Health Evidence Review Commission's Value-based Benefits Subcommittee

October 7, 2021

8:00 AM - 1:00 PM

Online Meeting

Join online meeting here

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Section 1.0

Call to Order

AGENDA
VALUE-BASED BENEFITS SUBCOMMITTEE
10/7/2021
8:00am - 1:00pm
Online Meeting
All times are approximate

Note: public testimony on specific agenda topics will be taken at the time that agenda item is discussed

I. Call to Order, Roll Call, Approval of Minutes – Kevin Olson **8:00 AM**

II. Staff report – Ariel Smits **8:05 AM**
- **A.** Errata
- **B.** RAC/COI survey
- **C.** Update on Ancillary Guideline A4
- **D.** Other staff items
- **E.** In lieu of services (David Inbody, CCO operations manager)

III. Straightforward/Consent agenda – Ariel Smits **8:45 AM**
- **A.** Consent table
- **B.** Straightforward guideline corrections
- **C.** Septoplasty coding corrections
- **D.** Items not reviewed in the past 5 years
    - A. Wireless capsule endoscopy

IV. COVID-19 Coding Updates **9:00 AM**
- **A.** New COVID-19 codes
- **B.** COVID coding for dental providers

V. Previous discussion items **9:10 AM**
- **A.** Clarification of when neuropsychological testing is covered prior to epilepsy surgery

VI. New discussion items **9:30 AM**
- **A.** Fall prevention programs
- **B.** Diabetic monitoring
    - A. Continuous glucose monitors for type 2 diabetes and gestational diabetes
    - B. Limits on diabetic test strips
- **C.** Treatment of acquired penile anomalies
- **D.** Neurectomy for wrist arthritis
- **E.** Cranial electrical stimulation for treatment of anxiety, depression and insomnia, re-review

F. Minimally invasive treatments for spinal conditions
    A. Minimally Invasive Lumbar Decompression for Spinal Stenosis
    B. Interspinous/interlaminar process spacer devices

G. Vitiligo

H. Interventional therapies for treatment of acute and chronic pain
    A. Therapies with no evidence of effectiveness
    B. Kyphoplasty and vertebroplasty
    C. Radiofrequency ablation for sacroiliac pain

VII. Public comment **12:55 PM**

VIII. Adjournment – Kevin Olson **1:00 PM**

Value-based Benefits Subcommittee Recommendations Summary
For Presentation to:
Health Evidence Review Commission on August 12, 2021

For specific coding recommendations and guideline wording, please see the text of the 8/12/2021 VbBS minutes.

RECOMMENDED CODE MOVEMENT (changes to the 10/1/21 Prioritized List unless otherwise noted)

- Add various codes for COVID monoclonal antibody therapy and vaccination to funded lines
- Add the 2022 ICD-10-CM codes to various lines and other lists
- Delete the diagnosis code for occipital neuralgia from one funded line and add to another.
- Move the diagnosis code for thrush from an uncovered to a funded line
- Add laparoscopic radiofrequency ablation as a covered treatment for uterine fibroids (effective 1/1/22)
- Add radiofrequency water vapor ablation of the prostate as a treatment for lower urinary tract symptoms in men with benign prostatic hypertrophy (effective 1/1/22)
- Add the procedure codes for deep brain stimulation to the epilepsy surgery line (effective 1/1/22)
- Make various straightforward coding and guideline note changes

ITEMS CONSIDERED BUT NO RECOMMENDATIONS FOR CHANGES MADE

- Coverage of femoroacetabular impingement syndrome was reviewed and no changes made

RECOMMENDED GUIDELINE CHANGES (changes to the 10/1/21 Prioritized List unless otherwise noted)

- Edit the guideline regarding coverage for COVID antibody testing to include additional indications for inpatient testing.
- Edit the guideline around cancer genetic testing to allow Breast Cancer Index to be used for node positive patients to inform decision making about extended endocrine therapy
- Edit the PET scan guideline to allow limited coverage for breast cancer in very specific circumstances, to allow brain PET prior to initiation of certain medications for Alzheimer's disease, and reorganized for clarity.
- Edit the brain imaging in dementia guideline to allow PET and MRI scans for patients prior to initiation or during therapy with certain medications for Alzheimer's disease
- Edit the Preventive Services Guideline to specify that Bright Futures is OHP's EPDST periodicity schedule, and to update the colon cancer screening coverage to reflect USPSTF's updated recommendations.
- Edit the guideline for wigs to include two ICD-10-CM codes
- Update the smoking cessation guideline to exclude cataract and similar bloodless surgeries and to clarify that the guideline does not apply to surgical consultations.
- Update the guideline for cervicogenic headache to reference a new, more precise, ICD-10-CM code
- Update the guideline for leiomyomata to include laparoscopic radiofrequency ablation
- Add new guideline clarifying when septoplasty is covered
- Add new guideline clarifying when rhinoplasty is covered
- Add new guideline for deep brain stimulation for refractory epilepsy (effective 1/1/22)

VALUE-BASED BENEFITS SUBCOMMITTEE
Virtual Meeting
August 12, 2021
8:00 AM – 1:00 PM

Members Present: Kevin Olson, MD, Chair; Holly Jo Hodges, MD, MBA, Vice-chair; Cris Pinzon, MPH, BSN, BS, RN; Kathryn Schabel, MD; Brian Duty, MD (arrived 9AM); Regina Dehen, ND, LAc.

Members Absent: Adriane Irwin, PharmD; Mike Collins

Staff Present: Ariel Smits, MD, MPH; Jason Gingerich; Liz Walker, PhD, MPH; Daphne Peck.

Also Attending: Bethany Godlewski PhD and Val King MD, MPH, (OHSU Center for Health Policy); Christy Simila; Cole Malibiran; Deb Espesete; Elizabeth Schmidt; floralum; Holli Thomas; Jason Daniels; kamodeo; Leslie Dennis (Adventist Health); Marci Herrall; Max Salganik (Biotheranostics); Melissa Wood (Exact Sciences); Michael Levitt; Molly Peltzman; Nisha Nagarkatti-Gude MD; Petra Wilson; Richard Kohl PhD; Sabrina Riggs (OSAA); Shauna Durbin; Tahmina Karimyar; Tamara R. Fountain MD.

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

  The meeting was called to order at 8:00 am and roll was called. A quorum of members was present at the meeting. Minutes from the May 20, 2021 VbBS meeting were reviewed and approved.

  Gingerich gave an update on membership. He announced that Gary Allen is retiring from the Commission, which will leave a vacancy on the Commission for a dentist. He also reviewed the RAC process underway to update the HERC's administrative rules to incorporate the HERC recently approved bylaws regarding conflict of interest declaration requirements. Gingerich also provided a legislative update. The legislative session has ended and no legislation passed that directly affects the HERC.

  There were no errata to report.

- **Topic: Straightforward/Consent Agenda**

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

Recommended Actions:

1) Remove Q52.9 (Congenital malformation of female genitalia, unspecified) from line 332 CONDITIONS REQUIRING HYPERBARIC OXYGEN THERAPY and add to line 353 STRUCTURAL CAUSES OF AMENORRHEA
2) Add C9778 (Colpopexy, vaginal; minimally invasive extra-peritoneal approach (sacrospinous)) to lines 455 URINARY INCONTINENCE and 466 UTERINE PROLAPSE; CYSTOCELE
3) Add S46.10 (Unspecified injury of muscle, fascia and tendon of long head of biceps) to lines 418 DISORDERS OF SHOULDER, INCLUDING SPRAINS/STRAINS GRADE 4 THROUGH 6 and 608 SPRAINS AND STRAINS OF ADJACENT MUSCLES AND JOINTS, MINOR
    a. Remove S46.10 from line 634 SUPERFICIAL WOUNDS WITHOUT INFECTION AND CONTUSIONS
4) Add S46.20 (Unspecified injury of muscle, fascia and tendon of other parts of biceps) to lines 376 DISRUPTIONS OF THE LIGAMENTS AND TENDONS OF THE ARMS AND LEGS, EXCLUDING THE KNEE, RESULTING IN SIGNIFICANT INJURY/IMPAIRMENT and 608 SPRAINS AND STRAINS OF ADJACENT MUSCLES AND JOINTS, MINOR
    a. Remove S46.20 from line 634 SUPERFICIAL WOUNDS WITHOUT INFECTION AND CONTUSIONS
5) Remove 20912 (Cartilage graft; nasal septum) from line 160 TRAUMATIC AMPUTATION OF ARM(S), HAND(S), THUMB(S), AND FINGER(S) (COMPLETE)(PARTIAL) WITH AND WITHOUT COMPLICATION
6) Advise HSD to remove G0452 (Molecular pathology procedure; physician interpretation and report) from the SUSPEND FOR REVIEW file and add to the DIAGNOSTIC PROCEDURES file
7) Do not include the new wig guideline from the March 2021 meeting in the October 1, 2021 Prioritized List
8) Modify Guideline Note 157 as shown in Appendix A
9) Effective January 1, 2022
    a. Rename Line 168 COMPLICATED HERNIAS; ~~UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER;~~ PERSISTENT HYDROCELE.
    b. Rename 524 UNCOMPLICATED HERNIA AND VENTRAL HERNIA (OTHER THAN ~~INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER OR~~ DIAPHRAGMATIC HERNIA)
    c. Modify Guideline Note 24 as shown in Appendix A
10) Modify Diagnostic Guideline D8 as shown in Appendix A
11) Modify Guideline Note 27 as shown in Appendix A
12) Delete Guideline Note 118
13) Add the following CPT codes to line 312 GENDER DYSPHORIA/TRANSEXUALISM
    a. 19370 Revision of peri-implant capsule, breast, including capsulotomy, capsulorrhaphy, and/or partial capsulectomy
    b. 19371 Peri-implant capsulectomy, breast, complete, including removal of all intracapsular contents
    c. 15273-15274 Application of skin substitute graft to trunk
    d. 51040 Cystostomy, cystotomy with drainage
    e. 64856 Suture of major peripheral nerve, arm or leg, except sciatic; including transposition
    f. 64859 Suture of each additional major peripheral nerve

14) Make no change in the current placement of the ICD-10 or CPT codes for femoroacetabular impingement syndrome (FAI) and no change to the current guideline regarding surgical procedures for treatment of FAI.

MOTION: To approve the recommendations stated in the consent agenda. CARRIES 5-0. *(Absent: Duty)*

- **Topic: COVID Coding Issues**

Discussion: Smits reviewed the summary document. There was minimal discussion.

Recommended Actions:

1) Add to line 3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS
    a. HCPCS M0243 (Intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring)
    b. CPT 0003A Immunization administration by intramuscular injection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, mRNA-LNP, spike protein, preservative free, 30 mcg/0.3 mL dosage, diluent reconstituted; third dose [Pfizer COVID vaccine]
    c. HCPCS M0201 Covid-19 vaccine administration inside a patient's home; reported only once per individual home per date of service when only covid-19 vaccine administration is performed at the patient's home
    d. HCPCS M0244 Intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring the home or residence; this includes a beneficiary's home that has been made provider based to the hospital during the covid 19 public health emergency
2) Add to line 399 INFLUENZA, COVID-19 AND OTHER NOVEL RESPIRATORY VIRAL ILLNESS
    a. HCPCS M0244 Intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring the home or residence; this includes a beneficiary's home that has been made provider based to the hospital during the covid 19 public health emergency
    b. HCPCS M0246 Intravenous infusion, bamlanivimab and etesevimab, includes infusion and post administration monitoring in the home or residence; this includes a beneficiary's home that has been made provider based to the hospital during the covid 19 public health emergency [note: not open for payment until FDA re-allows distribution]
    c. HCPCS M0247 Intravenous infusion, sotrovimab, includes infusion and post administration monitoring
    d. HCPCS M0248 Intravenous infusion, sotrovimab, includes infusion and post administration monitoring in the home or residence; this includes a beneficiary's home that has been made provider-based to the hospital during the covid-19 public health emergency
    e. HCPCS M0249 Intravenous infusion, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) only, includes infusion and post administration monitoring, first dose

f. HCPCS M0250 second dose

3) Advise HSD to add to the ANCILLARY PROCEDURES FILE
    a. HCPCS Q0244 Injection, casirivimab and imdevimab, 1200 mg
    b. HCPCS Q0247 Injection, sotrovimab, 500 mg
    c. HCPCS Q0249 Injection, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) only, 1 mg
4) Modify Diagnostic Guideline D27 as shown in Appendix A

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

- **Topic: ICD-10-CM Code Placement**

Discussion: Smits reviewed the straightforward code suggestions. There was no discussion.

Smits reviewed the codes requiring discussion. There was discussion about the following codes:

1) **L24.A and L24.B** Irritant contact dermatitis due to body fluids: the group felt that all of the subcodes should be placed on covered lines. Changes to the staff recommended placements: L24.A0, L24.A9 and L24.A2 were added to line 455 URINARY INCONTINENCE. L24.A1 was added to line 71 NEUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES
2) **U09.9** Post COVID-19 condition, unspecified: There was discussion about possible pairing with acupuncture or other CAM therapy. Smits noted that such therapy was not included in the CDC or expert recommendations. There was discussion about the lack of evidence of effectiveness for any treatments for "long-haul" COVID, mainly due to the new nature of this condition. There was concern about adding pairings with various treatments when there is no evidence about their utility. Smits noted that all other COVID related coverage (e.g. monoclonal antibody therapy, vaccines) are based on CDC recommendations, although it was noted that these types of therapies do have evidence supporting their use. The final decision was to accept the staff recommendation, and direct staff to bring this topic back in approximately six months for reconsideration of pairings for possible changes to the October 2022 Prioritized List.

Recommended Actions:

1) 2022 ICD-10-CM code placement as shown in Appendix C
2) Modify the new guideline on cervicogenic headache as shown in Appendix B

MOTION: To recommend the code and guideline note changes as amended. CARRIES 6-0.

- **Topic: Breast Cancer Index**

Discussion: Smits reviewed the summary document. There was no discussion.

Public testimony
Max Salganik, Associate Director of Medical Affairs for Biotheranostics: Mr. Salganik testified that the breast cancer index's (BCI's) role is to inform extended endocrine therapy. He agreed with including both node negative and node positive patients based on NCCN recommendations. All of their studies have had a mix of node negative and positive patients. BCI could be used for identifying very low risk patients who could avoid chemotherapy, but he was not requesting coverage for such an indication.

Recommended Actions:
1) Modify GN148 as shown in Appendix A

MOTION: To recommend the guideline note changes as presented. CARRIES 6-0.

- **Topic: PET scans**

Discussion: Smits reviewed the summary document for PET scan use in breast cancer.

Public testimony
Holli Thomas: Ms. Thomas said she is a breast cancer patient and expressed her support for the newly revised proposed guideline. She questioned the use of the word "tumor" in the staff recommended guideline but agreed with the general staff recommended changes.

The group discussed alternatives to the word "tumor" in the revised guideline and decided that "neoplasm" was a more appropriate word. The guideline changes were approved with that amendment.

Smits reviewed the summary document for use of PET and other neuroimaging for patients with Alzheimer's disease being evaluated for treatment with certain medications. There was no discussion of the staff recommended changes.

Smits reviewed the summary document for guideline revisions for clarity. There was no discussion.

Recommended Actions:
1) Modify Diagnostic Guideline D22 as shown in Appendix A
2) Modify Diagnostic Guideline D7 as shown in Appendix A

MOTION: To recommend the guideline note changes as amended. CARRIES 6-0.

- **Topic: Preventive Services Guideline**

Discussion: Smits reviewed the summary documents. There was no discussion regarding use of Bright Futures as OHP's EPDST periodicity schedule.

Public testimony

1) Leslie Dennis, Quality Director for Adventist Health: Ms. Dennis testified about Cologuard as an option for colorectal cancer screening. Hawaii and California Medicaid cover this test, but not Oregon Medicaid. Adventist is requesting inclusion of all options to increase CRC screening. During the pandemic, she said Adventist has had a high return rate of mailed Cologuard tests and are increasing their colorectal cancer screening rates. She also said they were using Cologuard to reduce the number of colonoscopies that can be done due to COVID-19. Dennis noted that Adventist is seeing a higher return rate for Cologuard as compared to FIT. Cologuard also has a 3-year testing interval rather than a 1-year interval of FIT. Cologuard has an outreach program which is why she feels there is an increased return rate.

   Olson commented that Providence also sees increased testing uptake with Cologuard and raised concerns about ability to achieve screening goals without this option, especially with limits on colonoscopy availability during the pandemic. Pinzon asked Ms. Dennis about the cost difference to their health system between the two tests. Dennis answered FIT tests are paid for by the health system which takes the loss if the test is not returned but Cologuard takes the loss if their test is not returned. Pinzon asked what was Cologuard's rate of follow up for positive patients. Dennis replied that Adventist tries to reach out to positive patients to schedule a diagnostic colonoscopy. She could provide no data on whether there is higher rate of actual follow up with FIT versus Cologuard screening.

2) Melissa Wood, Exact Sciences: Ms. Wood testified that patient follow up and adherence is more challenging in the Medicaid population compared to other populations. However, Cologuard has seen a greater than 50% return rate nationwide in Medicaid populations. She said that flex sigmoidoscopy is not being used anymore. FIT has low return rate, which gets lower over each year in the 10-year screening cycle. Cologuard is 92% sensitive for early stage cancer. Cologuard has no longitudinal data on reducing CDC incidence or mortality. In Oregon, the only patients not covered for Cologuard are underserved patients.

The subcommittee briefly discussed coverage of Cologuard. Staff was directed to bring coverage of Cologuard back to a future meeting to discuss in more detail.

Recommended Actions:

1) Modify GN106 as shown in Appendix A
2) Add HCPCS G0327 (Colorectal cancer screening; blood-based biomarker) to line 502 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS and modify the entry in GN172 as shown in Appendix A
3) Staff will bring coverage of Cologuard back to a future meeting for further discussion

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

- **Topic: Occipital Neuralgia**

Discussion: Smits reviewed the summary document. There was no discussion.

Recommended Actions:

1) Add ICD-10-CM M54.81 (occipital neuralgia) to line 410 MIGRAINE HEADACHES and remove from line 402 CONDITIONS OF THE BACK AND SPINE

MOTION: To recommend the code changes as presented. CARRIES 6-0.

- **Topic: Smoking Cessation and Elective Surgery**

Discussion: Smits introduced the summary document. Schabel noted that the evidence in hip and knee arthroplasty shows that smoking cessation improves surgical outcomes. However, she said that the current policy is having unintended consequences. Her orthopedic group will not see an OHP patient who is smoking even for a consultation. This policy is thus causing access barriers, as well as frustration among patients, providers, and referring physicians. Pinzon suggested revising the guideline to allow consultations without smoking cessation. Hodges suggested noting in the minutes that the guideline is not intended to apply to surgical consultations but rather procedures. Schabel suggested adding wording to the guideline itself to clarify that it is not intended to prohibit elective surgical consultation. Hodges expressed support for this language as long as no timeline is included.

Public testimony
Tamara Fountain, ophthalmologist in Chicago and President of the American Academy of Ophthalmology (AAO): Dr. Fountain requested coverage of cataract surgery regardless of smoking status. Cataracts can lead to blindness and surgery is the only definitive treatment for cataracts. The AAO supports the HERC staff recommendation. There is no evidence that smoking status impacts cataract surgery outcomes. Current guidelines do not address smoking cessation prior to this surgery. The Centers for Medicare and Medicaid Services (CMS) local coverage determination does not include any smoking cessation prior to cataract surgery.

Nisha Nagarkatti-Gude, ophthalmologist in Portland, board member of the Oregon Academy of Ophthalmology: Dr. Nagarkatti-Gude agreed with the staff recommendation to exclude cataract and other bloodless surgeries. Cataract surgery is not always elective. Cataracts affect ability to drive, work, take medication, or perform other activities of life. Unlike other surgeries, cataract surgery does not have the risks of many complications. It involves a very small incision and no sutures. No adverse events have been seen in healing with smoking. Active smoking status and use of anesthesia is a concern, but most patients have little to no anesthesia for cataract surgery.

Further discussion amongst the subcommittee resulted in additional wording being added to the guideline to clarify that the guideline did not apply to surgical consultation.

Recommended Actions:
1) Modify Ancillary Guideline A4 as shown in Appendix A

MOTION: To recommend the guideline note changes as amended. CARRIES 6-0.

- **Topic: Rhinoplasty and septoplasty**

Discussion: Smits reviewed the summary document, as well as a late comment by Dr. Tom Wang, a facial reconstructive surgeon.

Public testimony
Richard Kohl: Dr. Kohl testified regarding lack of coverage for deviated septum repair for his daughter, who is an OHP patient. He discussed the impact of deviated septum on her physical and mental health. Staff offered to conduct research to see whether a change to the List may be appropriate and offered to connect him with appropriate resources to deal with individual circumstances.

The subcommittee discussed the proposed new guidelines. Dr. Wang's suggested changes were accepted.

Recommended Actions:
1) Adopt a new guideline regarding coverage of septoplasty as shown below in Appendix B
2) Remove CPT 30520 (Septoplasty or submucous resection, with or without cartilage scoring, contouring or replacement with graft) from line 202 SLEEP APNEA, NARCOLEPSY AND REM BEHAVIORAL DISORDER
3) Adopt a new guideline regarding coverage of rhinoplasty as shown below in Appendix B
4) Remove CPT 30420 (Rhinoplasty, primary; including major septal repair) from line 561 ALLERGIC RHINITIS AND CONJUNCTIVITIS, CHRONIC RHINITIS

MOTION: To recommend the code and guideline note changes as amended. CARRIES 6-0.

- **Topic: Radiofrequency Ablation for Uterine Fibroids**

Discussion: Smits reviewed the summary document. There was no discussion. If approved, the recommended changes would take effect 1/1/2022.

Recommended Actions:
1) Add CPT **58674** (Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency) to line 404 UTERINE LEIOMYOMA AND POLYPS
2) Remove CPT 58674 from line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS and remove the related entry from Guideline Note 173 as shown in Appendix A
3) Modify Guideline Note 40 as shown below
4) Add transcervical radiofrequency ablation (CPT 0404T) to line 662/GN173 as shown in Appendix A

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

- **Topic: Radiofrequency Water Vapor Ablation of Prostate for LUTS**

Discussion: Smits reviewed the summary document. There was no discussion. If approved, the recommended changes would take effect 1/1/2022.

Recommended Actions:

1) Add CPT **53854** (Transurethral destruction of prostate tissue; by radiofrequency generated water vapor) to line 327 FUNCTIONAL AND MECHANICAL DISORDERS OF THE GENITOURINARY SYSTEM INCLUDING BLADDER OUTLET OBSTRUCTION
2) Remove CPT 53854 from line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS
3) Modify Guideline Note 173 as shown in Appendix A

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

- **Topic: Thrush**

Discussion: Smits reviewed the summary document. There was no discussion.

Recommended Actions:

1) Add ICD-10-CM B37.0 (Candidal stomatitis) to line 18 FEEDING PROBLEMS IN NEWBORNS
2) Remove ICD-10-CM B37.0 from lines 275 UROLOGIC INFECTIONS and 583 CANDIDIASIS OF MOUTH, SKIN AND NAILS
3) Change the line name of line 583 to CANDIDIASIS OF ~~MOUTH,~~ SKIN AND NAILS

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

- **Topic: Coverage Guidance—Deep Brain Stimulation for Refractory Epilepsy**

Discussion: King reviewed the evidence summary. Smits reviewed the values and preferences. Smits also reviewed the Prioritized List changes required to operationalize the coverage guidance. Hodges requested that "multiple" medications be defined. King noted that the studies included patients who had failed three or more medications, which is also the FDA licensing requirement. The guideline was amended to define multiple as three or more. This new benefit would be effective January 1, 2022.

Recommended Actions:

1) Add to line 174 GENERALIZED CONVULSIVE OR PARTIAL EPILEPSY WITHOUT MENTION OF IMPAIRMENT OF CONSCIOUSNESS
    a. CPT 61863-61868 Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array
    b. CPT 61880 Revision or removal of intracranial neurostimulator electrodes
    c. CPT 61886 Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to two or more electrode arrays
2) Add a new guideline to line 174 as shown in Appendix B

MOTION: To approve the recommended changes to the Prioritized List as amended based on the draft Deep Brain Neurostimulators for Refractory Epilepsy coverage guidance scheduled for review by HERC at their August 12, 2021 meeting. CARRIES 6-0.

- **Public Comment:**

  Petra Wilson: Ms. Wilson testified she was a transgender woman on the Oregon Health Plan who is requesting coverage for electrolysis for facial hair. The current exceptions process requires severe psychosocial comorbidities for coverage of facial feminization, which acts as an inducement to present that kind of behavior in order to receive care. Ms. Wilson requested clarification of when electrolysis is covered around surgical sites, and stated that it should be covered for the top of breasts and between the breasts as well as for facial hair. Does this include around the surgical site or just at the incision? She cited a 2016 statement from the World Professional Association of Transgender Health (WPATH) which says that the WPATH 7.0 guideline intended to recommend electrolysis for facial hair as medically necessary.

  Olson and Smits said these issues can be addressed at a future meeting during the planned extensive review of gender dysphoria-related coverage.

- **Issues for next meeting:**
  No carryover topics.

- **Next meeting:**

  October 7, 2021 as a virtual meeting.

- **Adjournment:**

  The meeting adjourned at 12:50 PM.

Appendix A
Revised Guideline Notes

ANCILLARY GUIDELINE A4, SMOKING CESSATION AND ELECTIVE SURGICAL PROCEDURES

Surgical consultation is covered for patients who actively smoke and who are referred for surgical consultations; if elective surgery is recommended based on a consultation, the requirements of this guideline note apply.

Smoking cessation is required prior to elective surgical procedures for active tobacco users. Cessation is required for at least 4 weeks prior to the procedure and requires objective evidence of abstinence from smoking prior to the procedure.

Elective surgical procedures in this guideline are defined as surgical procedures which are flexible in their scheduling because they do not pose an imminent threat nor require immediate attention within 1 month. Procedures for contraceptive/sterilization purposes, procedures targeted to active cancers (i.e. when a delay in the procedure could lead to cancer progression), ~~and~~ diagnostic procedures, and bloodless surgery (e.g. cataract surgery, certain skin procedures) are not subject to the limitations in this guideline note. This guideline applies regardless of procedure location and anesthesia type.

The well-studied tests for confirmation of smoking cessation include cotinine levels and exhaled carbon monoxide testing. However, cotinine levels may be positive in nicotine replacement therapy (NRT) users, smokeless tobacco and e-cigarette users (which are not contraindications to elective surgery coverage). In patients using nicotine products aside from combustible cigarettes the following alternatives to urine cotinine to demonstrate smoking cessation may be considered:

- Exhaled carbon monoxide testing
- Anabasine or anatabine testing (NRT or vaping)

Certain procedures, such as lung volume reduction surgery, bariatric surgery, erectile dysfunction surgery, and spinal fusion have 6 month tobacco abstinence requirements. See Guideline Notes 8, 100, 112 and 159.

DIAGNOSTIC GUIDELINE D7, NEUROIMAGING IN DEMENTIA

Neuroimaging is covered:

A) To rule out reversible causes of dementia (tumors, normal pressure hydrocephalus and chronic subdural hematoma) via structural neuroimaging only
B) MRI is covered for monitoring for adverse effects of aducanumab or similar FDA-approved medications for treatment of Alzheimer's disease

Neuroimaging is not covered:

A) For screening of asymptomatic patients for dementia
B) To predict progression of the risk of developing dementia in patients with mild cognitive impairment
C) For screening, diagnosis, or monitoring of dementia, with functional neuroimaging (PET, SPECT or fMRI)
    1) PET scans are covered for patients being considered for treatment with aducanumab or similar FDA-approved medications for treatment of Alzheimer's disease.

Appendix A
Revised Guideline Notes

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

DIAGNOSTIC GUIDELINE D8, DIAGNOSTIC TESTING FOR OBSTRUCTIVE SLEEP APNEA (OSA) ~~IN ADULTS~~

For adults over the age of 18 years:

A) For patients ~~In adults~~ with clinical signs and symptoms consistent with obstructive sleep apnea (OSA), a home sleep study is the first-line diagnostic test for most patients, when available.
    1) For portable devices, Type II-III are included on this line. Type IV sleep testing devices must measure three or more channels, one of which is airflow, to be included on this line. Sleep testing devices that are not Type I-IV and measure three or more channels that include actigraphy, oximetry, and peripheral arterial tone, are included on this line.

B) Polysomnography in a sleep lab is indicated as a first-line test for patients with significant cardiorespiratory disease, potential respiratory muscle weakness due to a neuromuscular condition, awake hypoventilation or suspicion of sleep related hypoventilation, chronic opioid medication use, history of stroke or severe insomnia.

C) If a patient has had an inconclusive (or negative) home sleep apnea test and a clinical suspicion for OSA remains, then attended polysomnography is included on this line. Split night diagnostic protocols are required when a diagnosis of OSA is confirmed in the first portion of the night.

~~For portable devices, Type II-III are included on this line. Type IV sleep testing devices must measure three or more channels, one of which is airflow, to be included on this line. Sleep testing devices that are not Type1 IV and measure three or more channels that include actigraphy, oximetry, and peripheral arterial tone, are included on this line~~.

For children age of 18 years or younger:

A) Obstructive sleep apnea (OSA) ~~in children (18 or younger)~~ must be diagnosed by
    1) nocturnal polysomnography with an AHI >5 episodes/h or AHI>1 episodes/h with history and exam consistent with OSA, OR
    2) nocturnal pulse oximetry with 3 or more SpO2 drops <90% and 3 or more clusters of desaturation events, or alternatives desaturation (>3%) index >3.5 episodes/h, OR
    3) use of a validated questionnaire (such as the Pediatric Sleep Questionnaire or OSA 18), OR
    4) consultation with a sleep medicine specialist.

B) Polysomnography and/or consultation with a sleep medicine specialist to support the diagnosis of OSA and/or to identify perioperative risk is recommended for
    1) high-risk children (i.e. children with cranio-facial abnormalities, neuromuscular disorders, Down syndrome, etc.)
    2) children with equivocal indications for adenotonsillectomy (such as discordance between tonsillar size on physical examination and the reported severity of sleep-disordered breathing), children younger than three years of age

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

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DIAGNOSTIC GUIDELINE D22, PET SCANS ~~GUIDELINES~~

Diagnosis:

PET Scans are covered for diagnosis ~~of the following cancers~~ only when:

1) The PET scan is for evaluation of either
    a. Solitary pulmonary nodules and non-small cell lung cancer, OR
    b. Evaluation of cervical lymph node metastases when CT or MRI do not demonstrate an obvious primary tumor~~.~~, AND
2) the PET scan will
    a. ~~For diagnosis, PET is covered only when it will~~ avoid an invasive diagnostic procedure, OR
    b. will assist in determining the optimal anatomic location to perform an invasive diagnostic procedure.

Initial staging:

PET scans are covered for the initial staging when ~~of the following cancers~~:

1) The staging is for one of the following cancers/situations:
    a. Cervical cancer only when initial MRI or CT is negative for extra-pelvic metastasis
    b. Head and neck cancer when initial MRI or CT is equivocal
    c. Colon cancer
    d. Esophageal cancer
    e. Solitary pulmonary nodule
    f. Non-small cell lung cancer
    g. Lymphoma
    h. Melanoma,
    i. Breast cancer ONLY when metastatic disease is suspected AND standard imaging results are equivocal or suspicious; AND
2) ~~For initial staging, PET is covered when~~ clinical management of the patient will differ depending on the stage of the cancer identified and either:
    a. the stage of the cancer remains in doubt after standard diagnostic work up, OR
    b. PET replaces one or more conventional imaging studies when they are insufficient for clinical management of the patient.

Monitoring:

1) For monitoring tumor response during active therapy for purposes of treatment planning, PET is covered for classic Hodgkin's lymphoma treatment ~~only~~.
2) metastatic breast cancer ONLY when a change in therapy is contemplated AND PET scan was the imaging modality initially used to find the neoplasm being monitored.

~~PET is not covered to monitor tumor response during the planned course of therapy for any other cancer~~.

Restaging:

Restaging is covered only when:

1) ~~for cancers for which staging is covered and~~ the cancer has staging covered above OR for thyroid cancer if recurrence is suspected and I131 scintography is negative, AND
2) ~~For restaging, PET is covered after completion of treatment~~ Initial therapy has been completed, AND
3) ~~for the purpose of~~ The PET scan is conducted for

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a. detecting residual disease, or
b. ~~for~~ detecting suspected recurrence, or
c. ~~to~~ determin~~e~~ing the extent of a known recurrence.

~~PET scans are NOT indicated for routine follow up of cancer treatment or routine surveillance in asymptomatic patients~~.

Other indications:
PET scans are ~~also indicated~~ covered for preoperative evaluation of the brain in patients who have intractable seizures and are candidates for focal surgery. PET scans are covered for patients being considered for treatment with aducanumab or similar FDA approved medications for treatment of Alzheimer's disease. ~~PET scans are NOT indicated for cardiac evaluation.~~

Non-covered conditions/situations:
1) PET scans are NOT covered to monitor tumor response during the planned course of therapy for any cancer other than classic Hodgkin's lymphoma or the limited indication described above for metastatic breast cancer.
2) PET scans are NOT covered for routine follow up of cancer treatment or routine surveillance in asymptomatic patients.
3) PET scans are NOT covered for cardiac evaluation.

DIAGNOSTIC GUIDELINE D27, SARS-COV-2 (COVID-19) TESTING
Testing for SARS-CoV-2 (COVID-19) virus RNA or viral antigen is a covered diagnostic service.

Antibody testing for SARS-CoV-2 (COVID-19; CPT 86413, 86328 or 86769) is covered as diagnostic only when such testing meets the following criteria:

A) Testing is done using tests that have FDA Emergency Use Authorization (EUA) or FDA approval; AND
B) Testing is used as part of the diagnostic work up in hospitalized patients of
   1) acute COVID-19 infection in a patient with a previous negative COVID-19 antibody test and a negative COVID-19 RNA or viral antigen test; OR
   2) complications of COVID-19 infection, such as myocarditis, coagulopathy, or multisystem inflammatory syndrome in children (MIS-C) or multisystem inflammatory syndrome in adults (MIS-A).

Effective January 1, 2022
GUIDELINE NOTE 24, COMPLICATED HERNIAS
Lines 168,524
Complicated inguinal and femoral hernias in men are included on Line 168 if the hernia

1) causes symptoms of intestinal obstruction and/or strangulation; OR
2) is incarcerated (defined as non-reducible by physical manipulation); OR
3) causes pain and functional limitations as assessed and documented by a medical professional OR
4) Affects the patient's ability to obtain or maintain gainful employment.

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Repair of inguinal and femoral hernias in women and in children age 18 and younger are included on Line 168 due to the different natural history of disease in ~~this~~ these populations.

Ventral hernias are included on line 524. Incarcerated ventral hernias (including incarcerated abdominal incisional and umbilical hernias) are included on Line 524, because the chronic incarceration of large ventral hernias does not place the patient at risk for impending strangulation. Ventral hernias are defined as anterior abdominal wall hernias and include primary ventral hernias (epigastric, umbilical, Spigelian), parastomal hernias and most incisional hernias (ventral incisional hernias). K42.0, K43.0, K43.3, K43.6 and K46.0 are included on Line 524 when used to designate incarcerated abdominal incisional and umbilical hernias without intestinal obstruction or gangrene.

GUIDELINE NOTE 27, TREATMENT OF SLEEP APNEA

Line 202

For adults over the age of 18 years:

A) CPAP is covered initially when all of the following conditions are met:
   1) 12 week 'trial' period to determine benefit. This period is covered if apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) is greater than or equal to 15 events per hour; or if between 5 and 14 events with additional symptoms including one or more of the following:
   2) excessive daytime sleepiness defined as either an Epworth Sleepiness Scale score>10 or daytime sleepiness interfering with ADLs that is not attributable to another modifiable sedating condition (e.g. narcotic dependence), or
   3) documented hypertension, or
   4) ischemic heart disease, or
   5) history of stroke
   6) Additionally
      a) Providers must provide education to patients and caregivers prior to use of CPAP machine to ensure proper use; and
      b) Positive diagnosis through polysomnogram (PSG) or Home Sleep Test (HST).

B) CPAP coverage subsequent to the initial 12 weeks is based on documented patient tolerance, compliance, and clinical benefit. Compliance (adherence to therapy) is defined as use of CPAP for at least four hours per night on 70% of the nights during a consecutive 30-day period.

C) Mandibular advancement devices (oral appliances) are covered for those for whom CPAP fails or is contraindicated.

D) Surgery for sleep apnea in adults is not included on this line (due to lack of evidence of efficacy). Surgical codes are included on this line only for children who meet criteria below ~~according to Guideline Note 118 OBSTRUCTIVE SLEEP APNEA DIAGNOSIS AND TREATMENT FOR CHILDREN~~.

E) Hypoglossal nerve stimulation for treatment of obstructive sleep apnea is not included on this line due to insufficient evidence of effectiveness and evidence of harm.

For children age of 18 years or younger:

A) Adenotonsillectomy is an appropriate first line treatment for children with OSA. ~~Weight loss is recommended in addition to other therapy in patients who are overweight or obese.~~ Adenoidectomy without tonsillectomy is only covered when a child with OSA has previously had a tonsillectomy, when tonsillectomy is contraindicated, or when tonsillar hypertrophy is not

present. More complex surgical treatments are only included on this line for children with craniofacial anomalies.

B) Intranasal corticosteroids are an option for children with mild OSA in whom adenotonsillectomy is contraindicated or for mild postoperative OSA.

C) CPAP is covered for a 3 month trial for children through age 18 who have
   1) undergone surgery or are not candidates for surgery, AND
   2) have documented residual sleep apnea symptoms (sleep disruption and/or significant desaturations) with residual daytime symptoms (daytime sleepiness or behavior problems)

D) CPAP will be covered for children through age 18 on an ongoing basis if:
   1) There is documentation of improvement in sleep disruption and daytime sleepiness and behavior problems with CPAP use, AND
   2) Annual re-evaluation for CPAP demonstrates ongoing clinical benefit and compliance with use, defined as use of CPAP for at least four hours per night on 70% of the nights in a consecutive 30 day period

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

Effective January 1, 2022

GUIDELINE NOTE 40, UTERINE LEIOMYOMA

Line 404

Hysterectomy, myomectomy, ~~or~~ uterine artery embolization, or laparoscopic radiofrequency ablation for leiomyomata may be indicated when all of the following are documented (A-D):

A) One of the following (1 or 2):
   1) Patient history of 2 out of 3 of the following (a, b and c):
      a. Leiomyomata enlarging the uterus to a size of 12 weeks or greater gestation
      b. Pelvic discomfort cause by myomata (i or ii or iii):
         i) Chronic lower abdominal, pelvic or low backpressure
         ii) Bladder dysfunction not due to urinary tract disorder or disease
         iii) Rectal pressure and bowel dysfunction not related to bowel disorder or disease
      c. Rapid enlargement causing concern for sarcomatous changes of malignancy
   2) Leiomyomata as probable cause of excessive uterine bleeding evidenced by (a, b, c and d):
      a. Profuse bleeding lasting more than 7 days or repetitive periods at less than 21-day intervals
      b. Anemia due to acute or chronic blood loss (hemoglobin less than 10 or hemoglobin less than 11 g/dL if use of iron is documented)
      c. Documentation of mass by sonography
      d. Bleeding causes major impairment or interferes with quality of life

B) Nonmalignant cervical cytology, if cervix is present

C) Assessment for absence of endometrial malignancy in the presence of abnormal bleeding

D) Negative preoperative pregnancy test result unless patient is postmenopausal or has been previously sterilized

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GUIDELINE NOTE 106, PREVENTIVE SERVICES

Lines 3,622

Included on Line 3 are the following preventive services:

A) US Preventive Services Task Force (USPSTF) "A" and "B" Recommendations in effect and issued prior to January 1, 2020.
   1) http://www.uspreventiveservicestaskforce.org/Page/Name/uspstf-a-and-b-recommendations/
      a) Treatment of falls prevention with exercise interventions is included on Line 292.
   2) USPSTF "D" recommendations are not included on this line or any other line of the Prioritized List.

B) American Academy of Pediatrics (AAP) Bright Futures Guidelines:
   1) http://brightfutures.aap.org. Periodicity schedule available at http://www.aap.org/en-us/professional-resources/practice-support/Periodicity/Periodicity Schedule_FINAL.pdf.
      a) Bright Futures is the periodicity schedule for screening for EPSDT for the Oregon Health Plan.
   2) Screening for lead levels is defined as blood lead level testing and is indicated for Medicaid populations at 12 and 24 months. In addition, blood lead level screening of any child between ages 24 and 72 months with no record of a previous blood lead screening test is indicated.

C) Health Resources **and Services Administration (HRSA) Women's Preventive Services-Required Health Plan Coverage Guidelines a**s updated by HRSA in December 2019. Available at https://www.hrsa.gov/womens-guidelines-2019 as of September 4, 2020.

D) Immunizations as recommended by the Advisory Committee on Immunization Practices (ACIP): http://www.cdc.gov/vaccines/schedules/hcp/index.html or approved for the Oregon Immunization Program: https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Documents/DMAPvactable.pdf
   1) COVID-19 vaccines are intended to be included on this line even if the specific administration code(s) do not yet appear on the line when the vaccine has both 1) FDA approval or FDA emergency use authorization (EUA) and 2) ACIP recommendation.

Colorectal cancer screening is included on Line 3 for average-risk adults aged ~~50~~ 45 to 75, using one of the following screening programs:

A) Colonoscopy every 10 years
B) Flexible sigmoidoscopy every 5 years
C) Fecal immunochemical test (FIT) every year
D) Guaiac-based fecal occult blood test (gFOBT) every year

CT colonography CPT 74263), FIT-DNA (CPT 81528) and mSEPT9 (HCPCS G0327) are included on line 502 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS.

Colorectal cancer screening for average-risk adults aged 76 to 85 is covered only ~~for those who~~ after informed decision making between patients and clinicians which includes consideration of the patient's overall health, prior screening history, and preferences.

~~B) Are healthy enough to undergo treatment if colorectal cancer is detected, and~~

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C) Do not have comorbid conditions that would significantly limit their life expectancy.

Note: CPT code 96110 (Developmental screening (eg, developmental milestone survey, speech and language delay screen), with scoring and documentation, per standardized instrument) can be billed in addition to other CPT codes, such as evaluation and management (E&M) codes or preventive visit codes.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

GUIDELINE NOTE 118, OBSTRUCTIVE SLEEP APNEA DIAGNOSIS AND TREATMENT FOR CHILDREN

Line 202

Obstructive sleep apnea (OSA) in children (18 or younger) must be diagnosed by

A) nocturnal polysomnography with an AHI >5 episodes/h or AHI>1 episodes/h with history and exam consistent with OSA, OR
B) nocturnal pulse oximetry with 3 or more SpO2 drops <90% and 3 or more clusters of desaturation events, or alternatives desaturation (>3%) index >3.5 episodes/h, OR
C) use of a validated questionnaire (such as the Pediatric Sleep Questionnaire or OSA 18), OR
D) consultation with a sleep medicine specialist.

Polysomnography and/or consultation with a sleep medicine specialist to support the diagnosis of OSA and/or to identify perioperative risk is recommended for

A) high risk children (i.e. children with cranio-facial abnormalities, neuromuscular disorders, Down syndrome, etc.)
B) children with equivocal indications for adenotonsillectomy (such as discordance between tonsillar size on physical examination and the reported severity of sleep-disordered breathing),
C) children younger than three years of age

Adenotonsillectomy is an appropriate first line treatment for children with OSA. Weight loss is recommended in addition to other therapy in patients who are overweight or obese. Adenoidectomy without tonsillectomy is only covered when a child with OSA has previously had a tonsillectomy, when tonsillectomy is contraindicated, or when tonsillar hypertrophy is not present. More complex surgical treatments are only included on this line for children with craniofacial anomalies.

