

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

For specific coding recommendations and guideline wording, please see the text of the 8-14-14 VbBS minutes.

RECOMMENDED CODE MOVEMENT (effective 10/1/14 unless otherwise noted)

- Make various straightforward coding changes
- Remove various nerve block procedure codes from lines on the Prioritized List and recommend they be returned to the Ancillary List
- Add diagnosis codes for diabetic retinopathy to the diabetic retinopathy line
- Add ICD-10 diagnosis codes for certain types of diabetes to the appropriate diabetes lines (effective 1/1/15)
- Remove diagnosis codes for chiropractic and osteopathic manipulation from the migraine headache line
- Add a new coding specification to the tension headache line specifying that chiropractic and osteopathic manipulation are on this line only for pairing with cervicogenic headache
- Move the diagnostic code for unspecified myopathy from the covered dysfunction lines to the new fibromyalgia line (effective 1/1/16)
- Add the diagnostic code for chronic fatigue syndrome to the new fibromyalgia line (effective 1/1/16)
- Remove diagnosis codes for osteomyelitis from the hyperbaric oxygen therapy line (to be reviewed by HERC in November, 2014)
- Add chemodenervation of the anal sphincter to the uncovered chronic anal fissure line
- Remove chemodenervation of extraocular muscles from the covered amblyopia line but leave on two covered strabismus lines
- Add various surgical codes for sex reassignment surgery to the gender dysphoria line (effective 1/1/15)

ITEMS CONSIDERED BUT NO RECOMMENDATIONS FOR CHANGES MADE

- Did not change the placement of tympanic membrane perforation diagnosis codes
- Leave diagnosis codes for unspecified rheumatism and fasciitis on a very low priority line rather than moving them to the new fibromyalgia line
- Did not change placement for botulinum toxin injections for treatment of neck or lower back pain or chronic daily headaches

RECOMMENDED GUIDELINE CHANGES (effective 10/1/14 unless otherwise noted)

- Eliminate the proposed guideline for treatments for Hepatitis C (which had been approved at the August 8, 2014 meeting)
- Modify the nerve block guideline to include the CPT codes for these procedures and make into an ancillary guideline

- Add a new guideline which specifies that removal of tympanostomy tubes is a covered service
- Modify the hyperbaric oxygen therapy guideline to add diabetic wounds as an indication, with specifics about when hyperbaric oxygen therapy would be appropriate (to be reviewed by HERC in November)
- Modify the spinal disorders guideline to require objective evidence of neurologic injury or radiculopathy
- Modify the rehabilitation guideline to limit the total number of therapy visits for all conditions to 30 per year, except for certain neurological conditions or when in an inpatient rehabilitation facility
- Modify the lymphedema guideline to specify that compression dressings/garments are covered for treatment of lymphedema even in the absence of complications
- Delete the Synagis guideline for RSV prophylaxis
- Add several new coding specifications regarding use of botulinum toxin and delete the guideline note regarding botulinum toxin use for bladder indications
- Modify the gender dysphoria guideline to add specifications for when cross-sex hormone therapy and sex reassignment surgery are appropriate (effective 1/1/15)

DRAFT

VALUE-BASED BENEFITS SUBCOMMITTEE
Meridian Park Health
Community Health Education Center, Room 117B&C
Tualatin, OR
August 14, 2014
8:30 AM – 1:00 PM

Members Present: Kevin Olson, MD, Chair; James Tyack, DMD; David Pollack, MD (left at 12:35 PM); Susan Williams, MD; Mark Gibson; Irene Crosswell, RPh; Holly Jo Hodges, MD.

Members Absent: Laura Ocker, LAc.

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

Also Attending: Jesse Little, Actuarial Services Unit of DMAP; Laura Hill and Becky Reynolds, Abbvie; Sarah Schmidt, Zoll; Camille Kerr and Deirdre Monroe, Allergan; Amy Burns and Mark Bradshaw, AllCare CCO; Josh Balloch, Pac/West Communications; Seth Adams, WVP Health Authority; Kim Blood, WVCH; Jim Gardner, PhRMA; Bill Struyk, Johnson & Johnson; Paul Neilsen, Astra Zeneca (Medimmune); Lisa Valaika, Genzyme; Rachel Seltzer, OHSU/OHA; Brian Neiuburt, OHA; John Beckwith and Debbie Christensen, Sacred Heart Hospital; Aubrey Harrison, Danielle Askini, and Alex Lausen, Basic Rights Oregon; Megan Bird, MD, Legacy Health Systems; Ann Murray, BMS; Shannon Beatty, Medimmune; Kathleen Klemann, FamilyCare; Lorren Sandt, Caring Ambassadors; Seth Johnstone and Jenn Burleton, TransActive; Eric Larsson, Lovaas Institute; Jim Murray, Hill-Ray; BJ Cavnor, One in Four Chronic Health; Kent Benner, MD, Oregon Clinic.

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

The meeting was called to order at 8:35 am and roll was called. Minutes from the June, 2014 VbBS meeting were previously reviewed and approved at the August 8th meeting. The minutes from the August 8th meeting are not yet available and will be reviewed and approved at the November, 2014 VBBS meeting.

Coffman reviewed the timing of upcoming Prioritized Lists. The HERC retreat has been set for October 30, 2014. There was some discussion about whether this was a public meeting; staff will review the agenda and public meetings law and advise the commission.

Note: line numbers referenced in these minutes are in the format of *October 1, 2014 line/January 1, 2015 line*

➤ **Topic: Straightforward/Consent Agenda**

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

MOTION: To approve the consent agenda as presented. CARRIES 7-0.

Recommended Actions:

- 1) Add 40530 (Resection of lip, more than 1/4, without reconstruction) to line 292/279 CANCER OF SKIN, EXCLUDING MALIGNANT MELANOMA
- 2) Add 77418 (Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session) and 77421 (Stereoscopic X-ray guidance for localization of target volume for the delivery of radiation therapy) to lines 252/242 CANCER OF OVARY and 459/439 CANCER OF GALLBLADDER AND OTHER BILIARY
- 3) Add 35606 (Bypass graft, with other than vein; carotid-subclavian) to line 440/419 TRANSIENT CEREBRAL ISCHEMIA; OCCLUSION/STENOSIS OF PRECEREBRAL ARTERIES WITHOUT OCCLUSION
- 4) Add 35452 (Transluminal balloon angioplasty, open; aortic) to line 472/452 ATHEROSCLEROSIS, AORTIC AND RENAL
- 5) Add 15120 (Split-thickness autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; first 100 sq cm or less, or 1% of body area of infants and children) and 15121 (each additional 100 sq cm, or each additional 1% of body area of infants and children, or part thereof) to line 448/427 COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT
- 6) Add 14040 (Adjacent tissue transfer or rearrangement, forehead, cheeks, chin, mouth, neck, axillae, genitalia, hands and/or feet; defect 10 sq cm or less) to line 459/438 HYPOSPADIAS AND EPISPADIAS
- 7) Add 62311 (Injection(s), of diagnostic or therapeutic substance(s), including anesthetic, antispasmodic, opioid, steroid, other solution, not including neurolytic substances, including needle or catheter placement, includes contrast for localization when performed, epidural or subarachnoid; lumbar or sacral) to lines 78/75 NEUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS; ATTENTION TO OSTOMIES and 318/297 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS
- 8) Add 90670 (Pneumococcal conjugate vaccine, 13 valent) to line 3 PREVENTIVE SERVICES, BIRTH TO 10 YEARS OF AGE and 4 PREVENTIVE SERVICES, OVER AGE OF 10 of the October 1, 2014 list and line 3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS of January 1, 2015 list
 - a. Advise DMAP to remove 90670 from the Excluded List.

➤ **Topic: Nerve blocks**

Discussion: Smits introduced the summary document regarding nerve blocks. The subcommittee felt that the return of these codes to the Ancillary List was the better of the two proposed staff recommendations. This will allow the nerve blocks to continue to be treated as anesthesia for the peri-operative uses. Additionally, HERC staff could not find previous discussion/rationale for moving these codes from Ancillary to the Prioritized List. The Subcommittee felt that this was likely a mistake and should be corrected. The guideline note is recommended to be changed to an Ancillary Guideline.

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

Recommended Actions:

- 1) Remove all nerve block CPT codes (64400-64450) from lines on the Prioritized List
- 2) DMAP was advised to place CPT codes (64400-64450) on the Ancillary List
- 3) Make the current nerve block guideline into an Ancillary Guideline and modify to add the CPT codes. See Appendix A for final approved wording.
- 4) Note: The meeting materials mistakenly listed the code range as 64400-64550

➤ **Topic: Diabetic retinopathy codes**

Discussion: Smits presented the staff summary for this topic. Allergan representatives informed staff that GN 116 needs to be considered for modification to allow pairing of intraocular steroids with the new FDA approved indication for limited use in diabetic retinopathy. Staff agreed to look into this possible GN change and bring back for further discussion at the November, 2014 VbBS meeting.

