causes functional deficit]

ICD-10 codes not covered for indications listed in the CPB:

Q67.7	Pectus carinatum

Poland's syndrome:

CPT codes covered if selection criteria are met:

11960	Insertion of tissue expander(s) for other than breast, including subsequent expansion
11970	Replacement of tissue expander with permanent prosthesis
11971	Removal of tissue expander(s) without insertion of prosthesis
19340	Immediate insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19342	Delayed insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction
19357	Breast reconstruction, immediate or delayed, with tissue expander, including subsequent expansion
19361	Breast reconstruction with latissimus dorsi flap, without prosthetic implant
19364	Breast reconstruction with free flap
19366	Breast reconstruction with other technique
19367	Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM), single pedicle, including closure of donor site
19368	with microvascular anastomosis (supercharging)
19369	Breast reconstruction with transverse rectus abdominis myocutaneous flap (TRAM), double pedicle, including closure of donor site
20900	Bone graft, any donor area; minor or small (e.g., dowel or button)
20902	major or large

ICD-10 codes covered if selection criteria are met:

Q79.8	Other congenital malformations of musculoskeletal system [Poland's syndrome]

The above policy is based on the following references:

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Additional Information

- Clinical Policy Bulletin Notes

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Retractile Testicles

Question: Should the diagnosis code for retractile testicles (Q55.22) be returned to a covered line?

Question source: David Lashley, MD, pediatric urologist

Issue: during the ICD-10 urology review, ICD-9 752.52 and ICD-10 Q55.22 (retractile testicles) were moved from line 98 UNDESCENDED TESTICLE to line 662 GENITOURINARY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY, as there is no effective treatment for this condition.

Dr. Lashley has raised concerns that this condition needs continued monitoring by the patient's PCP, and in many cases, by a pediatric urologist. The initial consultation for this condition is covered, but not any follow up visits for monitoring. While he agrees that there is no treatment for this condition, he feels that it should be on a covered line to allow monitoring.

Retractile testis is considered as a testis that is located at the upper scrotum or lower inguinal canal and that can be made to descend completely into the scrotum without resistance by manual reduction but returns to its original position. Retractile testis has traditionally been considered as a variant of normal testis because it usually descends into the scrotum during adolescence and shows no difference in testicular volume or childbearing capacity compared with the normal testis. However, **Bae (2012)** found that 14% of boys with retractile testicle develop undescended testicle and require orchiopexy. That article concludes "Retractile testis has a risk of requiring orchiopexy. The risk is higher in the population diagnosed at a younger age. Boys with retractile testis should be observed periodically until the testis is descended in the normal position."

From Dr. Lashley:

> PCP's send us a lot of kids with a concern about undescended testicle..?25% or more of the time the testicles are retractile and do not require surgery. No problem…they are new patient visits so they get covered regardless of the diagnosis. I tell the family:
>
> Retractile testicles: The family and I talked about treatment options for retractile testicles. Etiologies of retractile testicles were discussed with the family including the benign nature of this condition, the lack of association with the future development of testicular cancer, and the tendency for the testicles to drop permanently into the scrotum normally between now and puberty. The family and I talked about the fact that surgery in general is not indicated as a treatment of retractile testicles. Alternative treatment options were discussed with the patient in detail. All questions were answered. The family gave fully informed consent to proceed with conservative therapy for their retractile testicles at this time.
>
> On occasion (7-12%) these retractile testicles may "ascend" with the child's linear

growth and subsequently require surgical repair. For this reason I recommend that annual genital examinations at his well child visits continue to document the ability to bring the testicles into the dependant scrotum. I would be happy to see him back if there are ongoing questions or concerns. The patient/family was given instructions to call for incomplete descent of the testicles over time, scrotal/groin/abdominal pain, especially if associated with nausea, vomiting, swelling redness, etc.

so when the pcp checks the next year and can not get the testicle(s) into the scrotum they send them back for re eval. if the testicle is ascended..i am covered as the dx is now above the line. if the testicle is still retractile then i am not covered. it is a total hassle because pcp's will send the kids back to us with undescended testicle diagnosis and thus will not have the follow up visit authorized. i did not realize the retractile code is now BTL so i have a few claims which will not pay. The pcp's want to serve their patients so they often refer BTL diagnosis with ATL codes..which gets them in my door..but then i am often stuck trying to get paid for a BTL visit.

Utilization: For the period 1/1/14-9/30/15, more than >10000 billings (in any diagnosis position), with 4,402 are in the primary diagnosis position on the billing

HERC staff recommendation:

1) Remove ICD-10 Q55.22 (retractile testicle) from line 662 GENITOURINARY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY and add to line 98 UNDESCENDED TESTICLE
    a. Will allow specialty consultation and monitoring visits

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Pediatric Urology

Long-Term Outcomes of Retractile Testis

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Purpose: Retractile testis is considered to be a variant of normal testis in prepubertal boys. There is no agreed-upon management of retractile testis. The aim of this study was to provide data on the long-term outcomes of patients with retractile testis.

Materials and Methods: This study retrospectively reviewed the medical record of 43 boys who were referred for suspected undescended or retractile testis and were finally diagnosed with retractile testis between January 2001 and December 2008. All boys were biannually examined by a pediatric urologist to evaluate the presence of retractile, descended, or undescended testis and testicular volume.

Results: Of 43 boys, there were 22 boys with unilateral retractile testis (51.1%) and 21 boys with bilateral retractile testis (48.9%). Their mean age was 3.0±2.7 years and the follow-up duration was 4.4±1.7 years. Of 64 retractile testes, 29 (45.3%) succeeded in descending, 26 (40.6%) remained retractile, and 9 (14.1%) became undescended testis or of a decreased size requiring orchiopexy. The mean initial diagnostic age of the patients who underwent orchiopexy was 1.3±0.9 years; meanwhile, the mean initial diagnostic age of those who went on to have normal testis was 4.3±3.3 years (p=0.009). The mean follow-up duration was 3.6±1.5 years in the orchiopexy group, 4.0±1.4 years in the descended testis group, and 5.1±1.8 years in group with remaining retractile testis.

Conclusions: Retractile testis has a risk of requiring orchiopexy. The risk is higher in the population diagnosed at a younger age. Boys with retractile testis should be observed periodically until the testis is descended in the normal position.

Key Words: *Cryptorchidism; Orchiopexy; Testis*

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INTRODUCTION

Boys with retractile testis are often transferred from primary health clinics because of suspected cryptorchidism [1]. In many studies, retractile testis is considered as a testis that is located at the upper scrotum or lower inguinal canal and that can be made to descend completely into the scrotum without resistance by manual reduction but returns to its original position by the cremasteric reflex [2-4]. Retractile testis has traditionally been considered as a variant of normal testis because it usually descends into the scrotum during adolescence and shows no difference in testicular volume or childbearing capacity compared with the normal testis [5]. In general, patients with retractile testis are periodically reviewed until the end of adolescence or until the testis has completely descended into the scrotum. However, surgical correction is necessary if testicular maturation appears to be poor or if the testis fails to descend into the scrotum and cryptorchidism develops secondarily.

Some previous studies conducted with boys with retractile testis reported that 18 to 32% of patients required surgical correction owing to the development of undescended testis or decreases in testicular volumes [6,7]. One study reported tissue degeneration among patients with retractile testis that was similar to that of undescended testis [8]. Another study suggested a possible relation between retractile testis and sterility owing to the fact that adults with retractile testis who receive follow-up care show abnormalities in semen analysis compared with normal adults [9]. Treatments of retractile testis remain

controversial, but domestic research on the clinical follow-up of boys with retractile testis is insufficient. This study followed up and observed boys diagnosed with retractile testis to investigate the natural course of retractile testis and to analyze the need and the appropriate time of surgical treatments.

MATERIALS AND METHODS

Eighty-eight boys were transferred from primary health clinics to the department of urology in the hospital for suspected retractile testis or undescended testis between January 2001 and December 2008. Among them, 43 boys were included in this study who attended follow-up for longer than 1 year. Their medical records were retrospectively analyzed. Boys who underwent hormonal therapy were excluded.

Retractile testis was defined as a testis that was located in the upper scrotum or lower inguinal canal but that could be made to descend completely into the scrotum by manual reduction and then returned to the original position by the cremasteric reflex. Undescended testis was defined as a testis located in the upper scrotum or inguinal canal that could not be made to descend into the scrotum by manual reduction or that showed any resistance to reduction or returning immediately to its original position.

All patients were examined by a pediatric urologist. Their testicular location, mobility, and volume were compared with the results of their previous examination at the outpatient department every 6 months after the first diagnosis. According to testicular location, mobility, and volume, the patients were classified into the retractile testis, normal, and orchiopexy groups. Follow-up was terminated once the testis had descended into the scrotum or if any of the boys were diagnosed with undescended testis. Otherwise, the boys having retractile testis were subjected to further follow-ups. If testicular volume was smaller than the previously observed volume or smaller than that of the opposite testis, follow-up was also terminated owing to the judgment that testicular maturation had become poor. Testicular volume was measured with an orchidometer. Orchiopexy was performed for the boys whose testis had become undescended testis or whose testicular volume had decreased. We analyzed their long-term outcomes according to patients' age at the time of the diagnosis, testicular positions, and the status of the contralateral testis and changes in testicular volume.

One-way analysis of variance was used to compare the mean values of the normal, retractile, and orchiopexy groups and chi-square and linear-to-linear association tests were performed to analyze the categorical data. Results were considered to be significant if the p-value was less than 0.05.

RESULTS

There were 22 boys (51.1%) with unilateral retractile testis and 21 boys (48.9%) with bilateral retractile testis among a total of 64 retractile testes. Of these 64 retractile testes, 29 cases (45.3%) succeeded in descending into the normal scrotum. By contrast, 9 cases (14.1%) underwent orchiopexy owing to decreased testicular volume (5 cases) or persistent undescended testis (4 cases). Twenty-six cases (40.6%) remained retractile testis until the end of adolescence. The mean follow-up period of the 43 boys was 4.4±1.7 years, and the mean follow-up period of the boys with persistent retractile testis until the last follow-up was 5.1±1.8 years. The mean diagnostic age was 3.0±2.7 years. The mean age of the patients whose testis succeeded in descending into the scrotum was 4.3±3.3 years, showing that it had taken an average of 4.0±1.4 years until their testis came to descend in the normal scrotum. By contrast, the mean age of the boys who underwent orchiopexy was 1.3±0.9 years, showing that it had taken an average of 3.6±1.5 years. The mean diagnostic age of the boys who underwent orchiopexy was significantly younger than that of the boys whose testis came to descend in the scrotum without surgical correction (p=0.009). There were no statistical differences according to position or bilaterality (p=0.284, 0.292) (Table 1).

TABLE 1. Comparison of the patients' characteristics according to the final outcomes of retractile testis

	Final outcome				
	Normal	Retractile	Orchiopexy	Total	p-value
No. of patients (%)	20 (41.9)	16 (41.9)	7 (16.3)	43	
No. of testis (%)	29 (45.3)	26 (40.6)	9 (14.1)	64	
Age, diagnosis (yr)	4.3±3.3	2.3±1.7	1.3±0.9		0.009
Follow-up duration (yr)	4.0±1.4	5.1±1.8	3.6±1.5		0.069
Testis location					
Upper scrotum	1 (20.0)	3 (60.0)	1 (20.0)	5	
Inguinal canal	29 (49.2)	22 (37.3)	8 (13.6)	59	0.284
Testis bilaterality					0.292
Unilateral	11 (55.0)	6 (37.5)	5 (71.4)	22	
Bilateral	9 (45.0)	10 (62.5)	2 (28.6)	21	

Values are presented as number (%) or mean±SD.

TABLE 2. Change in testicular volume

Testicular volume		No. of patients
Initial	Final	
Normal	Normal	57
Normal	Small[a]	4[b]
Small	Normal	2
Small	Small	1[b]

[a]:Smaller than the contralateral testis, [b]:Orchiopexy was performed.

TABLE 3. Final outcomes according to the state of the contralateral testis

Contralateral testis	Final outcome			p-value
	Normal	Retractile	Orchiopexy	
Normal	6	7	4	0.328
Retractile	9	10	2	0.328
Undescended	3	1	1	0.328

Among the total 64 cases, 61 cases showed normal volume and 3 cases had smaller volumes at the first diagnosis compared with the contralateral testis. According to the follow-up results, 4 cases among those 61 cases with normal volume showed a decrease in volume and underwent orchiopexy, whereas 57 cases maintained a normal volume. Among those 3 cases with smaller volumes, 2 cases recovered to a normal volume when the testis succeeded in descending into the normal scrotum, whereas 1 case showed a decrease in volume and underwent orchiopexy (Table 2).

The authors subdivided the subjects into 3 groups according to the status of the contralateral testis. Among the total 43 boys, 17 boys had a unilateral retractile testis and normal opposite testis, 21 boys had bilateral retractile testis, and 5 boys had a unilateral retractile testis and undescended opposite testis that previously underwent surgical correction. Of the 17 boys with unilateral retractile testis and normal opposite testis, 4 boys (23.5%) underwent orchiopexy, 8 boys (47.1%) came to have descended testis, and the other 5 boys (29.4%) continued to have retractile testis. Of the 5 boys with unilateral retractile testis and undescended opposite testis, 1 patient (20%) underwent orchiopexy, 3 patients (60%) came to have descended testis, and 1 patient (20%) continued to have a retractile testis. Of the 21 boys with bilateral retractile testis, 2 patients (9.5%) underwent orchiopexy for bilaterally persistent undescended testis, 9 patients (42.9%) came to have both testes in the scrotum, and 10 patients (47.6%) continued to have bilateral retractile testis. There was no statistically significant difference between the 3 groups (p=0.611) (Table 3).

DISCUSSION

Management methods for retractile testis remain controversial, whereas treatment methods for undescended testis have been well established through many studies [10-12]. It has been reported that retractile testis is accompanied by histological changes; abnormality on semen analysis was found during follow-up when patients with retractile testis became adults [8,9]. In addition, La Scala and Ein [7] reported that boys with retractile testis need periodic follow-up.

Testicular maturation requires a 2°C to 4°C lower temperature than the normal core body temperature of 36.5°C, and a normal scrotum can meet such a requirement by protrusion. However, a retractile testis goes up and down between the inside of the normal scrotum and the inguinal canal, and the temperature of the inguinal canal exerts an adverse effect on testicular maturation because it is close to the core body temperature. It is difficult, however, to accurately assess how long the testis stays inside the normal scrotum or in the upper scrotum. Therefore, it is essential to examine testicular volume and any changes affecting testicular maturation during the follow-up of patients with retractile testis. If there is any decrease in testicular volumes, immediate surgical correction will be required. It has been reported that a shrunken testis can recover to the normal level of testicular volume after surgical correction [13,14]. This result implies that the appropriate decrease in the temperature around the testis after surgical correction allows for testicular maturation. In this study, 4 of 9 patients underwent surgical correction after showing shrinkage of the ipsilateral testis compared with the contralateral testis or compared with the results of the previous physical examination before surgery. All 4 of these cases showed testicular growth after surgical correction, resulting in testicular volumes similar to those of the contralateral testis. Surgical correction is also required if the following abnormalities are detected during the physical examination. First, an undescended testis that fails to descend into the normal scrotum is developed; second, the development of a sliding testis secondary to increased spermatic cord tension in which the testis can descend into the normal scrotum but immediately returns to the original position; and finally, the development of pain during the descent of the testis, although the testis can descend into the normal scrotum [3]. In this study, 4 boys showed failure of complete descent and subsequently developed undescended testis during the follow-up period; therefore, they underwent orchiopexy.

There are contradictory results concerning histological changes in a retractile testis. Some previous studies reported that the retractile testis had the histological structure of the normal testis [4,15], whereas recent studies showed conflicting results. Recent studies have suggested that surgical correction is necessary to prevent histological changes if patients with retractile testis develop undescended testis [8,16,17]. However, according to research that investigated the testicular volumes and childbearing

capacity of adults who had a medical history of retractile testis in both testes but did not undergo surgical correction, these variables were similar to those of a control group [18].

This study showed that a large number of boys with retractile testis diagnosed at a younger age tended to develop undescended testis, whereas none of the subjects diagnosed at the age of 6.5 years or older underwent surgical correction. Agarwal et al. [6] reported a similar result, claiming that the risk of development of undescended testis was higher in boys younger than 7 years old. However, this study included only 8 boys whose age was 6.5 or older at the time of the diagnosis. Therefore, further research with larger samples will be required in the future.

Previous studies showed that between 6.9% and 32% of boys with retractile testis require orchiopexy; in particular, 50.8 to 56% of boys with any resistance of the spermatic cord require orchiopexy [6,7,19]. The ratio of the boys who underwent orchiopexy in this study was 16.3%. A testis with any resistance against manual reduction was considered an undescended testis in this study. In previous studies, undescended testis was often misdiagnosed as retractile testis, which was subject to follow-up. This suggests that it is highly possible that the total sum of surgical candidates among patients with retractile testis may be much larger than the actual number. This result implies that care should be taken during the examination of patients with retractile testis to make a differential diagnosis with undescended testis. Much research has shown that a retractile testis may become an undescended testis during follow-up and annual or biannual follow-up for boys with retractile testis has been recommended [3,6,20]. In this study, the ratio of boys requiring orchiopexy for any reason was 16.3%. Therefore, we also agree with this recommendation that patients with retractile testis be examined closely concerning testicular location or volume until the testis has completely descended into the scrotum.

In addition, this study also analyzed outcomes according to the status of the contralateral testis. Agarwal et al. [6] reported that boys with 1 descended and 1 retractile testis had a higher probability for the retractile testis to be descended and boys with 1 undescended and 1 retractile testis had a higher probability for the retractile testis to be remained undescended. However, in this study, there was no significant difference in descent according to the status of the contralateral testis. All bilateral retractile testes had similar outcomes.

Hormonal therapy with human chorionic gonadotropin or gonadotrophin-releasing hormone is the most common treatment for undescended testis [21,22]. The action of hormones is similar to that of luteinizing hormones leading to a stimulation of the testis; the testis may then descend as it grows [23,24]. However, proof of the efficacy of hormonal therapy for undescended testis is limited as yet. There was a report that the practice of hormone therapy for less than 1 week was almost not effective for boys with unilateral undescended testis although it was found to be effective in about 56% of boys with bilateral undescended testis [25]. A number of studies have been conducted regarding hormone therapy among patients with retractile testis, and testicular descent was achieved by short-term hormone therapy. However, although short-term hormone therapy was effective, the therapy failed to prevent the return to retractile testis during follow-up [26]. Miller et al. [27] reported a response rate to hormonal therapy of 58% in a study conducted with 26 retractile testes among 16 patients and a response rate of 40% among patients with a retractile testis located in the inguinal canal. Boys who underwent hormonal therapy were excluded from the present study, because the aim of this study was to investigate the natural course of retractile testis. The rate of natural descent of the retractile testes located in the inguinal canal was 49.2% in this study.

This study demonstrated that boys who were diagnosed with retractile testis at a younger age were more likely to undergo orchiopexy. The status of the contralateral testis and testicular positions had no correlation to orchiopexy. Therefore, we suggest that boys with retractile testes, especially those diagnosed at a younger age, need closer observation and more frequent follow-up (annually or semiannually).

The limitations of this study include the error of selecting boys through retrospective investigations; the lack of a random design; judgements based only on physical examination without testicular biopsy; and the lack of complete follow-up until the end of adolescence in some boys. Other limitations are that the number of boys involved in the research was not large enough and that the results do not reflect the progress of patients who failed to attend the follow-up. Future research can address such limitations by involving a larger number of patients in a multi-center study that would allow the investigation of more details concerning the natural course of retractile testis.

CONCLUSIONS

About 16.3% of the boys diagnosed with retractile testis required surgical correction during long-term follow-up. The risk of orchiopexy was higher in the population diagnosed at a younger age. Judging from the results of this study, retractile testis might be considered as a variant of normal testis. Yet, close observation regarding testicular position, mobility, and volume through periodic follow-up is necessary until the testis has successfully descended into the scrotum or until the end of adolescence.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

ACKNOWLEDGEMENTS

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Telemedicine for Retinopathy of Prematurity

Question: Should remote screening and monitoring (CPT 92227 and 92228) of infants for retinopathy of prematurity (ROP) be a covered service?

Question source: Dr. Michael Chiang, ophthalmologist at Casey Eye Institute

Issue: Premature infants in rural NICU's may not have access to pediatric ophthalmologists for the detection and treatment of retinopathy of prematurity, a leading treatable cause of childhood blindness in the US. Remote screening and monitoring via telemedicine is becoming increasingly common, and is endorsed by the American Academy of Pediatrics and the American Academy of Ophthalmology. Currently, remote imaging for retinal disease detection or monitoring (CPT 92227 and 92228) is on the diabetes lines, and on the chorioretinal inflammation line and the birth trauma line. Retinopathy of prematurity (ICD-10 H35.1) is located on line 278 RETINOPATHY OF PREMATURITY.

Fierson et al (2015) reviewed telemedicine for ROP. (http://pediatrics.aappublications.org/content/pediatrics/135/1/e238.full.pdf study not included in packet due to length)The review included 8 level one studies (1715 patients). The PPV was found to be 62-100%, and the NPV was found to be 68-100%. The final conclusion of the paper was that telemedicine was a useful adjunct to bedside binocular indirect ophthalmoscopy, but should not replace it. The paper reviews technical issues which should be addressed in future studies.

Current list status:
H35.1 (Retinopathy of prematurity) is on line 278 RETINOPATHY OF PREMATURITY
P07.2 (Extreme immaturity of newborn) is on lines 17 VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS) and 23 LOW BIRTH WEIGHT (1500-2500 GRAMS)
P07.3 (Preterm newborn) is on lines 17 and 23

92227 (Remote imaging for detection of retinal disease (eg, retinopathy in a patient with diabetes) with analysis and report under physician supervision, unilateral or bilateral) is on lines 8, 30, 100, 353, and 365
92228 (Remote imaging for monitoring and management of active retinal disease (eg, diabetic retinopathy) with physician review, interpretation and report, unilateral or bilateral) is on lines 100, 353, and 365

HERC staff recommendations:

1) Add CPT 92227 (Remote imaging for detection of retinal disease (eg, retinopathy in a patient with diabetes) with analysis and report under physician supervision, unilateral or bilateral) and 92228 (Remote imaging for monitoring and management of active retinal disease (eg, diabetic retinopathy) with physician review, interpretation and report, unilateral or bilateral) to lines 17 VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS) and 23 LOW BIRTH WEIGHT (1500-2500 GRAMS) and 278 RETINOPATHY OF PREMATURITY

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December 28, 2015

Mr. Darren D. Coffman
Director, Health Services Commission
1225 Ferry Street NE
Salem, OR 97301
Email: HERC.Info@state.or.us

RE: Prioritized List Addition Request

Dear Mr. Coffman:

We occasionally notice that the condition and treatment pairs list is either missing ocular diagnoses or their corresponding treatments. We are concerned that there may be a lack of understanding of ocular disease processes or their therapy, including surgical repair. We also feel that many conditions/treatments missing, or below-the-line, meet medical necessity criteria and are considered standard of care, not experimental.

Please consider the following for inclusion on the Prioritized List:

- CPT 92227/92228 are covered on lines 8, 30, 100, 351, and 363. But not for prematurity or retinopathy of prematurity (ROP).
- The associated ICD-10 codes are H35.101-H35.139 (ROP), and P07.20-P07.39 (prematurity).
- This is important because ROP is the leading cause of treatable childhood blindness in the United States. Screening is increasingly been done by telemedicine, particularly in rural areas. Telemedicine diagnosis of ROP is within the standard of care according to published policy guidelines by the American Academy of Pediatrics & American Academy of Ophthalmology (attached).
- Because infants with ROP can go blind if not diagnosed and treated properly, this issue has enormous clinical, public health, and medico-legal significance.

Thank you for your consideration of adding this condition/treatment to the Prioritized List. Do not hesitate to contact me if further clarification is needed.

Sincerely,

Michael F. Chiang, MD

Cc: Ms. Elizabeth Cottle (OHSU Department of Ophthalmology)

Implantable Cardiac Event Monitors

Question: Should implantable cardiac event monitors be a covered service?

Question source: Tracy Muday, MD, OHP Medical Director

Issue: Implantable cardiac event monitors (CPT 33282 and HCPCS C1764) are currently Excluded. Dr. Muday received a request for placement of this device for evaluation of cryptogenic stroke. The HSC reviewed this device in 2000 and placed it on the Excluded List; the rationale and documentation for this decision is not available. The minutes note that this decision was made with the input of specialty groups familiar with the procedure. This device has not been reviewed since 2000.

An insertable cardiac monitor, also referred to as an implantable loop recorder (ILR), is a small insertable device that continuously monitors heart rhythms and records them either automatically or when a hand-held patient assistant is used. Unlike Holter monitors (monitor for 1-7 days) or external cardiac loop recorders (monitor for 3-4 weeks), the ILR's record for about 3 years. They are most commonly used to evaluate fainting spells/transient loss of consciousness that remain unexplained after initial evaluation. ILRs are also used for evaluation of seizures, recurrent palpitations, lightheadedness and dizziness.

Cryptogenic ischemic stroke, one in which the origin of the emboli cannot be determined after full evaluation (e.g. ECG, 24 hours of telemetry, echocardiogram, carotid ultrasound), make up nearly a quarter of all ischemic strokes. There is growing interest in the use of ICLRs to identify occult paroxysmal atrial fibrillation in patients with cryptogenic stroke (MED 2015).

Code	Code description	Placement
33282	Implantation of patient-activated cardiac event recorder	Services recommended for non-coverage table
33284	Removal of an implantable, patient-activated cardiac event recorder	290 COMPLICATIONS OF A PROCEDURE ALWAYS REQUIRING TREATMENT
C1764	Event recorder, cardiac (implantable)	Ancillary

Evidence

1) **MED 2015**, Implantable Loop Recorders for the Evaluation of Cryptogenic Stroke
    a. There is no high-quality comparative evidence on the use of implantable cardiac loop records or other ambulatory monitoring modalities on the initiation of oral anticoagulation or stroke recurrence in patients diagnosed with occult atrial fibrillation.
    b. In the past two years, four systematic reviews found increased detection of occult atrial fibrillation by ILCRs compared to other ambulatory monitoring efforts. However, these reviews do not report on change in management nor

impact on stroke recurrence (Afzal et al., 2015; Dussault et al., 2015; Kishore et al., 2014; Sposato et al., 2015). None of the systematic reviews identified head-to-head comparative trials of different ICLR devices or extended monitoring devices. The limited data available for inclusion in the reviews were based on observational trials with short follow up periods.

c. In a small, poor-quality cohort study of 61 patients receiving ICLRs, all received weeklong serial ECGs as well. The authors reported that within the first week of use, ILCR compared to serial ECG detected cases of intermittent atrial fibrillation at a 3:1 ratio. The authors did not discuss the potential clinical significance of this finding. This study did not observe any recurrent stroke or TIAs in their short follow-up period.
d. In a fair-quality, industry funded, RCT of 441 patients, higher rates of stroke and lower use of oral anticoagulation were observed in those randomized to conventional monitoring compared to ICLRs (i.e. baseline and serial ECGs every 6 months, thus not meeting strict inclusion criteria). At 6-and 12-months follow-up, the ICM group compared to controls had statistically significantly higher percentages of participants that received anticoagulation (6 months: 10.1% vs. 4.6%, P=0.04 and 12 months: 14.7% vs. 6.0%, P=0.007).
e. Among the included studies, adverse events were rare and included site infection, pocket erosion, pain, and irritation. A single patient experienced device failure from sub-optimal placement preventing rhythm detection.
f. Summary: Patients with ischemic stroke found to have atrial fibrillation on initial evaluation experience decreased risk of recurrent stroke with the use of oral anticoagulation therapy. In patients with cryptogenic stroke, despite an extensive initial evaluation without detection of atrial fibrillation, the use of prolonged monitoring demonstrates increased detection of paroxysmal or occult atrial fibrillation. The current literature is limited on the impact of the detection of occult atrial fibrillation through prolonged monitoring and subsequent initiation of anticoagulation on stroke recurrence. Clinicians and researchers are advocating for more comparative research to be conducted on ICLRs and their use in cryptogenic stroke, as well as the clinical impact of detecting occult atrial fibrillation in those with cryptogenic stroke.

2) **Parry 2010**, review of ILR for evaluation of unexplained syncope
   a. Conclusion: The ILR has entered routine clinical practice over the last 15 years with surprisingly few rigorous data. In this era of evidence-based practice, this requires to be addressed with a focus on high quality trials of up-to-the minute technology. In the interim, the ILR offers a useful adjunct in the investigation of unexplained syncope, particularly where an arrhythmic cause is suspected. Further controlled data are required to inform clinical practice with attention focused on empowering ILR-guided diagnosis, establishing the optimal timing of ILR use in syncope and embracing new technological advancements

Expert groups

1) **European Society of Cardiology 2009**, (http://europace.oxfordjournals.org/content/11/5/671 study not included in packet due to length) ILR position statement
    a. For management of transient loss of consciousness (TLoC)
        i. Class I. ILR is indicated:
            1. In an early phase of evaluation of patients with recurrent syncope of uncertain origin who have:
                a. absence of high-risk criteria that require immediate hospitalization or intensive evaluation and
                b. a likely recurrence within battery longevity of the device (Level of evidence A)
            2. In high-risk patients in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to specific treatment (Level of evidence B)
        ii. Class II A. ILR may be indicated:
            1. To assess the contribution of bradycardia before embarking on cardiac pacing in patients with suspected or certain neurally mediated syncope presenting with frequent or traumatic syncopal episodes (Level of evidence B)
        iii. Class II B. ILR may be indicated:
            1. In patients with T-LOC of uncertain syncopal origin in order to definitely exclude an arrhythmic mechanism (Level of evidence C)
    b. For diagnosis of undocumented palpitations
        i. Class IIA: ILRs may be indicated in selected cases with severe infrequent symptoms when ELRs and other ECG monitoring systems fail to document the underlying cause (Level of evidence B). The outcome of asymptomatic arrhythmias remains uncertain.
    c. For diagnosis of atrial fibrillation
        i. Continuous monitoring by implantable devices further increases the detection of AF, but it is hampered by misdetections and artefacts.
        ii. Technological improvements are required for significant reduction of maldetection. Manual analysis can improve diagnostic yield if stored electrograms are provided. The results of some on-going studies with new generation devices are awaited
        iii. The clinical relevance of Loop Recorders to guide medical and device therapy has yet to be demonstrated
    d. For risk stratification after MI
        i. The clinical usefulness of ILR to guide medical and device therapy in patients surviving myocardial infarction has yet to be demonstrated
        ii. ILRs have a potential role in identifying the correlation between symptoms and suspected ventricular tachyarrhythmia in selected high-risk patients affected by Brugada ECG pattern, long or short QT,

hypertrophic cardiomyopathy, and arrhythmogenic right ventricular dysplasia.

Other policies

1) **NICE 2010** http://guidance.nice.org.uk/cg109 (Study not included in packet due to length)
    - **a.** For evaluation of transient loss of consciousness (TLoC) in adults: For people with a suspected cardiac arrhythmic cause of syncope, offer an ambulatory ECG and do not offer a tilt test as a first-line investigation. The type of ambulatory ECG offered should be chosen on the basis of the person's history (and, in particular, frequency) of TLoC. For people who have TLoC infrequently (less than once every 2 weeks), offer an implantable event recorder.
2) **Aetna 2015**
    - a. Aetna considers an implantable loop recorder (e.g., Reveal Insertable Loop Recorder by Medtronic, Inc.) medically necessary for evaluation of recurrent unexplained episodes of pre-syncope, syncope, "seizures", palpitations, or dizziness when both of the following criteria are met:
        - i. A cardiac arrhythmia is suspected as the cause of the symptoms; *and*
        - ii. Either of the following criteria is met:
            1. For persons with heart failure, prior myocardial infarction or significant ECG abnormalities (see appendix), noninvasive ambulatory monitoring, consisting of 30-day presymptom external loop recordings or MCT, fails to establish a definitive diagnosis; *or*
            2. For persons without heart failure, prior myocardial infarction or significant ECG abnormalities (see appendix), symptoms occur so infrequently and unpredictably (less frequently than once per month) that noninvasive ambulatory monitoring (MCT or external loop recorders) are unlikely to capture a diagnostic ECG.
    - b. Aetna considers implantable loop recorders experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.
3) **Cigna 2015**
    - a. Cigna covers the use of an implantable loop recorder (CPT codes 33282, 33284, 93285, 93291, 93297, 93298, 93299, C1764, E0616) as medically necessary for the evaluation of recurrent unexplained episodes of fainting when ALL of the following criteria are met:
        - i. cardiac arrhythmia is suspected to be the cause of fainting
        - ii. noninvasive ambulatory monitoring failed to establish a definitive diagnosis because the symptoms occur so infrequently and unpredictably that the length of the monitoring period may have been inadequate to capture a diagnostic electrocardiogram (ECG) rhythm disorder
        - iii. tilt-table testing is negative or nondiagnostic

HERC staff summary:
The use of implantable loop recorders (ILRs) appears to have evidentiary support and expert recommendations for use for evaluation of recurrent transient loss of consciousness in patients in whom a comprehensive evaluation including noninvasive ambulatory monitoring did not demonstrate a cause of the TLoC or lead to specific treatment, and in whom a cardiac cause is suspected, and in whom an event is expected to recur within the battery life of the ILR.

The use of ILRs for evaluation for possible atrial fibrillation as the cause of cryptogenic stroke appears to be an area of active research and controversy.

HERC staff recommendations:

1) Add coverage for the use of implantable loop recorders (ILRs) for the evaluation of recurrent transient loss of consciousness in selected patients. Do not add coverage for other indications due to their experimental nature
    a. Advise HSD to add CPT 33282 (Implantation of patient-activated cardiac event recorder) to the Diagnostic Procedures File and remove from the Services Recommended for Non-Coverage Table
    b. Advise HSD to add HCPCS C1764 (Event recorder, cardiac (implantable)) to the Diagnostic Procedures File and remove from the Ancillary List
    c. Adopt the following Diagnostic Guideline Note

DIAGNOSTIC GUIDELINE DX, IMPLANTABLE LOOP RECORDERS
Use of an implantable cardiac loop recorder (ILR) is a covered service only when the patient meets all of the following criteria:

1) The evaluation is for recurrent transient loss of consciousness (TLoC); and
2) A comprehensive evaluation including noninvasive ambulatory cardiac monitoring did not demonstrate a cause of the TLoC; and
3) A cardiac arrhythmia is suspected to be the cause of the TLoC; and
4) There is a likely recurrence of the TLoC within the battery longevity of the device.

ILRs are not a covered service for evaluation of cryptogenic stroke or any other indication.

Implantable loop recorders in the investigation of unexplained syncope: a state of the art review

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ABSTRACT

Since its introduction 15 years ago, the implantable loop recorder (ILR) has become the investigative tool of choice in recurrent unexplained syncope following negative initial investigations. This is based on very few randomised controlled clinical trials and modestly sized observational studies. Further controlled data are required to inform clinical practice with attention focused on empowering ILR-guided diagnosis, establishing the optimal timing of ILR use in syncope and embracing new technological advancements.

INTRODUCTION

Syncope accounts for 1–6% of emergency attendances and 0.6–1.0% of hospital admissions.[1] The 10-year cumulative incidence of syncope in the Framingham study was 6% with increasing burden in tandem with advancing years.[2] The majority of cases are neurally-mediated in origin, but syncope is a common presentation of cardiac rhythm disturbance. The sporadic nature of presentation makes syncope a logical target for prolonged cardiac rhythm monitoring.

The implantable loop recorder (ILR) is a device implanted in the subcutaneous tissue of the left hemithorax under local anaesthetic. The ILR records a high fidelity bipolar ECG signal stored as a loop, frozen at the time of symptoms using a handheld activator. Newer devices have programmable automatic recognition (typically >160 beats/min, <30 beats/min or pauses >3 s).

The majority of clinical studies involving the ILR have focused on the investigation of recurrent unexplained syncope or neurally-mediated syncope. We reviewed the English language scientific literature by searching MEDLINE from 1966 through January 2009 using the PubMed interface under the terms syncope [MeSH] OR neurally mediated syncope [MeSH] AND ILR. The reference lists from articles identified by this search were also reviewed for relevant publications. A total of 139 articles were identified, with those representing the strongest evidence included in our review which confines itself to the adult population and the key evidence concerning ILR use in these contexts. Gaps in the evidence base will be highlighted and suggestions for future research proposed.

RECURRENT SYNCOPE

The initial clinical experience with the ILR was in a population of highly symptomatic patients with recurrent unexplained syncope.[3] Sixteen patients with a mean of 8.4±4.4 episodes of previous syncope, all with negative ambulatory monitoring, tilt table testing and electrophysiological (EP) study, underwent device implantation. Fifteen of the 16 patients (94%) had recurrent syncope during follow-up (13±8.4 months). A diagnosis was obtained in all 15 patients with symptom-rhythm correlation possible in 9 of them (60%). Treatment was instituted in all 15 with no recurrence of syncope by study termination.

This initial success paved the way for further work[4–31] in using the ILR as part of the diagnostic strategy in recurrent unexplained syncope (table 1). The considerable majority of these studies are observational, small and/or retrospective. While conclusions drawn from them individually are tempered by the inherent flaws of this study design, collectively they form a limited but persuasive evidence base to justify the clinical use of the ILR in recurrent unexplained syncope.

Randomised controlled trials

Clinical effectiveness

Only two randomised trials studies involving ILRs have been undertaken, both of which compared the role of the ILR with a conventional testing strategy. The Randomised Assessment of Syncope Trial (RAST)[6] involved 60 consecutive patients attending a specialist syncope service with recurrent unexplained syncope or a single episode of syncope with injury warranting cardiovascular investigation. At baseline all 60 patients had a negative initial evaluation similar to that recommended by the European Society of Cardiology guidelines on the management of syncope,[32] in common with the remainder of the ILR studies. An ILR was implanted in 30 patients; the remainder underwent prolonged external monitoring, tilt table testing and EP study. If the allocated strategy did not provide a diagnosis, patients were offered crossover to the alternative arm. A diagnosis was established in 14 patients in the ILR arm compared with 6 patients in the conventional arm (52% vs 20%, p=0.012). Six patients in the ILR group and 21 in the conventional testing group crossed over. Overall, when combining the primary strategy with crossover, a diagnosis was established in 55% with a prolonged monitoring strategy compared with 19% with conventional testing (p=0.0014).

The other randomised study is the Eastbourne Syncope Assessment Study (EaSyAS).[27] Two hundred and one unselected patients presenting to a single institution with recurrent syncope without a definite diagnosis following initial clinical investigation were randomly assigned to ILR implantation (n=103) or conventional investigation and management (n=98). There were further syncopal events in 43 (43%) of the ILR group compared with

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Cardiac Event Monitors

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Policy

I. Aetna considers external intermittent cardiac event monitors (i.e., external loop recorders) and external intermittent cardiac event monitors with real-time data transmission and analysis (e.g., eCardio eVolution) medically necessary for any of the following conditions:

   A. To document an arrhythmia in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring (see CPB 0019 - Holter Monitors); *or*
   B. To document ST segment depression for suspected ischemia; *or*
   C. To document the benefit after initiating drug therapy for an arrhythmia; *or*
   D. To document the recurrence of an arrhythmia after discontinuation of drug therapy; *or*
   E. To document the results after an ablation procedure for arrhythmia; *or*
   F. To evaluate syncope and lightheadedness in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring.

   Aetna considers external loop recorders experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.

II. Aetna considers mobile cardiovascular telemetry (MCT) (e.g., CardioNet Mobile Cardiac Outpatient Telemetry (MCOT) Service; Cardiac Telecom and Health Monitoring Services of America's Telemetry @ Home Service; Heartbreak ECAT (External Cardiac Ambulatory Telemetry) (Med net Healthcare Technologies), HEARTLink™ II ECG Arrhythmia Detector and Alarm System by Cardiac Telecom Corporation, LifeStar ACT by LifeWatch®, Inc., a subsidiary of Card Guard Scientific, SAVI® (Mediacom), Telemetry™ (Scott Care Cardiovascular Solutions) and Trove® (Biomedical Systems)) medically necessary for evaluation of recurrent unexplained episodes of pre-syncope, syncope, palpitations, or dizziness when both of the following criteria are met:

A. A cardiac arrhythmia is suspected as the cause of the symptoms; *and*
B. Members have a non-diagnostic Holter monitor, or symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring.

Aetna considers MCT experimental and investigational for other indications because its effectiveness for indications other than the ones listed above has not been established.

III. Aetna considers an implantable loop recorder (e.g., Reveal Insertable Loop Recorder by Medtronic, Inc.) medically necessary for evaluation of recurrent unexplained episodes of pre-syncope, syncope, "seizures", palpitations, or dizziness when both of the following criteria are met:

A. A cardiac arrhythmia is suspected as the cause of the symptoms; *and*
B. Either of the following criteria is met:

1. For persons with heart failure, prior myocardial infarction or significant ECG abnormalities (see appendix), noninvasive ambulatory monitoring, consisting of 30-day presymptom external loop recordings or MCT, fails to establish a definitive diagnosis; *or*
2. For persons without heart failure, prior myocardial infarction or significant ECG abnormalities (see appendix), symptoms occur so infrequently and unpredictably (less frequently than once per month) that noninvasive ambulatory monitoring (MCT or external loop recorders) are unlikely to capture a diagnostic ECG.

Aetna considers implantable loop recorders experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.

Note: Depending on clinical presentation, the individual may have had a negative or non-diagnostic electrophysiological study (EPS); however, EPS is no longer considered a prerequisite to insertion of an implantable loop recorder.

IV. Aetna considers the use of long-term (greater than 48 hours) external ECG monitoring by continuous rhythm recording and storage (e.g., Zio Patch) medically necessary for the following indications:

A. To evaluate syncope and lightheadedness in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring (see CPB 0019 - Holter Monitors); *or*

B. To document an arrhythmia in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring.

V. Aetna considers the AliveCor Heart Monitor (iPhoneECG) experimental and investigational because its clinical value has not been established.

Requests for cardiac event monitoring that do not meet the above criteria and requests for repeat studies within 1 year of a previous study are subject to medical necessity review.

Background

Cardiac event monitors are small portable devices worn by a patient during normal activity for up to 30 days. The device has a recording system capable of storing several minutes of the individual's electrocardiogram (EKG) record. The patient can initiate EKG recording during a symptomatic period of arrhythmia. Cardiac event monitors have primarily been used to diagnose and evaluate cardiac arrhythmias. These monitors are particularly useful in obtaining a record of arrhythmia that would not be discovered on a routine EKG or an arrhythmia that is so infrequent that it is not detected during a 24-hour period by a Holter monitor.

Two different types of cardiac event monitors are available. Pre-symptom (looping memory) event monitors are equipped with electrodes attached to the chest, and are able to capture EKG rhythms before the cardiac event monitor is triggered (pre-symptom recording) (Healthwise, 2003). This feature is especially useful for people who lose consciousness when arrhythmias occur.

Post-symptom event monitors do not have chest electrodes (Healthwise, 2003). One type of post-symptom event monitor is worn on the wrist. When symptoms occur, the patient presses a button to trigger an EKG recording. Another type of post-symptom event monitor is a device that the patient carries within easy reach. When symptoms occur, the patient presses the electrodes on the device against their chest and presses a button to trigger the EKG recording.

Cardiac event monitors have been developed with automatic trigger capabilities, which are designed to automatically trigger an EKG recording when certain arrhythmias occur. Automated trigger cardiac event monitors are thought to be more sensitive, but less specific, than manually-triggered cardiac event monitors for significant cardiac arrhythmias. The simplest automatic trigger cardiac event monitors detect a single type of arrhythmia (e.g., atrial fibrillation), whereas more sophisticated monitors are capable of detecting several types of arrhythmias (e.g., PDSHEART, 2001; Instromedix, 2002; LifeWatch, 2004; Medicomp, 2005; eCardio Diagnostics, 2004). Automatic trigger cardiac event monitors may be especially useful for persons with asymptomatic arrhythmias, persons with syncope, and other persons (children, mentally retarded persons) who can not reliably trigger the monitor when symptoms occur.

Cardiac event monitors may come with 24-hour remote monitoring. Usually, EKG results are transmitted over standard phone lines at the end of each day to an attended monitoring center, where a technician screens EKG results and notifies the patient’s physician of any significant abnormal results, based on predetermined notification criteria. Newer cardiac event monitors allow EKG results to be transmitted via e-mail over the internet (CardioPhonics, 2006). Some cardiac event monitors allow the patient to transmit EKG over standard telephone lines to the attended monitoring center immediately after symptoms occur (e.g., Versweyveld, 2001; Transmedex, 2001); other cardiac event monitors have been adapted to also allow immediate transmission of EKG results by cellular telephone (Philips, 2003; Schiller, 2004; CRY, 2004; HealthFrontier, 2004). If test results suggest a life-threatening emergency, monitoring center personnel may instruct the patient to go to the hospital or call an ambulance (Daja et al, 2001). The development of mobile technology may extend the use of cardiac event monitors from primarily diagnostic purposes to use primarily as an alarm system, to allow rapid intervention for the elderly and others at increased risk of cardiac events (Cox, 2003; Lloyds, 1999).

Standard cardiac event monitors come with 5 to 10 mins of memory. Cardiac event monitors with expanded memory capabilities have been developed, extending memory from approximately 20 to 30 mins (Instromedix, 2002; LifeWatch, 2002; Philips Medical Systems, 2003; PDSHeart, 2006) to as much as several hours (CardioPhonics, 2001; CardioPhonics, 2006). Extended memory is especially useful for automatic trigger cardiac event monitors, because the automatic trigger may not reliably discriminate between clinically significant arrhythmias (true positives) and EKG artifacts (false positives), such that a more limited memory would be filled with false positives.

Mobile cardiovascular telemetry (MCT) refers to non-invasive ambulatory cardiac event monitors with extended memory capable of continuous measurement of heart rate and rhythm over several days, with transmission of results to a remote monitoring center. Mobile cardiovascular telemetry is similar to standard cardiac telemetry used in the hospital setting.

CardioNet (Philadelphia, PA) has developed an MCT device with extended memory, automatic ECG arrhythmia detector and alarm that is incorporated into a service that CardioNet has termed "Mobile Cardiac Outpatient Telemetry (MCOT)." The CardioNet device couples an automatic arrhythmia detector and cellular telephone transmission so that abnormal EKG waveforms can automatically be transmitted immediately to the remote monitoring center. The CardioNet device also has an extended memory characteristic of digital Holter monitors; the CardioNet device is capable of storing up to 96 hours of EKG waveforms. These ECG results are transmitted over standard telephone lines to the remote monitoring center at the end of each day. The physician receives both urgent and daily reports.

The manufacturer states that an important advantage of MCOT is that it is capable of detecting asymptomatic events and transmitting them immediately, even when the patient is away from home, allowing timely intervention should a life-threatening arrhythmia may occur. The CardioNet device's extended memory allows the physician to examine any portion of the ECG waveform over an entire day. This extended memory ensures that it does not fill with EKG artifact (false positives) where the CardioNet's automated ECG trigger is unable to reliably discriminate between artifact and significant arrhythmias (true positives). Potential uses of MCOT include diagnosis of previously unrecognized arrhythmias, ascertainment of cause of symptoms, and initiation of anti-arrhythmic drug therapy.

The CardioNet ambulatory ECG arrhythmia detector and alarm is cleared for marketing by the Food and Drug Administration (FDA) based on a 510(k) premarket notification due to the FDA's determination that the CardioNet device was substantially equivalent to devices that were currently on the market. The CardioNet device is not intended for monitoring patients with life-threatening arrhythmias (FDA, 2002).

There is reliable evidence that MCT is superior to patient-activated external loop recorders for diagnosing cardiac arrhythmias. Rothman et al (2007) reported on a randomized controlled clinical study comparing the diagnostic yield of MCT (CardioNet MCOT) to patient-activated external looping event monitors for symptoms thought to be due to an arrhythmia. Subjects with symptoms of syncope, pre-syncope, or severe palpitations who had a non-diagnostic 24-hour Holter monitor were randomized to MCT or an external loop recorder for up to 30 days. The primary endpoint was the confirmation or exclusion of a probable arrhythmic cause of their symptoms. A total of 266 patients who completed the monitoring period were analyzed. A diagnosis was made in 88 % of MCT subjects compared to 75 % of subjects with standard loop recorders ($p = 0.008$). The authors noted that cardiac arrhythmias without associated symptoms, but nonetheless capable of causing the index symptoms, were the major determining factor accounting for the difference in diagnostic yield of MCT and patient-activated external loop recorders.

There is also evidence to suggest that MCT is superior to auto-triggered external loop recorders for diagnosing symptoms thought to be due to a cardiac arrhythmia. Loop recorders with auto-trigger algorithms have been used to improve the diagnostic yield of event monitors (Strickberger et al, 2006). Rothman et al (2007) explained that their study of MCT was not designed to evaluate auto-triggered loop recorders, as this type of recorder was not available at all study sites. However, 2 of the 17 study sites used looping event recorders with an auto-trigger algorithm in all of their randomized patients (Rothman et al, 2007). A total of 49 subjects, or 16 % of the randomized population were from these 2 sites. In a post-hoc analysis of this subgroup of patients, a diagnosis was made in 88 % of MCT subjects compared to 46 % of patients with auto-triggered external loop recorders. One possible factor accounting for the poor diagnostic yield of the auto-trigger loop recorders employed in this study is that they may have had

limited memory which quickly filled with artifact. In addition, the CardioNet MCOT device used in this study uses dual EKG leads, whereas the auto-trigger loop recorders may have used single leads.

One limitation of the study by Rothman et al (2007) was the lack of blinding of the investigators or subjects. The investigators sought to overcome this bias by having all monitoring strips and diagnoses evaluated by another electrophysiologist that was blinded to assignment. Another limitation of this study is that it did not explore the potential for work-up bias; the study did not describe whether any of the study subjects had ever had previous work-ups for cardiac arrhythmias that included evaluation with an external loop recorder.

A number of retrospective uncontrolled studies have been published that have described the experience with MCT. Olson et al (2007) retrospectively examined the records of 122 consecutive patients evaluated using MCT for palpitations (n = 76), pre-syncope/syncope (n = 17), or to monitor the effectiveness of anti-arrhythmic therapy (n = 29). The investigators reported on the proportion of patients with syncope/pre-syncope and palpitations whose diagnosis was established by MCT, and the proportion of patients monitored for medication titration who had dosage adjustments. This study is of similar design to an earlier study by Joshi et al (2005), which reported on the first 100 consecutive patients monitored by MCT.

Vasamreddy et al (2006) reported on a small (n = 19) prospective exploratory study examining the feasibility and results of using MCT for monitoring patients with atrial fibrillation before and after catheter ablation for atrial fibrillation. The authors concluded that MCT has potential utility for this use. The authors noted, however, that poor patient compliance with the study's MCT monitoring protocol represented an important limitation; only 10 of 19 subjects that were enrolled in the study completed the protocol, which required subjects to wear the MCT monitor 5 days per month for 6 months following the ablation.

Cardiac Telecom Corporation (Greensburg, PA) and Health Monitoring Services of America (Boca Raton, FL) have developed an MCT service called "Telemetry @ Home" that shares many similarities to the CardioNet Service. The Telemetry @ Home Service utilizes Cardiac Telecom's Heartlink II Monitor, which has automatic arrhythmia detection and extended memory. The Heartlink II Monitor is able to wirelessly transmit abnormal EKG waveforms from a base station in the home to a remote monitoring center. Unlike the CardioNet Service, the Heartlink II Monitor does not have a built-in cellular telephone, so that the monitor does not automatically transmit abnormal waveforms when the patient is away from home out of range of the base station. The Heartlink II Monitor was cleared by the FDA based upon a 510(k) premarket notification.

Biowatch Medical (Columbia, SC) offers an MCT service called "Vital Signs Transmitter (VST)" that shares many similarities to other MCT services. According to the manufacturer, VST provides continuous, real-time, wireless ambulatory patient monitoring of 2 ECG channels plus respiration and temperature (Biowatch Medical. 2008; Gottipaty et al, 2008). The VST is a wireless belt-like device with non-adhesive electrodes that is worn around the patient's chest. The VST has an integrated microprocessor and wireless modem to automatically detect and transmit abnormal ECG waveforms. The monitor transmits ECG data via an integrated cellular telephone, when activated by the patient or by the monitor's real-time analysis software, to a central monitoring station, where the tracing is analyzed by technicians. The technicians can then notify the patient's physician of any serious arrhythmias, transmit ECG tracings, and provide patient intervention if required. The monitoring center also provides daily reports that can be accessed by the patient's physician over the Internet. According to the manufacturer, a new VST device is being developed that will also provide data on the patient's oxygen saturation, blood pressure, and weight (Biowatch Medical, 2008). The VST was cleared by the FDA based on a 510(k) premarket notification.

Lifewatch Inc. (Rosemount, IL) has developed an MCT service called LifeStar Ambulatory Cardiac Telemetry (ACT). The LifeStar ACT is similar to the CardioNet MCOT in that it has built-in cellular transmission so that results can be transmitted away from home. The LifeStar ACT cardiac monitoring system utilizes an auto-trigger algorithm to detect atrial fibrillation, tachycardia, bradycardia, and pauses, and requires no patient intervention to capture or transmit an arrhythmia when it occurs. The device can also be manually triggered by the patient during symptoms. Upon arrhythmia detection or manual activation, the LifeStar ACT transmits data via the integrated cellular telephone to LifeWatch, where the ECG is analyzed. The LifeStar ACT has a longer continuous memory loop that can be retrieved as needed by the monitoring center. The LifeWatch ACT was cleared by the FDA based on a 510(k) premarket notification.

A systematic evidence review of remote cardiac monitoring prepared for the Agency for Healthcare Research and Quality by the ECRI Evidence-based Practice Center (AHRQ, 2007) reached the following conclusions about the evidence for MCT: "This study [by Rothman et al, 2007] was a high-quality multicenter study with few limitations. Therefore, the evidence is sufficient to conclude that real-time continuous attended monitoring leads to change in disease management in significantly more patients than do certain ELRs [external loop recorders]. However, because this is a single multicenter study, the strength of evidence supporting this conclusion is weak. Also, the conclusion may not be applicable to ELRs with automatic event activation, as this model was underrepresented in the RCT [by Rothman et al, 2007] (only 16 % of patients used this model)."