Intranasal corticosteroids are an option for children with mild OSA in whom adenotonsillectomy is contraindicated or for mild postoperative OSA.

CPAP is covered for a 3 month trial for children through age 18 who have

A) undergone surgery or are not candidates for surgery, AND
B) have documented residual sleep apnea symptoms (sleep disruption and/or significant desaturations) with residual daytime symptoms (daytime sleepiness or behavior problems)

CPAP will be covered for children through age 18 on an ongoing basis if:

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- ~~There is documentation of improvement in sleep disruption and daytime sleepiness and behavior problems with CPAP use~~
- ~~Annual re-evaluation for CPAP demonstrates ongoing clinical benefit and compliance with use, defined as use of CPAP for at least four hours per night on 70% of the nights in a consecutive 30 day period~~

GUIDELINE NOTE 148, BIOMARKER TESTS OF CANCER TISSUE

Lines 157,184,191,229,262,271,329

The use of tissue of origin testing (e.g. CPT 81504) is included on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS.

For early stage breast cancer, the following breast cancer genome profile tests are included on Line 191 when the listed criteria are met. One test per primary breast cancer is covered when the patient is willing to use the test results in a shared decision-making process regarding adjuvant chemotherapy. Lymph nodes with micrometastases less than 2 mm in size are considered node negative.

- Oncotype DX Breast Recurrence Score (CPT 81519) for breast tumors that are estrogen receptor positive, HER2 negative, and either lymph node negative, or lymph node positive with 1-3 involved nodes.
- EndoPredict (CPT 81522) and Prosigna (CPT 81520 or PLA 0008M) for breast tumors that are estrogen receptor positive, HER2 negative, and lymph node negative.
- MammaPrint (using CPT 81521 or HCPCS S3854) for breast tumors that are estrogen receptor or progesterone receptor positive, HER2 negative, lymph node negative, and only in those cases categorized as high clinical risk.

For early stage breast cancer that is estrogen receptor positive, HER2 negative, and either lymph node negative or lymph node positive with 1-3 involved nodes, Breast Cancer Index (CPT 81518) is included on line 191 when the patient is willing to use the test results in a shared decision-making process regarding prolonged adjuvant endocrine therapy.

EndoPredict, Prosigna, and MammaPrint are not included on Line 191 for early stage breast cancer with involved axillary lymph nodes. Oncotype DX Breast Recurrence Score is not included on Line 191 for breast cancer involving four or more axillary lymph nodes or more extensive metastatic disease.

Oncotype DX Breast DCIS Score (CPT 81479) is ~~and Breast Cancer Index (CPT 81518) are~~ included on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS.

For melanoma, BRAF gene mutation testing (CPT 81210) is included on Line 229. DecisionDx-Melanoma (CPT 81529) is included on Line 662.

For lung cancer, epidermal growth factor receptor (EGFR) gene mutation testing (CPT 81235) is included on Line 262 only for non-small cell lung cancer. KRAS gene mutation testing (CPT 81275) is not included on this line.

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For colorectal cancer, KRAS gene mutation testing (CPT 81275) is included on Line 157. BRAF (CPT 81210) and Oncotype DX are not included on this line. Microsatellite instability (MSI) is included on the Line 662.

For bladder cancer, Urovysion testing is included on Line 662.

For prostate cancer, Oncotype DX Genomic Prostate Score, Prolaris Score Assay (CPT 81541), and Decipher Prostate RP (CPT 81542) are included on Line 662.

For thyroid cancer, Afirma gene expression classifier (CPT 81546) is included on Line 662.

The development of this guideline note was informed by a HERC coverage guidance on Biomarkers Tests of Cancer Tissue for Prognosis and Potential Response to Treatment; the prostate-related portion of that coverage guidance was superseded by a Coverage Guidance on Gene Expression Profiling for Prostate Cancer. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

GUIDELINE NOTE 157, WIGS

Line 424,586

Wigs (HCPCS A9282) are covered only for hair loss due to chemotherapy or radiation therapy.

ICD-10-CM codes L58.0 (Acute radiodermatitis), L64.0 (Drug-induced androgenic alopecia) and L65.8 (Other specified nonscarring hair loss) are only included on line 424 for pairing with HCPC A9282 (Wig). Otherwise, these ICD10 codes are included on line 586.

GUIDELINE NOTE 218, CERVICOGENIC HEADACHE

Line 540

Osteopathic manipulative treatment and chiropractic manipulative treatment (CPT 98926-98929, 98940-98943) pair on this line only with cervicogenic headache (~~R51~~ G44.86).

GUIDELINE NOTE 172, INTERVENTIONS WITH MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS FOR CERTAIN CONDITIONS

Line 502

The following interventions are prioritized on Line 502 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS:

Procedure Code	Intervention Description	Rationale	Last Review
74263, 81528, 81327, G0327	Screening CT colonography, FIT-DNA (Cologuard), mSEPT9, Chromoscopy	Insufficient evidence for use in population screening	August 2021 ~~September, 2017~~ ; ~~August 2020 (Cologuard)~~

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GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
0404T	Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency	Insufficient evidence of effectiveness	August 2021
~~53854~~	~~Transurethral destruction of prostate tissue; by radiofrequency generated water vapor~~	~~Insufficient evidence of effectiveness~~	~~November, 2018~~
~~58674~~	~~Laparoscopy, surgical, ablation of uterine fibroid(s)~~	~~Insufficient evidence of effectiveness~~	~~November, 2016~~

Appendix B
New Guideline Notes

GUIDELINE NOTE XXX SEPTOPLASTY

Lines 42,119,246,287,465,506,525

Septoplasty is included on these lines when

A) The septoplasty is done to address symptomatic septal deviation or deformity which
    1) Fails to respond to a minimum 6 week trial of conservative management (e.g. nasal corticosteroids, decongestants, antibiotics); AND
    2) Results in one or more of the following:
        a. Persistent or recurrent epistaxis, OR
        b. Documented recurrent sinusitis felt to be due to a deviated septum and the patient meets criteria for sinus surgery in Guideline Note 35, SINUS SURGERY; OR
        c. Nasal obstruction with documented absence of other causes of obstruction likely to be responsible for the symptoms (for example, nasal polyps, tumor, etc.) [note: this indication is included only on line 506]; OR
B) Septoplasty is performed in association with cleft lip or cleft palate repair or repair of other congenital craniofacial anomalies; OR
C) Septoplasty is performed as part of a surgery for a neoplasm or facial trauma involving the nose.

Septoplasty is not covered for obstructive sleep apnea.

GUIDELINE NOTE XXX RHINOPLASTY

Lines 42,119,202,246,287,465,506,525

Rhinoplasty is included on these lines when

A) It is performed to correct a nasal deformity secondary to congenital cleft lip and/or palate or other severe congenital craniofacial anomaly; OR
B) It is performed as part of reconstruction after accidental or surgical trauma or disease (e.g., Wegener's granulomatosis, choanal atresia, nasal malignancy, abscess, septal infection with saddle deformity, or congenital deformity) AND
    1) There is prolonged, persistent obstructed nasal breathing unresponsive to a six week trial of conservative management (e.g. nasal corticosteroids, decongestants, antibiotics); AND
    2) Airway obstruction will not respond to septoplasty and turbinectomy alone; AND
    3) Photographs demonstrate an external nasal deformity; AND
    4) There is significant obstruction of one or both nares, documented by nasal endoscopy, computed tomography (CT) scan or other appropriate imaging modality; OR
C) There is nasal airway obstruction causing chronic rhinosinusitis when all of the following are met:
    1) The criteria for sinus surgery are met in Guideline Note 35, SINUS SURGERY; AND
    2) Airway obstruction will not respond to septoplasty and turbinectomy alone; AND
    3) Photographs demonstrate an external nasal deformity; AND
    4) There is significant obstruction of one or both nares), documented by nasal endoscopy, computed tomography (CT) scan or other appropriate imaging modality

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GUIDELINE NOTE XXX DEEP BRAIN STIMULATION FOR TREATMENT OF REFRACTORY EPILEPSY

Line 174

Deep brain stimulation for treatment of refractory epilepsy is included on this line only when

1) the surgery is performed at a Level 4 epilepsy center, AND
2) the patient has failed multiple (three or more) anti-seizure medications, AND
3) the patient is ineligible for resective surgery OR has failed vagus nerve stimulation or resective surgery

Appendix C
2022 ICD-10-CM Code Placement

ICD10 Code	Code Description	Recommended Placement
A79.82	Anaplasmosis [A. phagocytophilum]	268 RICKETTSIAL AND OTHER ARTHROPOD-BORNE DISEASES
C56.3	Malignant neoplasm of bilateral ovaries	238 CANCER OF OVARY
C79.63	Secondary malignant neoplasm of bilateral ovaries	238 CANCER OF OVARY
C84.7A	Anaplastic large cell lymphoma, ALK-negative, brea	158 NON-HODGKIN'S LYMPHOMAS Treatment: MEDICAL THERAPY 163 NON-HODGKIN'S LYMPHOMAS Treatment: BONE MARROW TRANSPLANT
D55.21	Anemia due to pyruvate kinase deficiency	194 HEREDITARY ANEMIAS, HEMOGLOBINOPATHIES, AND DISORDERS OF THE SPLEEN
D55.29	Anemia due to other disorders of glycolytic enzyme	194 HEREDITARY ANEMIAS, HEMOGLOBINOPATHIES, AND DISORDERS OF THE SPLEEN
D75.838	Other thrombocytosis	158 NON-HODGKIN'S LYMPHOMAS
D75.839	Thrombocytosis, unspecified	158 NON-HODGKIN'S LYMPHOMAS
D89.44	Hereditary alpha tryptasemia	652 ENDOCRINE AND METABOLIC CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
E75.244	Niemann-Pick disease type A/B	60 METABOLIC DISORDERS 99 END STAGE RENAL DISEASE 71,292,345,377 Dysfunction lines
F32.A	Depression, unspecified	203 DEPRESSION AND OTHER MOOD DISORDERS, MILD OR MODERATE
F78.A1	SYNGAP1-related intellectual disability	71,292,345,377 Dysfunction lines
F78.A9	Other genetic related intellectual disability	71,292,345,377 Dysfunction lines
G04.82	Acute flaccid myelitis	71,292,345,377 Dysfunction lines 535 VIRAL, SELF-LIMITING ENCEPHALITIS, MYELITIS AND ENCEPHALOMYELITIS
G44.86	Cervicogenic headache	540 TENSION HEADACHE
G92.00	Immune effector cell-associated neurotoxicity syndrome, grade unspecified	313 DISORDERS INVOLVING THE IMMUNE SYSTEM 71,292,345,377 Dysfunction lines
G92.01	Immune effector cell-associated neurotoxicity syndrome, grade 1	313 DISORDERS INVOLVING THE IMMUNE SYSTEM 71,292,345,377 Dysfunction lines

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G92.02	Immune effector cell-associated neurotoxicity syndrome, grade 2	313 DISORDERS INVOLVING THE IMMUNE SYSTEM 71,292,345,377 Dysfunction lines
G92.03	Immune effector cell-associated neurotoxicity syndrome, grade 3	313 DISORDERS INVOLVING THE IMMUNE SYSTEM 71,292,345,377 Dysfunction lines
G92.04	Immune effector cell-associated neurotoxicity syndrome, grade 4	313 DISORDERS INVOLVING THE IMMUNE SYSTEM 71,292,345,377 Dysfunction lines
G92.05	Immune effector cell-associated neurotoxicity syndrome, grade 5	313 DISORDERS INVOLVING THE IMMUNE SYSTEM 71,292,345,377 Dysfunction lines
G92.8	Other toxic encephalopathy	71,292,345,377 Dysfunction lines
G92.9	Unspecified toxic encephalopathy	71,292,345,377 Dysfunction lines
I5A	Non-ischemic myocardial injury (non-traumatic)	INFORMATIONAL DIAGNOSES
K22.81	Esophageal polyp	638 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM
K22.82	Esophagogastric junction polyp	638 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM
K22.89	Other specified disease of esophagus	56 ULCERS, GASTRITIS, DUODENITIS, AND GI HEMORRHAGE
K31.A0	Gastric intestinal metaplasia, unspecified	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A11	Gastric intestinal metaplasia without dysplasia, involving the antrum	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A12	Gastric intestinal metaplasia without dysplasia, involving the body (corpus)	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A13	Gastric intestinal metaplasia without dysplasia, involving the fundus	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A14	Gastric intestinal metaplasia without dysplasia, involving the cardia	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A15	Gastric intestinal metaplasia without dysplasia, involving multiple sites	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A19	Gastric intestinal metaplasia without dysplasia, unspecified site	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS

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K31.A21	Gastric intestinal metaplasia with low grade dysplasia	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A22	Gastric intestinal metaplasia with high grade dysplasia	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
K31.A29	Gastric intestinal metaplasia with dysplasia, unspecified	528 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
L24.A0	Irritant contact dermatitis due to friction or contact with body fluids, unspecified	455 URINARY INCONTINENCE
L24.A1	Irritant contact dermatitis due to saliva	71 EUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES
L24.A2	Irritant contact dermatitis due to fecal, urinary or dual incontinence	455 URINARY INCONTINENCE
L24.A9	Irritant contact dermatitis due friction or contact with other specified body fluids	455 URINARY INCONTINENCE
L24.B0	Irritant contact dermatitis related to unspecified stoma or fistula	71 EUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES
L24.B1	Irritant contact dermatitis related to digestive stoma or fistula	71 EUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES
L24.B2	Irritant contact dermatitis related to respiratory stoma or fistula	71 EUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES
L24.B3	Irritant contact dermatitis related to fecal or urinary stoma or fistula	71 EUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES
M31.10	Thrombotic microangiopathy, unspecified	175 POLYARTERITIS NODOSA AND ALLIED CONDITIONS
M31.11	Hematopoietic stem cell transplantation-associated thrombotic microangiopathy [HSCT-TMA]	285 COMPLICATIONS OF A PROCEDURE ALWAYS REQUIRING TREATMENT
M31.19	Other thrombotic microangiopathy	175 POLYARTERITIS NODOSA AND ALLIED CONDITIONS

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M35.05	Sjogren syndrome with inflammatory arthritis	330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M35.06	Sjogren syndrome with peripheral nervous system involvement	330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M35.07	Sjogren syndrome with central nervous system involvement	330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M35.08	Sjogren syndrome with gastrointestinal involvement	330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M35.0A	Sjogren syndrome with glomerular disease	59 END STAGE RENAL DISEASE Treatment MEDICAL THERAPY INCLUDING DIALYSIS 99 END STAGE RENAL DISEASE Treatment RENAL TRANSPLANT 330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M35.0B	Sjogren syndrome with vasculitis	330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M35.0C	Sjogren syndrome with dental involvement	53 PREVENTIVE DENTAL SERVICES 330 SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME
M45.A0	Non-radiographic axial spondyloarthritis of unspecified sites in spine	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A1	Non-radiographic axial spondyloarthritis of occipito-atlanto-axial region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A2	Non-radiographic axial spondyloarthritis of cervical region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A3	Non-radiographic axial spondyloarthritis of cervicothoracic region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A4	Non-radiographic axial spondyloarthritis of thoracic region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A5	Non-radiographic axial spondyloarthritis of thoracolumbar region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A6	Non-radiographic axial spondyloarthritis of lumbar region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS

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M45.A7	Non-radiographic axial spondyloarthritis of lumbosacral region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.A8	Non-radiographic axial spondyloarthritis of sacral and sacrococcygeal region	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M45.AB	Non-radiographic axial spondyloarthritis of multiple sites in spine	402 CONDITIONS OF THE BACK AND SPINE 529 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS
M54.50	Low back pain, unspecified	402 CONDITIONS OF THE BACK AND SPINE
M54.51	Vertebrogenic low back pain	402 CONDITIONS OF THE BACK AND SPINE
M54.59	Other low back pain	402 CONDITIONS OF THE BACK AND SPINE
P00.82	Newborn affected by (positive) maternal group B streptococcus (GBS) colonization	2 BIRTH OF INFANT
P09.1	Abnormal findings on neonatal screening for inborn errors of metabolism	DIAGNOSTIC WORKUP FILE (DWF)
P09.2	Abnormal findings on neonatal screening for congenital endocrine disease	DIAGNOSTIC WORKUP FILE (DWF)
P09.3	Abnormal findings on neonatal screening for congenital hematologic disorders	DIAGNOSTIC WORKUP FILE (DWF)
P09.4	Abnormal findings on neonatal screening for cystic fibrosis	DIAGNOSTIC WORKUP FILE (DWF)
P09.5	Abnormal findings on neonatal screening for critical congenital heart disease	DIAGNOSTIC WORKUP FILE (DWF)
P09.6	Abnormal findings on neonatal screening for neonatal hearing loss	DIAGNOSTIC WORKUP FILE (DWF)
P09.8	Other abnormal findings on neonatal screening	DIAGNOSTIC WORKUP FILE (DWF)
P09.9	Abnormal findings on neonatal screening, unspecified	DIAGNOSTIC WORKUP FILE (DWF)
R05.1	Acute cough	DIAGNOSTIC WORKUP FILE (DWF)
R05.2	Subacute cough	DIAGNOSTIC WORKUP FILE (DWF)
R05.3	Chronic cough	DIAGNOSTIC WORKUP FILE (DWF)
R05.4	Cough syncope	DIAGNOSTIC WORKUP FILE (DWF)
R05.8	Other specified cough	DIAGNOSTIC WORKUP FILE (DWF)
R05.9	Cough, unspecified	DIAGNOSTIC WORKUP FILE (DWF)
R35.81	Nocturnal polyuria	DIAGNOSTIC WORKUP FILE (DWF)
R35.89	Other polyuria	DIAGNOSTIC WORKUP FILE (DWF)
R45.88	Nonsuicidal self-harm	203 DEPRESSION AND OTHER MOOD DISORDERS, MILD OR MODERATE
R63.30	Feeding difficulties, unspecified	DIAGNOSTIC WORKUP FILE (DWF)

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R63.31	Pediatric feeding disorder, acute	149 FEEDING AND EATING DISORDERS OF INFANCY OR CHILDHOOD
R63.32	Pediatric feeding disorder, chronic	149 FEEDING AND EATING DISORDERS OF INFANCY OR CHILDHOOD
R63.39	Other feeding difficulties	DIAGNOSTIC WORKUP FILE (DWF)
R79.83	Abnormal findings of blood amino-acid level	DIAGNOSTIC WORKUP FILE (DWF)
S06.A0XA	Traumatic brain compression without herniation, initial encounter	196 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN
S06.A0XD	Traumatic brain compression without herniation, subsequent encounter	196 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN
S06.A0XS	Traumatic brain compression without herniation, sequela	INFORMATIONAL DIAGNOSIS
S06.A1XA	Traumatic brain compression with herniation, initial encounter	196 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN
S06.A1XD	Traumatic brain compression with herniation, subsequent encounter	196 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN
S06.A1XS	Traumatic brain compression with herniation, sequela	196 SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN
T40.711A	Poisoning by cannabis, accidental (unintentional), initial encounter	71,292,345,377 Dysfunction lines 102 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS
T40.711D	Poisoning by cannabis, accidental (unintentional), subsequent encounter	71,102,292,345,377
T40.711S	Poisoning by cannabis, accidental (unintentional), sequela	71,102,292,345,377
T40.712A	Poisoning by cannabis, intentional self-harm, initial encounter	71,102,292,345,377
T40.712D	Poisoning by cannabis, intentional self-harm, subsequent encounter	71,102,292,345,377
T40.712S	Poisoning by cannabis, intentional self-harm, sequela	INFORMATIONAL DIAGNOSIS
T40.713A	Poisoning by cannabis, assault, initial encounter	71,102,292,345,377
T40.713D	Poisoning by cannabis, assault, subsequent encounter	71,102,292,345,377
T40.713S	Poisoning by cannabis, assault, sequela	INFORMATIONAL DIAGNOSIS

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T40.714A	Poisoning by cannabis, undetermined, initial encounter	71,102,292,345,377
T40.714D	Poisoning by cannabis, undetermined, subsequent encounter	71,102,292,345,377
T40.714S	Poisoning by cannabis, undetermined, sequela	INFORMATIONAL DIAGNOSIS
T40.715A	Adverse effect of cannabis, initial encounter	102 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS
T40.715D	Adverse effect of cannabis, subsequent encounter	102 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS
T40.715S	Adverse effect of cannabis, sequela	INFORMATIONAL DIAGNOSIS
T40.716A	Underdosing of cannabis, initial encounter	DIAGNOSTIC WORKUP FILE (DWF)
T40.716D	Underdosing of cannabis, subsequent encounter	DIAGNOSTIC WORKUP FILE (DWF)
T40.716S	Underdosing of cannabis, sequela	INFORMATIONAL DIAGNOSIS
T40.721A	Poisoning by synthetic cannabinoids, accidental (unintentional), initial encounter	71,292,345,377 Dysfunction lines 102 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS
T40.721D	Poisoning by synthetic cannabinoids, accidental (unintentional), subsequent encounter	71,102,292,345,377
T40.721S	Poisoning by synthetic cannabinoids, accidental (unintentional), sequela	INFORMATIONAL DIAGNOSIS
T40.722A	Poisoning by synthetic cannabinoids, intentional self-harm, initial encounter	71,102,292,345,377
T40.722D	Poisoning by synthetic cannabinoids, intentional self-harm, subsequent encounter	71,102,292,345,377
T40.722S	Poisoning by synthetic cannabinoids, intentional self-harm, sequela	INFORMATIONAL DIAGNOSIS
T40.723A	Poisoning by synthetic cannabinoids, assault, initial encounter	71,102,292,345,377
T40.723D	Poisoning by synthetic cannabinoids, assault, subsequent encounter	71,102,292,345,377
T40.723S	Poisoning by synthetic cannabinoids, assault, sequela	INFORMATIONAL DIAGNOSIS
T40.724A	Poisoning by synthetic cannabinoids, undetermined, initial encounter	71,102,292,345,377
T40.724D	Poisoning by synthetic cannabinoids, undetermined, subsequent encounter	71,102,292,345,377
T40.724S	Poisoning by synthetic cannabinoids, undetermined, sequela	INFORMATIONAL DIAGNOSIS

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T40.725A	Adverse effect of synthetic cannabinoids, initial encounter	102 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS
T40.725D	Adverse effect of synthetic cannabinoids, subsequent encounter	102 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS
T40.725S	Adverse effect of synthetic cannabinoids, sequela	INFORMATIONAL DIAGNOSIS
T40.726A	Underdosing of synthetic cannabinoids, initial encounter	DIAGNOSTIC WORKUP FILE (DWF)
T40.726D	Underdosing of synthetic cannabinoids, subsequent encounter	DIAGNOSTIC WORKUP FILE (DWF)
T40.726S	Underdosing of synthetic cannabinoids, sequela	INFORMATIONAL DIAGNOSIS
T80.82XA	Complication of immune effector cellular therapy, initial encounter	424 COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT
T80.82XD	Complication of immune effector cellular therapy, subsequent encounter	424 COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT
T80.82XS	Complication of immune effector cellular therapy, sequela	INFORMATIONAL DIAGNOSIS
Y35.899A	Legal intervention involving other specified means, unspecified person injured, initial encounter	INFORMATIONAL DIAGNOSES
Y35.899D	Legal intervention involving other specified means, unspecified person injured, subsequent encounter	INFORMATIONAL DIAGNOSES
Y35.899S	Legal intervention involving other specified means, unspecified person injured, sequela	INFORMATIONAL DIAGNOSES
Z55.5	Less than a high school diploma	INFORMATIONAL DIAGNOSES
Z58.6	Inadequate drinking-water supply	INFORMATIONAL DIAGNOSES
Z59.00	Homelessness unspecified	INFORMATIONAL DIAGNOSES
Z59.01	Sheltered homelessness	INFORMATIONAL DIAGNOSES
Z59.02	Unsheltered homelessness	INFORMATIONAL DIAGNOSES
Z59.41	Food insecurity	INFORMATIONAL DIAGNOSES
Z59.48	Other specified lack of adequate food	INFORMATIONAL DIAGNOSES
Z59.811	Housing instability, housed, with risk of homelessness	INFORMATIONAL DIAGNOSES
Z59.812	Housing instability, housed, homelessness in past 12 months	INFORMATIONAL DIAGNOSES
Z59.819	Housing instability, housed unspecified	INFORMATIONAL DIAGNOSES
Z59.89	Other problems related to housing and economic circumstances	INFORMATIONAL DIAGNOSES
Z71.85	Encounter for immunization safety counseling	3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS

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Z91.014	Allergy to mammalian meats	INFORMATIONAL DIAGNOSES
Z91.51	Personal history of suicidal behavior	INFORMATIONAL DIAGNOSES
Z91.52	Personal history of nonsuicidal self-harm	INFORMATIONAL DIAGNOSES
Z92.850	Personal history of Chimeric Antigen Receptor T-cell therapy	INFORMATIONAL DIAGNOSES
Z92.858	Personal history of other cellular therapy	INFORMATIONAL DIAGNOSES
Z92.859	Personal history of cellular therapy, unspecified	INFORMATIONAL DIAGNOSES
Z92.86	Personal history of gene therapy	INFORMATIONAL DIAGNOSES
U09.9	Post COVID-19 condition, unspecified	345 NEUROLOGICAL DYSFUNCTION IN COMMUNICATION CAUSED BY CHRONIC CONDITIONS 399 INFLUENZA, COVID-19 AND OTHER NOVEL RESPIRATORY VIRAL ILLNESS

Section 2.0

Staff Report

Section 3.0

Consent Agenda-

Straightforward Items

Consent Agenda Issues—October 2021

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
64792	Excision of neurofibroma or neurolemmoma; extensive (including malignant type)	199 CANCER OF SOFT TISSUE 207 DEEP OPEN WOUND, WITH OR WITHOUT TENDON OR NERVE INVOLVEMENT 527 DEFORMITIES OF UPPER BODY AND ALL LIMBS	CPT 64792 is on several inappropriate lines and should also be added to line 199 to pair with ICD-10-CM C47.2 (Malignant neoplasm of peripheral nerves)	Remove 64792 from lines 207 and 527 Add 64792 to line 199
45800	Closure of rectovesical fistula	230 URINARY FISTULA	CPT 45800 currently only appears on line 100 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION. Similar CPT 45820 is on line 230	Add 45800 to line 230
95873 95874	Electrical stimulation for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure) Needle electromyography for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)	410 MIGRAINE HEADACHES	Per coding guidelines, 95874 and 95873 are add-on codes to be billed with CPT codes 64612,64615, 64616, 64642, 64643, 64644, 64645, 64646, 64647, 64653, 64999. Currently, 95873 and 95874 are on lines 292 and 362 and pair with all the 64XXX codes other than 64615. CPT 64615 is on line 410	Add 95873 and 95874 to line 410

Straightforward Guideline Changes

1) Ancillary Guideline A4 SMOKING CESSATION AND ELECTIVE SURGICAL PROCEDURES was modified at the August 2021 meeting to allow "bloodless surgery." The discussion was entirely around cataract surgery. The other example proposed in the guideline was "certain skin procedures." The CCO medical directors are asking for clarification of what types of procedures would qualify. HERC staff feel that leaving the example simply as "e.g. cataract surgery" would be preferable. See proposed edits below (purple text shows what was approved at the 8/12/21 meeting):

ANCILLARY GUIDELINE A4, SMOKING CESSATION AND ELECTIVE SURGICAL PROCEDURES
Surgical consultation is covered for patients who actively smoke and who are referred for surgical consultations; if elective surgery is recommended based on a consultation, the requirements of this guideline note apply.

Smoking cessation is required prior to elective surgical procedures for active tobacco users. Cessation is required for at least 4 weeks prior to the procedure and requires objective evidence of abstinence from smoking prior to the procedure.

Elective surgical procedures in this guideline are defined as surgical procedures which are flexible in their scheduling because they do not pose an imminent threat nor require immediate attention within 1 month. Procedures for contraceptive/sterilization purposes, procedures targeted to active cancers (i.e. when a delay in the procedure could lead to cancer progression), ~~and~~ diagnostic procedures, and bloodless surgery (e.g. cataract surgery~~, certain skin procedures~~) are not subject to the limitations in this guideline note. This guideline applies regardless of procedure location and anesthesia type.

The well-studied tests for confirmation of smoking cessation include cotinine levels and exhaled carbon monoxide testing. However, cotinine levels may be positive in nicotine replacement therapy (NRT) users, smokeless tobacco and e-cigarette users (which are not contraindications to elective surgery coverage). In patients using nicotine products aside from combustible cigarettes the following alternatives to urine cotinine to demonstrate smoking cessation may be considered:

- Exhaled carbon monoxide testing
- Anabasine or anatabine testing (NRT or vaping)

Certain procedures, such as lung volume reduction surgery, bariatric surgery, erectile dysfunction surgery, and spinal fusion have 6 month tobacco abstinence requirements. See Guideline Notes 8, 100, 112 and 159.

2) Biofeedback was removed from the Ancillary List and placed on a couple of lines on the Prioritized List in January 2021. The codes were also added to GN173/line 662. HSD has asked to have the code removed from line 662/GN173 as it is highly difficult in MMIS to have a code on a covered line and on line 662. Removing these codes from line 662/GN173 will allow their use only if paired with a diagnosis on the migraine or tension headache lines or when used for cancer (Statement of Intent 1). HERC staff recommends the removal shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
~~90875-90876~~ ~~90901~~	~~Individual psychophysiological therapy incorporating biofeedback training by any modality~~ ~~Biofeedback training by any modality~~	~~Insufficient evidence of effectiveness~~	~~January 2021~~
90912-90913	Biofeedback training, perineal muscles, anorectal or urethral sphincter, including EMG and/or manometry, when performed	Insufficient evidence of effectiveness	January 2021

Septoplasty Coding Clarification

Issue: At the August, 2021 VBBS/HERC meeting, new guidelines were adopted regarding rhinoplasty and septoplasty. It has been brought to HERC staff attention that there are issues with the placement of diagnosis and procedure codes related to septoplasty. Multiple codes are missing from lines that would allow pairing which, although below the line, would be available for use with the co-morbidity rule

Current Prioritized List status

Code	Code Description	Current Placement
CPT 30520	Septoplasty or submucous resection, with or without cartilage scoring, contouring or replacement with graft	42 CLEFT PALATE WITH AIRWAY OBSTRUCTION 119 CHOANAL ATRESIA 246 LIFE-THREATENING EPISTAXIS 287 CANCER OF ORAL CAVITY, PHARYNX, NOSE AND LARYNX 465 CHRONIC SINUSITIS 506 NASAL POLYPS, OTHER DISORDERS OF NASAL CAVITY AND SINUSES 525 BENIGN NEOPLASM OF NASAL CAVITIES, MIDDLE EAR AND ACCESSORY SINUSES
CPT 30620	Septal or other intranasal dermatoplasty	42,246,465,506,576
ICD J34.2	Deviated nasal septum	576 DEVIATED NASAL SEPTUM, ACQUIRED DEFORMITY OF NOSE, OTHER DISEASES OF UPPER RESPIRATORY TRACT
ICD Q67.4	Other congenital deformities of skull, face and jaw Includes "Deviation of nasal septum, congenital" as a subdiagnosis	256 DEFORMITIES OF HEAD 661 MISCELLANEOUS CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY

New guideline adopted August 12, 2021
GUIDELINE NOTE 118 SEPTOPLASTY

Lines 42,119,246,287,465,506,525

Septoplasty is included on these lines when

A) The septoplasty is done to address symptomatic septal deviation or deformity which
    1) Fails to respond to a minimum 6 week trial of conservative management (e.g. nasal corticosteroids, decongestants, antibiotics); AND
    2) Results in one or more of the following:
        a. Persistent or recurrent epistaxis, OR
        b. Documented recurrent sinusitis felt to be due to a deviated septum and the patient meets criteria for sinus surgery in Guideline Note 35, SINUS SURGERY; OR
        c. Nasal obstruction with documented absence of other causes of obstruction likely to be responsible for the symptoms (for example, nasal polyps, tumor, etc.) [note: this indication is included only on line 506]; OR
B) Septoplasty is performed in association with cleft lip or cleft palate repair or repair of other congenital craniofacial anomalies; OR
C) Septoplasty is performed as part of a surgery for a neoplasm or facial trauma involving the nose.

Septoplasty Coding Clarification

Septoplasty is not covered for obstructive sleep apnea.

HERC staff recommendations:

1) Add CPT 30520 (Septoplasty or submucous resection, with or without cartilage scoring, contouring or replacement with graft) to line 576 DEVIATED NASAL SEPTUM, ACQUIRED DEFORMITY OF NOSE, OTHER DISEASES OF UPPER RESPIRATORY TRACT
2) Add ICD-10-CM Q67.4 (Other congenital deformities of skull, face and jaw) to line 576
3) Modify the new septoplasty guideline as shown below

GUIDELINE NOTE XXX SEPTOPLASTY

Lines 42,119,246,287,465,506,525,576

Septoplasty is included on these lines when

A) The septoplasty is done to address symptomatic septal deviation or deformity which
    1) Fails to respond to a minimum 6 week trial of conservative management (e.g. nasal corticosteroids, decongestants, antibiotics); AND
    2) Results in one or more of the following:
        a. Persistent or recurrent epistaxis, OR
        b. Documented recurrent sinusitis felt to be due to a deviated septum and the patient meets criteria for sinus surgery in Guideline Note 35, SINUS SURGERY; OR
        c. Nasal obstruction with documented absence of other causes of obstruction likely to be responsible for the symptoms (for example, nasal polyps, tumor, etc.) [note: this indication is included only on line ~~506~~ 576]; OR
B) Septoplasty is performed in association with cleft lip or cleft palate repair or repair of other congenital craniofacial anomalies; OR
C) Septoplasty is performed as part of a surgery for a neoplasm or facial trauma involving the nose.

Septoplasty is not covered for obstructive sleep apnea.

Wireless Capsule Endoscopy Rereview
October 2021

Question: Should any changes be made to the current coverage of various wireless diagnostic tests for the gastrointestinal tract?

Question source: Holly Jo Hodges, CCO medical director; HERC staff

Issue: Multiple wireless tests exist for evaluating the gastrointestinal tract. One test, capsule endoscopy (CPT 91110), is on two covered lines with a guideline. Multiple other tests are on line 662/GN173, with last review dates between 2010 and 2015. Based on the HERC policy of reviewing topics not reviewed in the past 5 years, these procedures were all re-reviewed to look for new evidence that might support moving to a covered line.

There are several tests that have been trialed for the evaluation and diagnosis of transit and motility disorders of the gastrointestinal (GI) tract. The gold standard and most commonly performed test to evaluate gastric emptying is gastric scintigraphy, a radionuclide gastric emptying study used for the evaluation of gastrointestinal motility disorders, and gastroparesis. Colonic motility studies are used to assess the flow of intraluminal contents, the motions of the colonic wall that induce flow, and the control systems that integrate and regulate these processes.

Current Prioritized List status
91110 (Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus through ileum, with interpretation and report) is on lines 29 REGIONAL ENTERITIS, IDIOPATHIC PROCTOCOLITIS, ULCERATION OF INTESTINE and 56 ULCERS, GASTRITIS, DUODENITIS, AND GI HEMORRHAGE

GUIDELINE NOTE 9, WIRELESS CAPSULE ENDOSCOPY

Lines 29,56

A) Wireless capsule endoscopy is included on these lines for diagnosis of:
   1) Obscure GI bleeding suspected to be of small bowel origin with iron deficiency anemia or documented GI blood loss
   2) Suspected Crohn's disease with prior negative work up
B) Wireless capsule endoscopy is not included on these lines for:
   1) Colorectal cancer screening
   2) Confirmation of lesions of pathology normally within the reach of upper or lower endoscopes (lesions proximal to the ligament of Treitz or distal to the ileum)
C) Wireless capsule endoscopy is only included on these lines when the following conditions have been met:
   1) Prior studies must have been performed and been non-diagnostic
      a) GI bleeding: upper and lower endoscopy
      b) Suspected Crohn's disease: upper and lower endoscopy, small bowel follow through
   2) Radiological evidence of lack of stricture
   3) Only covered once during any episode of illness
   4) FDA approved devices must be used
   5) Patency capsule should not be used prior to procedure

Wireless Capsule Endoscopy Rereview
October 2021

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS
Line 662
The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
91111	Capsule endoscopy, esophagus	No evidence of effectiveness	December, 2012
91112	Gastrointestinal transit and pressure measurement	Insufficient evidence of effectiveness	December, 2012

Evidence

1) **NICE 2014**: Assessing motility of the GI tract using a wireless capsule
    a. The evidence on assessing motility of the gastrointestinal tract using a wireless capsule raises no major safety concerns. There is evidence of efficacy in measuring gastrointestinal function but uncertainty about the clinical benefit of this, and about patient selection. Therefore, this procedure should be used only with special arrangements for clinical governance, consent and audit or research.
    b. One systematic review (12 studies, 745 patients) identified
        i. sensitivity of the wireless motility capsule in comparison with clinical diagnosis of gastroparesis to be 65 to 68% and specificity to be 82 to 87% in a subset of 560 patients (reported by 7 studies included in the systematic review).
        ii. sensitivity of the capsule in comparison with gastric emptying scintigraphy to be 59 to 86% and specificity to be 64 to 81% in a subset of 560 patients (reported by 7 studies included in the systematic review).
        iii. sensitivity of the capsule compared with a radiopaque marker to be 37% and specificity to be 95% in a subset of 78 patients (reported by 1 study included in the systematic review) with constipation.
        iv. In a subset of 3 studies, using the wireless capsule altered management (medicine, diet or surgery) in 50 to 69% of patients with suspected gastroparesis
    c. A case series of 187 patients with constipation reported 7 adverse events as being possibly or definitely related to the capsule: 2 cases of abdominal pain, 1 case of diarrhea, 2 cases of dysphagia and 2 cases of nausea. Device malfunction was reported in 4% (8/180)
2) **AHRQ 2013,** systematic review of gastric and colonic transit studies
    a. N=12 studies (7 gastric emptying; 9 colonic motility)
    b. Gastric or colonic scintigraphy was used as the "gold standard" test
        i. Gastric emptying: low strength of evidence (SOE) that wireless capsule endoscopy (WMC) alone was comparable to scintigraphy for diagnostic accuracy, accuracy of motility assessment, effect on treatment decisions, and effect on resource utilization. Sensitivity of WMC compared with gastric scintigraphy ranged from 59 to 86 percent and specificity ranged from 64 to 81 percent.

ii. Colonic motility: moderate SOE for diagnostic accuracy, accuracy of motility assessment, and harms. WMC was comparable to radiopaque markers (ROM), with concordance ranging between 64 percent and 87 percent. Few harms were reported. The evidence was insufficient to justify conclusions about effects of WMC on treatment decisions and resource utilization.

c. **Conclusions.** WMC is comparable in accuracy to current modalities in use for detection of slow transit constipation and gastric emptying delay, and is therefore another viable diagnostic modality. Little data are available to determine the optimal timing of WMC for diagnostic algorithms

Other expert guidelines

1) **American Society for Gastrointestinal Endoscopy 2013**, technology review on wireless capsule endoscopy https://www.giejournal.org/action/showPdf?pii=S0016-5107%2813%2902091-9
    a. Over the last decade, WCE has established itself as a valuable test for imaging the small intestine. It is a safe and relatively easy procedure to perform that can provide valuable information in the diagnosis of small-bowel conditions. Its applications still remain limited within the esophagus and colon

Other payer policies

1) Aetna 2021
    a. Aetna considers the use of colonic motility studies (colonic manometry) medically necessary to guide decision-making for surgery in children with refractory colonic motility / defecatory disorders.
    b. Aetna considers a wireless capsule for measuring gastric emptying parameters (SmartPill GI Monitoring System) experimental and investigational for the evaluation of gastric disorders (e.g., gastroparesis), intestinal motility disorders (e.g., chronic constipation), and all other indications because of inadequate published evidence of its diagnostic performance and clinical utility over conventional means of measuring gastric emptying.

2) Cigna 2021
    a. Esophageal Capsule Endoscopy (CPT® 91111) is indicated in the following clinical scenario:
        i. When endoscopic procedures may be inappropriate or contraindicated, such as:
            1. Individuals with non-reversible coagulopathy OR
            2. Recent MI OR
            3. Evaluation of esophageal varices in cirrhotic individuals who are unable to tolerate or undergo EGD

Wireless Capsule Endoscopy Rereview
October 2021

HERC staff summary

Major evidence sources (NICE, AHRQ) and specialty society guidelines (ASGE) do not find strong evidence for use of wireless capsule endoscopy for evaluation of gastroparesis or intestinal motility issues. The American Society for Gastrointestinal Endoscopy finds limited application for the use of capsule endoscopy in the esophagus or colon.

HERC staff recommendations:

1) Make no changes in current coverage of wireless capsule endoscopy
2) Update the GN173 entries as shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
91111	Capsule endoscopy, esophagus	~~No~~ Insufficient evidence of effectiveness	~~December, 2012~~ October 2021
91112	Gastrointestinal transit and pressure measurement	Insufficient evidence of effectiveness	~~December, 2012~~ October 2021

NICE guidance

Assessing motility of the gastrointestinal tract using a wireless capsule

Interventional procedure guidance
Published: 21 January 2014
nice.org.uk/guidance/ipg502

1 Recommendations

1.1 The evidence on assessing motility of the gastrointestinal tract using a wireless capsule raises no major safety concerns. There is evidence of efficacy in measuring gastrointestinal function but uncertainty about the clinical benefit of this, and about patient selection. Therefore, this procedure should be used only with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to assess motility of the gastrointestinal tract using a wireless capsule should take the following actions:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.
- Audit and review clinical outcomes of all patients having the motility of the gastrointestinal tract assessed using a wireless capsule (see section 7.1).

1.3 NICE encourages further research into the use of a wireless capsule to assess motility of the gastrointestinal tract. Studies should include clear details of patient selection. They should report on the diagnostic accuracy of the

procedure in different parts of the gastrointestinal tract, and should provide data on the clinical benefits of the procedure for patients.

2 Indications and current treatments

2.1 The procedure is used to investigate gastrointestinal (GI) motility-related symptoms. Motility disorders can sometimes be difficult to diagnose. They include conditions such as gastroparesis and slow transit constipation. Gastroparesis is a chronic disorder of the stomach, characterised by delayed gastric emptying in the absence of mechanical obstruction. Treatment includes medical therapies (such as erythromycin and metoclopramide), botulinum toxin, gastric electrical stimulation, jejunostomy and parenteral nutrition. Slow transit constipation comprises a number of symptoms including straining, hard stools, sensation of incomplete evacuation and infrequent bowel movements. Management includes medical therapies such as laxatives and lifestyle advice (for example, increasing exercise, and intake of water and fibre).

2.2 The standard procedure used to assess upper GI motility is gastric emptying scintigraphy. It involves ingestion of a standardised radiolabelled meal. An X-ray is taken after 4 hours to determine the extent of gastric emptying.

2.3 Slow transit constipation is assessed using a radiopaque marker examination. The patient ingests a number of radiopaque markers and has an X-ray(s) after a predefined time period (usually 4 or 5 days) to determine whether markers have been evacuated.

3 The procedure

3.1 The aim of the wireless capsule procedure is to measure gastrointestinal (GI) motility (that is, gastric emptying time, small bowel transit time or colonic transit time) by assessing temperature, pressure and pH.