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

Recommended Actions:

- 1) Add the 362.0x codes (diabetic retinopathy, mild/moderate/severe, with or without proliferative retinopathy, and diabetic macular edema) to line 106/100 DIABETIC AND OTHER RETINOPATHY
 - a. Advise DMAP to remove the 362.0x codes from the Excluded List
 - b. Note: there was a typographical error in the meeting materials. The correct ICD-9 code is 362.0x, not 367.0x
- 2) Add all codes in the E10.3xx family (Type 1 diabetes mellitus with ophthalmologic complications) to line 100 DIABETIC AND OTHER RETINOPATHY for the January 1, 2015 Prioritized List

- 3) Add all codes in the E08.3xx family (diabetes due to underlying condition with retinopathy), E09.3xx family (drug or chemical induced diabetes with retinopathy), E11.3xx family (Type 2 diabetes mellitus with ophthalmologic complications), and E13.3xx family (other specified diabetes with retinopathy) to line 30 TYPE 2 DIABETES MELLITUS for the January 1, 2015 Prioritized List
- 4) Staff will review possible changes to GN116 for the November, 2014 VbBS meeting

➤ **Topic: Tympanostomy tube removal**

Discussion: Livingston reviewed the material in the packet for this topic. There was minimal discussion.

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

Recommended Actions:

- 1) Make no changes to the placement of tympanic membrane perforation diagnosis codes
- 2) Add a new guideline specifying that retained tympanostomy tube removal is a covered procedure even if the underlying diagnosis for placement of these tubes was a non-covered diagnosis. See Appendix B for guideline wording.

➤ **Topic: Spinal manipulation for tension and migraine headaches**

Discussion: Smits reviewed the materials in the meeting packet for this topic. The subcommittee discussed that the evidence for treatment of migraine headache and tension headache showed moderate to good evidence of lack of effectiveness, which is generally a rationale for removing a service from a Prioritized List pairing. There was some discussion about adding a guideline note specifying what is meant by “cervicogenic headache.” The group decided that such a guideline note could be added later if the health plans required assistance with this definition.

MOTION: To approve the code changes and coding specification as presented. CARRIES 6-1 (Opposed: Hodges).

Recommended Actions:

- 1) Remove osteopathic and chiropractic manipulation (CPT 98926- 98929, 98940-98943) from line 435/414 MIGRAINE HEADACHES
- 2) Add the following coding specifications to line 563/546 TENSION HEADACHES
 - i. “OMT and CMT (CPT 98926- 98929, 98940-98943) pair on this line only with cervicogenic headache (R51).”

➤ **Topic: Wearable cardiac defibrillators**

Discussion: Smits reviewed the packet materials regarding wearable cardiac defibrillators. Sarah Schmidt, representing Zoll, the company which manufactures Life Vest, gave testimony that the purpose of this device is a temporary use until ICD placement or until the patient has his or her medications optimized and no longer will need an ICD. Ms. Schmidt noted that the studies regarding the effectiveness of Life Vest have difficulties in their methodology, although she was unsure what the issues with the methodology actually were. These methodology issues are the reason that no mortality benefit was seen in these studies. Ms. Schmidt stated that there are studies which show what the therapeutic shock rates were, and noted that she can provide these studies to HERC staff. She noted that in the Zoll studies, 74% of patients who received a shock were alive 6 months later. She noted that the Life Vest allows discharge from hospital sooner. Zoll is currently conducting an RCT of the Life Vest with planned release of the results in fall 2015.

Subcommittee discussion centered around how successfully the vests stop ventricular fibrillation or ventricular tachycardia, and how often the shocks given by the vests are for these arrhythmias. It was noted that the lethal rhythms treated by this device generally have no symptoms other than sudden death, and so cannot be adequately treated by other means besides a bedside defibrillator. There is increasing numbers of requests for these devices. Hospitals and physicians are hesitant to discharge patients without these devices, as there is not another method in place to treat any fatal arrhythmias which might occur at home. Olson requested data on how often these devices are successfully converting serious arrhythmias. It was noted that the lack of evidence of effective reduction in mortality might stem from lack of patient compliance with wearing the device. Hodges noted that Life Vest use can be monitored, and that her health plan takes back the device if it is not being worn 21 or more hours a day.

The decision was made to table this topic and have HERC staff find more information on the rate of successful shock of such lethal rhythms as ventricular fibrillation or ventricular tachycardia.

Action:

- 1) This topic was tabled until the November, 2014 VBBS meeting.

➤ **Topic: Fibromyalgia related diagnoses (general conditions and chronic fatigue syndrome)**

Discussion: Smits reviewed the materials of general conditions related to fibromyalgia. The subcommittee felt that Rheumatism, unspecified and Fasciitis,

unspecified should not be moved to the fibromyalgia line as this would raise their priority on the Prioritized List.

Smits also reviewed the materials summarizing the research and recommendations regarding chronic fatigue syndrome. There was minimal discussion.

MOTION: To approve the code changes and line name change as amended. CARRIES 7-0.

Recommended Actions:

- 1) Move ICD-9 359.9 (Myopathy, unspecified) from lines 75,297,349,381 to the new fibromyalgia line
- 2) Keep ICD-10 G72.9 (Myopathy, unspecified) on the Excluded List.
- 3) Add chronic fatigue syndrome (ICD-9 780.71/ICD-10 R53.82) to the new fibromyalgia line
 - a. Advise DMAP to remove ICD-9 780.71/ICD-10 R53.82 from the Excluded List
- 4) Change line name to “Fibromyalgia, [Chronic Fatigue Syndrome, and Related Disorders](#)”

➤ **Topic: Coverage guidance—Hyperbaric Oxygen**

Discussion: Smits reviewed the packet materials regarding hyperbaric oxygen coverage. There was minimal discussion.

MOTION: To approve the code and guideline note change as presented. CARRIES 7-0.

Recommended Actions:

For the biennial review (to be reviewed by HERC later in the day)

- 1) Combine the two hyperbaric oxygen lines (lines 336 and 373) into one line placed at line 336 for the next biennial Prioritized List.

For review by HERC in November, along with the coverage guidance, for potential inclusion in January 1, 2015 list:

- 1) Add ICD-9 250.7, 250.8 and ICD-10 E11.5x,E11.621,E11.622,E11.628, S07.xxx,S17.xxx,S38.xxx, S57.xxx,S67.xxx, S77.xxx,S87.xxx,S97.xxx, and T79.Axx, to line 336_TOXIC EFFECT OF GASES, FUMES, AND VAPORS REQUIRING HYPERBARIC OXYGEN
- 2) Remove ICD-9 526.4, 686.00-686.09,709.3 and ICD-10 M46.20-M46.39 and M86.9 from line 336
- 3) Modify GN 107 as shown in Appendix A

➤ **Topic: Coverage guidance—percutaneous interventions for cervical spine pain**

Discussion: The summary document was reviewed. A mistake in the recommendations was found: CPT 64490-64495 was proposed for exclusion as well as for addition to 3 lines on the Prioritized List. The proposed placement on the Excluded list was a mistake.

Hodges cautioned that there would be a large demand for these types of procedures if coverage is added. Gibson expressed concern that the recommendations from HTAS to cover cervical epidural steroid injections and facet joint neurotomy were weak and based on a weak level of evidence. Shaffer commented that HTAS was led to recommend coverage based on the evidence plus clinical expertise and a desire to avoid more costly alternatives, such as spinal surgery. Gibson noted that the CCOs could elect to cover these procedures for cases in which they would help avoid a surgery, without adding these services to the Prioritized List and requiring coverage in all cases. He was concerned about adding these procedures to the Prioritized List based on weak evidence and provider testimony. The HTAS report was reviewed. The rationale for recommending adding coverage for epidural spinal steroid injections was found to be “Though quality of evidence from trusted sources is very low, there is evidence from additional sources, namely a retrospective single cohort study, of some benefit when the recommended criteria are met. Additionally, other payer policies include a similar recommendation, namely Medicare and Washington State’s payer policies.” Williams expressed concern over using a retrospective cohort study as the basis for the decision. There was general concern over the low level of evidence and over using other payer policies as a deciding factor for adding a service to the Prioritized List. However, some members noted that these types of procedures may prevent surgery, reduce ER visits, lower narcotic use, and have other beneficial outcomes.

HERC staff clarified that currently, epidural steroid injections are ancillary. This was felt to give these procedures the same status as procedures already included for coverage on the Prioritized List—such procedures must have evidence of ineffectiveness or evidence of harm or lower cost effectiveness compared to other procedures in order to be taken off the Prioritized List and therefore take away existing coverage. Procedures considered for initial addition to the list have a higher bar—they must have good evidence of effectiveness. The group initially felt that ancillary procedures should have the lower bar of evidence for inclusion on the List. However, this topic was readdressed later in the meeting, and several subcommittee members expressed concern with this policy. It was felt that many ancillary procedures were never formally reviewed and had a formal placement decision. Therefore, these procedures should be fully reviewed before addition to the List, just like new procedures. HERC staff agreed that this policy needed to be discussed further and placed it on the agenda for the VBBS/HERC retreat in October.

Hodges noted that clarification of when epidural steroids should be covered, such as in the proposed guideline, would be very helpful for the CCOs as these procedures are currently covered as ancillary. Shaffer noted that these injections are treatments and do not belong on the Ancillary List. Therefore, some placement decision needs to be made.

The subcommittee members noted that facet joint neurotomy was currently excluded. The evidence summary in the HTAS report stated that the recommendation for addition to coverage was based on the following: "Though quality of evidence from trusted sources is very low, the evidence shows there is some benefit when the recommended criteria are met. Coverage with these criteria was recommended by appointed expert." There was general agreement that expert opinion was not good enough evidence to justify coverage when the quality of evidence from trusted sources was very low. The group felt that facet joint neurotomy should not be added to the List.

Initially, the subcommittee voted to approve the addition of epidural steroid injections with the appropriate guideline and to not approve the addition of facet joint injections (Vote 6-0 with Pollack abstaining). However, this decision was reopened at a later point in the meeting and voided (Vote 7-0). The subcommittee wished to have this topic returned for further discussion to their November meeting.