The Zio Patch (iRhythm Technologies, Inc., San Francisco, CA) is a recording device that provides continuous single-lead ECG data for up to 14 days (Mittal et al, 2011). The Zio Patch uses a patch that is placed on the left pectoral region. The patch does not require patient activation. However, a button on the patch can be pressed by the patient to mark a symptomatic episode. At the end of the recording period, the patient mails back the recorder in a prepaid envolope to a central monitoring station(Mittal et al, 2011). A report is provided to the ordering physician within a few days. The manufacturer states that it is indicated for use in patients who may be asymptomatic or who may suffer from transient symptoms (e.g., anxiety, dizziness, fatigue, light-headedness, palpitations, pre-syncope, shortness of breath, and syncope). The Zio ECG Utilization Service (ZEUS) system is a comprehensive system that processes and analyzes received ECG data captured by long-duration, single-lead, continuous recording diagnostic devices (e.g., the Zio Patch and Zio Event Card). However, the clinical outcomes and cost-effectiveness of extended cardiac monitoring by means of the Zito Patch, the ZEUS system and similar devices have not been shown to be superior to other available approaches. Mittal et al (2011) noted that "clinical experience [with the Zio Patch] is currently lacking". The author stated that it is not known how well patients can tolerate the patch for 1 to 2 weeks, and whether the patch can yield a high-quality artifact-free ECG recording through the entire recording period. The authors stated, furthermore, that "the clinical implications of not having access to ECG information within the recording period need to be determined".

Rosenberg et al (2013) compared the Zio Patch, a single-use, non-invasive waterproof long-term continuous monitoring patch, with a 24-hour Holter monitor in 74 consecutive patients with paroxysmal atrial fibrillation (AF) referred for Holter monitoring for detection of arrhythmias. The Zio Patch was well-tolerated, with a mean monitoring period of 10.8 +/- 2.8 days (range of 4 to 14 days). Over a 24-hour period, there was excellent agreement between the Zio Patch and Holter for identifying AF events and estimating AF burden. Although there was no difference in AF burden estimated by the Zio Patch and the Holter monitor, AF events were identified in 18 additional individuals, and the documented pattern of AF (persistent or paroxysmal) changed in 21 patients after Zio Patch monitoring. Other clinically relevant cardiac events recorded on the Zio Patch after the first 24 hours of monitoring, including symptomatic ventricular pauses, prompted referrals for pacemaker placement or changes in medications. As a result of the findings from the Zio Patch, 28.4 % of patients had a change in their

clinical management. The authors concluded that the Zio Patch was well-tolerated, and allowed significantly longer continuous monitoring than a Holter, resulting in an improvement in clinical accuracy, the detection of potentially malignant arrhythmias, and a meaningful change in clinical management. Moreover, they stated that further studies are necessary to examine the long-term impact of the use of the Zio Patch in AF management.

Turakhia and colleagues (2013) noted that although extending the duration of ambulatory electrocardiographic monitoring beyond 24 to 48 hours can improve the detection of arrhythmias, lead-based (Holter) monitors might be limited by patient compliance and other factors. These researchers, therefore, evaluated compliance, analyzable signal time, interval to arrhythmia detection, and diagnostic yield of the Zio Patch, a novel leadless, electrocardiographic monitoring device in 26,751 consecutive patients. The mean wear time was 7.6 ± 3.6 days, and the median analyzable time was 99 % of the total wear time. Among the patients with detected arrhythmias (60.3 % of all patients), 29.9 % had their first arrhythmia and 51.1 % had their first symptom-triggered arrhythmia occur after the initial 48-hour period. Compared with the first 48 hours of monitoring, the overall diagnostic yield was greater when data from the entire Zio Patch wear duration were included for any arrhythmia (62.2 % versus 43.9 %, $p < 0.0001$) and for any symptomatic arrhythmia (9.7 % versus 4.4 %, $p < 0.0001$). For paroxysmal atrial fibrillation (AF), the mean interval to the first detection of AF was inversely proportional to the total AF burden, with an increasing proportion occurring after 48 hours (11.2 %, 10.5 %, 20.8 %, and 38.0 % for an AF burden of 51 % to 75 %, 26 % to 50 %, 1 % to 25 %, and less than 1 %, respectively). The authors concluded that extended monitoring with the Zio Patch for less than or equal to 14 days is feasible, with high patient compliance, a high analyzable signal time, and an incremental diagnostic yield beyond 48 hours for all arrhythmia types. These findings could have significant implications for device selection, monitoring duration, and care pathways for arrhythmia evaluation and AF surveillance.

Higgins (2013) stated that a number of substantial improvements to the 60-year old concept of the Holter monitor have recently been developed. One promising advance is the Zio Patch (iRhythm Technologies, Inc., CA), a small 2 × 5-inch patch, which can continuously record up to 14 days of a single ECG channel of cardiac rhythm without the need for removal during exercise, sleeping or bathing. Its ease-of-use, which enables optimal long-term monitoring, has been established in the ambulatory setting, although some insurance carriers have been reluctant to reimburse appropriately for this advance, an issue characteristic of other heart monitors, treated as 'loss-leaders'. In this article, in addition to discussing possible reasons for this reluctance, a novel model for direct-to-consumer marketing of heart monitoring, outside of the traditional health insurance reimbursement model, is also presented. Additional current and future advances in heart rhythm recording are also discussed. Such potentially revolutionary opportunities have only recently become possible as a result of technologic advances.

The Center for Medicare and Medicaid Services (CMS) (2004) has determined that an ambulatory cardiac monitoring device or service is eligible for Medicare coverage only if it can be placed into the following categories:

I. Patient/Event Activated Intermittent Recorders:

   A. Pre-symptom memory loop (insertable or non-insertable)

      - Attended;
      - Non-attended.

   B. Post-symptom (no memory loop)

      - Non-attended

II. Non-activated Continuous Recorders:

- Dynamic electrocardiography (e.g., Holter monitor)
- Non-attended.

The CMS has determined that an ambulatory cardiac monitoring device or service is not covered if it does not fit into these categories. The CMS noted that it may create new ambulatory electrocardiographic monitoring device categories "if published, peer-reviewed clinical studies demonstrate evidence of improved clinical utility, or equal utility with additional advantage to the patient, as indicated by improved patient management and/or improved health outcomes in the Medicare population (such as superior ability to detect serious or life-threatening arrhythmias) as compared to devices or services in the currently described categories".

Hanke et al (2009) noted that 24-hr Holter monitoring (24HM) is commonly used to assess cardiac rhythm after surgical therapy of atrial fibrillation (AF). However, this "snapshot" documentation leaves a considerable diagnostic window and only stores short-time cardiac rhythm episodes. To improve accuracy of rhythm surveillance after surgical ablation therapy and to compare continuous heart rhythm surveillance versus 24HM follow-up intra-individually, these investigators evaluated a novel implantable continuous cardiac rhythm monitoring (IMD) device (Reveal XT 9525, Medtronic Inc., Minneapolis, MN). A total of 45 cardiac surgical patients (male 37, mean age of 69.7+/-9.2 years) with a mean pre-operative AF duration of 38 +/- 45 m were treated with either left atrial epicardial high-intensity focus ultrasound ablation (n = 33) or endocardial cryothermy (n = 12) in case of concomitant mitral valve surgery. Rhythm control readings were derived simultaneously from 24HM and IMD at 3-month intervals with a total recording of 2,021 hours for 24HM and 220,766 hours for IMD. Mean follow-up was 8.30 +/- 3.97 m (range of 0 to 12 m). Mean post-operative AF burden (time period spent in AF) as indicated by IMD was 37 +/- 43 %. Sinus rhythm was documented in 53 readings of 24HM, but in only 34 of these instances by the IMD in the time period before 24HM readings (64 %, $p < 0.0001$), reflecting a 24HM sensitivity of 0.60 and a negative-predictive value (NPV) of 0.64 for detecting AF recurrence. The authors concluded that for "real-life" cardiac rhythm documentation, continuous heart rhythm surveillance instead of any conventional 24HM follow-up strategy is necessary. This is particularly important for further judgment of ablation techniques, devices as well as anti-coagulation and anti-arrhythmic therapy.

Hindricks et al (2010) quantified the performance of the first implantable leadless cardiac monitor (ICM) with dedicated AF detection capabilities. Patients (n = 247) with an implanted ICM who were likely to present with paroxysmal AF were selected. A special Holter device stored 46 hours of subcutaneously recorded ECG, ICM markers, and 2 surface ECG leads. The ICM automatic arrhythmia classification was compared with the core laboratory classification of the surface ECG. Of the 206 analyzable Holter recordings collected, 76 (37 %) contained at least 1 episode of core laboratory classified AF. The sensitivity, specificity, positive-predictive value, and NPV for identifying patients with any AF were 96.1 %, 85.4 %, 79.3 %, and 97.4 %, respectively. The AF burden measured with the ICM was very well-correlated with the reference value derived from the Holter (Pearson coefficient = 0.97). The overall accuracy of the ICM for detecting AF was 98.5 %. The authors concluded that in this ICM validation study, the dedicated AF detection algorithm reliably detected the presence or absence of AF and the AF burden was accurately quantified.

Ip et al (2012) examined the outcomes of surgical ablation and post-ablation AF surveillance with a leadless ICM. A total of 45 patients with drug-refractory paroxysmal or persistent AF underwent video-assisted epicardial ablation using a bipolar radiofrequency clamp. An ICM was implanted subcutaneously post-ablation to assess AF recurrence. AF recurrence was defined as greater than or

equal to 1 AF episode with a duration of greater than or equal to 30 s. The device-stored data were down-loaded weekly over the internet, and all transmitted events were reviewed. A total of 1,220 AF automatic and patient-activated AF episodes were analyzed over a follow-up of 12 +/- 3 months. Of these episodes, 46 % were asymptomatic. Furthermore, only 66 % of the patient-activated episodes were AF. Recurrence of AF was highest in first 4 weeks and substantially decreased 6 months post-ablation. The overall freedom from AF recurrence at the end of follow-up was 60 %. When 48-hr Holter recordings were compared with the device-stored episodes, the sensitivity of the device to detect AF was 98 %, and the specificity was 71 %. The authors concluded that ICM provides an objective measure of AF ablation success and may be useful in making clinical decisions.

The AliveCor Heart Monitor (AliveCor, Inc., San Francisco, CA) is an iPhone-enabled heart monitor that has been known as the "iPhoneECG". It is in a thin case with 2 electrodes that snaps onto the back of an iPhone 4 or 5. To obtain an electrocardiogram (ECG) recording, the patient just holds the device while pressing fingers from each hand onto the electrodes. The device can also obtain an ECG from the patient's chest. The AliveCor ECG iPhone application can record rhythm strips of any duration to be stored on the phone and uploaded securely for later analysis, sharing, or printing through AliveCor's website. The AliveCor Heart Monitor will operate for about 100 hours on a 3.0 V coin cell battery.

However, there is currently a lack of evidence to support the clinical value of the AliveCor Heart Monitor. Prospective, randomized controlled studies are needed to ascertain how the use of the AliveCor Heart Monitor would improve clinical outcomes in patients with cardiovascular diseases/disorders.

According to the company, research studies are currently in progress to explore effectiveness of the AliveCor Heart Monitor in the following areas: http://www.medgadget.com/2012/12/alivecor-iphone-ecg-receives-fda-clearance.html

- Expanding physician assistant/registered nurse data collection abilities
- Long-term atrial fibrillation remote monitoring
- Medication-induced QT-duration response monitoring
- Multi-specialty care integration
- Post-ablation follow-up
- Preventive pediatric care
- Stress induced rhythm morphology changes

The implantable loop recorder (ILR) is a subcutaneous, single-lead, ECG monitoring device used for diagnosis in patients with recurrent unexplained episodes of palpitations or syncope. The 2009 ESC syncope guidelines include the following recommendations for use of ILRs:

- ILR is indicated for early phase evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria (see appendix), and a high likelihood of recurrence within the battery life of the device.
- An ILR is recommended in patients who have high-risk features (see appendix) in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment.
- An ILR should be considered to assess the contribution of bradycardia before embarking on cardiac pacing in patients with suspected or certain reflex syncope with frequent or traumatic syncopal episodes.

Ziegler et al (2012) stated that the detection of undiagnosed atrial tachycardia/atrial fibrillation (AT/AF) among patients with stroke risk factors could be useful for primary stroke prevention. These researchers analyzed newly detected AT/AF (NDAF) using continuous monitoring in patients with stroke risk factors but without previous stroke or evidence of AT/AF. Newly detected AT/AF (AT/AF greater than 5 mins

on any day) was determined in patients with implantable cardiac rhythm devices and greater than or equal to 1 stroke risk factors (congestive heart failure, hypertension, age greater than or equal to 75 years, or diabetes). All devices were capable of continuously monitoring the daily cumulative time in AT/AF. Of 1,368 eligible patients, NDAF was identified in 416 (30%) during a follow-up of 1.1 ± 0.7 years and was unrelated to the CHADS2 score (congestive heart failure, hypertension [blood pressure consistently greater than 140/90 mm Hg or hypertension treated with medication], age greater than or equal to 75 years, diabetes mellitus, previous stroke or transient ischemic attack). The presence of AT/AF greater than 6 hours on greater than or equal to 1 day increased significantly with increased CHADS2 scores and was present in 158 (54 %) of 294 patients with NDAF and a CHADS2 score of greater than or equal to 2. Newly detected AT/AF was sporadic, and 78 % of patients with a CHADS2 score of greater than or equal to 2 with NDAF experienced AT/AF on less than 10 % of the follow-up days. The median interval to NDAF detection in these higher risk patients was 72 days (interquartile range: 13 to 177). The authors concluded that continuous monitoring identified NDAF in 30 % of patients with stroke risk factors. In patients with NDAF, AT/AF occurred sporadically, high-lighting the difficulty in detecting paroxysmal AT/AF using traditional monitoring methods. However, AT/AF also persisted for greater than 6 hours on greater than or equal to 1 day in most patients with NDAF and multiple stroke risk factors. Whether patients with CHADS2 risk factors but without a history of AF might benefit from implantable monitors for the selection and administration of anti-coagulation for primary stroke prevention merits additional investigation.

Cotter et al (2013) examined the usefulness of ILR with improved AF detection capability (Reveal XT) and the factors associated with AF in the setting of unexplained stroke. A cohort study was reported of 51 patients in whom ILRs were implanted for the investigation of ischemic stroke for which no cause had been found (cryptogenic) following appropriate vascular and cardiac imaging and at least 24 hours of cardiac rhythm monitoring. Age of patients ranged from 17 to 73 (median of 52) years. Of the 30 patients with a shunt investigation, 22 had a patent foramen ovale (73.3 %; 95 % CI: 56.5 % to 90.1 %). Atrial fibrillation was identified in 13 (25.5 %; 95 % CI: 13.1 % to 37.9 %) cases. Atrial fibrillation was associated with increasing age ($p = 0.018$), inter-atrial conduction block ($p = 0.02$), left atrial volume ($p = 0.025$), and the occurrence of atrial premature contractions on preceding external monitoring ($p = 0.004$). The median (range) of monitoring prior to AF detection was 48 (0 to 154) days. The authors concluded that in patients with unexplained stroke, AF was detected by ILR in 25.5 %. Predictors of AF were identified, which may help to target investigations. They stated that ILRs may have a central role in the future in the investigation of patients with unexplained stroke.

Mittal et al (2013) stated that in patients with atrial flutter who undergo cavo-tricuspid isthmus ablation, long-term ECG monitoring may identify new onset of AF. These investigators ascertained, through the use of an ILR with a dedicated AF detection algorithm, the incidence, duration, and burden of new AF in these patients and developed an optimal post-ablation ECG monitoring strategy. These researchers enrolled 20 patients with flutter, a CHADS2 score of 2 to 3, and no prior episode of AF. After cavo-tricuspid isthmus ablation, these investigators implanted an ILR, which was interrogated routinely; all stored ECGs were adjudicated. During a mean follow-up of 382 ± 218 days, 3 patterns were observed: (i) in 11 (55 %) patients, stored ECGs confirmed AF at 62 ± 38 days after ablation; (ii) in 4 (20 %) patients, although the ILR suggested AF, episodes actually represented sinus rhythm with frequent premature atrial contractions and/or over-sensing; (iii) in 5 (25 %) patients, no AF was observed. Episodes less than 4 hours were associated with low AF burden (less than 1 %) or false detections. The 1-year freedom from any episode of AF greater than 4 and greater than 12 hours was 52 % and 83 %, respectively. The authors concluded that these findings showed that many (but not all) patients develop new AF within the first 4 months of flutter ablation. Since external ECG monitoring for this duration is impractical, the ILR has an important role for long-term AF surveillance. They stated that future research should be directed toward identifying the relationship between duration/burden of AF and stroke and improving existing ILR technology.

An UpToDate review on "Cryptogenic stroke" (Prabhakaran and Elkind, 2013) states that "Paroxysmal atrial fibrillation (AF), if transient, infrequent, and largely asymptomatic, may be undetected on standard cardiac monitoring such as continuous telemetry and 24 or 48-hour Holter monitors. In a study that assessed longer-term monitoring using an outpatient telemetry system for a median duration of 21 days among 56 patients with cryptogenic stroke, paroxysmal AF was detected in 13 patients (23 %). The median time to detection of AF was 7 days. The majority of patients with paroxysmal AF were asymptomatic during the fleeting episodes. Other reports have noted that the detection rate of paroxysmal AF can be increased with longer duration of cardiac monitoring, and that precursors of AF such as frequent premature atrial contractions may predict those harboring paroxysmal AF. The optimal monitoring method -- continuous telemetry, ambulatory electrocardiography, serial electrocardiography, transtelephonic ECG monitoring, or implantable loop recorders -- is uncertain, though longer durations of monitoring are likely to obtain the highest diagnostic yield".

Appendix

Table: Short-Term High Risk Criteria Which Require Prompt Hospitalization or Intensive Evaluation

- *Severe structural or coronary artery disease* (heart failure, low LVEF, or previous myocardial infarction)
- *Clinical or ECG features suggesting arrhythmic syncope*
    - Syncope during exertion or supine
    - Palpitations at the time of syncope
    - Family history of SCD
    - Non-sustained VT
    - Bifascicular-block (LBBB or RBBB combined with left anterior or left posterior fascicular block) or other intraventricular conduction abnormalities with QRS duration ≥120 ms
    - Inadequate sinus bradycardia (<50 bpm) or sinoartrial block in absence of negative chronotropic medications or physical training
    - Pre-excited QRS complex
    - Prolonged or short QT interval
    - RBBB pattern with ST-elevation in leads V1-V3 (Brugada pattern)
    - Negative T waves in right precordial leads, epsilon waves, and ventricular late potentials suggestive of ARVC
- *Important co-morbidities*
    - Severe anemia
    - Electrolyte disturbance

Key: ARVC: arrhythmogenic right ventricular cardiomyopathy; bpm: beats per minute; LBBB: left bundle branch block; LVEF: left ventricular ejection fraction; RBBB: right bundle branch block; SCD: sudden cardiac death; VT: ventricular tachycardia.

Source: Task Force for the Diagnosis and Management of Syncope; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA); Heart Failure Association (HFA); Heart Rhythm Society (HRS), Moya A, Sutton R, Ammirati F, et al. Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J. 2009;30(21):2631-2671.

CPT Codes / HCPCS Codes / ICD-9 Codes

External intermittent cardiac event monitors (i.e., external loop recorders) and external intermittent cardiac event monitors with real-time data transmission and analysis :

CPT codes covered if selection criteria are met:

93268	External patient and, when performed, auto activated electrocardiographic rhythm derived event recording with symptom-related memory loop with remote download capability up to 30 days, 24-hour attended monitoring; includes transmission, review and interpretation by a physician or other qualified health care professional
93270	recording (includes connection, recording, and disconnection)
93271	transmission and analysis
93272	preview and interpretation by a physician or other qualified health care professional

Other CPT codes related to the CPB:

93224 - 93227	Electrocardiographic monitoring [Holter monitors and other event recording]

ICD-9 codes covered if selection criteria are met:

426.0 - 426.9	Conduction disorders [in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia or syncope is unlikely to be diagnosed by Holter monitoring]
427.0 - 427.9	Cardiac dysrhythmias [in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia or syncope is unlikely to be diagnosed by Holter monitoring]
780.2	Syncope and collapse [in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia or syncope is unlikely to be diagnosed by Holter monitoring]
780.4	Dizziness and giddiness [light-headedness] [in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia or syncope is unlikely to be diagnosed by Holter monitoring]
785.1	Palpitations

Other ICD-9 codes related to the CPB:

410.00 - 414.9	Ischemic heart disease [to document ST segment depression for suspected ischemia]
V15.1	Personal history of surgery to heart and great vessels [ablation procedure for arrhythmia]
V58.69	Long-term (current) use of other medications [to document the benefit after initiating drug therapy for arrhythmia]

Mobile cardiovascular telemetry (MCT):

CPT codes covered if selection criteria are met:

93228	External mobile cardiovascular telemetry with electrocardiographic recording, concurrent computerized real time data analysis and greater than 24 hours of accessible ECG data storage (retrievable with query) with ECG triggered and patient selected events transmitted to a remote attended surveillance center for up to 30 days; review and interpretation with report by a physician or other qualified health care professional
93229	technical support for connection and patient instructions for use, attended surveillance, analysis and physician prescribed transmission of daily and emergent data reports as prescribed by a physician or other qualified health care professional

ICD-9 codes covered if selection criteria are met - see below:

Criteria - a cardiac arrhythmia is suspected as the cause in members that have a non-diagnostic Holter monitor, or symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring

426.0 - 426.9	Conduction disorders
427.0 - 427.9	Cardiac dysrhythmias
780.2	Syncope and collapse [pre-syncope]
780.4	Dizziness and giddiness [light-headedness]
785.1	Palpitations

Implantable loop recorder:

CPT codes covered if selection criteria are met:

33282	Implantation of patient-activated cardiac event recorder
33284	Removal of an implantable, patient-activated cardiac event recorder
93285	Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional; implantable loop recorder system
93291	Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional , includes connection, recording and disconnection per patient encounter; implantable loop recorder system, including heart rhythm derived data analysis
93298	Interrogation device evaluation(s), (remote) up to 30 days; implantable loop recorder system, including analysis of recorded heart rhythm data, analysis, review (s) and report(s) by a physician or other qualified health care professional
93299	implantable cardiovascular monitor system or implantable loop recorder system, remote data acquisition(s), receipt of transmissions and technician review, technical support and distribution of results

HCPCS codes covered if selection criteria are met:

C1764	Event recorder, cardiac (implantable)
E0616	Implantable cardiac event recorder with memory, activator, and programmer

ICD-9 codes covered if selection criteria are met:

412	Old myocardial infarction [noninvasive ambulatory monitoring consisting of 30-day presymptom external loop recordings or MCT fails to establish a definitive diagnosis]
428.0 - 428.9	Heart failure [noninvasive ambulatory monitoring consisting of 30-day presymptom external loop recordings or MCT fails to establish a definitive diagnosis]
780.2	Syncope and collapse [pre-syncope] [symptoms occur so infrequently and unpredictably (less frequently than once per month) that noninvasive ambulatory monitoring (MCT or external loop recorders) are unlikely to capture a diagnostic ECG]
780.39	Other convulsions [seizures NOS] [symptoms occur so infrequently and unpredictably (less frequently than once per month) that noninvasive ambulatory monitoring (MCT or external loop recorders) are unlikely to capture a diagnostic ECG]
780.4	Dizziness and giddiness [light-headedness] [symptoms occur so infrequently and unpredictably (less frequently than once per month) that noninvasive ambulatory

	monitoring (MCT or external loop recorders) are unlikely to capture a diagnostic ECG]
785.1	Palpitations [symptoms occur so infrequently and unpredictably (less frequently than once per month) that noninvasive ambulatory monitoring (MCT or external loop recorders) are unlikely to capture a diagnostic ECG]
794.31	Abnormal electrocardiogram [ECG] [EKG] [significant ECG abnormalities & noninvasive ambulatory monitoring consisting of 30-day presymptom external loop recordings or MCT fails to establish a definitive diagnosis]

Long-term (greater than 48 hours) external ECG monitoring by continuous rhythm recording and storage:

CPT codes covered if selection criteria are met:

0295T - 0298T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; includes recording, scanning analysis with report, review and interpretation [Zio Patch]

ICD-9 codes covered if selection criteria are met [in persons with a non-diagnostic Holter monitor, or in persons whose symptoms occur infrequently (less frequently than daily) such that the arrhythmia is unlikely to be diagnosed by Holter monitoring]:

426.0 - 426.9	Conduction disorders
427.0 - 427.9	Cardiac dysrhythmias
780.2	Syncope and collapse [pre-syncope]
780.4	Dizziness and giddiness [light-headedness]
785.1	Palpitations

AliveCor Heart Monitor (iPhoneECG):

CPT codes not covered for indications listed in the CPB:

93040	Rhythm ecg, one to three leads; with interpretation and report

HCPCS codes not covered for indications listed in the CPB:

No specific code

Appendix - Short-Term High Risk Criteria Which Require Prompt Hospitalization or Intensive Evaluation:

Other ICD-9 codes related to the CPB:

412	Old myocardial infarction
428.0 - 428.9	Heart failure
794.31	Abnormal electrocardiogram [ECG] [EKG]

The above policy is based on the following references:

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Policy History

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- Definitions

Additional Information

- Clinical Policy Bulletin Notes

- Web Privacy
- Legal Statement
- Privacy Information

- Member Disclosure

Cigna Medical Coverage Policy

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Coverage Policy Number **0085**

Subject **Cardiac Event Monitors**

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Hyperlink to Related Coverage Policies

Telemedicine
Tilt Table Testing

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna companies including plans formerly administered by Great-West Healthcare, which is now a part of Cigna. Coverage Policies are intended to provide guidance in interpreting certain ***standard*** *Cigna benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document* ***always supercedes*** *the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2012 Cigna*

Coverage Policy

Continuous 24- to 48-hour External Unattended Cardiac Monitoring Device

Cigna covers the use of a 24- to 48-hour continuous external unattended cardiac monitoring device (e.g., Holter monitor™ [HM]) (Current Procedural Terminology [CPT] code 93224, 93225, 93226, 93227) as medically necessary for ANY of the following indications:

- as a diagnostic tool to evaluate symptoms suggestive of cardiac arrhythmias (e.g., frequent palpitations, unexplained dizziness, or syncope)
- assessment of pacemaker or implantable cardioverter defibrillator (ICD) function for **ANY** of the following:
    - frequent symptoms of palpitation, syncope, or near syncope
    - suspected component failure or malfunction
    - assessment of response to drug therapy in an individual with an ICD
- assessment of potential myocardial ischemia in suspected variant angina or known coronary artery disease when such information will impact management
- assessment of antiarrhythmic drug therapy in an individual with a treated arrhythmia
- child with **ANY** of the following:
    - hypertrophic or dilated cardiomyopathy
    - possible long QT syndrome

- congenital heart disease accompanied by a significant residual hemodynamic abnormality when surgery is being considered
- assessment of the adequacy of antiarrhythmic therapy during rapid growth
- asymptomatic non-paced congenital complete atrioventricular (AV) block

Patient or Event Recorder (Loop Recorder)

Cigna covers the use of an external loop recorder (CPT code 93268, 93270, 93271, 93272) as medically necessary for the identification of a suspected cardiac arrhythmia despite normal findings on ambulatory electrocardiography (AECG).

Cigna covers the use of an implantable loop recorder (CPT code 33282, 33284, 93285, 93291, 93297, 93298, 93299, C1764, E0616) as medically necessary for the evaluation of recurrent unexplained episodes of fainting when ALL of the following criteria are met:

- cardiac arrhythmia is suspected to be the cause of fainting
- noninvasive ambulatory monitoring failed to establish a definitive diagnosis because the symptoms occur so infrequently and unpredictably that the length of the monitoring period may have been inadequate to capture a diagnostic electrocardiogram (ECG) rhythm disorder
- tilt-table testing is negative or nondiagnostic

External Mobile Outpatient Cardiac Telemetry System

Cigna does not cover an external mobile outpatient cardiac telemetry system (CPT code 93228, 93229) for any indication because it is considered experimental, investigational or unproven.

Long-term Continuous 48 hour to 21 day External Unattended Cardiac Monitoring Device

Cigna does not cover a 48 hour to 21 day external continuous unattended cardiac monitoring device (CPT code 0295T—0298T) for any indication because it is considered experimental, investigational or unproven.

General Background

Cardiac arrhythmias or abnormal heartbeats represent a major source of morbidity and mortality among patients with cardiovascular disease. While some patients with arrhythmias may experience palpitations, weakness, dizziness, or syncope, other patients may have no symptoms at all. Some arrhythmias pose a significant health threat and require prompt treatment. Treatments for arrhythmias include medical therapy, artificial pacemakers, implanted cardiac defibrillators, and ablation of malfunctioning cardiac tissue. Effective treatment of arrhythmias requires an early diagnosis. This can be difficult, since arrhythmias can occur infrequently and unpredictably and may be asymptomatic. Therefore, devices that monitor a patient's heartbeat for an extended period of time and can automatically detect certain arrhythmias are desirable (ECRI, 2010).

Remote cardiac monitoring technologies allow home ECG monitoring of patients with suspected cardiac arrhythmias or at risk for developing arrhythmias. This is also referred to as ambulatory electrocardiography (AECG). Because certain abnormalities may occur only during sleep or with mental, emotional, or exercise-induced changes in cardiac oxygenation or function, an ECG may need to be recorded over long periods of time. AECG has proven to be useful for the diagnosis and management of patients at high risk for life-threatening cardiac arrhythmias (Agency for Healthcare Research and Quality [AHRQ], 2007; Hammill, 2007; Kadish, et al., 2001).

The categories of remote cardiac monitoring technologies include (AHRQ, 2007; Mittal, et al., 2011; U.S. Food and Drug Administration (FDA), 2012):

- continuous 24- to 48-hour external unattended cardiac monitoring device (e.g., Holter monitoring™ [HM])

- long-term continuous 48- to 21-day external unattended cardiac monitoring device
- patient- or event-activated device

    - externally-worn presymptom memory loop recorder (attended and unattended)
    - implantable/insertable presymptom memory loop recorder (attended and unattended)
    - post-symptom patient activated recorder

- real-time continuous attended cardiac monitoring system

Continuous 24- to 48-hour External Unattended Cardiac Monitoring Device: The most common device used is called a Holter monitor™ (HM). The recording device of an HM is worn on a strap at the waist or over the shoulder. The electrical signals of the heart are picked up by two electrodes attached to the chest, and these are connected to the recorder by wires. HM generally provides a continuous 24- to 48-hour record of the electrical signals from the heart. While wearing the HM, the individual keeps a diary of all activities and symptoms. The data is computer analyzed and interpreted by a physician at a later time (Olgin, 2011; Noble, et al., 2004).

The American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines for ambulatory electrocardiography (AECG) state there are two categories of AECG recorders: continuous and intermittent recorders. The authors assigned their highest level (i.e., Class I) of evidence to the following indications for AECG (Crawford, et al., 1999). There have been no updates to these guidelines since 1999:

- to assess symptoms possibly related to rhythm disturbances

    - patients with unexplained syncope, near syncope, or episodic dizziness in whom the cause is not obvious; patients with unexplained recurrent palpitations

- to assess antiarrhythmic therapy:

    - to assess antiarrhythmic drug response in individuals in whom baseline frequency of arrhythmia has been characterized as reproducible and sufficient to permit analysis

- to assess pacemaker and implantable cardioverter defibrillator (ICD) function:

    - evaluation of frequent symptoms of palpitation, syncope, or near syncope to assess device function to exclude myopotential inhibition and pacemaker-meditated tachycardia, and to assist in the programming of enhanced features such as rate responsivity and automatic switching
    - evaluation of suspected component failure or malfunction when device interrogation is not definitive in establishing a diagnosis
    - to asses the response to adjunctive pharmacological therapy in patients receiving frequent ICD therapy

- for ischemic monitoring:

    - patients with suspected variant angina

- for pediatric patients:

    - syncope, near syncope, or dizziness in patients with recognized cardiac disease, previously documented arrhythmia, or pacemaker dependency
    - syncope or near syncope associated with exertion when the cause is not established by other methods
    - evaluation of patients with hypertrophic or dilated cardiomyopathies
    - evaluation of possible or documented long QT syndromes
    - palpitation in the patient with prior surgery for congenital heart disease and significant residual hemodynamic abnormalities
    - evaluation of antiarrhythmic drug efficacy during rapid somatic growth

- asymptomatic congenital complete atrioventricular (AV) block, nonpaced

Patient or Event Recorder (Loop Recorder): The patient or event recorders can be used for a longer time (e.g., 30 days) than a HM and is more likely to record infrequent abnormal heart rhythms. The information collected by a patient or event recorder can be sent over the phone to a doctor's office, clinic, or hospital. The advantage of event recorders over the continuous ambulatory systems is that the ECG is more likely to be obtained while the patient is experiencing clinical symptoms, therefore allowing a direct correlation between the patient's symptoms and the ECG recorded at that instant (Miller, et al., 2011; AHRQ, 2007; Hammill, 2007; Noble, et al., 2004). Examples of patient or event recorders include:

- Externally-worn presymptom memory loop recorders (attended and unattended): This is a small device that attaches to the chest with electrodes. The standard external loop recorder records several minutes of activity at a time and then starts over, a process referred to as memory loop recording. The patient activates this device to record when a symptom occurs and then data from the device is typically transmitted to a monitoring center for immediate review. This process is repeated whenever symptoms occur over a period of 20–30 days (which is the typical amount of time the device is worn by the patient). Since the data that are recorded by the device are typically associated with a symptom, a physician can also determine whether that symptom is a result of a cardiac arrhythmia. However, due to the need for the patient to signal an event, the standard cardiac event monitor typically only captures events associated with a patient's symptoms and not those events that are asymptomatic.

  The auto-trigger external loop recorder also memory loop records, capturing several minutes of heart activity at a time before starting over. In addition, the auto-trigger external loop recorder uses systems to automatically detect events that may not be associated with a patient experiencing symptoms. Unlike a standard external loop recorder, an auto-trigger external loop recorder does not rely on the patient's ability to activate it and, as a result, is able to capture asymptomatic events in addition to symptomatic ones. However, the auto-trigger device still relies on the patient to call in and transmit the event by reaching the physician or a technician at a physician's office or a monitoring center and holding the cardiac event monitor up to a telephone to transmit the event data.

- Implantable/insertable presymptom memory loop recorders (attended and unattended).
  An implantable or insertable memory loop recorder (ILR) is inserted under the patient's skin at about the second rib on the left front of the chest and is activated by passing a special magnet over the device. The main difference between the ILR and the external loop recorders is that the ILR can be used for a much longer time period. Current models are capable of recording from 14–20 months before being surgically removed. It is capable of recording up to 42 minutes of a single ECG channel that can be partitioned for one to seven episodes, with up to 20 minutes of preactivation ECG saved for subsequent downloading to a programming unit for analysis. The device can be configured to store patient-activated, automatically activated recordings (e.g., heart rate outside preset parameters), or a combination of these. The ILR is used when syncope is infrequently detected by either an HM or a 30-day event recorder.

- Post-symptom patient-activated recorders: This handheld device is used only when symptoms occur. It does not have electrodes that are attached to the chest. When symptoms occur, the patient presses a button to start the ECG recording. The back of the device has small metal discs that function as the electrodes. The post-event monitor typically stores the data for up to 30 days which is transmitted telephonically or through a computer to a receiving center or doctor's office after the event.

U.S. Food and Drug Administration (FDA)
Continuous External Unattended Cardiac Monitoring Devices (HM) and Patient or Event Recorder (Loop Recorder): There are numerous manufacturers of continuous external unattended cardiac monitoring devices and patient or event recorders which can be found on the FDA Center for Devices and Radiologic Health 510(k) database (FDA, 2010). Examples of implantable memory loop recorders include the Reveal® Insertable Loop Recorder (Medtronic, Inc., Minneapolis, MN) which received 510(k) premarket approval from the FDA in February 2001 as a Class II device (FDA, 2001).

Literature Review

Continuous 24- to 48-hour External Unattended Cardiac Monitoring Device/Patient or Event Recorder (Loop Recorder): The peer-reviewed medical literature supports the clinical utility of standard cardiac event monitors such as the HM and loop recorders. Evidence in the published literature consists of systematic reviews, case studies and few well-designed clinical trials (Hindricks, et al., 2010; Giada, et al., 2007; Brignole, et al., 2006; Reiffel, et al., 2005; Farwell, et al., 2004; Sivakumaran, et al., 2003; Krahn, et al., 2001; Krahn, et al., 1999).

Long-term Continuous 48 hour to 21 day External Unattended Cardiac Monitoring Device: Long-term continuous external unattended cardiac monitoring devices provide continuous recording of the electrical activity of the heart for more than 48 hours and up to 21 days. These devices are suggested to increase detection of arrhythmias. A physician analyzes the recording to identify heart rhythm abnormalities. An example of these devices is the Zio® Patch (iRhythm Technologies, Inc., San Francisco, CA), which can record up to 14 days of activity (Mittal, et al., 2011).

U.S. Food and Drug Administration (FDA)

Long-term Continuous External Unattended Cardiac Monitoring Device: The FDA indications for use for the Zio® Patch (iRhythm Technologies, Inc., San Francisco, CA) states it is a prescription only single patient use, continuous recording EGG monitor that can be worn for up to 14 days. It is indicated for use on patients who experience transient symptoms such as syncope, palpitations, shortness of breath, or chest pains (FDA, 2012).

Literature Review

Long-term Continuous External Unattended Cardiac Monitoring Device: There is a lack of evidence in the published peer-reviewed medical literature supporting the clinical utility of long-term continuous external unattended cardiac monitoring devices. Studies are required to evaluate how long-term continuous external unattended cardiac monitoring devices can change treatment management and improve health outcomes compared to standard cardiac event monitors.

External Mobile Outpatient Cardiac Telemetry System: The external mobile outpatient cardiac telemetry continuous attended monitoring systems have been promoted for use as alarm systems for long-term monitoring in patients. When using this technology, the patient wears a portable electrocardiogram sensor with leads attached to the patient's skin for continuous monitoring of cardiac rhythms during daily activities. If the algorithm of the monitoring system detects an arrhythmic event, the system will automatically transmit the ECG data wirelessly or through a phone line to a service center. Here, experienced monitoring specialists analyze the data, respond to events, and report results in the manner prescribed by the physician. The patient can also manually send the ECG data by pressing a button when experiencing a symptom. Physicians can monitor a patient's cardiac rhythm for weeks (ECRI, 2010).

U.S. Food and Drug Administration (FDA)

External Mobile Outpatient Cardiac Telemetry System: CardioNet Mobile Cardiac Outpatient Telemetry™ (MCOT™) Services uses the CardioNet (Philadelphia, PA) home-based, real-time cardiac surveillance system. The CardioNet ambulatory ECG monitor received initial 510(k) premarket approval from the FDA in May 2001. The 2001 FDA intended use states, "The CardioNet Ambulatory ECG Monitor is a 3 channel ambulatory ECG monitor capable of recording and transmitting up to 24 hours of ECG data for the purpose of cardiac monitoring and diagnosis by a medical professional. The system includes recording and trans-telephonic transmitting circuitry, a graphic LCD and firmware. The system records ECG and transmits the ECG data to a remote central receiving station. The quality of the ECG data is suitable for analysis by another device to identify cardiac rhythm disorders, heart rate variability, reporting of QT interval and ST changes. The device is not intended to sound any alarms".

The CardioNet ECG Monitor with Arrhythmia Detection received 510(k) premarket approval from the FDA in February 2002. The CardioNet ECG Monitor with Arrhythmia Detection is referred to as the subject device and is a modification to the CardioNet Ambulatory ECG Monitor. The subject device includes the addition of an ECG analysis capability that allows detection of cardiac arrhythmia. The indications for use for the subject device is as follows:

- Patients who have demonstrated a need for cardiac monitoring and are at low risk of developing primary ventricular fibrillation or sustained ventricular tachycardia.
- Patients with dizziness or lightheadedness
- Patients with palpitations
- Patients with syncope of unknown etiology
- Patients who require monitoring for life-threatening arrhythmias, such as atrial fibrillation, other supra-ventricular arrhythmias, evaluation of bradyarrhythmias and intermittent bundle branch block. This includes post operative monitoring of these arrhythmias.
- Patients recovering from CABG surgery who require monitoring for arrhythmias.
- Patients requiring monitoring for arrhythmias induced co-morbid conditions such as hyperthyroidism or chronic lung disease.
- Patients with obstructive sleep apnea to evaluate possible nocturnal arrhythmias.
- Patients requiring arrhythmia evaluation for etiology of stroke or transient cerebral ischemia, possibly secondary to atrial fibrillation.
- Data from the device may be used by another device to analyze, measure or report QT interval. The device is not intended to sound any alarms for QT changes.

Another real-time system is the HEARTLink™ II, manufactured by Cardiac Telecom Corporation (Greensburg, PA) which uses Telemetry@ Home (FDA, 1998). Other examples of real-time systems include the CG-6108 Arrhythmia ECG Event Recorder (Card Guard Scientific Survival Ltd, Rehovot, Israel) which is also known as the Lifestar Ambulatory Cardiac Telemetry (ACT) by Life Watch Services, Inc. (Rosemont, IL), the Vital Signs Transmitter (VST)™ (Biowatch Medical, Inc., Columbia, SC), NUVANT™ Mobile Cardiac Telemetry (MCT) System (Corventis™, San Jose, CA) (FDA, 2009; FDA, 2006; FDA, 2004).

Literature Review

External Mobile Outpatient Cardiac Telemetry System: There is limited evidence in the published peer-reviewed medical literature supporting the clinical utility of external mobile outpatient cardiac telemetry systems. Many of the studies lack a comparator and do not report long-term outcomes. Additional studies with long-term follow-up are required to evaluate how real-time surveillance systems can change treatment management and improve health outcomes compared to standard cardiac event monitors.

Kadish et al. (2010) retrospectively analyzed patient characteristics, diagnostic yield, and diagnoses of patients in a large commercial database (LifeWatch Services, Inc., Rosemont, Illinois). The purpose of the present study was to evaluate the potential advantage of the immediate response feature. All patients (n=26,438) who underwent monitoring from April to December 2008 at a single service provider formed the patient population of this study. Arrhythmic events noted in these patients were defined as those requiring physician notification and those that represented potentially life-threatening arrhythmias. Of the 26,438 patients included in the study, 5459 (21%) had arrhythmic events meeting physician notification criteria during a mean monitoring period of 21 days. Of these, 262 patients (1%) had arrhythmic events that could potentially be classified as emergent. These included 120 patients with wide complex tachycardia >15 beats at >120 beats/min, 100 patients with pauses >6 seconds, and 42 patients with sustained heart rates <30 beats/min. An additional 704 patients (3%) had narrow complex tachycardia >180 beats/min at rest. Limitations of the study include lack of a comparison group, no information on patient outcomes and detailed information on the patient population was not reported.

In a case series study, Tayal et al. (2008) analyzed 56 patients with cryptogenic transient ischemic attack (TIA) or stroke after diagnostic evaluation and Mobile MCOT for up to 21 days. Demographic, radiographic, echocardiographic, and MCOT results were reviewed. The inclusion criteria were: age greater than 18 years; ischemic stroke or TIA within the last three months; and diagnosis of cryptogenic TIA/stroke. TIA was defined as sudden-onset focal neurologic symptoms or signs that resolved within 24 hours and was not associated with high-intensity abnormality in the diffusion-weighted sequence. TIA symptoms and signs included hemiplegia/hemiparesis, monoplegia/monoparesis, aphasia, transient monocular blindness, vertigo, dysarthria, and isolated sensory symptoms. The exclusionary criteria included: history of AF; admission ECG, inpatient cardiac telemetry monitoring, or 24-hour Holter data that demonstrated AF prior to initiation of MCOT; and prothrombotic state. The median MCOT monitoring duration was 21 (range 5–21) days resulting in an AF detection rate of 23% (13/56). AF was first detected after a median of 7 (range 2–19) days of monitoring. Twenty-seven asymptomatic AF episodes were detected in the 13 patients, of which 85% (23/27) were <30 seconds and the remaining 15% (4/27) were 4–24 hours in duration. Prior to the initiation of MCOT, 82.1%

(46/56) of the patients were receiving antiplatelet medication, 14.3% (8/56) were receiving warfarin, and 3.6% (2/56) were receiving both antiplatelet medication and warfarin. MCOT results altered patient management in the 13 patients found to have new onset AF by MCOT. Five patients had their antiplatelet medication changed to warfarin, six patients were maintained on the warfarin they were taking prior to MCOT, and two patients were maintained on antiplatelet medication. A reported limitation of this study was the absence of an age-matched control group without a history of TIA/stroke. In addition, not all patients underwent a transesophageal echocardiography (TEE) in this cohort. Another limitation of this study was lack of reported long-term follow-up to determine whether altered patient management improved health outcomes.

In a retrospective study, Saarel et al. (2008) reported on the use of the MCOT system for evaluation of children and adolescents with suspected cardiac arrhythmia. Patients older than 21 years and those with previously documented arrhythmia were excluded. A total of 59 MCOT studies were performed. Five patients met exclusion criteria leaving 54 subjects (mean age 12.4+/-4.5 years; range 3.2–19.7 years; 46% male) for inclusion. Half of the subjects had been previously monitored with a Holter (n=24), transtelephonic electrocardiographic event monitors (n=1), or both (n=2). Among these subjects, the diagnostic yield for MCOT was similar to the overall study population (59%, n=16/27). Twenty-one subjects (39%) did not experience symptoms during MCOT, yielding a diagnostic rate of 61% (n = 33). Of the 33 diagnostic studies, 9% (n=3; mean age 16.9+/-0.6 years; range 16.2–17.3 years; one male) showed supraventricular tachycardia and 9% (n=3; mean age 11.1+/-2.7 years; range 8.2–13.5 years; one male) showed supraventricular or ventricular ectopy. Minor skin irritation at sites of electrode placement was the only complication of MCOT (n=5). The reported limitations of this study include small sample size, retrospective data analysis, and nonrandomized design. Another limitation of this study was lack of follow-up to determine whether patient outcomes were improved as a result of diagnostic information provided by MCOT.

Rothman et al. (2007) conducted a multicenter, randomized, nonblinded controlled trial evaluating the CardioNet system versus a patient-activated external loop event monitor for symptoms thought to be due to a cardiac arrhythmia. The study included 305 patients at 17 centers. The inclusion criteria were: a high clinical suspicion of a malignant arrhythmia; symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours (presyncope was defined as transient dizziness, lightheadedness, unsteadiness, or weak spells without loss of consciousness; severe palpitations were defined as palpitations that would warrant referral for cardiac monitoring); and a nondiagnostic 24-hour Holter or telemetry monitor within 45 days prior to enrollment. Exclusion criteria were New York Heart Association (NYHA) Class IV heart failure, myocardial infarction within the prior three months, unstable angina, candidate for or recent valvular cardiac surgery, history of sustained ventricular tachycardia or ventricular fibrillation, complex ectopy defined as ventricular premature depolarizations ≥ 10/hour with a documented ejection fraction ≤ 35%, patients < 18 years of age, and a concomitant condition prohibiting completion of or compliance with the protocol. The primary endpoint was the confirmation or exclusion of a probable arrhythmic cause of the patient's symptoms (e.g., syncope, presyncope, or palpitations). Arrhythmias were classified as either clinically significant or clinically insignificant, and then the investigators evaluated the temporal relationship of any symptoms and the likelihood that a clinically significant arrhythmia caused the patient's presenting symptoms.

The patients were randomized to 30 days of monitoring with MCOT (MCOT Group n=134) or with an external patient activated loop monitor (Loop Group n=132). Out of the 305 randomized patients, 266 patients completed a minimum of 25 days of monitoring. The most common reason for not completing the protocol was patient noncompliance (13 MCOT patients and seven LOOP patients). Seven patients found the devices too difficult or cumbersome to use; seven patients had an allergic reactions or skin irritation to the electrodes; and six patients stated the monitors interfered with their work or travel. Most of the patients in the Loop Group were required to activate the recorder when they experienced symptoms; however, 49 (18%) patients were at centers that had autotriggered recording of cardiac events. During monitoring, clinically significant arrhythmias were detected in 55 (41%) patients in the MCOT Group versus 19 (14%) patients in the Loop Group, a statistically significant difference ($p<0.001$). For patients who had syncope or presyncope, clinically significant arrhythmias were detected in 52% of patients with MCOT and in 15% of patients with loop recorders. In most cases, the arrhythmias detected were AF, atrial flutter, or ventricular tachycardia. A subgroup analysis was performed at the institutions that used autotriggered loop monitoring rather than patient-activated monitoring. A definitive diagnosis was obtained in this subgroup for 88% of MCOT Group patients versus 46% of Loop Group patients ($p<0.0025$).However, this subgroup analysis involved a relatively small number of patients, and the autotriggered devices may have had single ECG leads, whereas the CardioNet system uses double ECG leads. The authors state the proportion of patients reporting symptoms was similar in both groups (79% in MCOT and

76% in LOOP), suggesting equal compliance during the early portion of the monitoring period when most transmissions and reported symptoms occurred. This study did not address the impact of the real-time monitoring features on the long-term health outcomes compared to the loop monitor. This study did not discuss how patient treatment changed as a result of the diagnostic information obtained from the CardioNet system.

In a case series study, Olson et al. (2007) evaluated the records of 122 consecutive patients using MCOT for palpitations (n=76), presyncope/syncope (n=17), or to monitor the efficacy of a specific antiarrhythmic therapy (n=29). Ten of 17 patients (59%) studied for resyncope/syncope had a diagnosis made with MCOT. Eight of these 17 patients had a previous negative evaluation for presyncope/syncope (e.g., holter or event monitor) and five had an event correlated with the heart rhythm during the monitoring period. Nineteen patients monitored for palpitations or presyncope/syncope were asymptomatic during monitoring but had a prespecified arrhythmia detected. When MCOT was used as the first ambulatory monitoring system to evaluate palpitations (n=18), 73% of patients correlated their symptoms with the underlying cardiac rhythm. Seven of 21 patients monitored for medication titration had dosage adjustments during outpatient monitoring. Eight patients underwent MCOT monitoring following radiofrequency ablation for atrial fibrillation (AF) (n=5), atrial flutter (n=1), premature ventricular complexes (n=1), and inappropriate sinus tachycardia (n=1). Two patients experienced symptoms during MCOT monitoring. One patient experienced symptomatic premature atrial complexes and the other had sinus rhythm during their symptomatic episode. There was one occurrence of asymptomatic AF in a patient following radiofrequency ablation of AF. A limitation of this study is the uncontrolled study design. There is no comparison to other ambulatory monitoring systems. No long-term health outcomes were reported.

In a small uncontrolled study, Vasamreddy et al. (2006) used the CardioNet monitoring system to assess the efficacy of cardiac tissue ablation procedures for treatment of atrial fibrillation. This is the first study reporting the outcomes of mobile cardiac telemetry monitoring following catheter ablation of AF. A total of 19 patients with highly symptomatic drug refractory AF underwent catheter ablation. Each was provided with an MCOT monitor and was asked to wear it five days immediately before the ablation, and five days per month starting with the ablation for six consecutive months. When patients experienced any symptoms, they were asked to activate the system and to record associated symptoms. Out of the total 390 events triggered by patient's symptoms, 40% were confirmed as AF events (156) and 60% were confirmed as non-AF events (234). Only shortness of breath and chest discomfort were highly associated with AF ($p< 0.05$). At the end of six months of follow-up, out of 10 patients who completed the study, seven (70%) patients were free of symptomatic AF recurrences, whereas only five (50%) patients achieved success when asymptomatic AF recurrences were included in the outcome. Poor patient compliance with a very intensive monitoring protocol was reported as an important limitation of using the CardioNet monitoring system. Only 53% of the study participants were able to complete the study protocol. A limitation of this study was the lack of a comparator and lack of long-term follow-up to determine whether patient outcomes were improved as a result of diagnostic information provided by CardioNet.

In a case series study, Joshi et al. (2005) reported data from the first 100 consecutive patients monitored by an MCOT system who were undergoing treatment for known arrhythmias or who were suspected to have arrhythmias based on symptoms such as palpitations, dizziness, or syncope. The effectiveness of MCOT was assessed based on detection of arrhythmias and changes in patient management after MCOT. A clinically significant arrhythmia was detected in 51 patients, but 25 (49%) did not have any symptoms during the arrhythmia. Thirteen of the 17 patients (76%) found to have atrial flutter/fibrillation had no symptoms during the arrhythmia. Thirty patients had been previously monitored by either an HM or an event recorder. MCOT detected an arrhythmia in 16 of the patients that was not found by a previous monitoring system. One patient had sustained ventricular tachycardia who required an implantable cardioverter-defibrillator. Following MCOT, physicians prescribed the following changes in treatment on a perpatient basis: drug treatment started (n=14), permanent pacemaker inserted (n=5), cardiac tissue ablated (n=4), drug treatment changed (n=3), cardioverter defibrillator implanted (n=2), anticoagulation stopped (n=2), pacemaker replaced (n=1), and drug treatment stopped (n=1). A limitation of this study was the lack of a comparator and long-term follow-up to determine whether patient outcomes were improved as a result of diagnostic information provided by MCOT.