3.2 The wireless capsule system consists of a single-use, non-digestible, wireless transmitting capsule, a receiver for acquiring and storing signals from the capsule and software for displaying data on a computer. The patient fasts for several hours before the procedure and then drinks some water and eats a standardised meal replacement before swallowing the capsule. The patient then fasts for several more hours and is advised to avoid vigorous exercise. While in

the body, the capsule samples bowel contents and transmits data about pH, pressure and temperature to a portable receiver (worn by the patient) at regular intervals as it travels through the GI tract. The patient can record meals, sleep and bowel movements by pushing an event button on the receiver. The capsule is passed out of the bowel with the faeces. If not seen in the stool, loss of the recording signal or an abrupt temperature drop on the recording profile confirm exit of the capsule from the body.

4 Efficacy

This section describes efficacy 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 interventional procedure overview.

4.1 A systematic review of 745 patients (12 studies) with suspected motility problems reported sensitivity of the wireless motility capsule in comparison with clinical diagnosis of gastroparesis to be 65 to 68% and specificity to be 82 to 87% in a subset of 560 patients (reported by 7 studies included in the systematic review).

4.2 The systematic review of 745 patients (12 studies) with suspected motility problems reported sensitivity of the capsule in comparison with gastric emptying scintigraphy to be 59 to 86% and specificity to be 64 to 81% in a subset of 560 patients (reported by 7 studies included in the systematic review).

4.3 The systematic review of 745 patients (12 studies) with suspected motility problems reported sensitivity of the capsule compared with a radiopaque marker to be 37% and specificity to be 95% in a subset of 78 patients (reported by 1 study included in the systematic review) with constipation. A case series of 187 patients with constipation reported sensitivity of the capsule in comparison with radiopaque marker assessment for colonic transit time of 80% (95% confidence interval [CI] 67 to 98%, p=0.01) and specificity of 91% (95% CI 83 to 96%, p=0.00001). The same study reported sensitivity of the capsule in comparison with radiopaque marker assessment for small and large bowel transit time of 79% (95% CI 67 to 89%, p=0.01) and specificity of 91% (95% CI 83 to 96%, p=0.00001).

4.4 A case series of 86 patients with suspected symptoms of upper GI or lower GI dysmotility reported that using the capsule confirmed the clinical diagnosis in 58% (50/86) of patients and that radiopaque marker examination or gastric emptying scintigraphy confirmed the clinical diagnosis in 44% (38/86) of patients ($p<0.05$).

4.5 A case series of 83 patients with suspected gastroparesis, intestinal dysmotility or slow transit constipation reported that in 53% (44/83) of patients, using the capsule led to a new diagnosis. In a case series of 43 patients with gastroparesis comparing the capsule with gastric emptying scintigraphy, the reported overall diagnostic gain with the capsule (defined as the difference between the percentage of patients with abnormal motility detected by the capsule but normal scintigraphy, and the percentage of patients with normal capsule findings but abnormal scintigraphy) was 19% ($p=0.04$).

4.6 The systematic review of 745 patients (12 studies) with suspected motility problems reported data from a subset of 3 studies. In these 3 studies, using the wireless capsule altered management (medicine, diet or surgery) in 50 to 69% of patients with suspected gastroparesis.

4.7 The specialist advisers listed key efficacy outcomes as pan-enteric measurement of transit (units of time) and motility (units of pressure or descriptive measures) in gut regions.

5 Safety

This section describes 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 interventional procedure overview.

5.1 A case series of 187 patients with constipation reported 7 adverse events as being possibly or definitely related to the capsule: 2 cases of abdominal pain, 1 case of diarrhoea, 2 cases of dysphagia and 2 cases of nausea.

5.2 Device malfunction was reported in 4% (8/180) of those who ingested the wireless motility capsule in the case series of 187 patients with symptomatic constipation.

5.3 Software malfunction resulting in missing data was reported in 7% (12/165) of participants (group not specified) in a comparative study of 165 people (78 patients with chronic constipation versus 87 healthy subjects).

5.4 The specialist advisers stated theoretical adverse events included impaction of the capsule in patients with strictures, and the capsule not progressing beyond the stomach in patients with severe gastroparesis.

6 Committee comments

6.1 The Committee noted the difficulties of validating the accuracy of diagnostic procedures in the gastrointestinal tract, especially for patients with complex motility disorders, in whom a range of diagnostic procedures may be used. These issues contributed to the difficulty in assessing the efficacy of this procedure.

6.2 The Committee noted the particular difficulty of validating diagnostic procedures for motility disorders of the small bowel.

7 Further information

7.1 For related NICE guidance, see the NICE website.

This guidance requires that clinicians undertaking the procedure make special arrangements for audit. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

Information for patients

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

About this guidance

NICE interventional procedures 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.

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

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.

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

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 have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

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Effective Health Care Program

Comparative Effectiveness Review
Number 110

Wireless Motility Capsule Versus Other Diagnostic Technologies for Evaluating Gastroparesis and Constipation:

A Comparative Effectiveness Review

Agency for Healthcare Research and Quality
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Wireless Motililty Capsule Versus Other Diagnostic Technologies for Evaluating Gastroparesis and Constipation: A Comparative Effectiveness Review

Structured Abstract

Objectives. To systematically review the evidence comparing wireless motility capsule (WMC) with other diagnostic tests used for the evaluation of gastroparesis and slow-transit constipation, in terms of diagnostic accuracy, accuracy of motility assessment, effect on treatment decisions, effect on patient-centered outcomes, harms, and effect on resource utilization.

Data sources. We searched Medline ® and Embase ® from inception through July 2012. Additionally, we scanned reference lists of relevant articles and queried experts.

Review methods. We included studies in any language that compared WMC with other diagnostic tests among patients with suspected gastroparesis or slow-transit constipation. Two reviewers independently assessed articles for eligibility, serially abstracted data from relevant articles, independently evaluated study quality, and graded the strength of the evidence (SOE). We summarized results qualitatively rather than quantitatively because of the heterogeneity of studies.

Results. We included 12 studies (18 publications). Seven studies evaluated diagnosis of gastric emptying delay; we found low SOE that WMC alone was comparable to scintigraphy for diagnostic accuracy, accuracy of motility assessment, effect on treatment decisions, and effect on resource utilization. Sensitivity of WMC compared with gastric scintigraphy ranged from 59 to 86 percent and specificity ranged from 64 to 81 percent. We found two studies evaluating WMC as an add-on to other testing. The SOE was low for diagnostic accuracy and for the accuracy of motility assessment by WMC in combination with other modalities. The addition of WMC increased diagnostic yield. Nine studies analyzed colon transit disorders and provided moderate SOE for diagnostic accuracy, accuracy of motility assessment, and harms. WMC was comparable to radiopaque markers (ROM), with concordance ranging between 64 percent and 87 percent. Few harms were reported. The evidence was insufficient to justify conclusions about effects of WMC on treatment decisions and resource utilization.

Conclusions. WMC is comparable in accuracy to current modalities in use for detection of slow-transit constipation and gastric emptying delay, and is therefore another viable diagnostic modality. Little data are available to determine the optimal timing of WMC for diagnostic algorithms.

Section 4.0

New Codes

COVID-19 Related Codes
October 2021

Issues:

1) A new code was added for a booster (third dose) of the Moderna vaccine on August 16, 2021. The initial FDA EUA expansion was for immunocompromised patients only. However, this indication is expected to broaden in the next few months
2) New codes for repeat administration of monoclonal antibodies were released on June 20, 2021

HERC staff recommendations:

1) Add CPT 0013A (IMM ADMN SARSCOV2 100 MCG/0.5 ML 3RD DOSE) to line 3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS
2) Add HCPCS M0240 (Intravenous infusion or subcutaneous injection, casirivimab and imdevimab includes infusion or injection, and post administration monitoring, subsequent repeat doses) and M0241 (Intravenous infusion or subcutaneous injection, casirivimab and imdevimab includes infusion or injection, and post administration monitoring in the home or residence, this includes a beneficiary's home that has been made provider-based to the hospital during the covid-19 public health emergency, subsequent repeat doses) to line 399 INFLUENZA, COVID-19 AND OTHER NOVEL RESPIRATORY VIRAL ILLNESS

COVID Coding for Dental Providers

Issue: On June 14, 2021, a series of CDT codes became effective to allow dentists to provide COVID-19 testing and vaccination. These codes need to be added to the Diagnostic List or the COVID line.

HERC staff recommendation:

1) Place the codes below as indicated

CDT code	Code Description	Recommended Placement
D0606	molecular testing for a public health-related pathogen, including coronavirus	Diagnostic Procedure File
D1701	Pfizer-BioNTech COVID-19 vaccine administration — first dose	3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS
D1702	Pfizer-BioNTech COVID-19 vaccine administration — second dose	3
D1703	Moderna COVID-19 vaccine administration — first dose	3
D1704	Moderna COVID-19 vaccine administration — second dose	3
D1705	AstraZeneca COVID-19 vaccine administration — first dose	3
D1706	AstraZeneca COVID-19 vaccine administration — second dose	3
D1707	Janssen COVID-19 vaccine administration	3

Section 5.0

Previously Discussed Items

Clarification of the Neuropsychological Testing Guideline
October 2021

Question: Should the neuropsychological testing guideline be clarified as to whether the pre-epilepsy surgery clause is only for patients who have surgery planned or is for patients being evaluated for possible epilepsy surgery?

Question source: HSD hearing division

Issue: In 2020, the neuropsychological testing guideline was modified to allow testing before and after epilepsy surgery. The epilepsy specialists who requested this change indicated that testing was done prior to epilepsy "… to see if the epilepsy surgery will affect various areas of functioning." The HSD hearing division has seen multiple hearings regarding CCO denying coverage of neuropsychological testing until a patient has been determined to be a surgical candidate. The original intent of the change was to allow the testing as part of the determination of whether a patient is actually a surgical candidate. HSD hearing division requests that the guideline be clarified regarding this point.

HERC staff recommendation:

1) Modify the neuropsychological testing guideline as shown below

DIAGNOSTIC GUIDELINE D26, NEUROBEHAVIORAL STATUS EXAMS AND NEUROPSYCHOLOGICAL TESTING

Neurobehavioral status exams (CPT 96116 and 96121) and neuropsychological testing services (CPT 96132 and 96133) are only covered when all of the following are met:

A) Symptoms are not explained by an existing diagnosis; AND
B) When the results of such testing will be used to develop a care plan.

OR when neuropsychological testing is done as part of the pre-operative evaluation prior to epilepsy surgery as part of the process to determine if the patient is an appropriate surgical candidate or post-operative follow up after epilepsy surgery.

Section 7.0

New Discussion Items

Evidence Based Falls Prevention Programs

Question: Should CPT codes to be used for evidence based falls prevention programs be added to the preventive services line with a new guideline?

Question source: OHA

Issue: HSD requested that the HERC review the evidence supporting fall prevention programs and consider adding coverage to the Prioritized List. Falls are an important problem in the elderly, and can lead to fractures, hospitalizations, and other complications. OHA has been working with community partners to try to increase training and access for fall prevention programs. Fall risk is multifactorial, but one component can be reduced strength and balance, which are addressed in fall prevention programs.

The HERC has previously supported adding several of these codes to the diabetes and preventive services lines for use in the Diabetes Prevention Program and other diabetes self-management programs. These programs were shown to have evidence of effectiveness found in a MED review and in a systematic review for the Community Preventive Services Task Force.

Programs supported by OHA:

Evidence-Based Falls Prevention Programs:

- Tai Chi: Moving for Better Balance
- Stepping On: Falls Prevention Program
- The Otago Exercise Program (Otago)
- OHSU "Matter of Balance" Program

Current Prioritized List status

CPT Code	**Code Description**	**Current Placement**
98961	Education and training for patient self-management by a qualified, nonphysician health care professional using a standardized curriculum, face-to-face with the patient (could include caregiver/family) each 30 minutes; 2-4 patients	1 PREGNANCY 3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS 8 TYPE 1 DIABETES MELLITUS 27 TYPE 2 DIABETES MELLITUS
98962	5-8 patients	1,3,8,27
HCPCS code	**Code Description**	**Current Placement**
S9445	Patient education, not otherwise classified, non-physician provider, individual, per session	ANCILLARY PROCEDURES
S9446	Patient education, not otherwise classified, non-physician provider, group, per session	ANCILLARY PROCEDURES
S9451	Exercise classes, non-physician provider, per session	401 CONDITIONS OF THE BACK AND SPINE
ICD-10 code	**Code Description**	**Current Placement**
Z91.81	History of falling	3 292 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS

Evidence

1) **Sherrington 2020,** abridged Cochrane systematic review on exercise for fall prevention in community living older adults
    a. N=108 RCTs (23,407 participants)
    b. Exercise (all types) reduces the rate of falls by 23% compared with control (rate ratio (RaR) 0.77, 95% CI 0.71 to 0.83; 12 981 participants, 59 studies, I2=55%; high-certainty evidence).
    c. Subgroup analyses found a larger effect of exercise (all types) in trials where interventions were delivered by a health professional (usually a physiotherapist, RaR 0.69, 95% CI 0.61 to 0.79; 4511 participants, 25 studies, I2=47%) than in trials where the interventions were delivered by trained instructors who were not health professionals (RaR 0.82, 95% CI 0.75 to 0.90; 8470 participants, 34 studies, I2=57%); test for subgroup differences: Chi2=4.44, df=1, p=0.04, I2=78%. Notably, both approaches resulted in reductions in the rate of falls.
    d. Exercise interventions that were classified as being primarily balance and functional reduce the rate of falls by 24% compared with control (RaR 0.76, 95% CI 0.70 to 0.81; 7920 participants, 39 studies, I2=29%, high-certainty evidence).
    e. Multiple types of exercise (commonly balance and functional exercises plus resistance exercises) probably reduce the rate of falls by 34% (RaR 0.66, 95% CI 0.50 to 0.88; 1374 participants, 11 studies; moderate-certainty evidence).
    f. Exercise interventions that were classified as 3D (Tai Chi or similar) may reduce the rate of falls by 19% compared with control (RaR 0.81, 95% CI 0.67 to 0.99; 2655 participants, 7 studies, I2=74%; low-certainty evidence).
    g. Conclusion: There is high-certainty evidence from 59 RCTs that exercise reduces the rate of falls in older adults living in the general community. Greater provision and implementation of these programs is an urgent challenge for the global sport and exercise medicine community and broader health and social support systems.
2) **Guirguis-Blake 2018,** USPSTF systematic review and evidence report on interventions to prevent falls in older adults
    a. N=21 RCTS of exercise (7297 participants)
        i. 5 good quality and 16 fair quality
        ii. Mean duration of the exercise interventions was approximately 12 months, and the most common frequency was 3 exercise sessions per week. The exercise interventions varied by the type and number of exercise components included and whether the exercise was conducted primarily alone or as a group. The most common type of exercise component was gait, balance, and functional training
        iii. Most of the control groups in the trials were instructed to maintain usual activity levels or usual activity plus minimal control (pamphlet, social visit, brief falls risk advice).
    b. In pooled analyses, exercise interventions were associated with a reduced risk of falling (15 trials [n = 4926]; RR, 0.89 [95% CI, 0.81-0.97]; *P* = .01; *I2* = 43.9%), with a median absolute decrease in participants falling of 3.8 percentage points and a reduced rate of injurious falls (10 trials [n = 4622]; IRR, 0.81 [95% CI, 0.73-0.90]; *I2* = 0.0%), with a median decrease of 0.35 falls per person-year
    c. Three trials (n = 2047) that evaluated fractures showed a reduced rate of fall related fractures, with IRR estimates ranging from 0.26 to 0.92, and 5 trials (n = 2776) that

evaluated risk of injurious falls showed a reduced risk, with IRR estimates ranging from 0.61 to 0.90. Pooled analyses showed no statistically significant association between exercise interventions and mortality (11 trials [n = 4263]; RR, 0.93 [95% CI, 0.71-1.22]; *P* = .60; *I2* = 0.0%)

d. Eight of 21 exercise trials (n = 4107) reported harms in the intervention group. Two of these trials also reported harms in the control group for comparison and reported no difference in the rate of serious injuries between the intervention and control groups. Harms reported for these exercise interventions were minor and included pain, bruising, or fall injuries or fractures that occurred during the exercise sessions.

e. Conclusions: Exercise interventions are associated with fewer people experiencing a fall, injurious falls, and people experiencing an injurious fall in average- and high-risk community-dwelling older adults

3. Gillespie 2012, Cochrane review of interventions for preventing falls in older people living in the community

a. N=59 trials (13,264 participants)
    i. Most trials compared a fall prevention intervention with no intervention or an intervention not expected to reduce falls.

b. Multiple-component group exercise significantly reduced rate of falls (RaR 0.71, 95% CI 0.63 to 0.82; 16 trials; 3622 participants) and risk of falling (RR 0.85, 95% CI 0.76 to 0.96; 22 trials; 5333 participants), as did multiple-component home-based exercise (RaR 0.68, 95% CI 0.58 to 0.80; 7 trials; 951 participants and RR 0.78, 95% CI 0.64 to 0.94; 6 trials; 714 participants).

c. For Tai Chi, the reduction in rate of falls bordered on statistical significance (RaR 0.72, 95% CI 0.52 to 1.00; 5 trials; 1563 participants) but Tai Chi did significantly reduce risk of falling (RR 0.71, 95% CI 0.57 to 0.87; 6 trials; 1625 participants).

d. Overall, exercise interventions significantly reduced the risk of sustaining a fall-related fracture (RR 0.34, 95% CI 0.18 to 0.63; 6 trials; 810 participants).

<u>Expert recommendations</u>

1) **USPSTF 2018,** interventions to reduce falls in community-dwelling older adults

a. The USPSTF found adequate evidence that exercise interventions have a moderate benefit in preventing falls in older adults at increased risk for falls

b. The USPSTF recommends exercise interventions to prevent falls in community-dwelling adults 65 years or older who are at increased risk for falls. (B recommendation)

HERC staff summary

Exercise interventions have high certainty evidence of effectiveness for prevention of falls and fall-related fractures in the elderly. Exercise interventions are a "B" recommendation from the USPSTF for persons aged 65 and older. The CDC recommends encouragement of wide-scale implementation of these programs. These programs have the support of OHA and are available in many locations and in culturally appropriate formats in Oregon.

HERC staff recommendations

1) Add explicit coverage for supervised exercise for falls prevention
    a. Add HCPCS S9451 (Exercise classes, non-physician provider, per session) to line 3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS
        i. CPT codes (98961, 98962) for these types of services are already on line 3
        ii. ICD-10 Z91.81 (History of falling) is on line 3
    b. Modify Guideline Note 106 below
        i. Also change date of USPSTF recommendation per federal rules

GUIDELINE NOTE 106, PREVENTIVE SERVICES

Lines 3,622

Included on Line 3 are the following preventive services:

A) US Preventive Services Task Force (USPSTF) "A" and "B" Recommendations in effect and issued prior to January 1, 2021 ~~2020~~.
    1) http://www.uspreventiveservicestaskforce.org/Page/Name/uspstf-a-and-b-recommendations/
        a) Treatment of falls prevention with exercise interventions is included on Line 292.
    2) USPSTF "D" recommendations are not included on this line or any other line of the Prioritized List.

B) American Academy of Pediatrics (AAP) Bright Futures Guidelines:
    1) http://brightfutures.aap.org. Periodicity schedule available at http://www.aap.org/en-us/professional-resources/practice-support/Periodicity/Periodicity Schedule_FINAL.pdf.
        a) Bright Futures is the periodicity schedule for screening for EPSDT for the Oregon Health Plan.
    2) Screening for lead levels is defined as blood lead level testing and is indicated for Medicaid populations at 12 and 24 months. In addition, blood lead level screening of any child between ages 24 and 72 months with no record of a previous blood lead screening test is indicated.

C) Health Resources **and Services Administration (HRSA) Women's Preventive Services-Required Health Plan Coverage Guidelines a**s updated by HRSA in December 2019. Available at https://www.hrsa.gov/womens-guidelines-2019 as of September 4, 2020.

D) Immunizations as recommended by the Advisory Committee on Immunization Practices (ACIP): http://www.cdc.gov/vaccines/schedules/hcp/index.html or approved for the Oregon Immunization Program: https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Documents/DMAPvactable.pdf
    1) COVID-19 vaccines are intended to be included on this line even if the specific administration code(s) do not yet appear on the line when the vaccine has both 1) FDA approval or FDA emergency use authorization (EUA) and 2) ACIP recommendation.

Colorectal cancer screening is included on Line 3 for average-risk adults aged 45 to 75, using one of the following screening programs:

A) Colonoscopy every 10 years
B) Flexible sigmoidoscopy every 5 years
C) Fecal immunochemical test (FIT) every year
D) Guaiac-based fecal occult blood test (gFOBT) every year

CT colonography CPT 74263), FIT-DNA (CPT 81528) and mSEPT9 (HCPCS G0327) are included on line 502 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS.

Colorectal cancer screening for average-risk adults aged 76 to 85 is covered only after informed decision making between patients and clinicians which includes consideration of the patient's overall health, prior screening history, and preferences.

Supervised evidence-based exercise programs for fall prevention for persons age 65 and older who are at increased risk of falls are included on line 3 using CPT 98961 or 98962 or HCPCS S9451. HCPCS S9451 is only included on Line 3 for the provision of supervised exercise therapy for fall prevention. Programs should be culturally tailored/culturally appropriate when feasible.

Note: CPT code 96110 (Developmental screening (eg, developmental milestone survey, speech and language delay screen), with scoring and documentation, per standardized instrument) can be billed in addition to other CPT codes, such as evaluation and management (E&M) codes or preventive visit codes.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

Exercise for preventing falls in older people living in the community: an abridged Cochrane systematic review

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ABSTRACT

Objectives To assess the effects of exercise interventions for preventing falls in older people living in the community.

Selection criteria We included randomised controlled trials evaluating the effects of any form of exercise as a single intervention on falls in people aged 60+years living in the community.

Results Exercise reduces the rate of falls by 23% (rate ratio (RaR) 0.77, 95% CI 0.71 to 0.83; 12 981 participants, 59 studies; high-certainty evidence). Subgroup analyses showed no evidence of a difference in effect on falls on the basis of risk of falling as a trial inclusion criterion, participant age 75 years+ or group versus individual exercise but revealed a larger effect of exercise in trials where interventions were delivered by a health professional (usually a physiotherapist). Different forms of exercise had different impacts on falls. Compared with control, balance and functional exercises reduce the rate of falls by 24% (RaR 0.76, 95% CI 0.70 to 0.81; 7920 participants, 39 studies; high-certainty evidence). Multiple types of exercise (commonly balance and functional exercises plus resistance exercises) probably reduce the rate of falls by 34% (RaR 0.66, 95% CI 0.50 to 0.88; 1374 participants, 11 studies; moderate-certainty evidence). Tai Chi may reduce the rate of falls by 19% (RaR 0.81, 95% CI 0.67 to 0.99; 2655 participants, 7 studies; low-certainty evidence). We are uncertain of the effects of programmes that primarily involve resistance training, dance or walking.

Conclusions and implications Given the certainty of evidence, effective programmes should now be implemented.

INTRODUCTION

At least one-third of community-dwelling people over 65 years of age fall each year,[1 2] and the rate of fall-related injuries increases with age.[3] Falls can have serious consequences, such as fractures and head injuries.[3]

Falls are associated with reduced quality of life,[4] and can have psychological consequences: fear of falling and loss of confidence that can result in self-restricted activity levels leading to a reduction in physical function and social interactions.[5] Paradoxically, this restriction of activities may increase the risk of further falls by contributing to deterioration in physical abilities.

A previous Cochrane Review found exercise as a single intervention, prevents falls,[6] and to be the most commonly tested single fall prevention intervention. Economic evaluations accompanying randomised trials have found exercise to be a cost effective fall-prevention strategy.[7] Exercise interventions have been found to be effective when delivered in a group-based setting or on an individual basis. The optimal features of successful fall prevention exercise programmes are not yet clear, but programmes that are multicomponent (eg, target both strength and balance),[6] and programmes that include balance training appear to be particularly effective.[8]

An update of the effects of exercise interventions on falls is warranted given the number of new trials published, the increasing number of older people living in the community and the major long-term consequences associated with falls and fall-related injuries to both the individual and to society. Different exercise programmes may have different effects on falls and so careful analysis of the impact of different programmes is crucial to optimise the prescription of exercise interventions and inform public health promotion initiatives for healthy ageing.

This systematic review of randomised controlled trials (RCTs) aimed to assess the effects of exercise interventions for preventing falls in older people living in the community when compared with control. The present report focuses on the review's primary outcome, rate of falls. Please refer to the full Cochrane Review[9] for reports of other outcomes as well as more detailed methods, descriptions of included studies and forest plots.

METHODS

Protocol

The protocol for this review was published.[10]

Eligibility criteria

We included RCTs, either individual or cluster randomised, evaluating the effects of exercise interventions on falls or fall-related fractures in older people living in the community. We included trials if they specified an inclusion criterion of 60 years of age or over. Trials that included younger participants were included if the mean age minus one SD was more than 60 years. We included trials where the majority of participants were living in the community, either at home or in places of residence that, on the whole, do not provide residential health-related care or rehabilitative services; for example, retirement villages, or sheltered housing. We excluded studies that only included participants

JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Interventions to Prevent Falls in Older Adults
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Falls are the most common cause of injury-related morbidity and mortality among older adults.

OBJECTIVE To systematically review literature on the effectiveness and harms of fall prevention interventions in community-dwelling older adults to inform the US Preventive Services Task Force.

DATA SOURCES MEDLINE, PubMed, Cumulative Index for Nursing and Allied Health Literature, and Cochrane Central Register of Controlled Trials for relevant English-language literature published through August 2016, with ongoing surveillance through February 7, 2018.

STUDY SELECTION Randomized clinical trials of interventions to prevent falls in community-dwelling adults 65 years and older.

DATA EXTRACTION AND SYNTHESIS Independent critical appraisal and data abstraction by 2 reviewers. Random-effects meta-analyses using the method of DerSimonian and Laird.

MAIN OUTCOMES AND MEASURES Number of falls (number of unexpected events in which a person comes to rest on the ground, floor, or lower level), people experiencing 1 or more falls, injurious falls, people experiencing injurious falls, fractures, people experiencing fractures, mortality, hospitalizations, institutionalizations, changes in disability, and treatment harms.

RESULTS Sixty-two randomized clinical trials (N = 35 058) examining 7 fall prevention intervention types were identified. This article focused on the 3 most commonly studied intervention types: multifactorial (customized interventions based on initial comprehensive individualized falls risk assessment) (26 trials [n = 15 506]), exercise (21 trials [n = 7297]), and vitamin D supplementation (7 trials [n = 7531]). Multifactorial intervention trials were associated with a reduction in falls (incidence rate ratio [IRR], 0.79 [95% CI, 0.68-0.91]) but were not associated with a reduction in other fall-related morbidity and mortality outcomes. Exercise trials were associated with statistically significant reductions in people experiencing a fall (relative risk, 0.89 [95% 13 CI, 0.81-0.97]) and injurious falls (IRR, 0.81 [95% CI, 0.73-0.90]) and with a statistically nonsignificant reduction in falls (IRR, 0.87 [95% CI, 0.75-1.00]) but showed no association with mortality. Few exercise trials reported fall-related fractures. Seven heterogeneous trials of vitamin D formulations (with or without calcium) showed mixed results. One trial of annual high-dose cholecalciferol (500 000 IU), which has not been replicated, showed an increase in falls, people experiencing a fall, and injuries, while 1 trial of calcitriol showed a reduction in falls and people experiencing a fall; the remaining 5 trials showed no significant difference in falls, people experiencing a fall, or injuries. Harms of multifactorial and exercise trials were rarely reported but generally included minor musculoskeletal injuries.

CONCLUSIONS AND RELEVANCE Multifactorial and exercise interventions were associated with fall-related benefit, but evidence was most consistent across multiple fall-related outcomes for exercise. Vitamin D supplementation interventions had mixed results, with a high dose being associated with higher rates of fall-related outcomes.

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Supplemental content

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Interventions for preventing falls in older people living in the community (Review)

Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson L, Lamb SE

Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson L, Lamb SE.
Interventions for preventing falls in older people living in the community.
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WILEY

[Intervention Review]

Interventions for preventing falls in older people living in the community

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ABSTRACT

Background

Approximately 30% of people over 65 years of age living in the community fall each year. This is an update of a Cochrane review first published in 2009.

Objectives

To assess the effects of interventions designed to reduce the incidence of falls in older people living in the community.

Search methods

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (February 2012), CENTRAL (*The Cochrane Library* 2012, Issue 3), MEDLINE (1946 to March 2012), EMBASE (1947 to March 2012), CINAHL (1982 to February 2012), and online trial registers.

Selection criteria

Randomised trials of interventions to reduce falls in community-dwelling older people.

Data collection and analysis

Two review authors independently assessed risk of bias and extracted data. We used a rate ratio (RaR) and 95% confidence interval (CI) to compare the rate of falls (e.g. falls per person year) between intervention and control groups. For risk of falling, we used a risk ratio (RR) and 95% CI based on the number of people falling (fallers) in each group. We pooled data where appropriate.

Main results

We included 159 trials with 79,193 participants. Most trials compared a fall prevention intervention with no intervention or an intervention not expected to reduce falls. The most common interventions tested were exercise as a single intervention (59 trials) and multifactorial programmes (40 trials). Sixty-two per cent (99/159) of trials were at low risk of bias for sequence generation, 60% for attrition bias for falls (66/110), 73% for attrition bias for fallers (96/131), and only 38% (60/159) for allocation concealment.

Multiple-component group exercise significantly reduced rate of falls (RaR 0.71, 95% CI 0.63 to 0.82; 16 trials; 3622 participants) and risk of falling (RR 0.85, 95% CI 0.76 to 0.96; 22 trials; 5333 participants), as did multiple-component home-based exercise (RaR 0.68, 95% CI 0.58 to 0.80; 7 trials; 951 participants and RR 0.78, 95% CI 0.64 to 0.94; 6 trials; 714 participants). For Tai Chi, the reduction in rate of falls bordered on statistical significance (RaR 0.72, 95% CI 0.52 to 1.00; 5 trials; 1563 participants) but Tai Chi did significantly reduce risk of falling (RR 0.71, 95% CI 0.57 to 0.87; 6 trials; 1625 participants). Overall, exercise interventions significantly reduced the risk of sustaining a fall-related fracture (RR 0.34, 95% CI 0.18 to 0.63; 6 trials; 810 participants).

Multifactorial interventions, which include individual risk assessment, reduced rate of falls (RaR 0.76, 95% CI 0.67 to 0.86; 19 trials; 9503 participants), but not risk of falling (RR 0.93, 95% CI 0.86 to 1.02; 34 trials; 13,617 participants).

Overall, vitamin D did not reduce rate of falls (RaR 1.00, 95% CI 0.90 to 1.11; 7 trials; 9324 participants) or risk of falling (RR 0.96, 95% CI 0.89 to 1.03; 13 trials; 26,747 participants), but may do so in people with lower vitamin D levels before treatment.

Home safety assessment and modification interventions were effective in reducing rate of falls (RaR 0.81, 95% CI 0.68 to 0.97; 6 trials; 4208 participants) and risk of falling (RR 0.88, 95% CI 0.80 to 0.96; 7 trials; 4051 participants). These interventions were more effective in people at higher risk of falling, including those with severe visual impairment. Home safety interventions appear to be more effective when delivered by an occupational therapist.

An intervention to treat vision problems (616 participants) resulted in a significant *increase* in the rate of falls (RaR 1.57, 95% CI 1.19 to 2.06) and risk of falling (RR 1.54, 95% CI 1.24 to 1.91). When regular wearers of multifocal glasses (597 participants) were given single lens glasses, all falls and outside falls were significantly reduced in the subgroup that regularly took part in outside activities. Conversely, there was a significant *increase* in outside falls in intervention group participants who took part in little outside activity.

Pacemakers reduced rate of falls in people with carotid sinus hypersensitivity (RaR 0.73, 95% CI 0.57 to 0.93; 3 trials; 349 participants) but not risk of falling. First eye cataract surgery in women reduced rate of falls (RaR 0.66, 95% CI 0.45 to 0.95; 1 trial; 306 participants), but second eye cataract surgery did not.

Gradual withdrawal of psychotropic medication reduced rate of falls (RaR 0.34, 95% CI 0.16 to 0.73; 1 trial; 93 participants), but not risk of falling. A prescribing modification programme for primary care physicians significantly reduced risk of falling (RR 0.61, 95% CI 0.41 to 0.91; 1 trial; 659 participants).

An anti-slip shoe device reduced rate of falls in icy conditions (RaR 0.42, 95% CI 0.22 to 0.78; 1 trial; 109 participants). One trial (305 participants) comparing multifaceted podiatry including foot and ankle exercises with standard podiatry in people with disabling foot pain significantly reduced the rate of falls (RaR 0.64, 95% CI 0.45 to 0.91) but not the risk of falling.

There is no evidence of effect for cognitive behavioural interventions on rate of falls (RaR 1.00, 95% CI 0.37 to 2.72; 1 trial; 120 participants) or risk of falling (RR 1.11, 95% CI 0.80 to 1.54; 2 trials; 350 participants).

Trials testing interventions to increase knowledge/educate about fall prevention alone did not significantly reduce the rate of falls (RaR 0.33, 95% CI 0.09 to 1.20; 1 trial; 45 participants) or risk of falling (RR 0.88, 95% CI 0.75 to 1.03; 4 trials; 2555 participants).

Thirteen trials provided a comprehensive economic evaluation. Three of these indicated cost savings for their interventions during the trial period: home-based exercise in over 80-year-olds, home safety assessment and modification in those with a previous fall, and one multifactorial programme targeting eight specific risk factors.

Authors' conclusions

Group and home-based exercise programmes, and home safety interventions reduce rate of falls and risk of falling.

Multifactorial assessment and intervention programmes reduce rate of falls but not risk of falling; Tai Chi reduces risk of falling.

Overall, vitamin D supplementation does not appear to reduce falls but may be effective in people who have lower vitamin D levels before treatment.

PLAIN LANGUAGE SUMMARY

Interventions for preventing falls in older people living in the community

As people get older, they may fall more often for a variety of reasons including problems with balance, poor vision, and dementia. Up to 30% may fall in a year. Although one in five falls may require medical attention, less than one in 10 results in a fracture.

This review looked at the healthcare literature to establish which fall prevention interventions are effective for older people living in the community, and included 159 randomised controlled trials with 79,193 participants.

Group and home-based exercise programmes, usually containing some balance and strength training exercises, effectively reduced falls, as did Tai Chi. Overall, exercise programmes aimed at reducing falls appear to reduce fractures.

Continuous Glucose Monitoring for Type 2 Diabetes

Questions:

1) Should coverage of continuous glucose monitors be extended to include insulin-dependent type 2 diabetics?
2) Should coverage of continuous glucose monitors be extended to include women with gestational diabetes and/or pregnant women with pre-existing diabetes who require insulin therapy?

Question sources:

1) HERC staff
2) Several CCOs

Issue: Continuous glucose monitors (CGMs) are devices designed to measure interstitial blood glucose, and sensor-augmented insulin pumps (SAPs) integrate CGM blood glucose readings into the function of the pump. These devices have been proposed for use to aid in the treatment of type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM). Currently, only T1DM is paired with CGMs on the Prioritized List.

Continuous glucose monitoring has been discussed at multiple meetings since 2012. This topic was most recently reviewed as part of the coverage guidance process in 2017. As a result of the 2017 coverage guidance review, coverage was added for type 1 diabetics meeting guideline criteria. Recently, several new studies have been published regarding the efficacy of continuous glucose monitoring in type 2 diabetics who are insulin dependent. Additionally, MED has conducted a systematic review of this topic.

From the 2017 coverage guidance on Continuous Glucose Monitoring:

> In adults with type 2 diabetes, we found insufficient evidence regarding the effects of CGM on long-term clinical outcomes or on severe hypoglycemia, and CGM does not improve treatment satisfaction. We have low confidence that improvements in HbA1c levels seen in type 2 diabetes studies are clinically significant. Given the prevalence of type 2 diabetes in the U.S. adult population, use of CGM would add significant cost without known population health benefit.
>
> No systematic reviews or randomized controlled trials of CGM for children and adolescents with type 2 diabetes were identified in the literature search. There is insufficient evidence to draw conclusions about CGM for any outcome in this population.

Current Prioritized List status

On line 8 TYPE 1 DIABETES MELLITUS

95350 Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; physician or other qualified health care professional (office) provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording

95251 analysis, interpretation and report

ICD-10-CM O24.0X (Pre-existing type 1 diabetes mellitus, in pregnancy), O24.11X (Pre-existing type 2 diabetes mellitus, in pregnancy), O24.31X (Unspecified pre-existing diabetes mellitus in pregnancy), O24.414 (Gestational diabetes mellitus in pregnancy, insulin controlled), O24.81X (Other pre-existing diabetes mellitus in pregnancy) and O24.91X (Unspecified diabetes mellitus in pregnancy) are on line 1 PREGNANCY

Type 2 diabetes mellitus (multiple codes) is on line 27 TYPE 2 DIABETES MELLITUS

GUIDELINE NOTE 108, CONTINUOUS GLUCOSE MONITORING

Line 8

Real-time (personal) continuous glucose monitoring (CGM) is included on Line 8 for:

A) Adults with type 1 diabetes mellitus not on insulin pump management:
   1) Who have received or will receive diabetes education specific to the use of CGM AND
   2) Who have used the device for at least 50% of the time at their first follow-up visit AND
   3) Who have baseline HbA1c levels greater than or equal to 8.0%, frequent or severe hypoglycemia, or impaired awareness of hypoglycemia (including presence of these conditions prior to initiation of CGM).

B) Adults with type 1 diabetes on insulin pump management (including the CGM-enabled insulin pump):
   1) Who have received or will receive diabetes education specific to the use of CGM AND
   2) Who have used the device for at least 50% of the time at their first follow-up visit.

C) Women with type 1 diabetes who are pregnant or who plan to become pregnant within six months without regard to HbA1c levels.

D) Children and adolescents under age 21 with type 1 diabetes:
   1) Who have received or will receive diabetes education specific to the use of CGM AND
   2) Who have used the device for at least 50% of the time at their first follow-up visit.

CPT 95250 and 95251 (Ambulatory continuous glucose monitoring) are included on this line for services related to real-time continuous glucose monitoring but not retrospective (professional) continuous glucose monitoring

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

Continuous Glucose Monitoring for Type 2 Diabetes

Evidence

1) **MED 2021**: Real-Time Continuous Glucose Monitors and Sensor Augmented Insulin Pumps: Evidence, Payer Policies, and Clinical Practice Guidelines
    a. Efficacy in adults with type 2 diabetes
        i. For studies conducted in populations with T2D, we included 5 poor- to good-methodological-quality systematic reviews1 and 2 additional fair-methodological-quality RCTs2 that reported outcomes on mean HbA1c changes. There was significant overlap of the studies included by the systematic reviews.
        ii. All of the systematic reviews that we included reported a significant reduction in mean HbA1c levels in adults that ranged from -0.25 to -0.48 when comparing rtCGMs with SMBG at various lengths of follow-up.
            1. While the point estimates of these analysis do not meet the threshold for clinical significance, the upper confidence intervals of Dicembrini et al., Park and Le, Garcia-Lorenzo et al. and Skelly et al. all cross the 0.5% threshold, but the entire confidence interval is not above the 0.5% minimally important clinical threshold.
    b. Adverse events in adults with type 2 diabetes
        i. Hypoglycemia
            1. We identified 3 systematic reviews and 1 additional RCT of adults with T2D that reported on hypoglycemic outcomes
            2. All 3 poor- to fair-methodological-quality systematic reviews that reported on hypoglycemic outcomes for individuals with T2D when comparing rtCGMs with SMBG noted that none of the included individual studies reported any severe hypoglycemic events
            3. Taylor et al., a fair-methodological-quality single-site RCT in Australia of 20 adults aged 20 to 75 years, compared rtCGM use and a low-carbohydrate diet with SMBG use and a low-carbohydrate diet. The authors found no significant differences between groups in mean time spent in hypoglycemia (< 70 mg/dL).
        ii. Hyperglycemia
            1. We did not identify any systematic reviews that reported on hyperglycemic events for individuals with T2D who used rtCGM compared to SMBG.
            2. Taylor et al. a fair-methodological-quality-single site RCT in Australia of 20 adults aged 20 to 75 years, compared rtCGM use and a low-carbohydrate diet with SMBG use and a low-carbohydrate diet. The authors found no significant differences between groups in mean time spent in hyperglycemia (> 180 mg/dL).
    c. Efficacy in pregnant women with pre-existing diabetes
        i. For pregnant women with preexisting diabetes, we included 2 systematic reviews that reported on HbA1c outcomes for rtCGM use
            1. Neither review found any significant differences between groups for change in maternal HbA1c from baseline at any study length of follow-up (range, 3 to 9 months).17,23 In addition, Jones et al. did not find any difference between groups in achieving maternal HbA1c less than or equal to 6.5% at 34 weeks gestation
    d. Adverse events in pregnant women with pre-existing diabetes

i. We identified a single good-methodological-quality systematic review17 on the use of rtCGMs versus SMBG in pregnant women with preexisting T1 or T2 diabetes. Jones et al. found no significant difference in severe maternal hypoglycemia, based on 1 study that followed women up to 34 weeks of gestation.

e. Effects on maternal and neonatal outcomes for pregnant women with pre-existing diabetes
   i. For maternal outcomes, Jones et al. found a significant decrease in a composite outcome of hypertensive disorders of pregnancy that included preeclampsia, pregnancy-induced hypertension, and eclampsia (risk ratio, 0.58; 95% CI, 0.39 to 0.85; *P* = .01), but did not find any differences between rtCGM and SMBG groups for the individual outcomes of preeclampsia, pregnancy-induced hypertension, or cesarean birth. Skelly et al. found a significant reduction in risk of cesarean section operations in pregnant women with preexisting T1D when using rtCGMs compared with SMBG (risk difference, -0.11; 95% CI, -0.21 to -0.01; *P* = .04), but no difference in risk of developing preeclampsia.
   ii. For neonatal outcomes, Jones et al.17 found a significant reduction in the risk for neonatal hypoglycemia (risk ratio, 0.66; 95% CI, 0.48 to 0.93; *P* = .02), but not for any of the reported neonatal outcomes (large for gestational age, small for gestational age, birth weight, head circumference, length, adiposity, birth trauma [shoulder dystocia, bone fracture, nerve palsy], shoulder dystocia, respiratory distress syndrome, neonatal hyperbilirubinemia, gestational age at birth, preterm birth [< 37 weeks gestation], preterm birth [< 34 weeks gestation], macrosomia, cord blood c-peptide levels > 566 pmol/L or > 2,725 pmol/L, perinatal mortality [stillbirth and neonatal mortality], morality or morbidity composite [pregnancy loss, birth injury, neonatal glycemia, hyperbilirubinemia, respiratory distress, and high level of neonatal care > 24 hours], miscarriage, stillbirth, neonatal mortality, and major and minor anomalies). Skelly et al did not find any significant differences between groups of pregnant women with T1D who used rtCGMs compared those who used SMBG for any neonatal outcome reported (birth weight, large for gestational age, gestational age, severe neonatal hypoglycemia, miscarriage, and preterm delivery [at < 34 or 37 weeks gestation]).

f. Efficacy in women with gestational diabetes
   i. We identified 1 good-methodological-quality systematic review and 1 additional poor-methodological-quality RCT of women with GDM that reported on HbA1c outcomes from rtCGM use.
      1. The single good-methodological-quality systematic review we identified did not find any significant changes in maternal HbA1c at 32 to 36 weeks of gestation between rtCGM or SMBG groups, based on a single study.
      2. Lane et al., a poor-methodological-quality single-site RCT in the US of 40 adult women with GDM (aged 18 to 45 years), found no significant differences in mean HbA1c levels or time spent in the target range of 70 to 140 mg/dL between women in the rtCGM and blinded CGM groups at week 1 and week 4 of the trial.

g. Adverse events in women with gestational diabetes

   i. We identified a single good-methodological-quality systematic review17 on the use of rtCGMs versus SMBG in pregnant women with preexisting T1 or T2 diabetes. Jones et al. found no significant difference in severe maternal hypoglycemia, based on 1 study that followed women up to 34 weeks of gestation.

h. Maternal and neonatal outcomes in women with gestational diabetes
   i. We included a single good-methodological-quality systematic review21 and 1 additional poor-methodological-quality RCT28 that reported on maternal and neonatal outcomes in women with GDM when comparing rtCGMs and SMBG use. Raman et al. (good methodological quality) found a significant decrease in gestational maternal weight gain (mean difference in kg, -1.26; 95% CI, -2.28 to -0.24; *P* = .02), and an increased risk in use of additional pharmacotherapy (risk ratio, 2.86; 95% CI, 1.47 to 5.56; *P* = .00) for individuals with GDM who used rtCGMs compared with SMBG.21 Raman et al. did not find any significant differences between groups on all other reported maternal (cesarean birth) and neonatal outcomes (perinatal mortality, stillbirth, neonatal mortality, birth weight, large for gestational age, small for gestational age, gestational age at birth, preterm birth [< 37 weeks], macrosomia, neonatal hypoglycemia, hyperbilirubinemia or jaundice).

i. Conclusion:
   i. For adults with T2D, the use of real time continuous glucose monitoring (rtCGM), compared to self-monitoring of blood glucose (SMBG), would likely reduce HbA1c levels, especially if there was near daily adherence. The majority of studies required individuals to be on an insulin treatment regimen for study inclusion and did not include people who were using oral medications only. The use of rtCGM, would likely not affect the number of hypoglycemic or hyperglycemic events, or the number of hospitalizations or emergency department visits (for older adults) when compared with SMBG. No studies reported on the number of diabetic ketoacidosis events. These findings are based on a review of 5 poor- to good-methodological-quality systematic reviews of 12 RCTs and 2 additional fair-methodological-quality RCTs (14 RCTs in total).
   ii. For pregnant women with preexisting diabetes, the use of rtCGM would likely result in no difference in HbA1c levels, number of severe hypoglycemic events, number of diabetic ketoacidosis events, or adverse maternal or neonatal outcomes, when compared to SMBG. However, rtCGM use does have the potential to reduce neonatal intensive care unit (NICU) lengths of stay greater than 24 hours. These findings are based on a review of 1 good-methodological-quality systematic review of 4 RCTs (4 RCTs in total).
   iii. For women with gestational diabetes, the use of rtCGM would likely result in no difference in HbA1c levels, time in hypoglycemic or hyperglycemic ranges, adverse maternal or neonatal outcomes, or hospitalizations, when compared to SMBG. These findings are based on a review of 1 good-methodological-quality systematic review of 2 RCTs and 1 additional poor-methodological-quality RCT (3 RCTs in total).

j. Children and adolescents with type 2 diabetes were not included in this review

k. Payer policies
   i. There was significant variation in the rtCGM and SAP coverage criteria across the 6 Medicaid program and Medicare data we reviewed. Some payers

(Oklahoma and Texas Medicaid, and Medicare) limit coverage of rtCGM to therapeutic devices, whereas others allow for coverage of adjunctive devices or therapeutic devices, but do not allow simultaneous billing of both sets of Healthcare Common Procedural Coding System (HCPCS) codes (New York and Washington Medicaid). New York, Oklahoma, and Oregon Medicaid programs cover rtCGMs for individuals with T1D, whereas Texas Medicaid covers individuals with T1D and T2D and Minnesota Medicaid and Medicare allow coverage for all individuals with diabetes. Washington State Medicaid covers adjunctive or therapeutic CGMs for individuals with T1D, adults with T2D with specific criteria, and pregnant women with preexisting T1D, preexisting T2D on insulin therapy prior to pregnancy or for whom blood glucose is not well-controlled and insulin is required, or with GDM for whom blood glucose is not well-controlled and insulin is required.