Actions:

- 1) HERC staff will add a discussion about the level of evidence required for adding ancillary procedures to the Prioritized List to the VBBS/HERC agenda for the October retreat
- 2) This topic was tabled for further discussion in November.

➤ **Topic: Guideline Note 37, Disorders Of Spine With Neurologic Impairment**

Discussion: Smits introduced the summary document on this topic. There was no discussion.

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

Recommended Action:

- 1) GN 37 was modified as shown in Appendix A

➤ **Topic: Rehabilitation guideline**

Discussion: Smits reviewed the packet materials regarding suggested changes to the rehabilitation guideline. Olson expressed frustration with the medical directors requesting changes to VbBS decisions when they are not coming to

VbBS meetings. Smits noted that there has not been a medical director representative on the VbBS for over a year, since Chris Kirk left. This meeting is the first official meeting for the new medical director representative, Holly Jo Hodges, who promised to bring the medical directors input to the VbBS meetings going forward.

The subcommittee felt that the staff recommended wording, including the suggesting additional wording, for the rehabilitation guideline was acceptable.

MOTION: To approve the guideline note changes as presented with additional optional language in the meeting materials. CARRIES 7-0.

Recommended Action:

- 1) Modify the rehabilitation guideline wording as shown in Appendix A

➤ **Topic: Lymphedema guideline**

Discussion: Smits presented the summary on proposed changes to the lymphedema guideline. John Beckwith, PT, testified that he was very concerned that the language in the guideline be very clear that compression dressings/garments were covered even when no complications were present. The subcommittee felt that the wording was sufficient. Hodges requested that clarification be made to the guideline to specify whether compression dressings included compression garments. Smits offered amended wording, adding in the term "garments." Beckwith requested that chronic venous insufficiency (CVI) be covered for compression dressings when appropriate. Smits reviewed her previous findings that CVI includes a range of conditions, from very mild to quite severe. It would be difficult to write a guideline specifying at what stage CVI was covered. The subcommittee requested that HERC staff work with experts to see if some coverage of compression dressings/garments should be done for CVI.

MOTION: To approve the guideline note changes as amended. CARRIES 7-0.

Recommended Actions:

- 1) GN 43 was modified as shown in Appendix A
- 2) HERC staff to evaluate potential coverage of compression dressings/garments for chronic venous insufficiency and bring back for subcommittee review at a future date

➤ **Topic: Denture guideline**

Discussion: This topic was tabled until the November, 2014 VbBS meeting.

➤ **Topic: Adenoidectomy—revisions to the obstructive sleep apnea guideline and sinusitis surgery guideline**

Discussion: This topic was tabled until the November, 2014 VbBS meeting.

➤ **Topic: RSV guideline**

Discussion: Livingston reviewed the summary document for proposed revisions to the RSV guideline. The CCO representatives testified that referring to P&T criteria would not be acceptable to them. The CCOs have their own committees and develop their own coverage criteria. They do not attend or participate in DMAP's P&T Committee meetings and do not feel that their preferences or opinions are taken into account in the P&T decision making process. If no guideline referring to P&T was adopted, then coverage of Synagis would revert to the individual CCO P&T committee decisions (or DMAP P&T coverage guidance for fee-for-service patients). This was felt to be the preferable alternative.

There was also public comment received from Paul Nielson, AstraZeneca, who raised concerns about the quality of the new American Academy of Pediatrics guideline on RSV prophylaxis.

The subcommittee decided to not adopt a new guideline referring to DMAP P&T criteria. However, it was recognized that the current Synagis guideline was out of compliance with national coverage recommendations by the American Academy of Pediatrics. Because DMAP and CCO P&T committee decisions can be much more timely than VbBS/HERC guideline note changes, the subcommittee decided to remove the Synagis guideline and similar drug related guidelines and not add any guidelines referring to DMAP P&T decisions.

MOTION: To approve the guideline note deletion but reject the proposed new guideline note. CARRIES 7-0.

Recommended Action:

- 1) Delete GN 69

➤ **Topic: Botulinum toxin**

Discussion: Smits reviewed the summary document regarding Botox. The VbBS had previously indicated that they did not wish to have guidelines referring to the DMAP P&T coverage criteria (see "RSV guideline" discussion above). The proposed new guideline referring to P&T criteria was therefore not accepted.

MOTION: To approve the coding changes, coding specifications and guideline note deletion but not the proposed new guideline note. CARRIES 7-0.

Recommended Actions:

- 1) Add 46505 (Chemodenervation of internal anal sphincter) to line 506/532
CHRONIC ANAL FISSURE
- 2) Remove 67345 (Chemodenervation of extraocular muscle) from line 397/372
AMBLYOPIA
- 3) Do not add coverage for botulinum toxin injections for treatment of neck or
lower back pain or chronic daily headaches
- 4) Keep the coding specification shown below on line 388/364 DYSTONIA
(UNCONTROLLABLE); LARYNGEAL SPASM AND STENOSIS
 - a. "Chemodenervation with botulinum toxin injection (CPT 64612, 64616) is
included on this line only for treatment of blepharospasm (ICD-9
333.81/ICD-10-CM G24.5), spasmodic torticollis (ICD-9 333.83/ICD-10-
CM G24.3), and other fragments of torsion dystonia (ICD-9 333.89/ICD-
10-CM G24.9)."
- 5) Add the coding specification shown below to line 318/297 NEUROLOGICAL
DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC
CONDITIONS
 - a. "Chemodenervation with botulinum toxin injection (CPT 64642-64647) is
included on this line for treatment of upper and lower limb spasticity (ICD-
9 333.6x, 333.7x, 340.xx, 341.0, 342.xx, 343.xx, 344.0x, 344.1, 344.2,
344.3x, 344.4x, 344.5, 344.89, 344.9, 359.0-359.2, 438.2x-438.5x/ICD-10
G24.02, G24.1, G35, G36.0, G71.xx, G80-G83, I69.03-I69.06).
- 6) Add the coding specification shown below to lines 452 STRABISMUS
WITHOUT AMBLYOPIA AND OTHER DISORDERS OF BINOCULAR EYE
MOVEMENTS; CONGENITAL ANOMALIES OF EYE/354 STRABISMUS
DUE TO NEUROLOGIC DISORDER and 398 STRABISMUS WITHOUT
AMBLYOPIA AND OTHER DISORDERS OF BINOCULAR EYE
MOVEMENTS; CONGENITAL ANOMALIES OF EYE; LACRIMAL DUCT
OBSTRUCTION IN CHILDREN
 - a. "Chemodenervation with botulinum toxin injection (CPT 67345) is included
on this line for the treatment of strabismus due to other neurological
disorders (ICD-9 378.73 /ICD-10 H50.89)."
- 7) Add the coding specification shown below to line 421 ACHALASIA, NON-
NEONATAL/382 ESOPHAGEAL STRICTURE; ACHALASIA
 - a. "Chemodenervation with botulinum toxin injection (CPT 43201) is included
on this line for treatment of achalasia (ICD-9 530.0/ICD-10 K22.0)."
- 8) Add the coding specification shown below to line 542/523 DISORDERS OF
SWEAT GLANDS
 - b. "Chemodenervation with botulinum toxin injection (CPT 64650, 64653) is
included on this line for the treatment of axillary hyperhidrosis and palmar
hyperhidrosis (ICD-9 705.2 and 780.8/ICD-10 L74.52, R61).
- 9) Delete GUIDELINE NOTE 103, CHEMODENERVATION OF THE BLADDER

➤ **Topic: Gender dysphoria**

Discussion: Smits reviewed the summary document in the meeting packet. There was considerable discussion regarding concerns for lack of an age restriction for surgical procedures. Smits reviewed that the Oregon age of consent for surgical procedures is age 15. Olson felt that these types of procedures should not be singled out for restriction until age 18 or even higher, as many other procedures which have life-long impact can be consented to at age 15. Expert testimony by Danielle Askini from Basic Rights Oregon and Jenn Burleton from TransActive indicated that youth are required to have extensive evaluations by qualified mental health professionals and that the year of hormone therapy required in the guideline acts as another safeguard against rash decisions by youth.

There was a minor edit to the proposed guideline to add in a missing word.

MOTION: To approve the line rescoring, updated treatment description, and the addition of cross-sex hormone therapy and various surgical procedures related to sex reassignment to the gender dysphoria line, and the new guideline as amended. CARRIES 5-1 (Opposed: Tyack, Absent: Pollack).

Recommended Actions:

- 1) Change the treatment description of the gender dysphoria line to ~~MEDICAL/PSYCHOTHERAPY~~ MEDICAL AND SURGICAL TREATMENT; PSYCHOTHERAPY
- 2) Rescore the gender dysphoria line as shown below:
 - a. Scoring proposal
Category: 6
HL: 6
Suffering: 4
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 3
Effectiveness: 2
Need for service: 1
Net cost: 2
Score: 1040
Approximate line placement: 312
- 3) Add cross-sex hormone therapy to the new gender dysphoria line
- 4) Add CPT 19301-19304, 53430, 54125, 54400-54417, 54520, 54660, 54690, 55175-55180, 55970, 55980, 56625, 56800, 56805, 56810, 57106-57107, 57110-57111, 57291-57292, 57335, 58150, 58180, 58260-58262, 58275-58291, 58541-58544, 58550-58554, 58570-58573, 58661, 58720 to the new gender dysphoria line
 - a. Advise DMAP to remove CPT 55970 and 55980 from the Excluded List

- 5) Modify the guideline for the new gender dysphoria line as shown in Appendix A
- 6) Note that all of these recommended actions would take effect on January 1, 2015 when the new gender dysphoria line appears on the Prioritized List

➤ **Topic: Hepatitis C**

Discussion: Livingston reviewed the summary document regarding treatments for hepatitis C in the meeting packet. Written testimony from CCOs, legislators and concerned citizens was received.