Systematic Review

The Centers for Medicare & Medicaid Services (CMS) requested that the AHRQ commission an evidence report to evaluate remote cardiac monitoring devices. The AHRQ contracted the Evidence-based Practice Center (ECRI) to prepare an evidence report on this topic. The systematic review focused on two major categories of remote cardiac monitoring devices. The first category included patient- or event-activated devices, which include externally-worn presymptom memory loop recorders (attended and unattended), implantable/insertable

presymptom memory loop recorders (attended and unattended), and post-symptom patient-activated recorders. The second category comprises real-time continuous attended cardiac monitoring systems. Continuous unattended cardiac monitoring (e.g., Holter monitoring), prehospital (in ambulance) monitoring and transmission, as well as monitoring solely for the purpose of detecting device failure, was beyond the scope of this report. The systematic review focused on the downstream utility of a diagnostic technology. The overall conclusions state that "Patients with unexplained syncope are more likely to undergo a change in disease management when using ILR monitoring or real-time continuous attended monitoring than used with conventional assessment (i.e., Holter monitoring and/or tilt table testing). Patients with severe palpitations occurring less than once per 24 hours are also more likely to undergo a change in disease management when using real-time continuous attended monitoring. The strength of evidence is moderate for ILR and weak for real-time continuous monitoring (based on one high-quality multicenter trial). Due to small numbers of studies identified and numerous quality flaws, the evidence was insufficient to evaluate the effect of other remote monitoring devices (ELRs and post-event recorders) on change in disease management. For the same reasons, the evidence is also insufficient to determine any class of remote cardiac monitoring devices leads to better clinical outcomes than conventional monitoring" (AHRQ, 2007).

Professional Societies/Organizations
The American Heart Association (AHA)/American College of Cardiology (ACC) focused update to the 2006 practice guideline on the management of patients with atrial fibrillation mentions a 24-hour Holter recording for evaluating the heart rate over an extended period. The authors reported that no standard method for assessment of heart rate control has been established to guide management of patients with AF (Wann, et al., 2011). This practice guideline does not mention external mobile outpatient cardiac telemetry systems.

The European Society of Cardiology (ESC) Task Force guidelines for the diagnosis and management of syncope, updated in 2009, include recommendations for electrocardiographic monitoring. The guideline states that currently several systems of ECG ambulatory monitoring are available: conventional ambulatory Holter monitoring, in-hospital monitoring, event recorders, external or implantable loop recorders, and remote (at home) telemetry. Remote (at home) telemetry is not in the electrocardiographic monitoring recommendations. The guideline states that the potential role of the remote telemetry systems in the diagnostic work-up of patients with syncope needs to be further evaluated (Moya, et al, 2009). There has been no update to this guideline since 2009.

The AHA/ACC scientific statement on the evaluation of syncope states: "The type and duration of ambulatory ECG monitoring is dictated by the frequency of symptoms. A Holter monitor is appropriate for episodes that occur at least every day. Event monitoring is ideal for episodes that occur at least once a month. An implantable loop monitor allows the correlation of symptoms with the cardiac rhythm in patients in whom the symptoms are infrequent. In patients with unexplained syncope, use of an implantable loop recorder for one year yielded diagnostic information in more than 90% of patients. This approach is more likely to identify the mechanism of syncope than is a conventional approach that uses Holter or event monitors and electrophysiological testing" (Strickberger, et al., 2006). There have been no updates to this statement since 2006.

The AHA/ACC/ European Society of Cardiology Committee (ESC) guideline on the management of patients with ventricular arrhythmias and prevention of sudden cardiac death assigns Class levels and levels of evidence to their recommendations for ambulatory electrocardiography (AECG) (Zipes, et al., 2006). There have been no updates to this guideline since 2006. This guideline does not mention external mobile outpatient cardiac telemetry systems.

Guideline recommendations are classified as Class I, Class IIa, Class IIb, and Class III. The classification system is described as follows:

- Class I: Benefit >>>Risk; Procedure/Treatment should be perfomed/administered
- Class IIa: Benefit >> Risk; Additional studies with focused objectives needed. It is reasonable to perform procedure/administer treatment
- Class IIb: Benefit ≥ Risk; Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/treatment may be considered.
- Class III: Risk ≥ Benefit; Procedure/treatment should not be performed/administered, since it is not helpful and may be harmful.

The weight of evidence supporting each recommendation is classified as follows:

- Level A: Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.
- Level B: Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.
- Level C: Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care.

The following recommendations for AECG are included in the guideline:

Class I

- AECG is indicated when there is a need to clarify the diagnosis by detecting arrhythmias, QT interval changes, T-wave alternans, or ST changes, to evaluate risk, or to judge therapy. *(Level of Evidence: A)*
- Event monitors when symptoms are sporadic to establish whether or not they are caused by transient arrhythmias. *(Level of Evidence: B)*
- Implantable recorders are useful in patients with sporadic symptoms suspected to be related to arrhythmias such as syncope when a symptom-rhythm correlation cannot be established by conventional diagnostic techniques. *(Level of Evidence: B)*

The ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias states, "Ambulatory 24-hour Holter recording can be used in patients with frequent (i.e., several episodes per week) but transient tachycardias. An event or wearable loop recorder is often more useful than a 24-hour recording in patients with less frequent arrhythmias. Implantable loop recorders may be helpful in selected cases with rare symptoms (i.e., fewer than two episodes per month) associated with severe symptoms of hemodynamic instability" (Blomstrom-Lundqvist, et al., 2003). There have been no updates to this guideline since 2003.

The ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography states that the indications for ambulatory ECG were addressed in the 1999 clinical guidelines (Crawford, et al., 1999). The competence statement states there are no specific guidelines that distinguish patients for whom it is appropriate to perform continuous monitoring from those for whom intermittent ambulatory monitoring is adequate. However, when monitoring is performed to evaluate the cause of intermittent symptoms, the frequency of symptoms should dictate the type of recording (Kadish, 2001).

Summary
The peer-reviewed medical literature and the American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines for ambulatory electrocardiography (AECG) support the clinical utility of standard cardiac event monitors.

There is a lack of evidence in the published peer-reviewed medical literature supporting the clinical utility of long-term continuous external unattended cardiac monitoring devices. Studies are required to evaluate how long-term continuous external unattended cardiac monitoring devices can change treatment management and improve health outcomes compared to standard cardiac event monitors.

There is insufficient evidence in the published peer-reviewed medical literature supporting the clinical utility of external mobile outpatient cardiac telemetry systems. Many of the studies lack a comparator and do not report long-term outcomes. Additional studies with long-term follow-up are required to evaluate how external mobile outpatient cardiac telemetry systems can change treatment management and improve health outcomes compared to standard cardiac event monitors.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Continuous 24- to 48-hour External Unattended Cardiac Monitoring Device

Covered when medically necessary to report 24- to 48-hour continuous external unattended cardiac monitoring device (e.g., Holter monitor™ [HM]):

CPT®* Codes	Description
93224	External electrocardiographic recording up to 48 hours by continuous rhythm recording and storage; includes recording, scanning analysis with report, physician review and interpretation
93225	External electrocardiographic recording up to 48 hours by continuous rhythm recording and storage; recording (includes connection, recording, and disconnection)
93226	External electrocardiographic recording up to 48 hours by continuous rhythm recording and storage; scanning analysis with report
93227	External electrocardiographic recording up to 48 hours by continuous rhythm recording and storage; physician review and interpretation

ICD-9-CM Diagnosis Codes	Description
410.00-410.92	Acute myocardial infarction
411.1	Intermediate coronary syndrome, unstable angina
413.1	Prinzmetal angina
414.8	Other specified forms of chronic ischemic heart disease
414.9	Unspecified chronic ischemic heart disease
425.11	Hypertrophic obstructive cardiomyopathy
425.18	Other hypertrophic cardiomyopathy
425.4	Other primary cardiomyopathies
426.0-426.9	Conduction disorders
427.0-427.9	Cardiac arrhythmias
780.2	Syncope and collapse
780.4	Dizziness and giddiness
785.1	Palpitations

Patient or Event Recorder (Loop Recorder)

Covered when medically necessary to report external loop recorder:

CPT®* Codes	Description
93268	External patient and, when performed, auto-activated electrocardiographic rhythm derived event recording with symptom-related memory loop with remote download capability up to 30 days, 24-hour attended monitoring; includes transmission, physician review and interpretation
93270	External patient and, when performed, auto-activated electrocardiographic rhythm derived event recording with symptom-related memory loop with remote download capability up to 30 days, 24-hour attended monitoring; recording (includes connection, recording, and disconnection)
93271	External patient and, when performed, auto-activated electrocardiographic rhythm derived event recording with symptom-related memory loop with remote download capability up to 30 days, 24-hour attended monitoring; transmission download and analysis
93272	External patient and, when performed, auto-activated electrocardiographic rhythm derived event recording with symptom-related memory loop with remote download capability up to 30 days, 24-hour attended monitoring; physician review and interpretation

ICD-9-CM Diagnosis Codes	Description
427.0-427.9	Cardiac dysrhythmias

Covered when medically necessary to report implantable loop recorder:

CPT®* Codes	Description
33282	Implantation of patient-activated cardiac event recorder
33284	Removal of an implantable, patient-activated cardiac event recorder
93285	Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with physician analysis, review and report; implantable loop recorder system
93291	Interrogation device evaluation (in person) with physician analysis, review and report, includes connection, recording and disconnection per patient encounter; implantable loop recorder system, including heart rhythm derived data analysis
93297	Interrogation device evaluation(s), (remote) up to 30 days; implantable cardiovascular monitor system, including analysis of 1 or more recorded physiologic cardiovascular data elements from all internal and external sensors, physician analysis, review(s) and report(s)
93298	Interrogation device evaluation(s), (remote) up to 30 days; implantable loop recorder system, including analysis of recorded heart rhythm data, physician analysis, review(s) and report(s)
93299	Interrogation device evaluation(s), (remote) up to 30 days; implantable cardiovascular monitor system or implantable loop recorder system, remote data acquisition(s), receipt of transmissions and technician review, technical support and distribution of results

HCPCS Codes	Description
C1764	Event recorder, cardiac (implantable)
E0616	Implantable cardiac event recorder with memory, activator and programmer

ICD-9-CM Diagnosis Codes	Description
427.0-427.9	Cardiac arrhythmias
780.2	Syncope and collapse

External Mobile Outpatient Cardiac Telemetry System

Experimental/Investigational/Unproven/Not Covered to report an external mobile outpatient cardiac telemetry system:

CPT®* Codes	Description
93228	External mobile cardiovascular telemetry with electrocardiographic recording, concurrent computerized real time data analysis and greater than 24 hours of accessible ECG data storage (retrievable with query) with ECG triggered and patient selected events transmitted to a remote attended surveillance center for up to 30 days; physician review and interpretation with report
93229	External mobile cardiovascular telemetry with electrocardiographic recording, concurrent computerized real time data analysis and greater than 24 hours of accessible ECG data storage (retrievable with query) with ECG triggered and

	patient selected events transmitted to a remote attended surveillance center for up to 30 days; technical support for connection and patient instructions for use, attended surveillance, analysis and physician prescribed transmission of daily and emergent data reports

ICD-9-CM Diagnosis Codes	Description
	All codes

Experimental/Investigational/Unproven/Not Covered:

CPT®* Codes	Description
0295T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; includes recording, scanning analysis with report, review and interpretation (Code effective 01/01/2012)
0296T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; recording (includes connection and initial recording) (Code effective 01/01/2012)
0297T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; scanning analysis with report (Code effective 01/01/2012)
0298T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; review and interpretation (Code effective 01/01/2012)

ICD-9-CM Diagnosis Codes	Description
	All codes

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
Cigna HealthCare	4/15/2008	0085	Cardiac Event Monitors

Electric Tumor Treatment Fields for Glioblastoma

Question: Should electric tumor treatment field therapy be covered for initial treatment of glioblastoma?

Question source: Andy Luther, MD, OHP medical director

Issue: Electric tumor treatment field therapy (ETTF) involves a portable device which delivers low-intensity, intermediate frequency electric fields via non-invasive, transducer arrays. It is thought to physically interfere with tumor cell division. Glioblastoma is a very difficult to treat cancer of the brain with a typical life expectancy with current therapy of 1-2 years. Standard treatment involves surgical resection, radiation therapy, and chemotherapy.

ETTF therapy was reviewed for treatment of recurrent glioblastoma in May, 2014. At that time, little evidence was found to support its effectiveness and it was found to be less cost effective than conventional therapy for recurrent glioblastoma. The HCPCS codes for this therapy (HCPCS A4555 and E0766) were placed on the Services Recommended for Non-Coverage Table.

ETTF recently received FDA approval for initial treatment of glioblastoma. This approval was based on the results of a single trial of 695 participants.

A4555	Electrode/transducer for use with electrical stimulation device used for cancer treatment, replacement only
E0766	Electrical stimulation device used for cancer treatment, includes all accessories, any type

From Dr. Luther:

> … had a request for the Optune "tumor treating fields" system for treatment of glioblastoma in conjunction with temozolomide. It was FDA approved in October for certain patients, but Up-To-Date is fairly cautious about it's use given data available so far. We have an unfortunate patient that it might be appropriate for, and of course it is very expensive, OHP coverage not clear. There is now (as of October) an indication for treatment for newly diagnosed glioblastoma, after rad/chemo, in conjunction with ongoing temozolomide. I think the ancillary GL only addresses recurrent glioblastoma, so this may deserve another look, as it seems likely to keep coming up.

Originally approved entry in the Services Recommended for Non-Coverage Table
ELECTRONIC TUMOR TREATMENT FIELDS
Most recent review date: May, 2014
Electronic tumor treatment field therapy (ETTF; HCPCS A4555 and E0766) has been found to have significantly lower cost effectiveness compared to conventional chemotherapy for treatment of recurrent glioblastoma. See VBBS/HERC minutes from 5/8/14 for details [link].

Current entry in the Services Recommended for Non-Coverage Table

HCPCS A4555, E0766	Electronic tumor treatment field (ETTF) therapy	June, 2014	Found to have comparable effectiveness to conventional treatments, but significantly higher cost[3]

Evidence

Stupp 2015 (http://www.ncbi.nlm.nih.gov/pubmed/?term=26670971 Study not included due to length)

1) Randomized, non-controlled trial, open label trial of temozolomide chemotherapy alone vs temozolomide chemotherapy followed by TTF therapy for initial treatment of glioblastoma
2) N=695 patients (466 TTF+chemo, 229 chemo alone)
    a. Trial stopped after analysis of 315 patients (280 actually included in analysis after exclusions)
    b. Excluded patients who progressed rapidly after initial diagnosis and thus had the poorest prognoses
3) Intention to treat trial, endpoint was progression free survival
4) Median follow up 38 months (range, 18-60 months).
5) Median progression-free survival in the intent-to-treat population was 7.1 months (95%CI, 5.9-8.2 months) in the TTFields plus temozolomide group and 4.0 months (95%CI, 3.3-5.2 months) in the temozolomide alone group (hazard ratio [HR], 0.62 [98.7%CI, 0.43-0.89]; *P* = .001). Median overall survival in the per-protocol population was 20.5 months (95%CI, 16.7-25.0 months) in the TTFields plus temozolomide group (n = 196) and 15.6 months (95%CI, 13.3-19.1 months) in the temozolomide alone group (n = 84) (HR, 0.64 [99.4%CI, 0.42-0.98]; *P* = .004).
6) Further data analysis and follow up will be done; however, control patients were allowed to cross over to the ETTF group after official study termination and therefore future study results will be difficult to interpret
7) Significant differences in chemotherapy received by the TFF and control groups
    a. Number of cycles of temozolomide in the TTF group until disease progression=6 vs 4 cycles in the control group
    b. Second line chemotherapy received in 67% of the TTF group vs 57% of the temozolomide alone group
    c. Unclear if due to benefit of TTF (longer healthy life) or whether the additional chemotherapy explains some or all of the observed TTF benefit
    d. Question about whether the open-label use of TTF impacted provider or patient decision making regarding additional therapies (see **Sampson 2015** critique)
8) No increase in adverse events seen in the TTF group compared to the temozolomide alone group
9) CONCLUSIONS AND RELEVANCE In this interim analysis of 315 patients with glioblastoma who had completed standard chemoradiation therapy, adding TTFields to maintenance temozolomide chemotherapy significantly prolonged progression-free and overall survival.

10) Industry sponsored trial

Major guidelines:

NCCN 2015

1) ETTF mentioned as a possible therapy option for treating recurrent glioblastoma
    a. "Consider alternating electric field therapy for glioblastoma (category 2B)"
    b. No change from recommendation reviewed by HERC in 2014
2) No mention of ETTF as possible therapy for treatment of initial treatment of glioblastoma

European Society for Medical Oncology 2014

(http://annonc.oxfordjournals.org/content/early/2014/04/29/annonc.mdu050 Guideline not included due to length)

1) Reviewed ETTF as treatment for recurrent glioblastoma and did not find evidence to support its use
2) Use for initial treatment of glioblastoma was not reviewed

HERC staff summary:

The current evidence to support the use of electric tumor treatment fields in the initial treatment of glioblastoma is based on a single trial, which had questions regarding the trial methodology. No major specialty group is currently including ETTF as a recommended treatment for initial glioblastoma treatment. However, this does appear to be a rapidly evolving field and a promising treatment.

HERC staff recommendations:

1) Do not add ETTF (HCPCS A4555 and E0766) as an initial treatment for glioblastoma
2) Amend the entry to the Services Recommended for Non-Coverage as shown below

HCPCS A4555, E0766	Electronic tumor treatment field (ETTF) therapy	June, 2014 (Affirmed March 2016) March, 2016	For recurrent glioblastoma: Found to have comparable effectiveness to conventional treatments, but significantly higher cost[3] For initial treatment of glioblastoma: Experimental[2]

Footnotes 2 and 3 refer to OARs

Introduction to Issues Regarding Services for Autism and Dementia

Questions:

1) Should autism and dementia diagnoses continue to appear on the dysfunction lines, or should they only appear on the specific lines for these conditions?
    a. If moved off the dysfunction lines, what services should pair with autism and dementia diagnoses that currently only pair with them on the dysfunction lines?
2) What guideline restrictions should be placed on rehabilitative and habilitative services for autism and dementia and other behavioral health conditions?
3) Should the current rehabilitation services guideline be modified?

Question sources: HERC staff, OHA, HSD, medical directors

Issues: Autism and dementia both have unique lines (lines 197 AUTISM SPECTRUM DISORDERS and 206 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS), but also appear on the four dysfunction lines. The services available on the dysfunction lines are far more extensive than those on the autism and dementia specific lines, including PT/OT/Speech services, and, for autism, inpatient and SNF care. HERC staff would like to discuss whether autism and dementia should be removed from the dysfunction lines; if so, what types of services that now appear on the dysfunction lines should be added to the condition specific lines to continue to pair with these diagnoses?

As background, the evidence base/literature for PT and OT services is not robust. The majority of the literature focuses on a specific modality (for example, ultrasound or soft tissue mobilization) and its effectiveness for treatment of a specific condition. There are some studies of PT as a general service for certain conditions, such as back pain, but again, this literature is limited to one or a set of closely related conditions. In general, the evidence supporting the use of PT and OT for most services is weak or lacking. Most Medicaid programs and private insurers use medical necessity and, in some cases, arbitrary number limits to manage the use of these services.

If autism and dementia are removed from the dysfunction lines, GN6 Rehabilitative Therapies will no longer apply to these conditions. This GN could be added to the autism and dementia lines in its current form; or some modified guideline could be applied. HERC staff would like to discuss what restrictions, if any, should be placed on PT/OT/Speech services for autism, dementia, and similar behavioral health conditions. As background for this discussion, VBBS/HERC members will need to have information on possible conflicts between GN6 as it applies to behavioral health services and national laws and regulations.

1) GN6 may conflict with several national laws and regulations
    a. EPSDT laws (Title XIX). The Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefit provides comprehensive and preventive health care services for children under age 21 who are enrolled in Medicaid.
    b. CMS rules regarding habilitative services
    c. Federal Mental Health Parity laws

    d. Essential Health Benefit (EHB) discrimination language
2) Pending guidance for the Oregon Department of Justice regarding legal issues with GN6
3) Possible issues with Oregon's Medicaid waiver and CMS requirements and rules for these types of services.

A new CMS regulation was issued in January, 2016 which impacts the types of restrictions for habilitative services which might be governed by GN6, Rehabilitative Services, such as many of the PT, OT and speech services for autism and dementia (see published rule in meeting packet). Habilitative services are defined as "health care services and devices that help a person keep, learn, or improve skills and functioning for daily living (habilitative services). Examples include therapy for a child who is not walking or talking at the expected age. These services may also include physical and occupational therapy, speech-language pathology and other services for people with disabilities in a variety of inpatient and/or outpatient settings." The new rule states:

> The state must not impose limits on habilitative services and devices that are more stringent than limits on rehabilitative services and devices (see 45 CFR 156.115(a)(5)(ii)). This provision is effective immediately and requires that states review the coverage in the ABP to ensure that limits are in compliance with this provision.
>
> Separate coverage limits must also be established for rehabilitative and habilitative services and devices (see 45 CFR 156.115(a)(5)(iii)) for plan years beginning on or after January 1, 2017. A combined limit that cannot be exceeded based on medical necessity is not permissible. States will need to assess any existing limits on this coverage to determine if an amendment to the ABP SPA is required.

Additional concerns about GN6 in general have been raised by various CCO medical directors and by HERC staff. HERC staff would like to discuss possible revisions to GN6 as it applies to non-behavioral health conditions. Some specific concerns include:

1) General concerns among the CCOs about the language and desire to eliminate the clause about 30 additional visits per year being authorized for "exceptional circumstances." This clause is considered difficult to interpret.
2) Consideration of the addition of pulmonary rehabilitation to the guideline. The current guideline has a global limit for the combination of PT, OT, speech and cardiac rehabilitation services
3) Cardiac rehabilitation involves more than just PT, and the cardiac lines are not even mentioned in the guideline note. Cardiac rehabilitation should considered for removal from the guideline note.
4) HERC staff has reviewed a 2015 MED report on PT/OT services in other state Medicaid programs, which finds Oregon to be more restrictive than nearly all other states, particularly for children. Staff would like to discuss consideration of removal of the strict numerical limit on visits, possibly only for children. Historically, the limit on

services was quite low and the current 30 visit all-encompassing limit was an expansion of coverage.

HSD has rules and regulations regarding when PT and OT services are appropriate. These are published as OARs.

1. OAR definition of Medical Appropriateness:
    a. Service is consistent with symptoms or treatment of the health condition
    b. Generally recognized as effective
    c. Not for convenience of provider, patient or vendor
    d. Most cost effective alternative
2. OAR definition of Medical Necessity:
    a. If less than 30+ visits won't be effective
    b. Patient will suffer harm if not treated with more than 30

MED 2015 Summary of state policies on coverage of PT, OT and speech therapy

1) Survey of 10 states policies/coverage
2) Common elements that states use to determine medical necessity are:
    a. Referral by a licensed health care practitioner
    b. Diagnosis requiring skilled professional services
    c. Reasonable expectation of improvement
    d. Plan of care with measurable goals and outcomes
    e. Additional elements states may consider include:
        i. Acute vs chronic conditions
        ii. Therapeutic goals (e.g., improvement, maintenance, prevention of deterioration)
3) Quantitative visit limits
    a. Few states specify limits on coverage for children, even those states with limits on adult services.
    b. States with no limits or limits only on the number of units billable per day for adults and children: Alabama, Colorado, Minnesota
    c. Arizona - Adults: 15 outpatient visits and 25 inpatient days/year each for PT and OT; Children: Limits not specified
    d. Maine - No more than 1 unit/day of supervised modalities per modality; Maintenance care: 2 visits/year, or 6 visits/year if needed to maintain function; Sensory integration: 2 visits/year, 1 evaluation or re-evaluation per condition or event; no limits specified for children
    e. Michigan - Up to 144 units/year (rehabilitative or habilitative) or after 24 visits in 60 days in the home setting (adults or children not specified)
    f. New York - 20 visits per year of PT and 20 visits of OT for adults; no limits for children
    g. Washington - adults limited to 24 units of PT and 24 units of OT per year with additional limits by procedure; no limits for children

h. Wisconsin - up to 35 units of PT and 35 units of OT per year, additional available by PA approval; same for adults and children over age 3

Current guideline

GUIDELINE NOTE 6, REHABILITATIVE THERAPIES

Lines 34,50,61,72,75,76,78,85,95,96,135,136,140,154,157,164,182,187,188,200,201,205, 206,212,259,261,276,290,292,297,305,306,314,322,346,350,351,353,360,361,364,366,381, 382,392,406,413,421,423,427,428,436,447,459,467,470,471,482,490,501,512,532,558,561, 574,592,611,666 (Lines 351, 366 and 532 represent lines 374, 412 and 545 from the Oct. 1, 2015 Prioritized List†)

A total of 30 visits per year of rehabilitative therapy (physical, occupational and speech therapy, and cardiac and vascular rehabilitation) are included on these lines when medically appropriate. Additional visits, not to exceed 30 visits per year, may be authorized in exceptional circumstances, such as in cases of rapid growth/development.

Physical, occupational and speech therapy, and cardiac and vascular rehabilitation are only included on these lines 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 the therapy,
2. there is objective, measurable documentation of clinically significant progress toward the therapy plan of care goals and objectives,
3. the therapy plan of care requires the skills of a medical provider, and
4. the client and/or caregiver cannot be taught to carry out the therapy regimen independently.

No limits apply while in a skilled nursing facility for the primary purpose of rehabilitation, an inpatient hospital or an inpatient rehabilitation unit.

Spinal cord injuries, traumatic brain injuries, or cerebral vascular accidents are not subject to the visit limitations during the first year after an acute injury.

HERC staff recommendations:

1) Discuss whether autism and dementia should remain on the dysfunction lines
    a. If autism and dementia are removed from the dysfunction lines, discuss which services should be added to the disease specific lines
        i. The Behavioral Health Advisory Panel (BHAP) may need to be tasked with review of the appropriateness of certain CPT codes
    b. See Appendix A for details
2) Give staff feedback and direction on guideline(s) for rehabilitative services and habilitative services for behavioral health conditions such as autism and dementia. Possible options include, but are not limited to:
    a. Applying GN6 Rehabilitative Services to the autism and dementia lines, in an edited form or in the current form
    b. Creating a new guideline for habilitative and rehabilitative services for behavioral health conditions such as autism and dementia
3) Give staff feedback and direction on possible revisions to GN6 Rehabilitative Therapies for physical health conditions. Possible options include, but are not limited to:
    a. Consider deleting the guideline entirely and allow HSD to create rules on appropriate use of services
    b. Consider deleting the number of visit limits and only include wording about medical necessity
    c. Consider removing the additional 30 visit clause for “rapid growth and development” and have the GN apply only to adults; no limits for children

Appendix A

Diagnoses which appear on the Dysfunction lines related to autism and/or dementia

1) Autism related diagnoses on both the dysfunction lines and line 197 AUTISM SPECTRUM DISORDERS
    a. F84.0 Autistic disorder
    b. F84.3 Other childhood disintegrative disorder
    c. F84.8 Other pervasive developmental disorders
2) Autism related diagnoses appearing only on the dysfunction lines
    a. F84.2 Rett's syndrome
3) Dementia related diagnoses appearing on the dysfunction lines and on line 206 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS
    a. F01.5 Vascular dementia
    b. F03.9 Unspecified dementia
    c. F06.1 Catatonic disorder due to known physiological condition
    d. F06.8 Other specified mental disorders due to known physiological condition
    e. F07.89 Other personality and behavioral disorders due to known physiological condition

Services Currently Only Pairing with Autism and/or Dementia on the Dysfunction Lines

1) Services appearing on the dysfunction lines but not both lines 197 AUTISM SPECTRUM DISORDERS and 206 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS
    a. Multiple procedures not felt to related to specifically to autism and dementia
        i. Examples: injections, osteotomy, arthrodesis, tracheostomy, gastroduodenostomy, colectomy, neurostimulator pumps, CMT, OMT, ophthalmologic examinations
        ii. These would still be available if paired with an appropriate diagnosis that the person with the autism or dementia condition might also have
    b. Speech therapy
        i. 92507-92508 Treatment of speech, language, voice, communication, and/or auditory processing disorder
        ii. 92521-92524 Evaluation of speech
        iii. 92526 Treatment of swallowing dysfunction and/or oral function for feeding
        iv. 92607-92609 Evaluation and therapeutic services for speech-generating augmentative and alternative communication device
        v. 92633 Auditory rehabilitation; postlingual hearing loss
    c. Speech therapy related
        i. 21084 Impression and custom preparation; speech aid prosthesis
        ii. 92526 Treatment of swallowing dysfunction and/or oral function for feeding
    d. CPT 96150-96154 Health and behavior assessment
    e. PT Services

    i. 97012 Application of a modality to 1 or more areas; traction, mechanical
    ii. 97022 Application of a modality to 1 or more areas; whirlpool
    iii. 97110-97129 Therapeutic procedure
    iv. 97140 Manual therapy techniques
    v. 97150 Therapeutic procedure(s), group (2 or more individuals)
    vi. 97530 Therapeutic activities, direct (one-on-one) patient contact (use of dynamic activities to improve functional performance)
    vii. 97535 Self-care/home management training (eg, activities of daily living (ADL) and compensatory training, meal preparation, safety procedures, and instructions in use of assistive technology devices/adaptive equipment)
    viii. 97542 Wheelchair management (eg, assessment, fitting, training)
    ix. 97760-97762 Orthotic(s) management and training
f. 99070 Supplies and materials (except spectacles), provided by the physician or other qualified health care professional over and above those usually included with the office visit or other services rendered (list drugs, trays, supplies, or materials provided)
g. 99078 Physician or other qualified health care professional qualified by education, training, licensure/regulation (when applicable) educational services rendered to patients in a group setting (eg, prenatal, obesity, or diabetic instructions)
h. 99184 Initiation of selective head or total body hypothermia in the critically ill neonate
i. 99281-99285 ER visits
j. 99291-99292 ICU care
k. 99354-99355 Prolonged evaluation and management or psychotherapy service(s) (beyond the typical service time of the primary procedure) in the office or other outpatient setting requiring direct patient contact beyond the usual service
l. 99356-99360 Prolonged service in the inpatient or observation setting
m. 99363-99364 Anticoagulant management
n. 99367-99368 Medical team conference with interdisciplinary team of health care professionals
o. 99374-99375 Supervision of a patient under care of home health agency
p. 99377-99378 Supervision of a hospice patient
q. 99379-99380 Supervision of a nursing facility patient (patient not present) requiring complex and multidisciplinary care modalities involving regular development and/or revision of care plans by that individual, review of subsequent reports of patient status, review
r. 99381-99429 Preventive medicine evaluation and management or service, alcohol and drug screening
s. 99379-99380 Supervision of a nursing facility patient (patient not present) requiring complex and multidisciplinary care modalities involving regular development and/or revision of care plans by that individual

t. 99468-99480 NICU/PICU

2) Services appearing on the dysfunction lines but not line 197 AUTISM SPECTRUM DISORDERS (already appear on line 206)
    a. 97001-97004 PT evaluation and re-evaluation
    b. 97532 Development of cognitive skills to improve attention, memory, problem solving (includes compensatory training), direct (one-on-one) patient contact, each 15 minutes
    c. 99217-99220 Inpatient observation
    d. 99221-99239 Inpatient hospital care
    e. 99304-99318 SNF care
    f. 99605-99607 Medication therapy management service(s) provided by a pharmacist

March 3, 2016

Via E-mail (darren.d.coffman@state.or.us)

Darren Coffman
Director, Health Evidence Review Commission
Health Policy & Analytics
Oregon Health Authority (OHA)
500 Summer Street, NE, E-20
Salem, OR 97301-1097

Re: Comments on OHP Coverage of Applied Behavior Analysis
And Other Therapies for Autism Spectrum Disorders

Dear Mr. Coffman:

Autism Speaks is the world's leading autism science and advocacy organization and has been at the forefront of increasing coverage of healthcare treatments for autism spectrum disorders (ASD). Autism Speaks is submitting these comments in response to the current limits on OHP coverage of treatments of autism spectrum disorders (ASD) including applied behavior analysis (ABA), speech therapy (ST), physical therapy (PT), and occupational therapy (OT).

We note that the age and visit limits on care as set forth in the Prioritized List of Health Services, Guideline Notes 6 and 75 are contrary to generally accepted treatment standards recognized across the country and highly detrimental to Oregon children who will face futures of reduced functionality at enormous personal loss and substantial long-term costs to the state.[1] The caps on care also violate Medicaid's EPSDT mandate and no other state imposes such limits on this coverage.[2]

[1] Ganz, M. (2007) The Lifetime Distribution of the Incremental Societal Costs of Autism, Arch Pediatric Adolescent Medicine, 161: 343-349 (estimating costs of 3.2 million dollars over the lifetime of a child without adequate treatment).

[2] EPSDT-A Guide for States: Coverage in the Medicaid Benefit for Children and Adolescents (2014), Centers for Medicare & Medicaid Services (hereinafter "EPSDT Coverage Guide"),pp. 23-24 (construing the requirement for individualized determinations under the correct or ameliorate standard: "For example, while a state may place in its State Plan a limit of a certain number of physical therapy visits per year for individuals age 21 and older, such a "hard" limit could not be applied to children."). *See* Centers for Medicare & Medicaid Services Amended Waiver List and Expenditure Authority, Number 21-W-00013/10 and 11-W-00160/10, Oregon Health Plan (OHP), p. 20 (("All mandatory and optional Medicaid State Plan

In any event, the proposed quantitative treatment limitations plainly violate the provisions of the Wellstone-Domenici Mental Health Parity and Addiction Equity Act (MHPAEA),[3] and for that reason alone, should be stricken.

As CMS has instructed, beneficiaries receiving services for treatment of a mental health condition through managed care organizations (MCOs) are entitled to parity protections under MHPAEA whether mental health services are delivered entirely through MCOs or by a combination of MCOs and other service delivery systems.[4] Parity requirements are to track those imposed on commercial insurers.[5] Services in excess of the state plan are to be provided when necessary to comply with MHPAEA.[6]

There is no question that the proposed age and hour caps on treatments for ASD violate MHPAEA. The Oregon Insurance Division has already so concluded in its official Bulletins applicable to commercial insurers as have other states. This applies to caps on ST, PT and OT[7] as well as caps on ABA.[8] Accordingly, the current limits on ASD

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eligible children younger than 21 years old are entitled to elect to receive direct Medicaid coverage outside of OHP including all State Plan and EPSDT covered services (populations 3, 4, 5, 6, 7, and 8 in Attachment D)").

[3] 29 U.S.C. § 1185a; 42 U.S.C. § 300gg-5; 26 U.S.C. § 9812.See Proposed Rule by the Centers for Medicare & Medicaid Services regarding Application of Mental Health Parity Requirements on Coverage, 80 FR 19418, available at http://www.gpo.gov/fdsys/pkg/FR-32015-04-10/pdf/2015-08135.pdf at p. 19419 (MCOs must comply with MHPAEA).

[4] Medicaid and Children's Health Insurance Programs; Mental Health Parity and Addiction Equity Act of 2008; the Application of Mental Health Parity Requirements to Coverage Offered by Medicaid Managed Care Organizations, the Children's Health Insurance Program (CHIP), and Alternative Benefit Plans, 80 Fed. Reg. 19418, 19420 (April 10, 2015). Final Action on the Proposed Rule is anticipated by April 2016. http://www.reginfo.gov/public/do/eAgendaViewRule?pubId=201510&RIN=0938-AS24.

[5] Medicaid Fact Sheet: Mental Health Parity Proposed Rule for Medicaid and CHIP (April 6, 2015), p.1 ("[S]tates that have contracts with managed care organizations will be required to meet the parity requirements regarding financial and treatment limitations consistent with the regulation applicable to private insurers" this "prevents inequity between beneficiaries who have mental health or substance use disorder conditions in the commercial market (including the state and federal marketplace) and Medicaid.")

[6] *See* 80 FR 19421 (States to base capitation rates on "provision of a benefit package that is compliant with these proposed parity requirements even if services go beyond what is in the state plan"). *See also* Medicaid Fact Sheet, *supra* n. 5 at p.1 ("States will be required to include contract provisions requiring compliance with parity standards in all applicable contracts for these Medicaid managed care arrangements . . . states that have contracts with managed care organizations will be required to meet the parity requirements regarding financial and treatment limitations consistent with the regulation applicable to private insurers. States will have the flexibility to include the cost of providing additional services or removing treatment limitations in their capitation rate methodology.")

[7] Oregon Insurance Division Bulletin INS 2015-1, p.7 ("Similarly, the 30-visit limits for speech therapy, occupational therapy and physical therapy in Oregon's Essential Health Benefits package are quantitative treatment limitations prohibited by MHPAEA when the therapy is to treat a mental health condition.")

[8] Oregon Insurance Division Bulletin INS 2015-2, p.3 ("The provisions of SB 365 that establish quantitative standards—the 25-hour per week coverage standard and the nine-year old age standard—are floors, not limitations on ABA coverage. As floors these provisions do not violate the MHPAEA. If applied as limits, these provisions would violate MHPAEA and its regulations, unless the insurer imposed the same limits as the predominant treatment limitation on substantially all of its medical or surgical outpatient coverage.")

coverage, including limits on ST, OT, PT and ABA, are not enforceable and should be eliminated.

Thank you for your consideration of these comments. If I can provide you with any additional information, please do not hesitate to contact me.

Respectfully submitted,

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March 2, 2016

Via Email: Darren.d.coffman@state.or.us

Mr. Darren Coffman
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Re: Comments on OHP Coverage of Applied Behavior Analysis and Other Services & *HERC Evaluation of Evidence: Applied Behavior Analysis for Autism Spectrum Disorder*

Dear Mr. Coffman:

The Center for Autism and Related Disorders (CARD) respectfully submits these comments in response to the above-referenced HERC report and OHP's limits on autism treatment coverage. CARD is among the world's largest and oldest organizations treating autism spectrum disorder (ASD) and the nation's third largest non-governmental organization contributing to autism research. CARD provides services to thousands of individuals diagnosed with ASD and employs a workforce of over 1,800 dedicated professionals in nearly 50 locations, including locations in Beaverton, Salem, and Eugene.

CARD has many concerns about the limited nature of the evidence review described in *HERC Evaluation of Evidence: Applied Behavior Analysis for Autism Spectrum Disorders (2014)* (hereinafter "HERC's 2014 Report") and the treatment limitations that arose from this review. Hour, age, and duration limits such as those contained in HERC's 2014 Report plainly violate the Federal Mental Health Parity & Addiction Equity Act (MHPAEA) and impose limits on autism treatment coverage that are not imposed by any other state.

Specifically, regarding HERC 2014 Report's research evaluation, any review of evidence-based interventions for autism spectrum disorder (ASD) that excludes single-subject research disregards the extensive body of research that has documented the effectiveness of applied behavior analysis (ABA) in treating ASD and the ethical and practical concerns that preclude randomized controlled trials (RCTs). As you may know, RCTs require a control group, i.e., a group that receives no treatment. Autism researchers, treatment providers, parents, and caregivers individually and collectively recognize the effectiveness of applied behavior analysis (ABA) in the treatment of autism spectrum disorder (ASD) and the importance of treating the deficits and behaviors commonly associated with ASD as early as possible. When an existing treatment is known to be effective, it is unethical to deprive a patient of that treatment as would be required in an RCT. The delay in providing ABA to a child with ASD in order to conduct an RCT can mean the difference between equipping a child with the skills to live independently in the community and grappling with the needs of a child who will require constant care and support throughout his/her lifetime. This delay is so consequential that the American Academy of Pediatricians (AAP) states that evidence-based intervention should be provided as soon

as an ASD diagnosis is *"seriously considered."*[1] Additionally, the heterogeneity that characterizes ASD and the individualized nature of treatment hobble any effort to find children with enough common variables to comprise a meaningful group. For these reasons, it is critical to include single-subject research in any comprehensive analysis of the effectiveness of ABA in treating ASD. Since HERC's review did not include single-subject research or even small groups, it is not surprising that its conclusions, in addition to violating MHPAEA, do not align with widely accepted conclusions regarding best practices in autism treatment.

Furthermore, please note that research has consistently demonstrated that "intensive" behavioral intervention such as that required to ameliorate the deficits and behaviors associated with ASD is defined as 30-40 hours per week, not the 25 hours recommended in the HERC report.[2] Indeed, the seminal study that first used ABA to treat ASD described intensity as "most…waking hours."[3] Since that first study, thousands of studies have demonstrated that outcomes are maximized only when a child receives sufficient hours of ABA. For many children, their ability to grow up and become adults who function independently in the community depends on early intensive behavioral intervention (EIBI) of 30-40 hours per week of ABA. Children who receive fewer hours are likely to require services over the course of their lifetime, the cost of which has been estimated at $3.2 million per capita[4].

Additionally, the HERC report states, "Ongoing coverage should be based on demonstrated progress towards meaningful predefined objectives" (page 19). Plateaus and regression are not uncommon in ASD treatment. Indeed, extinction bursts, wherein a challenging behavior increases dramatically, is actually an anticipated event in effective ABA-based autism treatment. Lack of progress toward a treatment goal may indicate that a change in the teaching strategy or intervention is warranted; may reflect other challenges in the child's life; and may actually represent progress when the child has traditionally regressed in a specific area where s/he now maintains the skill but does not demonstrate active progress. Additionally, circumstances not within the control of the child, the child's family, or the provider may affect the child's progress, such as illness or the death of a loved one. While lack of progress warrants analysis, OHA should not deprive children of medically necessary care based on this variable. Continued treatment may also be medically necessary to maintain skills and functioning and prevent regression. As such, access to ongoing treatment should not be conditioned on progress.

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[1] Pediatrics, Vol, 120, No, 5, Identification and Evaluation of Children with Autism Spectrum Disorders (2007), p. 1163.

[2] Behavior Analyst Certification Board (2014) Applied Behavior Analysis Treatment of Autism Spectrum Disorder: Practice Guidelines for Healthcare Funders and Managers, Second Edition, 14.

[3] Lovaas, O.I. (1987) Behavioral Treatment and Normal Educational and Intellectual Functioning in Young Autistic Children, *Journal of Consulting and Clinical Psychology,* 55, 3-9.

[4] Ganz, M. (2007) The Lifetime Distribution of the Incremental Societal Costs of Autism, *Arch Pediatric Adolescent Medicine,* 161: 343-349.

Application of Federal Mental Health Parity & Addiction Equity Act to Medicaid and Medicaid CCOs requires limitations to be eliminated.

The Federal Mental Health Parity & Addiction Equity Act (MHPAEA) provides that mental health services be delivered at parity with substantially all other medical/surgical services. MHPAEA clearly applies to managed care organizations administering Medicaid benefits.[5] Recommendations in HERC's 2014 Report, however, are at variance with MHPAEA in that they include specific age and hour limits. Such limits also violate EPSDT's Medicaid mandate.[6] The Oregon Insurance Division has issued official bulletins applicable to commercial insurers that clearly state that benefits for medically necessary autism treatment, including ABA[7] and speech and occupational therapy[8], cannot be capped. Similarly, OHA is currently in compliance with MHPAEA regarding delivery of ABA because it has made clear that the autism benefit has no age or hour limits. Regarding speech and occupational therapy, however, OHA is currently enforcing visit limits OHP guideline note 6), and those limits should be lifted immediately to bring OHA into compliance with MHPAEA, which applies to speech and occupational therapy when delivered to treat ASD.

As OHA prepares to transition administration of its autism benefit to CCOs, it is critical that CCOs have clear guidance that complies with MHPAEA[9]. Given that age, hour, and duration limits violate both MHPAEA and

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[5] 29 U.S.C. § 1185a; 42 U.S.C. § 300gg-5; 26 U.S.C. § 9812. See Proposed Rule by the Centers for Medicare & Medicaid Services regarding Application of Mental Health Parity Requirements on Coverage, 80 FR 19418, available at http://www.gpo.gov/fdsys/pkg/FR-32015-04-10/pdf/2015-08135.pdf at p. 19419 (MCOs must comply with MHPAEA); EPSDT-A Guide for States: Coverage in the Medicaid Benefit for Children and Adolescents).

[6] EPSDT-A Guide for States: Coverage in the Medicaid Benefit for Children and Adolescents (2014), Centers for Medicare & Medicaid Services, pp. 23-24 ("For example, while a state may place in its State Plan a limit of a certain number of physical therapy visits per year for individuals age 21 and older, such a 'hard' limit could not be applied to children."). *See* Centers for Medicare & Medicaid Services Amended Waiver List and Expenditure Authority, Number 21-W-00013/10 and 11-W-00160/10, Oregon Health Plan (OHP), p. 20 ("All mandatory and optional Medicaid State Plan eligible children younger than 21 years old are entitled to elect to receive direct Medicaid coverage outside of OHP including all State Plan and EPSDT covered services….").

[7] Oregon Insurance Division Bulletin INS 2015-2, p.3 ("The provisions of SB 365 that establish quantitative standards—the 25-hour per week coverage standard and the nine-year old age standard—are floors, not limitations on ABA coverage. As floors these provisions do not violate the MHPAEA. If applied as limits, these provisions would violate MHPAEA and its regulations, unless the insurer imposed the same limits as the predominant treatment limitation on substantially all of its medical or surgical outpatient coverage.")

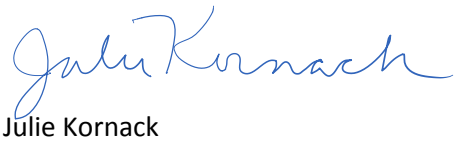
[8] Oregon Insurance Division Bulletin INS 2015-1, p.7 ("Similarly, the 30-visit limits for speech therapy, occupational therapy and physical therapy in Oregon's Essential Health Benefits package are quantitative treatment limitations prohibited by MHPAEA when the therapy is to treat a mental health condition.")

[9] Medicaid Fact Sheet: Mental Health Parity Proposed Rule for Medicaid and CHIP (April 6, 2015), p.1 ("[S]tates that have contracts with managed care organizations will be required to meet the parity requirements regarding financial and treatment limitations consistent with the regulation applicable to private insurers" this "prevents inequity between beneficiaries who have mental health or substance use disorder conditions in the commercial market (including the state and federal marketplace) and Medicaid.")

EPSDT, CARD respectfully urges HERC to update its recommendations to remove age, hour, and duration limits from its Prioritized List of Health Services. Because these limits violate MHPAEA, time is of the essence. As such, CARD respectfully urges OHA to update its guidelines and the Prioritized List of Health Services as soon as possible and prior to transitioning services to CCOs in July, 2016, as we have experienced extraordinary confusion among managed care organizations when they are confronted with contradictory guidance. Ensuring that OHA guidelines are in harmony with MHPAEA and EPSDT is critical to the smooth transition to CCOs that we seek to facilitate.

Thank you for your consideration of these comments. Should you have any questions or concerns, please do not hesitate to contact me at J.Kornack@centerforautism.com or at (818) 345-2345, extension 1070.

Sincerely,



Julie Kornack
Director of Public Policy

Section 8.0

Coverage Guidances

Skin Substitutes

Draft Coverage Guidance for VbBS Consideration

March 10, 2016

Oregon Health Authority

Oregon Health & Science University

Center For Evidence-based Policy

Background – Skin Ulcers

- Common types of skin ulcers
  - Diabetic foot ulcers (DFU)
    - Caused by atherosclerosis impeding blood flow to extremities and neuropathy that reduces person's ability to detect an injury
    - DFU can lead to infection (e.g., osteomyelitis) and amputation
  - Venous leg ulcers (VLU)
    - Caused by venous insufficiency
  - Pressure ulcers (i.e., bed sores)
    - Occurs when person is unable to reposition themselves, leading to prolonged pressure on a part of the body

Background – Treatments

- Standard treatments for skin ulcers
  - Cleaning and debridement
  - Moist dressing of the ulcer
  - Removing of any pressure on the part of the body with the ulcer (off-loading)
  - Care for the underlying conditions causing the ulcers:
    - DFU: controlling diabetes, blood pressure, etc.
    - VLU: improving circulation with compression stockings, revascularization procedures

Background – Skin Substitutes

- Skin substitutes were originally designed for the treatment of burns.
- Skin ulcers occur more frequently than burns, and skin substitutes are now used more commonly for treatment of ulcers.
- Skin substitutes are indicated for the treatment of chronic ulcers, usually defined as not healing within 30 days using standard treatments.

Background – Skin Substitutes

- Skin substitutes stimulate the body to regenerate lost tissue.
- These products do this by mimicking the body's skin structure.
- The FDA regulates skin substitutes based on how they are derived or produced:
  - Products derived from human donor tissue
  - Products derived from living human or animal tissues and cells
  - Acellular animal–derived products
  - Biosynthetic products

Background – Skin Substitutes

- There are over 70 skin substitute products approved for use in humans (see Table 1 in the CG, pp. 17-18)
- Not all products may be indicated for each type of wound (burns, DFU, VLU)

PICO Statement

- Population: Adults with chronic skin ulcers
- Intervention: Skin substitutes
- Comparator: Usual care
- Outcomes:
  - Deep soft tissue or bone infections (critical)
  - Complete wound healing (critical)
  - Quality of life (critical)
  - Time to complete wound healing (important)
  - Adverse effects (important)

Key Questions

1. What is comparative effectiveness of different types of skin substitutes compared with wound care alternatives for individuals with chronic skin ulcers? Include consideration of:
    a. Age
    b. Body mass index (BMI)
    c. Comorbidities
    d. Site of ulcer
    e. Ulcer etiology (e.g., infectious, pressure or circulatory)
    f. Wound severity
    g. Prior need for skin substitute
    h. Failure of prior therapies
2. What adverse events are associated with skin substitutes?
3. What are contraindications to the use of skin substitutes?

Evidence Sources

- Full search of core sources
  - AHRQ systematic review (Snyder, 2015) identified as the most comprehensive recent review for DFU and VLU: good-quality.
  - Other systematic reviews
    - Game (2015) for DFU: good-quality
    - Jones (2013) for VLU: good-quality
    - Felder (2012) for chronic foot ulcers: fair quality

Evidence Sources

- Medline search
  - Indexed in Medline and published 2012 - October 2015 (corresponding to dates after AHRQ systematic review search)
  - Inclusion criteria: Randomized control trials (RCT) that were not in one of the systematic reviews; product available in U.S.
  - One RCT found
  - During public comment period, one more additional RCT was published and then included in the CG

Evidence Review

- No evidence identified for treatment of pressure ulcers
- The identified evidence evaluated the effectiveness of eight skin substitutes currently sold in the US
- None of the studies found evidence for the critical outcome - quality of life
- Evidence review done separately for
  - Diabetic foot ulcers (DFU)
  - Venous leg ulcers (VLU)

Evidence Summary

Evidence shows moderate or low certainty of benefit

	Diabetic Foot Ulcers	Venous Leg Ulcers
Apligraf®	Complete wound healing: *moderate certainty of benefit* Adverse events: *low certainty of no harm*	Complete wound healing: *low certainty of benefit* Time to complete wound healing: *Low certainty of benefit*
Dermagraft®	Complete wound healing: *low certainty of benefit* Time to complete wound healing: *low certainty of benefit*	
EpiFix®		
Grafix®		

Evidence Summary

Evidence shows moderate or low certainty of benefit

	Diabetic Foot Ulcers	Venous Leg Ulcers
Graftjacket®		
OASIS®	Complete wound healing: *low certainty of benefit*	Complete wound healing: *low certainty of benefit*
Talymed®		
Theraskin®		

Public Comment

- Submitted by Soluble Systems
  - Suggested addition of three studies
    - One study was in AHRQ systematic review
    - One study was not RCT - non-comparative retrospective case series
    - One study not indexed in Medline, small (n=23), poor-quality RCT
  - Discussed coverage by other payers
- Submitted by Smith & Nephew
  - New study: Cazzell (2015) – fair quality RCT of 82 patients comparing OASIS to standard care for treatment of DFU
  - At 12 weeks, wound healing was greater in the OASIS group (54%) compared to standard care group (32%) (p=0.021)

EbGS Decision Factors

- Coverage recommendation divided by “low” versus “very low” quality evidence

Late breaking studies

- Late breaking studies
  - included RCTs, SRs, MAs
  - if submitted by end of public comment period
  - some were not indexed in Medline
- Will wait for a 2 year re-review before adding additional products (there are alternatives)

Complex reimbursement issues

- Costs of product
  - will vary by plan, setting of care, contractual issues
  - Varied number of applications, product sizes, shelf life
- Applications table (revised) included as an appendix for plan information. No max application language included in box.
- Language on reference pricing and bundling omitted

Prerequisites

- Based on combination of study criteria and expert input
- Appropriate wound care required
- Appropriate patient characteristics
  - Diabetic control (<12)
  - Adequate blood flow
  - Failure of prior therapy
  - *Participation* in tobacco cessation required

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: SKIN SUBSTITUTES FOR CHRONIC SKIN ULCERS

DRAFT for VbBS/HERC meeting materials 3/10/2016

HERC Coverage Guidance

Skin substitutes for chronic venous leg ulcers and chronic diabetic foot ulcers are recommended for coverage *(weak recommendation)* when all of the following criteria are met:

1. Product is recommended for the type of ulcer being treated (see table below)
2. FDA indications and contraindications are followed, if applicable
3. Wound has adequate arterial flow (ABI > 0.7), no ongoing infection and a moist wound healing environment
4. For patients with diabetes, Hba1c level is < 12.
5. Prior appropriate wound care therapy (including but not limited to appropriate offloading, multilayer compression dressings and smoking cessation counseling) has failed to result in significant improvement (defined as at least a 50 percent reduction in ulcer surface area) of the wound over at least 30 days
6. Ulcer improves significantly over 6 weeks of treatment with skin substitutes, with continued significant improvement every 6 weeks required for coverage of ongoing applications
7. Patients is able to adhere to the treatment plan

The following products are recommended/not recommended for coverage as shown below. All recommendations are weak recommendations.

Product	Diabetic foot ulcers	Venous leg ulcers
Dermagraft	Recommended	Not recommended
Apligraf	Recommended	Recommended
OASIS Wound Matrix	Recommended	Recommended
Epifix	Not recommended	Not recommended
Grafix	Not recommended	Not recommended
Graftjacket	Not recommended	Not recommended
Talymed	Not recommended	Not recommended
Theraskin	Not recommended	Not recommended
Other skin substitutes	Not recommended	Not recommended

The use of skin substitutes is not recommended for coverage of chronic skin ulcers other than venous leg ulcers and diabetic foot ulcers (e.g. pressure ulcers) *(weak recommendation).*

Note: Definitions for strength of recommendation are provided in Appendix A *GRADE Informed Framework Element Description*.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows standard methodology to translate evidence reviews into a policy decision. Coverage guidances are based on a thorough review of the evidence by the Evidence-based Guideline Subcommittee or the Heath Technology Assessment Subcommittee. The evidence review used in the coverage guidance development process may use existing systematic reviews of the evidence on a given topic and incorporate additional individual studies published more recently than the included systematic reviews. Included evidence sources are generally published within the last three to five years. A full description of the evidence review methodology is included in each coverage guidance as an appendix. The translation of the evidence review to a policy decision is based on a GRADE-informed framework, as described below

GRADE-Informed Framework

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are several elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Estimates of effect are derived from the evidence presented in this document. The level of confidence in the estimate is determined by the Commission based on assessment of two independent reviewers from the Center for Evidence-based Policy. Unless otherwise noted, estimated resource allocation, values and preferences, and other considerations are assessments of the Commission.