2. **Martens 2021**, RCT of CGM in Type 2 Diabetics on Insulin Therapy
    a. N=116 CGM vs N=59 with traditional blood glucose meter
        i. mean [SD] baseline HbA1c level, 9.1% [0.9%]
        ii. 165 (94%) completed the trial.
        iii. Follow up time 8 months
        iv. On basal insulin without prandial insulin
    b. Mean HbA1c level decreased from 9.1% at baseline to 8.0% at 8 months in the CGM group and from 9.0% to 8.4% in the BGM group (adjusted difference, −0.4% [95%CI, −0.8%to −0.1%]; *P* = .02).
    c. In the CGM group, compared with the BGM group, the mean percentage of time at greater than 250mg/dL was 11% vs 27% (adjusted difference, −16% [95%CI, −21% to −11%]; *P* < .001)
    d. Severe hypoglycemic events occurred in 1 participant (1%) in the CGM group and in 1 (2%) in the BGM group.
    e. Conclusion: Among adults with poorly controlled type 2 diabetes treated with basal insulin without prandial insulin, continuous glucose monitoring, as compared with blood glucose meter monitoring, resulted in significantly lower HbA1c levels at 8 months.

HERC staff summary

New systematic review and RCT data show that continuous glucose monitoring in an insulin treated type 2 diabetes population does not have a clinically significant impact. Hemoglobin A1C measurements fell significantly with CGM use, but did not reach a clinically significant threshold (-0.5%). Episodes of hypoglycemia did not appear to be impacted by CGM use in this population.

Use of CBM in pregnant women with pre-existing diabetes or with gestational diabetes did not improve diabetic control, hypoglycemic events, or maternal or neonatal outcomes.

HERC staff recommendation:

1) Make no changes to the current guideline note, which limit coverage of CGM to certain patients with type 1 diabetes.

JAMA | Original Investigation

Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin
A Randomized Clinical Trial

Thomas Martens, MD; Roy W. Beck, MD, PhD; Ryan Bailey, MS; Katrina J. Ruedy, MSPH; Peter Calhoun, PhD; Anne L. Peters, MD; Rodica Pop-Busui, MD, PhD; Athena Philis-Tsimikas, MD; Shichun Bao, MD, PhD; Guillermo Umpierrez, MD; Georgia Davis, MD; Davida Kruger, MSN, APN-BC; Anuj Bhargava, MD; Laura Young, MD, PhD; Janet B. McGill, MD; Grazia Aleppo, MD; Quang T. Nguyen, DO; Ian Orozco, MD; William Biggs, MD; K. Jean Lucas, MD; William H. Polonsky, PhD; John B. Buse, MD, PhD; David Price, MD; Richard M. Bergenstal, MD; for the MOBILE Study Group

IMPORTANCE Continuous glucose monitoring (CGM) has been shown to be beneficial for adults with type 2 diabetes using intensive insulin therapy, but its use in type 2 diabetes treated with basal insulin without prandial insulin has not been well studied.

OBJECTIVE To determine the effectiveness of CGM in adults with type 2 diabetes treated with basal insulin without prandial insulin in primary care practices.

DESIGN, SETTING, AND PARTICIPANTS This randomized clinical trial was conducted at 15 centers in the US (enrollment from July 30, 2018, to October 30, 2019; follow-up completed July 7, 2020) and included adults with type 2 diabetes receiving their diabetes care from a primary care clinician and treated with 1 or 2 daily injections of long- or intermediate-acting basal insulin without prandial insulin, with or without noninsulin glucose-lowering medications.

INTERVENTIONS Random assignment 2:1 to CGM (n = 116) or traditional blood glucose meter (BGM) monitoring (n = 59).

MAIN OUTCOMES AND MEASURES The primary outcome was hemoglobin A_{1c} (HbA_{1c}) level at 8 months. Key secondary outcomes were CGM-measured time in target glucose range of 70 to 180 mg/dL, time with glucose level at greater than 250 mg/dL, and mean glucose level at 8 months.

RESULTS Among 175 randomized participants (mean [SD] age, 57 [9] years; 88 women [50%]; 92 racial/ethnic minority individuals [53%]; mean [SD] baseline HbA_{1c} level, 9.1% [0.9%]), 165 (94%) completed the trial. Mean HbA_{1c} level decreased from 9.1% at baseline to 8.0% at 8 months in the CGM group and from 9.0% to 8.4% in the BGM group (adjusted difference, −0.4% [95% CI, −0.8% to −0.1%]; $P = .02$). In the CGM group, compared with the BGM group, the mean percentage of CGM-measured time in the target glucose range of 70 to 180 mg/dL was 59% vs 43% (adjusted difference, 15% [95% CI, 8% to 23%]; $P < .001$), the mean percentage of time at greater than 250 mg/dL was 11% vs 27% (adjusted difference, −16% [95% CI, −21% to −11%]; $P < .001$), and the means of the mean glucose values were 179 mg/dL vs 206 mg/dL (adjusted difference, −26 mg/dL [95% CI, −41 to −12]; $P < .001$). Severe hypoglycemic events occurred in 1 participant (1%) in the CGM group and in 1 (2%) in the BGM group.

CONCLUSIONS AND RELEVANCE Among adults with poorly controlled type 2 diabetes treated with basal insulin without prandial insulin, continuous glucose monitoring, as compared with blood glucose meter monitoring, resulted in significantly lower HbA_{1c} levels at 8 months.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03566693

Visual Abstract
Editorial
Related article
Supplemental content

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Diabetic Test Strips

Question: should the number of allowed diabetic test strips be modified?

Question source: Kelly Jamison, HSD claims reviewer

Issue: Diabetic test strips are used to measure blood glucose. Kelly Jamison asked the HERC to review the current limitations on test strips due to CMS issuing a new Medicare National Coverage Determination (NCD) for test strips. Additionally, test strip coverage has not been reviewed in the past 5 years and therefore is up for re-consideration.

Test strip coverage was reviewed through the Coverage Guidance process in 2013 and reaffirmed in 2016. The Coverage Guidance "blue box" reads:

> For patients with type 1 diabetes and those with type 2 diabetes using multiple daily insulin injections, home blood glucose monitors and related diabetic supplies are recommended for coverage (*strong recommendation*).
>
> For patients with type 2 diabetes not requiring multiple daily insulin injections, fifty test strips and related supplies are recommended for coverage at the time of diagnosis (*weak recommendation*). For those who require diabetic medication that may result in hypoglycemia, up to 50 test strips per 90 days are recommended for coverage (*weak recommendation*). If there is an acute change in glycemic control or active diabetic medication adjustment, an additional 50 strips are recommended for coverage (*weak recommendation*).
>
> For all diabetic patients who are prescribed diabetic test strips, a structured education and feedback program for self-monitoring of blood glucose is recommended for coverage (*strong recommendation*).
>
> *Note: This guidance does not apply to pregnant women.*

Current Prioritized List status

ANCILLARY GUIDELINE A2, SELF-MONITORING OF BLOOD GLUCOSE IN DIABETES

For patients with type 1 diabetes and those with type 2 diabetes using multiple daily insulin injections, home blood glucose monitors and related diabetic supplies are covered.

For patients with type 2 diabetes not requiring multiple daily insulin injections, 50 test strips and related supplies are covered at the time of diagnosis. For those who require diabetic medication that may result in hypoglycemia, up to 50 test strips per 90 days are covered. If there is an acute change in glycemic control or active diabetic medication adjustment, an additional 50 strips are covered.

All diabetic patients who are prescribed diabetic test strips should have a structured education and feedback program for self-monitoring of blood glucose.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

Evidence

1) **Gomes 2017**, Association of a Blood Glucose Test Strip Quantity-Limit Policy with Patient Outcomes
    a. Population
        i. N=834,309 patients for outcome of emergency department visits for hypoglycemia or hyperglycemia
        ii. N=83,347 patients for outcome of hemoglobin a1c levels
    b. ED visits for hypoglycemia and hyperglycemia
        i. Among those younger than 65 years, the rate of hypoglycemia and hyperglycemia declined over the study period (from 4.9 to 3.0 visits per 1000 Ontario drug benefit [ODB]-eligible patients and from 4.2 to 3.6 emergency department visits per 1000 ODB-eligible patients, respectively) and was not significantly associated with the introduction of quantity limits (*P* = .67 and *P* = .37, respectively).
        ii. Among those aged 65 years and older, rates of hypoglycemia and hyperglycemia declined over the study period (from 2.9 to 1.3 visits per 1000 eligible patients and from 0.8 to 0.5 visits per 1000 eligible patients, respectively) and was not significantly associated with the introduction of quantity limits (*P* = .12 and *P* = .24, respectively).
    c. Hemoglobin a1c levels
        i. After a slight rise from 7.2 in Q2 2008 to 7.5 in Q2 2009, mean HbA1c levels remained stable (range from 7.4 to 7.7) over the remainder of the study period among individuals younger than 65 years and was not impacted by the BGTS policy (*P* = .80). We observed a similar pattern among those aged 65 years and older with a slight rise in mean HbA1c levels from6.7 to 7.0 from Q2 2008 to Q2 2009 after which HbA1c levels stabilized and ranged between 7.0 and 7.2 over the remainder of the study period. There was no evidence of an impact of the BGTS policy on this trend (*P*= .97)
    d. When stratified by diabetes therapy group, rates of hypoglycemia and hyperglycemia were higher among insulin treated patients and lowest among those treated with nonhypoglycemia-inducing OHAs and those receiving no drug therapy. All outcomes were stable over the study period after stratifying by diabetes therapy group
    e. CONCLUSIONS AND RELEVANCE The imposition of quantity limits for blood glucose test strips was not associated with worsening short-term outcomes, suggesting that these policies can reduce costs associated with test strips without causing patient harm.
2) **Xu 2019**, Systematic review and meta-analysis of the impact of self monitoring of blood glucose (SMBG) in type 2 diabetics not on insulin therapy
    a. N=12 RCTs (3350 patients)
        i. All studies found to have inadequate blinding of patients
    b. Performing SMBG for 8 to 14 times per week was correlated with a better HbA1c control at 6 months (MD −0.46%, 95% CI −0.54 to −0.39) and 12 months (MD −0.20%, 95% CI −0.29 to −0.11). However, up to seven measurements of SMBG per week did not significantly affect glycemic control.
        i. NOTE: clinically significant a1c change is defined as >0.5%
    c. Among the four RCTs in which physicians applied the results of SMBG to adjust diabetes medication, a statistically significant reduction in HbA1c levels was observed in the intervention arm compared to the control arm (MD: −0.23, 95% CI −0.31 to −0.15, *P* <

0.00001). Hypoglycemic drugs were adjusted more often in the intervention group compared to the control group in these four studies.
    i. NOTE: clinically significant a1c change is defined as >0.5%
d. **Conclusions:** Eight to 14 measurements of SMBG per week were associated with a statistical improvement in glycemic control and a reduced BMI in patients with T2D not using insulin

3) **Young 2017,** RCT of glucose self-monitoring in non-insulin treated diabetic patients
    a. N=418 patients
    b. Randomized to no self-monitoring, once-daily self monitoring, and once-daily self-monitoring with enhanced patient feedback
    c. There were no significant differences in hemoglobin A1c levels across all 3 groups (*P* = .74; estimated adjusted mean hemoglobin A1c difference, SMBG with messaging vs no SMBG, −0.09%; 95%CI, −0.31% to 0.14%; SMBG vs no SMBG, −0.05%; 95%CI, −0.27%to 0.17%). There were also no significant differences found in HRQOL. There were no notable differences in key adverse events including hypoglycemia frequency, health care utilization, or insulin initiation.
    d. CONCLUSIONS AND RELEVANCE In patients with non–insulin-treated type 2 diabetes, we observed no clinically or statistically significant differences at 1 year in glycemic control or HRQOL between patients who performed SMBG compared with those who did not perform SMBG. The addition of this type of tailored feedback provided through messaging via ammeter did not provide any advantage in glycemic control.

<u>Other payer policies</u>

CMS 2021

Usual Utilization

For a beneficiary who is not currently being treated with insulin administrations, up to 100 test strips and up to 100 lancets every 3 months are covered if the basic coverage criteria (1)-(2) are met

1) The beneficiary has diabetes (Refer to the ICD-10 code list in the LCD-related Policy Article for applicable diagnoses); and
2) The beneficiary's treating practitioner has concluded that the beneficiary (or the beneficiary's caregiver) has sufficient training using the particular device prescribed as evidenced by providing a prescription for the appropriate supplies and frequency of blood glucose testing.

For a beneficiary who is currently being treated with insulin administrations, up to 300 test strips and up to 300 lancets every 3 months are covered if basic coverage criteria (1)-(2) (above) are met.

High Utilization

For a beneficiary who is not currently being treated with insulin administrations, more than 100 test strips and more than 100 lancets every 3 months are covered if criteria (a) – (c) below are met.
For a beneficiary who is currently being treated with insulin administrations, more than 300 test strips and more than 300 lancets every 3 months are covered if criteria (a) – (c) below are met.

a) Basic coverage criteria (1)-(2) listed above for all home glucose monitors and related accessories and supplies are met; and,
b) Within the six (6) months prior to ordering quantities of strips and lancets that exceed the utilization guidelines, the treating practitioner has had an in-person visit with the beneficiary to evaluate their diabetes control and their need for the specific quantity of supplies that exceeds the usual utilization amounts described above; and,

c) Every six (6) months, for continued dispensing of quantities of testing supplies that exceed the usual utilization amounts, the treating practitioner must verify adherence to the high utilization testing regimen.

If neither basic coverage criterion (1) or (2) is met, all testing supplies will be denied as not reasonable and necessary. If quantities of test strips or lancets that exceed the utilization guidelines are provided and criteria (a) – (c) are not met, the amount in excess will be denied as not reasonable and necessary.

Diabetic Test Strips

HERC staff summary

In a meta-analysis of the use of diabetes self-monitoring in non-insulin using diabetic patients published since the last coverage guidance review, there was no clinically meaningful change in hemoglobin a1c found with increased test strip use. Similarly, in an RCT published after the last review of this topic, no clinical difference in health care utilization or hemoglobin a1c level was found between patients who did diabetes self-monitoring compared to those who did not. A population level pre/post-analysis of an Ontario policy to limit test strip numbers found no significant change in ED utilization or hemoglobin a1c levels with diabetic test strip limits.

HERC staff recommendation:

1) Make no change in the current limitations on diabetic test strips for patients with diabetes who don't use multiple daily insulin injections.

JAMA Internal Medicine | Original Investigation

Association of a Blood Glucose Test Strip Quantity-Limit Policy With Patient Outcomes
A Population-Based Study

Tara Gomes, MHSc; Diana Martins, MSc; Mina Tadrous, PharmD, PhD; J. Michael Paterson, MSc; Baiju R. Shah, MD, PhD; Jack V. Tu, MD, PhD; David N. Juurlink, MD, PhD; Anna Chu, MHSc; Muhammad M. Mamdani, PharmD, MA, MPH

IMPORTANCE Given their high costs, payers have considered implementing quantity limits for reimbursement of blood glucose test strips. The effect of these limits on patient outcomes is unknown.

OBJECTIVE To determine whether the introduction of quantity limits for blood glucose test strips in August 2013 was associated with changes in clinical outcomes.

DESIGN, SETTING, AND PARTICIPANTS Cross-sectional time series analysis from April 2008 to March 2015 of residents of Ontario, Canada, aged 19 years and older with diabetes who were eligible for public drug coverage. In a sensitivity analysis, we studied high-volume users of test strips, who were most likely to be affected by the quantity limits.

EXPOSURES Eligible patients were stratified into 4 mutually exclusive groups based on diabetes therapy: insulin, hypoglycemia-inducing oral diabetes agents, nonhypoglycemia-inducing oral diabetes agents, and no drug therapy.

MAIN OUTCOMES AND MEASURES The primary outcome was emergency department visits for hypoglycemia or hyperglycemia, and the secondary outcome was mean hemoglobin A1c (HbA1c) levels. Outcomes were measured for all patients in each quarter, stratified by age group (<65 vs ≥65 years) and diabetes therapy.

RESULTS By the end of the study period, 834 309 people met inclusion criteria. Among those younger than 65 years, the rate of hypoglycemia and hyperglycemia declined over the study period (from 4.9 to 3.0 visits per 1000 Ontario drug benefit [ODB]-eligible patients and from 4.2 to 3.6 visits per 1000 ODB-eligible patients, respectively) and was not significantly associated with the introduction of quantity limits ($P = .67$ and $P = .37$, respectively). Similarly, among those aged 65 years and older, rates of hypoglycemia and hyperglycemia declined over the study period (from 2.9 to 1.3 visits per 1000 eligible patients and from 0.8 to 0.5 visits per 1000 eligible patients, respectively) and was not significantly associated with the introduction of quantity limits ($P = .12$ and $P = .24$, respectively). Results were consistent for the secondary outcome of mean HbA1c levels and in the sensitivity analysis of high-volume test strip users.

CONCLUSIONS AND RELEVANCE The imposition of quantity limits for blood glucose test strips was not associated with worsening short-term outcomes, suggesting that these policies can reduce costs associated with test strips without causing patient harm.

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Supplemental content

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META-ANALYSIS

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Evaluating the impact of self-monitoring of blood glucose frequencies on glucose control in patients with type 2 diabetes who do not use insulin: A systematic review and meta-analysis

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Abstract

Aims: International diabetes guidelines have not established the frequencies of self-monitoring of blood glucose in patients with type 2 diabetes (T2D) who do not use insulin. The present study aimed to assess the impact of self-monitoring of blood glucose (SMBG) frequencies on the glucose control and other outcomes in non-insulin-treated patients with T2D.

Methods: A literature search was performed in four databases. Randomised controlled trials with ≥6-month follow-up duration that compared the impact of different frequencies of SMBG on glycated haemoglobin A1c (HbA1c) were included. Studies with abstract only or reported effects of SMBG as a secondary outcome were excluded.

Results: Of the 1557 studies identified, 12 RCTs with a total of 3350 patients were analysed. Overall, performing SMBG for 8 to 14 times per week was correlated with a better HbA1c control at 6 months (MD −0.46%, 95% CI −0.54 to −0.39) and 12 months (MD −0.20%, 95% CI −0.29 to −0.11). However, up to seven measurements of SMBG per week did not significantly affect glycaemic control. In addition, performing SMBG between 8 and 14 times per week was also associated with improved BMI (MD −0.46, 95% CI −0.84 to −0.08). When the results of SMBG were applied to adjust diabetes medication, a significant reduction in HbA1c levels was observed in the intervention arm compared to the control arm.

Conclusions: Eight to 14 measurements of SMBG per week were associated with an improved glycaemic control and a reduced BMI in patients with T2D not using insulin.

1 | INTRODUCTION

Self-monitoring of blood glucose (SMBG) has been accepted as an integral component of diabetes management.[1] SMBG allows diabetic patients to become aware of their glycaemic levels, facilitating them to adjust diets and medication to improve their glycaemic control.[2-4] When used appropriately, SMBG can help to reduce the risk of hypo- and hyperglycaemia.[2,5,6]

Self-monitoring of blood glucose is considered beneficial to the management of type 1 diabetes (T1D) and insulin-treated type 2 diabetes (T2D).[1,7,8] The American Diabetes Association guideline provides specific recommendations for the timing of SMBG for patients using intensive insulin regimens: prior to meals and exercise, occasionally postprandially and at bedtime.[9] However, international diabetes guidelines have not established the frequencies of SMBG in non-insulin-treated T2D.

Several systematic reviews and meta-analyses have explored the effects of SMBG on glycaemic control in non-insulin-treated T2D patients, showing a reduction of glycated haemoglobin A1c (HbA1c) from 0.21% to 0.34% and a slight improvement in body mass index

JAMA Internal Medicine | Original Investigation

Glucose Self-monitoring in Non–Insulin-Treated Patients With Type 2 Diabetes in Primary Care Settings
A Randomized Trial

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IMPORTANCE The value of self-monitoring of blood glucose (SMBG) levels in patients with non–insulin-treated type 2 diabetes has been debated.

OBJECTIVE To compare 3 approaches of SMBG for effects on hemoglobin A_{1c} levels and health-related quality of life (HRQOL) among people with non–insulin-treated type 2 diabetes in primary care practice.

DESIGN, SETTING, AND PARTICIPANTS The Monitor Trial study was a pragmatic, open-label randomized trial conducted in 15 primary care practices in central North Carolina. Participants were randomized between January 2014 and July 2015. Eligible patients with type 2 non–insulin-treated diabetes were: older than 30 years, established with a primary care physician at a participating practice, had glycemic control (hemoglobin A_{1c}) levels higher than 6.5% but lower than 9.5% within the 6 months preceding screening, as obtained from the electronic medical record, and willing to comply with the results of random assignment into a study group. Of the 1032 assessed for eligibility, 450 were randomized.

INTERVENTIONS No SMBG, once-daily SMBG, and once-daily SMBG with enhanced patient feedback including automatic tailored messages delivered via the meter.

MAIN OUTCOMES AND MEASURES Coprimary outcomes included hemoglobin A_{1c} levels and HRQOL at 52 weeks.

RESULTS A total of 450 patients were randomized and 418 (92.9%) completed the final visit. There were no significant differences in hemoglobin A_{1c} levels across all 3 groups ($P = .74$; estimated adjusted mean hemoglobin A_{1c} difference, SMBG with messaging vs no SMBG, −0.09%; 95% CI, −0.31% to 0.14%; SMBG vs no SMBG, −0.05%; 95% CI, −0.27% to 0.17%). There were also no significant differences found in HRQOL. There were no notable differences in key adverse events including hypoglycemia frequency, health care utilization, or insulin initiation.

CONCLUSIONS AND RELEVANCE In patients with non–insulin-treated type 2 diabetes, we observed no clinically or statistically significant differences at 1 year in glycemic control or HRQOL between patients who performed SMBG compared with those who did not perform SMBG. The addition of this type of tailored feedback provided through messaging via a meter did not provide any advantage in glycemic control.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT02033499

Editor's Note page 929

Author Video Interview and JAMA Report Video

Supplemental content

CME Quiz at jamanetwork.com/learning

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: A complete list of the Monitor Trial Group members is provided in at the end of the article.

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Acquired Penile Anomalies

Question: When are treatment for acquired penile anomalies covered?

Question source: Medical Management Committee

Issue: A guideline adopted in 2015 specifies when various congenital penile deformities were included on a covered line. Some of the criteria require a certain degree of curvature or rotation in order to receive surgical repair. There have been multiple cases before the Medical Management Committee at OHA in which the patient has acquired penile anomalies, generally after a circumcision. MMC would like guidance on whether the Guideline Note 73 PENILE ANOMALIES criteria should apply to coverage of such acquired anomalies, or if other criteria should be considered for eligibility for treatment.

Currently, circumcision is only covered for a very limited set of indications. However, complications of circumcision are eligible for treatment, similar to complications of other elective procedures such as cosmetic breast augmentation.

Current Prioritized list status

ICD-10-CM N48.89 (Other specified disorders of penis) is on line 658 GENITOURINARY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY. Among the sub-diagnoses of N48.89 are chordee, acquired synechiae of foreskin of penis, and penile pain. ICD-10-CM T81.9XXA (Unspecified complication of procedure, initial encounter) is on line 571 OTHER COMPLICATIONS OF A PROCEDURE. This code is intended for complications after neonatal circumcision.

Congenital equivalents to circumcision complications, such as congenital chordee (ICD-10-CM Q54.4) or curvature of penis (ICD-10-CM Q55.61) are on line 433 HYPOSPADIAS AND EPISPADIAS as well as line 658 GENITOURINARY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY. Guideline Note 73 governs when the diagnosis is on the covered line.

CPT 54162 (Lysis or excision of penile post-circumcision adhesions) is on line 571 OTHER COMPLICATIONS OF A PROCEDURE

GUIDELINE NOTE 73, PENILE ANOMALIES

Lines 433,658

Anomalies of the penis (ICD-10-CM Q54.4, Q55.5 and Q55.6) are included on Line 433 only when they

A. Are associated with hypospadias, OR
B. Result in documented urinary retention, OR
C. Result in repeated urinary tract infections, OR
D. Result in recurrent infections such as meatitis or balanitis, OR
E. Involve 35 degrees of curvature or greater for conditions resulting in lateral or ventral curvature, OR
F. Involve 60 degrees of rotation or greater for conditions resulting in penile torsion, OR
G. Involve aplasia/congenital absence of the penis.

Otherwise, these diagnoses are included on Line 658.

Acquired Penile Anomalies

Expert input

Dr. Chris Austin, OHSU pediatric urology

I feel that adding phimosis N47.1 and acquired buried penis N48.83 would provide better coverage for the problems that we see after circumcision- The 2 most common procedures that need treatment for after circumcision are when the scar contracts and traps the penis- I call this a "trapped penis" (likely coded as an acquired buried penis or phimosis). This can initially be treated with topical steroids and stretching of the skin, but if this fails surgery is the only option. The proposed rules that are used for the treatment of penile anomalies fall short in that a trapped penis after a circumcision that fails topical therapy or penile skin bridges won't improve with time and leave the patient with a condition that would result in deformities or pain to their genitalia in the future without surgical care.

I think that all skin bridges (as opposed to simple penile adhesions) should be approved for treatment. They are due to the scar from the circumcision healing to the glans, creating a permanent scar formation that won't release over time. While they may create some angulation or twist to the penis, that degree would vary and is really not an indicator of severity of the problem or the risk of future problems. In my opinion, the risk if future problems for skin bridges and a trapped penis is more just the mere presence of the condition, unlike congenital anomalies, where the severity is a predictor of future problems.

HERC staff recommendations:

1) Add to line 424 COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT
    a. CPT 54162 (Lysis or excision of penile post-circumcision adhesions)
    b. ICD-10-CM N48.89 (Other specified disorders of penis)
    c. T81.9XXA (Unspecified complication of procedure, initial encounter)
    d. Keep all 3 codes on line 571 OTHER COMPLICATIONS OF A PROCEDURE
2) Add to line 424 COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT
    a. ICD-10-CM N48.83 (Acquired buried penis)
    b. Keep on line 658 GENITOURINARY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
3) Modify GN75 as shown below

GUIDELINE NOTE 73, PENILE ANOMALIES

Lines 424,433,571,658

Congenital a~~A~~nomalies of the penis (ICD-10-CM Q54.4, Q55.5 and Q55.6) are included on Line 433 only when they

A. Are associated with hypospadias, OR
B. Result in documented urinary retention, OR
C. Result in repeated urinary tract infections, OR
D. Result in recurrent infections such as meatitis or balanitis, OR
E. Involve 35 degrees of curvature or greater for conditions resulting in lateral or ventral curvature, OR
F. Involve 60 degrees of rotation or greater for conditions resulting in penile torsion, OR
G. Involve aplasia/congenital absence of the penis.

Otherwise, these diagnoses are included on Line 658

Acquired anomalies of the penis (ICD-10-CM N48.83, N48.89 or T81.9XXA) are included on line 424 only when they are the result of a prior penile procedure AND either

A. Result in a skin bridge. OR
B. Result in a buried penis; OR
C. Are associated with hypospadias, OR
D. Result in documented urinary retention, OR
E. Result in repeated urinary tract infections, OR
F. Result in recurrent infections such as meatitis or balanitis, OR
G. Involve 35 degrees of curvature or greater for conditions resulting in lateral or ventral curvature, OR
H. Involve 60 degrees of rotation or greater for conditions resulting in penile torsion.

Otherwise, these diagnoses are included on line 571 or 658.

Cranial Electrical Stimulation
2021 Re-Review

Question: should cranial electrical stimulation (CES) devices be included on the Prioritized List for pairing with any condition?

Question source: Allevia Health, Alpha-Stim manufacturer

Issue: Cranial electrotherapy stimulation (CES) is a form of non-invasive brain stimulation that applies a small, pulsed electric current across a person's head with the intention of treating a variety of conditions such as anxiety, depression and insomnia. CES is a form of transcutaneous electrical nerve stimulation (TENS). CES is FDA approved for treatment of pain, insomnia, anxiety, and/or depression.

Cranial electrical stimulation was last reviewed in 2017. That review found no evidence of effectiveness for CES for treatment of chronic pain in trusted evidence sources (Cochrane). Mixed results were found in small studies on anxiety and depression. Based on lack of data, use of CES for anxiety, depression or insomnia was judged to lack sufficient evidence of effectiveness and was placed on line 662/GN173. The current entry that includes CES has a date of last review of January 2020 due to a review of TENS therapy.

The manufacturer has brought updated studies and requests a re-review of non-coverage of CES. The evidence supplied by the manufacturer regarded treatment of depression, anxiety, pain and insomnia.

Current Prioritized List status

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
97014, 97032, 0278T, E0720, E0730, G0283	Transcutaneous electrical nerve stimulation (TENS), frequency specific microcurrent therapy, microcurrent electrical stimulation, and all similar therapies; Scrambler therapy; all similar transcutaneous electrical neurostimulation therapies	Insufficient evidence of effectiveness for chronic pain and all other indications	January 2020

Cranial Electrical Stimulation
2021 Re-Review

Evidence

Depression

1) **NICE 2015,** Transcranial direct current stimulation (tDCS) for depression
    a. Conclusion: The evidence on transcranial direct current stimulation (tDCS) for depression raises no major safety concerns. There is some evidence of efficacy but there are uncertainties about the specific mode of administration, the number of treatments needed and the duration of effect. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.
    b. A systematic review and meta-analysis of 7 RCTs (259 patients)
        i. active transcranial direct current stimulation (tDCS; n=137) or sham tDCS (n=122)
        ii. significantly greater improvement in depressive symptoms in the active tDCS group (Hedges' g=0.37; 95% confidence interval [CI] 0.04 to 0.7) compared against the sham tDCS group.
        iii. Significantly better treatment response rates (defined as an improvement greater than 50% in depression scores from baseline to end point) in the active tDCS group
        iv. Significantly better remission rates in the active tDCS group compared against the sham tDCS group, with scores lower than 8 in the Hamilton Depression Rating Scale (several variables assessed and measured on 5-point or 3-point scales, with low values indicating less depression), or lower or equal to 10 in the MADRS (OR 2.5, 95% CI 1.26 to 4.99).
    c. An RCT of 120 patients treated by active tDCS plus sertraline (n=30), active tDCS plus placebo (n=30), sham tDCS plus sertraline (n=30), or sham tDCS plus placebo (n=30) reported significantly lower Montgomery–Åsberg Depression Rating Scale (MADRS) scores (10 items measured on a scale of 0 to 6 with low values indicating less depression) after 6 weeks in patients treated by active tDCS plus sertraline compared against patients treated by sham tDCS plus sertraline (mean difference 8.5 points; 95% CI 2.96 to 14.03; p=0.002). Significantly lower MADRS scores after 6 weeks were also reported in patients treated by active tDCS plus placebo compared against patients treated by sham tDCS plus placebo (mean difference 5.6 points; 95% CI 1.30 to 10.01; p=0.01). This study found remission rates (according to MADRS scores) after 6 weeks were 47% (14/30) for patients treated by active tDCS plus sertraline, 40% (12/30) for patients treated by active tDCS plus placebo, 30% (9/30) for patients treated by sham tDCS plus sertraline and 13% (4/30) for patients treated by sham tDCS plus placebo (p=0.03 between groups).
    d. Adverse events included mania or hypomania, skin lesions, skin redness, headache, lightheadedness, somnolence and burning sensation
2) **Shekelle 2018,** systematic review of cranial electrical stimulation for pain, depression, anxiety and insomnia
    a. N=3 trials (N=40, 16, 20) involved patients with depression
        i. The trials with 40 and 16 patients used the Fisher Wallace Stimulator
        ii. The study with 20 patients used Alpha-Stim
    b. The trial with 40 patients reported no difference between groups in HAM-D scores over time, with nearly identical values in actively treated and sham-treated patients

c. The trial with 16 patients found no difference between groups in HAM-D scores at 1 week and 2 weeks and a statistically significant 8-point difference in the Beck Depression Inventory at 2 weeks favoring the CES group (with 5 points considered to be the minimal clinically important difference)
d. The trial with 20 patients used the Alpha-Stim unit and randomly assigned community-recruited volunteers to active versus sham CES. The groups did not differ in change in Beck Depression Inventory outcomes at 3 weeks

3) **Price 2021**, meta-analysis of cranial electrotherapy stimulation in the treatment of depression
    e. Note: submitted by Allevia Health
    f. Note: study sponsored by Electromedical Products International and all authors repot being an employee or consultant of this company
    g. N=5 RCTs (242 patients) and 12 observational studies (N=1173 patients)
        i. Noted to be at high risk of selection bias
        ii. RCTs had limited number of patients meeting DSM criteria for major depression
    a. The average effect for the 5 RCTs was calculated as *d* = -0.69 (*i.e.,* the mean depression level at posttest for the active group was 0.69 standard deviations lower than the mean depression level for the sham group), a medium effect. The additional 12 NRSI studies analyzed show a small effect of *d* = -0.43 in favor of the active treatment group.
    b. *Conclusion:* We conclude that CES has a small to medium significant effect in symptoms of depression

Anxiety and depression

1) **NICE 2021,** Alpha-Stim for anxiety disorders https://www.nice.org.uk/guidance/mtg56/resources/alphastim-aid-for-anxiety-disorders-pdf-64372119603397
    a. Conclusion: Alpha-Stim AID shows promise for managing anxiety disorders. However, there is not enough good-quality evidence to support the case for routine adoption
    b. N=6 studies (3 RCTs [one unpublished], 3 non-comparative observational studies)
        i. All studies noted to be small (N=12 to 197)
    c. The 3 randomized controlled trials showed a statistically significant improvement in patient-reported anxiety scores with Alpha-Stim AID compared with drugs alone, a sham device or no treatment in people with anxiety disorders. The benefit of Alpha-Stim AID in relieving anxiety symptoms was also reported consistently in the observational studies.
    d. The studies were of short duration (usually 5 to 6 weeks) with only 1 observational study reporting longer-term outcomes at 24 weeks.
    e. Adverse events reported with Alpha-Stim AID in 2 studies included mild headache, dizziness, nausea and feeling strange
    f. The randomized controlled trial evidence showed short-term relief of anxiety symptoms with Alpha-Stim AID in people with anxiety disorders. However, the committee noted that the quality of the evidence was low because of a high risk of bias. The committee was concerned about the possibility of a significant placebo effect with Alpha-Stim AID

g. No convincing evidence was available on the longer-term benefits of Alpha-Stim AID

2) **Shekelle 2018,** systematic review of cranial electrical stimulation for pain, depression, anxiety and insomnia
    i. N=5 trials with patients with anxiety and depression
        1. 4 were done more than 40 yrs ago with devices no longer available
    ii. One study (N=115 patients) compared CES to usual care
        1. The baseline HAM-A and HAM-D scores were about 29 and 14 points, respectively. Weekly measurements of HAM-A and HAM-D scores showed a steady decline (improvement) in both groups, but decreases were greater for patients treated with active CES: about 6.5 points on the HAM-A and 3.5 points on the HAM-D at 5 weeks. Both differences were statistically significant, although the HAM-D difference was of borderline clinical significance

Insomnia

1) **Shekelle 2018,** systematic review of cranial electrical stimulation for pain, depression, anxiety and insomnia
    a. Two trials enrolled patients with insomnia (N=36 and 10). One, done more than 40 years ago, used a CES device that is no longer marketed (Electrodorm). Together, the 2 studies had inconclusive results

<u>Other payer policies</u>:

1) All private payers surveyed considered CES to be experimental

Cranial Electrical Stimulation
2021 Re-Review

HERC staff summary: Trusted sources (NICE) and well conducted systematic reviews do not find sufficient evidence of effectiveness of cranial electrical stimulation for the treatment of depression, anxiety or insomnia.

HERC staff recommendation:

1) Keep cranial electrical stimulation on line 662/GN173
    a. Modify the date of last review in the GN173 entry as shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
97014, 97032, 0278T, E0720, E0730, G0283	Transcutaneous electrical nerve stimulation (TENS), frequency specific microcurrent therapy, microcurrent electrical stimulation, and all similar therapies; Scrambler therapy; all similar transcutaneous electrical neurostimulation therapies	Insufficient evidence of effectiveness for chronic pain and all other indications	January 2020 for TENS October 2021 for cranial electrical stimulation

Cranial Electrical Stimulation
2021 Re-Review

Appendix A
Disposition of submitted articles

CES for insomnia:
Price 2021: unable to locate study in Medline
Aseem 2019: unable to locate study in Medline

NICE guidance

Transcranial direct current stimulation (tDCS) for depression

Interventional procedures guidance
Published: 26 August 2015
nice.org.uk/guidance/ipg530

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Recommendations

1.1 The evidence on transcranial direct current stimulation (tDCS) for depression raises no major safety concerns. There is some evidence of efficacy but there are uncertainties about the specific mode of administration, the number of treatments needed and the duration of effect. Therefore, this procedure should

only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to do tDCS for depression should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.
- Audit and review clinical outcomes of all patients having tDCS for depression (see section 7.2).

1.3 NICE encourages further research into tDCS for depression, which should document how patients were selected and any other treatments they were having. It should describe the precise method and regime used for administering tDCS. Outcome measures should include the duration of effect. NICE may update the guidance on publication of further evidence.

2 Indications and current treatments

2.1 Depression is a common disorder, characterised by persistent sadness, loss of interest or pleasure, feelings of guilt, low self-worth, tiredness, poor concentration, and disturbed sleep, appetite and libido. It is often accompanied by feelings of hopelessness and suicidal thoughts. Depression can last from weeks to years, and can be recurrent. It can substantially impair a person's ability to function at work or cope with daily life.

2.2 Treatments for depression include a range of psychological therapies, and antidepressant medications. In severe depression that has not responded to other treatments, electroconvulsive therapy is sometimes used.

3 The procedure

3.1 Transcranial direct current stimulation (tDCS) is a non-invasive method of electrical stimulation of the brain using a weak direct current applied to the scalp through electrodes. The aim is to modify cortical excitability and activity in

the brain areas under the scalp electrodes. It is thought to work by the depolarisation and hyperpolarisation of cortical neurons.

3.2 The patient, who remains awake and alert during the procedure, is usually seated while a portable battery-operated stimulator delivers a constant low-strength direct current to 2 saline-soaked sponge electrodes placed on the scalp. Treatment sessions typically last for about 20–30 minutes, and are repeated daily for several weeks. Treatment is usually delivered by a trained clinician, but it can also be self-administered by the patient. tDCS may be used alone or in addition to other treatments for depression.

4 Efficacy

This section describes efficacy 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 interventional procedure overview.

4.1 A systematic review and meta-analysis of 7 randomised controlled trials (RCTs) including 259 patients treated by active transcranial direct current stimulation (tDCS; n=137) or sham tDCS (n=122) reported a significantly greater improvement in depressive symptoms in the active tDCS group using Hedges' g as the measure of the effect size, which standardises studies using different depression scales (Hedges' g=0.37; 95% confidence interval [CI] 0.04 to 0.7) compared against the sham tDCS group. An RCT of 120 patients treated by active tDCS plus sertraline (n=30), active tDCS plus placebo (n=30), sham tDCS plus sertraline (n=30), or sham tDCS plus placebo (n=30) reported significantly lower Montgomery–Åsberg Depression Rating Scale (MADRS) scores (10 items measured on a scale of 0 to 6 with low values indicating less depression) after 6 weeks in patients treated by active tDCS plus sertraline compared against patients treated by sham tDCS plus sertraline (mean difference 8.5 points; 95% CI 2.96 to 14.03; p=0.002). Significantly lower MADRS scores after 6 weeks were also reported in patients treated by active tDCS plus placebo compared against patients treated by sham tDCS plus placebo (mean difference 5.6 points; 95% CI 1.30 to 10.01; p=0.01).