The following public testimony was received verbally:

Amy Burns and Mark Bradshaw from AllCare presented a collaborative statement from 9 CCOs. The collective strongly discouraged a guideline note requiring CCOs to adhere to the P&T Committee's drug use criteria. They strongly felt that each CCO manages their own drug use and formularies and this drug class should be no different. They also had specific concerns about the criteria including:

- 1) Allowing off-label use of simeprevir and sofosbuvir
- 2) Allowing for off-label use for patients who are post transplant. This goes against OARs that do not allow for investigational or experimental practices. There is no outcome data to support this. The liver transplant population has not been studied and is not recommended in the Sovaldi package insert.
- 3) Subjective language around who can prescribe
- 4) Important psychosocial and medical factors around treatment that aren't addressed

Jim Gardner, Oregon Council for PhMRA, a paid advocate, recommended not looking at single therapeutic products and raised legal concerns with this approach.

Ann Murray, Bristol Myers Squibb, stated that she thinks this would be the first time HERC would have taken this approach, in which a treatments specific FDA-approved medication would be placed on an unfunded line while all other prescription medications for this condition remain funded ~~for a condition appear both on a funded and unfunded line.~~ Ms. Murray also submitted written testimony summarizing when treatments for a condition appear on both funded and unfunded lines, which she testified did not contain any instances of only a single drug treatment being included on the lower line.

Subcommittee members made a request to PhRMA to decrease the cost of the drug, with the answer that they appreciated the comment.

Kimberly Wyatt, Willamette Valley Community Health CCO and Dr. Seth Adams, pharmacist with WVCH, offered public comment. They stated they have their own pharmacy and therapeutics committee and have already created PA criteria for approval of these medications. It is important to the CCOS to have freedom to develop their own criteria. If there was going to be accountability to another organization (DMAP's P&T Committee) then CCOs would have wanted to be responsible in the development of these criteria.

Subcommittee members asked about the CCOs concerns regarding criteria in the proposed guideline note for drug and alcohol testing. It was clarified that they felt 6 months sobriety was too short of a time. They also require a mental health evaluation to assess readiness to treat and ascertain whether patients are compliant with prescription drugs for other diseases, such as diabetes and hypertension.

Lorren Sandt, from Caring Ambassadors, and BJ Cavnor, 1 in 4 Chronic Disease, testified as well, both stating pharmaceutical funding for their organizations. Sandt requested hepatitis C drug treatments should remain above the funding line and that everyone with hepatitis C should be treated with these drugs. She also pointed to the AASLD/IDSA guideline not requiring abstinence or sobriety. Cavnor requested a workgroup that would follow national guidelines and demanded that all people be allowed to come to the table.

Dr. Kent Benner offered testimony with no current conflicts of interest. He spoke about the community standard that was developed by local hepatologists, and discussed the rationale for this.

Subcommittee members discussed the significant impact of these medications on the budget. There was a proposal to table the decision. Given the concerns CCOs have about the reference to P&T criteria, the need for ongoing dialogue, the new AASLD guidelines, it was felt that a final decision on this policy should be tabled until a future meeting.

It was clarified that there will be a pharmacoeconomic analysis available by the November meeting and that an updated DERP report and NICE guidelines may be available later this year or early next year as well.

MOTION: To reject the proposed new guideline regarding treatment of hepatitis C and table the topic until a future meeting. CARRIES 7-0.

Recommended Actions:

- 1) None

➤ **Topic: Proposed "Non covered" section of the Prioritized List**

Discussion: Smits introduced this topic and noted that the new “non-covered” table was presented for approval in concept only. There was minimal discussion.

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Actions:

- 1) HERC staff will continue to work on developing the “non-covered” table and will publish it as a new portion of the January 1, 2015 Prioritized List.

➤ **Topic: Applied behavioral analysis for treatment of non-autistic self-injurious behavior**

Discussion: This topic was tabled to the August HERC meeting.

Actions: See minutes from the August HERC meeting.

➤ **Topic: Standardized assessment tools for evaluating progress for autism spectrum disorder**

Discussion: This topic was tabled to the August HERC meeting.

Actions: See minutes from the August HERC meeting.

➤ **Public Comment:**

No additional public comment was received.

➤ **Issues for next meeting:**

- Wearable cardiac defibrillators
- Denture guideline
- Adenoidectomy—revisions to the obstructive sleep apnea guideline and the sinusitis surgery guideline
- Coverage guidance—percutaneous interventions for cervical spine pain
- A new breastfeeding supplies guideline
- Unilateral hearing loss in adults
- OMT/CMT and the dysfunction lines
- Tobacco cessation coverage
- Tobacco smoking and procedures
- PET scan for fever of unknown origin
- Unilateral tonsillar hypertrophy
- Various straightforward coding changes

➤ **Next meeting:**

November 13, 2014 at Meridian Park Health Education Center, Tualatin, OR
Room 117B&C.

➤ **Adjournment:**

The meeting was adjourned at 1:30 PM.

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Appendix A

Revised Guideline Notes

~~GUIDELINE NOTE 76~~ ANCILLARY GUIDELINE A3, NERVE BLOCKS (Effective October 1, 2014)

~~Lines 1,3,6,8,9,11,20,24,25,28,30,32,37-41,46-55,59-63,65,67,68,70-76,81-100,102-105,107,109-112,115-121,123-125,129-132,134-145,147,148,154,156-164,166-170,172-175,178,180,183-195,197-201,203,204,206,208,209,211-214,216-221,223,225-228,230,232-239,241-251,253-255,257-267,269,273-275,277-280,283-286,289-294,297-306,308-312,314-317,319-324,327,328,330-335,337-341,343,344,346,349,350,352,354-360,362-370,372,374-376,378-384,386,389,391,392,394,397-402,404-408,410,412,417,419-424,426-428,430-436,438-441,443-447,450,452,453,456,458,459,464-466,468-472,474,476,477,480-484,486,487,496,504,519,526,527,532,535,549,568,630~~

The Health Evidence Review Commission intends that single injection and continuous nerve blocks ([CPT 64400-64550](#)) should be covered services if they are required for successful completion of, perioperative pain control for, or post-operative recovery from a covered operative procedure when the diagnosis requiring the operative procedure is also covered. Additionally, nerve blocks are covered services for patients hospitalized with trauma, cancer, or intractable pain conditions, if the underlying condition is a covered diagnosis.

GUIDELINE NOTE 6, REHABILITATIVE THERAPIES (Effective October 1, 2014)

~~Lines 37,50-52,64,74-76,78,80,85,89,90,94,95,98-101, 108, 109, 115, 116, 122, 129, 139, 141-143,145,146,158,161,167,179,184,185,189, 190, 192, 194, 195, 201, 202, 208,209,216,226,237,239,270,271,273,274,279,288,289,293,297,302,304,307-309, 318, 336,342,349, 350, 363, 367, 369, 375,376,378, 382,384,385,387, 400,406, 407, 434, 441,443,448,455,467,478,489,493,507,516,535,549,562,580, 597,619,638~~

A total of 30 visits per year of rehabilitative therapy (physical, occupational and speech therapy, and cardiac and vascular rehabilitation) are included on these lines when medically appropriate. Additional visits, not to exceed 30 visits per year, may be authorized in exceptional circumstances, such as in cases of rapid growth/development.

Physical, occupational and speech therapy, and cardiac and vascular rehabilitation are only included on these lines when the following criteria are met:

- 1) therapy is provided by a licensed physical therapist, occupational therapist, speech language pathologist, physician, or other practitioner licensed to provide the therapy,
- 2) there is objective, measurable documentation of clinically significant progress toward the therapy plan of care goals and objectives,
- 3) the therapy plan of care requires the skills of a **therapist** [medical provider](#), and
- 4) the client and/or caregiver cannot be taught to carry out the therapy regimen independently.

Appendix A

No limits apply while in a skilled nursing facility for the primary purpose of rehabilitation, an inpatient hospital or an inpatient rehabilitation unit.

Spinal cord injuries, traumatic brain injuries, or cerebral vascular accidents are not subject to the visit limitations during the first year after an acute injury.

GUIDELINE NOTE 37, DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT (Effective October 1, 2014)

Lines 374,545

Diagnoses are included on Line 374 when objective evidence of neurologic impairment or radiculopathy is present, as defined as:

- 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

Otherwise, disorders of spine not meeting these criteria (e.g. pain alone) fall on Line 545.

GUIDELINE NOTE 43, LYMPHEDEMA (Effective October 1, 2014)

Lines 448,597,598

Lymphedema treatments are included on these lines when medically appropriate. These services are to be provided by a licensed practitioner who is certified by one of the accepted lymphedema training certifying organizations or a graduate of one of the National Lymphedema Network accepted training courses within the past two years. The only accepted certifying organization at this time is LANA (Lymphology Association of North America; <http://www.clt-lana.org>). Treatments for lymphedema are not subject to the visit number restrictions found in Guideline Note 6 REHABILITATIVE THERAPIES. It is the intent of the HERC that compression dressings/garments and other medical equipment needed for the treatment of lymphedema be covered even in the absence of ulcers or other complications.