Note: The Quality of Evidence rating was assigned by the primary evidence source, not the HERC Subcommittee. The GRADE framework elements are described in Appendix A. A GRADE Evidence Profile is provided in Appendix B.

Apligraf® / Graftskin

Coverage question: Should Apligraf® be recommended for coverage for treatment of chronic skin ulcers?		
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**
Deep soft tissue or bone infection *(Critical outcome)*	DFU[1]: osteomyelitis 2.7% vs 10.4% (p = 0.4) ●●○○ *(low certainty of no benefit, based on one good quality RCT)* DFU (Apligraf vs Theraskin): One amputation due to infection with Theraskin vs none for Apligraf (p-value not reported) ●○○○ (very low certainty of no comparative benefit, based on one fair quality RCT) VLU: osteomyelitis 8.1% vs 0% (no statistical analysis)	Incremental cost for adding Apligraf to a patient's course of treatment for a small leg ulcer (<25 cm^2) under Medicare FFS (using average national prices for October, 2015) would range from $771.20 for a single application in an ambulatory surgery center to $4,553.81 for three applications in the physician's office setting. Prices are somewhat higher for foot ulcers due to higher physician fees/bundled fees for application.

[1] DFU: Diabetic Foot Ulcer; VLU: Venous Leg Ulcer

Coverage question: Should Apligraf® be recommended for coverage for treatment of chronic skin ulcers?		
Outcomes	**Estimate of Effect for Outcome/** ***Confidence in Estimate***	**Resource allocation**
	●○○○ *(very low certainty of benefit, based on one good quality RCT)*	Product is sold in 44 cm^2 sheets. Up to 3 applications appear to be the maximum necessary based on included studies.
Complete wound healing *(Critical outcome)*	DFU: RR 1.5, 1.96 (p = 0.01, 0.03) ●●●○ *(moderate certainty of benefit, based on two good quality RCTs)* DFU (Apligraf vs Theraskin): 47.1% vs 66.7% (p-value not reported) ●○○○ (very low certainty of no comparative benefit, based on one fair quality RCT) VLU: RR 2.38 (p < 0.001) ●●○○ *(low certainty of benefit, based on one good quality RCT)* Unspecified non-healing ulcers: 100% vs 75% (p < 0.01) ●○○○ *(very low certainty of benefit, based on one poor quality RCT)*	
Quality of life *(Critical outcome)*	No evidence identified.	
Time to complete wound healing *(Important outcome)*	DFU: No evidence identified. VLU: 61 vs 191 days (statistical analysis not provided) ●●○○ *(low certainty of benefit, based on one good quality RCT)* Unspecified non-healing ulcers: 7 vs 51 weeks (statistical analysis not provided)	

Coverage question: Should Apligraf® be recommended for coverage for treatment of chronic skin ulcers?		
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**
	●○○○ *(very low certainty of benefit, based on one poor quality RCT)*	
Adverse effects *(Important outcome)*	DFU: Pooled data from 4 RCTs showed similar incidence of cellulitis, dermatitis, and peripheral edema with Apligraf® vs control (statistical analysis not reported) ●●○○ *(low certainty of no harm, based on four good quality RCT)* VLU: Infection rates of 8.2% vs 7.8% (statistical analysis not reported) ●○○○ *(very low certainty of no harm, based on one good quality RCT)*	
Rationale: Apligraf is recommended for coverage for venous leg ulcers and diabetic foot ulcers, based on improved complete wound healing, low variability in patient preference, and despite its cost. A strong recommendation was not made because only 2/5 of the predefined critical/important outcomes were addressed by the evidence and in favor of Apligraf for DFU. Coverage is recommended only when other conditions exist for wound healing (see Other Considerations section, below).		
Recommendation: Apligraf is recommended for coverage for diabetic foot ulcers and venous leg ulcers *(weak recommendation)* when conditions necessary for wound healing are present. Payers may wish to consider bundled payment, reference pricing, or other effective alternatives for smaller ulcers, as this product is sold in units of 44 cm^2 and has a short shelf life, which may lead to waste.		

Dermagraft®

Coverage question: Should Dermagraft® be recommended for coverage for treatment of chronic skin ulcers?		
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**
Deep soft tissue or bone infection *(Critical outcome)*	DFU: Osteomyelitis incidence 8.6% in both intervention and control groups ●○○○ *(very low certainty of no benefit, based on one fair quality RCT)*	Incremental cost for adding Dermagraft® to a patient's course of treatment for a small leg ulcer (<25 cm^2) under Medicare FFS (using average national prices for October, 2015) would range from $771.20 for a single application in an ambulatory surgery center to $11,960.80 for eight applications in the hospital outpatient setting. Up to 4 applications total appears equivalent efficacy to 8 applications. Product is sold in 37.5 cm^2 sheets.
Complete wound healing *(Critical outcome)*	DFU: OR 1.64 (95% CI, 1.10 to 2.43) in pooled data from 3 fair quality RCTs; one poor quality RCT with 38.5% versus 31.7% (p = 0.138) ●●○○ *(low certainty of benefit, based on three fair quality concordant RCTs and one poor quality discordant RCT)* *DFU (Dermagraft vs OASIS): 84.6% vs 76.9%, p = 0.62* ●○○○ *(very low certainty of no comparative benefit, based on one fair quality RCT)* VLU: RR 1.83 (95% CI, 0.47 to 7.21) and RR 3.04 (95%, CI 0.95 to 9.68) ●○○○ *(very low certainty of no benefit, based on two fair quality RCTs)*	
Quality of life *(Critical outcome)*	No evidence identified.	
Time to complete wound healing *(Important outcome)*	DFU: 13 weeks vs 28 weeks(statistical analysis not reported) ●●○○ *(low certainty of benefit, based on four poor to fair quality RCTs)* DFU (Dermagraft vs OASIS): 40.90 vs 35.67 days, p = 0.73	

	●○○○ (very low certainty of no comparative benefit, based on one fair quality RCT) VLU: 35 weeks vs 74 weeks, (statistical analysis not reported) ●○○○ *(very low certainty of benefit, based on one fair quality RCT)*	
Adverse effects *(Important outcome)*	DFU: 19% vs 32%, p = 0.007; second RCT no difference in rates of AE. ●○○○ *(very low certainty of benefit, based on two fair quality RCTs)* VLU: Similar number of AEs in all groups, statistical analysis not reported ●○○○ *(very low certainty of no harm, based on one fair quality RCT)*	
Rationale: Dermagraft is recommended for coverage for diabetic foot ulcers based on evidence of reduced time to wound healing and a higher likelihood of complete wound healing than usual care, with low variability in patient values and preferences. The recommendation is weak because of the low certainty of the evidence, and relatively high cost. Dermagraft is not recommended for coverage for venous leg ulcers based on insufficient evidence of benefit for any critical or important outcome and lack of FDA approval for this indication.		
Recommendation: Dermagraft is not recommended for coverage for venous leg ulcers *(weak recommendation)* Dermagraft is recommended for coverage for diabetic foot ulcers *(weak recommendation)* when conditions necessary for wound healing are present. Payers may wish to consider bundled payment, reference pricing, or other effective alternatives for smaller ulcers, as this product is sold in units of 37.5 cm^2 and has a short shelf life, which may lead to waste.		

OASIS® Wound Matrix

Coverage question: Should OASIS® Wound Matrix be recommended for coverage for treatment of chronic skin ulcers?		
Outcomes	**Estimate of Effect for Outcome/** ***Confidence in Estimate***	**Resource allocation**
Deep soft tissue or bone infection *(Critical outcome)*	No evidence identified.	Incremental cost for adding OASIS Wound Matrix to a patient's course of treatment for a small leg ulcer (<25 cm^2) under Medicare FFS (using average national prices for October, 2015) would be $235.69 for a single application in an ambulatory surgery center. In a physician's office, the cost would be $10.72 per cm^2 plus physician's fees of $143.73. The manufacturer recommends re-application every three to seven days as needed. Product is sold in units of varying sizes, the smallest of which is 10.5 cm^2. One study of DFU showed an average of 10 sheets. One study of VLU reported an average of 8 sheets. Study showed equivalence of 8 sheets of Oasis to 3 sheets of Dermagraft for DFU. One Medicare LCD limits to 12 weeks of therapy.
Complete wound healing *(Critical outcome)*	DFU: 49% vs 28% (p = 0.06) at 12 weeks; 54% vs 32% (p=0.021)at 12 weeks ●●○○ *(low certainty of benefit, based on two fair quality RCTs with inconsistency in comparator groups)* DFU *(OASIS vs Dermagraft): 76.9% vs 84.6%, p = 0.62* ●○○○ *(very low certainty of no comparative benefit, based on one fair quality RCT)* VLU: 80% vs 65% at 8 weeks (p < 0.05); 83% vs 46% at 16 weeks (p < 0.001); 55% vs 34% at 12 weeks, (p = 0.02) ●●○○ *(low certainty of benefit, based on three fair to good quality RCTs with inconsistency in comparator groups)*	
Quality of life *(Critical outcome)*	No evidence identified.	
Time to complete wound healing *(Important outcome)*	DFU: 5.4 vs 8.3 weeks, statistical analysis not reported; 67 vs 73 days (p = 0.245) ●●○○ *(low certainty of no benefit, based on two fair quality RCTs)* DFU (OASIS vs Dermagraft): 35.67 vs 40.90 days, p = 0.73 ●○○○ (very low certainty of no comparative benefit, based on one fair quality RCT) VLU: 63% vs 40% expected to heal at 12 weeks, p = 0.0226	

Coverage question: Should OASIS® Wound Matrix be recommended for coverage for treatment of chronic skin ulcers?		
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**
	●○○○ *(very low certainty of benefit, based on one good quality RCT*	
Adverse effects *(Important outcome)*	DFU: Approximately equal number of AEs between groups, statistical analysis not reported ●○○○ *(very low certainty of no benefit, based on one fair quality RCT)* VLU: Approximately equal number of AEs between groups, statistical analysis not reported ●○○○ *(very low certainty of no benefit, based on one good quality RCT)*	
Rationale: OASIS Wound Matrix is recommended for coverage for venous leg ulcers based on low-certainty evidence that it improves complete wound healing and time to complete wound healing, with low variability in values and preferences. OASIS Wound matrix is recommended for coverage for diabetic foot ulcers based on low certainty evidence of benefit of improved wound healing, low variability in values and preferences.		
Recommendation: OASIS is recommended for coverage for diabetic foot ulcers and venous leg ulcers (*weak recommendation*), when conditions necessary for wound healing are present.		

EpiFix®

Coverage question: Should EpiFix® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***
Deep soft tissue or bone infection *(Critical outcome)*	No evidence identified.

Coverage question: Should EpiFix® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***
Complete wound healing *(Critical outcome)*	DFU: 92% versus 8% (p < 0.0001) ●○○○ *(very low certainty of benefit, based on one RCT of fair quality)*
Quality of life *(Critical outcome)*	No evidence identified.
Time to complete wound healing *(Important outcome)*	No evidence identified.
Adverse effects *(Important outcome)*	No evidence identified.
Rationale: Epifix is not recommended for coverage due to insufficient evidence of effectiveness and the availability of effective alternatives *(weak recommendation).*	
Recommendation: EpiFix is not recommended for coverage for chronic skin ulcers (*weak recommendation*).	

Grafix®

Coverage question: Should Grafix® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***
Deep soft tissue or bone infection *(Critical outcome)*	DFU: "Wound-related infection" (undefined) 18.0% vs 36.2%, p = 0.044●○○○ *(very low certainty of benefit, based on one RCT of poor quality)*

Coverage question: Should Grafix® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***
Complete wound healing *(Critical outcome)*	DFU: 62% vs 21%, p < 0.01 ●○○○ *(very low certainty of benefit, based on one RCT of poor quality)*
Quality of life *(Critical outcome)*	No evidence identified.
Time to complete wound healing *(Important outcome)*	DFU: 42 days vs 69.5 days (statistical analysis not reported) ●○○○ *(very low certainty of benefit, based on one RCT of poor quality)*
Adverse effects *(Important outcome)*	DFU: 44% vs 66% (p = 0.031) ●○○○ *(very low certainty of benefit, based on one RCT of poor quality)*
Rationale: Grafix is not recommended for coverage for chronic skin ulcers due to insufficient evidence of effectiveness and the availability of effective alternatives *(weak recommendation).*	
Recommendation: Grafix is not recommended for coverage for chronic skin ulcers *(weak recommendation).*	

Graftjacket®

Coverage question: Should Graftjacket® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***
Deep soft tissue or bone infection *(Critical outcome)*	One trial had a single pt with hallux amputation due to infection in the treatment group and zero in control. ●○○○ *(very low certainty of harm, based on one RCT of poor quality)*

Coverage question: Should Graftjacket® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/** ***Confidence in Estimate***
Complete wound healing *(Critical outcome)*	DFU, vs moist dressing: 70% vs 46% (p = 0.03) DFU, vs Curasol: 86% vs 29% (p = 0.006) ●●○○ *(very low certainty of benefit, based on two poor to fair quality RCTs)*
Quality of life *(Critical outcome)*	No evidence identified.
Time to complete wound healing *(Important outcome)*	DFU: 11.92 vs 13.5 weeks and 5.7 vs 6.8 weeks, not significant ●○○○ *(very low certainty of no benefit, based on two poor to fair quality RCTs)*
Adverse effects *(Important outcome)*	DFU: Wound infection 21.4% vs 35.7%,statistical analysis not reported ●○○○ *(very low certainty of no harm, based on one poor quality RCT)*
Rationale: Graftjacket is not recommended for coverage because of the very low evidence of benefit for the critical outcome of complete wound healing, and a lack of efficacy for improving time to complete wound healing. Given only one application is required, fewer resources would be needed which would be an argument in favor, however, there is insufficient evidence to justify if even at the lower cost, this would provide significant benefit to patients.	
Recommendation: Graftjacket is not recommended for coverage for chronic skin ulcers (*weak recommendation*).	

Talymed®

Coverage question: Should Talymed® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/** ***Confidence in Estimate***
Deep soft tissue or bone infection *(Critical outcome)*	No evidence identified.
Complete wound healing *(Critical outcome)*	VLU: 86% vs 45% (p = 0.0005) ●○○○ *(very low certainty of benefit, based on one good quality RCT)*
Quality of life *(Critical outcome)*	No evidence identified.
Time to complete wound healing *(Important outcome)*	No evidence identified.
Adverse effects *(Important outcome)*	VLU: No significant treatment-related AEs ●○○○ *(very low certainty of no benefit, based on one good quality RCT)*
Rationale: Talymed is not recommended for coverage because of very low certainty of benefit, a lack of strong patient preferences for this, alternatives available, and its high cost.	
Recommendation: Talymed is not recommended for coverage for chronic skin ulcers (*weak recommendation*).	

TheraSkin®

Coverage question: Should Theraskin® be recommended for coverage for treatment of chronic skin ulcers?	
Outcomes	**Estimate of Effect for Outcome/** ***Confidence in Estimate***
Deep soft tissue or bone infection *(Critical outcome)*	DFU (Theraskin vs Apligraf): One amputation for infection, compared to none with Apligraf ●○○○ (very low certainty of no comparative benefit, based on one RCT of fair quality)
Complete wound healing *(Critical outcome)*	DFU (Theraskin vs Apligraf): 66.7% vs 41.3% (p = 0.21) ●○○○ (very low certainty of no comparative benefit, based on one RCT of fair quality)
Quality of life *(Critical outcome)*	No evidence identified.
Time to complete wound healing *(Important outcome)*	No evidence identified.
Adverse effects *(Important outcome)*	No evidence identified.
Rationale: Theraskin is not recommended for coverage because of insufficient evidence of benefit (limited evidence suggesting it is comparable to another effective product), a lack of strong patient preferences for this, alternatives available, and its cost.	
Recommendation: TheraSkin is not recommended for coverage for chronic skin ulcers (*weak recommendation*).	

EVIDENCE OVERVIEW

Clinical background

Diabetic foot ulcers (DFUs), venous leg ulcers (VLUs), and decubitus ulcers can be serious wounds, leading to severe health outcomes such as amputations and death. Diabetic foot ulcers are the result of atherosclerosis that impedes blood flow to the extremities and peripheral neuropathy that reduces the ability to sense injuries from extended pressure or other causes. Diabetic foot ulcers can lead to infections such as osteomyelitis and amputation. Appropriate treatment of these wounds can minimize the negative health outcomes and improve patient quality of life. Treatment for diabetic foot ulcers include cleaning, dressing, debridement, and pressure relief (Wound, Ostomy, and Continence Nurses Society, 2012). During the past 20 years, the prevalence of diabetes among adults in Oregon has more than doubled, to 9% in 2011. Among adults covered by the Oregon Health Plan, 17% have diabetes (Oregon Heart Disease and Stroke and Diabetes Prevention Programs, 2013). The annual incidence of foot ulcers among Medicare patients with diabetes is 6% (Margolis et al., 2011).

Venous leg ulcers are caused by chronic venous insufficiency. Treatment for venous leg ulcers include cleaning and dressing the wound, hemodynamic support to control the underlying disorder that caused the ulcer (e.g., medication or vascular bypass procedures), compression bandages, and compression stockings. The lifetime incidence of venous leg ulcers is about 1% (O'Meara, Al-Kurdi, & Ovington, 2008).

Decubitus ulcers or pressure ulcers (commonly called bed sores or pressure ulcers) occur when patients are unable to reposition themselves, most commonly in hospitals, long-term care facilities, and at home. Sustained pressure on a specific part of the body (often a bony prominence such as hip or sacrum) for long periods of time can cause a pressure ulcer. Treatment includes removing the pressure from the affected area, skin protection, debridement of necrotic tissues, cleaning, and dressing. Data from the National Nursing Home Survey indicate that 11% of nursing home residents had pressure ulcers (Park-Lee & Caffrey, 2009).

Skin substitutes have been used to treat ulcers that do not heal with the standard treatments. The most common use for skin substitutes is for the treatment of diabetic foot ulcers, venous leg ulcers, and decubitus ulcers. The etymologies of these ulcers make the wounds slower to heal, and the usual wound treatments are not always sufficient to ensure complete healing.

Indications

Skin substitutes are indicated for the treatment of chronic wounds, usually defined as having not healed within 30 days, having not responded to initial treatment, or persisting despite appropriate care. Skin substitutes were originally designed to treat burns, but now the most common usage is treating diabetic foot ulcers, venous leg ulcers, and decubitus ulcers.

Technology description

Skin substitutes promote healing and wound closure by mimicking or substituting for the skin structure. The skin substitute is designed to help the healing process by stimulating the host to regenerate lost

tissue and replace the wound with functional skin. Skin substitutes can be categorized (Snyder, Sullivan, & Schoelles, 2012) based upon how they are derived or produced:

- Products derived from human donor tissue
- Products derived from living human or animal tissues and cells
- Acellular animal –derived products
- Biosynthetic products

Currently, there are over 73 skin substitute products approved by the FDA for use in humans. While skin substitute products can be broadly grouped according to their source materials, the products are all sufficiently unique as to make generalization of efficacy across categories impracticable.

Table 1 shows skin substitute products available in the United States, categorized by how the product is derived and thus regulated by the FDA. This list of skin substitutes was created from the evidence and policy sources, and may not be complete. Products in the same category may not be equivalent in terms of effectiveness (Snyder, Sullivan, & Schoelles, 2012).

Human-derived skin substitute products that are minimally processed are regulated by the FDA as human cells, tissues, and cellular and tissue-based products (HCT/Ps). With HCT/Ps, tissue is obtained from human donors then processed and used in the same role in the patient (e.g., skin for skin, tendon for tendon). These HCT/Ps are regulated as human tissue intended for transplantation as long as the processing and clinical use are consistent with “Minimal Manipulation” and “Homologous Use” as defined in 21 CFR 1271. Products regulated as HCT/Ps must be registered with the FDA but are not required to demonstrate safety or effectiveness.

Cellular-derived material for wound healing cultured from human-derived tissues are regulated using the Biologics License Application (under the Federal Public Health Service Act) or with premarket approval (PMA) or as a Humanitarian Use Device obtained through a humanitarian device exemption depending on their composition and primary mode of action. The application for products regulated under the PMA process must include scientifically valid clinical studies demonstrating that the product is effective and safe.

Acellular animal-derived products and synthetic products are regulated under Section 510(k) of the Food, Drug and Cosmetic Act. This requires a premarket submission to the FDA to demonstrate that the device is substantially equivalent, i.e., at least as safe and effective, to a legally marketed device that is not subject to PMA. Submitters can compare their device to a device that was legally marketed prior to May 28, 1976 or a device which has been previously found to be substantially equivalent through the 510(k) process (Snyder, Sullivan, & Schoelles, 2012).

Table 1: Skin Substitutes

Products derived from human donor tissue, minimally processed	Products derived from living human and/or animal tissue	Acellular animal-derived products	Biosynthetic products
AlloDerm Regenerative Tissue Matrix	Apligraf®/Graftskin	Acell UBM Hydrafted Wound Dressing	Epicel™
Allpatch HD™	Dermagraft®	Acell UMB Lyophilized Wound Dressing	Hyalomatrix® (Laserskin®)
Alloskin™	AlloMax™	Aongen™ Collagen Matrix	Hyalomatrix®
Cymetra® Micronized AlloDerm	Celaderm®	Atlas Wound Matrix	Jaloskin®
Dermacell® and Arthroflex®	OrCel™	Avagen Wound Dressing	Suprathel®
Flex HD®	TransCyte™	Biobrane®	Talymed®
GammaGraft®		Collagen Sponge (Innocoll)	
Graftjacket® Regenerative Tissue Matrix		Collagen Wound Dressing (Oasis Research)	
Graftjacket® Express Scaffold		Collaguard®	
Matrix HD™		CollaSorb™	
Memoderm™		CollaWound™	
Puros® Dermis		Collexa®	
Repliform®		Collieva®	
TheraSkin®		Coreleader Colla-Pad	
		Dermadapt™ Wound Dressing	
		DressSkin	
		EndoForm Dermal Template™	
		Excellagen	
		E-Z Derm™	
		FortaDerm™ Wound Dressing	
		Helicoll	
		Integra® Dermal Regeneration Template	
		Integra™ Bilayer Matrix Wound Dressing	

Products derived from human donor tissue, minimally processed	Products derived from living human and/or animal tissue	Acellular animal-derived products	Biosynthetic products
		Integra™ Flowable Wound Matrix LTM Wound Dressing MatriStem Matristem Micromatrix® Matristem® Burn Matrix MatriStem® Wound Matrix Matrix Collagen Wound Dressing Medline Collagen Wound Dressing OASIS Burn Matrix™ OASIS Wound Matrix ™ Primatrix™ Primatrix™ Dermal Repair Scaffold SIS Wound Dressing II SS Matrix™ Stimulen™ Collagen TheraPorm™ Standard/Sheet Unite® Biomatrix Unite™ Biomatrix	

The following skin substitute products may not be available for chronic wounds in the US: Dermagen, EpiDex, Hyalograft, Kaloderm, Matriderm, PermaDerm, StrataGraft/ExpressGraft, and Xelma.

Key Questions and Outcomes

The following key questions (KQ) guided the evidence search and review described below. For additional details about the review scope and methods please see Appendix D.

1. What is comparative effectiveness of different types of skin substitutes compared with wound care alternatives for individuals with chronic skin ulcers? Include consideration of:
    a. Age
    b. Body mass index (BMI)
    c. Comorbidities

d. Site of ulcer
e. Ulcer etiology (e.g. infectious, pressure or circulatory).
f. Wound severity
g. Prior need for skin substitute
h. Failure of prior therapies

2. What adverse events are associated with skin substitutes?
3. What are contraindications to the use of skin substitutes?

Critical outcomes selected for inclusion in the GRADE table: deep soft tissue or bone infection, complete wound healing, and quality of life. *Important outcomes* selected for inclusion in the GRADE table: time to complete wound healing and adverse effects.

Evidence overview

Four systematic reviews and two additional RCTs address the use of skin substitutes for chronic skin ulcers; they are summarized in Tables 2 and 3. The outcomes considered critical for purposes of this coverage guidance are deep soft tissue or bone infection, complete wound healing, and quality of life. Time to complete wound healing and adverse effects are considered important outcomes. Complete wound healing is generally defined as "full epithelialization with no drainage, no exudate or eschar (scab) present" (Snyder, Sullivan & Schoelles, 2012, p. 48).

Although some products may have similar components or substrates, "[t]he results obtained from studies of a single product […] cannot be extrapolated to all products in a group because of differences in product components and healing properties" (Snyder, Sullivan & Schoelles, 2012, p. 48). Therefore, the results are organized by product type below.

Results are also separated by indication (diabetic foot ulcer or venous leg ulcer; the search did not identify any evidence for skin substitutes in the treatment of decubitus ulcers). Effectiveness for one type of wound cannot be extrapolated across indications "because of the difference in etiology and pathophysiology" between different types of wounds (Snyder, Sullivan & Schoelles, 2012, p. 56).

One limitation of the body of evidence is a lack of standardization of comparators. Some trials compare one skin substitute versus another, but many use "usual care" in the control group. Some treatments that fall into the category of usual care can include (but are not limited to):

- Diabetic Foot Ulcers – usual care techniques:
  - Nonadherent gauze dressing (Mepitel), covered with a secondary dressing including saline-moistened gauze and dry gauze
  - Saline-moistened, nonadherent gauze (Teapore) covered with a layer of saline-moistened gauze followed by dry gauze and petrolatum gauze layer
  - Nonadherent interface + saline moistened gauze
  - Saline moistened gauze
- Venous Leg Ulcers – usual care techniques:
  - Tegapore (gauze bolster), zinc oxide-impregnanted, paste bandage (Unna boot), and self-adherent elastic wrap

- Multilayered compression therapy

The body of evidence is also limited in the evidence addressing the considerations in Key Question 1. Where possible, discussion of study inclusion/exclusion criteria are presented.

Table 2. Summary of Included Systematic Reviews

Systematic Review (Quality) Total N	Population No. and Type of Included Studies	Skin Substitute Category	Outcomes of Interest
Game (2015) (Fair) N = 1461	Diabetic foot ulcers: 11 RCTs 1 Cohort 1 Case-control	• Allogeneic fetal fibroblasts on polyglactic matrix (Dermagraft) • Tissue engineered sheet of fibroblast/keratinocyte co-culture (Graftskin) • Living keratinocytes and fibroblasts (Apligraf®) • Amniotic membrane wound graft (Epifix)	• Complete wound healing • Time to complete wound healing
Felder (2012) (Fair) N = 2043	Chronic foot ulcers (diabetic, angiopathic, venous stasis, pressure-induced, or infected): 15 RCTs 1 Cohort 5 SRs	• Bilayer of neonatal keratinocytes and fibroblasts on hyaluronic acid matrix (Apligraf/Graftskin) • Neonatal fibroblasts and keratinocytes cultured onto bovine collagen matrix (OrCel) • Cryopreserved split-thickness skin allograft (TheraSkin) • Allogeneic fetal fibroblasts on polyglactic matrix (Dermagraft) • Autologous cultured keratinocytes on hyaluronic acid-derived,	• Complete wound healing • Time to complete wound healing • Infection rate • Complications • Ulcer recurrence

Systematic Review (Quality) Total N	Population No. and Type of Included Studies	Skin Substitute Category	Outcomes of Interest
		perforated lamina (Laserskin) • Decellularized cadaveric dermis (Graftjacket®) • Bovine collagen and chondroitin-6-sulfate scaffold with silicone covering (Synthetic Integra)	
Jones (2013) (Good) N = 438	Venous leg ulcers: 5 RCTs	• Allogenic bilaminar Composite Cultured Skin (OrCel™) • Cultured epidermal allograft (Autoderm™) • Products derived from live human/animal tissue (Apligraf®, Dermagraft®)	• Complete wound healing • Time to complete healing • Rate of change in ulcer area • Pain • Adverse events
Snyder (2012) (Good) N = 1,829	Diabetic foot ulcers: 12 RCTs Vascular leg ulcers: 6 RCTs	• Products derived from human donor tissue (Graftjacket®) • Products derived from live human/animal tissue (Apligraf®, Dermagraft®) • Acellular animal derived products (OASIS® Wound Matrix) • Biosynthetic products (Talymed®)	• Wound infection • Complete wound healing • Time to complete wound healing • Adverse events • Quality of life surrogate outcomes (return to baseline activities of daily living and function, pain reduction)

Table 3. Summary of Included Randomized Controlled Trials identified in additional Medline search

RCT (Quality) Total N	Population	Skin Substitute Category	Outcomes of Interest
Lavery 2014 (Poor) N = 97	Diabetic foot ulcers	• Placenta-derived human viable wound matrix (Grafix®)	• Complete wound healing • Time to complete healing • Adverse events • Wound-related infections

EVIDENCE SUMMARY

Snyder [AHRQ] (2012)

The AHRQ systematic review by Snyder, Sullivan and Schoelles (2012) included 18 RCTs (12 on DFUs, 6 on VLUs). Of the 18 studies, eight were assessed as a low risk of bias, nine as a moderate risk of bias, and one with an unclear risk of bias. The review authors limited study inclusion to RCTs that had a minimum of 10 patients per treatment arm. In addition to the outcomes described in Table 1, the AHRQ review evaluated wound recurrence, need for amputation, need for hospitalization, return to baseline activities of daily living and function, pain reduction, and exudate and odor reduction.

Felder (2012)

The systematic review by Felder, Goyal, and Attinger (2012) included 15 RCTs and one prospective cohort study as well as five systematic reviews. This SR was concerned with chronic foot ulcers of any origin. There is significant overlap in included studies (nine RCTS) between the AHRQ SR (Snyder, Sullivan and Schoelles, 2012) and this SR. Felder and colleagues (2012) included five additional studies (3 DFU, 1 VLU, 1 non-healing foot ulcer) that were not included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012). Of these five, one was assessed at low risk of bias, one at moderate risk of bias, and three at high risk of bias. Rate of complete wound healing was the primary outcome; secondary outcomes included time to complete wound healing, infection rates, and ulcer recurrence.

Jones [Cochrane] (2013)

The Jones systematic review (Jones, Nelson and Al-Hity, 2013) focused on the treatment of VLUs and included five RCTs on the use of skin substitutes, two of which overlap with the AHRQ review (Snyder, Sullivan and Schoelles, 2012). Of the remaining three studies, one is rated as unclear risk of bias, one at low risk of bias, and one at moderate risk of bias. Authors included any randomized study, regardless of

publication status or language, in which skin grafts or skin replacements for venous leg ulcers were compared against any other intervention (only studies involving skin substitutes are summarized in this coverage guidance), and which reported on the primary outcomes of wound healing, time to complete healing, or absolute rate of change of ulcer area.

Game (2015)

A systematic review by Game and colleagues (2015) assessed the effectiveness of various interventions for diabetic foot ulcers. This is the second update of a systematic review undertaken by the International Working Group of the Diabetic Foot (IWGDF) in 2006 and first updated in June 2010. Game and colleagues (2015) included all controlled studies, both prospective and retrospective, that evaluated treatment of chronic foot ulcers in adults (age 18 and older) with type 1 or type 2 diabetes. Primary outcomes were healing, time to healing, and reduction in wound area. The 2015 review included 11 RCTs relevant to skin substitutes; all but three of them overlap with the other SRs included in this report. Of those three, one was rated at medium risk of bias and the others at high risk of bias.

Apligraf® / Graftskin

Apligraf®, known previously as Graftskin, is a "living cell based bilayered skin substitute derived from bovine type 1 collagen and human fibroblasts and keratinocytes derived from neonatal foreskins" (Snyder, Sullivan, and Schoelles, 2012, pg 38).

The FDA has approved Apligraf®

> For use with standard therapeutic compression for the treatment of non-infected partial and full-thickness skin ulcers due to venous insufficiency of greater than 1 month duration and which have not adequately responded to conventional ulcer therapy. Apligraf is also indicated for use with standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers of greater than three weeks' duration which have not adequately responded to conventional ulcer therapy and which extend through the dermis but without tendon, muscle, capsule or bone exposure.
>
> Apligraf is contraindicated for use on clinically infected wounds. Apligraf is contraindicated in patients with known allergies to bovine collagen. Apligraf is contraindicated in patients with a known hypersensitivity to the components of the Apligraf agarose shipping medium." of non-infected partial and full-thickness skin ulcers due to venous insufficiency of greater than 1 month duration and which have not adequately responded to conventional ulcer therapy. Apligraf is also indicated for use with standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers of greater than three weeks' duration which have not adequately responded to conventional ulcer therapy and which extend through the dermis but without tendon, muscle, capsule or bone exposure (Snyder, Sullivan, and Schoelles, 2012, pg 38).

The prescribing information contains a caution; “The safety and effectiveness of Apligraf have not been established for patients receiving greater than 5 device applications.”

Inclusion criteria for trials of Apligraf® varied in the size and severity of wounds. Minimum duration was 2-4 weeks. Patients were excluded for conditions that would impair wound healing such as poor glycemic control (identified in one trial as hemoglobin A1c ≥12), active infection, immunocompromise (either from underlying disease, radiation, chemotherapy, or recent corticosteroid use), evidence of skin cancer at or near the wound, renal or hepatic impairment, drug or alcohol abuse, and Charcot foot or inability to offload the ulcer. Some studies excluded patients whose ulcers responded to usual care in a 7-14 day run-in period. The majority of patients were male and in their 50s or 60s.

Three early studies (Sabolinski, 1996; Falanga, 1998; Falanga & Sabolinski, 1999) all used the same protocol of up to five applications within the first 21 days of treatment. Ulcers were re-examined every few days and if less than 50% of the previous application “took,” researchers applied the product again, up to five times in total. The earliest study reported that 70% of patients got 1-3 grafts; the others did not report how many applications were required. A 2009 study re-examined patients at 4 and 8 weeks after initial application and re-applied as necessary. “In the Apligraf group, 13 of the 33 subjects required only 1 application of Apligraf, and 15 and 5 subjects received 2 or 3 applications, respectively. On average, subjects received 1.8 Apligraf applications during the course of the study” (Edmonds, 2009, pg. 14). The comparative study of Apligraf® vs TheraSkin® (DiDomenico, 2011) put no limits on the number of applications and allowed them at clinician discretion, they report an average of 1.53 applications (SD = 1.65).

Chang, 2000 used only a single application for all subjects, and reported on costs thusly:

At our institution, professional fee reimbursement for all skin graft procedures averages $1 350. A single 7-inch disk of Apligraf costs $1000 to the third-party insurer or the patient. The reimbursement for a 3- to 5-day hospital stay, including operating room and recovery room costs, average $8000-$11,000 for a Medicare patient. Therefore, Apligraf application in these patients costs $7000 to $10,000 less that an autologous skin graft. Moreover, further cost reductions may be possible as demand for this product increases. Finally, wound closure yields may further be improved with multiple applications of TESG and as the optimal dressing and management of TESG-treated wounds in this patient population become better defined (Chang, 2000, pg. 49).

Critical Outcome: Deep Soft Tissue or Bone Infection

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) included one trial that reported cases of osteomyelitis in patients with DFUs treated with either Apligraf®/Graftskin or usual care. The RCT compared Apligraf® to saline-moistened gauze (treatment group, n = 112; usual care group, n = 96). There was a significantly lower incidence of osteomyelitis in the Apligraf® group compared to usual care (2.7% vs 10.4%, p = 0.04).

For VLUs, the AHRQ review included a single RCT comparing Apligraf® to compression therapy (treatment group, n = 161; usual care group, n = 136) that reported incidence of osteomyelitis. Approximately eight percent of patients receiving Apligraf® developed osteomyelitis at the study site, compared with no patients in the comparison group developing a bone infection (no statistical analysis conducted).

Critical Outcome: Complete Wound Healing

Snyder and colleagues (2012) included three RCTs comparing Apligraf® to usual care. Two of the trials included patients with DFUs (total n = 280) and the third trial focused on VLUs (n = 275). The AHRQ review (Snyder, Sullivan and Schoelles, 2012) found the use of Apligraf® was associated with significantly greater percentage of wound closures compared to usual care for patients with DFUs at 12 weeks (Trial 1, n=72, 52% vs 26%, p=0.03, relative risk 1.96, 95% CI 1.05 to 3.66; Trial 2, n=208, 56% vs 38%, p=0.01, relative risk 1.5, 95% CI 1.11 to 2.04) and patients with VLUs at 12 weeks (53% vs 22%, p<0.001, relative risk 2.38, 95% CI 1.67 to 3.39).

Felder and colleagues (2012) included two additional RCTs comparing Apligraf® to usual care. The first was a subgroup analysis of a larger study which looked at 120 patients whose ulcers had been present for at least one year, comparing Apligraf® to multilayer compression wrap. In this hard-to-heal subgroup, complete healing occurred by six months in 47% of subjects receiving Apligraf® versus 19% of the control subjects. The second study included by Felder (2012) compared Apligraf® against saline gauze dressing in patients with chronic foot ulcers of any etiology who had undergone limb revascularization within 60 days. Complete closure by six months occurred in 100% of Apligraf® patients, compared to 75% of usual care patients ($p < 0.01$).

Apligraf® vs Theraskin®

One RCT included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) evaluated the comparative effectiveness of Apligraf® and Theraskin® for DFUs (n = 28). Average wound size was similar between groups. There were no significant differences reported in complete wound closure between the two products (Apligraf® 41% vs Theraskin® 67%, p=0.21).

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of Apligraf® on validated quality of life indicators. One RCT included in the AHRQ review reported on pain, noting that it improved significantly in both Apligraf® and control groups (Snyder, Sullivan and Schoelles, 2012).

Important Outcome: Time to Complete Wound Healing

Snyder and colleagues (2012) included one RCT that reported on the time to complete wound healing in the use of Apligraf® for VLU. In the single RCT, patients who received Apligraf® experienced shorted median time to wound closure (61 days) compared with usual care (i.e., Unna boot) (191 days).

Felder and colleagues (2012) included one RCT of patients with chronic foot ulcers who had recently (60 days) undergone limb revascularization, which found mean time to healing with Apligraf® was seven weeks, compared to 15 weeks in the group treated with saline-gauze dressing (p = 0.0021).

Important Outcome: Adverse Effects

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) included four studies that reported on adverse effects from Apligraf® for a total of 332 patients treated with the product and 283 patients treated with usual care. Two RCTs (N = 28 and N = 72) reported only "serious adverse events" in the treatment and follow-up phases, and these were roughly equivalent (3-5 patients in each group). One trial only reported on osteomyelitis, which is discussed above. In the fourth RCT (N = 297), there were approximately equal incidences of cellulitis (15.5% vs 13.2%), dermatitis (8.7% vs 8.8%), and peripheral edema (5.0% vs 5.0%) in the Apligraf® group compared to usual care.

Although not explicitly stated as a critical outcome, one trial reported on the incidence of death. Six cases of death reported in the Apligraf® group compared with five cases in the usual care group (reasons not described); there were no other deaths reported across the three other trials.

Felder and colleagues (2012) included one additional study (a subgroup of a previous study, separating out 120 patients with hard-to-heal venous ulcers present longer than one year) that reported infection rates of 8.2% in the Apligraf® treatment group (n = 72) versus 7.8% in the usual care control group (n = 48).

In addition to the adverse effects described above, trials also reported relatively rare incidence of rashes, pain, urinary tract infection, pain, dyspnea, congestive heart failure, accidental injury, pharyngitis, asthenia, arrhythmia, arthralgia, increased cough, erythema, and kidney failure.

Dermagraft®

Dermagraft® is a "cryopreserved human fibroblast-derived dermal substitute on a bioabsorbable polyglactin mesh scaffold. The fibroblasts are obtained from human newborn foreskin tissue" (Snyder, Sullivan and Schoelles, 2012, pg 38). It is indicated by the FDA

> [f]or use in the treatment of full-thickness diabetic foot ulcers greater than six weeks' duration which extend through the dermis, but without tendon muscle, joint capsule or bone exposure. Dermagraft® should be used in conjunction with standard wound care regimens and in patients that have adequate blood supply to the involved foot. Dermagraft is contraindicated for use in ulcers that have signs of clinical infection or in ulcers with sinus tracts. Dermagraft is contraindicated in patients with known hypersensitivity to bovine products, as it may contain trace amounts of bovine proteins from the manufacturing medium and storage solution (Snyder, Sullivan and Schoelles, 2012, pg 38).

The FDA prescribing information contains a caution than Dermagraft has not been studied in patients receiving greater than 8 device applications.

Trials of Dermagraft® included patients with adequate glycemic control and evidence of adequate circulation as measured by ankle brachial pressure index (ABPI). Patients were excluded for evidence of active infection, impaired mobility, and significant comorbidities such as HIV, severe peripheral vascular

disease, or a bleeding disorder. Patients were also generally excluded if their ulcers responded to usual care during a run-in or screening period. Average age ranged from 55 to 72 years.

Application regimens for Dermagraft® are diverse in the literature. Earlier trials involved weekly applications for up to 7 or 8 treatments (Gentzkow, 1996; Naughton, 1997; Marston, 2003). A study in 2003 divided patients into three different treatment arms; weekly applications for up to 12 weeks and a total of four applications at 0, 1, 4, and 8 weeks had identical efficacy (5/13 wounds healed). The most recent trial in this report (Omar, 2004) used this same 0, 1, 4, and 8 protocol and had a similar result (5/10 ulcers healed).

Critical Outcome: Deep Soft Tissue or Bone Infection

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) identified one RCT comparing Dermagraft® to saline-moistened gauze in the treatment of DFU that reported on incidence of osteomyelitis. Rates were 8.6% in both the intervention and the control groups.

Critical Outcome: Complete Wound Healing

Snyder and colleagues (2012) included three RCTs that reported on complete wound healing in the use of Dermagraft® for DFUs. All three RCTs on DFUs found that patients receiving Dermagraft® experienced greater rates of complete wound healing compared to usual care at 12 weeks. A meta-analysis found Dermagraft to be more effective for achieving wound closure compared to usual care (saline-moistened gauze) for patients with DFUs (odds ratio 1.64; 95% CI 1.10 to 2.43).

Felder and colleagues (2012) identified one additional RCT of Dermagraft® in care of DFUs, in which the metabolic activity of the graft was assessed and patients in the treatment arm were stratified by whether or not the Dermagraft® was “metabolically active within the therapeutic range” (Felder, 2012, p. 150). At twelve weeks, the rate of complete healing was 38.5% in the entire treatment group and 31.7% in the control group (p = 0.138), but was 50.8% in the “metabolically active” Dermagraft® group.

Snyder and colleagues (2012) identified one RCT that included patients with VLUs, which found greater rates of complete wound healing in the Dermagraft® group at 12 weeks, although this finding was not statistically significant (28% vs 15%, p=0.30, relative risk 1.83, 95% CI 0.47 to 7.21).

Jones and colleagues (2013) identified one additional RCT of Dermagraft® versus usual care in VLUs that used a four-piece protocol. They pooled this data with the results of the aforementioned RCT and found that “There was no evidence of overall benefit associated with four pieces of dermal skin replacement (at baseline, one, four and eight weeks) in the two studies (RR 3.04, 95% CI 0.95 to 9.68), when pooled using a fixed-effect model (44 participants)” (Jones, Nelson, and Al-Hity, 2013, p. 10).

Dermagraft® vs OASIS®

One RCT included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) evaluated the comparative effectiveness of Dermagraft® and OASIS® for DFUs (n = 26). Average wound size was similar between groups (p = 0.94). There were no significant differences reported in complete wound closure between the two products (Dermagraft® 84.6% vs OASIS® 76.9%, p = 0.62).

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of Dermagraft® on validated quality of life indicators or surrogate measures.

Important Outcome: Time to Complete Wound Healing

Felder and colleagues (2012) identified four RCTs that reported on time to complete healing for DFUs treated with Dermagraft®. In all four trials, generally speaking, healing was faster in the Dermagraft® group than in the control. A fair quality small RCT testing three different Dermagraft® regimens against usual care (N=50) found that weekly application of Dermagraft® resulted in mean time to healing of 12 weeks, while less frequent applications and usual care led to healing times greater than 12 weeks. A second, fair quality RCT (N=235) assessed the metabolic activity of the Dermagraft® product prior to application and found an improvement in healing time (13 weeks vs 28 weeks) only when the product was "metabolically active within the therapeutic range" (Felder, Goyal, and Attinger, 2012, p. 150). A poor quality RCT (N=281) published the same year had identical results (13 weeks vs 28 weeks), while the final RCT in this review (also poor quality, N=245) demonstrated that time to healing was significantly faster with Dermagraft than with control (p = 0.04)

Similarly, the one RCT included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) on the use of Dermagraft® for patient with VLUs found shorter wound closure time in the Dermagraft group compared with usual care (35 weeks vs 74 weeks).

Dermagraft® vs OASIS®

One RCT included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) evaluated the comparative effectiveness of Dermagraft® and OASIS® for DFUs (n = 26). There were no significant differences reported in time to complete wound closure between the two products (Dermagraft 40.90 ± 32.32 days vs OASIS® 35.67 ± 41.47 days, p = 0.73).

Important Outcome: Adverse Effects

Two trials identified by Felder and colleagues (2012) reported on adverse effects with Dermagraft®. One trial (n = 314) found that compared to usual care (saline-moistened gauze), patients who received Dermagraft® had lower rates of adverse effects (i.e., infection, osteo and cellulitis) (19% vs 32%, p=0.007). In the second trial, patients in the Dermagraft® groups had similar rates of adverse events (undefined, statistical significance not reported in the AHRQ review). Unrelated AEs in this study (N = 53) included syncope, skin excoriation, bleeding from biopsy site, latex allergy, development of bullous pemphigoid, and cerebrovascular accident.

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) reported adverse events from one fair quality RCT (N=53) of Dermagraft® in treatment of VLUs. With 13-14 subjects in each treatment group, total number of adverse events was 15-18 per group, Serious adverse events were not reported in the control group; the three treatment groups each had at least one serious adverse event, with four serious events in the most intensive treatment arm.

EpiFix®

EpiFix® is derived from human amniotic membrane and is marketed both in a skin allograft form as well as an injectable form. It does not presently have any FDA indications. This evidence review identified one small RCT of EpiFix®. Patients were 56-62 years old, were 69% and 58% male in the intervention and control groups, respectively, and had ulcers averaging 2.8cm^2 in the intervention group and 3.4 cm^2 in the controls. Other inclusion/exclusion criteria were not described and significance of baseline differences were not reported.

In this RCT (Zelen, 2013), patients who had incomplete epithelialization received an additional application at weeks 2, 4, 6, 8, and 10. The authors state, "Five patients (45%) healed with one dHAM application, one (9.1%) healed with two applications, one (9.1%) healed with three applications, two (18%) healed with four applications, and one (9.1%) healed after five applications." This is an average of 2.3 applications.

Critical Outcome: Deep Soft Tissue or Bone Infection

No SRs or RCTs reported on the effect of EpiFix® on deep soft tissue or bone infection.

Critical Outcome: Complete Wound Healing

Game and colleagues (2015) identified one RCT of Epifix®, an amniotic membrane graft product, in the treatment of DFUs. This was a small pilot study in which 13 patients with an average wound size of 2.8 cm^2 were treated with EpiFix® and 12 patients with an average wound size of 3.4 cm^2 were treated with moistened gauze and silver; all patients received compression dressings. At four weeks, complete healing was 77% in the EpiFix® group and 0% in the control group ($p < 0.0001$). By six weeks, rates of complete healing were 92% and 8%, respectively ($p < 0.0001$). This is an unexpectedly low rate of healing in the control group.

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of EpiFix® on validated quality of life indicators or surrogate measures.

Important Outcome: Time to Complete Wound Healing

No SRs or RCTs reported on the effect of EpiFix® on time to complete wound healing.

Important Outcome: Adverse Effects

No SRs or RCTs reported on the adverse effects of EpiFix®.

Grafix®

Grafix® is another product derived from cryopreserved human placental membrane. It is approved by the FDA as a "wound cover" for both acute and chronic wounds. According to the manufacturer it intends to submit a Biologics License Application for more clinical indications. This evidence review identified only one RCT of poor quality. Patients in this trial had wounds of four to 52 weeks' duration, and of one to 15 cm^2 in area. Patients were excluded for A1c ≥12, inadequate ABPI, presence of active

infection, and response to usual care during a one-week screening period. Other subject characteristics were not reported. Patients received weekly applications for up to 84 days (Lavery, 2014).

Critical Outcome: Deep Soft Tissue or Bone Infection

No SRs or RCTs reported on the effect of Grafix® on deep soft tissue or bone infection. The RCT by Lavery and colleagues (2014) did report that patients randomized to Grafix® did experience significantly fewer wound infections than the usual-care group (18.0% versus 36.2%, p = 0.044), and a trend to fewer infection-related hospitalizations (6% versus 15%, p = 0.15).

Critical Outcome: Complete Wound Healing

Lavery and colleagues (2014) conducted an RCT of Grafix® versus standard wound care for DFUs. Patient groups were similar at baseline. Complete wound healing occurred in 62% of patients treated with Grafix® and in 21% of the control group (p < 0.01). The quality of this study is poor due to having no description of randomization methodology, nor concealment or blinding efforts. The study was funded by manufacturer.

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of Grafix® on validated quality of life indicators or surrogate measures.

Important Outcome: Time to Complete Wound Healing

In the poor quality RCT by Lavery and colleagues (2014), time to complete healing was a secondary outcome. Patients treated with Grafix® experienced complete wound healing in a median time of 42 days, compared to 69.5 days in the control group (p = 0.019).

Important Outcome: Adverse Effects

Lavery and colleagues (2014) reported that patients treated with Grafix® were less likely to experience any adverse event than patients in the control group (44% versus 66%, p = 0.031). One control group subject underwent amputation due to an adverse event; there were no amputations in the intervention arm. There was no discussion of whether any of the adverse events were thought to be related to treatment.

Graftjacket®

Graftjacket® is derived from donated human tissue, and is composed of extracellular components of human dermis (collagen, elastin, and proteoglycans). One RCT included patients with non-infected ulcers and a palpable/audible pulse to the affected extremity, but did not describe other inclusion/exclusion criteria. A second RCT included only patients with good diabetic control (Hgb A1c < 12, serum creatinine < 3.0 mg) and adequate ABPI, and excluded patients who had received biomedical or topical growth factors within 30 days. Other subject characteristics were not reported. Both RCTs used a single application in the treatment group (Brigido, 2006; Reyzelman, 2009).

Critical Outcome: Deep Soft Tissue or Bone Infection

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) identified one RCT that reported wound infection rates in the use of Graftjacket®. In 46 patients treated with Graftjacket®, one patient experienced a wound infection that eventually ended with amputation; there were no cases of wound infection in the 39 control group subjects.

Critical Outcome: Complete Wound Healing

Two RCTs were included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) that evaluated the use of Graftjacket® in patients with DFUs (total n = 113). The authors of both studies report a significantly greater proportion of wound closure compared to usual care at 12 weeks (compared with moist-wound therapy dressings: 70% vs 46%, p=0.03, relative risk 1.51, 95% CI 1.02 to 2.22; compared with Curasol: 86% vs 29%, p=0.006). In the AHRQ review, one of these RCTs was assessed at moderate risk of bias; the other was determined to be at low risk of bias after author communications clarified the randomization procedures. However, Felder and colleagues (2012) point out other flaws in this second RCT, specifically that the dropout rate was twice as high in the treatment group as in the control group, that the average pretreatment wound size was biased in favor of the Graftjacket arm (3.6cm^2 in the treatment subjects versus 5.1cm^2 in the control subjects), and that the control group "had a higher percentage of foot wounds, which are more likely to be weight-bearing and therefore more difficult to heal" (Felder, Goyal and Attinger, 2012, p. 60).

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of Graftjacket® on validated quality of life indicators or surrogate measures.

Important Outcome: Time to Complete Wound Healing

The AHRQ SR (Snyder, Sullivan and Schoelles, 2012) included two RCTs that reviewed the effectiveness of Graftjacket for DFUs. In one trial, time to complete healing was 11.92 weeks in the treatment group versus 13.5 weeks in the control group; in the other, it was 5.7 weeks in the treatment group versus 6.8 weeks in the control. While both studies reported a shortened time to would closure compared to a usual care group, neither finding was statistically significant.

Important Outcome: Adverse Effects

One RCT reported wound infection rates of 21.4% versus 35.7% in the treatment and control groups, respectively (Felder, Goyal and Attinger, 2012). The other RCT reported on a control group patient who experienced altered mental status and hypotension and another who developed an abscess; in the treatment group, one patient had an infection leading to amputation (discussed above), and a second required vascular surgery.

OASIS® Wound Matrix

OASIS® is derived from hydrolyzed bovine collagen and is approved by the FDA "[f]or the management of wounds including full thickness and partial thickness wounds, pressure ulcers, venous ulcers, ulcers caused by mixed vascular etiologies, diabetic ulcers, second-degree burns, donor sites and other

bleeding surface wounds, abrasions, traumatic wounds healing by secondary intention, dehisced surgical incisions" (Snyder, Sullivan and Schoelles, 2012, pg. ES-12). The AHRQ review identified five RCTs evaluating the effectiveness of OASIS®. Patients were enrolled with a wound of >4 weeks duration (in one trial, > 6 months). Patients with conditions that would slow wound healing were excluded from all trials, for example, malnutrition (albumin < 2.5 g/dL), poor glycemic control (A1c >12), active smoker status, inadequate circulation to the affected limb, active infection, immunosuppression, use of steroids, vascular disease, and Charcot foot.

In three trials of OASIS® for DFU, the product was re-applied as deemed clinically necessary. One RCT (Niezgoda, 2005) reported an average use of 10 sheets of OASIS per patient. A trial of OASIS compared to Dermagraft® (Landsman, 2008) reported that up to eight applications of OASIS was similarly effective to up to three applications of Dermagraft®. The third trial (Romanelli, 2010) reported an average of 5.2 days between dressing changes for OASIS patients.