4.2 The systematic review of 7 RCTs including 259 patients reported significantly better treatment response rates (defined as an improvement greater than 50% in depression scores from baseline to end point) in the active tDCS group

compared against the sham tDCS group (odds ratio [OR] 1.63, 95% CI 1.26 to 2.12).

4.3 The systematic review of 7 RCTs including 259 patients reported significantly better remission rates in the active tDCS group compared against the sham tDCS group, with scores lower than 8 in the Hamilton Depression Rating Scale (several variables assessed and measured on 5-point or 3-point scales, with low values indicating less depression), or lower or equal to 10 in the MADRS (OR 2.5, 95% CI 1.26 to 4.99). In the RCT of 120 patients, remission rates (according to MADRS scores) after 6 weeks were 47% (14/30) for patients treated by active tDCS plus sertraline, 40% (12/30) for patients treated by active tDCS plus placebo, 30% (9/30) for patients treated by sham tDCS plus sertraline and 13% (4/30) for patients treated by sham tDCS plus placebo (p=0.03 between groups).

4.4 A follow-up study of 42 patients whose depression had responded ('responders') to tDCS treatment in the RCT of 120 patients reported a sustained response rate at 24 weeks in these 'responders' of 47% (95% CI, 27 to 64, measured by Kaplan–Meier survival analysis). Patients with treatment-resistant depression had a much lower 24-week sustained response rate than patients with non-refractory depression (10% versus 77%, OR 5.52; p<0.01). The same study reported a mean response duration (for 'responders', n=42) of 11.7 weeks.

4.5 The systematic review of 7 RCTs including 259 patients reported dropout rates of 8% (12/137) in the active tDCS group and 11% (15/122) in the sham tDCS group, with no difference in treatment acceptability (OR 0.73, 95% CI 0.32 to 1.69).

4.6 The specialist advisers listed key efficacy outcomes as improvement in depressive symptoms, remission, reduction in anxiety, effectiveness in treatment resistance and improvement in other parameters including cognitive function, pain and neurological symptoms.

5 Safety

This section describes 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 interventional procedure overview.

5.1 Six episodes of either treatment-emergent mania or hypomania (Young Mania Rating Scale score greater than 8) were reported in a randomised controlled trial (RCT) of 120 patients treated by active transcranial direct current stimulation (tDCS) plus sertraline, active tDCS plus placebo, sham tDCS plus sertraline, or sham tDCS plus placebo. Five episodes (including 2 manic episodes) were from the active tDCS plus sertraline group and 1 was from the tDCS-only group (no further details provided).

5.2 Skin lesions were reported in all (5/5) patients treated by 2 mA tDCS and in 1 (1/10) patient treated by 1 mA tDCS in a case series of 15 patients treated by 1 mA or 2 mA tDCS. Generally, the lesions occurred after the fourth or fifth stimulation, showed stable superficial extensions during further tDCS and healed without scars about 1–3 weeks after the end of the tDCS treatment.

5.3 A burning sensation was reported in 9% of the studies in the active tDCS group and in 10% of the studies in the sham tDCS group in a systematic review of 117 studies (p value not significant).

5.4 Skin redness 2 weeks after treatment was reported in 25% (13/60) of patients in the active tDCS group and in 8% (4/60) of patients in the sham tDCS group in the RCT of 120 patients (p=0.03). Skin redness was reported in 23% (10/42) of patients in a follow-up study of 42 patients whose depression had responded to tDCS treatment in the RCT of 120 patients.

5.5 Itching was reported in 39% of the studies in the active tDCS group and in 33% of the studies in the sham tDCS group in the systematic review of 117 studies (p value not significant and no details of timing provided). Tingling was reported in 22% of the studies in the active tDCS group and in 18% of the studies in the sham tDCS group in the systematic review of 117 studies (p value not significant and no details of timing provided).

5.6 Headache was reported in 15% of the studies in the active tDCS group and in 16% of the studies in the sham tDCS group in the systematic review of 117 studies (p value not significant). Headache was reported in 19% (8/42) of patients in the follow-up study of 42 patients whose depression had responded to tDCS treatment in the RCT of 120 patients.

5.7 Light-headedness was reported in 40% of patients when tDCS was administered weekly and in 17% when tDCS was administered once every 2 weeks in a case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.8 Somnolence was reported in 16% (7/42) of patients in the follow-up study of 42 patients whose depression had responded to tDCS treatment in the RCT of 120 patients. Fatigue was reported in 10% of patients when tDCS was administered weekly in the case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.9 Blurred vision was reported in 7% of patients when tDCS was administered weekly and in 11% when tDCS was administered once every 2 weeks in the case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.10 Panic attacks were reported in a single case report 5 days after starting tDCS treatment. It was hypothesised that the patient, who was left-handed and dyslexic, had right hemispheric dominance.

5.11 Nausea was reported in 10% of patients when tDCS was administered weekly and in 6% when tDCS was administered once every 2 weeks in the case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.12 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers reported induction of phosphenes ('flashing lights') with anterior stimulation positions as an anecdotal adverse event. They considered that the following were theoretical adverse events: precipitation of seizures, exacerbation of

depression, interference with implanted electrical devices and twitching of facial muscles.

6 Committee comments

6.1 The Committee was mindful that depression is a very common condition and that a range of other treatments is available. It considered that this increased the need for good evidence on transcranial direct current stimulation (tDCS).

6.2 The Committee noted the inconsistency of the outcomes reported after tDCS for depression between the various studies. Together with the uncertainties about the different modes of administration and number of treatments, this underpinned the recommendation for further research.

7 Further information

7.1 For related NICE guidance, see the NICE website.

7.2 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

Information for patients

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

About this guidance

NICE interventional procedures 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.

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

We have produced information for the public explaining this guidance. Tools to help you put the guidance into practice and information about the evidence it is based on are also available.

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

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 have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Accreditation

REVIEW

Annals of Internal Medicine

Benefits and Harms of Cranial Electrical Stimulation for Chronic Painful Conditions, Depression, Anxiety, and Insomnia

A Systematic Review

Paul G. Shekelle, MD, PhD; Ian A. Cook, MD; Isomi M. Miake-Lye, PhD; Marika Suttorp Booth, MS; Jessica M. Beroes, BS; and Selene Mak, MPH

Background: Cranial electrical stimulation (CES) is increasingly popular as a treatment, yet its clinical benefit is unclear.

Purpose: To review evidence about the benefits and harms of CES for adult patients with chronic painful conditions, depression, anxiety, and insomnia.

Data Sources: Several databases from inception to 10 October 2017 without language restrictions and references from experts, prior reviews, and manufacturers.

Study Selection: Randomized controlled trials of CES versus usual care or sham CES that reported pain, depression, anxiety, or sleep outcomes in any language.

Data Extraction: Single-reviewer extraction checked by another; dual independent quality assessment; strength-of-evidence grading by the first author with subsequent group discussion.

Data Synthesis: Twenty-eight articles from 26 randomized trials met eligibility criteria. The 2 trials that compared CES with usual care were small, and neither reported a statistically significant benefit in pain or anxiety outcomes for patients with fibromyalgia or anxiety, respectively. Fourteen trials with sham or placebo controls involving patients with painful conditions, such as headache, neuromuscular pain, or musculoskeletal pain, had conflicting results. Four trials done more than 40 years ago and 1 from 2014 provided low-strength evidence of a possible modest benefit compared with sham treatments in patients with anxiety and depression. Trials in patients with insomnia (n = 2), insomnia and anxiety (n = 1), or depression (n = 3) had inconclusive or conflicting results. Low-strength evidence suggested that CES does not cause serious side effects.

Limitation: Most trials had small sample sizes and short durations; all had high risk of bias due to inadequate blinding.

Conclusion: Evidence is insufficient that CES has clinically important effects on fibromyalgia, headache, neuromusculoskeletal pain, degenerative joint pain, depression, or insomnia; low-strength evidence suggests modest benefit in patients with anxiety and depression.

Primary Funding Source: Veterans Affairs Quality Enhancement Research Initiative. (PROSPERO: CRD42016023951)

Ann Intern Med. 2018;168:414-421. doi:10.7326/M17-1970 **Annals.org**
For author affiliations, see end of text.
This article was published at Annals.org on 13 February 2018.

Cranial electrical stimulation (CES) is a noninvasive method of applying low-intensity electrical current to the head. It is related to but distinct from other forms of transcranial electrical stimulation, including electroconvulsive therapy and transcranial direct current stimulation. Versions of transcranial electrical stimulation vary in the placement of electrodes and the intensity and waveform of the current (1). According to Guleyupoglu and colleagues (1), CES evolved from the concept of "electrosleep," first investigated at the beginning of the 20th century. Most early research and applications occurred in Russia. Beginning in the 1960s, electrosleep became more popular in the United States. Because of the belief that the treatment did not actually induce sleep, the name was changed from "electrosleep" to "cranial electrical stimulation" (1). Other proposed names, which have not persisted, included "transcerebral electrotherapy" and "Neuro-Electric Therapy." The latter is noteworthy because it gave its name to an early CES device, the Neurotone 101 (NeuroSystems), the first such device approved by the U.S. Food and Drug Administration (FDA) (1). The FDA has cleared all subsequent CES devices for marketing on the basis of equivalency to the Neurotone 101. The status of CES devices and FDA regulation remains a matter of some controversy.

Cranial electrical stimulation is among a growing number of noninvasive brain stimulation interventions that change brain function and have been used to treat diseases like depression and anxiety (2). An early meta-analysis by Klawansky and colleagues (3) identified 8 sham-controlled randomized trials of CES for anxiety, 2 randomized controlled trials for brain dysfunction, 2 trials for headache, and 2 trials for insomnia. Pooled effects for anxiety were statistically significant, favoring active treatment. The analysis found no benefit for insomnia or brain dysfunction and a small beneficial effect for headache. The authors cautioned, however, that the quality of included studies was "quite low," mostly because of inadequate blinding.

Among the most commonly used CES devices in the United States are the Alpha-Stim products and the Fisher Wallace Stimulator (Fisher Wallace) (4). They differ in electrode location (ear clips in the former and sponge electrodes at the temples in the latter) and in the amount and type of current. Both are FDA-cleared

See also:

Editorial comment 446

Web-Only
Supplement

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A meta-analysis of cranial electrotherapy stimulation in the treatment of depression

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ARTICLE INFO

Keywords:
Depression
Cranial electrotherapy Stimulation (CES)
Meta-analysis
Randomized controlled trials (RCTs)
Non-randomized Studies on interventions (NRSIs)

ABSTRACT

Background: Depression rates have reached historic highs, with 49% of Americans reporting unabating symptoms and signs of depression, representing a 12% increase compared to the same time in 2019. With depression as a moderating factor for suicide, the need for efficacious treatments for depression has never been more pronounced. Although the armamentarium of the psychiatrist seems impressive having multiple medications and psychotherapy options, with guidelines for combination and augmentation treatments; many patients do not improve or are not suitable candidates for the usual, customary and reasonable (UCR) depression treatments. The use of various forms of brain stimulation technology as a complementary or alternative treatment for depression is growing and is expected to be part of the armamentarium of most psychiatrists by 2030. One form of brain stimulation, available in a phone sized prescription device, is cranial electrical stimulation (CES) which has been used as a treatment for depression since the 1970s. We have conducted two meta-analyses of CES research for depression separating randomized controlled trials (N = 5) from non-randomized studies on interventions (N = 12). For the double-blind RCTs 100 μA was used for 1 hour per day as 100 μA is a subsensory level of current so identical sham treatment devices could be used.

Methods: Our literature review followed Cooper's Taxonomy of Literature Reviews that is appropriate for the behavioral and physical sciences and the PRISMA reporting guidelines. The evaluation of strengths and limitations of the research studies included in this report adheres to recommended published guidelines in the Cochrane Handbook for Systematic Reviews of Interventions, and in the Handbook of Research Synthesis and Meta-Analysis. We used the Cohen's *d* effect size summary metric in all analyses. Homogeneity of effect sizes within the fixed and random effects models are reported. Meta-analyses were performed using the Compressive Meta-Analysis, version 3 program.

Results: The 5 RCTs represent a combined N of 242 and the 12 NRSIs represent 16 data sets with a combined N of 1173 for total of 1415 subjects across 17 studies. There were male and female subjects, from adolescents to 60 years old. The average effect for the 5 RCTs was calculated as $d = -0.69$ (*i.e.,* the mean depression level at posttest for the active group was −0.69 standard deviations lower than the mean depression level for the sham group), a medium effect. The additional 12 NRSI studies analyzed show a small effect of $d = -0.43$ in favor of the active treatment group.

Conclusion: We conclude that CES has a small to medium significant effect in symptoms of depression across moderate to severe patients in civilian, military, veterans, advanced cancer and pediatric populations.

1. Introduction

Depression is a debilitating condition that decimates patients' quality of life, their relationships, ability to work and care for themselves. It is broadly defined to include both pure depression and mixed anxiety-depression. The National Institute of Mental Health (NIMH, 2018) rates depression as one of the most diagnosed mental disorders, with more than 300 million people worldwide suffering from this disorder (James et al., 2018; WHO, 2017a). Lifetime prevalence worldwide is estimated to be between 10% and 18% of adults and between 5% and

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Minimally Invasive Lumbar Decompression for Spinal Stenosis

Question: Should the MILD (minimally invasive lumbar decompression) procedure be paired with lumbar spinal stenosis?

Question source: Vertos Medical

Issue: Vertos Medical has requested the review of the MILD procedure for treatment of lumbar spinal stenosis (LSS). MILD is a form of percutaneous image-guided lumbar decompression (PILD) for lumbar spinal stenosis. Percutaneous image-guided lumbar decompression (PILD) is a posterior decompression of the lumbar spine performed under indirect image guidance without any direct visualization of the surgical area. The use of a cannula and trocar provides a portal that allows access to the anatomic area for instruments used for resection. This is a procedure proposed as a treatment for symptomatic LSS unresponsive to conservative therapy. This procedure is generally described as a relatively non-invasive (compared to open surgery) procedure using specially-designed instruments to percutaneously remove a portion of the lamina and debulk the ligamentum flavum. Alternative treatments are generally epidural steroid injections, which are currently not covered on the Prioritized List for LSS.

This procedure has no prior history of review by the HSC or HERC.

Current Prioritized List status

Code	Code Description	Current Placement
0275T	Percutaneous laminotomy/laminectomy (interlaminar approach) for decompression of neural elements (with or without ligamentous resection, discectomy, facetectomy and/or foraminotomy), any method under indirect image guidance (eg, fluoroscopic, CT), single or multiple levels, unilateral or bilateral; lumbar	Never Reviewed
G0276	Blinded procedure for lumbar stenosis, PILD, or placebo control, performed in an approved coverage with evidence development (CED) clinical trial	Never Reviewed

Evidence

1) MiDAS 1 study (Chopko 2010, Mekhail 2012 and Chopko 2013)
    a. **Chopko 2013:** non-comparative cohort study--2 year follow up
        i. N=45 patients (58 patients reported at 1 year in initial paper)
        ii. At 2 years, patients demonstrated a statistically significant reduction of pain as measured by VAS, and improvement in physical function and mobility was significant as measured by Zurich Claudication Questionnaire and Oswestry Disability Index.
        iii. Chopko is a consultant for Vertos Medical

2) MiDAS ENCORE study (Benyamin 2015, Benyamin 2016, Staats 2016, Staats 2018). Study sponsored by Vertos Medical
    a. **Benyamin 2016**, RCT of MILD vs epidural steroid injections
        i. N=302 patients (149 MILD, 153 epidural steroid injections)
            1. Study limited by lack of blinding
        ii. At 1-year follow-up, ODI, NPRS, and all 3 ZCQ domains (Symptom Severity, Physical Function and Patient Satisfaction) demonstrated statistically significant superiority of MILD versus the active control.
        iii. The Oswestry Disability Index (ODI) responder rate was 58.0% in the MILD group versus 27.1% for the ESI group ($P < 0.001$), demonstrating clinically meaningful improvement in function for patients in the MILD group
        i. No change was seen in medication usage for either group, including opioids
        ii. Two patients who received MILD (2 events) and 2 patients who received ESIs (3 events) experienced device or procedure-related adverse events (1.3%, $P = 1.00$)
    b. **Staats 2018**, 2 year follow up of RCT of MILD vs epidural steroid injections [only first 6 months was an RCT, 2 year follow up is just the MILD cohort]
        i. N=119 patients treated with MILD at 1 year; N=99 patients treated with MILD at 2 yrs
        ii. At 2 years, Oswestry Disability Index improved by 22.7 points, Numeric Pain Rating Scale improved by 3.6 points, and Zurich Claudication Questionnaire symptom severity and physical function domains improved by 1.0 and 0.8 points, respectively.
3) **Mekhail 2021**: long term follow up of a retrospective cohort
    a. N=75 patients, single center study
        i. 7 patients lost to follow up
        ii. Study funded by the Cleveland Clinic
    b. Only 9 out of 75 patients required lumbar surgical decompression at 5 yr follow up (2.4% per year incidence)
    c. Subjects experienced statistically significant pain relief 3, 6, and 12 months compared to baseline.
        i. Numeric rating scale score change of 3.0-3.2, which is clinically significant
    d. Although only 24% of subjects (18/75) were treated with opioid medications before the *mild* intervention, there is a statistically significant change in opioid medications utilization between baseline and 3, 6, and 12-months after *mild* treatment ($p = 0.0048$, $p = 0.0015$, and $p = 0.0067$, respectively)
    e. 12 patients had minor complications (postoperative pain, ecchymosis, allergic dermatitis)

4) **Brown 2012,** RCT of mild vs epidural steroid injection
    a. N=38 patients (21 Mild, 17 ESI)
        i. Funded by Vertos Medical
    b. At 6- and 12-week follow-up, patients treated with mild reported significantly greater pain decrease over time ($P < 0.0001$), and significantly greater functional mobility improvement over time ($P < 0.0018$) than ESI patients. No major mild or ESI device or procedure-related complications were reported.

Expert recommendations

1) **Deer 2018**, MIST recommendations for minimally invasive spinal treatment for lumbar spinal stenosis
    a. West Virginia Society for Interventional Pain Physicians
    b. Funded by a grant from Vertos Medical
    c. Based on the systematic review of the available literature for PILD (Table 9), the consensus committee has determined that there is sufficient support to warrant Level I evidence using the USPSTF criteria. The 2 comparative prospective studies that led to reimbursement approval by the CMS are both Level I (USPSTF criteria). All RCT evidence compares PILD to lumbar ESI and not to open decompression (Grade A, Level I, Consensus strong).

Other payer coverage

1) **CMS 2016:** covers only with evidence development
2) **Aetna 2021:** considers MILD to be experimental
3) **Cigna 2021:** considers MILD to be experimental

HERC staff summary

Minimally invasive lumbar decompression for lumbar spinal stenosis has only been studied in small cohort studies or in RCTs comparing MILD to epidural steroid injections. No trials were found comparing MILD to standard medical care, other minimally invasive surgical procedures, lumbar fusion, or other treatments currently paired with lumbar spinal stenosis. The RCTs identified had major limitations including lack of ability to adequately blind investigators and small sample sizes. The cohort studies were limited by lack of comparison groups and small sample sizes. No private payer surveyed are covering this procedure and CMS only covers as part of clinical trials.

There is insufficient evidence in the medical literature to demonstrate the safety and efficacy of percutaneous laminotomy/laminectomy approaches, including the MILD procedure. Additional well-designed trials comparing MILD with other decompressive procedures (e.g., standard open laminectomy, minimally invasive decompression) with long-term outcome data are needed to determine how this procedure compares to available alternative treatments for lumbar stenosis that are currently covered on the Prioritized List (e.g. not epidural steroid injections).

HERC staff recommendations:

1) Add minimally invasive lumbar decompression to line 662/GN173 as shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
0275T	Percutaneous laminotomy/laminectomy (interlaminar approach) for decompression of neural elements (with or without ligamentous resection, discectomy, facetectomy and/or foraminotomy), any method under indirect image guidance (eg, fluoroscopic, CT), single or multiple levels, unilateral or bilateral; lumbar	Insufficient evidence of effectiveness	October 2021
G0276	Blinded procedure for lumbar stenosis, PILD, or placebo control, performed in an approved coverage with evidence development (CED) clinical trial		

Long-term Results of Percutaneous Lumbar Decompression for LSS

Two-Year Outcomes

Bohdan W. Chopko, PhD, MD

Objective: The aim of this report was to evaluate the long-term effectiveness and safety of mild lumbar decompression for the treatment of neurogenic claudication associated with lumbar spinal stenosis. This technique uses a percutaneous dorsal approach to remove small portions of ligament and lamina, thereby restoring space and decompressing the spinal canal.

Materials and Methods: Two-year data are reported for 45 patients treated with mild decompression at 11 US sites. Outcome measures included the Visual Analog Scale (VAS), Oswestry Disability Index, and Zurich Claudication Questionnaire. Safety was monitored throughout the procedural and follow-up period for all patients. Interim data are included for these patients at 1 week, 6 months, and 1-year follow-up.

Results: Seventy-one percent of patients reported improvement in VAS at the end of the reporting period. At 2 years, patients demonstrated a statistically significant reduction of pain as measured by VAS, and improvement in physical function and mobility was significant as measured by Zurich Claudication Questionnaire and Oswestry Disability Index. Tukey honestly significant different test found significant improvement in all outcome measures from baseline to each follow-up interval. Further, major improvement occurred by 1-week follow-up and showed no difference between each subsequent follow-up, signifying considerable stability and durability of the initial result over time. No major device or intraprocedural adverse events were reported.

Discussion: In this report of 2-year follow-up on 45 patients treated with mild percutaneous lumbar decompression, patients experienced statistically significant pain relief and improved functionality.

Key Words: lumbar spinal stenosis, neurogenic claudication, decompression, ligamentum flavum, mild

(*Clin J Pain* 2013;29:939–943)

Lumbar spinal stenosis (LSS) is a common geriatric condition that is associated with significant pain and disability. A complex degenerative process, symptomatic LSS results from compression of neural elements. This pathomorphologic narrowing of the spinal canal can be attributed to multiple factors including disk herniation, facet hypertrophy, and hypertrophic ligamentum flavum.[1–4] Occurring in an estimated 46% of LSS cases, ligamentum flavum hypertrophy is the most common contributing factor for these patients.[5]

Patients with spinal canal narrowing identified on radiography may be asymptomatic, or these patients can present with various symptoms.[1] The classic presentation is neurogenic claudication, described as pain upon ambulation, spinal extension, or standing, and relieved with lumbar flexion. LSS patients may also experience radicular pain, which is described as sharp pain that radiates in a dermatomal pattern.[6,7] It is important to determine the pathophysiology of symptomatic LSS pain, as it directly affects the path of treatment.

Neurogenic claudication was first described by Verbiest[8] in the 1950s as structural narrowing of the vertebral canal that compresses the cauda equina. Narrowing of the central vertebral canal is believed to cause venous hypertension resulting in nerve root ischemia and painful neurogenic claudication symptoms.[7,9–12] Exertion tends to exacerbate neurogenic claudication symptoms because of increased requirements for blood supply and, therefore, exaggerated venous insufficiency. Separately, radicular pain may be related to severe foraminal or subarticular stenosis that compromises the lateral recess leading to inflammation of the exiting nerve root as well as direct deformation of the nerve roots. The presence of neurogenic claudication has been reported to occur in 91% to 100% of the symptomatic LSS population, and radicular pain in close to 90%.[13–17]

The distinct pathophysiologic causes of neurogenic claudication versus radicular pain must be considered when developing treatment plans for LSS patients. Inflammation is believed to play a major role in the cause of radicular pain, and anti-inflammatory medications or epidural steroid injections (ESIs) may be helpful for these patients.[18] However, neurogenic claudication is much less related to inflammation, and it has been reported that ESIs have no beneficial effect on neurogenic claudication associated with spinal stenosis.[19] Patients with neurogenic claudication refractory to conservative measures, such as physical therapy, have historically been treated with surgical decompression as the next treatment option.

Initial conservative therapy for LSS patients with both neurogenic claudication and radicular pain typically begins with physical therapy and proceeds to the use of anti-inflammatory medications followed by ESIs. Although this conservative treatment regimen may alleviate the inflammation associated with radicular pain, it does not address

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From the Department of Anatomy and Neurobiology, Northeast Ohio Medical University, Rootstown, OH.

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Randomized Trial

MILD® is an Effective Treatment for Lumbar Spinal Stenosis with Neurogenic Claudication: MiDAS ENCORE Randomized Controlled Trial

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Disclaimer: Drs. Benyamin and Staats are Study Principal Investigators for the MiDAS ENCORE Study
* Investigators in the MiDAS ENCORE Study are listed in the Appendix.
Conflict of interest: Each author certifies that he, or member of his immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript. Disclaimer and Conflict of interest on P. 239.

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Free full manuscript: www.painphysicianjournal.com

Background: Lumbar spinal stenosis (LSS) is a common degenerative condition of the spine, which is a major cause of pain and functional disability for the elderly. Neurogenic claudication symptoms are a hallmark of LSS, where patients develop low back or leg pain when walking or standing that is relieved by sitting or lumbar flexion. The treatment of LSS generally begins with conservative management such as physical therapy, home exercise programs, and oral analgesics. Once these therapies fail, patients commonly move forward with interventional pain treatment options such as epidural steroid injections (ESIs) or MILD® as the next step.

Objective: To assess improvement of function and reduction in pain for Medicare beneficiaries following treatment with MILD (treatment group) in LSS patients with neurogenic claudication and verified ligamentum flavum hypertrophy and to compare to a control group receiving ESIs.

Study Design: Prospective, multi-center, randomized controlled clinical trial.

Setting: Twenty-six US interventional pain management centers.

Methods: Patients in this trial were randomized one to one into 2 study arms. A total of 302 patients were enrolled, with 149 randomized to MILD and 153 to the active control. Outcomes are assessed using the Oswestry Disability Index (ODI), Numeric Pain Rating Scale (NPRS) and Zurich Claudication Questionnaire (ZCQ). Primary efficacy is the proportion of ODI responders, tested for statistical superiority of the MILD group versus the ESI group. ODI responders are defined as patients achieving the validated Minimal Important Change (MIC) of ≥ 10 point improvement in ODI from baseline to follow-up. Similarly, secondary efficacy is the proportion of NPRS and ZCQ responders using validated MIC thresholds. Primary safety is the incidence of device- or procedure-related adverse events in each group. This report presents safety and efficacy results at 1-year follow-up. Outcomes at 2 years will be collected and reported for patients in the MILD group only.

Results: At 1-year follow-up, ODI, NPRS, and all 3 ZCQ domains (Symptom Severity, Physical Function and Patient Satisfaction) demonstrated statistically significant superiority of MILD versus the active control. For primary efficacy, the 58.0% ODI responder rate in the MILD group was higher than the 27.1% responder rate in the epidural steroid group ($P < 0.001$). The primary safety endpoint was achieved, demonstrating that there is no difference in safety between MILD and ESIs ($P = 1.00$).

Limitations: There was a lack of patient blinding due to considerable differences in treatment protocols, and a potentially higher non-responder rate for both groups versus standard-of-care due to adjunctive pain therapy study restrictions. Study enrollment was not limited to patients that had never received ESI therapy.

Conclusions: One-year results of this randomized controlled clinical trial demonstrate that MILD is statistically superior to ESIs in the treatment of LSS patients with neurogenic claudication and verified central stenosis due to ligamentum flavum hypertrophy. Primary and secondary efficacy outcome measures achieved statistical superiority in the MILD group compared to the control group. With 95% of patients in this study presenting with 5 or more LSS co-factors, it is important to note that patients with spinal co-morbidities also experienced statistically significant improved function that was durable through 1 year.

Key words: MILD, minimally invasive lumbar decompression, interlaminar epidural steroid injections, ESI neurogenic claudication, ligamentum flavum, ENCORE, PILD, CED Study, LSS

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ORIGINAL ARTICLE

OPEN

Long-Term Safety and Efficacy of Minimally Invasive Lumbar Decompression Procedure for the Treatment of Lumbar Spinal Stenosis With Neurogenic Claudication

2-Year Results of MiDAS ENCORE

Peter S. Staats, MD, MBA, Timothy B. Chafin, MD,† Stanley Golovac, MD,‡ Christopher K. Kim, MD,§ Sean Li, MD,|| William B. Richardson, MD,** Ricardo Vallejo, MD, PhD,†† Sayed E. Wahezi, MD,‡‡ Edward P. Washabaugh, III, MD,§§ and Ramsin M. Benyamin, MD†† for the MiDAS ENCORE Investigators*

Background and Objectives: This study evaluated the long-term durability of the minimally invasive lumbar decompression (MILD) procedure in terms of functional improvement and pain reduction for patients with lumbar spinal stenosis and neurogenic claudication due to hypertrophic ligamentum flavum. This is a report of 2-year follow-up for MILD study patients.

Methods: This prospective, multicenter, randomized controlled clinical study compared outcomes for 143 patients treated with MILD versus 131 treated with epidural steroid injections. Follow-up occurred at 6 months and at 1 year for the randomized phase and at 2 years for MILD subjects only. Oswestry Disability Index, Numeric Pain Rating Scale, and Zurich Claudication Questionnaire were used to evaluate function and pain. Safety was evaluated by assessing incidence of device-/procedure-related adverse events.

Results: All outcome measures demonstrated clinically meaningful and statistically significant improvement from baseline through 6-month, 1-year, and 2-year follow-ups. At 2 years, Oswestry Disability Index improved by 22.7 points, Numeric Pain Rating Scale improved by 3.6 points, and Zurich Claudication Questionnaire symptom severity and physical function domains improved by 1.0 and 0.8 points, respectively. There were no serious device-/procedure-related adverse events, and 1.3% experienced a device-/procedure-related adverse event.

Conclusions: MILD showed excellent long-term durability, and there was no evidence of spinal instability through 2-year follow-up. Reoperation and spinal fracture rates are lower, and safety is higher for MILD versus other lumbar spine interventions, including interspinous spacers, surgical decompression, and spinal fusion. Given the minimally invasive nature of this procedure, its robust success rate, and durability of outcomes, MILD is an excellent choice for first-line therapy for select patients with central spinal stenosis suffering from neurogenic claudication symptoms with hypertrophic ligamentum flavum.

Clinical Trial Registration: This study was registered at ClinicalTrials.gov, identifier NCT02093520.

(*Reg Anesth Pain Med* 2018;43: 789–794)

Neurogenic claudication due to lumbar spinal stenosis (LSS) is associated with debilitating pain in the lower back and extremities and is the cause of significant functional limitation, especially in the elderly population.[1] Neurogenic claudication symptoms are precipitated by walking and relieved by sitting. It is believed that spinal extension (walking and standing) produces neurogenic claudication symptoms by reducing the cross-sectional area of the central canal, resulting in nerve root compression and painful nerve root ischemia. This compression is relieved with spinal flexion, which causes the central canal to expand, leading to pain relief and resolution of neurogenic claudication symptoms.[2,3] Unlike symptoms of radicular pain, the distribution of symptoms related to neurogenic claudication is not usually dermatomal. Radicular pain is related to inflammation of an affected nerve root and generally radiates from the back and buttock into the leg in a dermatomal pattern.[4,5]

Patients suffering from neurogenic claudication almost always present with degenerative soft tissue and bony pathology related to a combination of disc protrusion, thickened or ossified ligamentum flavum, facet joint hypertrophy, or osteophytes.[1–3] In 1 report by Hansson and colleagues,[3] ligamentum flavum hypertrophy (LFH) contributed to between 50% and 85% of central canal narrowing, leading the authors to conclude that the ligamentum flavum plays a dominant role in the load-induced narrowing of the lumbar spinal canal. Further, one of the common characteristics of neurogenic claudication is the high frequency of multiple-level stenosis.[2,6]

The MiDAS ENCORE study was approved by the Centers for Medicare & Medicaid Services (CMS) as a Coverage with Evidence Development study for the purpose of providing level I evidence to support the safety and effectiveness of the MILD procedure. This randomized controlled trial assessed outcomes of the MILD procedure compared with epidural steroid injections (ESIs) in subjects with LSS and neurogenic claudication symptoms,

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P.S.S. and R.M.B. are study principal investigators for MiDAS ENCORE. In this role, they have been responsible for study oversight. Responsibilities include protocol review, assistance with site selection, site investigator support, oversight of patient enrollment and protocol compliance, and adjudication of adverse events.

This trial was sponsored by Vertos Medical. The sponsorship includes study-related supplies and expenses, as well as funding for statistical analysis services by an independent provider.

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

The durability of minimally invasive lumbar decompression procedure in patients with symptomatic lumbar spinal stenosis: Long-term follow-up

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Abstract

Background: Minimally invasive lumbar decompression (*mild*®) has been shown to be safe and effective for the treatment of lumbar spinal stenosis patients with hypertrophic ligamentum flavum as a contributing factor. This study examines the long-term durability of the *mild* procedure through 5-year follow-up. Pain relief and opioid medications utilization during 12-month follow-up were also assessed.

Methods: All patients diagnosed with lumbar spinal stenosis secondary to ligamentum flavum hypertrophy who underwent *mild* from 2010 through 2015 at the Cleveland Clinic Department of Pain Management were included in this retrospective longitudinal observational cohort study. The primary outcome measure was the incidence of open lumbar decompression surgery at the same level(s) as the *mild* intervention during 5-year follow-up. Secondary outcome measures were the change in pain levels using the Numeric Rating Scale and opioid medications utilization using Morphine Milligram Equivalent dose per day from baseline to 3, 6, and 12 months post-*mild* procedure. Postprocedural complications (minor or major) were also collected.

Results: Seventy-five patients received *mild* during the protocol-defined time period and were included in the study. Only 9 out of 75 patients required lumbar surgical decompression during the 5-year follow-up period. Subjects experienced statistically significant pain relief and reduction of opioid medications utilization at 3, 6, and 12 months compared to baseline.

Conclusion: Based on our analysis, the *mild* procedure is durable over 5 years and may allow elderly patients with symptomatic lumbar spinal stenosis to avoid lumbar decompression surgery while providing significant symptomatic relief.

KEYWORDS
back pain, *mild*®, minimally invasive lumbar decompression, pain relief, spinal stenosis, surgical lumbar decompression

ORIGINAL ARTICLE

A Double-blind, Randomized, Prospective Study of Epidural Steroid Injection vs. The *mild*® Procedure in Patients with Symptomatic Lumbar Spinal Stenosis

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■ **Abstract**

Background: Epidural steroid injections (ESIs) are commonly used to treat low back pain, including symptomatic lumbar spinal stenosis (LSS). Reports on LSS treatment with ESIs have not differentiated between neurogenic claudication, which is believed to result from nerve root compression, and lumbar radicular pain, thought to be caused by inflammation. While there is overlap between these groups, the clinical relevance of ESI treatment cannot be generalized between these 2 distinct diseases with completely different pathophysiological causes.

Methods: This was a double-blind, randomized, prospective study of ESI vs. the *mild* procedure in patients with symptomatic LSS, conducted at a single pain management center. Patient reported outcome measures included Visual Analog Scale, Oswestry Disability Index, and Zurich Claudication Questionnaire (ZCQ) patient satisfaction.

Results: Thirty-eight patients were randomized into 2 treatment groups, 21 in *mild* and 17 in ESI. At 6- and 12-week follow-up, patients treated with *mild* reported significantly greater pain decrease over time ($P < 0.0001$), and significantly greater functional mobility improvement over time ($P < 0.0018$) than ESI patients. At week 6, *mild* ZCQ patient satisfaction score of 2.2 indicated a higher level of satisfaction than for ESI with a score of 2.8. In addition, 12-week ZCQ satisfaction score was 1.8, demonstrating sustained near-term satisfaction in the *mild* group. No major *mild* or ESI device or procedure-related complications were reported.

Conclusions: This study demonstrated that in LSS patients suffering with neurogenic claudication, *mild* provides statistically significantly better pain reduction and improved functional mobility vs. treatment with ESI. ■

Key Words: low back pain, spine, lumbar decompression, lumbar spinal stenosis, ligamentum flavum, *mild*®, epidural steroid injection

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DOI. 10.1111/j.1533-2500.2011.00518.x

INTRODUCTION

Degenerative lumbar spinal stenosis (LSS) is a common disease of the lumbar spine with symptom onset generally

ORIGINAL ARTICLE

The MIST Guidelines: The Lumbar Spinal Stenosis Consensus Group Guidelines for Minimally Invasive Spine Treatment

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Table 9. Systematic Review of PILD Literature

Study	Study Type	Details	U.S. Preventative Services Task Force Rating[2]
MiDAS (Benyamin et al., 2016; Staats & Benyamin, 2016)[8,64]	RCT	MILD vs. LESI with follow-up at 6 months, 1 and 2 years (in press) for the MILD arm Outcome measures: VAS, ODI, ZCQ, SF-12	Level I
Brown (2012)[63]	RCT	21 subjects randomized to MILD and 17 to LESI with VAS, ODI, and ZCQ and followed at 6 and 12 weeks. Improved satisfaction at 6 and 12 weeks for PILD vs. LESI; PILD also demonstrated improved pain and function scores vs. LESI in the 12-week period.	Level I
Deer et al. (2012)[79]	Observational, prospective	46 subjects with LSS followed prospectively at 12 weeks, 6 months, and 1 year following PILD Outcome measures: VAS, ODI, ZCQ	
Chopko & Caraway (2010)[73]	Observational, prospective	78 patients followed prospectively Outcome measures: VAS, ODI, ZCQ, SF-12	
Mekhail et al. (2012)[77]	Observational, retrospective	58 subjects with LSS followed retrospectively at 11 U.S. sites Outcome measures: VAS, ODI, ZCQ, SF-12 Results: Significant decrease in pain; physical function significantly improved by all measures	
Basu (2012)[78]	Observational, prospective	27 subjects with LSS enrolled in single site Outcome measures: ODI, ZCQ, VAS at baseline and 6 months	
Chopko (2011)[75]	Observational, prospective	14 subjects with LSS receiving MILD Outcome measures: VAS, ODI Results: Significantly improved VAS while ODI failed to improve	
Lingreen & Grider (2010)[74]	Observational, retrospective	42 subjects with LSS at 2 U.S. centers Outcome measures: VAS, patient self-reported improvement to stand and ambulate for >15 minutes pre- and post-procedure. 40% reduction in pain with 86% subjects suggesting they would recommend the PILD procedure.	
Wong (2012)[76]	Observational, retrospective	17 subjects with LSS receiving PILD Outcome measures: ODI, VAS followed 1 year Results: 70% reduction in VAS and significant improvement in ODI at 1 year	

LESI, lumbar epidural steroid injection; LSS, lumbar spinal stenosis; MiDAS, mild® Decompression Alternative to Open Surgery; MILD, minimally invasive lumbar decompression; ODI, Oswestry Disability Index; PILD, percutaneous image-guided lumbar decompression; RCT, randomized controlled trial; SF-12, Short Form 12 Health Survey; ZCQ, Zurich Claudication Questionnaire.

(Carlsbad, CA, U.S.A.). Prior to the S-IDS, the X-STOP® interspinous spacer (X-ISS) decompression system by Medtronic (Minneapolis, MN, U.S.A.) was the most commonly utilized ISS in the United States. The device was approved for use by the U.S. Food and Drug Administration (FDA) in 2005; however, Medtronic ultimately discontinued distribution in 2015 citing minimal long-term benefit and a relatively high rate of complications, which included dislodgement of the device.[82] Later that year, the S-IDS was approved by the FDA. The device was intended to rectify the deficiencies of the X-ISS (ie, device movement) and introduce a percutaneous implantation technique that could be utilized by interventional spine specialists.

The S-IDS is an H-shaped, 1-piece implant composed of titanium alloy as opposed to the X-ISS, which was a 2-piece implant composed of polyetheretherketone (PEEK) polymer. The X-ISS required an open implantation through an incision approximately 1-inch in length (per level), whereby the 2 components would be assembled at the level of the spine. In contrast, the S-IDS is delivered percutaneously, as a single piece, through a cannula, using a series of dilators to open tissues leading to the intralaminar opening. The S-IDS has superior and inferior cam lobes that rotate during deployment, so as to capture the superior and inferior spinous processes, respectively (Figure 9). The S-IDS is indicated to treat skeletally mature patients with intermittent neurogenic claudication secondary to a diagnosis of moderate degenerative LSS, with or without Grade 1 spondylolisthesis, confirmed by imaging, with evidence of thickened LF, narrowed lateral recess, and/or central canal or foraminal narrowing. The S-IDS may be implanted at 1 or 2 adjacent lumbar levels in patients in whom treatment is indicated at no more than 2 levels, from L1 to L5.[83,84]

Literature Review of Interspinous Spacers. The sentinel article establishing the efficacy of ISS for the treatment of intermittent neurogenic claudication secondary to moderate LSS was published by Zucherman et al. in *Spine* in 2005.[85] This was a multicenter, prospective, randomized trial comparing the X-ISS ($n = 100$) to nonoperative therapy ($n = 91$). At 2 years, the X-ISS

Decision Memo for Percutaneous Image-guided Lumbar Decompression for Lumbar Spinal Stenosis (CAG-00433R)

Links in PDF documents are not guaranteed to work. To follow a web link, please use the MCD Website.

Decision Summary

After considering public comments as required by section 1862(l) of the Social Security Act, CMS will finalize its proposal to continue CED and expand the January 2014 NCD. CMS will cover through a prospective longitudinal study PILD procedures using an FDA-approved/cleared device that successfully completed a CMS-approved RCT that met the criteria listed in Section 150.13 of the NCD manual.

In addition, the CMS-approved prospective longitudinal study must answer at least one of the following questions:

1. *Does PILD provide a clinically meaningful improvement of function (e.g., reduced acute and post-acute hospitalizations, nursing home care or inpatient rehabilitation services) and/or quality of life in Medicare beneficiaries with LSS compared to other treatments?*
2. *Does PILD provide a clinically meaningful reduction in pain (e.g., as measured by class, dose, duration of prescription pain medication use) in Medicare beneficiaries with LSS compared to other treatments?*
3. *Does PILD affect the overall clinical management of LSS and decision making, including use of other medical treatments or services (e.g., repeat PILD procedures, other interventions and surgical treatments), compared to other treatments?*

The prospective longitudinal study must also meet the following criteria:

1. The protocol must specify a statistical analysis and a minimum length of patient follow-up time that evaluates the effect of beneficiary characteristics on patient health outcomes as well as the duration of the benefit.
2. The eligibility requirements, both inclusion and exclusion criteria that were specified in the CMS-approved RCT protocol, must be maintained in the new prospective longitudinal study.
3. All study sites and study results must be listed in the ClinicalTrials.gov database.

All CMS-approved clinical research studies must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
b. The rationale for the study is well supported by available scientific and medical evidence.
c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
d. The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
e. The study is sponsored by an organization or individual capable of completing it successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.
g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare

requirements.

i. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
j. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Research & Quality (AHRQ) Registry of Patient Registries (RoPR).
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessibly manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
l. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
m. The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

All clinical research study protocols must be reviewed and approved by CMS. The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity (a. through m. listed above), as well as the investigator's contact information, to the address below.

Director, Coverage and Analysis Group
Re: PILD CED
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Baltimore, MD 21244-1850

Email address for protocol submissions: clinicalstudynotification@cms.hhs.gov
Email subject line: "CED [NCD topic (i.e. PILD)] [name of sponsor/primary investigator]"

The information will be reviewed, and approved studies will be identified on the CMS website - https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html.

See Appendix B for our proposed manual language.