GUIDELINE NOTE 43, LYMPHEDEMA (Effective January 1, 2016)

Lines ~~427,577,579~~ XXX (new lymphedema line ~427)

Lymphedema treatments are included on this line ~~these lines~~ when medically appropriate. These services are to be provided by a licensed practitioner who is certified by one of the accepted lymphedema training certifying organizations or a graduate of one of the National Lymphedema Network accepted training courses within the past two years. The only accepted certifying organization at this time is LANA (Lymphology

Appendix A

Association of North America; <http://www.clt-lana.org>). Treatments for lymphedema are not subject to the visit number restrictions found in Guideline Note 6 REHABILITATIVE THERAPIES. It is the intent of the HERC that compression dressings/garments and other medical equipment needed for the treatment of lymphedema be covered even in the absence of ulcers or other complications.

GUIDELINE NOTE 107, HYPERBARIC OXYGEN (Effective date pending HERC review of coverage guidance, not to be prior to January 1, 2015)

Lines 336, ~~373~~ (delete only for biennial review List)

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

- ~~when paired with ICD-9-CM code 526.4 for osteomyelitis of the jaw only~~
- when paired with ICD-9-CM codes 250.7x and 250.8x/ICD-10-CM E11.5x and E11.621, E11.622, E11.623 for diabetic wounds with gangrene OR diabetic wounds of the lower extremities in patients who meet the all of the following criteria:
 - Patient has Type 1 or Type 2 diabetes and has a lower extremity wound that is due to diabetes, AND
 - Patient has a wound classified as Wagner grade III or higher, AND
 - Patient has failed an adequate course of standard wound therapy including arterial assessment, with no measurable signs of healing after at least thirty days, AND
 - Wounds must be evaluated at least every 30 days during administration of hyperbaric oxygen therapy. Continued treatment with hyperbaric oxygen therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.
- when paired with ICD-9-CM codes 526.89/ ICD-10--CM codes M27.8 for osteoradionecrosis of the jaw only
- when paired with ICD-9-CM codes 639.0, 670.02, and 670.04/ ICD-10--CM codes O08.0, M60.000-M60.09 only if the infection is a necrotizing soft-tissue infection
- ~~when paired with ICD-9-CM codes 730.10-730.99/ICD-10-CM M46.20-M46.39, M86.9 only for chronic refractory osteomyelitis unresponsive to conventional medical and surgical management~~
- when paired with ICD-9-CM codes 927-929/ICD-10 CM codes S07.xxx, S17.xxx, S38.xxx, S47.1xxA-S47.1xxD, S47.2xxA-S47.2xxD, S47.9xxA-S47.9xxD, S57.xxx, S67.xxx, S77.xxx, S87.xxx, S97.xxx, T79.Axx, only for posttraumatic crush injury of Gustilo type III B and C
- when paired with ICD-9-CM codes 990/ ICD-10--CM codes T66.xxxA only for osteoradionecrosis and soft tissue radiation injury
- when paired with ICD-9-CM codes 996.52, 996.7/ ICD-10--CM codes T86.820-T86.829, T82.898A, T82.898D, T82.9xxA, T82.9xxD, T83.89xA, T83.89xD, T83.9xxA, T83.9xxD, T84.89xA, T84.89xD, T84.9xxA, T84.9xxD, T85.89xA, T85.89xD, T859xxA, T859xxD only for compromised myocutaneous flaps.

Appendix A

GUIDELINE XXX GENDER DYSPHORIA (Effective January 1, 2015)

Line 413

Hormone treatment is included on this line for use in delaying the onset of puberty and/or continued pubertal development with GnRH analogues for gender questioning children and adolescents. This therapy should be initiated at the first physical changes of puberty, confirmed by pubertal levels of estradiol or testosterone, but no earlier than Tanner stages 2-3. Prior to initiation of puberty suppression therapy, adolescents must fulfill eligibility and readiness criteria, and must have a comprehensive mental health evaluation. Ongoing psychological care is strongly encouraged for continued puberty suppression therapy.

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

- 1) have persistent, well-documented gender dysphoria
- 2) have the capacity to make a fully informed decision and to give consent for treatment
- 3) have any significant medical or mental health concerns reasonably well controlled
- 4) have a thorough psychosocial assessment by a qualified mental health professional with experience in working with patients with gender dysphoria

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

- 1) have persistent, well documented gender dysphoria
- 2) have completed twelve months of continuous hormone therapy as appropriate to the member's gender goals unless hormones are not clinically indicated for the individual
- 3) have completed twelve months of living in a gender role that is congruent with their gender identity unless a medical and a mental health professional both determine that this requirement is not safe for the patient
- 4) have the capacity to make a fully informed decision and to give consent for treatment
- 5) have any significant medical or mental health concerns reasonably well controlled
- 6) have two referrals from qualified mental health professionals with experience in working with patients with gender dysphoria who have independently assessed the patient. Such an assessment should include the clinical rationale supporting the patient's request for surgery, as well as the rationale for the procedure(s)

Appendix B

New Guideline Notes

GUIDELINE NOTE XXX RETAINED TYMPANOSTOMY TUBES (*Effective October 1, 2014*)

Lines 178, 308, 405, 418, 502

Removal of retained tympanostomy tubes under anesthesia, if indicated (CPT code 69424 Ventilating tube removal requiring general anesthesia) or as part of an office visit, are intended to be covered for Line 502 diagnoses with the Line 405 ICD-9 code 383.83 (Retained foreign body of middle ear).

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Code	Description	Placement	Comments
C9741	Right heart catheterization with implantation of wireless pressure sensor in the pulmonary artery, including any type of measurement, angiography, imaging supervision, interpretation, and report	Diagnostic List	Similar code 93451 (Right heart catheterization including measurement(s) of oxygen saturation and cardiac output, when performed) is Diagnostic
C9742	Laryngoscopy, flexible fiberoptic, with injection into vocal cord(s), therapeutic, including diagnostic laryngoscopy, if performed	209 SUPERFICIAL ABSCESSSES AND CELLULITIS 364 DYSTONIA (UNCONTROLLABLE); LARYNGEAL SPASM AND STENOSIS	Similar code 31513 (Laryngoscopy, indirect; with vocal cord injection) is on lines 209,364
G0277	Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval	336 ANAEROBIC INFECTIONS REQUIRING HYPERBARIC OXYGEN 373 TOXIC EFFECT OF GASES, FUMES, AND VAPORS REQUIRING HYPERBARIC OXYGEN	Hyperbaric oxygen guideline will apply
G0279	Diagnostic digital breast tomosynthesis, unilateral or bilateral (list separately in addition to g0204 or g0206)	Non-Covered List	77061-77063 (Digital breast tomosynthesis) on 2015 CPT code review was placed on Non-Covered List
G0464	Colorectal cancer screening; stool-based dna and fecal occult hemoglobin (e.g., kras, ndrg4 and bmp3)	Non-Covered List	
G0466	Federally qualified health center (fqhc) visit, new patient; a medically-necessary, face-to-face encounter (one-on-one) between a new patient and a fqhc practitioner during which time one or more fqhc services are rendered and includes a typical bundle of	Outpatient medical lines	
G0467	Federally qualified health center (fqhc) visit, established patient; a medically-necessary, face-to-face encounter (one-on-one) between an established patient and a fqhc practitioner during which time one or more fqhc services are rendered and includes a	Outpatient medical lines	
G0468	Federally qualified health center (fqhc) visit, ippe or awv; a fqhc visit that includes an initial preventive physical examination (ippe) or annual wellness visit (awv) and includes a typical bundle of medicare-covered services that would be furnished per	3 PREVENTION SERVICES WITH EVIDENCE OF EFFECTIVENESS	
G0469	Federally qualified health center (fqhc) visit, mental health, new patient; a medically-necessary, face-to-face mental health encounter (one-on-one) between a new patient and a fqhc practitioner during which time one or more fqhc services are rendered and	Mental health lines	
G0470	Federally qualified health center (fqhc) visit, mental health, established patient; a medically-necessary, face-to-face mental health encounter (one-on-one) between an established patient and a fqhc practitioner during which time one or more fqhc services	Mental health lines	

G0471	Collection of venous blood by venipuncture or urine sample by catheterization from an individual in a skilled nursing facility (snf) or by a laboratory on behalf of a home health agency (hha)	Diagnostic List	
G0472	Hepatitis c antibody screening, for individual at high risk and other covered indication(s)	Diagnostic List	
G0473	Face-to-face behavioral counseling for obesity, group (2-10), 30 minutes	325 OBESITY (ADULT BMI \geq 30, CHILDHOOD BMI \geq 95 PERCENTILE)	Group nutrition counseling (97804) is on line 325, but not on lower obesity line (594)
G6001	Ultrasonic guidance for placement of radiation therapy fields	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6002	Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6003	Radiation treatment delivery, single treatment area,single port or parallel opposed ports, simple blocks or no blocks: up to 5mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6004	Radiation treatment delivery, single treatment area,single port or parallel opposed ports, simple blocks or no blocks: 6-10mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6005	Radiation treatment delivery, single treatment area,single port or parallel opposed ports, simple blocks or no blocks: 11-19mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6006	Radiation treatment delivery, single treatment area,single port or parallel opposed ports, simple blocks or no blocks: 20mev or greater	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6007	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: up to 5mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6008	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: 6-10mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6009	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: 11-19mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6010	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: 20 mev or greater	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6011	Radiation treatment delivery,3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; up to 5mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines

G6012	Radiation treatment delivery,3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 6-10mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6013	Radiation treatment delivery,3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 11-19mev	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6014	Radiation treatment delivery,3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 20mev or greater	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6015	Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic mlc, per treatment session	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Intensity modulated therapy is on the radiation therapy lines
G6016	Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6017	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (eg,3d positional tracking, gating, 3d surface tracking), each fraction of treatment	97,116,117,119,129,130,133,137,139,161,195,199,203,204,212,214,162,218,219,233,238,241,242,262,263,265,266,274,279,291,292,299,319,320,321,333,359,376, 401, 402, 424, 439,533,600,611	Radiation therapy lines
G6018	Ileoscopy,through stoma; with transendoscopic stent placement (includes predilation)	32 REGIONAL ENTERITIS, IDIOPATHIC PROCTOCOLITIS, ULCERATION OF INTESTINE 46 INTUSSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	2015 CPT code 44384 (Ileoscopy, through stoma; with placement of endoscopic stent (includes pre- and post-dilation and guide wire passage, when performed)) placed on these lines
G6019	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	46 INTUSSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 60 ULCERS, GASTRITIS, DUODENITIS, AND GI HEMORRHAGE 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 170 ANAL, RECTAL AND COLONIC POLYPS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	44392 (Colonoscopy through stoma; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps) and 44394 (snare technique) are on lines 46,105,161,170,647 Line 60 is also appropriate <u>Add 44392 and 44394 to line 60</u>

G6020	Colonoscopy through stoma; with transendoscopic stent placement (includes predilation)	32 REGIONAL ENTERITIS, IDIOPATHIC PROCTOCOLITIS, ULCERATION OF INTESTINE 46 INTUSSUSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	New CPT 44402 (Colonoscopy through stoma; with endoscopic stent placement) is on lines 32, 46, 105, 161, 647
G6021	Unlisted procedure, intestine	Ancillary Codes File	Will require manual review
G6022	Sigmoidoscopy, flexible; with ablation of tumor(s), polyp(s), or other lesions(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	46 INTUSSUSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 60 ULCERS, GASTRITIS, DUODENITIS, AND GI HEMORRHAGE 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 170 ANAL, RECTAL AND COLONIC POLYPS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	Similar code 45333 (Sigmoidoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps) is on lines 46,105,161,170,647 Line 60 is also appropriate <u>Add 45333 to line 60</u>
G6023	Sigmoidoscopy, flexible; with transendoscopic stent placement (includes predilation)	32 REGIONAL ENTERITIS, IDIOPATHIC PROCTOCOLITIS, ULCERATION OF INTESTINE 46 INTUSSUSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	New CPT code 45347 (Sigmoidoscopy, flexible; with placement of endoscopic stent (includes pre- and post-dilation and guide wire passage, when performed)) placed on lines 32, 46, 105, 161, 647
G6024	Colonoscopy, flexible; proximal to splenic flexure; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	46 INTUSSUSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 60 ULCERS, GASTRITIS, DUODENITIS, AND GI HEMORRHAGE 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 170 ANAL, RECTAL AND COLONIC POLYPS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	45384 (Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps) and 45385 (snare technique) are on lines 46,60,105,161,170,647

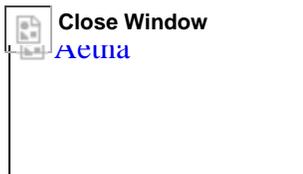
G6025	Colonoscopy, flexible, proximal to splenic flexure; with transendoscopic stent placement (includes predilation)	32 REGIONAL ENTERITIS, IDIOPATHIC PROCTOCOLITIS, ULCERATION OF INTESTINE 46 INTUSSUSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, HAZARDOUS FOREIGN BODY IN GI TRACT WITH RISK OF PERFORATION OR OBSTRUCTION 105 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION 161 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS 647 BENIGN NEOPLASMS OF DIGESTIVE SYSTEM	New CPT code 45389 (Colonoscopy, flexible; with endoscopic stent placement) placed on lines 32, 46, 105, 161, 647
G6027	Anoscopy, high resolution (hra) (with magnification and chemical agent enhancement); diagnostic, including collection of specimen(s) by brushing or washing when performed	Diagnostic List	
G6028	Anoscopy, high resolution (hra) (with magnification and chemical agent enhancement); with biopsy(ies)	Diagnostic List	
G6030	Amitriptyline	Diagnostic List	
G6031	Benzodiazepines	Diagnostic List	
G6032	Desipramine	Diagnostic List	
G6034	Doxepin	Diagnostic List	
G6035	Gold	Diagnostic List	
G6036	Assay of imipramine	Diagnostic List	
G6037	Nortriptyline	Diagnostic List	
G6038	Salicylate	Diagnostic List	
G6039	Acetaminophen	Diagnostic List	
G6040	Alcohol (ethanol); any specimen except breath	Diagnostic List	
G6041	Alkaloids, urine, quantitative	Diagnostic List	
G6042	Amphetamine or methamphetamine	Diagnostic List	
G6043	Barbiturates, not elsewhere specified	Diagnostic List	
G6044	Cocaine or metabolite	Diagnostic List	
G6045	Dihydrocodeinone	Diagnostic List	
G6046	Dihydromorphinone	Diagnostic List	
G6047	Dihydrotestosterone	Diagnostic List	
G6048	Dimethadione	Diagnostic List	
G6049	Epiandrosterone	Diagnostic List	
G6050	Ethchlorvynol	Diagnostic List	
G6051	Flurazepam	Diagnostic List	
G6052	Meprobamate	Diagnostic List	
G6053	Methadone	Diagnostic List	
G6054	Methsuximide	Diagnostic List	
G6055	Nicotine	Diagnostic List	
G6056	Opiate(s), drug and metabolites, each procedure	Diagnostic List	
G6057	Phenothiazine	Diagnostic List	
G6058	Drug confirmation, each procedure	Diagnostic List	

2015 HCPCS Code Review Issues

Stool Based DNA and Fecal Occult Hemoglobin Testing (HCPCS G0464)

- 1) Definition: stool based DNA and fecal occult hemoglobin testing is a new test (Cologuard™) approved by the FDA in August, 2014. This test detects the presence of red blood cells and multiple types of DNA mutations that may indicate the presence of certain kinds of abnormal growths that may be cancers such as colon cancer or precursors to cancer. It is an alternative screening test for colorectal cancer.
- 2) Evidence reviews
 - a. **USPSTF 2008**
 - i. The USPSTF concludes that the evidence is insufficient to assess the benefits and harms of computed tomographic colonography and fecal DNA testing as screening modalities for colorectal cancer. I recommendation
 - ii. Currently has an update to this review in progress
 - b. **Imperiale 2014**
 - i. Trial of screening with fecal immunochemical test (FIT, fecal occult blood testing) vs fecal DNA testing
 1. All patients underwent colonoscopy as gold standard for screening
 - ii. N=9989 average risk persons
 1. 65 (0.7%) found to have colorectal cancer and 757 (7.6%) had advanced precancerous lesions (advanced adenomas or sessile serrated polyps measuring ≥ 1 cm in the greatest dimension) on colonoscopy.
 2. The sensitivity for detecting colorectal cancer was 92.3% with DNA testing and 73.8% with FIT (P = 0.002).
 3. The sensitivity for detecting advanced precancerous lesions was 42.4% with DNA testing and 23.8% with FIT (P<0.001).
 4. The rate of detection of polyps with high-grade dysplasia was 69.2% with DNA testing and 46.2% with FIT (P = 0.004); the rates of detection of serrated sessile polyps measuring 1 cm or more were 42.4% and 5.1%, respectively (P<0.001).
 5. Specificities with DNA testing and FIT were 86.6% and 94.9%, respectively, among participants with nonadvanced or negative findings (P<0.001) and 89.8% and 96.4%, respectively, among those with negative results on colonoscopy (P<0.001).
 6. The numbers of persons who would need to be screened to detect one cancer were 154 with colonoscopy, 166 with DNA testing, and 208 with FIT.
 7. Conclusions In asymptomatic persons at average risk for colorectal cancer, multitarget stool DNA testing detected significantly more cancers than did FIT but had more false positive results.
 - iii. **Yang 2013**, meta-analysis of stool DNA testing
 1. N=20 studies (5876 patients)

2. Multiple DNA markers had a sensitivity of 75.9% and specificity of 88.3 for cancer and 68.3% sensitivity and 91.8% specificity for advanced adenoma for high risk patients
 3. Less accurate for average-risk patients
 4. Conclusions: fecal DNA testing for multiple markers had strong diagnostic significance for cancer and advanced adenoma in high-risk patients
- 3) Other guidelines
- a. American College of Gastroenterology 2008 (**Rex 2008**)
 - i. Fecal DNA testing every 3 years is an acceptable alternative screening strategy (Grade 2 B)
 - ii. Based on older fecal DNA tests
 - iii. FIT costs much less than fecal DNA testing and should be the preferred screening test
 - iv. Additional disadvantages of fecal DNA testing include no established data on which to determine an optimal interval, and the lack of clinical recommendations on how to respond to patients who have positive DNA tests and negative colonoscopies.
 - b. **NCCN 2014**
 - i. Emerging technologies such as stool DNA have shown increasing evidence as a reasonably accurate screening modality, but there are limited data to determine an interval between screening. At present, stool DNA is not considered a primary screening modality.
 - ii. For those unwilling or unable to have screening colonoscopy, there is increasing evidence that a stool DNA test may provide a valuable noninvasive option.
 - iii. Recommendation based on older generation stool DNA tests
- 4) Other policies
- a. **CMS 2014**
 - i. Covers once every 3 yrs for asymptomatic, average risk patients age 50 to 85 years,
 - b. **Aetna 2014**
 - i. Aetna considers colorectal cancer screening of stool using molecular genetic techniques (e.g., Cologuard, ColoSure, PreGen-Plus) experimental and investigational because of insufficient evidence in the peer-reviewed literature.
- 5) HERC staff recommendation:
- a. Place HCPCS G0464 on the **Non-Covered List**
 - i. Promising, but not included in the recommended screening strategies for either USPSTF or NCCN
 - ii. Readdress when new USPSTF review on screening for colorectal cancer is published



Clinical Policy Bulletin:
Colorectal Cancer Screening
Number: 0516

Policy

1. Routine Screening

Aetna considers *any* of the following colorectal cancer screening tests medically necessary preventive services for members aged 50 years and older when these tests are recommended by their physician:

- Colonoscopy (considered medically necessary every 10 years for persons at average risk); *or*
- Double contrast barium enema (DCBE) (considered medically necessary every 5 years for persons at average risk); *or*
- Sigmoidoscopy (considered medically necessary every 5 years for persons at average risk).