Two RCTs reported on OASIS® in treatment of VLU. One (Mostow, 2005) reported an average of eight sheets per patient; the other (Romanelli, 2007) reported an average of 6.4 days between dressing changes but did not report on number of sheets of product used.

Critical Outcome: Deep Soft Tissue or Bone Infection

No SRs or RCTs reported on the effect of OASIS® on deep soft tissue or bone infection.

Critical Outcome: Complete Wound Healing

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) included one RCT of patients with DFUs (n = 98), comparing OASIS® Wound Matrix with Regranex Gel (contains platelet-derived growth factor) and found greater wound closure of plantar ulcers at 12 weeks in the OASIS® group (49% vs 28%, p=0.06).

A second RCT comparing OASIS® Wound Matrix with standard care was identified after the initial search and draft coverage guidance was completed. Cazzell and colleagues (2015) published results of an open-label RCT of 82 patients comparing OASIS® to standard care for treatment of DFU. In the intervention group, OASIS was applied once each week. Patients in the control group were also seen weekly and the standard care intervention was selected by the investigator (standard care included sliver dressing, Hydrogel, wet-to-dry, alginate, Manuka honey, or triple antibiotic dressing). Ulcer measurement was standardized by use of a digital image capture and wound measurement device. At 12 weeks, wound healing was greater in the OASIS group (54%) compared with the standard care group (32%) (p=0.021). Smith and Nephew funded the study and employs three of the authors. Aside from the conflicts of interest and open-label design, the study otherwise appears to be at low risk of bias. This fair quality RCT demonstrates improved DFU wound healing at 12 weeks for patients treated with OASIS compared to standard care.

Snyder and colleagues (2012) included three RCTs of patients with VLUs that evaluated the effectiveness of OASIS® Wound Matrix (total n = 222). The trials included disparate usual care groups (petrolatum-impregnated gauze with no compression, Jaloskin containing hyaluronan, nonadherent dressing with compression bandages). However, healing rates were greater in the OASIS® Wound Matrix arms across

all three trials and follow-up periods (80% vs 65% at 8 weeks, p<0.05; 83% vs 46% at 16 weeks, p<0.001; 55% vs 34% at 12 weeks, p=0.02; respectively).

OASIS® Wound Matrix vs Dermagraft®

The AHRQ SR (Snyder, Sullivan and Schoelles, 2012) included one RCT that compared OASIS® Wound Matrix with Dermagraft® for individuals with DFUs (n = 26). The study found no significant difference in complete wound closure between the two products (Dermagraft 84.6% vs OASIS® 76.9%, p = 0.62).

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of OASIS® on validated quality of life indicators. One RCT identified in the AHRQ review reported fewer wound dressings with OASIS® (6.46 ± 1.39 changes vs 2.54 ± 0.78), while a second reported lower pain levels in the intervention group as measured by a 10-point visual analog scale (3.7 vs 6.2, p < 0.05). A third RCT reported that 2/17 patients in the OASIS® group experienced pain, compared to 1/10 control patients.

Important Outcome: Time to Complete Wound Healing

Of the three RCTs included in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) that evaluated OASIS® Wound Matrix in patients with DFUs, only one trial reported a shorter time to wound closure compared to nonadherent dressing with compression bandages (5.4 weeks vs 8.3 weeks, statistical analysis not reported). A second RCT reported 35.67 ± 41.47 days in the OASIS® arm vs 40.90 ± 32.32 days in the control (not significant). The third RCT reported average time of 67 days with OASIS® and 73 days with control (p = 0.245). All three RCTs were of fair quality.

One RCT of OASIS® in VLUs did not report time to healing, but did estimate using Cox analysis that at twelve weeks, 63% of the treatment group vs 29% of the controls would be expected to achieve complete wound healing (Snyder, Sullivan and Schoelles, 2012).

OASIS® Wound Matrix vs Dermagraft®

The AHRQ SR included one RCT that compared OASIS® Wound Matrix with Dermagraft for individuals with DFUs. The study found no significant difference in the time to wound closure between the two products (Snyder, Sullivan and Schoelles, 2012).

Important Outcome: Adverse Effects

The AHRQ SR included one RCT that compared OASIS® with Regranex growth gel (Snyder, Sullivan and Schoelles, 2012). The authors reported adverse effects in the OASIS® group (n=17) including one patient with depression/mood disorder, one patient with gastrointestinal disorder, and three patients with infections in a non-study ulcer. In the Regranex group (n=10), there was one instance of infection in a non-study ulcer, two cases of limb injury, one respiratory tract infection, one case of septic arthritis, and one skin injury.

The AHRQ SR also reported on one trial in which eight patients received OASIS® and 15 were treated with compression. In this trial, three patients in each group experienced an allergic reaction or intolerance to the secondary dressing. One patient in the OASIS® group died of cardiovascular disease; one patient in the compression group developed a new ulcer from the compression. One patient in each

group developed an infection in another (non-target) wound, one patient receiving compression developed a seroma, and one patient in each group suffered skin injury.

Talymed®

Talymed® is a wound dressing product containing poly-N-acetyl glucosamine (pGlcNAc) derived from microalgae. (Snyder, Sullivan and Schoelles, 2012, pg. 56). This evidence review identified one small pilot RCT within the AHRQ review. Patients in this trial were 59-63 years old, 25-65% male, and had wounds ranging from 2.7 to 3.6 months duration. Patients in both intervention and control groups had comorbidities including hypertension, diabetes, obesity, arthritis, and blood clotting disorders. Patients were excluded for a variety of more severe indications such as collagen vascular disease, Charcot disease, previous radiation, current hemodialysis, or insufficient ABPI.

The RCT (Kelechi, 2011) included three treatment arms (single application, application every other week, or application every three weeks). Weekly application was equivalent to control (45%, n = 9 of 20). Complete healing occurred in 86.4% (n = 19 of 22) and 65.0% (n = 13 of 20) with applications every two and every three weeks, respectively. P-value was significant for every other week versus standard care ($p < 0.01$).

Critical Outcome: Deep Soft Tissue or Bone Infection

No SRs or RCTs reported on the effect of Talymed® on deep soft tissue or bone infection.

Critical Outcome: Complete Wound Healing

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) included a single RCT that evaluated the use of Talymed® in combination with usual care compared to usual care alone for VLUs (n=82). Patients receiving Talymed® with usual care every other week experienced higher wound closure rates than usual care alone at 20 weeks (86% vs 45%, p=0.0005). Snyder and colleagues (2012) note that patients receiving Talymed® once every three weeks or only receiving one application did not experience statistically significant results.

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of Talymed® on validated quality of life indicators or surrogate measures.

Important Outcome: Time to Complete Wound Healing

No SRs or RCTs reported on the effect of Talymed® on time to complete wound healing.

Important Outcome: Adverse Effects

In the AHRQ review (Snyder, Sullivan and Schoelles, 2012), a single RCT reported “no pain, edema, or significant treatment-related adverse events occurred” (p. C-65).

TheraSkin®

TheraSkin® is a cryopreserved human skin allograft (Snyder, Sullivan and Schoelles, 2012). This evidence review identified one RCT in which TheraSkin® was used as a comparison for Apligraf® for diabetic foot ulcers, discussed above. Patients in this trial had either Type I or Type II diabetes with A1c < 12.0 and the ability to comply with an offloading regimen as well as adequate ABPI (>0.75) and absence of infection, gangrenous tissue, or abscess. The study was rated at moderate risk of bias.

Patients in the RCT (DiDomenico, 2011) received up to five applications, in accordance with the manufacturer's recommendations. Authors report that most patients received only a single application and that the mean number of applications was 1.38 (SD = 0.29).

Critical Outcome: Deep Soft Tissue or Bone Infection

The AHRQ review (Snyder, Sullivan and Schoelles, 2012) identified one RCT in which TheraSkin® was used as the comparator to Apligraf®. In this trial, one patient treated with TheraSkin® was hospitalized due to infection, but no further information is available.

Critical Outcome: Complete Wound Healing

The RCT identified in the AHRQ review (Snyder, Sullivan and Schoelles, 2012) reported complete wound healing at two time points. By 12 weeks follow up, the TheraSkin® group had 66.7% complete healing, versus 41.3% in the Apligraf® group (p = 0.21). The difference was even smaller at 20 weeks, as no more patients in the TheraSkin group experienced complete healing (66.7% vs 47.1%, p not reported).

Critical Outcome: Quality of Life

No SRs or RCTs reported on the effect of TheraSkin® on validated quality of life indicators or surrogate measures.

Important Outcome: Time to Complete Wound Healing

No SRs or RCTs reported on the effect of TheraSkin® on time to complete wound healing.

Important Outcome: Adverse Effects

No SRs or RCTs reported on the adverse effects of TheraSkin®

Summary of the Evidence

The field of biologic skin substitutes for treatment of chronic skin ulcers such as venous leg ulcers and diabetic foot ulcers is rapidly expanding with a variety of new innovations and products. An AHRQ review in 2012 identified 57 unique products, while this updated search found 73 and there are likely more. Evidence for the effectiveness and safety of these products has not kept pace with their development, however, as this review was only able to find published trials of nine products (available in the US), and none dealing with pressure ulcers. While early tests are promising for these products in the treatment of serious and occasionally life-threatening wounds, our confidence in the estimates of effectiveness is generally very low. Studies are almost universally limited by small sample size and inconsistency in control groups and what is defined as "usual care." There is virtually no evidence to

illuminate the comparative effectiveness of these products, nor to compare their effectiveness versus other alternative types of wound dressings besides moist saline gauze and compression.

Our key question regarding subgroup analysis (considerations of age, BMI, comorbidities, etc.) went largely unanswered by these studies. Where inclusion/exclusion criteria were reported, in general the patients were predominantly male, between 50-70 years of age, had hemoglobin A1c < 12.0%, had no active infectious process, and had adequate circulation to the extremity as measured by ankle-brachial pressure index (ABPI). Some trials excluded other comorbidities such as immunosuppression.

Most trials did report on the likelihood of complete wound closure, which makes comparison of results across studies possible; however, the limitation is that many studies have a short follow-up time that may miss complete healing that takes place in the usual care group at a later time. The second critical outcome was incidence of deep soft tissue or bone infection; this outcome was not widely reported and could be inferred from some studies only by the occasion of an amputation. No information was identified related to validated quality of life indicators for any of the products, although there is very limited information about pain and number of dressing changes for a few products. Time to complete healing is another outcome considered important to this review. In these early trials, the skin substitutes do appear to reduce time to wound healing but it should be noted that none of the trials had adequate blinding and many are subject to selection as well as observer bias.

In the AHRQ review, Snyder and colleagues (2012) express concern about the external validity of this body of evidence:

> The overall applicability of the evidence base is limited to a small number of skin substitute products examining diabetic foot ulcers and venous and/or arterial leg ulcers and to patients in generally good health. Although these results are consistent in showing a benefit when using skin substitutes and suggest that skin substitutes could be used in treating diabetic foot ulcers and venous leg ulcers, the patients enrolled in these studies were in generally good health and free of infected wounds, medications that would impede wound healing, clinically significant medical conditions, significant peripheral vascular disease, malnutrition, or uncontrolled diabetes. The results of these studies may not easily translate to everyday clinical situations. The expected population with chronic wounds is likely to have these conditions; therefore, the results reported in studies without these patients may not extrapolate well. The applicability of the findings to sicker patients may be limited (Snyder, Sullivan and Schoelles, 2012, p. 74).

These products are dissimilar enough that even though they can be broadly categorized by derivation, results from a trial of one product cannot be extrapolated to other products in its category. With such a large number of products, it will be challenging to have high confidence in the evidence of their effectiveness without many, many more trials.

OTHER DECISION FACTORS –

Resource Allocation

Cost for a course of treatment with skin substitutes can vary widely, depending on the product used, the number of applications required, the amount of skin substitute purchased, where it is applied (inpatient hospital, outpatient hospital, ambulatory surgical center, office) and payer reimbursement policies. Costs for a course of treatment can vary from a few hundred dollars for an in-office treatment with a low-cost skin substitute such as OASIS® Wound Matrix to several thousand dollars for multiple applications of higher cost products such as Apligraf and Dermagraft. While these products are sometimes billed separately from the physician fees for applying them (including related debridement), some payers are bundling payment in order to incentivize the use of cost-effective products. For instance, in the ambulatory surgery center setting, Medicare fee for service bundles the professional fee with the product itself. In addition, in a form of reference pricing, Medicare groups these bundles into two groups--for high-cost and low cost products—in order to encourage the use of cost-effective products. Some other payers follow Medicare's practices, but others have their own reimbursement policies.

When not bundled, prices for the skin substitute product itself are usually based on the number of square centimeters purchased, though some products are only sold in relatively large pieces (creating waste when used for small ulcers), while others can be purchased in a variety of sizes. In addition, some products are perishable and must be ordered to arrive within a few days of use; others have a longer shelf life. If these products are effective at improving time to complete ulcer healing, or preventing amputations, they could be cost-effective. However, given the low quality evidence available on most of these products, it is difficult to determine whether or not the expected improvement is sufficient to justify the cost.

For products recommended for coverage, the GRADE-informed framework above shows examples of pricing for smaller ulcers for Medicare fee-for-service in various settings. Information about costs for a course of treatment in the GRADE-informed framework and in Appendix E reflects a certain number of applications, based on FDA approval criteria, other payers' coverage criteria or averages from studies.

When multiple effective skin substitutes are available for a given indication, strategizing preferred products based on price or using alternative payment strategies may create savings for payers.

Values and preferences

Ulcers can be painful, distressing, and debilitating to patients and patients would likely be highly motivated to have effective treatment. However, few of these products have any evidence of benefit at this point and patients would be unlikely to strongly prefer skin substitutes if benefit is unclear. Skin substitutes, however, do not appear to add much burden to the patient; they would continue to require frequent wound dressings, offloading, and other mediating treatments regardless of the use of skin substitutes, so adverse effects or impact on convenience would not be a strong consideration against these products.

Other considerations

Expert input and study inclusion criteria show that skin substitutes can only be effective when other conditions necessary for wound healing exist. These conditions include the following:

1. Product is recommended for the type of ulcer being treated (see table below)
2. FDA indications and contraindications are followed, if applicable
3. Appropriate offloading has been performed
4. Wound has adequate arterial flow, no ongoing infection and a moist wound healing environment
5. Multilayer compression dressings are used (when clinically appropriate)
6. Patient has not used tobacco products 4 weeks prior to placement
7. For patients with diabetes, Hba1c level is < 12.
8. No prior failure of the same skin substitute for the ulcer being treated
9. Prior appropriate wound care therapy has failed to result in significant improvement of the wound over at least 30 days
10. Ulcer improves significantly over 6 weeks of treatment with skin substitutes, required for coverage of ongoing applications
11. Patients is able to adhere to the treatment plan

POLICY LANDSCAPE

Quality measures

No quality measures related to skin substitutes were identified on the National Quality Measures Clearinghouse.

Payer coverage policies

Among the four private payers reviewed, two payers provide coverage of skin substitute products (Aetna and Cigna) and two payers do not have coverage criteria (Moda and Regence). Washington Medicaid only covers one skin substitute (Theraskin for diabetic foot ulcers) and requires prior authorization. No National Coverage Determinations were identified. However, there are four Local Coverage Determinations (LCDs) that specify coverage of skin substitutes. Two of the LCDs detail specific products covered (L34285 and L34593), while the other two do not (L36377 and L35041). Table 4 summarizes the coverage for skin substitutes to treat diabetic foot ulcers (DFU) and venous leg ulcers (VLU) across payers. None of the skin substitute coverage policies cover decubitus ulcers. All payers reviewed, except the Medicare NCD and Washington Medicaid, cover skin substitutes when a wound has not adequately responded to standard treatments, usually within 30 days. Many coverage policies have additional indications that limit use, such as the ulcer being infection-free (Aetna, L35041, L34593, and L34285), the foot having adequate blood supply (Aetna, Cigna, L 35041, and L34593), and HbA1C < 12% (Cigna). Some payers limit the number of applications of skin substitutes, for example, a maximum of four treatments of Apligraf or Epifix in 12 weeks and wound healing must be present (Cigna), not more than 10 applications per wound (L35041), Apligraf and Epifix limited to five applications (L34593), and Graftjacket is limited to one application (L34285).

Table 4. Summary of Other Payer Coverage of Skin Substitutes

Payer	Skin Substitutes						
	Apligraf®	Dermagraft®	Epifix®	Graftjacket®	OASIS®	Primatrix®	Theraskin®
Aetna	DFU, VLU	DFU	X	DFU	DFU, VLU	X	X
Cigna	DFU, VLU	DFU	DFU, VLU	DFU	DFU, VLU	X	DFU
Washington	X	X	X	X	X	X	DFU w/ author-ization
LCD-Alabama (L34285)	DFU, VLU	DFU	DFU, VLU	DFU	DFU, VLU	X	DFU, VLU
LCD-Iowa (L34593)	DFU, VLU	DFU	DFU, VLU	DFU	DFU, VLU	DFU, VLU	DFU, VLU
LCD-Delaware (L35041)	DFU, VLU – no specific products identified						
LCD-Florida (L36377)	DFU, VLU – no specific products identified						

Key: X – product is not covered

Abbreviations: DFU – diabetic foot ulcer; LCD – local coverage determination; VLU – venous leg ulcer

Clinical Practice Guidelines

Diabetic foot ulcers

Three clinical practice guidelines address care for diabetic foot ulcers (Braun, Kim, Margolis, Peters, & Lavery, 2006; NICE, 2011; Registered Nurses' Association of Ontario, 2013). The good-quality National Institute for Health and Care Excellence (NICE) clinical practice guidelines recommend to, "Consider dermal or skin substitutes as an adjunct to standard care when treating diabetic foot ulcers, only when healing has not progressed and on the advice of the multidisciplinary foot care service" (2015, p.18). The fair-quality guideline from the Registered Nurses' Association of Ontario and Braun and colleagues (2006) poor-quality update to the Wound Healing Society guideline did not include a recommendation on use of skin substitutes.

Venous leg ulcers

Three clinical practice guidelines address care of venous leg ulcers (AAWC, 2010; Australian Wound Management Association Inc. and the New Zealand Wound Care Society Inc., 2011; SIGN, 2010). One good-quality guideline, Australian and New Zealand Clinical Practice Guideline for Prevention and Management of Venous Leg Ulcers, and one poor-quality guideline from the Association for the Advancement of Wound Care (AAWC) recommend skin substitutes for non-healing or persistent venous

leg ulcers, but do not provide recommendations on the use of specific products. The good-quality SIGN guideline found that there is insufficient evidence on which to base a recommendation for including skin substitutes, or any skin grafting.

Pressure ulcers

The good-quality Institute for Clinical Systems Improvement (ICSI) guideline recommends that clinicians refer the patient to a wound-focused physician or clinician to select the appropriate skin substitute or other biological application for the treatment of chronic skin ulcers, such as platelet gels, platelet-derived growth factor therapy, or extracellular matrix sheets.

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Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

APPENDIX A. GRADE INFORMED FRAMEWORK – ELEMENT DESCRIPTIONS

Element	Description
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Other considerations	Other considerations include issue about the implementation and operationalization of the technology or intervention in health systems and practices within Oregon.

Strong recommendation

In Favor: The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Against: The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Weak recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Quality or strength of evidence rating across studies for the treatment/outcome[2]

High: The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.

Moderate: The subcommittee is moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

[2] Includes risk of bias, precision, directness, consistency and publication bias

***Low*:** The subcommittee's confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.

***Very low*:** The subcommittee has very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

APPENDIX B. GRADE EVIDENCE PROFILE[3]

Apligraf® / Graftskin

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
DFUs	1	RCT	Low	Unknown	Direct	Precise	*None*	Low confidence in estimate of effect ●●○○
VLUs	1	RCT	Low	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○
Complete Wound Healing								
DFUs	2	RCT	Low	Consistent	Direct	Precise	*None*	Moderate confidence in estimate of effect ●●●○
VLUs	1	RCT	Low	Unknown	Direct	Precise	*None*	Low confidence in estimate of effect ●●○○
Nonhealing foot ulcers – undefined	1	RCT	High	Unknown	Indirect	Precise	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								

[3] All GRADE Evidence Profiles in this Appendix are in comparison to usual care.

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Time to Complete Wound Healing								
VLUs	1	RCT	Low	Unknown	Direct	Precise	*None*	Low confidence in estimate of effect ●●○○
Nonhealing foot ulcers – undefined	1	RCT	High	Unknown	Indirect	Precise	*None*	Very low confidence in estimate of effect ●○○○
Adverse Effects								
DFUs	1	RCT	Low	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○
VLUs	1	RCT	Low	Unknown	Direct	Unknown	*None*	Very low confidence in estimate of effect ●○○○

Abbreviations: DFU – diabetic foot ulcer; RCT – randomized controlled trial; VLU – venous leg ucler

Dermagraft®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
DFU	1	RCT	Moderate	Unknown	Direct	Precise	None	Very low confidence in estimate of effect ●○○○
Complete Wound Healing								
DFUs	4	RCTs	Moderate to high	Inconsistent	Direct	Precise	*3 RCTs of moderate ROB are consistent, a high-risk RCT had a discrepant result*	Low confidence in estimate of effect ●●○○
VLUs	2	RCTs	Moderate	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
DFUs	4	RCT	Moderate to high	Consistent	Direct	Unknown	*None*	Low confidence in estimate of effect ●●○○
VLUs	1	RCTs	Moderate	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Adverse Effects								
DFUs	2	RCT	Moderate	Unknown	Direct	Unknown		Very low confidence in estimate of effect ●○○○
VLUs	1	RCT	Moderate	Unknown	Direct	Unknown		Very low confidence in estimate of effect ●○○○

Abbreviations: DFU – diabetic foot ulcer; RCT – randomized controlled trial; VLU – venous leg ulcer

EpiFix®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
No evidence identified								
Complete Wound Healing								
DFU	1	RCT	Moderate	Unknown	Direct	Precise	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
No evidence identified								

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Adverse Effects								
No evidence identified								

Abbreviations: DFU – diabetic foot ulcer; RCT – randomized controlled trial

Grafix®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
DFUs	1	RCT	High	Unknown	Direct	Precise	*"Wound-related infection" not defined*	Very low confidence in estimate of effect ●○○○
Complete Wound Healing								
DFU	1	RCT	High	Unknown	Direct	Precise	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
DFU	1	RCT	High	Unknown	Direct	Precise	*None*	Very low confidence in estimate of effect ●○○○

Abbreviations: DFU – diabetic foot ulcer; RCT – randomized controlled trial

Adverse Effects								
DFU	1	RCT	High	Unknown	Direct	Precise	*None*	Very low confidence in estimate of effect ●○○○

Graftjacket®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
No evidence identified								
Complete Wound Healing								
DFUs	2	RCT	Moderate to high	Consistent	Unknown	Precise	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
DFUs	2	RCTs	Moderate to high	Unknown	Direct	Unknown	*None*	Very low confidence in estimate of effect ●○○○
Adverse Effects								
DFUs	1	RCT	High	Unknown	Direct	Unknown	*None*	Very low confidence in estimate of effect ●○○○

Abbreviations: DFU – diabetic foot ulcer; RCT – randomized controlled trial

OASIS® Wound Matrix

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
No evidence identified								
Complete Wound Healing								
DFUs	1	RCT	Moderate	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○
VLUs	3	RCT	Low to moderate	Unknown	Direct	Imprecise	Effectiveness varied based on type of usual care	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
VLUs	3	RCTs	Low to moderate	Unknown	Direct	Imprecise	Effectiveness varied based on type of usual care	Very low confidence in estimate of effect ●○○○
Adverse Effects								
VLUs	1	RCT	Low	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○
DFUs	1	RCT	Moderate	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○

Abbreviations: DFU – diabetic foot ulcer; RCT – randomized controlled trial; VLU – venous leg ulcer

Talymed®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
No evidence identified								
Complete Wound Healing								
VLUs	1	RCT	Low	Unknown	Direct	Imprecise	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
No evidence identified								
Adverse Effects								
VLU	1	RCT	Low	Unknown	Direct	Unknown	None	Very low confidence in estimate of effect ●○○○

Abbreviations: RCT – randomized controlled trial; VLU – venous leg ulcer

TheraSkin® versus Apligraf®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
DFUs		RCT	Moderate	Unknown	Indirect	Unknown	*None*	Very low confidence in estimate of effect ●○○○
Complete Wound Healing								
DFUs	1	RCT	Moderate	Unknown	Indirect	Unknown	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
No evidence identified								
Adverse Effects								
No evidence identified								

Abbreviations: RCT – randomized controlled trial; DFU – diabetic foot ulcer

OASIS® versus Dermagraft®

Indication	Quality Assessment (Confidence in Estimate of Effect)							
	No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Deep Soft Tissue or Bone Infection								
No evidence identified								
Complete Wound Healing								
DFUs	1	RCT	Moderate	Unknown	Indirect	Unknown	*None*	Very low confidence in estimate of effect ●○○○
Quality of Life								
No evidence identified								
Time to Complete Wound Healing								
No evidence identified								
Adverse Effects								
No evidence identified								

Abbreviations: RCT – randomized controlled trial; DFU – diabetic foot ulcer

APPENDIX C. METHODS

Scope Statement

Populations

Adults with chronic skin ulcers

Population scoping notes: *Considered limiting scope to diabetic foot ulcers and venous leg ulcers, sacral decubitus ulcers, but decided on the broader definition above, considered burns and other types of wounds*

Interventions

Skin substitutes

Intervention exclusions: None

Comparators

Usual care

Outcomes

Critical: Deep soft tissue or bone infections, complete wound healing, quality of life

Important**:** Time to complete wound healing, adverse effects

Considered but not selected for the GRADE table: *Cellulitis, sepsis, death, need for surgical management, ulcer recurrence*

Key Questions

1. What is comparative effectiveness of different types of skin substitutes compared with wound care alternatives for individuals with chronic skin ulcers? Include consideration of:
    a. Age
    b. Body mass index (BMI)
    c. Comorbidities
    d. Site of ulcer
    e. Ulcer etiology (e.g. infectious, pressure or circulatory).
    f. Wound severity
    g. Prior need for skin substitute
    h. Failure of prior therapies
2. What adverse events are associated with skin substitutes?
3. What are contraindications to the use of skin substitutes?

Search Strategy

A full search of the core sources was conducted to identify systematic reviews, meta-analyses, technology assessments, and clinical practice guidelines using the terms “wound,” “ulcer,” “skin

substitute," or "bioengineered skin." Searches of core sources were limited to citations published after 2005.

The core sources searched included:

- Agency for Healthcare Research and Quality (AHRQ)
- Blue Cross/Blue Shield Health Technology Assessment (HTA) program
- BMJ Clinical Evidence
- Canadian Agency for Drugs and Technologies in Health (CADTH)
- Cochrane Library (Wiley Interscience)
- Hayes, Inc.
- Institute for Clinical and Economic Review (ICER)
- Medicaid Evidence-based Decisions Project (MED)
- National Institute for Health and Care Excellence (NICE)
- Tufts Cost-effectiveness Analysis Registry
- Veterans Administration Evidence-based Synthesis Program (ESP)
- Washington State Health Technology Assessment Program

A MEDLINE® (Ovid) search was then conducted to identify systematic reviews, meta-analyses, and technology assessments published after the search dates of the AHRQ report (Snyder et al, 2012). The search was limited to publications in English published after 2011 (the end search date for the AHRQ SR). Using the 2012 AHRQ systematic review as the predominant evidence source, a second MEDLINE® (Ovid) search was conducted to identify any randomized controlled trials published after the search dates of the AHRQ review (2011).

Searches for clinical practice guidelines were limited to those published since 2010. A search for relevant clinical practice guidelines was also conducted, using the following sources:

- Australian Government National Health and Medical Research Council (NHMRC)
- Centers for Disease Control and Prevention (CDC) – Community Preventive Services
- Choosing Wisely
- Institute for Clinical Systems Improvement (ICSI)
- National Guidelines Clearinghouse
- New Zealand Guidelines Group
- NICE
- Scottish Intercollegiate Guidelines Network (SIGN)
- United States Preventive Services Task Force (USPSTF)
- Veterans Administration/Department of Defense (VA/DOD)

Inclusion/Exclusion Criteria

Studies were excluded if they were not published in English, did not address the scope statement, or were study designs other than systematic reviews, meta-analyses, technology assessments, or clinical practice guidelines. A MEDLINE® search was conducted for randomized control trials published after the AHRQ systematic review.

The AHRQ systematic review (Snyder, Sullivan and Schoelles, 2012) was selected as the base systematic review for this topic based on its comprehensiveness; thus systematic reviews published prior to the AHRQ review were excluded. In addition, several systematic reviews published more recently than the AHRQ review were excluded because they did not include any additional studies that were not already summarized by the included systematic reviews. These four systematic reviews were excluded because they included only studies that were in the AHRQ systematic review:

Game , F. L., Hinchliffe, R. J., Apelqvist, J., Armstrong, D. G., Bakker, K., Hartemann, A., … Jeffcoate, W.J. (2012). A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. Diabetes Metab Res Rev, 28 Suppl 1:119-41. DOI: 10.1002/dmrr.2246.

Greer , N., Foman, N., Dorrian, J., Fitzgerald, P., MacDonald, R., Rutks, I., & Wilt, T. (2012). Advanced wound care therapies for non-healing diabetic, venous, and arterial ulcers: A systematic review. VA-ESP Project #09-009.. Retrieved from http://link.springer.com/article/10.1007%2Fs40257-014-0081-9.

Hankin , C. S., Knispel, J., Lopes, M., Bronstone, A., & Maus, E. (2012). Clinical and cost efficacy of advanced wound care matrices for venous ulcers. Journal of Managed Care Pharmacy, 18(5), 375-384. Retrieved from http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=15289.

Iorio, M. L.,Shuck, J., Attinger, C. E.(2014). Wound healing in the upper and lower extremities – A systematic review on the use of acellular dermal matrices. *Plastic and Reconstructive Surgery, 130*: 5S-2. DOI: 10.1097/PRS.0b013e3182615703.

The following systematic review was excluded because it only included studies found in the AHRQ systematic review or Jones and colleagues (2013):

Valle , M. F., Maruthur, N. M., Wilson, L. M., Malas, M., Qazi, U., Haberl, E., … Lazarus, G. (2014). Comparative effectiveness of advanced wound dressings for patients with chronic venous leg ulcers: A systematic review. Wound Repair and Regeneration, 22(2), 193-204. DOI: 10.1111/wrr.12151.

Finally, the following systematic review was excluded because it did not provide sufficient detail regarding outcomes reported in trials of skin substitutes:

Braun, L. R., Fisk, W. A., Lev-Tov, H., Kirsner, R.S., & Isseroff, R. R. (2014). Diabetic foot ulcer: an evidence-based treatment update. *Am J Clin Dermatol, 15*, 267–281. DOI: 10.1007/s40257-014-0081-9.

APPENDIX D. APPLICABLE CODES

CODES	DESCRIPTION
ICD-10 Diagnosis Codes	
E08.621 E09.621 E10.621 E11.621 E13.621	Diabetes mellitus due to underlying condition with foot ulcer Drug or chemical induced diabetes mellitus with foot ulcer Type I diabetes mellitus with foot ulcer Type II diabetes mellitus with foot ulcer Other diabetes mellitus with foot ulcer
L97-L97.9	Non-pressure chronic ulcer of lower limb
L89-L89.0	Pressure ulcer
L98.4	Non-pressure chronic ulcer of skin
CPT Codes	
15271	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
15272	Each additional 25 sq cm wound surface, or part thereof
15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
15276	Each additional 25 sq cm wound surface, or part there of
15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15274	Each additional 100 sq cm wound surface area or part thereof, or each additional 1% of body area of infants and children or part thereof
15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digitis, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound area, or 1% of body area of infants and children
15278	Each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children or part thereof
HCPCS Level II Codes	
C5271	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
C5272	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof (list separately in addition to code for primary procedure)
C5273	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5274	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or
C5275	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
C5276	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof (list

C5277	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of bod
C5278	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or
Q4100	Skin substitute, NOS
Q4101	Apligraf
Q4102	OASIS wound matrix
Q4103	OASIS burn matric
Q4104	Integra BMWD
Q4105	Integra DRT
Q4106	Dermagraft
Q4107	Graftjacket
Q4108	Integra Matrix
Q4110	Primatrix
Q4111	Gammagraft
Q4112	Cymetra injectable
Q4113	Graftjacket Xpress
Q4114	Integra Flowable Wound Matrix
Q4115	Alloskin
Q4116	Alloderm
Q4117	Hyalomatrix
Q4118	Matristem Micromatrix
Q4119	Matristem Wound Matrix
Q4120	Matristem Burn Matrix
Q4121	Theraskin
Q4122	Dermacell
Q4123	Alloskin
Q4124	Oaskis Tri-layer Wound Matrix
Q4125	Arthroflex
Q4126	Memoderm/derma/tranz/integup
Q4127	Taylmed
Q4128	Flexhd/Alopatchhd/matrixhd
Q4129	Unite Biomatrix
Q4131	Epifix
Q4132	Grafix core
Q4133	Grafix prime
Q4134	HMatrix
Q4135	Mediskin
Q4136	EZderm
Q4137	Amnioexcel or Biodmatrix, 1cc
Q4138	DioDfence DryFlex, 1cc
Q4139	Amniomatrix or Biodmatrix, 1cc
Q4140	Biodfence 1cm
Q4141	Alloskin ac, 1 cm
Q4142	Xcm biologic tiss matrix 1cm
Q4143	Repriza, 1cm
Q4145	Epifix, 1mg

Q4146	Tensix, 1 cm
Q4147	Architect ecm px fx 1 sq cm
Q4148	Neox 1k, 1cm
Q4149	Excellagen, 0.1cc
Q4150	Allowrap DS or Dry 1 sq cm
Q4151	AmnioBand, Guardian 1 sq cm
Q4152	Dermapure 1 square cm
Q4153	Dermavest 1 square cm
Q4154	Biovance 1 square cm
Q4155	NeoxFlow or ClarixFlo 1mg
Q4156	Neox 100 1 square cm
Q4157	Revitalon 1 square cm
Q4158	Marigen 1 square cm
Q4159	Affinity 1 square cm
Q4160	NuSheild 1 square cm
Q9349	Fortaderm, fortaderm antimic
Q9358	SergiMend, fetal
C9360	SurgiMend, neonatal
C9363	Integra Meshed Bil Wound Mat

ICD-10-PCS (Procedure Codes)						
Section	**Body System**	**Operation**	**Body Part**	**Approach**	**Device**	**Qualifier**
O (Medical and surgical)	**H** (skin and breast) **J** (subcutaneous tissue and fascia) **R** (mouth and throat)	**R** (replacement) **U** (supplement) **W** (revision)	All (0-X) except: Q finger nail R toe nail S hair	**O** (open) **3** (percu-taneous)	**J** (synthetic substitute) **K** (nonauto-logous tissue substitute)	**Z** (no qualifier)
CODES	**DESCRIPTION**					
0HR0	Skin, Scalp					
0HR1	Skin, Face					
0HR2	Skin, Right Ear					
0HR3	Skin, Left Ear					
0HR4	Skin, Neck					
0HR5	Skin, Chest					
0HR6	Skin, Back					
0HR7	Skin, Abdomen					
0HR8	Skin, Buttock					
0HR9	Skin, Perineum					
0HRA	Skin, Genitalia					
0HRB	Skin, Right Upper Arm					
0HRC	Skin, Left Upper Arm					
0HRD	Skin, Right Lower Arm					
0HRE	Skin, Left Lower Arm					
0HRF	Skin, Right Hand					
0HRG	Skin, Left Hand					
0HRH	Skin, Right Upper Leg					
0HRJ	Skin, Left Upper Leg					

0HRK	Skin, Right Lower Leg
0HRL	Skin, Left Lower Leg
0HRM	Skin, Right Foot
0HRN	Skin, Left Foot
0HRQ	Finger Nail
0HRR	Toe Nail
0HRS	Hair
0HRT	Breast, Right
0HRU	Breast, Left
0HRV	Breast, Bilateral
0HRW	Nipple, Right
0HRX	Nipple, Left

Note: Inclusion on this list does not guarantee coverage.

APPENDIX E: FREQUENCY OF APPLICATION AND COST OF SKIN SUBSTITUTES

Product	Proposed maximum covered applications	Rationale	Medicare cost information per application (National Average Fee For Service, October, 2015*)
Apligraf	5	Greater than 5 applications not studied per FDA. Early studies limited to 5 applications, and one later study found wound healing was completed within 3 applications. Cigna limits to 4 applications in 12 weeks. Two Medicare LCD limits to 5 applications.	ASC: $771 HOPD: $1,495 Phys. Off =$1,518
Derma-graft	8	The FDA prescribing information contains a caution than Dermagraft has not been studied in patients receiving greater than 8 device applications. 2003 study showed that 4 applications is equivalent to 8. Cigna limits to 8 applications in 12 weeks. One Medicare LCD limits to 8 applications.	ASC: $771 HOPD: $1,495 Phys. Off =$1,409
Epifix	5	One study limited to 5 applications. Cigna limits to 4 applications in 12 weeks. Two Medicare LCD limits to 5 applications.	ASC: $771 HOPD: $1,495 Phys. Office: $535
Grafix	12	Weekly applications up to 84 days in the one study	ASC: $771 HOPD: $1,495 Phys. Off **
Graft-jacket	1	Single application used in both studies. Cigna and one Medicare LCD limits to 1 application.	ASC: $771 HOPD: $1,495 Phys. Office: $1,672
Oasis Wound Matrix	12	One study of DFU showed an average of 10 sheets. One study of VLU reported an average of 8 sheets. Study showed equivalence of 8 sheets of Oasis to 3	ASC: $236 HOPD: $518

		sheets of Dermagraft. One Medicare LCD limits to 12 weeks of therapy.	Phys. Office: $262
Talymed	10	Study used applications every 1-3 weeks over 20 weeks. Found fewer applications ineffective.	ASC: $771 HOPD: $1,495 Phys. Office **
Thera-skin	5	Up to 5 applications received in the study, however, most patients only had 1. Cigna limits to 4 applications in 12 weeks. One Medicare LCD limits to 5 applications.	ASC: $771 HOPD: $1,495 Phys. Office: $612

ASC=ambulatory surgery center; DFU=diabetic foot ulcers; HOPD=hospital outpatient department; LCD=local coverage determination; VLU=venous leg ulcers

*Costs reported are for the smallest available product and include applicable professional fees for applying the skin substitute to a leg ulcer smaller than 25 cm^2. Fees are higher for some other body parts or larger applications.

**Physician's office average sales price (ASP) fees cannot be calculated, product not on ASP fee schedule.

References for pricing information:

Hospital outpatient bundle costs retrieved from https://www.cms.gov/apps/ama/license.asp?file=/hospitaloutpatientpps/downloads/2015-Jan-Addendum-B-File.zip

Ambulatory surgical center bundled rates retrieved from

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ASCPayment/Downloads/2015-October-ASC-Addenda.zip

Physician fees retrieved from

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/index.html?redirect=/PhysicianFeeSched/

October 2015 ASP Pricing file (for physician's office product fees) retrieved from:

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2015ASPFiles.html

All retrievals made October 29, 2015.

Cost information in this applications table did not affect the coverage guidance recommendations. Costs represent a single application; the appropriate number of applications for a patient may differ by product.

CG-Skin substitutes for diabetic foot ulcers and venous leg ulcers

Question: How should the Coverage Guidance on Skin Substitutes for Chronic Skin Ulcers be applied to the Prioritized List?

Question source: Evidence-based Guidelines Subcommittee (EbGS)

Issue: The EbGS made recommendation about specific skin substitutes, and about the clinical prerequisites necessary for a skin substitute to be appropriate. Many of the specific skin substitutes are HCPCS codes that are not typically included on the Prioritized List. A guideline would need to be developed addressing the prerequisites, and also indicating those skin substitutes which were found to have adequate evidence to support their use.

Skin substitutes are also covered for burns, but this was outside the scope of the Coverage Guidance.

There is information about typical number of applications and maximum number of applications based on a mixture of the evidence or other insurers. These are not consistently evidence- derived. VbBS needs to discuss whether or not maximum number of applications should be included in the Prioritized List's new Guideline Note.

Current Prioritized List Status:

Line: 384
Condition: CHRONIC ULCER OF SKIN (See Guideline Notes 62,64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT
ICD-10: E08.621-E08.622,E09.621-E09.622,E10.621-E10.622,E11.621-E11.622,E13.621-E13.622,I70.231-I70.25,I70.331-I70.35,I70.431-I70.45,I70.531-I70.55,I70.631-I70.65,I70.731-I70.75,I83.001-I83.029,I83.201-I83.229,I87.011-I87.019,I87.031-I87.039,I87.311-I87.319,I87.331-I87.339,L88,L89.000-L89.95,L97.101-L97.929,L98.411-L98.499
CPT: 10060,10061,11000-11047,14000-15136,15200-15221,15241-15770,15920-15958,27598,28122,28810,29445,29580-29584,36470-36479,37700-37785,64505-64530,96150-96154,97036,97605-97608,98966-98969,99051,99060,99070,99078,99184,99201-99239,99281-99285,99291-99404,99408-99416,99429-99449,99468-99480,99487-99498,99605-99607
HCPCS: D7920,G0396,G0397,G0406-G0408,G0425-G0427,G0458,G0463,G0466,G0467

Code	Code Descriptions	Current Lines
15271	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area	61,76,185,201,212,384
15272	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof (List separately in addition to code for primary procedure)	61,76,185,201,212,384
15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm	61,76,185,201,212,384

Code	Code Descriptions	Current Lines
	wound surface area, or 1% of body area of infants and children	
15274	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (List separately in addition to code for primary procedure)	Updated description Codes,61,76,185,201,212,384
15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area	61,76,185,201,212,384
15276	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof (List separately in addition to code for primary procedure)	61,76,185,201,212,384
15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children	Updated description Codes,61,76,185,201,212,384
15278	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (List separately in addition to code for primary procedure)	61,76,185,201,212,384

All Ancillary Codes

Q4100	Skin substitute, NOS
Q4101	Apligraf
Q4102	OASIS wound matrix

Q4103	OASIS burn matric
Q4104	Integra BMWD
Q4105	Integra DRT
Q4106	Dermagraft
Q4107	Graftjacket
Q4108	Integra Matrix
Q4110	Primatrix
Q4111	Gammagraft
Q4112	Cymetra injectable
Q4113	Graftjacket Xpress
Q4114	Integra Flowable Wound Matrix
Q4115	Alloskin
Q4116	Alloderm
Q4117	Hyalomatrix
Q4118	Matristem Micromatrix
Q4119	Matristem Wound Matrix
Q4120	Matristem Burn Matrix
Q4121	Theraskin
Q4122	Dermacell
Q4123	Alloskin
Q4124	Oaskis Tri-layer Wound Matrix
Q4125	Arthroflex
Q4126	Memoderm/derma/tranz/integup
Q4127	Taylmed
Q4128	Flexhd/Alopatchhd/matrixhd
Q4129	Unite Biomatrix
Q4131	Epifix
Q4132	Grafix core
Q4133	Grafix prime
Q4134	HMatrix
Q4135	Mediskin
Q4136	EZderm
Q4137	Amnioexcel or Biodmatrix, 1cc
Q4138	DioDfence DryFlex, 1cc
Q4139	Amniomatrix or Biodmatrix, 1cc
Q4140	Biodfence 1cm
Q4141	Alloskin ac, 1 cm
Q4142	Xcm biologic tiss matrix 1cm
Q4143	Repriza, 1cm
Q4145	Epifix, 1mg
Q4146	Tensix, 1 cm
Q4147	Architect ecm px fx 1 sq cm

Q4148	Neox 1k, 1cm
Q4149	Excellagen, 0.1cc
Q4150	Allowrap DS or Dry 1 sq cm
Q4151	AmnioBand, Guardian 1 sq cm
Q4152	Dermapure 1 square cm
Q4153	Dermavest 1 square cm
Q4154	Biovance 1 square cm
Q4155	NeoxFlow or ClarixFlo 1mg
Q4156	Neox 100 1 square cm
Q4157	Revitalon 1 square cm
Q4158	Marigen 1 square cm
Q4159	Affinity 1 square cm
Q4160	NuSheild 1 square cm
Q9349	Fortaderm, fortaderm antimic
Q9358	SergiMend, fetal

Recommendations:

1) Adopt a new guideline note

GUIDELINE NOTE XXX, SKIN SUBSTITUTES FOR CHRONIC SKIN ULCERS

Line 384

Skin substitutes for chronic skin ulcers (venous leg ulcers and diabetic foot ulcers only) are included on Line 384 only when all of the following criteria are met:

1. Product is indicated for inclusion on this Line for the type of ulcer being treated (see table below)
2. FDA indications and contraindications are followed, if applicable
3. Wound has adequate arterial flow (ABI > 0.7), no ongoing infection and a moist wound healing environment
4. For patients with diabetes, Hba1c level is < 12.
5. Prior appropriate wound care therapy (including but not limited to appropriate offloading, multilayer compression dressings and smoking cessation counseling) has failed to result in significant improvement (defined as at least a 50 percent reduction in ulcer surface area) of the wound over at least 30 days
6. Ulcer improves significantly over 6 weeks of treatment with skin substitutes, , with continued significant improvement every 6 weeks required for coverage of ongoing applications
7. Patients is able to adhere to the treatment plan

Skin substitutes table

Product	**Diabetic foot ulcers**	**Venous leg ulcers**
Dermagraft	Included	Not included
Apligraf	Included	Included
OASIS Wound Matrix	Included	Included
~~Epifix~~	~~Not included~~	~~Not included~~
~~Grafix~~	~~Not included~~	~~Not included~~

~~Graftjacket~~	~~Not included~~	~~Not included~~
~~Talymed~~	~~Not included~~	~~Not included~~
~~Theraskin~~	~~Not included~~	~~Not included~~
Other skin substitutes	Not included	Not included

2) Discuss whether above strikethrough language should remain or be deleted.

3) Discuss whether or not to include the maximum number of applications.
    a. Consider imbedding the following information into the Skin substitutes table:

Product	**Maximum applications**
Dermagraft	8
Apligraf	5
Oasis Wound Matrix	12

HERC Coverage Guidance – Skin Substitutes
Disposition of Public Comments

Table of Contents

Commenters

Identification	Stakeholder
A	Soluble Systems *[Submitted December 7, 2015]*
B	Smith & Nephew Advance Wound Management *[Submitted December 15, 2015]*

HERC Coverage Guidance – Skin Substitutes
Disposition of Public Comments

Public Comments

ID/#	Comment	Disposition
A1	"We would like to request that Oregon Medicaid reconsider the current non-coverage recommendation of Theraskin based on the following conclusions obtained from previously submitted clinical data. Upon review of the included references, Theraskin is as effective and at least equivalent to products currently recommended for coverage by Oregon Medicaid (Apligraf and Dermagraft)."	Thank you for your comment. We will address each of these studies individually below.
A2	"The 2011 Landman's study concluded that Theraskin healed (closed) 60% of previously non-progressing diabetic foot ulcers (DFUs) and venous leg ulcers (VLUs) at 12 weeks and 74% at 20 weeks."	Because this is a non-comparative retrospective case series, it does not meet individual inclusion criteria for the evidence review.
A3	"DiDomenico's 2011 study concluded that TheraSkin had a greater rate of wound healing than Apligraf, both at 12 weeks (66.7% vs. 41.3%) and 20 weeks (66.7% vs. 47.1%)."	This study is included in the systematic review by Snyder, Sullivan, & Schoelles (2014), and has thus already been included in the evidence review for the draft coverage guidance. DiDomenico and colleagues did not report a test of statistical significance of the difference observed in the trial; the authors of the AHRQ report found that the difference was not statistically significant (p=0.21).

HERC Coverage Guidance – Skin Substitutes
Disposition of Public Comments

ID/#	Comment	Disposition
A4	"Sanders 2014 clinical study showed wounds treated with TheraSkin are twice as likely to close by week 12, with half the number of grafts, versus wounds treated with Dermagraft."	This manuscript is not indexed in Medline and therefore was not included in the evidence review. Furthermore, this small (n=23) RCT is of poor quality because of uncertainty about allocation concealment; baseline differences in study population (particularly with respect to number of diabetes medications, peripheral arterial disease, tobacco use and wound duration before treatment); differences in the number of office visits in each treatment group and use of offloading techniques; and inadequate blinding of participants, personnel, and outcomes assessors. Additionally, two authors are paid consultants of Soluble Systems and the research was funded by Soluble Systems.
A5	"Snyder, Sullivan and Schoelles 2012 (AHRQ Review included on page 26 of Oregon's Draft Policy) evaluated the effectiveness of Apligraf and TheraSkin for DFUs with average wound sizes. The study also concluded that there were no significant differences reported in complete wound closure between the two products Apligraf 41% vs. Theraskin 67%, p=0.21."	The AHRQ systematic review concluded that there is insufficient evidence to draw conclusions about the comparative effectiveness of Theraskin and Apligraf. The single trial that informed this comparison (DiDomenico, 2011) was a small (n=28) and imprecise trial deemed to be at moderate risk of bias by the authors of the AHRQ review.

HERC Coverage Guidance – Skin Substitutes
Disposition of Public Comments

ID/#	Comment	Disposition
A6	"We respectfully recommend Oregon Medicaid to take into consideration that Theraskin is broadly and long accepted by the medical community and insurance carriers as medically and reasonably necessary therapy for the treatment of a broad range of chronic wound indications. ○ All A/B Medicare Administrative Contractors (MACs) across the U.S., including Oregon, cover Theraskin. ○ 41 Medicaid plans throughout the country, including many states surrounding Oregon, also provide Theraskin coverage. ○ Many large Private Health Plans cover Theraskin including Regence, Kaiser, Cigna, Blue Cross Independence, HCSC (BCBS IL/NM/OK/TX), Amerihealth, BCBS Highmark, United Health Care, Tricare, UPMC Health Plan, etc."	Thank you for your comment. Our review of Local Coverage Determinations (LCDs) as well as the policies of selected Medicaid programs and private health plans found that Theraskin is commonly, but not uniformly, covered.

ID/#	Comment	Disposition
A7	"Oregon Medicaid proposes a recommendation of non-coverage for Theraskin due to 'product cost being moderate compared to alternative treatment options.' Listed within the Oregon Medicaid draft policy under 'Frequency of application and cost of skin substitute' Apligraf and Dermagraft product costs were based upon clinical studies while Theraskin's product cost was based upon Medicare LCD limits. Thus, causing Theraskin associated cost-savings to appear modest when compared to alternative treatments. We respectfully recommend that Oregon Medicaid reevaluate Theraskin's product cost in a similar manner as Apligraf and Dermagraft or adults all product cost using Medicare's' LCFD maximum limits."	The right-hand column of the frequency of application document presented to EbGS was based on the maximum number of applications from the study, while lower limits were used for other products. The rationale column does note that most patients in the study only required a single application. At its November 3, 2015 meeting, the subcommittee recognized that costs and number of applications will vary by patient and that the cost of these products cannot be easily estimated at the population level. Therefore we have removed a specific number of applications for each product from the right column of the applications table and added information on application frequency used in the studies for those products recommended for coverage. However, the subcommittee still finds insufficient evidence of effectiveness to recommend this product for coverage.
B1	"In the draft guidance, the Commission recommends (with a weak recommendation) coverage of OASIS Wound Matrix for venous leg ulcers ('VLU'). We support the recommendation for coverage of OASIS for VLU, and we thank the Commission for its position."	Thank you for your comment.
B2	"By contrast, the Commission recommends against coverage of OASIS Wound Matrix for the treatment of diabetic foot ulcers ('DFU') concluding that there is 'inadequate evidence of benefit, other alternatives available, and its costliness.' We respectfully disagree with this recommendation for the reasons summarized below.	The study by Cazzell and colleagues was not indexed in Medline at the time of the search; it has subsequently been indexed. The previous RCTs of Oasis for DFU were included in the AHRQ review. Landsman, et al (2008) found no statistically significant difference between OASIS and Dermagraft for DFU wound healing at 12 weeks. Niezgoda, et al (2005) compared OASIS to Regranex Gel and found a

ID/#	Comment	Disposition
	There is new evidence, published after the 2012 Agency for Healthcare Research & Quality ('AHRQ') systematic review from supporting the use of OASIS in the treatment of diabetic foot ulcers. This evidence was not considered by the Commission. The findings from a prospective, randomized controlled trial of OASIS Ultra Trilayer Matrix versus standard care were published in 2015 in Advances in Wound Care. In this 16 week trial, 82 qualified patients were randomly assigned to 12 weeks' treatment with OASIS or standard care. The trial demonstrated that a greater proportion of the DFUs were closed by the end of the treatment period (week 12) for the OASIS group than for the standard care group (54% vs. 32%; p = 0.021). More ulcers were closed at each weekly study visit in the OASIS group than the standard care group beginning at week 3 (first visit showing ulcers closed). The overall treatment effect on proportion of ulcers closed over the 12 weeks and the interaction of treatment by week were found to be statistically significant (p = 0.047) in favor of the OASIS group. In the draft coverage guidance, the Commission defined five outcomes considered in its evaluation: ▪ Critical Outcomes – Deep soft tissue or bone infection – Complete wound healing ▪ Important Outcomes – Quality of life – Time to complete wound healing – Adverse effects The randomized, controlled study above included three of these outcomes and supports the use of OASIS compared to the standard care with statistically significant results."	difference in healing at 12 weeks that approached statistical significance (49% vs 28% respectively, p=0.06). Cazzell is an open-label RCT of 82 patients comparing OASIS to standard care for treatment of DFU. In the intervention group, OASIS was applied once each week. Patients in the control group were also seen weekly and the standard care intervention was selected by the investigator (standard care included sliver dressing, Hydrogel, wet-to-dry, alginate, Manuka honey, or triple antibiotic dressing). Ulcer measurement was standardized by use of a digital image capture and wound measurement device. At 12 weeks, wound healing was greater in the OASIS group (54%) compared with the standard care group (32%) (p=0.021). Smith and Nephew funded the study and employs three of the authors. Aside from the conflicts of interest and inadequate blinding, the study otherwise appears to be at low risk of bias. This fair quality RCT demonstrates improved DFU wound healing at 12 weeks for patients treated with OASIS compared to standard care.