Interlaminar Stabilization/Distraction Devices
2021 Re-review

Question: Should any change be made to the non-coverage of interlaminar stabilization/distraction devices?

Question source: Holly Jo Hodges, CCO medical director

Issue: Interspinous spacers are devices implanted between vertebral spinous processes for patients with back pain as an alternative to spinal fusion or decompression surgery. Interlaminar spacers are implanted between adjacent lamina and have 2 sets of wings that are placed around the inferior and superior spinous processes. These implants aim to restrict painful motion while otherwise enabling normal motion. The devices (spacers) distract the laminar space and/or spinous processes and restrict extension. This procedure theoretically enlarges the neural foramen and decompresses the cauda equina in patients with spinal stenosis and neurogenic claudication. These devices can be used as part of decompressive surgery or can be used alone as a minimally invasive surgery. Spinous process fixation is considered by some surgeons as a minimally invasive spine surgery technique that stabilizes the lumbar spine with less dissection and trauma to the vertebra than the current gold standard, pedicle screw (PS) fixation.

These devices were last reviewed as new CPT codes in November, 2016. That review included a systematic review and meta-analysis of interspinous spacers vs traditional decompressive surgery for lumbar spinal stenosis (Wu 2014) that found no significant difference in outcomes for pain and function, but a significantly higher rate of reoperation with the spacers. Also reviewed were two RCTS of interspinous spacers vs conservative therapy for lumbar spinal stenosis (Zucherman 2006 and Pullizzi 2014) with a total of 733 patients that found improvements in claudication symptoms and physical function with the spacers. Two case series (Kim 2013 and Barbagallo 2009) were reviewed for complications which found spinous process fractures in 11 out of 38 patients in one series and in 4 out of 69 patients in the other series. NICE reviewed this technology in 2010 and found that these procedures were efficacious in carefully selected patients with only short and medium term data available. All private insurers surveyed considered this technology to be experimental for all indications. The North American Spine Society (2011) found that there was insufficient evidence on this technology to make a recommendation.

The HERC staff summary in the 2016 review was “There is no evidence of benefit of these devices compared to traditional decompression surgery, but there is a higher complication and re-operation rate. Two trials have shown benefit of these devices compared to medical management; however, NASS and private insurers have not found sufficient evidence for use as a stand-alone procedure.”

Dr. Hodges requested a re-review of this technology due to appeals for denials in her CCO. As this technology was last reviewed more than 5 years ago, HERC staff conducted an updated evidence review.

Current Prioritized List status

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
22867-22870 C1821	Insertion of interlaminar/ interspinous process stabilization/ distraction device, without fusion, including image guidance when performed, with open decompression, lumbar Interspinous process distraction device (implantable)	Insufficient evidence of effectiveness	November, 2016

Evidence

1) **Lopez 2017**, Lumbar Spinous Process Fixation and Fusion: A Systematic Review and Critical Analysis of an Emerging Spinal Technology
    a. N=15 articles
        i. 4 comparative studies, 2 case series and 9 in vitro biomechanical studies
    b. Two studies compared interspinous fixation devices (IFD) to pedical screw (PS) surgery (Kim et al and Wang et al) which found comparable fixation rates and comparable reductions in VAS scores between the techniques. Kim reports decreases in adjacent segment disease with IFD. Both studies were judged to be at high risk for bias due to poor methodology in randomization and blinding.
    c. Conclusion: Insufficient literature on IFDs exists to recommend their use over PS fixation. Most notably, the literature lacks high class of evidence trials, a comparative study with follow- up of >1 year, and a comparison of complication rate or severity with that of PS fixation. Furthermore, the present studies have significant methodological flaws that impugn the conclusions drawn from their results.
2) **Zhong 2021**, retrospective cohort analysis of outcomes after single level interspinous implants vs single level laminectomy
    a. N=83 patients (37 laminectomy vs 46 interlaminar stabilization device (ISD)
    b. ISD patients had longer operative times (141.91 ± 47.88 vs. 106.81 ± 41.30 minutes, P=0.001), and longer length of stay (2.0 ± 1.5 vs. 1.1 ± 1.0 days, P=0.001).
    a. Total perioperative complications (21.7% vs. 5.4%, P=0.035) and instrumentation-related complication was higher in ISD (10.9% vs. 0% laminectomy group, P=0.039).
    b. Conclusion. Single-level CID devices had higher perioperative 90-day complications, longer operative time, length of stay, higher EBL compared to laminectomies alone. Similar overall revision and neurologic complication rates were noted compared to laminectomy at last follow-up.

NICE: no update to 2010 review found

Expert guidelines

1) **North American Spine Society 2018**: AANS and CNS Joint Section on Disorders of the Spine and Peripheral Nerves (DSPN) Comments on NASS Coverage Policy Recommendations on Lumbar Interspinous Device without Fusion and Decompression
    a. Stabilization with an ISP without fusion in conjunction with laminectomy may be indicated as an alternative to lumbar fusion for degenerative lumbar stenosis with or without low grade spondylolisthesis (less than or equal to 3mm of anterolisthesis on a lateral radiograph) with qualifying criteria when appropriate:
        i. Significant mechanical back pain is present (in addition to those symptoms associated with neural compression) that is felt unlikely to improve with decompression alone. Documentation should indicate that this type of back pain is present at rest and/or with movement while standing and does not have characteristics consistent with neurogenic claudication.
        ii. A lumbar fusion is indicated post-decompression as recommended in the NASS Coverage Recommendations for Lumbar Fusion.
        iii. A lumbar laminectomy is indicated as recommended in the NASS Coverage Recommendations for Lumbar Laminectomy

Other payer policies

1) MODA 2021, Wellmark BCBS 2021, Aetna 2021, and Cigna 2021 all consider interspinous/ interlaminar process spacer devices to be experimental

HERC staff summary

Updated evidence review and survey of payer policies found no evidence to change the prior staff conclusion that interspinous/interlaminar process spacer devices are equivalent to traditional fusion surgery in terms of improving pain and function but have a higher rate of complications and need for re-operation. All private payers continue to consider this technology to be experimental. In the 5 years since last review, the North American Spine Society has changed their recommendation to indicate that the procedure "may be indicated as an alternative to lumbar fusion."

HERC staff recommendations:

1) Do not add coverage for interspinous/interlaminar process spacer devices
2) Update GN173 entry regarding these devices as shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
22867-22870 C1821	Insertion of interlaminar/ interspinous process stabilization/ distraction device, without fusion, including image guidance when performed, with open decompression, lumbar Interspinous process distraction device (implantable)	Insufficient evidence of effectiveness	~~November, 2016~~ October 2021

Spine

SURGERY

SPINE Volume 46, Number 13, pp 893–900

Patient Outcomes After Single-level Coflex Interspinous Implants *Versus* Single-level Laminectomy

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Study Design. Retrospective cohort analysis.

Objective. The aim of this study was to compare postoperative outcomes of Coflex interspinous device *versus* laminectomy.

Summary of Background Data. Coflex Interlaminar Stabilization device (CID) is indicated for one- or two-level lumbar stenosis with grade 1 stable spondylolisthesis in adult patients, as an alternative to laminectomy, or laminectomy and fusion. CID provides stability against progressive spondylolisthesis, retains motion, and prevents further disc space collapse.

Methods. Patients ≥18 years' old with lumbar stenosis and grade 1 stable spondylolisthesis who underwent either primary single-level decompression and implantation of CID, or single-level laminectomy alone were included with a minimum 90-day follow-up at a single academic institution. Clinical characteristics, perioperative outcomes, and postoperative complications were reviewed until the latest follow-up. χ^2 and independent samples *t* tests were used for analysis.

Results. Eighty-three patients (2007–2019) were included: 37 cases of single-level laminectomy (48.6% female) were compared to 46 single-level CID (50% female). CID cohort was older (CID 69.0 ± 9.4 *vs.* laminectomy 64.2 ± 11.0, $P = 0.042$) and had higher American Society of Anesthesiologists (ASA) grade (CID 2.59 ± 0.73 *vs.* laminectomy 2.17 ± 0.48, $P = 0.020$). CID patients had higher estimated blood loss (EBL) (97.50 ± 77.76 *vs.* 52.84 ± 50.63 mL, $P = 0.004$), longer operative time (141.91 ± 47.88 *vs.* 106.81 ± 41.30 minutes, $P = 0.001$), and longer length of stay (2.0 ± 1.5 *vs.* 1.1 ± 1.0 days, $P = 0.001$). Total perioperative complications (21.7% *vs.* 5.4%, $P = 0.035$) and instrumentation-related complication was higher in CID (10.9% *vs.* 0% laminectomy group, $P = 0.039$). There were no other significant differences between the groups in demographics or outcomes.

Conclusion. Single-level CID devices had higher perioperative 90-day complications, longer operative time, length of stay, higher EBL compared to laminectomies alone. Similar overall revision and neurologic complication rates were noted compared to laminectomy at last follow-up.

Key words: Coflex, interlaminar device, lumbar stenosis, outcomes, laminectomy, spondylolisthesis.

Level of Evidence: 3

Spine 2021;46:893–900

Coflex Interlaminar Stabilization device (CID [RTI Surgical, Minnetonka, MN, formerly Paradigm Spine, New York, NY]) is a flexible titanium implant placed between adjacent spinous processes after direct central decompression.[1] Coflex aims to prevent disc height collapse after decompression to maintain foraminal height, stabilize the adjacent vertebral segments against translational instability, and preserve segmental motion. It is a new generation of interspinous devices, with previous-generation rigid devices having high complication and revision rates.[2] The Food and Drug Administration (FDA) has approved Coflex for one- to two-level lumbar stenosis from L1-L5 in skeletally mature patients with at least 6 months of conservative treatment whose spondylolisthesis is graded less than II.[3] Alternatives to CID are direct decompression with or without fusion. Two randomized control trials described laminectomy and fusion had similar patient-reported outcomes for treating lumbar stenosis, whereas

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Acknowledgment date: June 23, 2020. First revision date: September 29, 2020. Acceptance date: November 13, 2020.

The device(s)/drug(s) is/are FDA-approved or approved by corresponding national agency for this indication.

Paradigm Spine, New York, NY, USA funds were received in support of this work.

Relevant financial activities outside the submitted work: consultancy, grants, royalties, stocks.

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DOI: 10.1097/BRS.0000000000003924

Lumbar Spinous Process Fixation and Fusion

A Systematic Review and Critical Analysis of an Emerging Spinal Technology

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Study Design: A systematic review.

Objective: The available literature on interspinous rigid fixation/fusion devices (IFD) was systematically reviewed to explore the devices' efficacy and complication profile.

Summary of Background Data: The clinical application of new spinal technologies may proceed without well-established evidence, as is the case with IFDs. IFDs are plate-like devices that are attached to the lateral aspects of 2 adjacent spinous processes to promote rigidity at that segment. Despite almost a decade since the devices' introduction, the literature regarding efficacy and safety is sparse. Complications have been reported but no definitive study is known to the authors.

Methods: A systematic review of the past 10 years of English literature was conducted according to PRISMA guidelines. The timeframe was chosen based on publication of the first study containing a modern IFD, the SPIRE, in 2006. All PubMed publications containing MeSH headings or with title or abstract containing any combination of the words "interspinous," "spinous process," "fusion," "fixation," "plate," or "plating" were included. Exclusion criteria consisted of dynamic stabilization devices (X-Stop, DIAM, etc.), cervical spine, pediatrics, and animal models. The articles were blinded to author and journal, assigned a level of evidence by Oxford Centre of Evidence-Based Medicine (OCEBM) criteria, and summarized in an evidentiary table.

Results: A total of 293 articles were found in the initial search, of which 15 remained after examination for exclusion criteria. No class I or class II evidence regarding IFDs was found. IFDs have been shown by methodologically flawed and highly biased class III evidence to reduce instability at 1 year, without statistical comparison of complication rates against other treatment modalities.

Conclusions: Although IFDs are heavily marketed and commonly applied in modern practice, data on safety and efficacy are inadequate. The paucity of evidence warrants reexamination of these devices' value and indications by the spine surgery community.

Key Words: interspinous, spine, fusion, plate, pedicle screw, fixation, instability

(*Clin Spine Surg* 2017;30:E1279–E1288)

The principle tenets of minimally invasive spine surgery are to reduce approach-related morbidity without sacrificing a thorough and effective treatment of the patient's pathology.[1–3] Spinous process fixation is advertised as a minimally invasive spine surgery technique that stabilizes the lumbar spine with less dissection and trauma to the vertebra than the current gold standard, pedicle screw (PS) fixation.[4–7] Interspinous fixation devices (IFD) aim to provide rigidity comparable with PS fixation by bilaterally securing plates to the lateral aspects of 2 adjacent spinous processes, effectively clamping the motion segment together. IFD implantation has been applied to posterolateral and interbody fusion procedures. Certain IFD products are designed to achieve additional stability through interspinous bony fusion. Proponents have noted that IFD placement is a more expedient procedure that requires a single, less obtrusive midline incision.[8,9]

The primary evidence for IFDs rests with ex vivo biomechanical studies, which have demonstrated that stand-alone IFDs provide rigidity that is comparable with PSs in flexion-extension but not in axial rotation or lateral bending.[10,11] Moreover, these studies only evaluated the devices in a short-term setting and do not account for long-term in vivo stresses. IFDs also reduce disk load and preserve adjacent facet joint anatomy, potentially reducing the risk of developing adjacent segment disease (ASD).[9,12,13] Multiple IFDs have been designed and are indexed in the literature using various terminology, including spinous process clamps, plates, and anchors. These are not to be confused with interspinous spacers or "bumpers" (X-Stop, Wallis, or DIAM devices), which reduce extension through dynamic stabilization with the aim of decreasing symptoms of lumbar spinal stenosis.

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AANS and CNS Joint Section on Disorders of the Spine and Peripheral Nerves (DSPN)
Comments on NASS Coverage Policy Recommendations on Lumbar Interspinous Device without Fusion and Decompression

The American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) Joint Section on Disorders of the Spine and Peripheral Nerves (DSPN) appreciates the opportunity to provide comments on the North American Spine Society (NASS) coverage policy recommendations on Lumbar Interspinous Device without Fusion and Decompression. Below in italic print are recommendations from the NASS document followed by our comments in bold.

Interspinous devices (ISP) have been used previously for the purpose of indirect decompression without laminectomy through spinous process distraction. Importantly these coverage recommendations are for interspinous devices without fusion in conjunction with a direct decompression in the form of a lumbar laminectomy for patients with neurogenic claudication or radiculopathy secondary to spinal stenosis. Coflex for example is specifically approved for this indication. Interspinous fusion is importantly excluded.

AANS/CNS Joint Section on DSPN Comment:

The title of the policy may cause confusion. We suggest the title be changed to: "Lumbar Interspinous Device without Fusion *in conjunction with* Decompression" or alternatively "Decompression without Fusion when using Lumbar Interspinous Process Devices". Either one of these alternate titles clearly indicates that the surgeon is performing a decompression.

Stabilization with an ISP without fusion in conjunction with laminectomy may be indicated as an alternative to lumbar fusion for degenerative lumbar stenosis with or without low grade spondylolisthesis (less than or equal to 3mm of anterolisthesis on a lateral radiograph) with qualifying criteria when appropriate:

1. *Significant mechanical back pain is present (in addition to those symptoms associated with neural compression) that is felt unlikely to improve with decompression alone. Documentation should indicate that this type of back pain is present at rest and/or with movement while standing and does not have characteristics consistent with neurogenic claudication.*

2. *A lumbar fusion is indicated post-decompression as recommended in the NASS Coverage Recommendations for Lumbar Fusion.*

3. *A lumbar laminectomy is indicated as recommended in the NASS Coverage Recommendations for Lumbar Laminectomy.*

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AANS/CNS Joint Section on DSPN Comment:

The indications listed in the NASS coverage position are supported by the experience in the literature.

Interspinous (ISP) devices are NOT indicated in cases that do not fall within the above parameters. In particular, they are not indicated in the following scenarios and conditions:

1. *Degenerative spondylolisthesis of grade II or higher*
2. *Degenerative scoliosis or other signs of coronal instability*
3. *Dynamic instability as detected on flexion-extension views demonstrating at least 3 mm of change in translation*
4. *A fusion is otherwise not indicated as per the NASS Coverage Recommendations for Lumbar Fusion*
5. *A laminectomy is otherwise not indicated as per the NASS Coverage Recommendations for Lumbar Laminectomy*

AANS/CNS Joint Section on DSPN Comment:

The exclusion criteria are for the most part reasonable. ISP devices are not meant to be applied for the purpose of stabilizing an unstable spinal segment and are not meant to be a replacement for spinal fusion in the presence of spinal instability. Item number 4 above would seem to imply that the use of an ISP device is only indicated if the patient also meets the NASS Coverage Recommendations for Lumbar Fusion. Below in italics we have listed these recommendation and included our notes on each of these in parenthesis.

1. *Dynamic instability is present as documented by flexion-extension radiographs or comparison of a supine and upright image, defined as a difference in translational alignment between vertebrae greater than 2 mm between views.*

> **AANS/CNS Joint Section on DSPN note: This is essentially an exclusion criteria for the use of an ISP device**

2. *Spondylolisthesis (defined as at least 1-2 mm of anterolisthesis of the upper vertebra in relation to the lower vertebra) is present, either isthmic (i.e. secondary to a posterior arch stress fracture) or degenerative type.*

> ***AANS/CNS Joint Section on DSPN: note spondylolisthesis greater than 3 mm is a contraindication to the use of an ISP device.***

3. Cases in which decompression will likely result in iatrogenic instability, such as foraminal stenosis, during which greater than 50% of facet joint will be removed to adequately decompress the exiting nerve root.

> **AANS/CNS Joint Section on DSPN note: iatrogenic instability would also be a contraindication to the use of an ISP device**

4. *Adjacent level disease, stenosis that has developed at a level above or below a previous fusion.*

> **AANS/CNS Joint Section on DSPN note: that it is questionable that an ISP device could be used for this indication and it was not studied in the trials**

5. *Recurrent stenosis, e.g. that which developed at a level that has been previously operated*

AANS/CNS Joint Section on DSPN note: that this is also not an indication for the use of an ISP device

We are concerned that cross-referencing to the NASS lumbar fusion coverage recommendations may lead to potential confusion for the use of the ISP device. We suggest the fourth contraindication above--A fusion is otherwise not indicated as per the NASS Coverage Recommendations for Lumbar Fusion—be removed or modified.

Thank you for considering our comments. We hope our feedback on the NASS Coverage Policy Recommendations on the Decompression without Fusion when using Lumbar Interspinous Process Devices coverage position are helpful. Please let us know if we can provide any additional information. If at all possible, we would appreciate a greater period of time to provide a response for future coverage positions.

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Partial Neurectomy for Wrist Arthritis

Question: Should partial neurectomy be added as a treatment for wrist arthritis?

Question source: HSD Medical Management Committee

Issue: The posterior interosseous nerve neurectomy has been used as both an isolated and adjunct procedure treating patients with chronic dorsal wrist pain that is unresponsive to nonoperative treatments. HSD's MMC committee was recently asked to review a request for this procedure, and asked HERC to look at the evidence supporting its effectiveness.

Total wrist denervation is not generally done in the US. Partial neurectomy or the posterior or anterior interosseus nerves (PIN or AIN respectively) are typically the procedures used in the US. The posterior interosseus nerve is a deep motor branch of the radial nerve, the nerve fibers of which originate from the cervical segments C7 and C8. The anterior interosseous nerve is a motor branch from the median nerve which originates from C8 and T1.

Partial neurectomy is typically done in patients who otherwise would undergo total wrist arthroplasty but want to maintain a better range of motion.

Current Prioritized List status

CPT Code	**Code descriptions**	**Placement**
25825	Arthrodesis, wrist, with autograft	131,132,200,207,355,356,359,401,527,558
64772	Transection or avulsion of other spinal nerve, extradural	207 DEEP OPEN WOUND, WITH OR WITHOUT TENDON OR NERVE INVOLVEMENT
ICD-10-CM Code		
M19.03	Primary osteoarthritis, wrist	356 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE Treatment: ARTHROPLASTY/ RECONSTRUCTION 463 OSTEOARTHRITIS AND ALLIED DISORDERS Treatment: MEDICAL THERAPY, INJECTIONS
M19.13	Post-traumatic osteoarthritis, wrist	356, 463
M10.23	Secondary osteoarthritis, wrist	356,463

Evidence

1) **Chin 2019**: systematic review of selective denervation of the wrist for chronic pain
    a. N=12 studies (AIN, PIN or combination)
        i. Indications: chronic wrist pain, wrist arthritis, chronic fracture or non-union
    b. 6 studies (240 wrists) found pain improvement (VAS score) of 36-92%; rated low quality of evidence
    c. 5 studies (186 wrists) found grip strength improvement of 7-64%; rated low quality of evidence
    d. Postoperative complication rates, including re-operations (including permanent interventions, e.g. proximal row carpectomy) and persistent or worse pain, varied from 6% to 29%
    e. Conclusion: Treatment outcomes of both partial and complete denervations were favorable; however, variations in outcomes suggest the need for improving evidence regarding surgical technique and nerve identification.
2) **VandenBerge 2017**, systematic review of posterior interosseus nerve neurectomy
    a. N=6 studies (135 patients)
    b. At an average final follow-up of 51 months (range of study means, 16.3-138.1), 88.9% of patients were able to return to work at their full capacity
    c. After initial improvement, a recurrence of pain occurred in 25.5% of patients at an average of 12.3 months.
    d. Overall, only 1 complication (excluding recurrence of pain) was reported among 113 cases (0.9%), including 1 case of reflex sympathetic dystrophy
    e. **Conclusions:** Isolated PINN have shown excellent clinical outcomes, with few patients experiencing recurrent pain at long-term follow-up. PINN can provide relief in patient's chronic wrist pain.
3) **Milone 2018**, review of anterior and posterior interosseus nerurectomy
    a. N=7 studies (191 wrists), AIN or PIN or combination
    b. Results: 44-80% pain improvement
    c. Conclusions: At this time, partial denervation procedures should be limited to use for treatment of chronic wrist conditions for which the only alternative is an arthrodesis. Future studies are needed to assess optimal indications as well as duration of relief and possible acceleration of underlying pathology

Other payer policies:

1) **Aetna 2021**: considers wrist arthrodesis for wrist arthritis to be experimental. No policy found on wrist partial neurectomy

No other policies found on wrist arthrodesis or on wrist partial neurectomy

Expert input

Dr. Robert Orfaly, OHSU orthopedics

I do not perform PIN neurectomies as I believe that partial or complete wrist fusion produces predictable results in my hands. However, it is a widely-accepted treatment alternative to fusion since wrist arthroplasty is typically only considered in low demand patients with bilateral disease. As you state, the literature is certainly not definitive and is further problematic given the wide variety of underlying diagnoses leading to the arthritis being treated. Therefore, this would be a condition in which treatment alternatives are mostly established by expert consensus and I would say that partial neurectomy, partial and complete wrist fusion all would be supported.

Partial Neurectomy for Wrist Arthritis

HERC staff summary:
Partial neurectomy appears to reduce pain in patients with chronic wrist pain due to arthritis, injuries, or other causes. Experts recommend the use of these procedures only when the alternative is an arthrodesis.

HERC staff recommendation:

1) Add CPT 64772 (Transection or avulsion of other spinal nerve, extradural) to line 356 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE Treatment: ARTHROPLASTY/ RECONSTRUCTION
2) Add a new guideline to line 356 as shown below

GUIDELINE NOTE XXX PARTIAL WRIST NEURECTOMY
Line 356
CPT 64772 is only included on this line for partial wrist neurectomy and is only covered when the alternative is wrist arthrodesis.

Review Article

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Selective denervation of the wrist for chronic pain: a systematic literature review

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Abstract

Selective denervation of sensory nerve branches to the wrist is a palliative surgical treatment option for patients with chronic wrist pain when preserving the range of motion and function is preferred. Treatment varies from partial isolated denervation of the posterior interosseous nerve to extensive 'complete' denervations. This study aimed to provide an overview of the literature regarding treatment outcomes in the domains of pain, grip strength, patient satisfaction and return to work. MEDLINE (PubMed), EMBASE and Cochrane databases were systematically searched and identified 993 studies, of which 12 were eligible for analysis. Denervation resulted in high 'return to work' rates (up to 94%), patient satisfaction (up to 92%), increased grip strength (7%–64%) and improved average pain scores (36%–92%). Treatment outcomes of both partial and complete denervations were favourable; however, variations in outcomes suggest the need for improving evidence regarding surgical technique and nerve identification.

Keywords

Wrist denervation, chronic pain, anterior interosseous nerve, posterior interosseous nerve, neurectomy

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Introduction

Chronic pain in the hand and wrist is a common problem. In the UK, the prevalence of chronic (>3 months) pain was present in 13% of the surveyed population who had pain in multiple locations in the hand or wrist (Carnes et al., 2007). Patients eligible for denervation should have chronic wrist pain (>3 months) and be skeletally mature (Hofmeister et al., 2006). This procedure is a palliative option when preservation of the range of motion and function are preferred and conservative treatment has been inadequate (Hofmeister et al., 2006; Le Nen et al., 2011).

Denervation techniques of the wrist have been modified over the years from Wilhelm's 'complete' denervation in 1959 (Wilhelm, 2001) to less invasive 'partial' denervation using only a single incision (Berger, 1998; Grechenig et al., 2017). Partial denervation focuses on specific articular nerves, especially the anterior interosseous nerve (AIN) and posterior interosseous nerve (PIN). To determine the potential effect of denervation, the patient's response to a preoperative anaesthetic nerve block has been evaluated (Hofmeister et al., 2006; Ishida et al., 1993; Riches et al., 2016; Storey et al., 2011). However, other authors refrain from using diagnostic blocks because the analgesic response after the local block poorly correlated with the postoperative change in pain scores (Patil and Arenas-Prat, 2016; Weinstein and Berger, 2002). Surgical scarring, incomplete surgical denervation and/or re-innervation of the joint may lead to reduced pain reduction. Furthermore, the local analgesic might spread to smaller terminal nerve branches to the wrist joint that are not divided during surgery. The procedure is contraindicated in

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chronic conditions that are still treatable with conservative methods and in a dysfunctional joint due to a structural deformity (Hofmeister et al., 2006; Patil and Arenas-Prat, 2016).

We systematically reviewed the literature describing therapeutic effects of nerve denervation in the domains of wrist pain, grip strength, patient satisfaction and return to work (RTW).

Methods

Literature search

A systematic search of the available literature in MEDLINE using PubMed, EMBASE and Cochrane CENTRAL databases was performed in March of 2019. In PubMed, the title and abstract (tiab) and medical subject headings (MeSH Terms) were added to the keywords of the search to expand the scope of the search. For EMBASE, the title (ti) and abstracts (ab) and further keywords (kw) were also added to the primary search terms that were used for the queries. The primary search terms included 'wrist', 'denervation', 'neurectomy', 'neurotomy', 'nerve tissue', 'anterior interosseous nerve' and 'posterior interosseous nerve'. A search for additional trials was done in Cochrane CENTRAL. The complete search strategy is provided in the supplementary data (Table S1; Appendix S1). References in selected studies were screened for eligibility.

Inclusion and exclusion criteria

All clinical studies with their own patient cohort reporting outcomes on both complete and/or partial wrist denervation techniques on chronic wrist pain, regardless of the origin of the pain, were included. There was no limit for publication date. Non-English studies and studies on patients who underwent concomitant surgical procedures were excluded. Studies containing both patients with and without concomitant procedures were only included if the treatment and outcomes of the 'denervation only' group was reported separately.

Selection procedure

All studies from the search were screened on title and abstract for eligibility for analysis by two independent assessors (KC and AE) using an online referencing tool (Ouzzani et al., 2016). After selection based on title and abstract, full texts were screened for relevance of outcomes. In case of disagreement, both assessors discussed the eligibility of the study with the senior author (SS) acting as a referee until consensus was reached on final inclusion or exclusion.

Quality of selected studies

Guidelines from the Oxford Centre for Evidence-Based Medicine (CEBM) were followed to assess the quality of the included studies. Furthermore, the online GRADEpro Guideline Development Tool (McMaster University/Evidence Prime Inc., Hamilton, Ontario, Canada) was used to give an overall indication of the risk of bias and quality of the included studies according to guidelines set by the Cochrane Handbook for each outcome measure discussed.

Outcomes

Full text manuscripts were screened to obtain the detailed patient characteristics including age, follow-up time and denervation technique. The primary outcome was postoperative pain using the visual analogue scale (VAS) on a 0–10 (or 0–100) scale or pre- and postoperative grip strength (in kilograms). Secondary outcomes included, 'return to work' (RTW) rate, patient satisfaction and patient recommendation rates.

Results

Study selection

The literature search yielded a total of 993 studies (Figure 1). After removing duplicates, screening titles and abstracts, 969 studies were excluded from further analysis. After screening full texts of 24 studies, another 12 studies were excluded based on incomplete presentation of outcomes, such as the absence of both pre- and postoperative VAS scores or grip strength outcomes. Results from 12 studies were included for analysis (Table 1).

Indications for selective denervation

The 12 included studies reported a range of conditions for which patients were treated with selective denervations. These are summarized in Table 1.

Surgical techniques for selective denervation

The studies included can be subdivided according to surgical technique; (modified) complete denervation techniques and less invasive partial denervations (Table 1) (Berger, 1998; Wilhelm, 1965, 2001). The complete denervation, according to Wilhelm, targets the PIN, articular branch of the first interosseous space, articular branches of the lateral antebrachial cutaneous nerve, articular branch of the superficial radial nerve, articular fibres of the palmar branch of

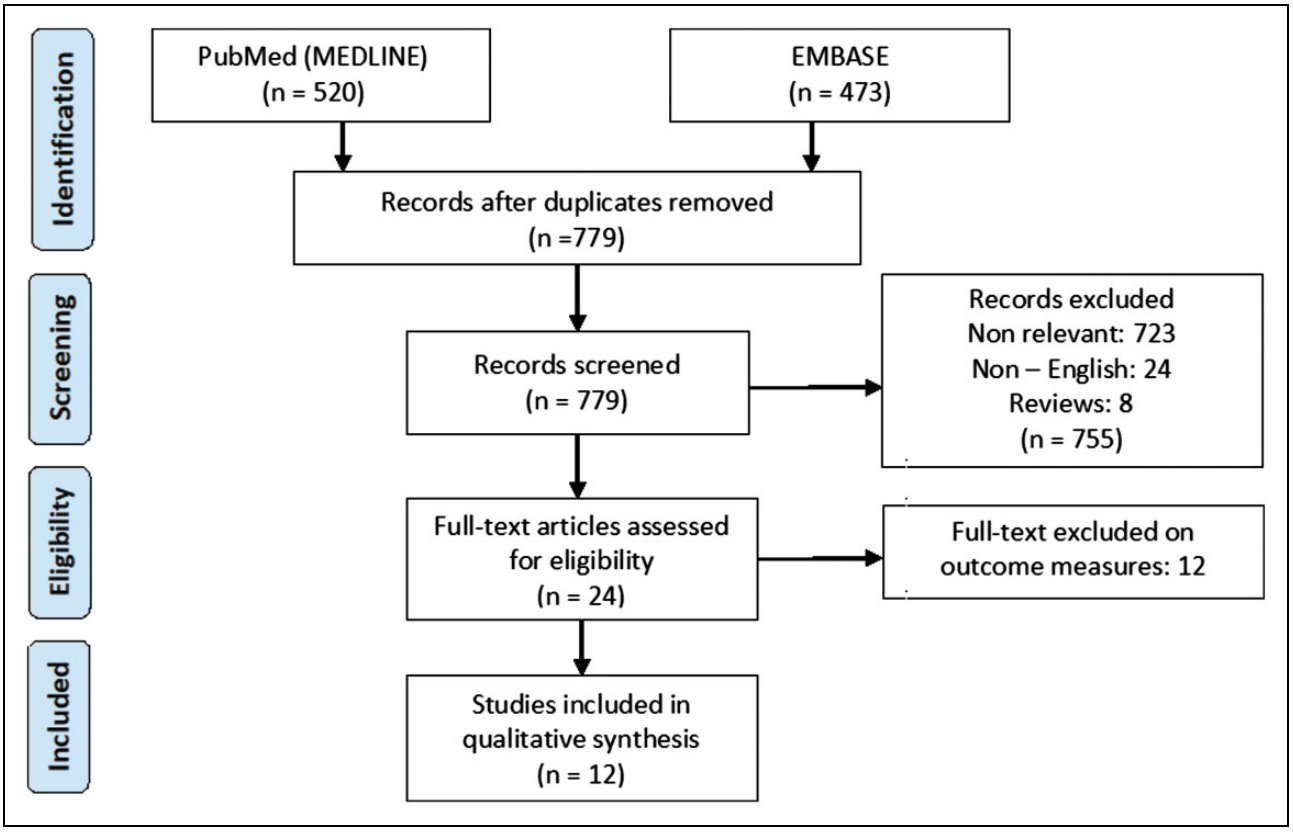

Figure 1. PRISMA flowchart of the screening process in PubMed (MEDLINE) and EMBASE.

the median nerve, articular fibres of the AIN, perforating fibres of the deep branch of the ulnar nerve, articular fibres of the dorsal branch of the ulnar nerve and the articular branch of the posterior antebrachial cutaneous nerve. Variations of Wilhelm's technique are targeting a number of the aforementioned nerves. The partial denervation techniques can be subdivided in resection of only the PIN (PIN only), the AIN and PIN (AIN & PIN), or the aforementioned combined with resection of, for example, cutaneous branches of the radial and/or median nerve (partial) (Delclaux et al., 2017; Patil and Arenas-Prat, 2016; Storey et al., 2011).

Pre- and postoperative pain scores

Five studies with a total of 240 patients described pre- and postoperative pain using the VAS (Table 2). Using the complete denervation technique, Fuchsberger et al. (2017) reported a median preoperative VAS of 84 with an improvement to 32, 6 weeks postoperatively. After 12 years follow-up the median VAS remained low (40) in 124 of the 135 patients. Riches et al. (2016) only resected the PIN. They scored pain according to the Modified Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands (MSACRAH) (Sautner et al., 2004), where Riches et al. (2016) observed a decrease in pain. Their MSACRAH pain score was based on a scale of 200 points. The remaining three studies used a variant of the partial denervation not limited to only the AIN and PIN. According to the GRADEpro tool, when pooled, all studies yielded a 'Low' level of quality for the outcome postoperative pain based on the overall lack of blinding, randomization and low number of patients.

Grip strength

The search resulted in five studies in which grip strength was described for 186 patients (Table 3). Four studies measured grip strength by using the JAMAR Hand Dynamometer (JAMAR Hand Dynamometer Model 1, Clifton, NJ, USA, or Baseline Fabrication Enterprises Inc., Irvington, NY, USA) (Braga-Silva et al., 2011; Delclaux et al., 2017; Hofmeister et al., 2006; Storey et al., 2011; Weinstein and Berger, 2002). The greatest relative improvement was seen in the cohort reported by Braga-Silva et al. (2011), which underwent complete denervation with an increase in grip strength of 64%. According to the GRADEpro tool, the studies yielded a 'Low' level of quality for the outcome grip strength based on the

Table 1. Overview of selected studies and their levels of evidence according to the CEBM guideline.

Studies	Wrists	Denervation techniques	Indications for denervation	Level of evidence (CEBM)
Sgromolo et al., 2018	10/3	AIN & PIN/ PIN only	Chronic idiopathic wrist pain	IV
Delclaux et al., 2017	33	Partial	SLAC, SNAC, (distal) radial fracture sequelae with advanced RC OA, post-traumatic ulnar carpal impingement	IV
Fuchsberger et al., 2017	135	Complete	Kienböck's, scaphoid pseudarthrosis, primary arthritis, secondary arthritis (radius) fracture	IV
Patil and Arenas-Prat, 2016	21	Partial	SLAC, SNAC, Kienböck's, DRUJ OA, post-traumatic OA of the RC joint, ulnocarpal abutment	IV
Riches et al., 2016	12	PIN only	Rheumatoid arthritis	II
Storey et al., 2011	37	Partial	SLAC, SNAC, Kienböck's, (distal) radial/ulna fracture sequelae, wrist OA, STTJ OA, rheumatoid arthritis, SR arthritis, ulnocarpal abutment, scaphoid nonunion, TFCC injury, carpal instability, ligament laxity, CRPS, congenital deformity, non-specific wrist pain	IV
Braga-Silva et al., 2011	49	Complete	SNAC, Kienböck's, primary degenerative OA	IV
Hofmeister et al., 2006	48	AIN & PIN	Dynamic wrist instability	IV
Schweizer et al., 2006	70	Complete	SLAC, Kienböck's, primary osteoarthritis, scaphoid non-union, distal radius fracture, fibrocartilage complex disorders, neurogenic, lupus	IV
Weinstein and Berger, 2002	19	AIN & PIN	SLAC, STTJ arthritis, rheumatoid arthropathy, scaphoid nonunion, post-traumatic RC degenerative joint disease, SL dissociation, SL instability, dorsal wrist pain	IV
Ishida et al., 1993	4/13	Partial/ complete	Kienböck's, (degenerative) arthritis, scaphoid nonunion, distal radius fracture, SL dissociation, sprain or idiopathic	IV
Röstlund et al., 1980	2/7	PIN only/ complete	Scaphoid nonunion, Kienböck's	IV

CEBM: Centre for Evidence-Based Medicine; AIN: anterior interosseous nerve; PIN: posterior interosseous nerve; SLAC: scapholunate advanced collapse; SNAC: scaphoid nonunion advanced collapse; RC: radiocarpal; OA: osteoarthritis; Kienböck's: Kienböck's disease; DRUJ: distal radio-ulnar joint; STTJ: scaphotrapezotrapezoidal joint; SR: scaphoradial; TTFC: triangular fibrocartilage complex; CRPS: chronic regional pain syndrome; SL: scapholunate; Level II of evidence: prospective cohort, comparative study; Level IV of evidence: retrospective case series, no control group.

Table 2. Overview of studies publishing pre- and postoperative pain scores according to the VAS.

Studies	Denervation techniques	Wrists	Mean follow-up (months)	Preoperative VAS	Postoperative VAS	Relative VAS improvement
Sgromolo et al., 2018	AIN & PIN/ PIN only	10/3	13	4 (2–6)[a]	2.2 (0–5)[a]	45%
Delclaux et al., 2017	Partial	33	41	7.1 (4–10)[a]	1.8 (0–8)[a]	75%
Fuchsberger et al., 2017	Complete	124	146	83[b]	40[b]	52%
Patil and Arenas-Prat, 2016	Partial	21	18	86 (75–100)[a]	30 (10–85)[a]	65%
Riches et al., 2016	PIN only	12	24	167 (SD 41)[c]	14 (SD 19)[c]	92%
Storey et al., 2011	Partial	37	18	In rest: 25 (1–46)[b] Activity: 74 (60–82)[b]	In rest: 16 (1–31)[b] Activity: 30 (14–64)[b]	In rest: 36% Activity: 60%

[a]Mean with range or standard deviation (SD).
[b]Median with/without interquartile range (IQR).
[c]M-SACRAH score, which used a 0–200 score.
VAS: visual analogue scale; AIN: anterior interosseous nerve; PIN: posterior interosseous nerve.

Table 3. Overview of studies reporting grip strength.

Studies	Denervation techniques	Wrists	Mean follow-up (months)	Preoperative grip strength (kg)	Postoperative grip strength (kg)	Relative grip improvement
Delclaux et al., 2017	Partial	33	41	33 (13–50)[a]	35 (26–55)[a]	7%
Storey et al., 2011	Partial	37	18	15 (10–24)[b]	21 (11–29)[b]	53%
Braga-Silva et al., 2011	Complete	49	72	11 (SD 3)[a]	18 (SD 3)[a]	64%
Hofmeister et al., 2006	AIN & PIN	48	28	34 (6–60)[a]	41 (21–65)[a]	18%
Weinstein and Berger, 2002	AIN & PIN	19	30	28	37.5	34%

[a]Mean with range or standard deviation (SD).
[b]Median with interquartile range (IQR).

Table 4. Overview of studies reporting return to work rate.

Studies	Denervation techniques	Wrists	Return to type of work	Return to work rate (former job)
Sgromolo et al., 2018	AIN & PIN/PIN only	10/3	2 former job, 6 lighter job, 5 stopped	15%
Delclaux et al., 2017	Partial	33	31 former job	94%
Schweizer et al., 2006	Complete	70	61 former job, 9 lighter job	87%
Weinstein and Berger, 2002	AIN & PIN	19	n/a	73%
Ishida et al., 1993	Partial/complete	4/13	6 former job, 2 lighter job, 4 stopped, 2 (partial/3 (complete) re-operated	35%
Röstlund et al., 1980	PIN/complete	2/7	6 former job, 2 lighter job, 1 other job	67%

AIN: anterior interosseous nerve; PIN: posterior interosseous nerve; n/a: data not available.

incomplete reports on the methods of measuring grip strength.

Return to work

When reported, the majority of patients could return to their former jobs or perform a physically less demanding job. The partial denervation group had a RTW rate ranging from 15% to 94%, while the complete denervation groups had a RTW rate ranging from 35% to 87% (Table 4). According to the GRADEpro tool, these studies yielded a 'Very Low' level of quality on RTW based on the risk of bias, indirectness and the reported categories of outcome measures used.

Patient satisfaction

Patients were generally positive concerning the outcome after denervation with up to 92% being satisfied (Table 5) (Delclaux et al., 2017; Hofmeister et al., 2006; Ishida et al., 1993; Riches et al., 2016; Röstlund et al., 1980; Storey et al., 2011; Weinstein and Berger, 2002). The cohort of Ishida et al. (1993) stands out as only 24% of their cohort was satisfied with the treatment (Ishida et al., 1993). Another criterion for patient satisfaction was the question about whether the patient would recommend selective denervation to others or would undergo the procedure again. This also yielded positive results (Fuchsberger et al., 2017; Riches et al., 2016; Schweizer et al., 2006; Weinstein and Berger, 2002). The assessment with the GRADEpro tool resulted a 'Very Low' level of quality for the patient satisfaction outcome due to the possible publication bias and reporting bias due to the categories used for assessing patient satisfaction.

Complications and re-operations

Postoperative complication rates, including re-operations (including permanent interventions, e.g. proximal row carpectomy) and persistent or worse pain, varied from 6% to 29% (Delclaux et al., 2017; Hofmeister et al., 2006; Storey et al., 2011; Weinstein and Berger, 2002). In the cohort of Ishida et al. (1993), two out of four partial denervation patients needed additional surgery due to persistent pain, in contrast to the three out of 13 complete denervation patients. Using a partial denervation technique,

Table 5. Overview of studies reporting patient satisfaction and recommendation rates.

Study	Denervation technique	Wrists	Satisfaction rate	Recommendation rate
Delclaux et al., 2017	Partial	33	75% (not specified)	n/a
Fuchsberger et al., 2017	Complete	135	n/a	79%
Riches et al., 2016	PIN only	12	92% very or fairly satisfied	100%
Storey et al., 2011	Partial	37	69% satisfied	n/a
Hofmeister et al., 2006	AIN & PIN	48	25 excellent (52%), 15 good (31%), 4 fair (8%), 4 poor (8%)	n/a
Schweizer et al., 2006	Complete	70	n/a	48 (69%) vs 19 (27%) would repeat, 3 undecided (4 %)
Weinstein and Berger, 2002	AIN &PIN	19	70% very or somewhat satisfied	90%
Ishida et al., 1993	Complete	13	3 extremely (23%), 1 satisfied (8%), 1 slightly (8%), 8 dissatisfied (61%)	n/a
Ishida et al., 1993	Partial	4	1 slightly (25%), 3 dissatisfied (75%)	n/a
Röstlund et al., 1980	PIN only, complete	9	4 very (44%), 4 satisfied (44%), 1 unsatisfied (11%)	n/a

n/a: data not available; AIN: anterior interosseous nerve; PIN: posterior interosseous nerve.