In addition, Aetna considers annual screening with immunohistochemical or guaiac-based fecal occult blood testing (FOBT), either alone or in conjunction with sigmoidoscopy, medically necessary preventive services for members beginning at age 50 years. Colorectal cancer screening beginning at age 45 is considered a medically necessary preventive service for African Americans because of the high incidence of colorectal cancer and a greater prevalence of proximal or right-sided polyps and cancerous lesions in this population. There is insufficient evidence to support earlier screening of members at increased risk from smoking or obesity.

Aetna considers screening upper endoscopy experimental and investigational. No current guidelines of leading medical professional organizations or Federal public health agencies recommend routine upper endoscopy screening of asymptomatic persons.

Aetna considers colorectal cancer screening of stool using molecular



Policy History

[Last](#)

[Review:](#) 08/12/2014

Effective: 02/28/2003

Next

[Review:](#) 06/11/2015

[Review History](#)

[Definitions](#)

Additional Information

[Clinical Policy](#)

[Bulletin Notes](#)

genetic techniques (e.g., Cologuard, ColoSure, PreGen-Plus) experimental and investigational because of insufficient evidence in the peer-reviewed literature.

Aetna considers colorectal cancer screening using methylated Septin 9 (ColoVantage) experimental and investigational because of insufficient evidence in the peer-reviewed literature.

Aetna considers colorectal cancer screening using microRNA experimental and investigational because of insufficient evidence in the peer-reviewed literature.

For the ColonSentry test for colorectal cancer screening, see [CPB 0352 - Tumor Markers](#).

2. High-Risk Testing:

Aetna considers colorectal cancer testing with sigmoidoscopy, DCBE, or colonoscopy as frequently as every 2 years medically necessary for members with *any* of the following risk factors for colorectal cancer:

- A first-degree relative (sibling, parent, child) who has had colorectal cancer or adenomatous polyps (screening is considered medically necessary beginning at age 40 years, or 10 years younger than the earliest diagnosis in their family, whichever comes first);
or
- Family history of familial adenomatous polyposis (screening is considered medically necessary beginning at puberty); *or*
- Family history of hereditary non-polyposis colorectal cancer (HNPCC) (screening is considered medically necessary beginning at age 20 years); *or*
- Family history of MYH-associated polyposis in siblings (screening is considered medically necessary beginning at age 25 years); *or*
- Diagnosis of Cowden syndrome (screening is considered medically necessary beginning at age 35 years).

Aetna considers annual FOBT, alone or in conjunction with sigmoidoscopy, medically necessary for testing of members with any of the above risk factors for colorectal cancer.

3. Surveillance:

Aetna considers colorectal cancer surveillance with colonoscopy, flexible sigmoidoscopy or DCBE medically necessary as frequently as every year for members who meet *any* of the following criteria:

- Member has inflammatory bowel disease (including ulcerative colitis or Crohn's disease) (colorectal cancer surveillance is considered medically necessary as frequently as every year); *or*
- Personal history of adenomatous polyps (surveillance is considered

- medically necessary as frequently as every 2 years); *or*
- Personal history of colorectal cancer (surveillance is considered medically necessary as frequently as every year).

Aetna considers annual FOBT, alone or in conjunction with sigmoidoscopy, medically necessary for surveillance of colorectal cancer.

4. Diagnostic Testing:

Aetna considers diagnostic testing with FOBT, colonoscopy, sigmoidoscopy and/or DCBE medically necessary for evaluation of members with signs or symptoms of colorectal cancer or other gastrointestinal diseases. Diagnostic upper endoscopy is considered medically necessary for evaluation of persons with signs and symptoms of upper gastrointestinal disease.

5. Anal Pap Smear:

Aetna considers screening for anal cytological abnormalities (anal Pap smear) or for anal HPV infection experimental and investigational because of the lack of evidence that such screening improves clinical outcomes.

Note: The USPSTF guidelines apply to routine screening. The USPSTF have no A or B recommendations for high-risk screening. The USPSTF guidelines explain: “These recommendations apply to adults 50 years of age and older, excluding those with specific inherited syndromes (the Lynch syndrome or familial adenomatous polyposis) and those with inflammatory bowel disease. The recommendations do apply to those with first-degree relatives who have had colorectal adenomas or cancer, although for those with first-degree relatives who developed cancer at a younger age or those with multiple affected first-degree relatives, an earlier start to screening may be reasonable (USPSTF, 2008).”

See also [CPB 0140 - Genetic Testing](#), [CPB 0352 - Tumor Markers](#), [CPB 0535 - Virtual Gastrointestinal Endoscopy](#), and [CPB 0783 - In Vivo Analysis of Colorectal Polyps and Crohn's Disease](#).

Background

This policy is based on recommendations from the U.S. Preventive Services Task Force (USPSTF) and the American College of Gastroenterology (ACG).

Colorectal cancer (CRC) is the third most commonly diagnosed cancer among persons in the United States. The 5-year survival rate of CRC detected in early states is 90 %, but the 5-year survival rate is only 8 % for those diagnosed after the cancer has metastasized. Almost 90 % of CRC cases are found in persons

age 50 and older.

The American Cancer Society (Levin et al, 2008) recommends the following testing options for the early detection of adenomatous polyps and cancer for asymptomatic adults aged 50 years and older:

Tests that detect adenomatous polyps and cancer:

- Colonoscopy every 10 years; *or*
- Computed tomographic (CT) colonography every 5 years; *or*
- Double-contrast barium enema (DCBE) every 5 years; *or*
- Flexible sigmoidoscopy every 5 years.

Tests that primarily detect cancer:

- Annual fecal immunochemical test with high test sensitivity for cancer; *or*
- Annual guaiac-based fecal occult blood test with high sensitivity for cancer; *or*
- Stool DNA test with high sensitivity for cancer, interval uncertain.

More frequent screening has been recommended for persons with a first-degree relative (parent, sibling or child) with a history of CRC. The increased risk of developing cancer at younger ages may justify beginning screening before the age of 50 in persons with a positive family history, especially when affected relatives developed CRC at younger ages. The American Society of Colon and Rectal Surgeons (2010) recommends that people with a first-degree relative with colon cancer or adenomatous polyps diagnosed at age less than 60 years of age or 2 first degree relatives diagnosed at any age should be advised to have screening colonoscopy starting at age 40 years or 10 years younger than the earliest diagnosis in their family, whichever comes first, and repeated every 5 years. The American Society for Gastrointestinal Endoscopy (2006) has a similar position.

Regular colonoscopic screening is part of the routine diagnosis and management of individuals at high-risk of developing CRC, including those with a family history of hereditary syndromes (familial polyposis, hereditary non-polyposis colon cancer (HNPCC)); individuals with long-standing ulcerative colitis or Crohn's disease; or high-risk adenomatous polyps or colon cancer. Referral to specialists is appropriate. It has been recommended that persons with a family history of adenomatous polyposis begin screening at puberty, and persons with a family history of HNPCC begin screening at 20 to 30 years of age.

Randomized controlled trials (RCTs) have proven that the fecal occult blood test can detect CRC significantly lowers the rate of death from the disease.

Although there are no RCTs proving that sigmoidoscopy reduces the mortality rate from CRC, a number of case-control studies have suggested that

sigmoidoscopy is effective in reducing CRC mortality. The literature indicates that sigmoidoscopy can detect 70 to 80 % of CRC. However, sigmoidoscopy is unable to detect the substantial number of cancers that arise solely in the proximal colon. The literature indicates that some of the additional neoplasms that it misses can be detected by combining sigmoidoscopy with fecal occult blood testing.

Some have advocated whole-bowel screening with colonoscopy or DCBE because it is able to detect proximal colon lesions. One study found that approximately 30 % of cancers detected by colonoscopy would not have been detected by sigmoidoscopy. However, no direct evidence proves that whole-bowel screening, either by colonoscopy or DCBE, reduces mortality, although clinical trials are now underway to investigate this.

A study comparing the use of colonoscopy to DCBE for patients with previously identified polyps found that colonoscopy detected more polyps than DCBE. Double contrast barium enema found only 20 % of adenomatous polyps found by colonoscopy.

Although the rate of complications from colonoscopy has been shown to be low, complications from colonoscopy are more common than from other screening procedures. Perforation of the colon and complications from anesthesia have been reported to occur in 0.1 to 0.3 % of colonoscopies performed by gastroenterologists, and death occurs in 0.01 % of colonoscopies.