ID/#	Comment	Disposition
B3	"OASIS has the same level of general acceptance by the medical community as Apligraf. While not a consideration for coverage, the Commission does review the policy landscape and payer coverage policies. Under Medicare, with respect to local coverage determinations, the policy must be based on published authoritative evidence derived from definitive RCTs or other definitive studies, and general acceptance by the medical community (standard of practice), as supported by sound medical evidence. Use of OASIS in the treatment of DFU is well established in the payer community: ▪ All of the MACs cover OASIS for VLU and DFU ▪ OASIS has positive coverage based on medical necessity from 760 private payers"	Thank you for your comment. Our review of Local Coverage Determinations (LCDs) as well as the policies of selected Medicaid programs and private health plans found that OASIS is commonly, but not uniformly, covered.
B4	"OASIS is the least costly product per application compared with Apligraf and Dermagraft. The Commission's recommendation against coverage for OASIS for DFUs is based, in part, on the Commission's conclusion that the product is costly. In fact, as is shown below, OASIS has a lower cost per application compared with Apligraf and Dermagraft—two other products recommended for coverage for diabetic foot ulcers." *See chart in submitted comments.*	OASIS does have a lower unit cost than Apligraf and Dermagraft. However, as noted in the cost comparison chart, studies which showed effectiveness of OASIS used 8 to 10 applications of this product per patient versus smaller quantities used in the studies showing effectiveness for Dermagraft and Apligraf. The subcommittee does recognize that costs and number of applications will vary by patient and that the cost of these products cannot be easily estimated at the population level.
B5	"The Commission stated in the draft guidance that OASIS 'is not recommended for coverage for diabetic foot ulcers based on inadequate evidence of benefit, other alternatives available, and its costliness.' We believe that this new evidence, together with the position taken by private and public payers as well as the relative low cost of OASIS compared to Apligraf and Dermagraft, support coverage for OASIS for the treatment of diabetic foot ulcers."	Thank you for your comment.

References Provided by Commenters

ID/#	References
A2	Landsman A. S., Cook J., Cook E., Landsman A. R., Garrett P., Yoon J., Kirkwood A., Desman E. (2011). A retrospective clinical study of 188 consecutive patients to examine the effectiveness of a biologically active cryopreserved human skin allograft (TheraSkin®) on the treatment of diabetic foot ulcers and venous leg ulcers. Foot Ankle Spec. 4(1):29-41. DOI: 0.1177/1938640010387417.
A3	DiDomenico, L., Landsman, A. R., Emch, K. J., Landsman, A. (2011). A prospective comparison of diabetic foot ulcers treated with either a cryopreserved skin allograft or a bioengineered skin substitute. *Wounds, 23*(7):184-9.
A4	Sanders, L., Landsman, A. S., Landsman, A., Keller, N., Cook, J., Cook, E., Hopson, M. (2014). A prospective, multicenter, randomized, controlled clinical trial comparing a bioengineered skin substitute to a human skin allograft. *Ostomy Wound Manage, 60*(9):26-38
B2	Cazzell, S. M., Lange, D. L., Dickerson, J. E. Jr., Slade, H. B. (2015). The Management of diabetic foot ulcers with porcine small intestine submucosa tri-layer matrix: A randomized controlled trial. *Adv Wound Care, 4*:1-8. DOI: 10.1089/wound.2015.0645.

Section 9.0

Coverage Guidances

Bariatric Surgery

Draft Coverage Guidance for VbBS Consideration

March 10, 2016

Oregon Health Authority

OREGON HEALTH & SCIENCE UNIVERSITY

Center For Evidence-based Policy

Background – Obesity

- Obesity is defined as:
  - Adult: body mass index (BMI) >30 kg/m^2 in adults
    - Class I BMI 30-34.9 (obese)
    - Class II BMI 35-39.9 (severely obese)
    - Class III BMI 40-49.9 (morbidly obese)
    - Super obesity BMI>50 (super obese)
  - Children and adolescents: > 95^{th} percentile of age- and sex-specific BMI

Background – Obesity

- Obesity is common in the US
  - 35% of adults
  - 17% of 2 to 19 year olds
  - 8.1% of infants and toddlers
- Obesity is a risk factor for many conditions including heart disease, type 2 diabetes (T2DM), stroke, cancer, sleep apnea, and arthritis
- Obesity is costly
  - $147 to $210 billion in annual medical spending attributable to obesity

Background – Obesity

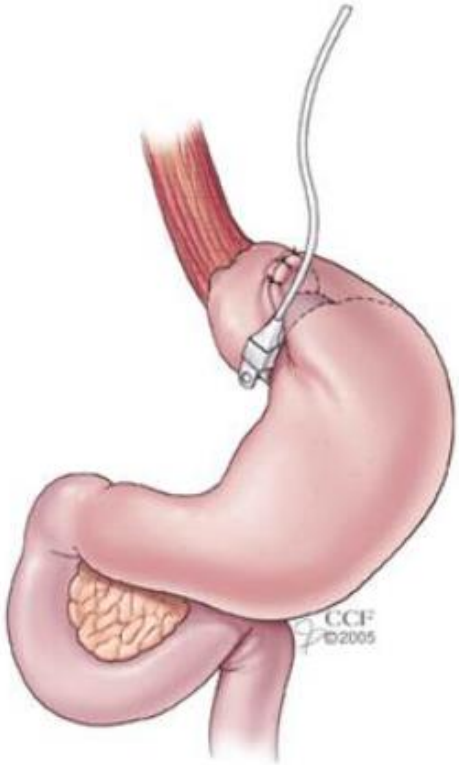
- In Oregon:
  - 24% of adults are obese
  - 38% of OHP-covered adults are obese
  - Approximately 11% of 8th graders are obese
  - Medicaid costs attributable to obesity were estimated at $333 million annually

Background – Treatments

- Structured programs to improve nutrition and physical activity
- Intensive behavioral counseling
- Medications (orlistat, lorcaserin, phentermine, liraglutide, naltrexone, topiramate)
- Devices (vagal nerve blockers, gastric balloons, endoliners)
- Bariatric surgery

Background – Surgery

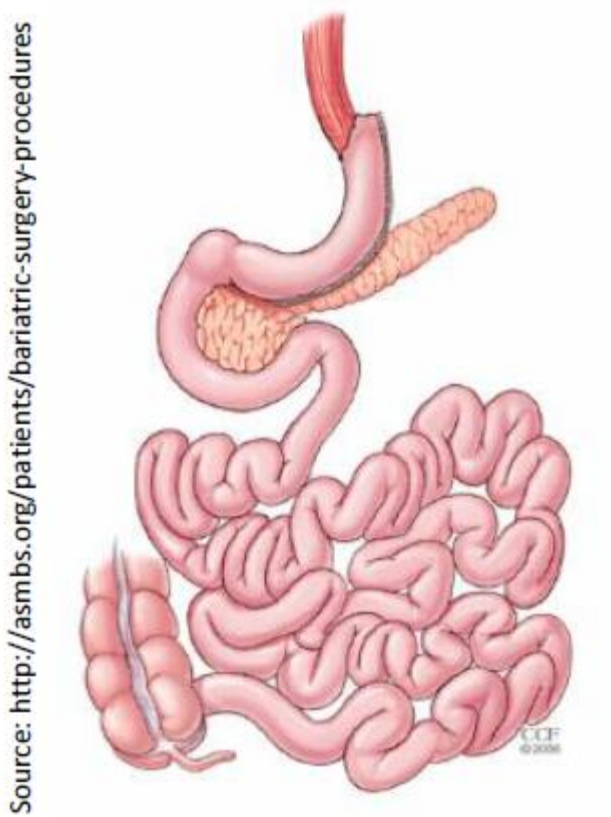
Adjustable gastric banding (AGB or LAGB)



Source: http://asmbs.org/patients/bariatric-surgery-procedures

Background – Surgery

Vertical sleeve gastrectomy (VSG)



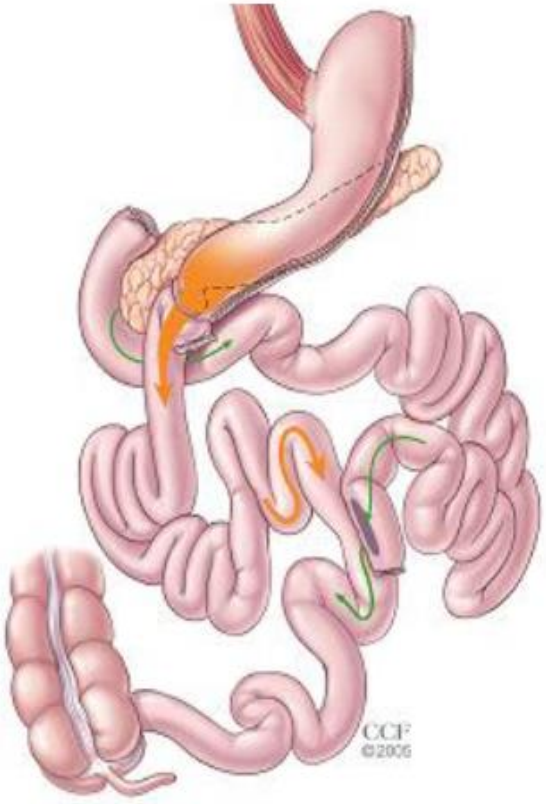
Source: http://asmbs.org/patients/bariatric-surgery-procedures

Background – Surgery

Roux-en-Y gastric bypass (RYGB)

Background – Surgery

- Biliopancreatic diversion/duodenal switch (BPD/DS)



Source: http://asmbs.org/patients/bariatric-surgery-procedures

Background – Surgery

	2011	2012	2013
RYGB	36.7%	37.5%	34.2%
Gastric band	35.4%	20.2%	14.0%
Sleeve gastrectomy	17.8%	33.0%	42.1%
BPD/DS	0.9%	1.0%	1.0%
Revisions	6.0%	6.0%	6.0%
Other	3.2%	2.3%	2.7%
TOTAL	100%	100%	100%
Total number of surgeries	158,000	173,000	179,000

Background – Surgery

	2011	2012	2013
RYGB	36.7%	37.5%	34.2%
Gastric band	**35.4%**	**20.2%**	**14.0%**
Sleeve gastrectomy	**17.8%**	**33.0%**	**42.1%**
BPD/DS	0.9%	1.0%	1.0%
Revisions	6.0%	6.0%	6.0%
Other	3.2%	2.3%	2.7%
TOTAL	100%	100%	100%
Total number of surgeries	158,000	173,000	179,000

PICO Statement

- Population: Obese adults and children
- Intervention: Bariatric or metabolic surgery
- Comparator: Non-surgical treatment
- Outcomes:
  - All-cause mortality (critical)
  - Major adverse cardiovascular events (critical)
  - Resolution of T2DM (important)
  - Resolution of hypertension (important)
  - Weight loss (important)

Key Questions

1. Should coverage be recommended for bariatric surgery in each of the scenarios in the table below?
2. What is the appropriate minimum age for bariatric surgery?
3. What components and systems of care are associated with improved health outcomes? (e.g., centers of excellence, surgeon's experience, etc.)
4. What preoperative assessments or requirements for preoperative weight loss should be recommended in patients being considered for bariatric surgery?

	BMI 30-34.9	BMI 35-39.9	BMI>=40
With DM2	Scenario 1	Scenario 2	Scenario 3
W/o DM2 nor other comorbidities	Scenario 4	Scenario 5	Scenario 6
W/o DM2 but with other comorbidities	Scenario 7	Scenario 8	Scenario 9

Sources

- Full search of core sources
  - Washington HTA report (2015) identified as the most recent and comprehensive review
- Medline search
  - Search dates: January 2014 – July 2015
  - Corresponding to end search date for WA HTA report
  - 13 additional systematic reviews met quality and inclusion criteria
- Clinical practice guideline search (last 5 years)
- Payer policy search

Evidence Strengths and Limitations

- Voluminous evidence base
  - More than 20 SRs published in the last 1.5 years spanning over 600 individual studies
  - Poor agreement on inclusion for individual SRs
- Of 179 studies in the WA HTA report
  - 26 (15%) were good quality
  - 74 (41%) were fair quality
  - 49 (44%) were poor quality

Evidence Strengths and Limitations

- Major limitations include:
  - Many non-comparative studies
  - Baseline differences in study groups
  - Differences in duration of follow-up between groups
  - Limited duration of follow-up and high rates of attrition
  - Inconsistent definitions of harms and outcomes
  - Specific bariatric procedures were variable

Evidence Review – Adults

- WA HTA (2015)
  - 179 comparative trials
    - 21 good or fair quality trials (14 RCTs, 7 cohort) compared bariatric surgery with non-surgical management
    - 13 RYGB, 6 AGB, 4 VSG, 3 BPD/DS
  - Meta-analytic results
    - Weight loss: Pooled mean difference in BMI 7.4 kg/m^2 (95% CI 6.2 to 8.6) favoring surgery
    - Resolution of T2DM: Odds ratio of 3.62 (95% CI 2.49 to 4.73) favoring surgery

Evidence Review – Adults

- WA HTA (2015), cont.
  - Non meta-analytic results
    - "[o]ther individual comorbidities commonly evaluated in these comparative studies included hypertension and hyperlipidemia. In studies evaluating resolution of these conditions and/or discontinuation of relevant medications as a binary variable, bariatric surgery was associated with two- to three-fold reductions in the prevalence of these comorbidities [hypertension and hyperlipidemia] at the end of follow-up, while nonsurgical management resulted in no appreciable change from baseline…"
  - Results stratified by BMI (Appendix F)
  - Cost-effectiveness analysis (Appendix G)

Evidence Review – Adults

- Chang (2014)
  - 164 studies of bariatric surgery (2003-2012)
  - Included studies spanned over 161,000 patients
  - Average pre-surgical BMI of 45; 26% had T2DM and 47% had hypertension
  - Meta-analytic results
    - Mortality within 30 days of surgery: 0.08% (95% CI 0.01 to 0.24) (RCTs) and 0.22% (95% CI 0.14 to 0.31) (OS)
    - Change in BMI at 1 year: -13.53 kg/m^2 (RCTs) and -11.79 kg/m^2 (OS)
    - Change in BMI at 5 years: -11.40% (RCTs) and -14.32% (OS)
    - T2DM remission: 92% (95% CI 84.68 to 97.18) for surgery compared to 17.4% (95% CI 0.98 to 69.27) in the control groups (RCTs)

Evidence Review – Adults

- Colquitt (2014)
  - 22 RCTs, 7 comparing bariatric surgery to non-surgical controls
  - Change in BMI: -7.4 kg/m^2 to -33.3 kg/m^2 with surgery compared to -0.5 kg/m^2 to -4.7 kg/m^2 in controls
  - T2DM remission: 42%-90% in surgical groups

- Hayes (2014)
  - Studies of adults with T2DM (2007-2014)
  - % BMI decrease: 20%-33% surgery vs. 1%-10% controls
  - T2DM remission: 38%-90% surgery vs. 0%-33% controls
  - RYGB and sleeve gastrectomy are equally effective in the treatment of T2DM

Evidence Review – Adults

- Kwok (2014)
  - 14 comparative cohort studies; average follow-up of 2-15 years
  - All-cause mortality: 1059/29,208 (3.6%) surgery vs. 18,962/166,200 (11.4%) controls, OR 0.48 (95% CI 0.35 to 0.64), NNT=13
- Muller-Stich (2014)
  - 13 studies (7 RCTs and 6 cohorts)
  - Focused on diabetic patients with BMI<35 kg/m^2 (n=818)
  - T2DM remission: 129/280 (46%) surgery vs. 6/252 (2.3%), OR 14.11 (95% CI 6.67 to 29.86), NNT=2 to 3

Evidence Review – Adults

- Puzziferri (2014)
  - 29 studies (10 RCTs, 8 cohorts, 11 case series) of RYGB, AGB, or VSG in patients with BMI>35
  - Minimum of 2 years of follow-up and <20% attrition
  - Strict definitions of T2DM and HTN remission
  - % Mean excess weight loss: 65.7% for RYGB, 64.5% for VSG, 45% for AGB
  - T2DM remission: 66.7% after RYGB, 28.6% after AGB
  - HTN remission: 38.2% after RYGB, 17.4% after AGB

Evidence Summary – Adults

- Bariatric surgery is associated with lower rates of all-cause mortality, despite a short-term increased risk of perioperative mortality and complications (based on low certainty evidence from cohort studies).
- Bariatric surgery is associated with significant reductions in BMI in adults (based on moderate certainty evidence from a mix of observational and randomized trials).
  - The effects on weight loss appear to be greatest in patients with baseline BMI ≥40.

Evidence Summary – Adults

- Bariatric surgery is associated with remission or resolution of T2DM and hypertension in adults with BMI ≥ 35 (based on moderate certainty evidence from a mix of observational and randomized trials).
  - The effects on remission of T2DM appear to be greatest in patients with baseline BMI ≥40
  - Preliminary evidence suggests that adults with BMI < 35 may also achieve significant reductions in BMI and improvement in comorbid T2DM and hypertension, though the long term effects are not yet clear.

Evidence Summary – Adults

- Harms of bariatric surgery
  - Perioperative mortality rate that probably ranges from 0.1 to 2%
  - Overall complication rate that is probably 8 to 25%
  - Estimated reoperation rate is likely between 2 and 13%.
  - Limited evidence from a single study that comorbid congestive heart failure, cardiac arrhythmias, and peripheral vascular disease are associated with higher rates of complications after bariatric surgery.

Evidence Summary – Patient Selection

- Low certainty conflicting evidence on the effects of preoperative weight loss requirements from one SR.
- Evidence from one SR indicates that the obesity surgery mortality risk score (OR-MRS) is a validated preoperative assessment of perioperative mortality risk and may be useful in selecting patients for surgery or counseling them on surgical risks.

Evidence Summary – Reoperation

- Most studies included in the six SRs were not methodologically rigorous and there are concerns about publication bias in this literature.
- Very low certainty evidence that revisional or conversion procedures may achieve additional weight loss (particularly conversion of AGB to RYGB or BPD/DS)
- Reoperations have a higher rate of complications
- No evidence that bariatric reoperation improved co-morbidity resolution.

Evidence Summary – Systems of Care

- Zevin (2012)
  - 24 observational studies examining the effects of surgeon and facility volume on outcomes
- Low certainty evidence that surgeon experience is associated with improved outcomes
- Very low certainty evidence that hospital bariatric surgical volume is associated with improved outcomes.

Evidence Review – Children

- General limitations
  - Primarily small, low quality observational studies (only a single RCT of AGB); largest trial included in the SRs was 81 patients
  - Shorter follow-up durations than adult studies (mostly 6 months to 3 years)

Evidence Review – Children

- Aikenhead (2011)
  - 37 studies (all but one observational), no meta-analysis
  - 13 studies of AGB
    - BMI reduction: 8.5 kg/m^2 to 43 kg/m^2
    - Resolution of comorbid conditions: 11% to 100%
  - 8 studies of RYGB
    - BMI reduction: 9 kg/m^2 to 25 kg/m^2
    - 100% resolution of dyslipidemia, asthma, DJD, and GERD in 3 of 4 studies reporting changes in comorbid conditions
  - 14 studies of other procedures (VSG, BPD/DS, gastroplasty)
    - BMI reduction: 9 kg/m^2 to 24 kg/m^2
    - No detailed information on resolution of comorbidities

Evidence Review – Children

- Black (2013)
  - 23 studies (1 RCT, 22 observational) comprising 637 patients
  - Weighted BMI difference (1 year post-op): -13.5 kg/m^2 (95% CI -15.1 to -11.9)
  - Rates of T2DM resolution were 50-100% (excluding one study with a single T2DM patient who did not experience resolution)
  - Rate of HTN resolution were 50% to 100%

Evidence Review – Children

- Treadwell (2008)
  - 18 studies, all observational, 1 with a comparative cohort
  - 6 studies of AGB
    - Change in BMI (95% CI) -13.7 kg/m^2 to -10.6 kg/m^2
    - T2DM remission 80%-100% (2 studies)
    - HTN remission 50%-100% (3 studies)
  - 6 studies of RYGB
    - Change in BMI (95% CI) -17.8 kg/m^2 to -22.3 kg/m^2
    - HTN remission 50%-100% (3 studies)

Evidence Summary – Children

- Bariatric surgery is associated with significant reductions in BMI in children and adolescents (based on low certainty evidence primarily from small, non-comparative observational trials).
- Bariatric surgery is associated with remission or resolution of T2DM and hypertension in children or adolescents (based on very low certainty evidence from a small number of trials).
- There is no evidence-based minimum age recommendation for pediatric bariatric surgery. Patients as young as five years old were included in the studies.

Public Comment

- One public comment, from Oregon Chapter of the American Society for Metabolic and Bariatric Surgery:
  - "We agree the information in the areas of adolescent surgery and surgical treatment of BMI less than 35 is incomplete and rapidly evolving. We believe these two areas should be reassessed in two years."

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: METABOLIC AND BARIATRIC SURGERY

DRAFT for 3/10/2016 VbBS/HERC meeting materials

HERC Coverage Guidance

Coverage of metabolic and bariatric surgery (including Roux-en-Y gastric bypass, gastric banding, and sleeve gastrectomy) is recommended for:

- Adult obese patients (BMI ≥ 35) with
  - Type 2 diabetes *(strong recommendation)* OR
  - at least two of the following other serious obesity-related comorbidities: hypertension, coronary heart disease, mechanical arthropathy in major weight bearing joint, sleep apnea *(weak recommendation)*
- Adult obese patients (BMI ≥ 40) *(strong recommendation)*

Metabolic and bariatric surgery is recommended for coverage in these populations only when provided in a facility accredited by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program *(weak recommendation).*

Metabolic and bariatric surgery is not recommended for coverage in:

- Patients with BMI <35, or 35-40 without the defined comorbid conditions above *(weak recommendation)*
- Children and adolescents *(weak recommendation)*

Note: Definitions for strength of recommendation are provided in Appendix B: GRADE Informed Framework – Element Descriptions.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline

Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

GRADE-INFORMED FRAMEWORK

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are several elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Estimates of effect are derived from the evidence presented in this document. The level of confidence in the estimate is determined by the Commission based on assessment of two independent reviewers from the Center for Evidence-based Policy. Unless otherwise noted, estimated resource allocation, values and preferences, and other considerations are assessments of the Commission.

Coverage question: Should bariatric surgery be recommended for coverage in adults?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
All-cause mortality (*Critical outcome)*	Odds ratio: 0.48 (95% CI 0.35 to 0.64) Crude event rates 3.6% with surgery and 11.4% without surgery Number needed to treat = 13 ●●○○ *(low certainty based on consistent but indirect observational studies)*	Bariatric surgery costs tens of thousands of dollars per surgery, but has been shown to be cost effective across BMI thresholds and surgery types.	Patients would balance surgery and its risks with risks of living with morbid obesity. Many patients who have failed conservative attempts at weight loss may elect surgery. The benefits of decreased mortality, dramatic weight loss, and regression of diabetes are important outcomes that patients and society	The greatest benefit may be with BMI ≥ 40 but otherwise specific subpopulations which would benefit the most from bariatric surgery are not well characterized. The pre-operative requirements for achieving optimal outcomes are unclear. Given the rate of complications and need for reoperation
Major adverse cardiovascular events (*Critical outcome*)	Odds ratio: 0.54 (95% CI 0.41 to 0.70) Crude event rates 2.4% with surgery and 4.0% without surgery Number needed to treat = 62			

Coverage question: Should bariatric surgery be recommended for coverage in adults?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
	●●○○ (*low certainty based on consistent but indirect observational studies)*		would strongly value. However, there would still be moderate variability because of the risks and costs associated with surgery, as well as the intensive peri- and post-operative follow up.	reported in the summary literature, benefit plans may wish to consider alternative payment methodologies like bundled payments or a pay-for-outcomes approach. Surgeon case volume, and to a lesser extent hospital case volume, appear to affect outcomes for patients undergoing bariatric surgery and requirements regarding surgeon or facility volume may be reasonable.
Type 2 DM remission/resolution (*Important outcome*)	Odds ratio: 3.6 to 52.4 (favoring surgery) Number needed to treat: 1 to 5			
	●●●○ *(moderate certainty based on a mix of RCTs and observational studies with consistent but imprecise effects)*			
Hypertension remission/ resolution (*Important outcome*)	Odds ratio: 2.99 to 3.12 (favoring surgery) Number needed to treat: 4			
	●●●○ *(moderate certainty based on a mix of RCTs and observational studies with consistent but imprecise effects)*			
Change in BMI (*Important outcome*)	Mean difference at 1 year: -5.5 to -33.35 kg/m^2 (favoring surgery) Pooled mean difference: -7.4 kg/m^2 (favoring surgery)			

Coverage question: Should bariatric surgery be recommended for coverage in adults?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
	●●●○ *(moderate certainty based on a mix of RCTs and observational studies with consistent but imprecise effects)*			

Rationale: Bariatric surgery appears to lower all-cause mortality and major adverse cardiovascular events in obese adults (low certainty), and significantly reduces BMI, and results in resolution of type 2 diabetes and hypertension. The greatest benefit appears to be with BMI ≥ 40. Though bariatric surgery is costly and carries significant perioperative risks, the clear long-term positive health benefits leads to a recommendation for coverage. The strength of the recommendation is based on the fact that there is a strong benefit on critical outcomes (particularly in diabetics), and patients desiring surgery would strongly prefer this intervention. For those without diabetes, and other comorbidities are present, the evidence is less clear, leading to a weak recommendation.

Recommendation:

Coverage of metabolic and bariatric surgery (including Roux-en-Y gastric bypass, gastric banding, and sleeve gastrectomy) is recommended for:

- Adult obese patients (BMI ≥ 35 and <40) with:
  - Type 2 diabetes *(strong recommendation)* OR
  - at least two of the following other serious obesity-related comorbidities: hypertension, coronary heart disease, mechanical arthropathy in major weight bearing joint, sleep apnea *(weak recommendation)*
- Adult obese patients (BMI ≥ 40) *(strong recommendation)*

Metabolic and bariatric surgery is recommended for coverage in these populations only when provided in a facility accredited by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program *(weak recommendation).*

Metabolic and bariatric surgery is not recommended for coverage in:

- Patients with BMI <35, or 35-40 without the defined comorbid conditions above *(weak recommendation)*

Note: GRADE framework elements are described in Appendix B. A GRADE evidence profile is provided in Appendix C.

Coverage question: Should bariatric surgery be recommended for coverage in children and adolescents?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
All-cause mortality (*Critical outcome*)	Insufficient evidence in this population *Insufficient evidence*	High cost (tens of thousands of dollars) but may be cost effective especially given the long time horizon if weight loss is maintained. However, uncertainty about the long-term balance of benefits and harms could significantly alter estimates of cost-effectiveness.	High variability. If conservative treatments have failed, children, adolescents and their parents would be highly motivated to find an effective alternative intervention. Children may have a significant fear of surgery, but the profound social and emotional impact of obesity may override their concerns. Parents are likely to be more concerned about the long term health impacts of obesity than children, and may be concerned about the	Parental involvement in weight management plans is likely necessary to assist the effectiveness of obesity treatments (based on expert opinion). Pediatric bariatric surgery is likely to be available at only a few highly specialized centers. The American Academy of Pediatrics has 10 criteria that pediatric bariatric surgery programs should meet.
Major adverse cardiovascular events (*Critical outcome*)	Insufficient evidence in this population *Insufficient evidence*			
Type 2 DM remission/resolution (*Important outcome*)	Rates of remission of T2DM ranged from 50 to 100% ●○○○ *(very low certainty based on mostly small observational trials with imprecise effects)*			
Hypertension remission/ resolution (*Important outcome*)	Rates of remission of hypertension ranged from 50 to 100% ●○○○ (*very low certainty based on mostly small observational trials with imprecise effects)*			

Coverage question: Should bariatric surgery be recommended for coverage in children and adolescents?				
Change in BMI (*Important outcome*)	Mean weighted difference in BMI at 1 year (from baseline): -10.5 to -17.2 kg/m^2 ●●○○ *(low certainty based on mostly small observational trials)*		uncertainty about the long term benefits.	
Rationale: Bariatric surgery likely results in significant reductions in BMI (low certainty) and is associated with remission of type 2 diabetes and hypertension (very low certainty). However, coverage is not recommended because of the limited evidence about overall long-term benefits and harms of bariatric surgery in this population as well as the high variability in values and preferences.				
Recommendation: Bariatric surgery is not recommended for coverage in children and adolescents *(weak recommendation).*				

Note: GRADE framework elements are described in Appendix B. A GRADE evidence profile is provided in Appendix C.

Coverage question: Should reoperative bariatric surgery for inadequate weight loss be recommended for coverage?					
Outcomes		**Estimate of Effect for Outcome** **Confidence in Estimate of Effect**	**Resource allocation**	**Values and Preferences**	**Other considerations**
Critical outcomes	All-cause mortality	Insufficient evidence in this population *Insufficient evidence*	A second high cost procedure (tens of thousands of dollars), with a history of prior failure may be	There would be high variability in patient preferences. With a prior failure of a bariatric procedure, some patients would be hesitant to try an additional procedure	There is evidence of greater complications rates with reoperation. There is insufficient evidence in the reoperation group to
		Insufficient evidence in this population			

Coverage question: Should reoperative bariatric surgery for inadequate weight loss be recommended for coverage?					
Outcomes		**Estimate of Effect for Outcome** **Confidence in Estimate of Effect**	**Resource allocation**	**Values and Preferences**	**Other considerations**
	Major adverse cardiovascular events	*Insufficient evidence*	more costly in total and less effective, however, the cost –effectiveness in this group is unknown.	given the burdens of surgery and prior ineffectiveness. Others would be motivated to try a different procedure in hopes that it would work better. Patients seeking reoperation have likely no other good potential option given failure of multiple previous alternatives (e.g. clinical, pharmacological, nutritional, physical activity, and surgical).	know if their outcomes would be substantially different that those undergoing their first operation. A significant proportion of these patients would be going from a band to a RYGB (from a procedure with a higher failure rate to a lower failure rate).
Important outcomes	Type 2 DM remission / resolution	Insufficient evidence in this population *Insufficient evidence*			
	Hypertension remission/ resolution	Insufficient evidence in this population *Insufficient evidence*			
	Change in BMI	Mean change in BMI (from baseline): +2.4 kg/m^2 to -17.2 kg/m^2 (follow-up ranging from 8 to 48 months) ●○○○ *(very low certainty based on small case series)*			
Rationale: Reoperation is associated with higher complication rates but also effective weight loss (based on very low quality evidence). While there are not long term health outcomes available, there is no reason to believe that significant weight loss in the reoperation group would be associated with less future health benefits. Therefore, the subcommittee makes no recommendation that the coverage criteria should be different between reoperation and primary surgery. Surgeons will also evaluate their patients and consider reasons for failure when deciding if the patient is a good candidate for reoperation.					
Recommendation: No recommendation that coverage criteria for re-operation should be different than for primary surgery.					

Note: GRADE framework elements are described in Appendix B GRADE evidence profile is provided in Appendix C.

EVIDENCE OVERVIEW

Clinical background

Obesity, generally defined as a body mass index (BMI) ≥ 30 kg/m^2 in adults or above the 95th percentile of age- and sex-specific BMI growth charts in children and adolescents, is common. Information from the National Health and Nutrition Examination Survey published in 2014 provides estimates of obesity prevalence of 35% of adults, 17% of 2 to 19 year olds, and 8.1% of infants and toddlers (Ogden, Carroll, Kit, & Flegal, 2014). Obesity is a risk factor for several medical conditions including heart disease, type 2 diabetes mellitus (T2DM), stroke, cancer, sleep apnea, osteoarthritis and others. The Centers for Disease Control and Prevention estimates that obesity is the second leading cause of preventable death and will likely overtake tobacco use as the leading cause of preventable death within the next decade. Older estimates from 2009 found that medical spending attributable to obesity is between $147 billion and $210 billion annually with at least $60 billion of those costs accruing to Medicare and Medicaid programs (Finkelstein, Trogdon, Cohen, & Dietz, 2009).

Data from the Oregon Behavioral Risk Factor Surveillance system in 2009 found that the overall prevalence of adult obesity in Oregon is 24%, though the prevalence of obesity in adults covered by the Oregon Health Plan is greater at 38%. The Oregon Healthy Teens Survey in 2009 estimated that approximately 11% of 8th graders were obese. The Oregon Department of Public Health estimated that costs of obesity related medical care in the Medicaid program alone exceeded $333 million in 2006 (State of Oregon, Department of Human Services, 2012).

There are a number of commonly used medical treatments for obesity including structured programs to promote improved nutrition and physical activity, intensive behavioral counseling for individuals or families, and medications. The Food and Drug Administration (FDA) approved pharmaceutical treatments for obesity include orlistat (Xenical®, Alli®), lorcaserin (Belviq®), phentermine/topiramate (Qsymi®), liraglutide (Victoza®, Saxenda®), and bupropion/naltrexone (Contrave®). Several other medications and herbal supplements are also promoted for weight loss. The FDA also recently approved a weight loss device called the Maestro® Rechargable System that works by blocking signals along the vagal nerve.

Bariatric surgical procedures (sometimes also referred to as metabolic surgery) are another treatment option for obesity.

Indications

Bariatric surgery (alone or in conjunction with non-surgical treatments) is indicated for the treatment of obesity. Guidelines regarding indications for bariatric surgery vary based on BMI thresholds and the presence of obesity-related comorbid conditions.

Technology description

Bariatric procedures commonly performed in the United States include adjustable gastric banding (AGB), vertical sleeve gastrectomy (VSG), Roux-en-Y gastric bypass (RYGB), and biliopancreatic diversion/ duodenal switch (BPD/DS). An excellent overview of the anatomic details of these procedures is available in the executive summary of the Washington Health Technology Assessment (WA HTA) report published in April 2015 (WA HTA, 2015).

The use of bariatric surgical procedures is growing, and approximately 179,000 procedures were performed in 2013 in the United States (U.S.). The distribution of procedure types in the U.S. has shifted with greater use of vertical sleeve gastrectomy and declining use of gastric banding. The estimated number and distribution of surgical procedures in the U.S. is summarized in Table 1.

Table 1. Estimated number and distribution of bariatric surgical procedures in the United States between 2011 and 2013.

	2011	2012	2013
Total	158,000	173,000	179,000
RYGB	36.7%	37.5%	34.2%
Gastric band	35.4%	20.2%	14.0%
Sleeve gastrectomy	17.8%	33.0%	42.1%
BPD/DS	0.9%	1.0%	1.0%
Revisions	6.0%	6.0%	6.0%
Other	3.2%	2.3%	2.7%

Reproduced from the American Society of Bariatric and Metabolic Surgeons, http://connect.asmbs.org/may-2014-bariatric-surgery-growth.html.

Abbreviations: BPD/DS – Biliopancreatic diversion/duodenal switch; RYGB – Roux-en-Y gastric bypass

Adjustable gastric banding and VSG are procedures that either functionally or anatomically reduce the size of the stomach. Adjustable gastric banding, alone among the bariatric surgical procedures, is completely reversible. Roux-en-Y gastric bypass and BPD/DS are more complicated procedures that reduce the size of the stomach and connect more distal portions of the small intestine to the gastric remnant thus bypassing varying lengths of small intestine and reducing the absorption of nutrients. For this reason, these surgeries are sometimes referred to as malabsorptive procedures, with the degree of malabsorption correlating to the length of small intestine that is bypassed. Vertical sleeve gastrectomy is sometimes performed as part of a two stage procedure for patients with extremely high BMIs (the second stage of the procedure is usually a malabsorptive procedure that is more technically feasible after the initial weight loss achieved by VSG).

These procedures can be performed laparoscopically and with robotic assistance. Adjustable gastric banding is sometimes performed on an outpatient basis, but the other procedures generally require a hospital stay that varies from one to seven days after surgery depending on the procedure and patient-specific characteristics. Recovery times vary from one to four weeks. All procedures require frequent follow-up, but AGB may require a greater number of follow-up visits to make adjustments to the band (done through a port located underneath the skin of the abdomen).

All of the bariatric surgical procedures entail operative and post-operative risks, though these vary by the type of procedure. Data regarding perioperative mortality, complications, need for reoperation, and serious adverse events reported in four systematic reviews are summarized in Table 2. It should be noted that definitions of complications and adverse events varied widely across studies. Operative risks include bleeding, infection, and damage to various abdominal organs. Nausea and vomiting are common after all these procedures and the malabsorptive surgeries sometimes cause persistent diarrhea. The malabsorptive procedures are associated with an increased risk of vitamin and mineral deficiencies, and certain types of kidney stones may become more common. Gastrointestinal bleeding from ulcers occurring at the surgical anastamoses also occurs. Infections of the subcutaneous port and erosion of the gastric band into the stomach are risks unique to AGB. The overall median complication rates reported in the Washington HTA report range from 8.8% for VSG to 26.9% for BPD (WA HTA, 2015).

Table 2. Mortality, complications, reoperations, and serious adverse events reported in four systematic reviews.

	Chang (2014)	Colquitt (2014)	Puzziferri (2014)	WA HTA (2015) Range, Median
Mortality <30 days	0.08% in RCTs 0.22% in OSs	NR	NR	NR
Mortality >30 days or not specified	0.31% in RCTs 0.35% in OSs	NR	1% for bypass procedures 0.2% for banding procedures	BPD: 0%-2.9%, 1.4% LAGB: 0%-2.0%, 0.15% RYGB: 0%-4.3%, 1.94% VSG: 0%-3.9%, 0.07%
Complication rate	17% in RCTs 10% in OSs	NR	NR	BPD: 8%-83%, 26.9% LAGB: 0%-53%, 10.1% RYGB: 0%-78%, 9.2% VSG: 0%- 80%, 8.8%
Reoperation rate	7% in RCTs 6% in OSs	2%-13%	NR	BPD: 0%-30%, 3.6% LAGB: 0%-44%, 7.4% RYGB: 0%-22%, 5.8%

	Chang (2014)	Colquitt (2014)	Puzziferri (2014)	WA HTA (2015) Range, Median
				VSG: 0%-17%, 3.9%
Serious adverse event rate	NR	0-37% in surgical groups 0-25% in non-surgical groups	NR	NR

Abbreviations: BPD – Biliopancreatic diversion; LAGB – Laparoscopic adjustable gastric banding; NR – Not reported; OS – Observational study; RCT – Randomized controlled trial; RYGB – Roux-en-Y gastric bypass; VSG – Vertical sleeve gastrectomy

Key Questions

The following key questions (KQ) guided the evidence search and review described below. For additional details about the review scope and methods please see Appendix A.

1. Should coverage be recommended for bariatric surgery in each of the scenarios in the table below? (Note that the "resolution of diabetes" would not be an applicable outcome in scenarios 4-9)

	BMI 30 – 34.9	BMI 35 – 39.9	BMI ≥ 40
With DM2	Scenario 1	Scenario 2	Scenario 3
W/o DM2 nor other comorbidities	Scenario 4*	Scenario 5*	Scenario 6*
w/o DM2 but with other comorbidities	Scenario 7*	Scenario 8*	Scenario 9*

*Resolution of type 2 diabetes isn't a relevant outcome for this population

2. What is the appropriate minimum age for bariatric surgery?
3. What components and systems of care are associated with improved health outcomes (e.g., centers of excellence, surgeon's experience, etc.)?
4. What preoperative assessments or requirements for preoperative weight loss should be recommended in patients being considered for bariatric surgery?

Critical outcomes selected for inclusion in the GRADE table were all-cause mortality and major adverse cardiovascular events. Important outcomes selected for inclusion in the GRADE table were weight loss (change in BMI), and remission or resolution of T2DM or hypertension.

Evidence review

General Limitations

The literature on bariatric surgery is voluminous. The search conducted by Center staff yielded more than 20 systematic reviews published in the last two years (see Appendix A for a detailed methods description). These reviews span more than 600 individual studies. It should be noted that there is little consistency in the inclusion of individual studies across reviews and that many of the systematic reviews did not perform meta-analysis, in part due to high levels of heterogeneity.

Furthermore, there are important concerns about the quality of much of the published research on bariatric surgery. As the Washington HTA report summarized:

> While the comparative evidence base for either head-to-head comparisons of bariatric procedures or comparisons of bariatric surgery to nonsurgical interventions has grown considerably over time, major challenges with the quality and applicability of available studies remains. Of the 179 comparative studies identified for this evaluation, we rated only 26 (15%) to be of good quality, based on comparable groups at baseline, comparable duration of follow-up, and limited sample attrition. An additional 74 studies (41%) were rated fair quality; issues with comparability, duration of follow-up, and/or attrition were identified in these studies, but attempts were made to control for confounding in the analytic methods (e.g., survival analysis techniques, multivariate regression). However, we considered another 79 studies (44%) to be of poor quality because at least one key quality issue was present and not adequately addressed in either study design or analysis. (WA HTA, 2015, p ES-6).

Additionally, there are at least nine ongoing trials of bariatric surgery that are expected to publish results over the next four years.

Systematic Reviews Addressing Effectiveness in Adults

Eight good quality systematic reviews address the effectiveness of bariatric surgery in adults (Chang et al., 2014; Colquitt, Pickett, Loveman, & Frampton, 2014; Hayes, 2014; Kwok et al., 2014; Muller-Stich et al., 2014; Puzziferri et al., 2014; Wang et al., 2015; WA HTA, 2015). These studies are summarized in Table 3 and discussed below by systematic review.

Table 3. Summary of Systematic Reviews – Effectiveness of Bariatric Surgery for Adults

Systematic Review (Quality) Total N	No. and Type of Included Studies	Population	Outcomes of Interest
Chang, 2014 (Good) N = 161,756	37 RCTs 127 observational studies	Pre-surgical BMI (mean): 45 kg/m^2 T2DM: 26% Hypertension: 47%	Mortality (within 30 days of surgery) Complication rate BMI (mean change at 1 and 5 years) T2DM remission Hypertension remission
Colquitt, 2014 (Good) N ~ 600	7 RCTs	Average pre-surgical BMI (mean): 27 – 55 kg/m^2 5 out of 7 studies required participants have T2DM	BMI T2DM remission Hypertension remission Serious adverse events
Hayes, 2014 (Good) N = 1,734	18 controlled or comparative studies	Pre-surgical BMI (mean): 25 – 55 kg/m^2 T2DM	BMI T2DM remission
Kwok, 2014 (Good) N = 195,408	14 comparative cohorts	Most studies enrolled participants with BMI > 35 kg/m2	All-cause mortality Cardiovascular adverse events
Muller-Stich, 2014 (Good) N = 766	7 RCTs 6 Comparative observational studies	Pre-surgical BMI (mean): < 35 – 37 kg/m^2	BMI T2DM remission Hypertension remission
Puzziferri, 2014 (Good) N = 8,678	10 RCTs 8 cohort studies 11 case series	Pre-surgical BMI (mean): 44 – 61 kg/m^2	Weight loss T2DM remission Hypertension remission Perioperative mortality

Systematic Review (Quality) Total N	No. and Type of Included Studies	Population	Outcomes of Interest
Wang, 2015 (Good) N = 256	4 RCTs	Pre-surgical BMI (mean): 30 – 47 kg/m^2	BMI T2DM remission
WA HTA, 2015 (Good) N = 2,083	14 RCTs 7 comparative cohort studies	Pre-surgical BMI (mean): 30 – 56 kg/m^2	BMI T2DM remission Perioperative mortality and complications

Abbreviations: BMI – body mass index; RCT – randomized controlled trial; T2DM – type 2 diabetes mellitus; WA HTA – Washington Health Technology Assessment Program

Chang (2014)

Chang et al. (2014) is a good quality systematic review and meta-analysis of 164 contemporary studies (37 randomized controlled trials [RCTs] and 127 observational studies) of bariatric surgery published between 2003 and 2012. The included studies spanned over 161,000 patients with an average age of 45 years and an average pre-surgical BMI of 45 kg/m^2. Twenty six percent of the included patients had T2DM and 47% had hypertension. More than two years of follow-up was available for 133,000 of the included patients. Results of RCTs and observational studies were reported separately in the meta-analysis.

The review and meta-analysis focused on surgical mortality and complications, change in BMI, and resolution of obesity-related comorbid conditions. The overall rate of mortality within 30 days of surgery was 0.08% (95% confidence interval [CI] 0.01% to 0.24%) in the RCTs and 0.22% (95% CI 0.14% to 0.31%) in the observational studies. The overall complication rate was 17% (95% CI 11% to 23%) in the RCTs and 9.8% (95% CI 7.4 to 13.0) in the observational studies.

The overall mean change in BMI at 1 year was -13.53 kg/m^2 in the RCTs and -11.79 kg/m^2 in the observational studies. For those studies reporting outcomes at five years of follow-up, the overall mean change in BMI was -11.40 kg/m^2 in the RCTs and -14.32 kg/m^2 in the observational studies.

In the RCTs, the T2DM remission rates in the surgical groups was 92% (95% CI 84.68 to 97.18) compared with a rate of 17.4% (95% CI 0.98 to 69.27) in the control groups. The observational studies found a T2DM remission rate of 86.5%. In the RCTs, the hypertension remission rate was 75% (95% CI 61.52 to 86.35) in the surgical groups compared with a rate of 49% (95% CI 0 to 99%). These comparisons are both indirect and imprecise because so few of the included studies compared surgical and non-surgical

groups directly. Additionally, duration of follow-up for the studies examining comorbid conditions was unclear.

Colquitt (2014)

Colquitt et al. (2014) is a good quality systematic review by the Cochrane Collaboration that includes 22 RCTs, of which 7 studies, comprising approximately 600 patients, compared bariatric surgery to non-surgical controls. Because of differences in the characteristics of participants, interventions, and comparators, meta-analysis was considered inappropriate, and the results were reported narratively.

In terms of BMI, the included studies reported mean changes of -7.4 kg/m^2 to -33.3 kg/m^2 with surgery compared to -0.5 kg/m^2 to -4.7 kg/m^2 in non-surgical controls. The authors conclude that "the direction of the effect was consistently in favour of surgery" based on moderate quality of evidence.

In terms of remission of T2DM, the included studies reported rates of remission ranging from 42% to 90% at 12 to 24 months in surgical groups (73% to 90% if one study with a more stringent definition of A1c < 6 is excluded) compared to remission rates of 0% to 32% in non-surgical controls. The authors conclude that "more people experienced remission following surgery" based on moderate quality of evidence.

Three studies included in the Cochrane review also reported on hypertension outcomes. Two studies reported rates of reduction or discontinuation of antihypertensive medications ranging from 49% to 80% between 12 and 24 months in the surgical groups compared to 0% to 70% in non-surgical controls. One additional study reported that the proportion of patients with systolic blood pressure less than130 mmHg at 12 months was 84% in the surgical group and 79% in non-surgical controls. The authors did not draw any conclusions based on these data.

Hayes (2014)

Hayes (2014) is a good quality systematic review and health technology assessment based on 18 controlled or comparative studies of RYGB in adults with T2DM published between2007 and 2014. Seven of the included studies (5 RCTs and 2 non-randomized controlled trials) compared RYGB with non-surgical treatments while the remaining 11 compared RYGB with other bariatric surgical procedures. The average follow-up across the included studies was 12 months to 5 years.

In patients undergoing RYGB, BMI was reduced by 20 to 33% compared to baseline and T2DM remission was reported in 38 to 90% of patients. In the non-surgical treatment groups, BMI change ranged from -10% to 1%, and T2DM remission rates ranged from 0 to 33%. Based on this, Hayes concluded that RYGB is superior to intensive lifestyle or medical interventions for the treatment of T2DM. The authors further conclude that RYGB and sleeve gastrectomy are equally effective in the treatment of T2DM. Finally, the authors note that preliminary evidence (from a single study) suggests the RYGB may be equally effective for treatment of T2DM in patients with BMI<35 kg/m^2 and BMI>35 kg/m^2, but that additional studies are needed to establish the safety and effectiveness of RYGB in patients with lower BMIs.

Kwok (2014)

Kwok et al. (2014) is a good quality systematic review and meta-analysis of 14 comparative cohort studies reporting mortality and cardiovascular outcomes amongst 29,208 bariatric surgery patients and 166,200 non-surgical controls. The follow-up period of the included studies ranged from 2 years to 14.7 years. The surgical procedures in the studies included AGB, RYGB, SG, banded gastroplasty, as well as other unspecified bariatric surgical procedures. Most of the included studies reported enrolling patients with BMI >35 kg/m^2. Of the 14 included studies, 10 were deemed to be at low to moderate risk of bias, while four studies were deemed to be at moderate-high risk of bias due to concerns over loss to follow-up and inadequate adjustment for confounding. See Appendix D for a detailed description of the included studies.

In the 14 studies included in the meta-analysis of all-cause mortality, the crude event rate was 1059/29,208 (3.6%) in the surgical group and 18,962/166,200 (11.4%) in the non-surgical control group. The odds ratio (OR) for mortality in the surgical group compared with the non-surgical group was 0.48 (95% CI 0.35 to 0.64). Considering only the 10 studies that reported adjusted estimates, the association was consistent but more conservative with an odds ratio for mortality of 0.60 (95% CI 0.49 to 0.74) favoring the surgical group over the non-surgical controls.

In the four studies included in the meta-analysis of composite cardiovascular adverse events, the crude event rate was 407/17,262 (2.4%) in the surgical group and 1108/27,726 (4.0%) in the non-surgical control group. The odds ratio for composite cardiovascular adverse events in the surgical group compared with the non-surgical group was 0.54 (95% CI 0.41 to 0.70). The pooled estimates for the odds ratio of myocardial infarction and stroke for surgical patient compared to non-surgical controls were 0.46 (95% CI 0.30 to 0.69) and 0.49 (95% CI 0.32 to 0.75) respectively.

Overall, the authors conclude that long-term follow-up data from comparative cohort studies suggest that bariatric surgery is associated with lower rates of mortality (3.6% vs 11.4% for non-surgical controls, number needed to treat [NNT] = 13) and composite adverse cardiovascular events (2.4% vs 4.0% for non-surgical controls, NNT = 62).

Muller-Stich (2014)

Muller-Stich et al. (2014) is a good quality systematic review and meta-analysis of studies comparing surgical and medical treatment of T2DM in non-severely obese patients. The systematic review included seven RCTs and six comparative observational studies comprising 818 diabetic patients. All of the studies included patients with BMI <35 kg/m^2 and eight of the studies were performed exclusively in patients with BMI <35 kg/m^2; among the remaining seven studies the highest average BMI was 37.1 kg/m^2. The surgical procedures performed in the included studies were AGB, BPD, RYGB, and SG. The follow-up periods ranged from 12 to 36 months.

In the meta-analysis of studies reporting remission of T2DM, 129 of 280 patients achieved remission in the surgical group compared with 6 of 252 patients in the medical treatment group. The combined odds

ratio for T2DM resolution after surgery compared with medical treatment was 14.11 (95% CI 6.67 to 29.86).

In the meta-analysis of studies reporting change in BMI, the absolute mean difference in BMI was -5.5 kg/m^2 (95% CI -6.7 to -4.3) favoring the surgical group.

In the meta-analysis of studies reporting presence of arterial hypertension at the end of the study, the 76 of 274 patients in the surgical group and 101/189 patients in the medical treatment group had arterial hypertension. The combined odds ratio for arterial hypertension after surgery compared with medical treatment was 0.25 (95% CI 0.12 to 0.50).

The authors performed a network meta-analysis to compare the treatment effects of the different surgical procedures. Although point estimates of the odds ratio for T2DM remission compared to medical treatment ranged from 12.23 for AGB to 55.05 for RYGB, the 95% confidence intervals overlapped for all four included procedures, and all were superior to medical treatment.

Overall, the authors conclude that among non-severely obese patients with T2DM bariatric surgery results in greater short-term improvements in diabetes remission, weight loss, and arterial hypertension when compared with medical treatment.

Puzziferri (2014)

Puzziferri et al. (2014) is a good quality systematic review and meta-analysis of 29 studies with long-term follow-up and low rates of attrition. Specifically, only studies of gastric bypass, gastric band, or sleeve gastrectomy performed in patients with a BMI of >35 and that reported outcomes with a minimum of two years of follow-up and at least 80% of the original study participants were included in the review. Only 29 studies (of nearly 8,000 citations reviewed) met the inclusion criteria. Among the included studies were 10 RCTs, one matched cohort, six prospective cohorts, one retrospective cohort, and 11 case series.

Weight loss outcomes in this review were reported as percentage of mean excess weight loss (EWL). The sample size weighted mean EWL was 65.7% after gastric bypass, 64.5% after sleeve gastrectomy, and 45% after gastric banding.

Six of the included studies reported on remission of T2DM (defined as glycated hemoglobin <6.5% without medications). Sample size weighted T2DM remission rates were 66.7% after gastric bypass and 28.6% after gastric banding.

Three of the included studies reported on remission of hypertension (defined as blood pressure <140/90 without medications). The reported hypertension remission rate was 38.2% after gastric bypass and 17.4% after gastric banding.

Wang (2015)

Wang et al. (2015) is a good quality, though narrowly focused, systematic review and meta-analysis of randomized controlled trials comparing laparoscopic RYGB with sleeve gastrectomy in overweight or obese adults with T2DM. Three RCTs judged to be at low risk of bias and one RCT with an unclear risk of

bias were included. The average baseline BMI in the studies ranged from 30 to 46 kg/m^2. Laparoscopic RYGB and sleeve gastrectomy resulted in similar improvements in HbA1c, fasting plasma glucose, need for any diabetic medication, and BMI. Improvements in HDL and LDL cholesterol were statistically significantly greater in the RYGB group. The absolute or relative improvements in these outcomes compared to baseline were not included. Overall, the authors conclude that RYGB and sleeve gastrectomy offer equivalent results in terms of weight loss and T2DM remission, but that RYGB affords greater improvements in lipid parameters and may thus significantly decrease cardiovascular risk.

Washington Health Technology Assessment Report (2015)

The WA HTA report (2015) is a good quality systematic review and health technology assessment summarizing results from 179 comparative studies (35 RCTs, 59 prospective cohorts, 85 retrospective cohorts). Notably, one large cohort study with long-term follow-up, the Swedish Obese Subjects study, was not included as a primary source for the Washington HTA report because most of the patients in that study received a surgical procedure (gastroplasty) that is no longer widely performed. Only 15% of the included studies were judged to be of high quality, with an additional 41% deemed fair quality. When performing meta-analysis, the authors included only good or fair quality RCTs.