Delclaux et al. (2017) reported persisting dysesthesia in 21% of patients, of which one patient developed a complex regional pain syndrome. Neuromas in 8% of patients and transient hypoesthesia were described anecdotally (Braga-Silva et al., 2011).

Denervation versus other surgical techniques

In 2016 Riches et al. published a prospective series of 94 patients with rheumatoid arthritis (RA) with a mean follow-up time of 3 years (Riches et al., 2016). These patients underwent one of eight surgical procedures (Swanson's arthroplasty, wrist arthrodesis, carpal tunnel decompression, RA nodule excision, synovectomy/tenosynovectomy, tendon repair/release and PIN denervation). The 12 patients who underwent PIN denervation did not differ significantly in terms of pain and functional recovery as compared with the other procedures.

Discussion

All studies showed reduction in reported VAS pain scores postoperatively as a result of denervation. Only two studies reported reduction in pain at rest and pain during activity separately (Delclaux et al., 2017; Storey et al., 2011), and both reported an improvement in both domains. Patients with longer follow-up times after denervation tended to benefit less from denervation (Ferreres et al., 1995; Fuchsberger et al., 2017; Röstlund et al., 1980). Progression of the underlying condition could have caused the pain to increase and/or limit the function of the wrist joint (Dellon, 1985). However, with the limited numbers of studies available, we were unable to conclude whether a complete denervation results in better long-term results compared with partial techniques or vice versa. To objectively assess the impact on the patients' well-being, whether positive or negative, the preferred outcome measure for pain is the VAS. Our search only yielded six studies in English in which the VAS was described on a scale of 0–10 or 0–100 (Table 2). In the remaining six studies, only relative changes in pre- and postoperative VAS were reported. The relative VAS improvement of the isolated PIN (PIN only) denervation by Riches et al. (2016) is higher than the other more extensive partial denervation techniques, however, that score is the result of the MSACRAH, which uses a combined pain score of the VAS during activity and in rest is used in contrast to most of the other studies (Table 2). It is unclear whether this explains the relatively high VAS improvement of Riches et al. (2016). The partial denervation studies show an overall higher trend in improvement compared with the complete denervation study of Fuchsberger et al. (2017).

Grip strength was increased after denervation overall, however a relative decrease has also been reported (Röstlund et al., 1980), but this was not included in Table 2, as only a relative difference was described in that report. Grip strength improved the most after complete denervation (Braga-Silva et al., 2011). A factor is that the mean preoperative grip strength in the cohort of Braga-Silva et al. (2011) is lower compared with the other studies, therefore a

similar increase in absolute grip strength resulted in a higher relative improvement in grip strength. Patient satisfaction was generally high after denervation in both the complete and partial denervation groups. The partial denervation group of Storey et al. (2011) and Ishida et al. (1993) showed a trend for more dissatisfied patients. Nevertheless, the majority of patients are still in favour of repeat selective denervation if they had the chance to initially choose again for a surgical treatment (Schweizer et al., 2006). The RTW rate was relatively high, despite the fact that a number (four and six, respectively) of patients in two studies had received financial compensation or were amidst a discharge procedure due to their incapacity to work (Sgromolo et al., 2018; Weinstein and Berger, 2002). Weinstein and Berger (2002) stated that a failure of the denervation was independently associated with workers' compensation claims.

The reported complication rates after denervation suggest that further improvement of the current procedures and standardization of complication reports for selective denervation is needed, because it is still unclear which denervation technique is superior regarding complications. The effectiveness of the complete, PIN only, AIN and PIN and other partial denervation techniques varied in the studies published over the years and can in part be explained by the anatomical variation that complicates the identification of relevant nerve branches (Berger, 1998; Braga-Silva et al., 2011; Buck-Gramcko, 1977; Buck-Gramcko, 1993; Delclaux et al., 2017; Dellon, 1985; Ekerot et al., 1983; Ferreres et al., 1995; Fukumoto et al., 1993; Geldmacher et al., 1972; Grechenig et al., 1998; Hofmeister et al., 2006; Ishida et al., 1993; Patil and Arenas-Prat, 2016; Riches et al., 2016; Röstlund et al., 1980; Schweizer et al., 2006; Storey et al., 2011; Weinstein and Berger, 2002; Wilhelm, 2001).

Improving nerve identification may ensure more selective denervation techniques with similar results to complete denervation (Ekerot et al., 1983) to treat chronic pain while preserving the range of motion (Sgromolo et al., 2018) and leaves the option open for other salvage procedures in case of insufficient pain relief. Despite heterogeneity in the literature and therefore without conclusive evidence of which technique is superior, denervation of the wrist shows a trend towards positive patient outcomes in regard to pain relief, RTW rate and patient satisfaction. Standardization of measuring and reporting outcomes (e.g. using standardized scoring systems for pain and grip strength) should be introduced in order to conclude which surgical technique is best for treating chronic pain. Further exploration of methods to overcome disappointing results due to anatomical variation and misidentification of the relevant sensory nerves could lead to more effective denervation procedures.

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Review

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Outcomes Following Isolated Posterior Interosseous Nerve Neurectomy: A Systematic Review

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Abstract

Background: Posterior interosseous nerve neurectomies (PINN) are an option in the treatment of chronic dorsal wrist pain. However, the literature describing PINN consists primarily of small case series, and the procedure is typically done as an adjunct treatment; therefore, the outcomes of the PINN itself are not well known. We performed a systematic review of the literature to provide characteristics of patients following a PINN. **Methods:** A systematic review of the literature was performed. Papers published in the PubMed database in English on isolated PINN were included. Articles in which a PINN was performed as an adjunct were excluded. Primary outcomes were return to work, patient satisfaction, pain/function scores, wrist range of motion, complications, and pain recurrence. Weighted averages were used to calculate continuous data, whereas categorical data were noted in percentages. **Results:** The search yielded 427 articles including 6 studies and 135 patients (136 cases). The average age was 43.6 years (range, 17-75), and most patients were female (54.1%). At an average final follow-up of 51 months, 88.9% of patients were able to return to work. After initial improvement, a recurrence of pain occurred in 25.5% of patients at an average of 12.3 months. Excluding recurrence of pain, the complication rate was 0.9%, including 1 reflex sympathetic dystrophy. Overall, 88.4% of patients experienced a subjective improvement and were satisfied with the procedure. **Conclusions:** Isolated PINN have shown excellent clinical outcomes, with few patients experiencing recurrent pain at long-term follow-up. PINN can provide relief in patient's chronic wrist pain.

Keywords: wrist denervation, posterior interosseous nerve neurectomy, chronic wrist pain, PINN, hand and wrist surgery

Introduction

The posterior interosseous nerve neurectomy (PINN) was first described in 1966 by Wilhelm who performed dorsal wrist denervation in patients presenting with pain due to trauma, necrosis of the lunate, arthritis, and scaphoid nonunions recalcitrant to conservative measures.[17] These findings were reinforced by a second German report 11 years later in which a combination of wrist denervations were performed, yielding good pain relief in 80% of patients after a follow-up of more than 2 years.[3]

Subsequently, PINN has been used as both an isolated[5,6,8,9,11,12] and adjunct procedure[1,4,13,18] treating patients with chronic dorsal wrist pain that is unresponsive to nonoperative treatments. Although several techniques for wrist denervation exist,[7,10] the PINN is the simplest technically to achieve, requires the least soft tissue handling, and the PIN innervates the central two-thirds of the wrist including to the wrist capsule, scaphoid, lunate, and dorsal distal radius.[15]

However, the PINN literature is comprised of short case series without controls. In addition, because the procedure is typically in addition to other treatments to include carpal excision,[13] wrist fracture,[1] nonunion,[18] or Kienbock disease,[4] the quality of and length of effect of wrist denervation alone are not well known. The goal of this study is to produce a large conglomeration of patients who have undergone an isolated PINN to give a better understanding of the advantages and disadvantages of the technique. A systematic review of the published literature was performed to show patients' demographics and elucidate outcomes, complications, and length of effect following an isolated PINN. We

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Partial Wrist Denervation: The Evidence Behind a Small Fix for Big Problems

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Wrist denervation addresses symptomatic wrist pain without the morbidity and complication profile of more extensive surgical procedures aimed to correct the underlying pathology. The concept of wrist denervation is not new, but its practical application has been modified over the past 50 years. A variety of techniques have been described for various indications, with generally good results. In the United States, a simple, single incision partial denervation consisting of neurectomies of the anterior and posterior interosseous nerves is most commonly performed. Although data on this procedure are limited, most patients are satisfied with pain relief in the short term. There is no evidence that partial denervation procedures alter proprioception of the wrist, and this procedure shows promise as a good option for palliating pain without prolonged postoperative immobilization or leave from work. Preoperative injections do not seem to correlate well with postoperative results. Future studies are needed to assess the duration of relief and possible acceleration of underlying pathology. *(J Hand Surg Am. 2018;43(3):272–277.*

Key words Anterior interosseous nerve, arthritis, denervation, nerve, posterior interosseous nerve.

INTRODUCTION

Wrist denervation describes neurectomies of terminal sensory fibers of peripheral nerves that innervate the wrist capsule and or ligaments.[1] Although popular internationally,[1–3] complete joint denervation is not commonly undertaken in the United States, where partial isolated denervation of the wrist through neurectomies of the anterior interosseous (AIN) and posterior interosseous nerves (PIN) is more routinely performed.[4]

The advantage of wrist denervation is that it offers pain relief while avoiding stiffness, postoperative immobilization, and other complications associated with arthrodesis procedures.[4,5] An unsuccessful neurectomy also does not preclude subsequent alternative treatment. For this reason, partial and total neurectomies have been described for the treatment of a variety of wrist pathologies including posttraumatic, degenerative, and inflammatory.

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HISTORY OF TOTAL WRIST DENERVATION

The concept of wrist denervation is not new. In 1862, John Hilton[6] put forth Hilton's law, which states that nerves crossing a joint innervate that joint. However, it was not until the 1940s and 1950s that surgeons first reported surgical denervation of the hip, knee, shoulder, and ankle joints.[5] In January, 1959, Albrecht Wilhelm[5] initially described the technique of a total wrist joint denervation performed in a 30-year-old German patient with arthritis associated with a scaphoid nonunion. Wilhelm's complete wrist denervation involves 5 skin incisions, 2 of which require epifascial mobilizations, to gain access to 10 terminal nerve branches (Table 1). Many international surgeons reported on modifications of Wilhelm's procedure,[7,8] and although a definitive

TABLE 1. Wrist Innervation

Branch	Nerve	Terminal Innervation
Median	Anterior interosseous	Volar radiocarpal joint, volar radiocarpal ligaments, carpal tunnel floor, distal radioulnar joint
	Palmar cutaneous branch	Transverse carpal ligament adjacent to scaphoid tubercle
Radial	Posterior interosseous	Dorsal radiocarpal joint, intercarpal joints, second to fourth CMC joints
	Superficial branch	Radiocarpal joint (10%)
	Articular branch of first interosseous space	First to second CMC joints (95%)
	Posterior antebrachial cutaneous	Radiocarpal joint (5%)
Ulnar	First articular branch	Pisotriquetral joint (55%)
	Deep branch perforators	Volar second to fifth CMC joints, distal intercarpal, and midcarpal joints
	Dorsal sensory branch	Ulnar carpus, ulnocarpal complex (70%), fourth to fifth CMC joints
Other	Lateral antebrachial cutaneous	Radial radiocarpal joint, radial intercarpal joints, first CMC joint
	Medial antebrachial cutaneous	Ulnocarpal complex (10%)

CMC, carpometacarpal.
Derived from anatomic findings of Fukumoto[10] in 20 specimens. Percentages report occurrence if less than 100%. All nerves except first articular branch of the ulnar are neurotomized by Wilhelm's[5] total denervation technique.

technique has not been established, results have been mostly favorable.[2]

RATIONALE FOR PARTIAL DENERVATION

Despite its international record, total wrist denervation is technically demanding, requires multiple incisions, and may result in the loss of protective proprioception.[4] It is not routinely performed in the United States, where surgeons have advocated for partial denervation procedures focusing on the PIN and AIN.[4,8] Although inherently incomplete, such a partial denervation is supported by anatomical studies highlighting the relative contributions of these nerves.[1,9]

The PIN is the main innervator dorsally, because it has been consistently shown to send fibers into the central two-thirds of the wrist.[1,10,11] Although anterior wrist innervation is less dominated by the AIN,[11,12] Van de Pol[1] reported that the AIN is the most important contributor to volar wrist innervation because it innervates volar periosteum at its capsule and ligament insertions.

In addition to being a technically relatively simple surgery supported by anatomic findings, an isolated AIN and PIN neurectomy affords the attractive option of a single-needle diagnostic nerve block, which is easy to perform in the office. Moreover, the patient may favor a procedure with quick recovery and immediate unrestricted activity to minimize work leave.[7,8,13,14]

PARTIAL DENERVATION TECHNIQUE

Berger[4] first formally defined the technique for a single-incision combined AIN and PIN neurectomy in 1998. He described a 3- to 4-cm longitudinal dorsal incision overlying the plane between the radius and ulna one finger-breadth proximal to the ulnar head. The PIN is identified overlying the interosseous membrane after dissection between the extensor digitorum communis and extensor indicis proprius. The AIN is identified after longitudinally incising the interosseous membrane. Both the PIN and AIN are neurectomized by sharply resecting 2 cm of nerve. Other surgeons have advocated for slightly more complex 2-incision approaches to access additional nerves.[1,8,15]

RESULTS OF PARTIAL DENERVATION

Unlike complete or extensive denervations, almost all published results of partial AIN and or PIN neurectomies were performed in the United States (Table 2).[1–3,12,16–18] In 1984 and 1985, Dellon et al[16] and Dellon,[17] respectively, reported good short-term results of isolated AIN or PIN neurectomy. However, those studies were limited by short follow-up and heterogeneous indications. In 1995, Ferreres[2] retrospectively reviewed 30 patients who underwent an isolated PIN neurectomy. Although the study found that pain improved initially and that radiographs did not deteriorate, two-thirds of patients had pain recur with activity

TABLE 2. Published Results of Partial Wrist Denervations

Year	Author	Country	Procedure	Wrists	Indication	Mean Follow-up, y	Results
1984	Dellon et al[16]	United States	AIN	11	Various pain "attributed to the terminal branch of the AIN" after hyperextension injury: 1 Colles fracture, 1 scaphoid nonunion, 1 volar wrist ganglion, 7 associated carpal tunnel syndromes	1.1	100% excellent
1985	Dellon[17]	United States	PIN	29	Various: 11 sprains, 8 Colles fractures, 4 carpal injuries, 4 postganglionectomy, 3 arthritidies	1.3	90% excellent
1995	Ferreres[2]	Spain	PIN	30	Various: 7 intra-articular distal radius fractures, 5 Colles fractures, 5 Kienböck's disease, 3 scaphoid nonunions, 2 sprains, 1 scapholunate instability, 5 miscellaneous	4.7	70% fair or good, worsening over time
2002	Weinstein et al[14]	United States	AIN + PIN	20	12 scapholunate advanced collapse wrists, 8 other	2.6	90% satisfied, 80% improved pain severity, 85% survival
2006	Hofmeister et al[13]	United States	AIN + PIN	50	Dynamic wrist instability	2.3	85% satisfied, 50% pain relief, 68% survival
2011	Storey et al[1]	United Kingdom	AIN + PIN + superficial branch of radial nerve	37	25 arthritic wrists, 12 other	1.5	60% decrease in pain scores, 81% continued relief
2014	Riches et al[3]	United States	PIN	14	Rheumatoid arthritis	1.8	44% improved pain, 78% satisfied

by 2 years. Concerned with this finding, the authors were able to conclude only that the procedure may be useful as an adjunct to other procedures. However, Riches et al[3] advocated for an isolated PIN denervation as an alternative to more difficult salvage procedures to treat rheumatoid patients with painful wrist arthritis after their study found no difference in function at a mean of 1.8 years in patients treated with either arthrodesis or isolated PIN denervation.

Since Berger's[4] description of single-incision isolated PIN and AIN denervation in 1998, only 2 studies have assessed the outcomes of this combined treatment.[13,14] In 2002, Weinstein and Berger[14] performed a retrospective cohort review of 20 cases, 12 of which were for painful scapholunate advanced collapse, with a mean follow-up of 31 months. The authors found that at final follow-up, 80% of patients reported improved pain severity, and 60% improved pain frequency; 45% of patients endorsed a subjective improvement in grip strength. The mean Disabilities of the Arm, Shoulder, and Hand (DASH) score was 31, and 73% returned to work. Only 3 patients required a subsequent operation, yielding an 85% survival rate. Importantly, 90% were satisfied and would retroactively choose the same treatment, including all 3 who underwent reoperation. Still, that study was limited by its relatively short follow-up; questions remain about the long-term durability of those outcomes.

In 2006, Hofmeister et al[13] evaluated the effectiveness of AIN and PIN neurectomy for chronic wrist instability. These authors studied 50 wrists at a mean follow-up of 28 months, selecting from a prospective database of adult patients with arthroscopically confirmed dynamic instability. The authors reported 50% pain relief from the neurectomy, with a mean DASH score improvement from 42 before surgery to 27 afterward and 85% patient satisfaction. Although the authors concluded by advocating for partial denervation as a viable treatment alternative that may obviate or delay the need for a motion-limiting procedure, the reported survival rate of 68% was lower than that reported by Weinstein and Berger[14]; 16 wrists failed this treatment by 28 months and required subsequent surgery: 4 ligament reconstructions and 12 arthrodeses. We suspect the reason for this higher failure rate to be their indications for denervation: nonarthritic wrists with dynamic instability, which could have been initially treated with a ligament reconstruction to prevent progression to a stage that required subsequent arthrodesis.

To supplement AIN and PIN neurectomies, surgeons have advocated for adding a second incision to denervate additional articular nerves.[1,8,15] However, there are limited data on such alternatives. Strauch[8] anecdotally reported that his 2-incision approach resulted in excellent to good pain relief in 6 of 8 patients at an average follow-up of 1.5 years. Storey et al[15] reported on denervations of the AIN, PIN, and superficial radial nerve in 37 patients, 25 of whom had arthritic wrist pain. Pain scores decreased by 60% from initial assessment levels at a mean of 18 months, and 75% of patients reported sustained pain relief at a mean of 10.3 years. Only 6 patients required reoperation at a mean of 2.6 years after surgery.

Partial wrist denervation has been less reported on than its complete denervation counterpart despite its relative preference in the United States. The few studies of single nerve denervations are limited by size and heterogeneity,[2,3,16,17] and only 2 recent publications describe the outcomes of single-incision AIN and PIN neurectomy.[13,14] One performed partial denervation proactively as an alternative to ligament reconstruction rather than as an alternative to wrist arthrodesis[11] and both were limited to less than 3 years' follow-up. These limited data suggest that with proper indications, namely end-stage wrist arthritis for which alternative treatment would be fusion, most patients are satisfied with pain relief at least in the short term. Still, little is known about the longevity of pain relief or potential for progression of pathology, although a single report adding neurectomy of the superficial branch of the radial nerve described sustained results.[15] Nonetheless, more studies are needed.

DIAGNOSTIC NERVE BLOCK

A theoretic benefit of wrist denervation procedures is that one can be afforded a trial of expected benefit via a preoperative diagnostic nerve block. Wilhelm[5] described these lidocaine injections as essential, and some authors[19] argued that denervation of the wrist is indicated only after confirmation that local anesthetic alleviates symptoms. Consequently, published results of neurectomies are often[5,19] but not always[7] reported in patients who were selected based on preoperative nerve block. However, authors[9,20] who studied the relationship between denervation outcomes and response to preoperative local anesthesia did not find strong correlations.

Weinstein and Berger[14] showed that postinjection pain relief did not correlate with postoperative pain frequency or severity, nor was postinjection pain and

grip improvement correlated with ultimate DASH scores. Hofmeister et al[13] found that diagnostic pain relief was not correlated with postoperative pain relief, although diagnostic grip strength changes were correlated with postoperative grip strength improvement. Radu et al[18] reported that a subgroup of patients who underwent diagnostic nerve block with satisfactory pain relief was not more likely to benefit from wrist denervation than was a large cohort that received no such preoperative injection.

These findings are surprising because they suggest that a preoperative response to injection is not predictive of postoperative outcomes. One possible explanation is that a percutaneous injection may miss its target, underestimating relief from denervation. Alternatively, and more plausibly, an excessive injection may infiltrate nerve branches that are not addressed during partial or even extensive neurectomies. A well-delivered injection can best be thought of as a screening test for potential relief, one with the added benefit of persuading a skeptical patient to consider a small or minimally invasive solution to what he or she views as a large problem.

PROPRIOCEPTION

Wrist ligaments and capsule contain mechanoreceptors reactive to joint pressure, motion, and velocity. Such proprioception not only assists balance and function, it provides a protective sensation for joints.[20,21] Consequently, a theoretical concern with complete and even partial neurectomy is loss of this protective proprioception, with an end result of Charcot arthropathy, as seen in the foot of patients with diabetic neuropathy.[9] Although anatomic studies have suggested that both PIN and AIN contribute to a possible ligamentomuscular reflex of the wrist joint, partial neurectomies may preserve proprioception by preserving other nerves that aid in this function.[4,21] Moreover, even complete denervation may allow for proprioception by preserving the contributions of muscular and cutaneous afferents.[9]

Still, it may be partially for proprioceptive reasons that the dynamically unstable patients of Hofmeister et al[13] progressed to require arthrodesis after partial neurectomy. This may also explain the concern Wilhelm[5] expressed that failures were attributed to progression of instability. However, no study of partial or total wrist denervation reported Charcot joints, and Weinstein and Berger[14] reported that no patients described an altered sense of joint position after partial denervation.

The few studies that directly assessed the potential deleterious effect of partial denervation on proprioception reported no such negative sequalae.[20,21] Patterson et al[21] found no difference between patients who underwent a PIN neurectomy and healthy volunteers. Similarly, when Gay et al[20] performed a randomized control trial of 80 healthy volunteers who received either lidocaine or placebo injections to the AIN and PIN, the authors found no difference in active and passive positioning tests over a 60° flexion-extension arc. Consequently, despite anatomic studies signifying that the PIN as well as other nerves targeted by denervation procedures are important for wrist proprioception, clinical studies suggest that partial and probably even complete denervation is safe in this regard.

SUMMARY

Devised and perpetuated internationally, total wrist denervation has been shown to be a viable treatment option for palliating wrist pain. Although it is more commonly performed in the United States, a morbidity-minimizing partial neurectomy of the AIN and PIN is less well-studied. Nonetheless, limited data suggest that this procedure can provide relief in the short term, and there is no evidence that proprioception is altered by a partial denervation. At this time, partial denervation procedures should be limited to use for treatment of chronic wrist conditions for which the only alternative is an arthrodesis. Future studies are needed to assess optimal indications as well as duration of relief and possible acceleration of underlying pathology.

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Vitiligo

Question: Should vitiligo (ICD-10-CM L80) be moved to a funded line?

Question source: Julie Dhossche and Sabra Leitenberger, OHSU pediatric dermatology

Issue: Vitiligo is an acquired pigmentary disorder of skin and mucous membranes, manifesting itself by expanding depigmented lesions. While the cause is not well understood, the observed variation in clinical manifestations of the condition has suggested several possible etiologies, including association with other medical conditions. Currently, vitiligo (ICD-10-CM L80) is on line 656 DERMATOLOGICAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY. No prior review of this condition was found in a search of HSC or HERC minutes. Vitiligo did not have any effective treatments at the time of the creation of the Prioritized List, which likely explains its low prioritization. Since the List was created, treatments for vitiligo have been developed. Additionally, the HERC has re-prioritized other skin conditions that have social impacts such as severe acne, severe atopic dermatitis, and port wine stain in recent years.

Previous HSD/HERC history
No previous review found in search of HSC/HERC minutes

From Dr. Dhossche:

> We were hoping to request a review of vitiligo. This diagnosis is currently below the line. However, we see children who are obviously devastated by this disease, especially in those with skin of color, and when there is facial involvement and large body surface area affected. There is more literature out there now about how this is not a cosmetic issue-- it's a disease with very real impact and psychosocial consequences.

Current Prioritized List status

Code	Code description	Current placement
L80	Vitiligo	656 DERMATOLOGICAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
96910	Photochemotherapy; tar and ultraviolet B (Goeckerman treatment) or petrolatum and ultraviolet B	158 NON-HODGKIN'S LYMPHOMAS 313 DISORDERS INVOLVING THE IMMUNE SYSTEM 426 SEVERE INFLAMMATORY SKIN DISEASE 489 DERMATOPHYTOSIS OF NAIL, GROIN, AND FOOT AND OTHER DERMATOMYCOSIS 508 CIRCUMSCRIBED SCLERODERMA 533 CONTACT DERMATITIS AND NON-INFECTIOUS OTITIS EXTERNA 541 MILD PSORIASIS; DERMATOPHYTOSIS: SCALP, HAND, BODY 656 DERMATOLOGICAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY
96912	Photochemotherapy; psoralens and ultraviolet A (PUVA)	158,313,426,489,508,533,541,656

96913	Photochemotherapy (Goeckerman and/or PUVA) for severe photoresponsive dermatoses requiring at least 4-8 hours of care under direct supervision of the physician (includes application of medication and dressings)	158,313,426,489,508,533,541,656
96920-96922	Laser treatment for inflammatory skin disease (psoriasis)	426,541

GUIDELINE NOTE 21, SEVERE INFLAMMATORY SKIN DISEASE

Lines 426,482,504,532,541,656

Inflammatory skin conditions included in this guideline are:

A) Psoriasis
B) Atopic dermatitis
C) Lichen planus
D) Darier disease
E) Pityriasis rubra pilaris
F) Discoid lupus

The conditions above are included on Line 426 if severe, defined as having functional impairment as indicated by Dermatology Life Quality Index (DLQI) ≥ 11 or Children's Dermatology Life Quality Index (CDLQI) ≥ 13 (or severe score on other validated tool) AND one or more of the following:

A) At least 10% of body surface area involved
B) Hand, foot or mucous membrane involvement.

Otherwise, these conditions above are included on Lines 482, 504, 532, 541 and 656.

For severe psoriasis, first line agents include topical agents, phototherapy and methotrexate. Second line agents include other systemic agents and oral retinoids and should be limited to those who fail, or have contraindications to, or do not have access to first line agents. Biologics are included on this line only for the indication of severe plaque psoriasis; after documented failure of first line agents and failure of (or contraindications to) a second line agent.

For severe atopic dermatitis/eczema, first-line agents include topical moderate- to high- potency corticosteroids and narrowband UVB. Second line agents include topical calcineurin inhibitors (e.g. pimecrolimus, tacrolimus), topical phosphodiesterase (PDE)-4 inhibitors (e.g. crisaborole), and oral immunomodulatory therapy (e.g. cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, or oral corticosteroids). Use of the topical second line agents (e.g. calcineurin inhibitors and phosphodiesterase (PDE)-4 inhibitors) should be limited to those who fail or have contraindications to first line agents. Biologic agents are included on this line for atopic dermatitis only after failure of or contraindications to at least one agent from each of the following three classes: 1) moderate to high

potency topical corticosteroids, 2) topical calcineurin inhibitors or topical phosphodiesterase (PDE)-4 inhibitors, and 3) oral immunomodulator therapy.

GUIDELINE NOTE 13, HEMANGIOMAS, COMPLICATED; PORT WINE STAINS

Lines 321,627,656

Dermatologic hemangiomas (ICD-10-CM D18.01 Hemangioma and Lymphangioma of skin and subcutaneous tissue) are included on Line 321 when they are ulcerated, infected, recurrently hemorrhaging, or function-threatening (e.g. eyelid hemangioma). Otherwise, they are included on Line 627.

ICD-10 Q82.5 (Congenital non-neoplastic nevus) is included on line 321 only when representing port wine stains. For all other diagnoses, it is included on line 656. Treatment of port wine stains is only included on line 321 when treatment is with pulsed dye lasers and:

1) When lesions are located on the face and neck; OR
2) When lesions are located on the trunk or extremities AND are associated with recurrent bleeding or painful nodules.

Otherwise, treatment of port wine stains is included on line 656.

Vitiligo

Evidence

Need for treatment

1) **Lai 2017**: systematic review and meta-analysis of vitiligo and depression
    a. N=25 studies (2708 patients)
        i. All observational studies
    b. Based on diagnostic codes, the pooled prevalence of depression among patients with vitiligo was 0.253 [95% confidence interval (CI) 0.16–0.34; P < 0.001)]. Using self-reported questionnaires, the pooled prevalence of depressive symptoms was 0.336 (95% CI 0.25–0.42; P < 0.001). The pooled odds ratio of depression among patients with vitiligo was 5.05 vs. controls (95% CI 2.21–11.51; P < 0.001).
    c. The pooled prevalence of impaired general health among patients with vitiligo based on GHQ was 0.34 (95% CI 0.29–0.38; P < 0.001)
    d. This study demonstrated that patients with vitiligo were at a significantly higher risk of clinical depression or depressive symptoms compared with those without a depigmenting disease. Approximately one-third of patients with vitiligo reported depressive symptoms or impaired general health, and up to one-quarter of them had clinical depression.
2) **Osinubi 2017**: systematic review and meta-analysis of psychological comorbidity in people with vitiligo
    a. N=29 studies (2530 patients)
    b. Pooled prevalence using depression-specific and anxiety-specific questionnaires was 0.29 [95% confidence interval (CI) 0.21– 0.38] and 0.33 (95% CI 0.18–0.49), respectively. Prevalence was lower for clinically diagnosed depression (0.21, 95% CI 0.15–0.28) and anxiety (0.15, 95% CI 0.06–0.24).
    c. High heterogeneity was observed.
    d. Conclusions A range of psychological outcomes are common in people with vitiligo.
3) **Morrison 2017**, systematic review and meta-analysis of quality of life in people with vitiligo
    a. N=12 studies (1799 patients)
        i. Mainly used the Dermatology Life Quality Index (DLQI)
    b. Quality of life (QOL) was significantly worse in patients with vitiligo vs healthy controls (SMD 1.98 CI 1.08-2.88)
    c. QOL was significantly better in patients with vitiligo vs patients with psoriasis (SMD -0.93 CI -1.36 to – 0.49)
    d. QOL was similar in patients with vitiligo vs patients with atopic dermatitis (SMD -1.25 CI -3.31 to 0.82)
    e. QOL was similar in patients with vitiligo vs patients with acne (SMD 0.66, CI -0.94 to 2.25))
    f. the review is limited by high heterogeneity because of methodological and clinical differences between the studies

Treatment efficacy

1) **Whitton 2015**, Cochrane review of interventions for vitiligo
    a. N=96 studies (4512 patients)
    b. Nine analyses from eight studies reported >75% repigmentation. In the following studies the repigmentation was better in the combination therapy group:
        i. calcipotriol plus PUVA (psoralen with UVA light) versus PUVA (paired OR 4.25, 95% CI 1.43 to 12.64, one study, N = 27)

   ii. hydrocortisone-17-butyrate plus excimer laser versus excimer laser alone (RR 2.57, 95% CI 1.20 to 5.50, one study, N = 84)
   iii. oral minipulse of prednisolone (OMP) plus NB-UVB (narrowband UVB) versus OMP alone (RR 7.41, 95% CI 1.03 to 53.26, one study, N = 47)
   iv. azathioprine with PUVA versus PUVA alone (RR 17.77, 95% CI 1.08 to 291.82, one study, N = 58) and 8-Methoxypsoralen (8-MOP) plus sunlight versus psoralen (RR 2.50, 95% CI 1.06 to 5.91, one study, N = 168).

c. We performed one meta-analysis of three studies, in which we found a non-significant 60% increase in the proportion of participants achieving >75% repigmentation in favor of NB-UVB compared to PUVA (RR 1.60, 95% CI 0.74 to 3.45; I^2 = 0%).
d. Studies assessing topical preparations, in particular topical corticosteroids, reported the most adverse effects. However, in combination studies it was difficult to ascertain which treatment caused these effects. We performed two analyses from a pooled analysis of three studies on adverse effects. Where NB-UVB was compared to PUVA, the NB-UVB group reported less observations of nausea in three studies (RR 0.13, 95% CI 0.02 to 0.69; I^2 = 0% three studies, N = 156) and erythema in two studies (RR 0.73, 95% CI 0.55 to 0.98; I^2 = 0%, two studies, N = 106), but not itching in two studies (RR 0.57, 95% CI 0.20 to 1.60; I^2 = 0%, two studies, N = 106).
e. Very few studies only assessed children or included segmental vitiligo. We found one study of psychological interventions but we could not include the outcomes in our statistical analyses. We found no studies evaluating micropigmentation, depigmentation, or cosmetic camouflage.
f. **Authors' conclusions** This review has found some evidence from individual studies to support existing therapies for vitiligo, but the usefulness of the findings is limited by the different designs and outcome measurements and lack of quality of life measures. There is a need for follow-up studies to assess permanence of repigmentation as well as high-quality randomized trials using standardized measures and which also address quality of life.

2) **Bae 2017,** systematic review and meta-analysis of phototherapy for vitiligo
   a. N=35 studies (1428 patients)
      i. 11 were single arm studies, 9 were within patient trials, and 15 were parallel trials.
   b. For narrow band UV-B (NBUVB) phototherapy, an at least mild response (≥ 25% repigmentation) occurred in 62.1% (95%CI, 46.9%-77.3%) of 130 patients in 3 studies at 3 months, 74.2% (95%CI, 68.5%-79.8%) of 232 patients in 11 studies at 6 months, and 75.0% (95%CI, 60.9%-89.2%) of 512 patients in 8 studies at 12 months. A marked response (≥ 75% repigmentation) was achieved in 13.0% (95%CI, 2.1%-23.9%) of 106 patients in 2 studies at 3 months, 19.2% (95%CI, 11.4%-27.0%) of 266 patients in 13 studies at 6 months, and 35.7% (95%CI, 21.5%-49.9%) of 540 patients in 9 studies at 12 months.
   c. For psoralen-UV-A (PUVA) phototherapy, an at least mild response occurred in 51.4%(95%CI, 28.1%-74.7%) of 103 patients in 4 studies at 6 months and 61.6%(95%CI, 20.2%-100%) of 72 patients in 3 studies at 12 months. marked response to PUVA phototherapy was achieved in 8.5% (95% CI, 0%- 18.3%) of 88 patients in 3 studies at 6months and 13.6% (95% CI, 4.2%-22.9%) of 72 patients in 3 studies at 12 months
   d. In the subgroup analyses, marked responses were achieved on the face and neck in 44.2%(95%CI, 24.2%-64.2%), on the trunk in 26.1%(95%CI, 8.7%-43.5%), on the

extremities in 17.3%(95%CI, 8.2%-26.5%), and on the hands and feet in none after at least 6 months of NBUVB phototherapy.

e. CONCLUSIONS AND RELEVANCE Long-duration phototherapy should be encouraged to enhance the treatment response in vitiligo. The greatest response is anticipated on the face and neck.

3) **Lee 2019**, systematic review and meta-analysis of topical calcineurin inhibitor therapy (TCI) for vitiligo
    a. N=46 studies (1499 patients)
        i. 36 studies (941 patients) were included in the TCI monotherapy group and 12 studies (558 patients) were in the TCI plus phototherapy group
    b. For TCI monotherapy, an at least mild response (≥ 25% repigmentation) was achieved in 55.0% (95%CI, 42.2%-67.8%) of 560 patients in 21 studies, an at least moderate response (≥50% repigmentation) in 38.5% (95%CI, 28.2%-48.8%) of 619 patients in 23 studies, and a marked response (≥75%repigmentation) in 18.1% (95%CI, 13.2%-23.1%) of 520 patients in 19 studies after median treatment duration of 3 months (range, 2-7 months).
    c. In the subgroup analyses, face and neck lesions showed an at least mild response in 73.1% (95%CI, 32.6-83.5%) of patients, and a marked response in 35.4% (95%CI, 24.9-46.0%) of patients.
    d. For TCI plus phototherapy, an at least mild response to TCI plus phototherapy was achieved in 89.5% (95%CI, 81.1-97.9%) of patients, and a marked response was achieved in 47.5% (95%CI, 30.6-64.4%) of patients.
    e. CONCLUSIONS AND RELEVANCE The use of TCIs, both as a monotherapy and in combination with phototherapy, should be encouraged in patients with vitiligo.
4) **Jeong Ju 2021:** systematic review and meta-analysis of surgical interventions with patients with vitiligo
    a. N=117 studies (8776 patients)
    b. Rate of repigmentation of greater than 90% for surgical interventions was 52.69% (95%CI, 46.87%-58.50%) and 45.76% (95%CI, 30.67%-60.85%) for punch grafting, 72.08% (95% CI, 54.26%-89.89%) for thin skin grafting, 61.68% (95%CI, 47.44%-75.92%) for suction blister grafting, 47.51% (95%CI, 37.00%-58.03%) for noncultured epidermal cell suspension, 36.24%(95%CI, 18.92%-53.57%) for noncultured follicular cell suspension, and 56.82% (95%CI, 48.93%-64.71%) for cultured epidermal cell suspension. The rate of repigmentation of greater than 50% after any surgical intervention was 81.01% (95%CI, 78.18%-83.84%). In meta-regression analyses, the treatment response was associated with patient age (estimated slope, −1.1418), subtype of vitiligo (estimated slope, 0.3047), and anatomical sites (estimated slope, −0.4050).
    c. CONCLUSIONS AND RELEVANCE The findings of this systematic review and meta-analysis suggest that surgical intervention can be an effective option for refractory stable vitiligo.

<u>Expert recommendations</u>

1) **Rodrigues 2017**, Vitiligo Working Group treatment recommendations
    a. Potent or ultrapotent topical corticosteroids administered in a cyclical fashion avoids adverse effects
    b. Topical tacrolimus 0.1% should be used twice daily for affected areas on the face and intertriginous areas

c. Narrowband ultraviolet B light phototherapy appears to be safe and effective when >5-10% body surface area is affected; focused narrowband ultraviolet B light phototherapy, such as hand and foot units or excimer laser, is useful in localized disease
d. Topical tacrolimus 0.1% used twice per week may help prevent relapse after repigmentation is achieved
e. Surgical techniques are most successful in late-stage segmental vitiligo. Surgery can be considered in those with nonresponsive, stable vitiligo. Noncultured epidermal melanocyte cell grafting demonstrates superior extent and quality of pigmentation compared with other surgical techniques

2) **Taieb 2015**: European Dermatology Forum consensus guidelines on management of vitiligo
   a. In children and adults, once-daily application of potent topical corticosteroids (TCS) can be advised for patients with limited, extrafacial involvement for a period no longer than 3 months, according to a continuous treatment scheme or, better, to a discontinuous scheme (15 days per month for 6 months with a strict assessment of response based on photographs).
   b. Facial lesions can be treated as effectively and with lesser side-effects by topical calcieurin inhibitors (TCI).
   c. topical ascomycin immunomodulating macrolactams (TIM) can be considered in adults and children with vitiligo as an alternative to topical steroids for new, act spreading, lesions on thin skin. The topical safety profile of TIM is better compared with potent TCS, especially concerning risks of skin atrophy.
   d. Oral PUVA is currently used in adult patients with generalized vitiligo as a second-line therapy. Compared with NB-UVB it has the disadvantage of lower efficacy and higher short- and long-term risks. As with NB-UVB, 12–24 months of continuous therapy may be necessary to acquire maximal repigmentation. For topical PUVA, psoralens should be formulated in creams at very low concentration.
   e. NB-UVB is indicated for generalized NSV. Total body treatment is suggested for lesions involving more than 15–20% of the body area. Total NB-UVB has also been considered as treatment for active spreading vitiligo, even if limited supportive data are available. Targeted phototherapies (laser and nonlaser) are indicated for localized vitiligo and in particular for small lesions of recent onset and childhood vitiligo, to avoid side-effects due to total body irradiation with UVB, and in all cases where contraindications exist for total body irradiation with conventional NB-UVB (risk for melanoma or nonmelanoma skin cancer, photoaggravated disease, etc.).
   f. Oral immunomodulating therapy is not considered useful for repigmenting stable vitiligo.
   g. Current data do not provide enough evidence to recommend immunosuppressants or biologics in patients with vitiligo. Moreover, the potential side-effects of these agents do not justify their use in vitiligo.
   h. The surgery option should be reserved for patients with stable vitiligo and other localized forms of vitiligo, after the documented failure of medical interventions.
   i. For NSV, patients with the stable form of the disease and a negative history of Koebner phenomenon are eligible, but the risk of relapse must be explained thoroughly to the patient.

Other payer policies

1) **Aetna 2021**
    a. Aetna considers the following established methods medically necessary for the treatment of vitiligo:
        i. Excimer laser (e.g., XTRAC, PhotoMedex, Radnor, PA; EX-308, Ra Medical Systems, Inc., Carlsbad, CA)
        ii. Narrow-band ultraviolet B (NB-UVB)
        iii. Topical and oral psoralen photochemotherapy (PUVA)
        iv. Topical tacrolimus
        v. Topical and systemic corticosteroids.
    b. Surgical treatments are considered experimental
2) **Cigna 2021** Vitiligo
    a. An initial regimen (i.e., for up to 12 weeks) of office-based phototherapy or photochemotherapy is considered medically necessary for the treatment of localized or generalized vitiligo when EITHER of the following criteria is met:
        i. vitiligo body surface area (BSA) involvement ≤ 10% with BOTH of the following:
            1. failure, intolerance or contraindication to an eight consecutive week trial of at least ONE topical corticosteroid
            2. failure, intolerance or contraindication to a twelve consecutive week trial of at least ONE topical calcineurin inhibitor (e.g., tacrolimus 0.03% or 0.1% ointment, pimecrolimus 1% cream)
        ii. vitiligo BSA involvement > 10%
    b. Continued office-based phototherapy or photochemotherapy beyond the initial 12 weeks and for up to 52 weeks is considered medically necessary for the treatment of localized or generalized vitiligo when there is a beneficial clinical response to the previous course of treatment. Continued office-based phototherapy or photochemotherapy beyond 52 weeks for up to and including 200 total treatments is considered medically necessary when there is a continued beneficial clinical response. More than 200 treatment sessions of office-based phototherapy or photochemotherapy for vitiligo is considered not medically necessary.
    c. An initial regimen (i.e., for up to 12 weeks) of office-based targeted excimer laser therapy (i.e., 308 nanometers [nm]) is considered medically necessary for the treatment of localized vitiligo when BOTH of the following criteria are met:
        i. failure, intolerance or contraindication to an eight consecutive week trial of at least ONE topical corticosteroid
        ii. failure, intolerance or contraindication to a twelve consecutive week trial of at least ONE topical calcineurin inhibitor (e.g., tacrolimus 0.03% or 0.1% ointment, pimecrolimus 1% cream)
    d. Continued office-based targeted excimer laser therapy (i.e., 308 nanometers [nm]) beyond the initial 12 weeks and for up to 52 weeks is considered medically necessary for the treatment of localized vitiligo when there is a beneficial clinical response to treatment Continued office-based targeted excimer laser therapy (i.e., 308 nanometers [nm]) beyond 52 weeks up to and including 200 total treatments is considered medically necessary when there is a continued beneficial clinical response. More than 200 treatment sessions of office-based targeted excimer laser therapy (i.e., 308 nanometers [nm]) for the treatment of vitiligo is considered not medically necessary.