Overall or cause-specific mortality was not directly addressed in the WA HTA report because none of the included comparative studies reported those outcomes. However, the WA HTA report does note that evidence from at least one recent comparative cohort study found significantly lower all-cause mortality at 1 to 14 years of follow-up in surgical subjects (hazard ratio [HR] 0.45, 95% CI 0.36 to 0.56) (Arterburn, 2015).

The comparison of bariatric surgery to non-surgical management included 21 good- or fair-quality studies (14 RCTs, 7 comparative cohorts). These studies reported on RYGB (13 studies), AGB (6 studies), VSG (4 studies) and BPD/DS (3 studies). The non-surgical comparators included diet and lifestyle interventions and/or medical interventions (some variably defined as “intensive”). Meta-analytic results were available for weight loss and resolution of T2DM. The pooled mean difference in BMI was 7.4 (95% CI 6.2 to 8.6) favoring surgery, based on 10 studies. Resolution of T2DM had a log odds ratio of 3.62 (95% CI 2.49 to 4.73) favoring surgery, based on nine studies. Meta-analysis of studies reporting resolution of HTN was not done, but the report noted that “[o]ther individual comorbidities commonly evaluated in these comparative studies included hypertension and hyperlipidemia. In studies evaluating resolution of these conditions and/or discontinuation of relevant medications as a binary variable, bariatric surgery was associated with two- to three-fold reductions in the prevalence of these comorbidities [hypertension and hyperlipidemia] at the end of follow-up, while nonsurgical management resulted in no appreciable change from baseline…” (WA HTA, 2015, p. 34).

The WA HTA report is the only systematic review staff identified that summarizes key clinical outcomes stratified by procedure and mean pre-operative BMI. Those tables are included in Appendix G. Nine good- or fair-quality RCTs and prospective cohorts comparing bariatric surgery and non-surgical management enrolled patients with BMI<35. Seven of those studies included presence of T2DM or

metabolic syndrome as an entry criterion, while two did not report comorbid condition-based entry criteria. The authors conclude that for those with a mean pre-operative BMI of 30 to 35.9 "patterns of weight loss across procedures were similar to those in studies of patients at higher BMI" (WA HTA, 2015, p. ES-41). Furthermore, among studies of patients at lower BMI levels that reported on remission of T2DM at 12 to 24 months the results favored surgery (remission rates of 26% to 73%) over non-surgical treatment (remission rates of 0% to 16%).

Systematic Reviews Addressing Effectiveness in Children and Adolescents

Three fair or good quality systematic reviews address the effectiveness of bariatric surgery in children and adolescents (Aikenhead, Knai, & Lobstein, 2011; Black, White, Viner, & Simmons, 2013; Treadwell, Sun, & Schoelles, 2011). These studies are summarized in Table 4 and discussed below by systematic review.

Table 4. Summary of Systematic Reviews – Effectiveness of Bariatric Surgery for Children and Adolescents

Systematic Review (Quality) Total N	No. and Type of Included Studies	Population	Outcomes of Interest
Aikenhead, 2011 (Fair) N = 831	1 RCT 8 cohort studies 14 observational studies 12 case series	≤ 19 years old	BMI
Black, 2013 (Fair) N = 637	1 RCT 22 observational studies	Pre-surgical BMI (mean): 46 – 52 Age: 5 – 23 years	BMI
Treadwell, 2008 (Treadwell) N = 644	18 Observational studies	Pre-surgical BMI (mean): 46 – 52 Age: 9 – 21 years	BMI

Abbreviations: BMI – body mass index; RCT – randomized controlled trial

Aikenhead (2011)

Aikenhead et al. (2011) is a fair quality narrative systematic review of 37 studies of effectiveness of bariatric surgery spanning 831 patients age 19 years old or younger. The authors note several general limitations of the pediatric bariatric surgery literature including predominately observational study designs, small sample sizes (the largest of the included trials had 68 patients), and sparse information on low frequency outcomes.

Thirteen of the included studies (all but one observational) assessed gastric banding. Twelve of these studies reported mean BMI reductions of 8.5 kg/m^2 to 43 kg/m^2, while one study (a case report of gastric banding and truncal vagotomy in an adolescent with a rare mutation in a gene implicated in regulation of appetite and energy balance) found an increase in BMI of 2.2 kg/m^2. Rates of resolution of comorbid conditions ranged from 11 to 100%.

Eight of the included studies (all observational) assessed RYGB. The studies reported mean reductions in BMI of 9 kg/m^2 to 25 kg/m^2. The authors note that four of the studies reported on comorbid conditions and three of those four studies found 100% rates of resolution for dyslipidemia, degenerative joint disease, asthma, and gastroesophageal reflux disease.

Fourteen of the included studies (all observational) reported on other bariatric procedures (sleeve gastrectomy, BPD/DS, vertical banded gastroplasty). These studies reported mean BMI reductions of 9 kg/m^2 to 24 kg/m^2. The authors note that changes in comorbid conditions were reported in 12 of the 14 studies, but additional details are not included.

The authors' overall conclusion is that "[i]n the context of a general lack of effective tools for primary prevention or behavioural treatment of obesity, surgical treatment may be advocated as a preferred and cost-effective solution for certain children and adolescents" (Aikenhead, 2011, p. 18)

Black (2013)

Black et al. (2013) is a fair quality systematic review and meta-analysis of bariatric surgery for obese children and adolescents. Twenty-three studies (22 observational and 1 RCT) comprising 637 patients undergoing RYGB, AGB, or SG were included. The mean pre-surgical BMI was 52.4 kg/m^2 in the RYGB studies, 49.6 kg/m^2 in the SG studies, and 46.1 kg/m^2 in the AGB studies. The ages of patients in the included studies ranged from 5 to 23 years old.

Overall, the average weighted BMI difference from baseline to one year postoperatively was -13.5 kg/m^2 (95% CI -15.1 to -11.9). The greatest BMI reductions were observed in patients undergoing RYGB (average weighted difference of -17.2 kg/m^2) and the smallest BMI reductions were observed in the AGB group (average weighted difference of -10.5 kg/m^2).

The authors note that they were unable to provide summary estimates of the effects on comorbidity resolution because the data were of poor quality and adequate definitions of resolution were not provided. The rates of reported resolution of T2DM from baseline to follow-up ranged from 0 to 100% in the eight studies that reported this outcome. However, excluding one study with only a single T2DM patient who did not experience resolution, the rate of resolution for T2DM would range from 50 to 100%. The rates of reported resolution of hypertension from baseline to follow-up ranged from 50 to 100% in the 10 studies that reported this outcome.

Treadwell (2008)

Treadwell et al. (2008) is a good quality systematic review and meta-analysis of bariatric surgery for pediatric obesity. This review included 18 studies of children ages 9 to 21 years (mean age 16.7 years) with mean BMI ranging from 45.8 kg/m^2 to 51.8 kg/m^2. In 14 of the 18 studies, patients must have failed

a trial of non-surgical weight loss before undergoing bariatric surgery. Only one of the included studies reported a non-surgical control group and significant differences in baseline characteristics between the groups were noted including baseline BMI and comorbidities. Thus, the authors note that, in effect, the included studies were all case series.

Meta-analysis of change in BMI in six studies of AGB found a 95% CI of -13.7 kg/m^2 to -10.6 kg/m^2 at mean length of follow-up of one to three years. Two of the studies of AGB reported T2DM remission rates of 80 to 100% and three of the studies reported hypertension remission rates of 50 to 100%.

Meta-analysis of change in BMI in six studies of RYGB found a 95% CI of -17.8 kg/m^2 to -22.3 kg/m^2 at mean length of follow-up of one to six years. Only one of the studies of RYGB reported remission of T2DM. Three studies of RYGB reported rates of hypertension remission of 50 to 100%.

Because of the small number of studies and patients undergoing other procedures, summary information on weight changes or comorbidity resolution was not presented.

Overall, the authors conclude that there is weak to moderate evidence that AGB achieves weight loss at one year or longer and weak evidence of resolution of T2DM and hypertension. For RYGB, the authors conclude that there is weak to moderate evidence of weight loss at one year or longer, weak evidence of resolution of hypertension, and insufficient evidence of resolution of T2DM. There was insufficient evidence for any outcomes from other bariatric procedures.

Systematic Reviews Addressing Bariatric Reoperation Procedures

As the use of primary bariatric surgical procedures has increased, so too has the rate of bariatric reoperation. The term “bariatric reoperation” captures several types of procedures (conversion, correction, revision, or reversal) that are performed for various indications. Inadequate weight loss (commonly, but not uniformly, defined as <50% EWL) is the most common indication for revision or conversion procedures. Reoperation is also performed to address both acute complications (including anastomotic leaks, bleeding, strictures, obstruction, and perforation) and chronic complications (including protein calorie malnutrition, severe GERD, band erosion, late or recurrent leaks, late strictures, and band intolerance.) Reversal procedures are rare, but are sometimes performed to address intractable nausea and vomiting, excessive or uncontrolled weight loss, severe malnutrition, recurrent anastomotic ulcers, severe hypoglycemia, and recalcitrant hypocalcaemia.

In general, bariatric reoperation is thought to be more technically challenging than primary bariatric surgery, at least in part because of the likelihood of surgical adhesions from the primary procedure. Nevertheless, many reoperative bariatric procedures can still be performed laparoscopically, though the complication rates may be higher when compared with primary bariatric procedures.

Five fair quality and one low quality systematic reviews address the effectiveness of bariatric reoperative procedures (Brethauer, et al., 2014; Cheung, Switzer, Gill, Shi, & Kamali, 2014; Coblijn, Verveld, van Wagensveld, & Lagard, 2013; Elnahas, Graybiel, Farrokhyar, Gmora, Anvari, & Hong, 2013;

Mahawar, Graham, Carr, Jennings, Schroeder, Balupuri, & Small, 2015; Schouten, Japink, Meesters, Nelemans, & Greve, 2011).

These systematic reviews of bariatric reoperation provide very low certainty evidence that revisional or conversion procedures performed after an initial bariatric surgery may achieve additional weight loss (particularly those procedures that convert AGB to RYGB or BPD/DS), but at the expense of a higher rate of complications. The systematic reviews offer no evidence that bariatric reoperation improved co-morbidity resolution. Most of the studies included in the systematic reviews were not methodologically rigorous and there are concerns about publication bias in this literature. Furthermore, the indications for bariatric reoperation varied across and within individual studies.

Brethauer (2014)

Brethauer et al. (2014) is a systematic review on indications for and outcomes of reoperative bariatric surgery that was conducted by the ASMBS Bariatric Surgery Revision Taskforce. The review was supported by an unrestricted educational grant from Covidien, a company that manufactures equipment used in bariatric surgical procedures. While the review states that 175 articles were included in the systematic review, the majority of these were single center retrospective case series and the evidence tables in the review provide details on only 35 "selected studies." Thus, the degree to which the narrative review and recommendations reflect an unbiased inclusion of studies identified in the systematic review is uncertain. Furthermore, the reporting of quantitative outcomes across indications and reoperative procedures was erratic. The conclusions of the authors, summarized here with the above caveats, are 1) reoperation for inadequate or failed weight loss generally improves weight loss, and 2) complication rates are generally higher with reoperative procedures.

Cheung (2014)

Cheung et al. (2014) is a systematic review of studies of revisional bariatric surgery following laparoscopic sleeve gastrectomy. The review includes 11 studies spanning a total of 218 patients. In most of the studies patients underwent revisional procedures because of insufficient weight loss or weight regain, although the former indication was variably defined. Intractable gastroesophageal reflux disease was an additional indication in 5 of the studies. The revisional procedures included laparoscopic butterfly gastroplasty, laparoscopic omega loop mini gastric bypass, laparoscopic re-sleeve gastrectomy, laparoscopic duodenal switch, and laparoscopic or open RYGB. Nine of the studies were cases series and two studies were case-controls. The largest single study enrolled 40 patients. The primary outcomes were change in BMI at various time points. At 24 months or greater, revisional procedures were associated with reductions in BMI. Revision of LSG to gastric bypass resulted in an average change in BMI of -6.2 kg/m^2. Revision of LSG to re-sleeve gastric bypass resulted in an average change in BMI of -3.2 kg/m^2. Revision of LSG to other surgical interventions (all other conversion procedures) resulted in an average change in BMI of -17.2 kg/m^2. In the three studies that examined the effects of revisional procedures on GERD complications, there was a 100% complete resolution rate, though it should be noted that the sample size for this outcome was very small (n=15). The authors note that their review

was limited by the small number of studies and patients, the very low methodological rigor of the study designs, and the absence of postoperative complication rates after revision.

Coblijn (2013)

Coblijn et al. (2013) is a systematic review of studies of revisional bariatric surgery (LSG or LRYGB) after an initial adjustable gastric banding procedure. The review includes 15 studies of LRYGB spanning 588 patients and 8 studies of LSG spanning 286 patients. Not all studies reported the indication for revisional surgery, but in those that did the most common indication was insufficient weight loss or weight regain (approximately 65% of patients). Most of the studies were consecutive case series and there were no randomized controlled trials. The primary outcomes of interest were perioperative morbidity and mortality. In the LRYGB studies that reported this outcome there were no perioperative deaths and the overall perioperative complication rate was 8.5%. In the LSG studies that reported this outcome, there were 3 perioperative deaths and the overall perioperative complication rate was 12.2%. The rate of reoperation after the revisional procedures was 6.5% for LRYGB and 3.5% for LSG. Though weight loss was not of primary interest for this review, the authors did note that 11 of the 15 LRYGB studies reported mean EWL of 23% to 74%, though the follow-up time was not clear. Weight loss achieved with revisional LSG appeared to be nearly comparable. The authors note several limitations to their review including the very low methodological rigor of the study designs and the possibility of publication bias, particularly for studies reporting on morbidity and mortality.

Elnahas (2013)

Elnahas et al. (2013) is a systematic review of conversion bariatric procedures after failed adjustable gastric banding. The review includes 24 studies reporting outcomes of conversion to LSG (n=106 patients), LRYGB (n=514 patients), and laparoscopic BPD/DS (n=71 patients). Patients in these studies underwent the conversion procedure due to inadequate weight loss or surgical complications with AGB. All of the included studies were retrospective case series. The primary outcome of interest was weight loss measured by change in BMI or percentage EWL. The mean change in BMI at 24 to 48 months after reoperation was -2.8 kg/m^2 for LSG, -8.5 kg/m^2 for LRYGB, and -13.3 kg/m^2 for BPD/DS. The weighted mean complication rates for conversion to LSG, LRYGB, and BPD/DS were 4.1%, 10.7%, and 24.4% respectively. The authors note several limitations to their study including the very low methodological rigor of the study designs and significant heterogeneity across studies.

Mahawar (2015)

Mahawar et al. (2015) is a systematic review of studies that compare the outcomes of revisional bariatric procedures to the outcomes of the same primary procedures. The review includes 14 studies comparing revisional and primary RYGB and 7 studies comparing revisional and primary SG. The designs of the primary studies were not made explicit, but all appeared to be case-control or retrospective cohort studies. Quantitative cumulative outcomes reported in the studies comparing revisional with primary RYGB included mortality (1.3% revisional vs 0.2% primary), complications (29.5% revisional vs 13.9% primary), reoperation (8.4% revisional vs 8.6% primary), and leaks (5.8% revisional vs 1.0%

primary). Quantitative cumulative outcomes reported in the studies comparing revisional SG with primary SG included mortality (0% revisional vs 0.1% primary), complications (10.5% revisional vs 5.2% primary), reoperation (4.8% revisional vs 1.6% primary), and leaks (1.9% revisional vs 1.5% primary). Weight loss outcomes were not cumulatively analyzed because of heterogeneity in the studies, but the authors do note that most of the studies that reported on weight loss outcomes found that the weight loss achieved with revisional procedures was either inferior to (10/14 studies of RYGB, 2/5 studies of SG) or not significantly different from the weight loss achieved with primary procedures (4/14 studies of RYGB, 3/5 studies of SG). The authors do not comment on limitations of their review other than noting the absence of any level I evidence on revisional bariatric surgery.

Schouten (2011)

Schouten et al. (2011) is a systematic review of studies examining reoperation following gastric banding procedures. The review included 11 studies of re-banding, 12 studies of conversion to LRYGB, 5 studies of conversion to laparoscopic BPD/DS, and 5 studies of conversion to LSG.

Among the 11 studies that examined re-banding, the most common indications were slippage, erosion, or pouch dilation. Ten of the 11 studies presented level III or level IV evidence, while one presented level II evidence. The follow-up period varied from 8 to 48 months after reoperation. The early complication rate ranged from 0% to 11%, the late complication rate ranged from 0% to 41%, and the reoperation rate ranged from 0% to 45%. Change in BMI was reported in 6 studies and ranged from +2.4 kg/m^2 to -5.8 kg/m^2.

Among the 12 studies of conversion to LRYGB, the most common indications were insufficient weight loss, band, erosion, and pouch dilation. Ten of the 12 studies presented level III or level IV evidence, while the remaining 2 presented level II evidence. The follow-up period ranged from 8.3 to 36 months after reoperation. The early complication rate ranged from 3% to 36%, the late complication rate ranged from 2% to 23%, and the reoperation rate ranged from 0% to 20%. Change in BMI was reported in 9 studies and ranged from -6.1 kg/m^2 to -13.2 kg/m^2. Percentage EWL was reported in 2 studies and ranged from 33% to 43%.

Among the 5 studies of conversion to BPD/DS, the most common indication was insufficient weight loss. All 5 studies presented level III or level IV evidence. The follow-up period ranged from 12 to 38 months after reoperation. The early complication rate ranged from 8% to 62%, the late complication rate ranged from 20.6% to >23.5%, and the reoperation rate ranged from 0% to 20.6%. Percentage of EWL was reported in 3 studies and ranged from 44% to 70%.

Among the 5 studies of conversion to LSG, the most common indication was insufficient weight loss. Four studies presented level IV evidence while 1 study presented level II evidence. The follow-up period ranged from 12 to 24 months after reoperation. The early complication rate ranged from 0% to 13.8%, the late complication rate ranged from 0% to 10.3%, and the reoperation rate ranged from 0% to 10.3%.

Percentage of EWL was reported in 2 studies and ranged from 20% to 65.7% while change in BMI was reported in 1 study as -4.4 kg/m^2.

The authors conclude that adjustable gastric banding should remain a first line procedure with re-banding or conversion to RYGB or BPD/DS as options for managing band failure.

Systematic Reviews Addressing Patient Selection

One poor quality and two good quality systematic reviews address patient selection criteria (Ochner, Dambkowski, Teomans, Teizeira, & Xavier Pi-Sunyer, 2012; Thomas & Agrqwal, 2012; WA HTA, 2015).

Ochner (2012)

Ochner et al. (2012) is a good quality narrative systematic review of 29 studies examining the effects of preoperative weight loss requirements on postoperative outcomes. The authors note that heterogeneity in the included studies precluded formal quantitative synthesis. Overall, the included studies were mostly observations and were mixed on the effects of preoperative weight loss requirements on postoperative weight loss outcomes. As the authors note, "studies of the relation between pre- and post-operative changes in body weight range from a positive relationship (preoperative weight loss associated with greater postoperative weight loss) to a negative relationship (preoperative weight loss associated with less postoperative weight loss) and many in between (no relationship)" (Ochner et al., 2012, p. 1381). The only included RCT deemed "viable" by the authors randomized 100 patients undergoing RYGB to a group with a requirement of 10% preoperative weight loss or a group with no preoperative weigh loss requirement. At six months after surgery, patients in the preoperative weight loss group had lost 54% of excess body weight compared to 51% excess body weight loss in the in the group without a preoperative weight loss requirement, but because only 37% of the original sample was analyzed at six months there was insufficient power to detect an effect.

The review also examined studies reporting on the effects of preoperative weight loss requirements on other outcomes including resolution of comorbid conditions. One study of 90 RYGB patients found that preoperative weight loss of >5% of excess body weight was associated with shorter operative times (36 minutes on average) but no difference in complications or resolution of comorbid conditions. Another study demonstrated that patients with preoperative weight loss of >5% of excess body weight were less likely to have a postoperative length of stay of >4 days. The RCT referenced above found no difference in the complication rate or resolution of comorbid conditions at six months. A fourth study found no correlation between preoperative weight changes and remission of diabetes or hypertension.

The authors' overall conclusion is that "[g]iven the inconsistency and questionable validity of the extant research…on the question of the effect of preoperative weight loss on peri- and postoperative outcomes, it is the opinion of these authors that insufficient evidence is currently available to justify a pre-bariatric surgery weight loss mandate" (Ochner et al., 2012, p. 1386).

Thomas (2012)

Thomas & Agarwal (2012) is a poor quality systematic review of a preoperative risk stratification tool known as the obesity surgery mortality risk score (OS-MRS). The OS-MRS assigns one point each for age greater than 45 years, male gender, BMI > 50 kg/m^2, hypertension, and known risk factors for pulmonary embolism. Scores of 0 to 1 are considered class A or lowest risk, scores of 2 to 3 reflect class B or intermediate risk, and scores of 4 to 5 are class C or high risk. This review included six studies reporting on 9,382 patients evaluating the validity of OS-MRS to predict postoperative mortality risk. Overall, there were 83 death in the 9,382 patients (0.88%). There were 13 deaths among the 4,912 class A patients (0.26%), 55 deaths among the 4,124 class B patients (1.33%), and 14 deaths among the 346 class C patients (4.34%). The mortality difference between classes were statistically significant at $p<0.05$. The authors conclude that use of the OS-MRS can stratify mortality risk in patients undergoing bariatric surgery (particularly RYGB which was the predominately studied procedure in the included studies).

WA HTA (2015)

The WA HTA report included a single retrospective comparative cohort study that stratified outcomes by patient adherence to preoperative program recommendations. In the laparoscopic AGB group, patients who did not attend >75% of their pre-procedure appointments had attenuated weight loss at 12 months of follow-up (23% EWL vs 32% EWL in patients with fewer missed appointment, p=0.01). There were no differences in RYGB performance related to pre-procedure appointment adherence.

A single study included in the WA HTA report concluded that patients with congestive heart failure and cardiac arrhythmias had a significantly increased risk of post-surgical complications compared with the overall cohort (40% vs 13.4% for open RYGB, 21.1% vs 8.6% for laparoscopic RYGB, and 17.4% vs 3.1% for laparoscopic AGB, all p-values <0.001). The same study reported that patients with peripheral vascular disease undergoing RYGB had significantly increased complication rates compared to those without peripheral vascular disease (32.0% vs 8.4%, p<0.001).

The WA HTA report also notes that it did not find studies that stratified outcomes by smoking status or psychosocial health that met inclusion criteria.

Systematic Reviews Addressing Systems of Care

One good quality systematic review addresses the effect of systems of care on bariatric surgery outcomes (Zevin, Aggarwal, & Grantcharov, 2012).

Zevin (2012)

Zevin et al. (2012) is a good quality systematic review of volume-outcome associations in bariatric surgery. The article reviews 24 observational studies comprising almost 460,000 patients. Meta-analysis was not performed due to a high level of heterogeneity that resulted, in part, from differences in duration of follow-up and risk-adjustment.

Thirteen studies addressed the relationship between annual surgeon case volume and patient outcomes. Across the five cohort studies that were included, there was consistent evidence of improved

outcomes with increasing surgeon volume. The results of lower quality studies (primarily retrospective cohorts) were mixed, but six of the eight studies supported an association between surgeon volume and outcomes.

Seventeen studies addressed the association between hospital volume and outcomes. While the two case-control studies that were included did not support an association between facility volume and outcomes, the preponderance of retrospective case series (14/15 studies) that were included found an association between facility volume and outcomes.

The authors conclude that there is strong evidence to support the association between surgeon volume and patient outcomes, and that weaker evidence supports the association between hospital volume and outcomes. Overall, they conclude that the literature "supports the BSCOE accreditation and the bariatric surgery fellowship training programs" (Zevin et al., 2012, p. 70).

WA HTA (2015)

The WA HTA report notes that pre-procedure support groups have shown little benefit, but that there is some evidence that patients in postoperative support groups experience improvements in psychological comorbidities and achieve greater weight loss. The WA HTA report cites one RCT of 144 Hispanic-American RYGB patients randomized to "comprehensive nutrition and lifestyle support or brief, printed healthy lifestyle guidelines…" At one year after surgery, patients in the comprehensive support group had greater reductions in BMI (6.48 kg/m^2 vs 3.63 kg/m^2, $p<0.001$).

Systematic Reviews Addressing Cost-effectiveness

WA HTA (2015)

The WA HTA report (2015) performed a cost-effectiveness analysis based on a model constructed by the authors. This analysis assumed a public payer perspective. The base-case analysis compared RYGB with standard care over a 10 year time horizon; other base-case assumptions included a procedural cost of $24,277, 20% worsening in BMI after 12 months, mean BMI at baseline of 40 kg/m^2, and a discounting rate of 3%. In the base-case analysis, the incremental cost-effectiveness of RYGB compared to standard care was $37,423 per quality-adjusted life year (QALY) gained. In the deterministic sensitivity analyses, the incremental cost-effectiveness estimates ranged from $5,444 per QALY to $84,971 per QALY. The estimates were most sensitive to changes in the time horizon, the cost of the bariatric surgical procedure, maintenance of weight loss after surgery, and baseline BMI. The WA HTA cost-effectiveness estimates, stratified by procedure and baseline BMI, are included in Appendix H.

There is very sparse evidence on the cost-effectiveness of bariatric surgery in children and adolescents. The only included systematic review which addresses this question is Aikenhead et al. (2011). The conclusions of this review are limited by the small number of studies, use of economic models that are not directly applicable to the U.S., and inferences from cost-effectiveness studies of bariatric surgery in adults.

EVIDENCE SUMMARY

Despite the existence of a large number of studies and systematic reviews, there remain substantial limitations to the evidence regarding bariatric surgery. Differences in patient characteristics, choice of surgical procedure, and individual components and intensity of non-surgical management arms make it difficult to summarize effects across studies. Variable measures of weight loss and wide variation in definitions of remission or resolution of comorbid conditions pose additional problems. Many of the studies included in the reviews were non-comparative, and the comparative observational studies suffer from risk of bias related to patient selection and residual confounding. The data from RCTs is limited by questions regarding proper allocation concealment and the universal absence of blinding. Perhaps the greatest concern is the limited long term follow-up of patients from RCTs and incomplete outcomes data due to high rates of attrition in most studies.

Overall, the following conclusions can be drawn based on review of the summary literature:

1. Bariatric surgery is associated with lower rates of all-cause mortality and major adverse cardiovascular events in adults, despite a short term increased risk of perioperative mortality and complications (based on low certainty evidence from cohort studies with long term follow-up, with study populations consisting predominantly of patients with BMI ≥35).
2. Bariatric surgery is associated with significant reductions in BMI in adults, despite a short term increased risk of perioperative mortality and complications (based on moderate certainty evidence from a mix of observational and randomized trials). The effects on weight loss appear to be greatest in patients with baseline BMI ≥40 based on the BMI stratification provided in the WA HTA report.
3. Bariatric surgery is associated with remission or resolution of T2DM and hypertension in adults with BMI ≥ 35, despite a short term increased risk of perioperative mortality and complications (based on moderate certainty evidence from a mix of observational and randomized trials).
    - The effects on remission of T2DM appear to be greatest in patients with baseline BMI ≥40 based on the BMI stratification provided in the WA HTA report.
    - Preliminary evidence suggests that adults with BMI < 35 may also achieve significant reductions in BMI and improvement in comorbid T2DM and hypertension, though the long term effects are not yet clear.
4. Bariatric surgery is associated with significant reductions in BMI in children and adolescents, despite a short term increased risk of perioperative mortality and complications (based on low certainty evidence primarily from small, non-comparative observational trials of bariatric surgery for pediatric obesity).

5. Bariatric surgery is associated with remission or resolution of T2DM and hypertension in children or adolescents, despite a short term increased risk of perioperative mortality and complications (based on very low certainty evidence from a small number of trials).
6. There is no evidence-based minimum age recommendation for pediatric bariatric surgery. Patients as young as five years old were included in the studies reported in the summary literature.
7. There is low certainty conflicting evidence on the effects of preoperative weight loss requirements.
8. The obesity surgery mortality risk score (OR-MRS) is a validated preoperative assessment of perioperative mortality risk (particularly for RYGB procedures) and may be useful in selecting patients for surgery or counseling them on surgical risks.
9. Harms of bariatric surgery include a perioperative mortality rate that probably ranges from 0.10 to 2%, and an overall complication rate that is probably on the order of 8 to 25%. The estimated reoperation rate is likely between 2 and 13%. There is limited evidence from a single study that comorbid congestive heart failure, cardiac arrhythmias, and peripheral vascular disease are associated with higher rates of complications after bariatric surgery.
10. There is low certainty evidence that surgeon experience is associated with improved outcomes and very low certainty evidence that hospital bariatric surgical volume is associated with improved outcomes.
11. There is very low certainty evidence that revisional or conversion procedures performed after an initial bariatric surgery may achieve additional weight loss (particularly those procedures that convert AGB to RYGB or BPD/DS), but at the expense of a higher rate of complications. Systematic reviews offer no evidence that bariatric reoperation improved co-morbidity resolution.

OTHER DECISION FACTORS

Resource allocation

Bariatric surgery for adults is costly, but improved outcomes compared with non-surgical management may offset these costs. The WA HTA report cites total costs of bariatric surgical procedures as ranging from $17,483 for gastric banding to $36,160 for biliopancreatic diversion. By comparison, standard non-surgical care has a reported total cost of $3,746. Accounting for reductions in BMI, resolution of comorbid conditions, and complications of surgery and projecting costs and effectiveness over a 10-year horizon, bariatric surgical procedures are uniformly cost-effective at a willingness-to-pay threshold of $100,000 per QALY gained. This was true across BMI thresholds and surgical procedures. Excerpts from the economic analysis in the WA HTA report are provided in Appendix H.

Bariatric surgery for children is also costly, but improved outcomes may offset these costs, and the beneficial effects could accrue over the longer time horizon afforded by earlier intervention in children and adolescents. However, there is very limited evidence of cost-effectiveness of pediatric bariatric surgery. The pediatric cost-effectiveness information included in the review by Aikenhead et al. in 2011 used assumptions from Australia that are likely too indirect to influence deliberations on resource allocation.

Reoperations for additional weight loss are sometimes requested; a second high cost procedure (tens of thousands of dollars), with a history of prior failure is unlikely to show a favorable cost-effectiveness ratio.

Values and preferences

Adults

Most people would prefer to avoid surgery and its attendant risks if similar results could be attained through safer and less invasive interventions. However, patients who have failed to achieve adequate weight loss with less invasive interventions may decide that the superior outcomes of bariatric surgery (including long term improvements in all-cause mortality, complete remission of diabetes, and significant weight loss) outweigh the upfront risks of surgery. Overall, there would be a moderate variability given these considerations.

Children and adolescents

Similar to adults, most children and their parents would prefer to avoid surgery and its attendant risks if similar results could be attained through safer and less invasive interventions. However, patients who may have failed to achieve adequate weight loss with less invasive interventions may decide that bariatric surgery offers the best chance at weight reduction. The significant social pressures of obesity at a young age may also push children and their parents to have strong interest in an effective treatment. Children though would likely have a great fear of surgery and the associated procedures and loss of social/academic participation. However, additional uncertainties related to malnutrition in this age group and its effects on growth, development, and reproductive capacity may make surgery less appealing in children and adolescents (to their caregivers). Long term remission rates of morbid obesity and recurrence of the comorbidities are unknown; most studies report outcomes at one year, although a few studies report outcomes at up to three years. Given these considerations, there would be high variability in children's and parents preferences.

Re-operations for inadequate weight loss

There would be high variability in patient preferences regarding reoperation. With a prior failure of the procedure, some patients would be hesitant to try an additional procedure given the burdens of surgery and prior ineffectiveness, but others would be motivated to try a different procedure in hopes that it would work. Patients seeking reoperation likely have no other good option given failure of multiple previous alternatives (e.g. clinical, pharmacological, nutritional, physical activity, surgical).

Other factors

Adults

The greatest health benefits may be with BMI ≥ 40 but otherwise specific subpopulations which would benefit the most from bariatric surgery are not well characterized.

The pre-operative requirements for achieving optimal outcomes are unclear.

Given the rate of complications and need for reoperation reported in the summary literature, benefit plans may wish to consider alternative payment methodologies like bundled payments or a pay-for-outcomes approach.

Surgeon case volume, and to a lesser extent hospital case volume, appear to affect outcomes for patients undergoing bariatric surgery and requirements regarding surgeon or facility volume may be reasonable.

Children and adolescents

Parental involvement in weight management plans is likely necessary to assist the effectiveness of obesity treatments (based on expert opinion).

Pediatric bariatric surgery is likely to be available at only a few highly specialized centers. The American Academy of Pediatrics has 10 criteria that pediatric bariatric surgery programs should meet.

Re-operations for inadequate weight loss

It is unclear from the evidence which modifiable patient factors that resulted in surgical failure would predict a high likelihood of success or failure of a second procedure.

POLICY LANDSCAPE SOURCES

Quality measures

One bariatric surgery-specific quality measure was identified when searching the National Quality Measures Clearinghouse:

- Prevention and management of obesity for adults: percentage of patients with a BMI greater than or equal to 40 who have been provided with a referral to a bariatric specialist (Institute for Clinical Systems Improvement)

Payer coverage policies

Medicare (National Coverage Determination [NCD] 100.1), Washington Medicaid, Aetna, Cigna, Regence Blue Cross Blue Shield, and Moda all provide coverage of bariatric surgery. Each coverage policy outlines specific coverage criteria that must be met prior to bariatric surgery being approved. These criteria are described below and provided in more detail in Appendix E.

Age

All six payers provide coverage of bariatric surgery for adults (defined as at least 18 years), and Aetna and Cigna additionally provides coverage for adolescents (defined as an individual with completed skeletal growth). Washington limits the procedure type to LAGB only for individuals aged 18 to 20 years.

Body Mass Index

For adults, Aetna, Cigna and Moda require individuals have a BMI of greater than or equal to 40 kg/m^2, or greater than or equal to 35 kg/m^2 with specific comorbidities. Washington and NCD 100.1 cover individuals with a BMI of greater than or equal to 35 kg/m^2 with comorbidities, and Regence BCBS requires that an individual have a BMI of greater than or equal to 40 kg/m^2 or a BMI of greater than, or equal to 35 kg/m^2 with type 2 diabetes or at least two other specified comorbidities. Washington is the only identified payer that explicitly requires individuals not be pregnant at the time of the surgery.

For adolescents, Aetna covers individuals with a BMI of greater than 40 kg/m^2 who have serious comorbidities, or individuals with a BMI of greater than 50 kg/m^2 with less serious comorbidities. Cigna uses the same BMI criteria as the adult population.

Comorbidities

Diabetes is the only comorbidity specified by all five payers. Payers specify various combinations of other comorbid conditions including coronary heart disease, dyslipidemia, hypertension, lower extremity lymphatic or venous obstruction, mechanical arthopathy in major weight bearing joint, rare comorbid conditions (e.g., pseudo tumor cerebri), and obstructive sleep apnea. Aetna specifies several less severe comorbidities for adolescents with a BMI of over 50 including gastroesphageal reflux disease, intertriginous soft-tissue infection, nonalcoholic steatohepatitis, obesity-related psychosocial distress, significant impairments in daily living, and stress urinary incontinence.

Pre-Surgical Requirements

Five payers require individuals to undergo a comprehensive psychosocial evaluation and participate in a formal weight loss program prior to being approved for bariatric surgery (Aetna, Cigna, Moda, Regence BCBS, and Washington). Three payers require a separate medical evaluation (Washington, Cigna, Moda), surgical evaluation (Washington, Cigna), and nutritional evaluation (Cigna, Moda) prior to surgery. The NCD 100.1 requires that individuals have been previously unsuccessful with medical treatment for obesity.

Payers require an individual attend a formal weight loss program within six months (Washington) to two years of surgery (Aetna, Regence BCBS, Moda). The weight loss program must be greater than or equal to three (Cigna) to six months in duration (Washington, Aetna, Regence BCBS, Moda). Both Washington and Moda require that individuals lose 5% of their initial body weight as part of the weight loss program prior to surgery. Aetna's policy states that there can be no net weight gain during weight loss program attendance. Payer coverage policies include a variety of additional required program components including counseling by a registered dietitian, patient journal of participation, regular face-to-face provider visits, behavior modification, supervised exercise regimen, and hypocaloric diet changes.

Provider Requirements

Washington Medicaid and Moda state that bariatric surgery is only covered if provided by an approved facility, defined by Moda as a Center of Excellence and by Washington with specific criteria. Bariatric surgery facilities approved by Washington Medicaid must have performed a minimum of 100 bariatric surgical procedures, be under the direction of an experienced board-certified surgeon, been in operation for at least five years, have a 2% or less mortality rate, have a 15% or less morbidity rate, have at least five years of patient follow-up data, have an average of at least 50% patient weight loss at five years, and have a reoperation/revision rate of 5% or less.

The Centers for Medicaid and Medicare have approved six facilities in Oregon to perform bariatric surgery: Bay Area Hospital, Legacy Good Samaritan Hospital and Medical Center, Oregon Health & Science University, Sacred Heart Medical Center, Salem Hospital, St. Charles Medical Center – Bend.

Repeat Surgery Coverage

Aetna, Cigna and Regence BCBS address repeat bariatric surgery and outline specific circumstances under which it is covered. All three payers provide coverage to correct complication from the initial surgery, and conversion from gastric banding to sleeve gastrectomy, RYGB or BPD/DS. Aetna and Cigna specify that conversion surgery is covered for individuals who have not lost more than 50% of their body weight two years following the primary bariatric surgery. Cigna will cover the adjustment of the silicone gastric band and repeat surgery for a failed dilation of a gastric pouch. Aetna will additionally cover removal of a gastric band, replacement of adjustable band, and repeat surgery for a failed dilation of a gastric pouch.

Non-Covered Procedures

Aetna, Cigna, and Regence BCBS outline specific conditions and procedures that are not in the coverage of bariatric surgery. Across all three payers, gastroplasty ("stomach stapling"), laparoscopic gastric plication, mini gastric bypass, transoral endoscopic surgery (e.g., OverStich suturing device, StomaphX™, TOGA®), are not covered. In addition, Aetna and Cigna do not cover gastrointestinal liners (e.g., EndoBarrier™), intragastric balloon, loop gastric bypass, silastic ring vertical gastric bypass (e.g., Fobi pouch), or vagus nerve blocking. Aetna and Regence BCBS do not cover band over bypass surgeries, band or sleeve gastrectomy surgeries, sclerotherapy for the treatment of dilated gastrojejunostomy following bariatric surgery, or for gastroesophageal reflux disease in non-obese individuals. Cigna and Regence BCBS do not cover intestinal bypass (jejunoileal bypass) or restorative obesity surgery (e.g., ROSE). Regence BCBS specifically does not cover vertical banded gastroplasty; Aetna covers this procedure for members who are at increased risk of adverse consequences from Roux-en-Y gastric bypass due to certain gastrointestinal conditions (see Appendix E).

The NCD 100.1 does not provide coverage for open adjustable gastric banding, open sleeve gastrectomy, open and laparoscopic vertical banded gastroplasty, intestinal bypass surgery, and gastric balloon for treatment of obesity.

Professional society guidelines

Adults

The Institute for Clinical Systems Improvement (ICSI) (Fitch et al., 2013a) (good quality), Veterans Administration (VA) (Management of Overweight and Obesity Working Group, 2014) (good quality), the American Association of Clinical Endocrinologists, Obesity Society, American Society for Metabolic & Bariatric Surgery (Mechanick et al., 2013) (poor quality primarily), the Australian National Health and Medical Research Council (NHMRC) (NHMRC, 2013) (good quality), and the National Institute for Health and Care Excellence (NICE) (NICE, 2014) (good quality) provide recommendations on the use of bariatric surgery in adults. The guideline from the American Heart Association/American College of Cardiology/The Obesity Society (Jensen et al., 2014) (good quality) provides a summary of the evidence related to the long-term effectiveness of bariatric surgeries and the long-term effects of these procedures on varying BMI levels with and without comorbidities. The guideline does not provide clinical practice recommendations.

All identified guidelines consistently recommend bariatric surgery for individuals with a BMI of greater than 40 kg/m^2, or greater than 35 kg/m^{2}with significant comorbidities. There is some variance between guidelines in what comorbidities are considered significant. For example, only two of the five guidelines list gastroesophageal reflux disease as a significant comorbidity. Four guidelines (AACD/OS/ASMBS, ICSI, NHMRC, NICE) recommend bariatric surgery be considered for individuals with a BMI of greater than 30 kg/m^{2}who have severe comorbidities such as diabetes, and NICE recommends bariatric surgery for individuals of Asian descent with recent-onset diabetes who may have a lower BMI than other

populations. The VA determined that there was insufficient evidence to recommend the use of bariatric surgery for individuals with a BMI less than 35 kg/m^2.

The AACD/OS/ASMBS and NICE guidelines recommend individuals have pre-surgical comprehensive medical and psychological evaluations. The use of multidisciplinary teams consisting of surgical, medical, nutrition, and psychological expertise is recommended by NICE and NHMRC.

Children

The ICSI (Fitch et al., 2013b) (good quality), the Australian NHMRC (NHMRC, 2013), and NICE (NICE, 2014) provide recommendations on indications for bariatric surgery in the pediatric population. Both the ICSI and NHMRC guidelines recommend bariatric surgery as an option for adolescents with a BMI greater than 40, or greater than 35 with severe comorbidities. The NHMRC specifies that only laparoscopic gastric banding performed by a specialist bariatric/pediatric surgical team is recommended for adolescents. The guideline from ICSI is the most comprehensive and recommends detailed pre-surgical evaluations, failed attempts at weight loss through formal weight loss programs, and the use of multidisciplinary team at regional bariatric centers of excellence. ICSI further recommends that children have attained Tanner stage 4 or 5 or have bone age of ≥13 years in girls or ≥15 years in boys before considering bariatric surgery. Pediatric bariatric surgery is not recommended by NICE except in the case of exceptional circumstances.

Assessment of congruence between guidelines and evidence

In general, the clinical practice guideline recommendations for adults are supported by the available evidence. Patients with BMI ≥40 kg/m^2 or with BMI 35 to 39.9 with obesity-related comorbid conditions have been well studied in the literature, and the clinical practice guidelines reflect this stronger evidence base. The divergence in the recommendations for patients with BMI 30 to 34.9 probably reflects the smaller number of studies that specifically address this population and the shorter follow-up periods reported in these studies. Recommendations regarding pre-surgical evaluations may reflect expert practice tips, but are not directly supported by the summary literature. Similarly, recommendations regarding preoperative weight loss are based on expert opinion and are not directly supported by the summary literature.

The wider variation in the recommendations for bariatric surgery in children reflects greater uncertainty about both the effectiveness and the adverse effects of surgery. When surgery is recommended for children, there is general agreement based on expert opinion that this should be performed at regional centers of excellence.

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Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

APPENDIX A. METHODS

Scope Statement

Populations

Obese individuals who are being considered for bariatric or metabolic surgery

Population scoping notes: *Include <18. Exclude overweight (BMI<30)*

Interventions

Bariatric or metabolic surgery (Adjustable gastric banding, Roux-en-y gastric bypass, biliopancreatic diversion, duodenal switch, vertical sleeve gastrectomy)

Intervention exclusions: *Gastric balloon (not FDA approved)*

Comparators

Nonsurgical treatment (medical management, pharmacotherapy, intensive multicomponent behavioral interventions, behavioral counseling, structured weight management programs (e.g. Weight Watchers)

Outcomes

Critical: All-cause mortality, Major Cardiac Events (MACE)

Important**:** Resolution of hypertension, weight loss, resolution of type 2 diabetes

Considered but not selected for the GRADE table: Hyperlipidemia, arthritis, sleep apnea, CPAP use, medication use

Key Questions

1. Should coverage be recommended for bariatric surgery in each of the scenarios in the table below? (Note that the "resolution of diabetes" would not be an applicable outcome in scenarios 4-9)

	BMI 30-34.9	BMI 35-39.9	BMI>=40
With DM2	Scenario 1	Scenario 2	Scenario 3
W/o DM2 nor other comorbidities	Scenario 4*	Scenario 5*	Scenario 6*
w/o DM2 but with other comorbidities	Scenario 7*	Scenario 8*	Scenario 9*

*Resolution of type 2 diabetes isn't a relevant outcome for this population

2. What is the appropriate minimum age for bariatric surgery?

3. What components and systems of care are associated with improved health outcomes? (e.g., centers of excellence, surgeon's experience, etc.)
4. What preoperative assessments or requirements for preoperative weight loss should be recommended in patients being considered for bariatric surgery?

Search Strategy

A full search of the core sources was conducted to identify systematic reviews, meta-analyses, technology assessments, and clinical practice guidelines using the terms "bariatric." Searches of core sources were limited to citations published after 2004 with one exception (see inclusion criteria).

The core sources searched included:

Agency for Healthcare Research and Quality (AHRQ)
Blue Cross/Blue Shield Health Technology Assessment (HTA) program
BMJ Clinical Evidence
Canadian Agency for Drugs and Technologies in Health (CADTH)
Cochrane Library (Wiley Interscience)
Hayes, Inc.
Institute for Clinical and Economic Review (ICER)
Medicaid Evidence-based Decisions Project (MED)
National Institute for Health and Care Excellence (NICE)
Tufts Cost-effectiveness Analysis Registry
Veterans Administration Evidence-based Synthesis Program (ESP)
Washington State Health Technology Assessment Program (WA HTA)

A recent technology assessment from the WA HTA program was identified as the most comprehensive review identified (WA HTA, 2015). A MEDLINE® (Ovid) search was then conducted to identify systematic reviews, meta-analyses, and technology assessments published after the search dates of the WA HTA report. The search was limited to publications in English published after 2014 (the end search date for the WA HTA systematic review).

Searches for clinical practice guidelines were limited to those published since 2010. A search for relevant clinical practice guidelines was also conducted, using the following sources:

Australian Government National Health and Medical Research Council (NHMRC)
Centers for Disease Control and Prevention (CDC) – Community Preventive Services
Choosing Wisely
Institute for Clinical Systems Improvement (ICSI)
National Guidelines Clearinghouse
New Zealand Guidelines Group
NICE
Scottish Intercollegiate Guidelines Network (SIGN)

United States Preventive Services Task Force (USPSTF)
Veterans Administration/Department of Defense (VA/DOD)

Inclusion/Exclusion Criteria

Due to the volume of available literature related to the effectiveness of bariatric surgery in adults (Key Question #1), reviews were limited to those published after 2013. Center staff dual quality assessed the identified reviews and only included those that were rated as good quality.

Studies were excluded if they were not published in English, did not address the scope statement, or were study designs other than systematic reviews, meta-analyses, technology assessments, or clinical practice guidelines. The following systematic review was excluded because it only included studies that were found in the other systematic reviews:

Ashrafian, H., Toma, T., Rowland, S. P., Harling, L., Tan, A., Efthimiou, E., … Athanasiou, T. (2014). Bariatric surgery or non-surgical weight loss for obstructive sleep apnoea? A systematic review and comparison of meta-analyses. *Obesity Surgery, 25*(7), 1239-50. DOI: 10.1007/s11695-014-1533-2.

APPENDIX B. GRADE INFORMED FRAMEWORK - ELEMENT DESCRIPTIONS

Element	Description
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Other considerations	Other considerations include issue about the implementation and operationalization of the technology or intervention in health systems and practices within Oregon.

Strong recommendation

In Favor: The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Against: The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Weak recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Quality or strength of evidence rating across studies for the treatment/outcome[1]

High: The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.

Moderate: The subcommittee is moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

[1] Includes risk of bias, precision, directness, consistency and publication bias

***Low*:** The subcommittee's confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.
***Very low*:** The subcommittee has very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

APPENDIX C. GRADE EVIDENCE PROFILE

Quality Assessment (Confidence in Estimate of Effect) – Adults							
No. of Studies	**Study Design(s)**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Factors**	**Quality**
All-cause Mortality[1]							
14	Cohort	Moderate	Consistent	Direct	No serious imprecision	Large effect size	Low confidence in estimate of effect ●●○○
Major Adverse Cardiovascular Events[1]							
4	Cohort	Moderate	Consistent	Direct	No serious imprecision	Large effect size	Low confidence in estimate of effect ●●○○
Type 2 DM Remission/Resolution[2]							
60	15 RCTs; 45 observational studies	Moderate to High	Consistent	Direct	Imprecise	None	Moderate confidence in estimate of effect ●●●○
Hypertension Remission/Resolution[2]							
52	13 RCTs; 39 observational studies	Moderate	Consistent	Direct	Imprecise	None	Moderate confidence in

Quality Assessment (Confidence in Estimate of Effect) – Adults							
No. of Studies	**Study Design(s)**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Factors**	**Quality**
							estimate of effect ●●●○
Change in BMI[2]							
101	28 RCTs; 73 observational studies	Moderate to High	Consistent	Direct	Imprecise	None	Moderate confidence in estimate of effect ●●●○

[1] Studies from Tables 1 and 2(Kwok, 2014). Strength of evidence assessment based on Table 2 in Kwok (2014).

[2]Studies and strength of evidence assessment based on Figure 2 of Colquitt (2014), Supplemental Table 1 of Muller-Stich (2015), and the description of study quality from the WA HTA review (2015, p.27-28). Chang (2014) does not provide individual study risk of bias assessments.

Quality Assessment (Confidence in Estimate of Effect) – Children and Adolescents							
No. of Studies	**Study Design(s)**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Factors**	**Quality**
All-cause Mortality							
0	NA	NA	NA	NA	NA	NA	Insufficient evidence
Major Adverse Cardiovascular Events							
0	NA	NA	NA	NA	NA	NA	Insufficient evidence

Quality Assessment (Confidence in Estimate of Effect) – Children and Adolescents							
No. of Studies	**Study Design(s)**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Factors**	**Quality**
Type 2 DM Remission/Resolution[1]							
13	13 observational studies	High	Consistent	Direct	Imprecise	None	Very low confidence in estimate of effect ●○○○
Hypertension Remission/Resolution[1]							
15	15 observational studies	High	Consistent	Direct	Imprecise	None	Very low confidence in estimate of effect ●○○○
Change in BMI[1]							
28	1 RCT; 27 observational studies	High	Consistent	Direct	Imprecise	None	Low confidence in estimate of effect ●●○○

[1] Studies from Black (2013) and Treadwell (2008).

APPENDIX D. MORTALITY BENEFIT OUTCOMES FROM KWOK (2014) SYSTEMATIC REVIEW AND META-ANALYSIS

Several large cohort studies with long-term follow-up comparing bariatric surgery patients to non-surgical controls have demonstrated a consistent reduction in all-cause mortality (as summarized in the meta-analysis in Kwok 2014). In the included cohort studies that performed direct subgroup analysis by BMI, the effects of bariatric surgery appear to be stronger in patients with higher BMI, though other cohorts that report proportional hazard ratios using BMI of 35-40 kg/m2 as the reference find increasing mortality in BMI groups >40. Only two of the cohorts reported outcomes by baseline comorbidities. In the Swedish Obese Subjects study (Sjostorm, 2012), patients with T2DM may have benefited more than those without T2DM, while patients with SBP <140 may have benefited more than hypertensive patients; however, in both scenarios the 95% confidence intervals overlap. It should be noted that Sjostrom reported on the incidence of cardiovascular events rather than mortality and that 70% of the patients received vertical banded gastroplasty, a procedure that is no longer used in the United States. Scott (2013) reports on a cohort of bariatric patients compared to matched controls undergoing either orthopedic or gastrointestinal procedures. There were no significant differences based on the presence of HTN in either group or T2DM in the bariatric-orthopedic comparison; among T2DM patients in the bariatric-GI comparison, there was a slight increase in the proportional hazard of mortality. Two other cohort studies (Arterburn, 2013 and Johnson, 2013) only included patients with T2DM at baseline.

Caution should be exercised in interpreting subgroup analyses from these cohorts given the potentially small number of patients involved. Individual studies with pre-specified inclusion criteria based on comorbidities are more likely to provide accurate estimates of the effects in these groups. On balance, there is insufficient evidence from these cohort studies to conclude that the effects of bariatric surgery on long-term mortality vary based on pre-operative BMI or the presence of comorbid conditions.