Expert input
Dr. Julie Dhossche, OHSU pediatric dermatology

> I think it's fine to add vitiligo to the severe inflammatory skin disease line, though one thing I want to point out is that the facial involvement in vitiligo is especially stigmatizing, and the guidelines on this line are 10% BSA or hand, foot or mucosal involvement. I would honestly be over the moon if we could add FACE in this guideline not just for vitiligo but for any of these diseases....

Vitiligo

HERC staff summary

Vitiligo has a significant effect on quality of life, similar to other severe skin conditions currently in the funded region of the Prioritized List (e.g. severe dermatitis and acne). Patients with vitiligo are significantly more likely to have clinical depression than healthy control subjects. Evidence was not found that treatment improved quality of life; however, such improvement can be inferred. Vitiligo has more of an impact on people with darker skin tones.

Based on the included systematic reviews and meta-analyses, the following therapies have evidence of effectiveness either alone or in combination: PUVA (psoralen with UVA light), narrow band UVB, excimer laser, topical/oral steroids and topical calcineurin inhibitors (TCI). These therapies are all covered by private insurers. Expert guidelines also recommend topical tacrolimus.

Surgical treatment of vitiligo appears based on one systematic review to be effective for treatment of vitiligo. Expert guidelines only recommend surgical treatment after failure of medical treatment. Major insurers consider surgical treatment of vitiligo to be experimental.

HERC staff summary

1) Add ICD-10 L80 (Vitiligo) to line 426 SEVERE INFLAMMATORY SKIN DISEASE
   a) Similar diagnoses are on this line, as are the CPT codes for PUVA and UVB
   b) Keep L80 on line 656 DERMATOLOGICAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY for cases that do not meet guideline criteria for coverage
   c) Note: no surgical intervention codes appear on line 426. Surgical treatment would need to be approved as an exception
2) Modify GN21 as shown below
   a) Adds vitiligo for coverage
   b) Adds facial involvement as a coverage criterion for all severe inflammatory skin conditions

GUIDELINE NOTE 21, SEVERE INFLAMMATORY SKIN DISEASE

Lines 426,482,504,532,541,656

Inflammatory skin conditions included in this guideline are:

A) Psoriasis
B) Atopic dermatitis
C) Lichen planus
D) Darier disease
E) Pityriasis rubra pilaris
F) Discoid lupus
G) Vitiligo

The conditions above are included on Line 426 if severe, defined as having functional impairment as indicated by Dermatology Life Quality Index (DLQI) ≥ 11 or Children's Dermatology Life Quality Index (CDLQI) ≥ 13 (or severe score on other validated tool) AND one or more of the following:

A) At least 10% of body surface area involved
B) Hand, foot, face, or mucous membrane involvement.

Otherwise, these conditions above are included on Lines 482, 504, 532, 541 and 656.

For severe psoriasis, first line agents include topical agents, phototherapy and methotrexate. Second line agents include other systemic agents and oral retinoids and should be limited to those who fail, or have contraindications to, or do not have access to first line agents. Biologics are included on this line only for the indication of severe plaque psoriasis; after documented failure of first line agents and failure of (or contraindications to) a second line agent.

For severe atopic dermatitis/eczema, first-line agents include topical moderate- to high- potency corticosteroids and narrowband UVB. Second line agents include topical calcineurin inhibitors (e.g. pimecrolimus, tacrolimus), topical phosphodiesterase (PDE)-4 inhibitors (e.g. crisaborole), and oral immunomodulatory therapy (e.g. cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, or oral corticosteroids). Use of the topical second line agents (e.g. calcineurin inhibitors and phosphodiesterase (PDE)-4 inhibitors) should be limited to those who fail or have contraindications to first line agents. Biologic agents are included on this line for atopic dermatitis only after failure of or contraindications to at least one agent from each of the following three classes: 1) moderate to high potency topical corticosteroids, 2) topical calcineurin inhibitors or topical phosphodiesterase (PDE)-4 inhibitors, and 3) oral immunomodulator therapy.

BJD
British Journal of Dermatology

Vitiligo and depression: a systematic review and meta-analysis of observational studies

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Summary

Vitiligo is a common depigmenting disorder with profound psychosocial impacts. Previous observational studies have suggested a link between vitiligo and psychiatric morbidity, such as depression. However, variability in study design makes it difficult to quantify accurately the relationship between vitiligo and depression. We aimed to investigate the underlying prevalence and risk of depression among patients with vitiligo. A comprehensive search of MEDLINE, Embase and the Cochrane Library was conducted. Cross-sectional, case–control or cohort studies that assessed the prevalence of depression among patients with vitiligo or the relationship between vitiligo and depression were included. DerSimonian and Laird random-effects models were utilized to calculate the pooled prevalence and relative risks. Publication bias was evaluated by funnel plots and Egger's tests. Twenty-five studies with 2708 cases of vitiligo were included. Based on diagnostic codes, the pooled prevalence of depression among patients with vitiligo was 0·253 [95% confidence interval (CI) 0·16–0·34; $P < 0·001$)]. Using self-reported questionnaires, the pooled prevalence of depressive symptoms was 0·336 (95% CI 0·25–0·42; $P < 0·001$). The pooled odds ratio of depression among patients with vitiligo was 5·05 vs. controls (95% CI 2·21–11·51; $P < 0·001$). Moderate-to-high heterogeneity was observed between the studies. Patients with vitiligo were significantly more likely to suffer from depression. Clinical depression or depressive symptoms can be prevalent, with the actual prevalence differing depending on screening instruments or, possibly, geographical regions. Clinicians should actively evaluate patients with vitiligo for signs/symptoms of depression and provide appropriate referrals to manage their psychiatric symptoms accordingly.

What's already known about this topic?

- Vitiligo can have profound psychosocial impacts and impair patients' quality of life.
- Studies have suggested a relationship between vitiligo and depression.

What does this study add?

- Patients with vitiligo were significantly more likely to suffer from depression than controls.
- The pooled prevalence and risk of depression vary depending on screening instruments or, possibly, geographical regions.

BJD
British Journal of Dermatology

The prevalence of psychological comorbidity in people with vitiligo: a systematic review and meta-analysis*

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Summary

Background Vitiligo is a chronic disorder causing skin depigmentation with global prevalence varying from 0·2% to 1·8%. U.K. guidelines recommend assessment of psychological state during clinical evaluation of vitiligo. However, the prevalence of psychological comorbidity in people with vitiligo has not been described.
Objectives To establish the prevalence of psychological symptoms or disorders in people with vitiligo and describe the outcome measures used.
Methods We performed a comprehensive search of MEDLINE, Embase, CINAHL and PsycINFO to identify observational studies assessing the prevalence of psychological symptoms or disorders (December 2016). DerSimonian and Lard random-effects models were used to estimate the overall pooled prevalence.
Results We identified 29 studies with 2530 people with vitiligo. Most studies included a measure of either depression (n = 25) or anxiety (n = 13). The commonest tools were the Hospital Anxiety and Depression Scale and the Centre for Epidemiology Studies Depression Scale. Ten studies provided information on 13 other psychological outcomes. Pooled prevalence using depression-specific and anxiety-specific questionnaires was 0·29 [95% confidence interval (CI) 0·21–0·38] and 0·33 (95% CI 0·18–0·49), respectively. Prevalence was lower for clinically diagnosed depression (0·21, 95% CI 0·15–0·28) and anxiety (0·15, 95% CI 0·06–0·24). When nonspecific tools were used the prevalence remained similar for depression (0·27, 95% CI 0·08–0·46) but increased for anxiety (0·46, 95% CI 0·39–0·52). High heterogeneity was observed.
Conclusions A range of psychological outcomes are common in people with vitiligo. The prevalence of anxiety was influenced by type of screening tool, suggesting the need for validation of psychological outcome screening tools in the field of dermatology.

What's already known about this topic?

- Vitiligo can have a profound psychosocial impact.
- People with vitiligo are more likely to experience depression than those without vitiligo.

What does this study add?

- People with vitiligo have a range of psychological symptoms or disorders.
- Approximately one in four people with vitiligo experience depression; however, the prevalence of anxiety is unclear as it varies substantially according to the screening tool used.

Interventions for vitiligo (Review)

Whitton ME, Pinart M, Batchelor J, Leonardi-Bee J, González U, Jiyad Z, Eleftheriadou V, Ezzedine K

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http://www.thecochranelibrary.com

WILEY

[Intervention Review]

Interventions for vitiligo

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ABSTRACT

Background

Vitiligo is a chronic skin disorder characterised by patchy loss of skin colour. Some people experience itching before the appearance of a new patch. It affects people of any age or ethnicity, more than half of whom develop it before the age of 20 years. There are two main types: generalised vitiligo, the common symmetrical form, and segmental, affecting only one side of the body. Around 1% of the world's population has vitiligo, a disease causing white patches on the skin. Several treatments are available. Some can restore pigment but none can cure the disease.

Objectives

To assess the effects of all therapeutic interventions used in the management of vitiligo.

Search methods

We updated our searches of the following databases to October 2013: the Cochrane Skin Group Specialised Register, CENTRAL in *The Cochrane Library* (2013, Issue 10), MEDLINE, Embase, AMED, PsycINFO, CINAHL and LILACS. We also searched five trials databases, and checked the reference lists of included studies for further references to relevant randomised controlled trials (RCTs).

Selection criteria

Randomised controlled trials (RCTs) assessing the effects of treatments for vitiligo.

Data collection and analysis

At least two review authors independently assessed study eligibility and methodological quality, and extracted data.

JAMA Dermatology | Original Investigation

Phototherapy for Vitiligo
A Systematic Review and Meta-analysis

Jung Min Bae, MD, PhD; Han Mi Jung, MD; Bo Young Hong, MD, PhD; Joo Hee Lee, MD; Won Joon Choi, MD; Ji Hae Lee, MD, PhD; Gyong Moon Kim, MD, PhD

IMPORTANCE References to the expected treatment response to phototherapy would be helpful in the management of vitiligo because phototherapy requires long treatment durations over several months.

OBJECTIVE To estimate the treatment response of vitiligo to phototherapy.

DATA SOURCES A comprehensive database search of MEDLINE, EMBASE, and the Cochrane library from inception to January 26, 2016, was performed for all prospective studies. The main keywords used were *vitiligo*, *phototherapy*, *psoralen*, *PUVA*, *ultraviolet*, *NBUVB*, and *narrowband*.

STUDY SELECTION All prospective studies reporting phototherapy outcome for at least 10 participants with generalized vitiligo were included. Of 319 studies initially identified, the full texts of 141 studies were assessed for eligibility, and 35 were finally included in the analysis. Of these, 29 studies included 1201 patients undergoing narrowband UV-B (NBUVB) phototherapy, and 9 included 227 patients undergoing psoralen–UV-A (PUVA) phototherapy.

DATA EXTRACTION AND SYNTHESIS Two reviewers independently extracted the following data: study design, number and characteristics of the participants, phototherapy protocol, and rate of repigmentation based on the quartile scale. Single-arm meta-analyses were performed for the NBUVB and PUVA groups. Sample size–weighted means were calculated using a random-effects model for the repigmentation rates of the included studies.

MAIN OUTCOMES AND MEASURES The primary outcomes were at least mild (≥25%), at least moderate (≥50%), and marked (≥75%) responses on a quartile scale. Response rates were calculated as the number of participants who showed the corresponding repigmentation divided by the number of all participants enrolled in the individual studies.

RESULTS The meta-analysis included 35 unique studies (1428 unique patients). For NBUVB phototherapy, an at least mild response occurred in 62.1% (95% CI, 46.9%-77.3%) of 130 patients in 3 studies at 3 months, 74.2% (95% CI, 68.5%-79.8%) of 232 patients in 11 studies at 6 months, and 75.0% (95% CI, 60.9%-89.2%) of 512 patients in 8 studies at 12 months. A marked response was achieved in 13.0% (95% CI, 2.1%-23.9%) of 106 patients in 2 studies at 3 months, 19.2% (95% CI, 11.4%-27.0%) of 266 patients in 13 studies at 6 months, and 35.7% (95% CI, 21.5%-49.9%) of 540 patients in 9 studies at 12 months. For PUVA phototherapy, an at least mild response occurred in 51.4% (95% CI, 28.1%-74.7%) of 103 patients in 4 studies at 6 months and 61.6% (95% CI, 20.2%-100%) of 72 patients in 3 studies at 12 months. In the subgroup analyses, marked responses were achieved on the face and neck in 44.2% (95% CI, 24.2%-64.2%), on the trunk in 26.1% (95% CI, 8.7%-43.5%), on the extremities in 17.3% (95% CI, 8.2%-26.5%), and on the hands and feet in none after at least 6 months of NBUVB phototherapy.

CONCLUSIONS AND RELEVANCE Long-duration phototherapy should be encouraged to enhance the treatment response in vitiligo. The greatest response is anticipated on the face and neck.

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Supplemental content

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JAMA Dermatology | Original Investigation

Treatment Outcomes of Topical Calcineurin Inhibitor Therapy for Patients With Vitiligo
A Systematic Review and Meta-analysis

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IMPORTANCE Topical calcineurin inhibitors (TCIs), including tacrolimus and pimecrolimus, have been widely used for the treatment of vitiligo; however, the efficacy of TCI monotherapy is often underestimated.

OBJECTIVES To estimate the treatment responses to both TCI monotherapy and TCI accompanied by phototherapy for vitiligo, based on relevant prospective studies, and to systematically review the mechanism of action of TCIs for vitiligo treatment.

DATA SOURCES A comprehensive search of the MEDLINE, Embase, Web of Science and Cochrane Library databases from the date of database inception to August 6, 2018, was conducted. The main key words used were *vitiligo*, *topical calcineurin inhibitor*, *tacrolimus*, *pimecrolimus*, and *FK506*.

STUDY SELECTION Of 250 studies initially identified, the full texts of 102 articles were assessed for eligibility. A total of 56 studies were identified: 11 studies on the TCI mechanism, 36 studies on TCI monotherapy, 12 studies on TCI plus phototherapy, and 1 study on TCI maintenance therapy.

DATA EXTRACTION AND SYNTHESIS Two reviewers independently extracted data on study design, patients, intervention characteristics, and outcomes. Random-effects meta-analyses using the generic inverse variance weighting were performed for the TCI monotherapy and TCI plus phototherapy groups.

MAIN OUTCOMES AND MEASURES The primary outcomes were the rates of at least mild (≥25%), at least moderate (≥50%), and marked (≥75%) repigmentation responses to treatment. These rates were calculated by dividing the number of participants in an individual study who showed the corresponding repigmentation by the total number of participants who completed that study.

RESULTS In the 56 studies included in the analysis, 46 (1499 patients) were selected to evaluate treatment response. For TCI monotherapy, an at least mild response was achieved in 55.0% (95% CI, 42.2%-67.8%) of 560 patients in 21 studies, an at least moderate response in 38.5% (95% CI, 28.2%-48.8%) of 619 patients in 23 studies, and a marked response in 18.1% (95% CI, 13.2%-23.1%) of 520 patients in 19 studies after median treatment duration of 3 months (range, 2-7 months). In the subgroup analyses, face and neck lesions showed an at least mild response in 73.1% (95% CI, 32.6-83.5%) of patients, and a marked response in 35.4% (95% CI, 24.9-46.0%) of patients. For TCI plus phototherapy, an at least mild response to TCI plus phototherapy was achieved in 89.5% (95% CI, 81.1-97.9%) of patients, and a marked response was achieved in 47.5% (95% CI, 30.6-64.4%) of patients.

CONCLUSIONS AND RELEVANCE The use of TCIs, both as a monotherapy and in combination with phototherapy, should be encouraged in patients with vitiligo.

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Supplemental content

CME Quiz at jamanetwork.com/learning and CME Questions page 992

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JAMA Dermatology | Original Investigation

Surgical Interventions for Patients With Vitiligo
A Systematic Review and Meta-analysis

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IMPORTANCE Surgical interventions are a key part of the therapeutic arsenal, especially in refractory and stable vitiligo. Comparison of treatment outcomes between the different surgical procedures and their respective adverse effects has not been adequately studied.

OBJECTIVE To investigate the reported treatment response following different surgical modalities in patients with vitiligo.

DATA SOURCES A comprehensive search of the MEDLINE, Embase, Web of Science, and Cochrane Library databases from the date of database inception to April 18, 2020, was conducted. The key search terms used were *vitiligo, surgery, autologous, transplantation, punch, suction blister,* and *graft*.

STUDY SELECTION Of 1365 studies initially identified, the full texts of 358 articles were assessed for eligibility. A total of 117 studies were identified in which punch grafting (n = 19), thin skin grafting (n = 10), suction blister grafting (n = 29), noncultured epidermal cell suspension (n = 45), follicular cell suspension (n = 9), and cultured epidermal cell suspension (n = 17) were used.

DATA EXTRACTION AND SYNTHESIS Three reviewers independently extracted data on study design, patients, intervention characteristics, and outcomes. Random effects meta-analyses using generic inverse-variance weighting were performed.

MAIN OUTCOMES AND MEASURES The primary outcomes were the rates of greater than 90%, 75%, and 50% repigmentation response. These rates were calculated by dividing the number of participants in an individual study who showed the corresponding repigmentation by the total number of participants who completed the study. The secondary outcomes were the factors associated with treatment response to the surgical intervention.

RESULTS Among the 117 unique studies and 8776 unique patients included in the analysis, rate of repigmentation of greater than 90% for surgical interventions was 52.69% (95% CI, 46.87%-58.50%) and 45.76% (95% CI, 30.67%-60.85%) for punch grafting, 72.08% (95% CI, 54.26%-89.89%) for thin skin grafting, 61.68% (95% CI, 47.44%-75.92%) for suction blister grafting, 47.51% (95% CI, 37.00%-58.03%) for noncultured epidermal cell suspension, 36.24% (95% CI, 18.92%-53.57%) for noncultured follicular cell suspension, and 56.82% (95% CI, 48.93%-64.71%) for cultured epidermal cell suspension. The rate of repigmentation of greater than 50% after any surgical intervention was 81.01% (95% CI, 78.18%-83.84%). In meta-regression analyses, the treatment response was associated with patient age (estimated slope, −1.1418), subtype of vitiligo (estimated slope, 0.3047), and anatomical sites (estimated slope, −0.4050).

CONCLUSIONS AND RELEVANCE The findings of this systematic review and meta-analysis suggest that surgical intervention can be an effective option for refractory stable vitiligo. An appropriate procedure should be recommended based on patient age, site and size of the lesion, and costs.

Supplemental content

CME Quiz at jamacmelookup.com and CME Questions page 363

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Review

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Current and emerging treatments for vitiligo

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Abstract

Clinicians should be aware that vitiligo is not merely a cosmetic disease and that there are safe and effective treatments available for vitiligo. It is important to recognize common and uncommon presentations and those with active disease, as well as their implications for clinical management; these were discussed in the first article in this continuing medical education series. Existing treatments include topical and systemic immunosuppressants, phototherapy, and surgical techniques, which together may serve to halt disease progression, stabilize depigmented lesions, and encourage repigmentation. We discuss how to optimize the currently available treatments and highlight emerging treatments that may improve treatment efficacy in the future.

Keywords: afamelanotide; biologics; corticosteroids; excimer lamp; excimer laser; grafting; leukoderma; methotrexate; narrowband ultraviolet light; phototherapy; pigmentation; tacrolimus; treatment; vitiligo.

BJD
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Guidelines for the management of vitiligo: the European Dermatology Forum consensus

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Summary

The aetiopathogenic mechanisms of vitiligo are still poorly understood, and this has held back progress in diagnosis and treatment. Up until now, treatment guidelines have existed at national levels, but no common European viewpoint has emerged. This guideline for the treatment of segmental and nonsegmental vitiligo has been developed by the members of the Vitiligo European Task Force and other colleagues. It summarizes evidence-based and expert-based recommendations (S1 level).

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Funding sources
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Conflicts of interest
None declared.

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Vitiligo is an acquired depigmenting disorder affecting 0·5% of the world population, without sex or racial differences. It affects all age groups.[1,2] According to the consensus definition given to generalized/vulgaris or nonsegmental vitiligo (NSV) by the Vitiligo European Task Force (VETF)[1] 'vitiligo vulgaris/NSV is an acquired chronic pigmentation disorder characterized by white patches, often symmetrical, which usually increase in size with time, corresponding to a substantial loss of functioning epidermal and sometimes hair follicle melanocytes'; however, this is not specific enough. It needs to be completed by a list of disorders (the acquired generalized hypomelanoses) which may clinically overlap with NSV, but which are clearly attributable to known aetiological factors. In cases of uncertain diagnosis, additional noninvasive and invasive procedures may be needed (Table 1).

Segmental vitiligo (SV) is defined descriptively as for NSV except for a unilateral distribution (asymmetric vitiligo) that may totally or partially match a cutaneous segment (e.g. dermatomal-like). Some specific features of SV are rapid onset and involvement of the hair follicle pigmentary system. One unique segment is involved in most patients (Table 2).

Concerning therapy and NSV topographic subtypes, acral lesions show the worst response rate.[3] Distinction between SV and NSV may affect prognosis in terms of resistance to

visibility, age and coping is outlined in Table 4 and the algorithm in Figure 1. A zero line is always possible, meaning no treatment if the disease is not bothering the patient. The environmental factors (occupation, Koebner phenomenon, sustained stress or anxiety) should always be discussed. For SV, triggering neurogenic factors are usually envisaged but good studies are lacking to prove this point. This stepwise approach should be considered as a proposal based mostly on evidence-based medicine data. However, there is much room for modulation and innovation based on this scheme.[119]

The polygenic and multifactorial background in vitiligo should be reflected in more personalized approaches in the future.[119] An early therapeutic intervention before the appearance of leucotrichia is recommended. Cutaneous inflammation may be a shared feature in all cases. Accordingly, a more aggressive anti-inflammatory therapy, including methotrexate, would probably be helpful. If the initial step preceding inflammation comes from a local predisposition of melanocytes to attach poorly to the basement membrane, there are possible targets to improve adhesion mechanisms. The issue of self-renewal ('stemness') aptitude of melanocytes has been raised especially for SV,[119] which clearly benefits from autologous grafting. If impairment of melanocyte survival mechanisms are a cause, growth factor supplementation, such as melanocyte-stimulating hormone (MSH) analogues[120,121] could be used. Improving the antioxidant status of the epidermis has been attempted, but more powerful tools using gene transfer might be used in the future.[122]

When melanocyte loss has been stopped, therapy needs to address repigmentation. New repigmenting therapies are emerging such as helium–neon (He–Ne) lasers and prostaglandin E_2.[123,124] Recent development in the field of melanocyte precursors are promising. If we can better stimulate the migration of those cells towards the epidermis and understand why they usually stop migrating when becoming pigmented, a major step would be achieved. Newer technologies derived from progenitors or reprogrammed skin cells[125] will probably further increase the possibility of surgical intervention.

Disclaimer

These guidelines are defined for dermatologists in the clinic and in private practice. Furthermore, they are meant to help health insurance organizations and political decision-makers.

Steps that can be considered part of every physician's general obligations when prescribing drugs (inquiring about allergies and intolerance reactions, as well as identifying potential contraindications) are not reported. It was considered obvious, and not declared, that all patients should be informed about the specific risks associated with any given systemic therapy.

During the preparation of this guideline, further clinical and experimental studies may have been carried out, proving or counteracting the guideline. Consequently, the authors can take no responsibility for dosage or treatment decisions taken in this rapidly changing field. Readers are advised to keep themselves abreast of new data and developments subsequent to the publication of the guidelines.

Table 4 General outline of management for vitiligo: therapy options, according to the clinical features

Type of vitiligo	Level	Usual management
SV or limited NSV (< 2–3% of body surface)	First line	Avoidance of triggering factors, local therapies (corticosteroids, calcineurin inhibitors)
	Second line	Localized NB-UVB therapy, especially excimer monochromatic lamp or laser
	Third line	Consider surgical techniques if repigmentation cosmetically unsatisfactory on visible areas
NSV	First line	Avoidance of triggering/aggravating factors. Stabilization with NB-UVB therapy, at least 3 months. Optimal duration at least 9 months, if response. Combination with systemic/topical therapies, including reinforcement with localized UVB therapy, possible
	Second line	Systemic steroids (e.g. 3–4-month minipulse therapy) or immunosuppressants if rapidly progressing disease or absence of stabilization under NB-UVB
	Third line	Graft in nonresponding areas especially with high cosmetic impact. However, Koebner phenomenon limits the persistence of grafts. Relative contraindication in areas such as dorsum of hands
	Fourth line	Depigmentation techniques (hydroquinone monobenzyl ether or 4-methoxyphenol alone or associated with Q-switched ruby laser) in nonresponding widespread (> 50%) or highly visible recalcitrant facial/hands vitiligo

A no treatment option (zero line) can be considered in patients with a fair complexion after discussion. For children, phototherapy is limited by feasibility in the younger age group and surgical techniques are rarely proposed before prepubertal age. There is no current recommendation applicable to the case of rapidly progressive vitiligo, not stabilized by ultraviolet (UV) therapy. For all subtypes of disease or lines of treatment, psychological support and counselling, including access to camouflage instructors, is needed. NSV, nonsegmental vitiligo; SV, segmental vitiligo; NB-UVB, narrowband UVB. Table adapted from Ref. 3.

Interventional Treatments for Acute and Chronic Pain
With No Evidence of Effectiveness

Issue: AHRQ recently updated their comparative effectiveness review for interventional treatments for acute and chronic pain. Multiple therapies were reviewed that were found to have no evidence of effectiveness. HERC staff have reviewed these therapies, some of which are included on line 662/GN173 and need to have the date of last review for entries updated.

Several other therapies were identified as have no evidence of effectiveness that do not have specific CPT or HCPCS codes. These therapies should be called out in the surgical treatments for conditions of the back and spine guideline. These therapies include intradiscal injection of platelet rich plasma, stem cells, methylene blue, or ozone.

Interventional therapies listed as having no effect of no evidence or insufficient evidence of effectiveness in the 2021 AHRQ systematic review

CPT/HCPCS Code	**Code Description**	**Procedure**	**Current Placement**
64633-64636 C9752, C9753	Destruction by neurolytic agent, paravertebral facet joint nerve(s)	Radiofrequency facet joint denervation	662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:
64640	Destruction by neurolytic agent; other peripheral nerve or branch	Radiofrequency denervation of the obturator nerve (hip pain)	662
64505	Injection, anesthetic agent; sphenopalatine ganglion	Sphenopalatine block	ANCILLARY PROCEDURES Note: covered by the nerve block guideline
64553	Percutaneous implantation of neurostimulator electrode array; cranial nerve	Occipital nerve stimulation	174 GENERALIZED CONVULSIVE OR PARTIAL EPILEPSY WITHOUT MENTION OF IMPAIRMENT OF CONSCIOUSNES
64555	Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)	Peripheral nerve stimulation of the ulnar, median or radial nerve	NEVER REVIEWED

Interventional Treatments for Acute and Chronic Pain
With No Evidence of Effectiveness

Evidence

1) **AHRQ 2021**, systematic review of interventional treatments for acute and chronic pain https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-247-interventional-treatments-acute-chronic-pain_0.pdf
    a. Evidence was insufficient to assess pulsed radiofrequency denervation for presumed facet joint pain versus sham denervation (1 trial, N=40) or continuous radiofrequency denervation (1 trial, N=40) (SOE: insufficient).
    b. Evidence was insufficient to assess intradiscal platelet-rich plasma injection for presumed discogenic back pain (1 trial, N=58) (SOE: insufficient).
    c. There were no differences between intradiscal platelet-rich plasma injection and saline injection in harms, including no serious adverse events, at up to 3 years following treatment (SOE: low).
    d. Evidence was insufficient to assess intradiscal stem cell injection for presumed discogenic back pain (1 trial, N=100) (SOE: insufficient).
    e. Intradiscal methylene blue for presumed discogenic back pain (1 trial, N=81) was associated with no difference versus sham at 6 weeks and 3 months. Evidence was insufficient to determine effects of intradiscal methylene blue at 6 months (2 trials, N=153, with conflicting results) and 12 months or longer (1 trial, N=72) (SOE: low for no difference at 6 weeks and 3 months; insufficient for 6, 12, and 24 months).
    f. Evidence was insufficient to assess intradiscal oxygen-ozone for radicular low back pain (1 trial, N=159) (SOE: insufficient).
    g. No trial evaluated intradiscal oxygen-ozone injection without corticosteroid or oxygen-ozone injection for presumed (nonradicular) discogenic low back pain.
    h. Evidence was insufficient to assess sphenopalatine block versus sham for headache (1 trial, N=41) (SOE: insufficient).
    i. Evidence was insufficient to assess occipital nerve stimulation versus sham stimulation for headache (1 trial, N=157) (SOE: insufficient).
    j. One trial (N=50) found piriformis injection with corticosteroid and local anesthetic for piriformis syndrome associated with no difference versus local anesthetic alone in pain at rest at 1 week; piriformis injection was associated with a moderate reduction in pain at rest versus local anesthetic at 1 month (SOE: low for no difference at 1 week and for benefit at 1 month).
    k. Evidence was insufficient to assess peripheral nerve stimulation for upper extremity peripheral neuropathic pain (SOE: insufficient).

HERC staff recommendations:

1) Add CPT 64555 to line 662
2) Modify GN173 as shown below
    a. Update dates of last review for several lines
    b. Add an entry for CPT 64555
3) Modify GN37 as shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
64555	Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)	Insufficient evidence of effectiveness	October 2021
64633-64634	Radiofrequency ablation of the cervical and thoracic spine	Insufficient evidence of benefit	~~March, 2015~~ October 2021
64635-64636 C9752, C9753	Radiofrequency ablation of the lumbar and sacral spine	Insufficient evidence of benefit	~~November, 2014~~ ~~Coverage guidance~~ October 2021
64640	Destruction by neurolytic agent; other peripheral nerve or branch	Insufficient evidence of effectiveness	~~March 2020~~ October 2021

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

Lines 346,529

Spine surgery is included on Line 346 only in the following circumstances:

A) Decompressive surgery is included on Line 346 to treat debilitating symptoms due to central or foraminal spinal stenosis, and only when the patient meets the following criteria:
    1) Has MRI evidence of moderate or severe central or foraminal spinal stenosis AND
    2) Has neurogenic claudication OR
    3) Has objective neurologic impairment consistent with the MRI findings. Neurologic impairment is defined as 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

Foraminal or central spinal stenosis causing only radiating pain (e.g. radiculopathic pain) is included only on Line 529.

B) Spinal fusion procedures are included on Line 346 for patients with MRI evidence of moderate or severe central spinal stenosis only when one of the following conditions are met:
1) spinal stenosis in the cervical spine (with or without spondylolisthesis) which results in objective neurologic impairment as defined above OR
2) spinal stenosis in the thoracic or lumbar spine caused by spondylolisthesis resulting in signs and symptoms of neurogenic claudication and which correlate with xray flexion/extension films showing at least a 5 mm translation OR
3) pre-existing or expected post-surgical spinal instability (e.g. degenerative scoliosis >10 deg, >50% of facet joints per level expected to be resected)

For all other indications, spine surgery is included on Line 529.

The following interventions are not included on these lines due to lack of evidence of effectiveness for the treatment of conditions on these lines, including cervical, thoracic, lumbar, and sacral conditions:

- local injections (including ozone therapy injections)
- botulinum toxin injection
- intradiscal electrothermal therapy
- therapeutic medial branch block
- coblation nucleoplasty
- percutaneous intradiscal radiofrequency thermocoagulation
- percutaneous laser disc decompression
- radiofrequency denervation
- corticosteroid injections for cervical pain
- intradiscal injections, including platelet rich plasma, stem cells, methylene blue, or ozone

Corticosteroid injections for low back pain with or without radiculopathy are only included on Line 529. Diagnostic anesthetic injections for selective nerve root blocks are included on Line 529 for lumbar or sacral symptoms.

The development of this guideline note was informed by HERC coverage guidances on Percutaneous Interventions for Low Back Pain, Percutaneous Interventions for Cervical Spine Pain, Low Back Pain: Corticosteroid Injections and Low Back Pain: Minimally Invasive and Non-Cordicosteroid Percutaneous Interventions. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

Interventional Treatments for Acute and Chronic Pain
Kyphoplasty and Vertebroplasty

Question: Should any changes be made in the current coverage of kyphoplasty and vertebroplasty?

Question source: HERC staff

Issue: AHRQ recently updated their comparative effectiveness review for interventional treatments for acute and chronic pain. Kyphoplasty and vertebroplasty were two interventions with some evidence of effectiveness found on review. These procedures are performed for vertebral compression fractures, which are often due to osteoporosis or metastatic disease. Vertebroplasty involves the injection of polymethyl methacrylate (PMMA), commonly known as bone cement, into the collapsed (fractured) vertebral body. In kyphoplasty, injection of PMMA is preceded by insertion and inflation of a balloon into the collapsed vertebral body to restore it.

Kyphoplasty and vertebroplasty were last reviewed in May, 2013 as part of the coverage guidance process. At that time, coverage was added for these procedures on line 478 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY, which is below the current funding line (line 471). A guideline applies to line 478 regarding with these procedures are covered.

Current Prioritized List status
CPT **22510-22512** (Percutaneous vertebroplasty) are on line 478 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY
CPT **22513-22515** (Percutaneous vertebral augmentation) are on line 478

GUIDELINE NOTE 109, VERTEBROPLASTY, KYPHOPLASTY, AND SACROPLASTY
Line 478
Vertebroplasty and kyphoplasty are not included on this line (or any other line) for the treatment of routine osteoporotic compression fractures.

Vertebroplasty and kyphoplasty are only included on this line for the treatment of vertebral osteoporotic compression fractures when they are considered non-routine and meet all of the following conditions:

A) The patient is hospitalized under inpatient status due to pain that is primarily related to a well-documented acute fracture, and
B) The severity of the pain prevents unassisted ambulation, and
C) The pain is not adequately controlled with oral or transcutaneous medication, and
D) The patient must have failed an appropriate trial of conservative management.

Sacroplasty is not included on these or any lines of the Prioritized List for coverage consideration.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx

Evidence

Interventional Treatments for Acute and Chronic Pain
Kyphoplasty and Vertebroplasty

1) **AHRQ 2021**, systematic review of interventional treatments for acute and chronic pain
    a. N=13 trials (1685 patients)
    https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-247-interventional-treatments-acute-chronic-pain_0.pdf
        i. 4 trials rated good quality, 5 rated fair quality and 4 rated poor quality
        ii. mean age 66 to 80 years
    b. Vertebroplasty
        i. Vertebroplasty for vertebral compression fracture was associated with a small reduction in pain intensity versus sham vertebroplasty or usual care at 1 to 2 weeks (10 trials, N=1093), 1 to 6 months (10 trials, N=1094), 6 to 12 months (8 trials, N=993), and 12 months and longer (9 trials, N=965); and a moderate reduction at 2 to 4 weeks (8 trials, N=918) (strength of evidence [SOE]: low at 1 to 2 weeks, moderate at other time points).
            1. Restricting to sham vertebroplasty controls (5 trials, N=536) tended to decrease benefits (no difference at 1 to 2 weeks and small at other time points), but the difference between sham and usual care trials was only statistically significant at 2 to 4 weeks (p for interaction=0.01). Benefits also tended to be larger in trials of patients with more acute compared with less acute pain, but differences were not statistically significant.
            2. Few trials evaluated the association between vertebroplasty versus sham or usual care and likelihood of experiencing a pain response (defined as pain at least moderately better,79 pain <4 on a 0 to 10 numeric rating scale (NRS), or pain improvement ≥30%). Results favored vertebroplasty at 2 to 4 weeks (3 trials), 1 to 6 months (2 trials), 6 to 12 months (2 trials), and 12 months and longer (2 trials), with relative risk (RR) estimates that ranged from 1.27 to 1.46. However, estimates were imprecise and nonstatistically significant.
        ii. There was insufficient evidence to determine effects of vertebroplasty on function at 1 to 2 weeks (7 trials, N=743), due to marked inconsistency between sham trials (no benefit) and usual care trials (small benefit) Vertebroplasty was associated with a small improvement versus sham or usual care in function at 2 to 4 weeks (6 trials, N=708), 1 to 6 months (7 trials, N=637), 6 to 12 months (6 trials, N=690), and ≥12 months (6 trials, N=612). (SOE: insufficient for 1 to 2 weeks, moderate for 1 to 6 months and 12 months and longer, and high for 2 to 4 weeks and 6 to 12 months).
            1. Only one trial (mean pain duration at enrollment 17.8 weeks) evaluated the association between vertebroplasty versus sham or usual care and likelihood of experiencing functional improvement (defined as RDQ improved ≥30%). Vertebroplasty was associated with reduced likelihood of functional improvement versus sham at 2 to 4 weeks (relative risk [RR] 0.66, 95% CI, 0.45 to 0.97), but increased likelihood at 12 months and longer (RR 1.56, 95% CI, 1.12 to 2.18).
        iii. Vertebroplasty was associated with a small improvement versus sham or usual care in general quality of life as measured by the EuroQOL 5-Dimension Questionnaire (EQ-5D) at 2 to 4 weeks (4 trials, mean difference 0.05, 95% CI, 0.02 to 0.09, I2=0%), and at 6 to 12 months (3 trials, mean difference 0.06, 95%

CI, 0.02 to 0.11, I2=0%). At other time points there were no differences or the difference was not statistically significant.

iv. Vertebroplasty was not associated with increased risk of incident vertebral fracture at 12 months and longer (7 trials, N=826); evidence on serious adverse events was sparse and imprecise but did not indicate increased risk (SOE: moderate for vertebral fracture, low for serious adverse events).

c. Kyphoplasty
   i. N= 2 trials (434 patients)
      1. mean age 64 and 73 years)
   ii. Kyphoplasty for vertebral compression fracture was associated with large reductions in pain and moderate to large improvement in function versus usual care at 1 week and 1 month in patients with or without cancer. No trial compared kyphoplasty against sham (SOE: low for function at 1 week; moderate for pain and for function at 1 month).
   iii. In one trial (N=300) of patients without cancer, effects on pain and function were small to moderate at 3 months to 2 years (SOE: low).
   iv. Evidence on incident or worsening vertebral fracture was inconsistent and imprecise, based on two trials (N=434) (SOE: insufficient).

d. Conclusions: Vertebroplasty is probably effective at reducing pain and improving function in older patients with vertebral compression fractures; benefits are small but similar to other therapies recommended for pain. Evidence was too limited to separate effects of control type and symptom acuity on effectiveness of vertebroplasty. Kyphoplasty has not been compared against sham, but is probably more effective than usual care for vertebral compression fractures in older patients.

HERC staff summary

The AHRQ systematic review found vertebroplasty and kyphoplasty to have a small benefit for pain and function. The current placement of these procedures on a non-funded line with a guideline appear appropriate and no changes are recommended.

HERC staff recommendation:

1) Make no changes in the current placement of CPT **22510-22512** (Percutaneous vertebroplasty) and CPT **22513-22515** (Percutaneous vertebral augmentation) on line 478 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY
2) Make no changes to GUIDELINE NOTE 109, VERTEBROPLASTY, KYPHOPLASTY, AND SACROPLASTY

Interventional Treatments for Acute and Chronic Pain
Radiofrequency Denervation for Sacroiliac Pain

Question: Should any changes be made in the current coverage of radiofrequency denervation for sacroiliac pain?

Question source: HERC staff

Issue: AHRQ recently updated their comparative effectiveness review for interventional treatments for acute and chronic pain. This review included radiofrequency denervation for sacroiliac pain. Conventional radiofrequency ablation involves the application of continuous high frequency electrical current to ablate nerve tissue thought to be the cause of pain. Cooled and pulsed radiofrequency have been proposed as potential alternatives to conventional radiofrequency. Like conventional radiofrequency ablation, the cooled radiofrequency procedure involves the application of high frequency electrical current. It differs from conventional radiofrequency ablation by using a larger, "cooled" (relative to conventional radiofrequency; heat is still generated) radiofrequency probe, potentially allowing for more targeted, larger and more effective lesions.

Radiofrequency denervation for sacroiliac pain was last reviewed in November 2019. At that time, a systematic review and metanalysis of 7 studies (240 patients; Sun 2018) and a systematic review including 17 studies (King 2015) were included as the evidence base. Both reviews included RCTs, as well as cohort and other observational trials. The conclusion was that the evidence based consisted of mostly small observational trials with considerable variation in diagnostic criteria, patient selection, treatment modality and outcomes measured. It was determined that this procedure had insufficient evidence of effectiveness and was placed on line 662/GN173

Current Prioritized List status
CPT **64625** Radiofrequency ablation, nerves innervating the sacroiliac joint, with image guidance (ie, fluoroscopy or computed tomography) is on line 662

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
64451, 64625	Anesthetic or steroid injection and/or radiofrequency ablation, nerves innervating the sacroiliac joint, with image guidance	Insufficient evidence of effectiveness	November 2019

Interventional Treatments for Acute and Chronic Pain
Radiofrequency Denervation for Sacroiliac Pain

Evidence

1) **AHRQ 2021**, systematic review of interventional treatments for acute and chronic pain https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-247-interventional-treatments-acute-chronic-pain_0.pdf
    a. N=2 trials (28 and 51 patients) with sham controls [Cohen 2008 and Patel 2012]
        i. Both trials required patients to have pain in the sacroiliac area for at least 6 months and persistent pain despite standard nonoperative therapies. Patients had to have at least 75 percent pain relief with a single or repeat diagnostic sacroiliac block
        ii. Both trials rated fair quality (unclear randomization methods and high crossover)
            1. Crossover was high: in one trial, 94 percent (16/17) of patients randomized to sham treatment crossed over to cooled radiofrequency denervation after 3 months and in the other, 64 percent (9/14) crossed over after 1 month.
        iii. NOTE: Cohen 2008 and Patel 2012 included in the King 2015 systematic review included in the 2019 HERC review of this topic
    b. Cooled radiofrequency denervation for sacroiliac pain was associated with a moderate to large reduction in pain (mean difference 1.0 to 2.9 points on a 0 to 10 pain scale) and small to large improvement in function versus sham radiofrequency at 1 month; improvements in pain and function at 3 months were moderate (1 trial, N=28, mean change in pain from baseline -2.4 vs -0.8) (SOE: moderate for pain and function at 3 months; low for function at 1 month).
    c. One trial reported no serious complications, though some patients reported temporary worsening pain typically lasting 5 to 10 days after the procedure; one patient in the cooled radiofrequency arm reported transient nonpainful buttock paresthesias.
    d. Conclusion: In younger populations, cooled radiofrequency denervation is probably more effective than sham for sacroiliac pain.

Interventional Treatments for Acute and Chronic Pain
Radiofrequency Denervation for Sacroiliac Pain

HERC staff summary

AHRQ review only includes RCTs of cooled radiofrequency ablation with sham controls. The total number of patients in the included trials was very small (N=79). AHRQ concluded that this technology was probably more effective than sham. This is different from the conclusion reached by HERC 2 years ago in their last review. The 2019 HERC review included the two RCTs in the AHRQ review, as well as other types of studies (RCTs of non-cooled RFA, cohort studies, etc.). Taken as a whole, HERC staff conclude that the evidence is still insufficient that radiofrequency ablation is effective for treatment of sacroiliac pain.

HERC staff recommendations:

1) Make no change to the placement of CPT 64625 (Radiofrequency ablation, nerves innervating the sacroiliac joint, with image guidance (ie, fluoroscopy or computed tomography)) on line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS
2) Update the date of last review in GN173 as shown below

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 662

The following Interventions are prioritized on Line 662 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
64625	Anesthetic or steroid injection and/or radiofrequency ablation, nerves innervating the sacroiliac joint, with image guidance	Insufficient evidence of effectiveness	~~November 2019~~ October 2021