Studies in the table below were reviewed in the following article: Kwok, C. S., Pradhan, A., Khan, M. A., Anderson, S. G., Keavney, B. D., Myint, P. K., … Loke, Y. K. (2014). Bariatric surgery and its impact on cardiovascular disease and mortality: a systematic review and meta-analysis. International Journal of Cardiology, 173(1), 20-28. DOI: 10.1016/j.ijcard.2014.02.026

Study	Population (surgical group)	Overall effect of surgery on mortality (95% CI)	Effect of surgery on mortality by BMI (95% CI)	Mortality effect by comorbidities (95% CI)
Adams (2007) Matched retrospective cohort	9,949 adults RYGB Avg BMI 44.9	HR 0.63 (0.53 to 0.74) (all subjects) HR 0.60 (0.45 to 0.67) (matched subjects)	BMI<45 HR 0.72 (0.53 to 0.99) BMI >45 HR 0.56 (0.43 to 0.74)	NR
Arterburn (2013) Retrospective cohort	1,395 adults 80% RYGB BMI>35 and T2DM	HR 0.54 (0.22 to 1.30)	NR	NR
Busetto (2007) Matched cohort	821 adults LAGB BMI>40	RR 0.36 (0.16 to 0.79)	BMI 40-49 RR 0.67 (0.23 to 1.94) BMI>50 RR 0.21 (0.21 to 0.75)	NR
Christou (2004) Retrospective cohort	1,035 adults RYGB Mean BMI 50.0	RR 0.11 (0.04 to 0.27)	NR	NR
Flum (2004) Retrospective cohort	3,328 adults Any gastric bypass "Morbidly obese" (by ICD codes) 13% T2DM	HR 0.67 (0.54 to 0.85)	NR	NR
Gentileschi (2012) Prospective cohort	208 adults RYGB, VSG, AGB Avg BMI 46.6 31% T2DM, 48% HTN	1/208[i] (surgical group) 4/81 (non-surgical group)	NR	NR

BMI=Body mass index (reported in kg/m^2), CAD=Coronary artery disease, HR=Hazard ratio, HTN=Hypertension, LAGB=Laparoscopic Adjustable gastric banding, NR=Not reported, RR=Relative risk,

Johnson (2013) Retrospective cohort	2,580 adults with T2DM Any bariatric surgery Avg BMI 47 82% HTN, 8.6% CAD	41/2580[ii] (surgical group) 985/13,371 (non-surgical group)	NR	NR
Maciejewski (2011) Retrospective cohort	850 adults (Vets) RYGB Avg BMI 47	HR 0.64[iii] (0.51 to 0.80)	BMI 35-39 HR 1.0 (reference)[iv] BMI 40-49 HR 1.22 (1.16 to 1.27) BMI >50 HR 1.71 (1.59 to 1.85)	NR
Miranda (2012) Retrospective cohort	2,020 adults 95% RYGB Avg BMI 49	HR 0.76 (0.60 to 0.96)	NR	NR
Peeters (2007) Prospective cohort	966 adults LAGB Avg BMI 45	HR 0.28 (0.10 to 0.85)	BMI <40 HR 0.89 BMI >40 HR 0.16	NR
Scott (2013) Retrospective Cohort	4,747 adults Any bariatric surgery "Morbid obesity" (by ICD codes) 41% T2DM, 71% HTN, 5% CAD	HR 0.72 compared to matched ortho surgery pts (0.58 to 0.89) HR 0.48 compared to matched GI surgery pts (0.39 to 0.61)	NR	Bariatric-ortho[v] HTN HR 1.02 (0.8 to 1.4) T2DM HR 1.14 (0.9 to 1.5) Bariatric-GI HTN HR 0.79 (0.6 to 1.1) T2DM HR 1.49 (1.1 to 2.0)

RYGB=Roux-en-Y gastric bypass, SBP=Systolic blood pressure (reported in mmHg), T2DM=Type 2 diabetes mellitus, VSG=Vertical sleeve gastrectomy

[i] Reported as crude event rates

[ii] Reported as crude event rates

Sjostrom (2012) Prospective cohort	2,010 adults 70% gastroplasty	HR 0.83[vi] (0.69 to 1.00)	BMI <40.8 HR 0.91 (0.70 to 1.18) BMI >40.8 HR 0.8 (0.60 to 1.06)	T2DM HR 0.63 (0.45 to 0.90) No TD2M HR 0.84 (0.67 to 1.06) SBP<140 HR 0.63 (0.46 to 0.86) SBP>140 HR 0.82 (0.64 to 1.04)
Sowemimo (2007) Retrospective cohort	908 adults Nearly all RYGB BMI>40 or >35 with comorbidities Mean BMI 54	HR 0.18 (0.09 to 0.35)	NR	NR

[iii] Reported after unadjusted Cox regression; after adjustment for covariates, the HR was 0.80 (95% CI 0.63 to 0.995). An analysis of propensity matched patients resulted in a HR of 0.83 (95% CI 0.61 to 1.14).

[iv] Reported as adjusted Cox proportional hazards

[v] Reported as Cox proportional hazards

[vi] Primary outcome in Sjostrom was not mortality but incidence of CV events (included here because of its analysis by comorbidity)

[vii] Reported as adjusted Cox proportional hazards

APPENDIX E. BARIATRIC SURGERY COVERAGE

Table E1. Bariatric Surgery Coverage – Adults

Coverage criteria	Payer				
	Washington Medicaid	Aetna[1]	Cigna[2]	Regence BCBS[3]	Moda
Patient Characteristics					
Age	18 – 20 yrs (LAGB obly) 21 – 59 yrs (all procedures)	≥ 18 yrs	≥ 18 yrs	≥ 18 yrs	≥ 18 yrs
BMI	≥ 35 with comorbidities 30-34.9 with DM2 (*see below*)	> 40 > 35 with comorbidities (*see below*)	≥ 40 ≥ 35 with comorbidities (*see below*)	≥ 40 ≥ 35 with DM2 or at least two other comorbidities (*see below*)	≥ 40 ≥ 35 with comorbidities (*see below*)
Not pregnant	√	---	---	---	---
Comorbidities					
Coronary heart disease	---	√	√	√	√
Diabetes	√	√	√	√	√
Dyslipidemia	---	---	√	√	---
Hypertension	---	√	√ (poorly controlled or pulmonary)	√	√
Lower extremity lymphatic or venous obstruction	---	---	√	---	---
Mechanical arthopathy in major weight bearing joint	√	---	√	---	√
Rare comorbid conditions (e.g., pseudo tumor cerebri)	√[4]	---	---	---	---
Sleep apnea	---	√	√	√	√
Absence of other medical conditions (e.g., multiple sclerosis)	√	---	---	---	√

Key: √ – required; --- – not in policy description

Abbreviations: BCBS – Blue Cross Blue Shield; BMI – body mass index; LAGB – laparoscopic adjustable gastric banding; yrs – years

Notes:

1. Specific to open or laparoscopic Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable silicone gastric banding (LASGB), open or laparoscopic sleeve gastrectomy, open or laparoscopic biliopancreatic diversion (BPD), and duodenal switch (DS).
2. Specific to open or laparoscopic Roux-en-Y gastric bypass, open or laparoscopic adjustable silicone gastric banding (LAP-BAND®, REALIZE™), open or laparoscopic biliopancreatic diversity with duodenal switch (BPD/DS) for individuals with a BMI >50, open or laparoscopic sleeve gastrectomy, open or laparoscopic vertical banded gastroplasty
3. Roux-en-Y with an alimentary limb of 150 cm or less, sleeve gastrectomy as a stand-alone procedure, or adjustable gastric banding
4. Must be medical evidence that bariatric surgery is medically necessary and that the benefits of bariatric surgery outweigh the risk of surgical mortality

Table E2. Bariatric Surgery Coverage – Children

Coverage criteria	Payer	
	Aetna[1]	Cigna[2]
Patient Characteristics		
Age	Adolescents who have completed bone growth (~13 yrs in girls, ~15 yrs in boys)	Reached full expected skeletal growth
BMI	> 40 with serious comorbidities > 50 with less serious comorbidities	≥ 40 ≥ 35 with comorbidities
Comorbidities		
Coronary artery disease	---	√
Diabetes	√ (>40 BMI)	√
Dislipidemias	√ (> 50 BMI)	√
Gastroesophageal reflux disease	√ (> 50 BMI)	---
Hypertension	√ (> 50 BMI)	√ (poorly controlled or pulmonary)
Intertriginous soft-tissue infection	√ (> 50 BMI)	---
Mechanical arthropathy in a major weight bearing joint	√ (> 50 BMI)	√
Nonalcoholic steatohepatitis	√ (> 50 BMI)	---
Obesity-related psychosocial distress	√ (> 50 BMI)	---
Rare comorbid conditions (e.g., pseudo tumor cerebri)	√ (>40 BMI)	---
Significant impairments in daily living	√ (> 50 BMI)	---
Sleep apnea	√ (>40 BMI)	√
Stress urinary incontinence	√ (> 50 BMI)	---
Venous stasis disease	√ (> 50 BMI)	√

Key: √ – required; --- – not in policy description Abbreviations; BMI – body mass index; yrs - years

Notes:

1. Specific to open or laparoscopic Roun-en-Y gastric bypass (RYGB), laparoscopic adjustable silicone gastric banding (LASGB), open or laparoscopic sleeve gastrectomy, open or laparoscopic biliopancreatic diversion (BPD), and duodenal switch (DS)
2. Specific to open or laparoscopic Roux-en-Y gastric bypass, open or laparoscopic adjustable silicone gastric banding (LAP-BAND®, REALIZE™), open or laparoscopic biliopancreatic diversity with duodenal switch (BPD/DS) for individuals with a BMI >50, open or laparoscopic sleeve gastrectomy, open or laparoscopic vertical banded gastroplasty

Table E3. Pre-Surgical Requirements

Coverage criteria	Payer				
	Washington Medicaid	**Aetna**[1]	**Cigna**[4]	**Regence BCBS**	**Moda**
Patient Evaluation					
Comprehensive psychosocial evaluation	√[2]	√[3]	√	√	√
Internal medicine evaluation	√	---	√	---	√
Surgical evaluation	√	---	√	---	---
Nutrition evaluation	---	---	√	---	√
Weight Loss Program					
Required	√	√ (physician-supervised *or* multi-disciplinary surgical prep regimen)	√ (physician- or registered dietician-supervised)	√ (physician-supervised)	√
Timing	Within 180 days of surgery	Within 2 years of surgery (physician-supervised) Within 6 months of surgery (surgical prep regimen)	Within 1 year of surgery	Within 2 years of surgery	Within 2 years of surgery
Duration	≥ 6 months	Cumulative total ≥ 6 months, one program ≥ 3 months (physician-supervised) ≥ 3 months (surgical prep regimen)	≥ 3 months	≥ 6 months	≥ 6 months
Required weight loss	5% of initial body weight	No net weight gain during program	---	----	5% of initial body weight over 6 months

Coverage criteria	Payer				
	Washington Medicaid	Aetna[1]	Cigna[4]	Regence BCBS	Moda
Program Components	Supervised by licensed provider; monthly provider visits; 2x/month counseling by a registered dietitian; patient journal of participation	Physician-supervised: medical record documentation with program compliance record; supervised nutrition and exercise program must have face-to-face component Surgical Prep Regimen: Behavior modification program; dietician or nutritionist consultation; medical record documentation; supervised exercise regimen; substantial face-to-face component; reduced-calorie diet supervised by a dietitian or nutritionist	---	Three visits for medical supervision (no more than 4 months apart); provided by MD, DO, NP, PA, or RD under supervision of MD, DO, NP or PA; assessment and counseling on weight, diet, exercise and behavior modification; clinical documentation of willingness to comply with pre- and post-operative treatment plan	Hypocaloric diet changes, nutritional education, physical activity, behavior change strategies; three or more primary care visits; completion of a 8-week health education, weight management program

Key: √ – required; --- – not in policy description

Abbreviations: DO – doctor of osteopathy; MD – medical doctor; NP – nurse practitioner; PA – physician assistant; RD – registered dietician

Notes:

1. Specific to open or laparoscopic Roun-en-Y gastric bypass (RYGB), laparoscopic adjustable silicone gastric banding (LASGB), open or laparoscopic sleeve gastrectomy, open or laparoscopic biliopancreatic diversion (BPD), and duodenal switch (DS)
2. Provider must be a psychiatrist, licensed psychiatric ARNP, or licensed independent social worker with a minimum of two years postmasters' experience in a mental health setting
3. For members who have a history of severe psychiatric disturbance (schizophrenia, borderline personality disorder, suicidal ideation, severe depression) or who are currently under the care of a psychologist/psychiatrist or who are on psychotropic medications
4. Specific to open or laparoscopic Roux-en-Y gastric bypass, open or laparoscopic adjustable silicone gastric banding (LAP-BAND®, REALIZE™), open or laparoscopic biliopancreatic diversity with duodenal switch

(BPD/DS) for individuals with a BMI >50, open or laparoscopic sleeve gastrectomy, open or laparoscopic vertical banded gastroplasty

Table E4. Facility Requirements

Approved Facility Requirements	Payers Washington Medicaid
Minimum number of bariatric surgical procedures performed	100
Direction	Experience board-certified surgeon
Time in operation	≥ 5 years
Mortality rate	≤ 2%
Morbidity rate	≤ 15%
Patient follow-up	≥ 5 years
Average patient weight loss at 5 years	≥ 50%
Reoperation/revision rate	≤ 5%

Table E5. Repeat Surgery Coverage

Circumstances	Payers		
	Aetna	Cigna	Regence BCBS
Adjustment of silicone gastric band	---	√	---
Removal of gastric band	√	---	---
Correct complications	√	√	√
Conversion to sleeve gastrectomy, RYGB or BPD/DS	√[1, 2, 3]	√[2]	√
Failed dilation of gastric pouch after primary surgery	√[1] (if primary surgery was successful in inducing weight loss)	√	---
Replacement of adjustable band	√ (for complications)	---	---

Key: √ – covered; --- – not in policy description

Abbreviations: BPD – biliopancreatic diversion; DS – duodenal switch RYGB – Roux-en-Y gastric bypass;

Notes:

1. If patient has been compliant with a prescribed nutrition and exercise program following the procedure
2. For members who have not lost > 50% of body weight 2 years following primary surgery
3. Conversion from adjustable band to sleeve gastrectomy, RYGB or BPD/DS, for complications that cannot be corrected with band manipulation, adjustments or replacement

Table E6. Non-Covered Conditions and Procedures

	Payers		
	Aetna	**Cigna**	**Regence BCBS**
Conditions			
Idiopathic intracranial hypertension	X	---	---
Infertility	X	---	---
DM2 w/BMI <35	X	X[1]	
Gastroesophageal reflux in non-obese persons	X	---	X
Gastroparesis	X	---	---
Procedures			
Band over bypass	X	---	X
Band over sleeve	X	---	X
Roux-en-Y gastric bypass combined with simultaneous BPD without DS	---	X	---
Gastrointestinal liners (EndoBarrier™)	X	X	---
Gastroplasty ("stomach stapling")	X	X	X
Intragastric balloon	X	X	
Laparoscopic gastric plication	X	X	X
Loop gastric bypass	X	X	
Mini gastric bypass	X	X	X
Sclerotherapy for the treatment of dilated gastrojejunostomy following bariatric surgery	X	---	X
Silastic ring vertical gastric bypass (Fobi pouch)	X	X	---
Transoral endoscopic surgery (OverStitch suturing device or StomaphyX™ device)	X	X (including TOGA®)	X
Vagus nerve blocking	X	X	---
Gastric electrical stimulation or gastric pacing	---	X	---
Intestinal bypass (jejunoileal bypass)	---	X	X
restorative obesity surgery, endoluminal (ROSE)	---	X	X
Vagus nerve stimulation	---	X	---

Distal gastric bypass (long limb gastric bypass, >150 cm)	---	---	X
Biliopancreatic bypass (Scopinaro procedure)	---	---	X
Biliopancreatic bypass with duodenal switch	---	---	X
Two-stage procedures	---	---	X
Vertical banded gastroplasty	---	---	X
EndoCinch™	---	---	X

Key: √ – covered; X – not covered; --- – not in policy description

Notes:

1. Not covered when performed solely for treatment of diabetes mellitus
2. Specific requirements for vertical banded gastroplasty (members who are at increased risk of adverse consequences from Roux-en-Y Gastric bypass due to the presence of:
    - Demonstrated complications from extensive adhesions involving the intestines from prior major abdominal surgery, multiple minor surgeries, or major trauma
    - Hepatic cirrhosis with elevated liver function tests
    - Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
    - Poorly controlled systemic disease
    - Radiation enteritis.

APPENDIX F. APPLICABLE CODES

CODES	DESCRIPTION
ICD-10	
E11.0 – E11.9	Diabetes, type 2
E66.01-E66.9	Overweight, Obesity and Morbid Obesity
G47.30 – G47.39	Sleep apnea
I10	Essential hypertension
ICD-9-CM Volume I Codes	
250.00, 250.02; 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, 250.92	Diabetes, Type II
278.00 – 278.03	Overweight, Obesity, and Morbid Obesity
327.20 – 327.29; 780.57	Sleep apnea
401.0 – 401.9	Hypertension
ICD-9-CM Volume III Codes	
43.82	Laparoscopic vertical (sleeve) gastrectomy
43.89	Open and other partial gastrectomy
44.31	High gastric bypass
44.38	Laparoscopic gastroenterostomy
44.5	Revision of gastric anastomosis
44.68	Laparoscopic gastroplasty
44.69	Other repair of stomach
44.95	Laparoscopic gastric restrictive procedure
44.96	Laparoscopic revision of gastric restrictive procedure
44.97	Laparoscopic removal of gastric restrictive device(s)
44.98	Laparoscopic) adjustment of size of adjustable gastric restrictive device

45.51	Isolation of segment of small intestine
45.91	Small-to-small intestinal anastomosis
CPT Codes	
43644	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and Roux-en-Y gastroenterostomy (roux limb 150 cm or less)
43645	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and small intestine reconstruction to limit absorption
43770	Laparoscopy, surgical, gastric restrictive procedure; placement of adjustable gastric restrictive device (e.g., gastric band and subcutaneous port components)
43771	Laparoscopy, surgical, gastric restrictive procedure; revision of adjustable gastric restrictive device component only
43772	Laparoscopy, surgical, gastric restrictive procedure; removal of adjustable gastric restrictive device component only
43773	Laparoscopy, surgical, gastric restrictive procedure; removal and replacement of adjustable gastric restrictive device component only
43774	Laparoscopy, surgical, gastric restrictive procedure; removal of adjustable gastric restrictive device and subcutaneous port components
43775	Laparoscopy, surgical, gastric restrictive procedure; longitudinal gastrectomy (i.e., sleeve gastrectomy)
43842	Gastric restrictive procedure, without gastric bypass, for morbid obesity; vertical-banded gastroplasty
43843	Gastric restrictive procedure, without gastric bypass, for morbid obesity; other than vertical-banded gastroplasty
43845	Gastric restrictive procedure with partial gastrectomy, pylorus-preserving duodenoileostomy and ileoileostomy (50 to 100 cm common channel) to limit absorption (biliopancreatic diversion with duodenal switch)
43846	Gastric restrictive procedure, with gastric bypass for morbid obesity; with short limb (150 cm or less) Roux-en-Y gastroenterostomy
43847	Gastric restrictive procedure, with gastric bypass for morbid obesity; with small intestine reconstruction to limit absorption
43848	Revision, open, of gastric restrictive procedure for morbid obesity, other than adjustable gastric restrictive device (separate procedure)
43886	Gastric restrictive procedure, open; revision of subcutaneous port component only
43887	Gastric restrictive procedure, open; removal of subcutaneous port component only
43888	Gastric restrictive procedure, open; removal and replacement of subcutaneous port component only

Note: Inclusion on this list does not guarantee coverage

HCPCS Level II Codes	
S2083	Adjustment of gastric band diameter via subcutaneous port by injection or aspiration of saline

APPENDIX G. OUTCOMES BY BASELINE MEAN BMI FROM THE WA HTA REPORT (P. 64-65)

Baseline Mean BMI Category									
		30-34.99		35-39.99		40-49.99		>50	
		Median	Range	Median	Range	Median	Range	Median	Range
% Decrease BMI	RYGB	25.4	(19.6-34.3)	26.0	(24.1-33.1)	32.2	(7.5-52.3)	34	(10.1-46.7)
	VSG	21.3	(21.3-21.3)	22.0	(19.1-22.5)	28.4	(15.0-37.1)	30.1	(11.0-39.4)
	LAGB	16.8	(11.8-21.7)	16.8	(13.0-17.5)	20.4	(6.0-46.8)	17.7	(1.0-31.8)
	BPD/DS	31.8	(17.3-46.3)			32.6	(15.9-50.8)	43.4	(39.2-47.7)
	Follow-up (months)	12.0	(3.0-45.2)	15.3	(12.0-60.0)	12.0	(0.5-120.0)	22.6	(1.2-84.0)
	No. Studies	7		6		79		22	
	Good/Fair/Poor	2/3/2		3/1/2		9/34/36		4/10/8	
% EWL	RYGB	70.0		77.0	(61.0-92.9)	67.0	(27.1-88.0)	61.8	(43.8-72.3)
	VSG			58.5	(51.0-66.0)	59.2	(30.7-83.0)	47.5	(25.4-75.0)
	LAGB	87.2		50.1	(34.0-62.5)	43.5	(18.2-78.8)	45.9	(31.0-73.0)
	BPD/DS					52.7	(34.9-70.4)	73.4	63.0-84.0)
	Follow-up (months)	18.0	(12.0-24.0)	30.0	(18.7-60.0)	24.0	(0.47-120)	24.0	(12.0-84.0)
	No. Studies	2		4		57		15	
	Good/Fair/Poor	1/0/1		1/1/2		6/27/24		1/8/6	
% Improvement Hypertension	RYGB			90.0		71.0	(22.0-100.0)	62.6	(60.7-69.2)
	VSG					64.3	(23.5-100.0)		
	LAGB			40.0		57.5	(18.0-100.0)	54.3	(33.3-66.7)
	BPD/DS	67.0				81.4	(68.6-87.0)	68.3	(66.7-69.9)
	Follow-up (months)	36.0		60.0		21.0	(3.5-84.0)	24.0	(12.0-50.4)
	No. Studies	1		1		29		5	
	Good/Fair/Poor	0/1/0		0/0/1		4/12/13		1/3/1	

Baseline Mean BMI Category									
		30-34.99		35-39.99		40-49.99		>50	
		Median	Range	Median	Range	Median	Range	Median	Range
% Improvement T2DM	RYGB	51.1	(33.0-92.3)	73.4	(66.7-80.0)	79.0	(33.0-100.0)	77.1	(40.0-100.0)
	VSG	50.0	(50.0-50.0)			77.3	(36.0-100.0)	88.9	(88.9-88.9)
	LAGB	33.0	(21.1-100.0)	50.0	(25.0-73.0)	50.0	(17.0-100.0)	52.3	(36.4-66.7)
	BPD/DS	84.8	(83.0-84.8)			87.1	(81.5-92.7)	91.4	(82.7-100.0)
	Follow-up (months)	12.0	(3.0-45.2)	24.0	(12.0-60.0)	16.0	(1.0-62.7)	24.0	(1.5-50.4)
	No. Studies	6		3		35		7	
	Good/Fair/Poor	0/3/3		2/0/1		3/14/18		1/4/2	
% Improvement Sleep Apnea	RYGB	89.0				70.5	(10.0-100.0)	56.7	(49.3-88.0)
	VSG					62.0	(6.0-99.0)		
	LAGB					29.0	(3.0-55.0)	46.2	(39.3-66.7)
	BPD/DS	90.0						79.5	(78.9-80.0)
	Follow-up (months)	45.15				21.6	(12.0-36.0)	20.1	(12.0-20.1)
	No. Studies	1		0		11		4	
	Good/Fair/Poor	0/0/1				2/5/4		1/3/0	
% Improvement Dyslipidemia	RYGB			100.0		64.5	(6.0-100.0)	52.9	(27.3-58.8)
	VSG					67.5	(35.0-67.5)		
	LAGB			38.0		36.5	(0.0-36.5)	34.4	(23.3-45.5)
	BPD/DS					90.0	(90.0-90.0)		
	Follow-up (months)			60.0		24.0	(12.0-62.7)	16.2	(12.0-50.4)
	No. Studies	0		1		18		3	
	Good/Fair/Poor	0		0/0/1		2/9/7		1/1/1	

APPENDIX H. COST-EFFECTIVENESS ESTIMATES FROM THE WA HTA REPORT (P. 80)

BMI Level/ Procedure	Cost ($)	Effectiveness (QALYs)	Cost-effectiveness ($/QALY gained)	
			Vs. SC	Vs. RYGB
BMI≥30				
Standard care	$34,923	7.5680	NA	NA
RYGB	$54,110	8.0807	$37,423	NA
VSG	$48,702	8.0417	$29,087	Less expensive & less effective
LAGB	$47,668	7.9252	$35,680	Less expensive & less effective
BPD/DS	$65,741	8.2307	$46,508	$77,574
BMI 30-34.9				
Standard care	$27,943	7.9418	NA	NA
RYGB	$49,735	8.3529	$53,021	NA
VSG	$44,298	8.3211	$43,122	Less expensive & less effective
LAGB	$42,738	8.2273	$51,826	Less expensive & less effective
BPD/DS	$61,410	8.4730	$63,011	$97,194
BMI 35-39.9				
Standard care	$32,538	7.6567	NA	NA
RYGB	$52,886	8.1351	$42,534	NA
VSG	$47,468	8.0986	$33,789	Less expensive & less effective
LAGB	$46,217	7.9898	$41,073	Less expensive & less effective
BPD/DS	$64,533	8.2751	$51,743	$83,224
BMI≥40				
Standard care	$40,329	7.2846	NA	NA
RYGB	$58,257	7.8630	$30,995	NA
VSG	$53,047	7.8194	$23,784	Less expensive & less effective
LAGB	$52,255	7.6882	$29,552	Less expensive & less effective
BPD/DS	$69,329	8.0322	$38,790	$65,431

BPD = biliopancreatic diversion; ICER = incremental cost-effectiveness ratio; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; VSG = vertical sleeve gastrectomy.

NOTE: Because of rounding, performing calculations may not produce the exact results shown.

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[i] Reported as crude event rates

[ii] Reported as crude event rates

[iii] Reported after unadjusted Cox regression; after adjustment for covariates, the HR was 0.80 (95% CI 0.63 to 0.995). An analysis of propensity matched patients resulted in a HR of 0.83 (95% CI 0.61 to 1.14).

[iv] Reported as adjusted Cox proportional hazards

[v] Reported as Cox proportional hazards

[vi] Primary outcome in Sjostrom was not mortality but incidence of CV events (included here because of its analysis by comorbidity)

Bariatric/Metabolic Surgery for Obesity

Issue: The HERC is reviewing treatments for obesity as part of its biennial review. The Health Technology Assessment Subcommittee (HTAS) has performed a detailed assessment of the evidence and developed a Draft Coverage Guidance on bariatric surgery for obesity. The Obesity Task Force can review the Draft Coverage Guidance recommendations and assist in discussing how this best should be implemented as part of the Prioritized List of Health Services.

Current Prioritized List Status:

Line: 30

Condition:	TYPE 2 DIABETES MELLITUS (See Coding Specification Below) (See Guideline Notes 8,62,64,65)
Treatment:	MEDICAL THERAPY, BARIATRIC SURGERY WITH BMI >= 35
ICD-10:	E08.00-E08.29,E08.311-E08.9,E09.00-E09.29,E09.311-E09.9,E11.00-E11.29,E11.311-E11.9,E13.00-E13.29,E13.311-E13.9,E16.1,Z46.51
CPT:	43644,43645,43770-43775,43846-43848,48155,64505-64530,90935-90947,90989-90997,92002-92014,92227,96150-96154,97605-97608,97802-97804,98960-98969,99051,99060,99070,99078,99184,99201-99239,99281-99285,99291-99404,99408-99416,99429-99449,99468-99480,99487-99498,99605-99607
HCPCS:	G0108,G0109,G0245,G0246,G0270,G0271,G0396,G0397,G0406-G0408,G0425-G0427,G0458,G0463,G0466,G0467,S2083,S9140-S9145,S9353,S9537

CPT codes 43644-43645 and 43846-43848 (Roux-En-Y gastric bypass) and 43770-43775 (laparoscopic adjustable gastric banding and sleeve gastrectomy) are only included on this line as treatment according to the requirements in Guideline Note 8 when paired with:

1) a primary diagnosis of E11 (Type II Diabetes with or without complication);
2) a secondary diagnosis of E66.01, E66.09, E66.2, E66.8 or E66.9 (Obesity); AND,
3) a tertiary diagnosis code of Z68.35-Z68.39 or Z68.4.

Line: 325

Condition:	OBESITY (ADULT BMI ≥ 30, CHILDHOOD BMI ≥ 95 PERCENTILE) (See Guideline Notes 5,64,65)
Treatment:	INTENSIVE NUTRITIONAL/PHYSICAL ACTIVITY COUNSELING AND BEHAVIORAL INTERVENTIONS
ICD-10:	E66.01-E66.9,Z68.30-Z68.45,Z68.54
CPT:	96150-96154,97802-97804,98966-98969,99051,99060,99070,99078,99201-99215,99281-99285,99341-99355,99358-99378,99381-99404,99408-99416,99429-99449,99487-99498
HCPCS:	G0396,G0397,G0447,G0463,G0466,G0467,G0473

Line: 589

Condition:	OBESITY (ADULT BMI ≥ 30, CHILDHOOD BMI ≥ 95 PERCENTILE) (See Guideline Notes 8,64,65)
Treatment:	NON-INTENSIVE NUTRITIONAL/PHYSICAL ACTIVITY COUNSELING AND BEHAVIORAL INTERVENTIONS; BARIATRIC SURGERY FOR OBESITY WITH A SIGNIFICANT COMORBIDITY OTHER THAN TYPE II DIABETES & BMI >=35 OR BMI>=40 WITHOUT A SIGNIFICANT COMORBIDITY
ICD-10:	E66.01-E66.9,Z68.30-Z68.45,Z68.54,Z71.3
CPT:	43644,43645,43770-43775,43846-43848,98966-98969,99051,99060,99070,99078,99201-99215,99281-99285,99341-99355,99358-99378,99381-99404,99408-99416,99429-99449,99487-99498,99605-99607
HCPCS:	G0396,G0397,G0447,G0463,G0466,G0467,G0473

Bariatric/Metabolic Surgery for Obesity

GUIDELINE NOTE 8, BARIATRIC SURGERY

Lines 30,589

Bariatric surgery is included under the following criteria:

A) Age ≥ 18
B) The patient has
   1) a BMI ≥ 35 with co-morbid type II diabetes for inclusion on Line 30 TYPE 2 DIABETES MELLITUS; OR
   2) BMI >=35 with at least one significant co-morbidity other than type II diabetes (e.g., obstructive sleep apnea, hyperlipidemia, hypertension) or BMI >= 40 without a significant co-morbidity for inclusion on Line 589
C) No prior history of Roux-en-Y gastric bypass or laparoscopic adjustable gastric banding, unless they resulted in failure due to complications of the original surgery.
D) Participate in the following four evaluations and meet criteria as described.
   1) Psychosocial evaluation: (Conducted by a licensed mental health professional)
      a) Evaluation to assess potential compliance with post-operative requirements.
      b) Must remain free of abuse of or dependence on alcohol during the six-month period immediately preceding surgery. No current use of nicotine or illicit drugs and must remain abstinent from their use during the six-month observation period. Testing will, at a minimum, be conducted within one month of the surgery to confirm abstinence from nicotine and illicit drugs.
      c) No mental or behavioral disorder that may interfere with postoperative outcomes[1].
      d) Patient with previous psychiatric illness must be stable for at least 6 months.
   2) Medical evaluation: (Conducted by OHP primary care provider)
      a) Pre-operative physical condition and mortality risk assessed with patient found to be an appropriate candidate.
      b) Optimize medical control of diabetes, hypertension, or other co-morbid conditions.
      c) Female patient not currently pregnant with no plans for pregnancy for at least 2 years post-surgery. Contraception methods reviewed with patient agreement to use effective contraception through 2nd year post-surgery.
   3) Surgical evaluation: (Conducted by a licensed bariatric surgeon associated with program[2])
      a) Patient found to be an appropriate candidate for surgery at initial evaluation and throughout period leading to surgery while continuously enrolled on OHP.
      b) Received counseling by a credentialed expert on the team regarding the risks and benefits of the procedure[3] and understands the many potential complications of the surgery (including death) and the realistic expectations of post-surgical outcomes.
   4) Dietician evaluation: (Conducted by licensed dietician)
      a) Evaluation of adequacy of prior dietary efforts to lose weight. If no or inadequate prior dietary effort to lose weight, must undergo six-month medically supervised weight reduction program.
      b) Counseling in dietary lifestyle changes

E) Participate in additional evaluations:
   1) Post-surgical attention to lifestyle, an exercise program and dietary changes and understands the need for post-surgical follow-up with all applicable professionals (e.g. nutritionist, psychologist/psychiatrist, exercise physiologist or physical therapist, support group participation, regularly scheduled physician follow-up visits).

[1] Many patients (>50%) have depression as a co-morbid diagnosis that, if treated, would not preclude their participation in the bariatric surgery program.

[2] All surgical services must be provided by a program with current certification by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP), or in active pursuit of such certification with all of the following: a dedicated, comprehensive, multidisciplinary, pathway-directed bariatric program in place; hospital to have performed bariatrics > 1 year and > 25 cases the previous 12 months; trained and credentialed bariatric surgeon performing at least 50 cases in past 24 months; qualified bariatric call coverage 24/7/365;appropriate bariatric-grade equipment in outpatient and inpatient facilities; appropriate medical specialty services to complement surgeons' care for patients; and quality improvement program with prospective documentation of surgical outcomes. If the program is still pursuing (MBSAQIP) certification, it must also restrict care to lower-risk OHP patients including: age < 65 years; BMI < 70; no major elective revisional surgery; and, no extreme medical comorbidities (such as wheel-chair bound, severe cardiopulmonary compromise, or other excessive risk). All programs must agree to yearly submission of outcomes data to Division of Medicaid Assistance Programs (DMAP).

[3] Only Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding and sleeve gastrectomy are approved for inclusion.

Evidence summary (GRADE table from HTAS draft Coverage Guidance):

Coverage question: Should bariatric surgery be recommended for coverage in adults?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
All-cause mortality (*Critical outcome)*	Odds ratio: 0.48 (95% CI 0.35 to 0.64) Crude event rates 3.6% with surgery and 11.4% without surgery Number needed to treat = 13 ●●○○ *(low certainty based on consistent but indirect observational studies)*	Bariatric surgery costs tens of thousands of dollars per surgery, but has been shown to be cost effective across BMI thresholds and surgery types.	Patients would balance surgery and its risks with risks of living with morbid obesity. Many patients who have failed conservative attempts at weight loss may elect	The greatest benefit may be with BMI ≥ 40 but otherwise specific subpopulations which would benefit the most from bariatric surgery are not well characterized.

Bariatric/Metabolic Surgery for Obesity

Coverage question: Should bariatric surgery be recommended for coverage in adults?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
Major adverse cardiovascular events (*Critical outcome*)	Odds ratio: 0.54 (95% CI 0.41 to 0.70) Crude event rates 2.4% with surgery and 4.0% without surgery Number needed to treat = 62 ●●○○ (*low certainty based on consistent but indirect observational studies)*		surgery. The benefits of decreased mortality, dramatic weight loss, and regression of diabetes are important outcomes that patients and society would strongly value. However, there would still be moderate variability because of the risks and costs associated with surgery, as well as the intensive peri- and post-operative follow up.	The pre-operative requirements for achieving optimal outcomes are unclear. Given the rate of complications and need for reoperation reported in the summary literature, benefit plans may wish to consider alternative payment methodologies like bundled payments or a pay-for-outcomes approach. Surgeon case volume, and to a lesser extent hospital case volume, appear to affect outcomes for patients undergoing bariatric surgery and requirements regarding surgeon or facility volume may be reasonable.
Type 2 DM remission/resolution (*Important outcome*)	Odds ratio: 3.6 to 52.4 (favoring surgery) Number needed to treat: 1 to 5 ●●●○ *(moderate certainty based on a mix of RCTs and observational studies with consistent but imprecise effects)*			
Hypertension remission/ resolution (*Important outcome*)	Odds ratio: 2.99 to 3.12 (favoring surgery) Number needed to treat: 4 ●●●○ *(moderate certainty based on a mix of RCTs and observational studies with consistent but imprecise effects)*			
Change in BMI (*Important outcome*)	Mean difference at 1 year: -5.5 to -33.35 kg/m^2 (favoring surgery) Pooled mean difference: -7.4 kg/m^2 (favoring surgery) ●●●○ *(moderate certainty based on a mix of RCTs and observational studies with consistent but imprecise effects)*			

Bariatric/Metabolic Surgery for Obesity

Coverage question: Should bariatric surgery be recommended for coverage in adults?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
Rationale: Bariatric surgery appears to lower all-cause mortality and major adverse cardiovascular events in obese adults (low certainty), and significantly reduces BMI, and results in resolution of type 2 diabetes and hypertension. The greatest benefit appears to be with BMI ≥ 40. Though bariatric surgery is costly and carries significant perioperative risks, the clear long-term positive health benefits leads to a recommendation for coverage. The strength of the recommendation is based on the fact that there is a strong benefit on critical outcomes (particularly in diabetics), and patients desiring surgery would strongly prefer this intervention. For those without diabetes, and other comorbidities are present, the evidence is less clear, leading to a weak recommendation.				

Recommendation:
Coverage of metabolic and bariatric surgery (including Roux-en-Y gastric bypass, gastric banding, and sleeve gastrectomy) is recommended for:
• Adult obese patients (BMI ≥ 35 and <40) with:
  ○ Type 2 diabetes *(strong recommendation)* OR
  ○ at least two of the following other serious obesity-related comorbidities: hypertension, coronary heart disease, mechanical arthropathy in major weight bearing joint, sleep apnea *(weak recommendation)*
• Adult obese patients (BMI ≥ 40) *(strong recommendation)*
 	
Metabolic and bariatric surgery is recommended for coverage in these populations only when provided in a facility accredited by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program *(weak recommendation).*
Metabolic and bariatric surgery is not recommended for coverage in:
• Patients with BMI <35, or 35-40 without the defined comorbid conditions above *(weak recommendation)*				

Note: GRADE framework elements are described in Appendix B. A GRADE evidence profile is provided in Appendix C.

Coverage question: Should bariatric surgery be recommended for coverage in children and adolescents?				
Outcomes	**Estimate of Effect for Outcome/ *Confidence in Estimate***	**Resource allocation**	**Values and Preferences**	**Other considerations**
All-cause mortality (*Critical outcome*)	Insufficient evidence in this population *Insufficient evidence*	High cost (tens of thousands of dollars) but may be cost effective especially given the long	High variability. If conservative treatments have failed, children, adolescents and their	Parental involvement in weight management plans is likely necessary to assist the

Bariatric/Metabolic Surgery for Obesity

Coverage question: Should bariatric surgery be recommended for coverage in children and adolescents?				
Major adverse cardiovascular events (*Critical outcome*)	Insufficient evidence in this population *Insufficient evidence*	time horizon if weight loss is maintained. However, uncertainty about the long-term balance of benefits and harms could significantly alter estimates of cost-effectiveness.	parents would be highly motivated to find an effective alternative intervention. Children may have a significant fear of surgery, but the profound social and emotional impact of obesity may override their concerns. Parents are likely to be more concerned about the long term health impacts of obesity than children, and may be concerned about the uncertainty about the long term benefits.	effectiveness of obesity treatments (based on expert opinion). Pediatric bariatric surgery is likely to be available at only a few highly specialized centers. The American Academy of Pediatrics has 10 criteria that pediatric bariatric surgery programs should meet.
Type 2 DM remission/resolution (*Important outcome*)	Rates of remission of T2DM ranged from 50 to 100% ●○○○ *(very low certainty based on mostly small observational trials with imprecise effects)*			
Hypertension remission/ resolution (*Important outcome*)	Rates of remission of hypertension ranged from 50 to 100% ●○○○ (*very low certainty based on mostly small observational trials with imprecise effects)*			
Change in BMI (*Important outcome*)	Mean weighted difference in BMI at 1 year (from baseline): -10.5 to -17.2 kg/m^2 ●●○○ *(low certainty based on mostly small observational trials)*			
Rationale: Bariatric surgery likely results in significant reductions in BMI (low certainty) and is associated with remission of type 2 diabetes and hypertension (very low certainty). However, coverage is not recommended because of the limited evidence about overall long-term benefits and harms of bariatric surgery in this population as well as the high variability in values and preferences.				
Recommendation: Bariatric surgery is not recommended for coverage in children and adolescents *(weak recommendation).*				

Note: GRADE framework elements are described in Appendix B. A GRADE evidence profile is provided in Appendix C.

Bariatric/Metabolic Surgery for Obesity

Coverage question: Should reoperative bariatric surgery for inadequate weight loss be recommended for coverage?					
Outcomes		**Estimate of Effect for Outcome** **Confidence in Estimate of Effect**	**Resource allocation**	**Values and Preferences**	**Other considerations**
Critical outcomes	All-cause mortality	Insufficient evidence in this population *Insufficient evidence*	A second high cost procedure (tens of thousands of dollars), with a history of prior failure may be more costly in total and less effective, however, the cost – effectiveness in this group is unknown.	There would be high variability in patient preferences. With a prior failure of a bariatric procedure, some patients would be hesitant to try an additional procedure given the burdens of surgery and prior ineffectiveness. Others would be motivated to try a different procedure in hopes that it would work better. Patients seeking reoperation have likely no other good potential option given failure of multiple previous alternatives (e.g. clinical, pharmacological, nutritional, physical activity, and surgical).	There is evidence of greater complications rates with reoperation. There is insufficient evidence in the reoperation group to know if their outcomes would be substantially different that those undergoing their first operation. A significant proportion of these patients would be going from a band to a RYGB (from a procedure with a higher failure rate to a lower failure rate).
	Major adverse cardiovascular events	Insufficient evidence in this population *Insufficient evidence*			
Important outcomes	Type 2 DM remission / resolution	Insufficient evidence in this population *Insufficient evidence*			
	Hypertension remission/ resolution	Insufficient evidence in this population *Insufficient evidence*			
	Change in BMI	Mean change in BMI (from baseline): +2.4 kg/m^2 to -17.2 kg/m^2 (follow-up ranging from 8 to 48 months) ●○○○ *(very low certainty based on small case series)*			
Rationale: Reoperation is associated with higher complication rates but also effective weight loss (based on very low quality evidence). While there are not long term health outcomes available, there is no reason to believe that significant weight loss in the reoperation group would be associated with less future health benefits. Therefore, the subcommittee makes no recommendation that the coverage criteria should be different between reoperation and primary surgery. Surgeons will also evaluate their patients and consider reasons for failure when deciding if the patient is a good candidate for reoperation.					
Recommendation: No recommendation that coverage criteria for re-operation should be different than for primary surgery.					

Note: GRADE framework elements are described in Appendix B GRADE evidence profile is provided in Appendix C

Bariatric/metabolic surgery for obesity

HTAS Coverage Recommendations

Coverage of metabolic and bariatric surgery (including Roux-en-Y gastric bypass, gastric banding, and sleeve gastrectomy) is recommended for:

- Adult obese patients (BMI ≥ 35) with
    - Type 2 diabetes *(strong recommendation)* OR
    - at least two of the following other serious obesity-related comorbidities: hypertension, coronary heart disease, mechanical arthropathy in major weight bearing joint, sleep apnea *(weak recommendation)*
- Adult obese patients (BMI ≥ 40) *(strong recommendation)*

Metabolic and bariatric surgery is recommended for coverage in these populations only when provided in a facility accredited by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program *(weak recommendation).*

Metabolic and bariatric surgery is not recommended for coverage in:

- Patients with BMI <35, or 35-40 without the defined comorbid conditions above *(weak recommendation)*

Children and adolescents *(weak recommendation)*

HERC Staff Assessment:

Currently, bariatric surgery only pairs in the funded region of the Prioritized List with type 2 diabetes. The Coverage Guidance suggests that coverage should be expanded to include those with comorbidities other than diabetes. Therefore, changing the primary indication for bariatric surgery on the List to be for obesity rather than diabetes makes sense and consolidating the bariatric surgery codes to the Obesity line is indicated. Having bariatric surgery codes on the lower obesity line (589) is confusing because of the comorbidity rule, when there are clearly defined comorbidities in the new proposed guideline note language.

HERC Staff Recommendations Pending Input from Obesity Task Force:

1) Add bariatric surgery to Line 325
    a. Change the Treatment title
    b. Add bariatric surgery codes (see Code Movement Table)
    c. Add reference to Guideline Note 8
2) Remove bariatric surgery from Line 30, Type 2 Diabetes
    a. Change title of the Treatment to not include bariatric surgery
    b. Remove bariatric surgery codes from line 30 (see Code Movement Table)
    c. Remove coding specification about bariatric surgery
    d. Remove reference to Guideline Note 8
3) If Line 589 is not deleted, remove bariatric surgery from Line 589
    a. Change the Treatment title

b. Remove bariatric surgery codes from Line 589 (see Code Movement Table)

4) Revise Guideline Note 8
   a. Discuss whether to remove the language that excludes reoperations (C)
   b. Discuss whether the preoperative and postoperative requirements should be modified

Line: 30
Condition: TYPE 2 DIABETES MELLITUS (See Coding Specification Below) (See Guideline Notes ~~8~~,62,64,65)
Treatment: MEDICAL THERAPY~~, BARIATRIC SURGERY WITH BMI >= 35~~
ICD-10: E08.00-E08.29,E08.311-E08.9,E09.00-E09.29,E09.311-E09.9,E11.00-E11.29,E11.311-E11.9,E13.00-E13.29, E13.311-E13.9,E16.1,Z46.51
CPT: ~~43644,43645,43770-43775,43846-43848,48155,~~64505-64530,90935-90947,90989-90997,92002-92014,92227, 96150-96154,97605-97608,97802-97804,98960-98969,99051,99060,99070,99078,99184,99201-99239,99281-99285,99291-99404,99408-99416,99429-99449,99468-99480,99487-99498,99605-99607
HCPCS: G0108,G0109,G0245,G0246,G0270,G0271,G0396,G0397,G0406-G0408,G0425-G0427,G0458,G0463,G0466, G0467,S2083,S9140-S9145,S9353,S9537

~~CPT codes 43644-43645 and 43846-43848 (Roux-En-Y gastric bypass) and 43770-43775 (laparoscopic adjustable gastric banding and sleeve gastrectomy) are only included on this line as treatment according to the requirements in Guideline Note 8 when paired with:~~
~~1) a primary diagnosis of E11 (Type II Diabetes with or without complication);~~
~~2) a secondary diagnosis of E66.01, E66.09, E66.2, E66.8 or E66.9 (Obesity); AND,~~
~~3) a tertiary diagnosis code of Z68.35-Z68.39 or Z68.4.~~

Line: 325
Condition: OBESITY (ADULT BMI ≥ 30, CHILDHOOD BMI ≥ 95 PERCENTILE) (See Guideline Notes 5,8,64,65)
Treatment: INTENSIVE NUTRITIONAL/PHYSICAL ACTIVITY COUNSELING AND BEHAVIORAL INTERVENTIONS, BARIATRIC SURGERY
ICD-10: E66.01-E66.9, Z68.30-Z68.45,Z68.54
CPT: 43644,43645,43770-43775,43846-43848,96150-96154,97802-97804,98966-98969,99051,99060,99070,99078, 99201-99215,99281-99285,99341-99355,99358-99378,99381-99404,99408-99416,99429-99449,99487-99498
HCPCS: G0396,G0397,G0447,G0463,G0466,G0467,G0473

Line: 589
Condition: OBESITY (ADULT BMI ≥ 30, CHILDHOOD BMI ≥ 95 PERCENTILE) (See Guideline Notes 8,64,65)
Treatment: NON-INTENSIVE NUTRITIONAL/PHYSICAL ACTIVITY COUNSELING AND BEHAVIORAL INTERVENTIONS~~; BARIATRIC SURGERY FOR OBESITY WITH A SIGNIFICANT COMORBIDITY OTHER THAN TYPE II DIABETES & BMI >=35 OR BMI>=40 WITHOUT A SIGNIFICANT COMORBIDITY~~
ICD-10: E66.01-E66.9,Z68.30-Z68.45,Z68.54,Z71.3
CPT: ~~43644,43645,43770-43775,43846-43848,~~98966-98969,99051,99060,99070,99078,99201-99215,99281-99285, 99341-99355,99358-99378,99381-99404,99408-99416,99429-99449,99487-99498,99605-99607
HCPCS: G0396,G0397,G0447,G0463,G0466,G0467,G0473

GUIDELINE NOTE 8, BARIATRIC SURGERY

Line~~s 30,589~~ 325

Bariatric/metabolic surgery (limited to Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding, and sleeve gastrectomy) is included on Line 325~~under~~ when the following criteria are met:

A) Age ≥ 18
B) The patient has obesity with a:
   1) BMI ≥ 40 OR
   2) BMI ≥ 35 with:
      a) Type 2 diabetes, OR

b) at least two of the following other serious obesity-related comorbidities: hypertension, coronary heart disease, mechanical arthropathy in major weight bearing joint, sleep apnea

~~3) a BMI ≥ 35 with co-morbid type II diabetes for inclusion on Line 30 TYPE 2 DIABETES MELLITUS; OR~~

~~4) BMI >=35 with at least one significant co-morbidity other than type II diabetes (e.g., obstructive sleep apnea, hyperlipidemia, hypertension) or BMI >= 40 without a significant co-morbidity for inclusion on Line 589~~

~~C) No prior history of Roux-en-Y gastric bypass or laparoscopic adjustable gastric banding, unless they resulted in failure due to complications of the original surgery.~~

D) Participate in the following four evaluations and meet criteria as described.

1) Psychosocial evaluation: (Conducted by a licensed mental health professional)
   a) Evaluation to assess potential compliance with post-operative requirements.
   b) Must remain free of abuse of or dependence on alcohol during the six-month period immediately preceding surgery. No current use of nicotine or illicit drugs and must remain abstinent from their use during the six-month observation period. Testing will, at a minimum, be conducted within one month of the surgery to confirm abstinence from nicotine and illicit drugs.
   c) No mental or behavioral disorder that may interfere with postoperative outcomes[1].
   d) Patient with previous psychiatric illness must be stable for at least 6 months.
2) Medical evaluation: (Conducted by OHP primary care provider)
   a) Pre-operative physical condition and mortality risk assessed with patient found to be an appropriate candidate.
   b) Optimize medical control of diabetes, hypertension, or other co-morbid conditions.
   c) Female patient not currently pregnant with no plans for pregnancy for at least 2 years post-surgery. Contraception methods reviewed with patient agreement to use effective contraception through 2nd year post-surgery.
3) Surgical evaluation: (Conducted by a licensed bariatric surgeon associated with program[2])
   a) Patient found to be an appropriate candidate for surgery at initial evaluation and throughout period leading to surgery while continuously enrolled on OHP.
   b) Received counseling by a credentialed expert on the team regarding the risks and benefits of the procedure~~3~~ and understands the many potential complications of the surgery (including death) and the realistic expectations of post-surgical outcomes.
4) Dietician evaluation: (Conducted by licensed dietician)
   a) Evaluation of adequacy of prior dietary efforts to lose weight. If no or inadequate prior dietary effort to lose weight, must undergo six-month medically supervised weight reduction program.
   b) Counseling in dietary lifestyle changes

E) Participate in additional evaluations:

1) Post-surgical attention to lifestyle, an exercise program and dietary changes and understands the need for post-surgical follow-up with all applicable professionals (e.g. nutritionist, psychologist/psychiatrist, exercise physiologist or physical therapist, support group participation, regularly scheduled physician follow-up visits).

[1] Many patients (>50%) have depression as a co-morbid diagnosis that, if treated, would not preclude their participation in the bariatric surgery program.

[2] All surgical services must be provided by a program with current certification by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP). ~~, or in active pursuit of such certification with all of the following: a dedicated, comprehensive, multidisciplinary, pathway-directed bariatric program in place; hospital to have performed bariatrics > 1 year and > 25 cases the previous 12 months; trained and credentialed bariatric surgeon performing at least 50 cases in past 24 months; qualified bariatric call coverage 24/7/365;appropriate bariatric-grade equipment in outpatient and inpatient facilities; appropriate medical specialty services to complement surgeons' care for patients; and quality improvement program with prospective documentation of surgical outcomes. If the program is still pursuing (MBSAQIP) certification, it must also restrict care to lower-risk OHP patients including: age < 65 years; BMI < 70; no major elective revisional surgery; and, no extreme medical comorbidities (such as wheel-chair bound, severe cardiopulmonary compromise, or other excessive risk). All programs must agree to yearly submission of outcomes data to Division of Medicaid Assistance Programs (DMAP).~~

~~[3] Only Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding and sleeve gastrectomy are approved for inclusion.~~

Code Movement Table

Code	Code Description	Staff Recommendation
Z46.51	Encounter for fitting and adjustment of gastric lap band	Remove from Line 30, and place on Line 325 only
43644	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and Roux-en-Y gastroenterostomy (roux limb 150 cm or less)	Remove from Line 30 and 589, and place on Line 325 only
43645	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and small intestine reconstruction to limit absorption	Remove from Line 30 and 589, and place on Line 325 only
43770	Laparoscopy, surgical, gastric restrictive procedure; placement of adjustable gastric restrictive device (eg, gastric band and subcutaneous port components)	Remove from Line 30 and 589, and place on Line 325 only
43771	Laparoscopy, surgical, gastric restrictive procedure; revision of adjustable gastric restrictive device component only	Remove from Line 30 and 589, and place on Line 325 only
43772	Laparoscopy, surgical, gastric restrictive procedure; removal of adjustable gastric restrictive device component only	Remove from Line 30 and 589, and place on Line 325 only
43773	Laparoscopy, surgical, gastric restrictive procedure; removal and replacement of adjustable gastric restrictive device component only	Remove from Line 30 and 589, and place on Line 325 only
43774	Laparoscopy, surgical, gastric restrictive procedure; removal of adjustable gastric restrictive device and subcutaneous port components	Remove from Line 30 and 589, and place on Line 325 only
43775	Laparoscopy, surgical, gastric restrictive procedure; longitudinal gastrectomy (ie, sleeve gastrectomy)	Remove from Line 30 and 589, and place on Line 325 only
43846	Gastric restrictive procedure, with gastric bypass for morbid obesity; with short limb (150 cm or less) Roux-en-Y gastroenterostomy	Remove from Line 30 and 589, and place on Line 325 only
43847	Gastric restrictive procedure, with gastric bypass for morbid obesity; with small intestine reconstruction to limit absorption	Remove from Line 30 and 589, and place on Line 325 only

Bariatric/metabolic surgery for obesity

Code	Code Description	Staff Recommendation
43848	Revision, open, of gastric restrictive procedure for morbid obesity, other than adjustable gastric restrictive device (separate procedure)	Remove from Line 30 and 589, and place on Line 325 only
S2083	Adjustment of gastric band diameter via subcutaneous port by injection or aspiration of saline	Remove from Line 30, place on Line 325

HERC Coverage Guidance – Metabolic and Bariatric Surgery
Disposition of Public Comments

Table of Contents

Commenters

Identification	Stakeholder
A	Oregon Chapter of the American Society for Metabolic and Bariatric Surgery *[Submitted January 18, 2016]*

Public Comments

ID/#	Comment	Disposition
A1	"[W]e would like to applaud the efforts to update the current policy on metabolic and bariatric surgery. We agreed with standardizing the indications for surgery to come in line with current clinical practice throughout the United States. We agree the information in the areas of adolescent surgery and surgical treatment of BMI less than 35 is incomplete and rapidly evolving. We believe these two areas should be reassessed in two years."	Thank you for your comment. The Oregon HERC assesses any new evidence every two years to determine if a new coverage guidance is needed.