The USPSTF released updated recommendations on CRC screening. In contrast to the 2002 USPSTF recommendation, which applied to all adults 50 years of age and older without regard to an age at which to stop screening, USPSTF now recommends routine CRC screening in adults beginning at age 50 and continuing only until age 75 (USPSTF, 2008). The USPSTF recommends the following screening modalities: high-sensitivity fecal occult blood testing (FOBT), sigmoidoscopy with interval FOBT, or colonoscopy. The risks and benefits of these screening methods vary. The USPSTF does not recommend routine screening for adults 76 to 85 years of age; however, there may be considerations that support CRC screening in an individual patient. The USPSTF recommends against screening adults older than 85 years of age. The USPSTF concluded that there is insufficient evidence to permit a recommendation for CT colonography and fecal DNA.

The USPSTF found good evidence that periodic FOBT reduces mortality from CRC and fair evidence that sigmoidoscopy alone or in combination with FOBT reduces mortality. The USPSTF did not find direct evidence that screening colonoscopy is effective in reducing CRC mortality; efficacy of colonoscopy is supported by its integral role in trials of FOBT, extrapolation from sigmoidoscopy studies, limited case-control evidence, and the ability of colonoscopy to inspect the proximal colon. The USPSTF determined that DCBE offers an alternative means of whole-bowel examination, but it is less sensitive than colonoscopy, and there is no direct evidence that it is effective in reducing mortality rates.

The USPSTF noted that it is unclear whether the increased accuracy of colonoscopy compared with alternative screening methods (e.g., the identification of lesions that FOBT and flexible sigmoidoscopy would not detect) offsets the procedure's additional complications, inconvenience, and costs.

The mortality reduction previously reported in FOBT trials was maintained in longer-term follow-up, and a meta-analysis estimated the overall CRC mortality reduction at 15 % for biennial FOBT. Screening with fecal DNA is still an evolving technology, with only 1 fair-quality study in average-risk patients providing data on sensitivity (better than Hemoccult II) and on the proportion of all tests that have positive results (higher than Hemoccult II). There are no new trials that report on mortality for colonoscopy and sigmoidoscopy or newer screening methods, such as fecal DNA and fecal immunochemical testing. The decision analytic modeling analysis performed for the USPSTF projected a comparative benefit to screening with colonoscopy, high-sensitivity fecal blood test, or flexible sigmoidoscopy every 5 years in combination with fecal testing every 3 years or mid-interval screening, relative to the other techniques studied. Despite the lack of direct evidence from clinical trials to ascertain which is the most effective strategy, any of the recommended screening methods is effective compared with no screening.

Guaiaic FOBTs have been recognized among various CRC screening methods as having the highest quality supporting evidence. Immunochemical tests (e.g., Flexsure OBT, InSure FOBT) may be used as an alternative to standard guaiac-based tests of fecal occult blood, and have several potential advantages that make them more convenient than guaiac tests: (i) unlike guaiac tests, a fecal smear is not required for immunochemical tests -- samples may be obtained from a brush sample of toilet bowl water; (ii) unlike guaiac tests, immunochemical tests are not affected by diet or medications, so that dietary and medicinal restrictions are not necessary prior to testing.

In an update of the clinical guidelines on CRC screening and surveillance that were prepared by a panel convened by the U.S. Agency for Health Care Policy and Research (AHRQ) and published in 1997 under the sponsorship of a consortium of gastroenterology societies, Winawer et al (2003) stated that promising new screening tests (virtual colonoscopy and tests for altered DNA in stool) are in development but are not yet ready for use outside of research studies.

Genetic testing of stool samples is also under study as a possible way to screen asymptomatic high-risk individuals for CRC. Colorectal cancer cells are shed into the stool, providing a potential means for the early detection of the disease by detecting specific tumor-associated genetic mutations in stool samples. Several genetic targets (e.g., mutations in p53 genes, deletions within the BAT26 locus, and mutations in K-RAS) are currently under investigation. Research conducted thus far has shown that these tests can detect CRC in people already diagnosed with this disease by other means. However, more

studies are needed to determine whether the test can detect CRC in asymptomatic individuals. The USPSTF notes that tests that incorporate genetic stool markers have not been evaluated with respect to mortality reduction.

A stool DNA test (PreGen-Plus), which looks for signs of mutant genes in stool, is made by Exact Sciences Corp (Marlborough, MA). A multi-center clinical trial (Imperiale et al, 2004) reported that analysis of fecal DNA detects a greater proportion of colorectal neoplasia than FOBT. However neither of these non-invasive screening tests approaches the accuracy of a colonoscopy, the gold standard for detecting CRC. In the study, 4,404 average-risk, asymptomatic persons aged 50 years or older provided one stool specimen for DNA testing, underwent standard Hemoccult II FOBT, and then underwent colonoscopy. The fecal DNA panel, which identifies 21 mutations, detected 16 (51.6 %) of 31 invasive cancers, whereas Hemoccult II detected 4 (12.9 %) of 31 cancers. The DNA panel detected 29 (40.8 %) of 71 invasive cancers plus adenomas with high-grade dysplasia compared with 10 (14.1 %) of 71 detected by Hemoccult II. Among 418 subjects with advanced neoplasia, the DNA panel was positive in 76 (18.2 %), and Hemoccult II was positive in 45 (10.8 %). Specificity in patients with negative findings on colonoscopy was 94.4 % for the fecal DNA panel and 95.2 % for Hemoccult II.

An accompanying editorial (Woolf, 2004) suggested that it is too early for the fecal DNA panel to replace FOBT as a screening test for CRC. Remaining questions include generalizability, low sensitivity in this study for both FOBT and the fecal DNA panel, inability to determine whether the health benefits of fecal DNA testing outweigh the harms, availability and cost of the fecal DNA test, and the need for public access to screening to be more systematic and of higher quality. This is in agreement with the observation of Agrawal and Syngal (2005) who stated that preliminary data on fecal DNA tests show better performance characteristics than FOBT. In their current form, however, it is not clear that the added sensitivity merits the additional cost. These tests must be studied in larger cohorts of asymptomatic patients before adequate comparison can be made to established colorectal cancer screening techniques.

A special report by the BlueCross BlueShield Association Technology Evaluation Center (2006) of fecal DNA analysis for CRC screening concluded that, although the impact of fecal DNA screening on cancer morbidity and mortality has not yet been studied, it seems reasonable to assume that attaining sensitivities equal to or better than that of FOBT would result in similar or improved outcomes. The report identified several questions that remain to be answered before fecal DNA screening can be widely recommended, including: whether sensitivity for large adenoma be significantly increased compared to FOBT; whether false-positive rates be maintained appropriately low for a screening program; what are the published performance characteristics of the test in an average-risk screening population; what is the optimal screening interval; which patients should not be screened with fecal DNA testing; does the test improve compliance with CRC screening recommendations; and is the

test cost-effective.

The Agency for Healthcare Research and Quality's review on "Fecal DNA Testing in Screening for Colorectal Cancer in Average Risk Adults" (AHRQ, 2012) concluded that there is currently insufficient evidence to support the use of fecal DNA tests to accurately screen adults at average risk and who show no symptoms for CRC. The review calls for further research about the effectiveness of fecal DNA testing, as well as acceptability and adherence to, fecal DNA testing compared to other stool-based screening tests.

A cost-effectiveness analysis of DNA stool testing prepared for the AHRQ (Zauber et al, 2007) found that all DNA stool test strategies considered were dominated by (i.e., more costly and less effective) other recommended CRC screening tests. The investigators concluded: "These results suggest that screening for CRC with the DNA stool test version 1.1 does provide a benefit in terms of life-years gained compared with no screening but the cost, relative to the benefit derived and to the availability and costs of other CRC screening tests, would need to be in the range of \$34 - \$60 to be a non-dominated option. Only if significant improvements for the DNA stool test characteristics or relative adherence with DNA stool testing compared with other available options can be demonstrated, will stool DNA testing at the current costs of \$350 be cost-effective. These estimates are based on a third-party payer analysis on an unscreened 65-year old cohort. Threshold costs are similar for a 50-year old cohort, but can be somewhat higher from a modified societal perspective (\$88 to \$134 for 5-yearly testing and \$73 to \$116 for 3-yearly testing)."

In August 2007, the Centers for Medicare & Medicaid Services (CMS) initiated a national coverage determination process for screening DNA stool testing for CRC. However, in October 2007, the U.S. Food and Drug Administration (FDA) sent a warning letter to EXACT Sciences, maker of the only commercially available stool DNA test, stating that their PreGen-Plus test is a medical device that requires FDA clearance or approval prior to marketing and is currently being marketed in violation of the Federal and Food Drug and Cosmetic Act. Because of the FDA action, CMS subsequently announced its intention not to expand the CRC screening benefit to include coverage of this test. CMS stated that they will consider a request for re-consideration when a commercially available stool DNA test has been cleared or approved by the FDA.

The American Cancer Society's guidelines on CRC screening recommend several methods of screening, including virtual colonoscopy, based in part upon the presumption that the availability of multiple methods of screening will improve compliance (Levin et al, 2008). Colorectal cancer screening guidelines from the American Cancer Society recommend CT colonography (virtual colonoscopy) performed every 5 years as an acceptable alternative to optical colonoscopy performed every 10 years for screening of average-risk persons. However, there are no studies demonstrating that virtual colonoscopy does, in fact, increase compliance. Virtual colonoscopy is similar to optical

colonoscopy in that it requires completion of a pre-procedure cathartic regimen. If a lesion is found on virtual colonoscopy, the patient must return another day and complete another cathartic regimen for an optical colonoscopy to remove the lesion. By contrast, optical colonoscopy allows for identification and removal of a lesion in one procedure.

An assessment of CT colonography prepared for the Washington State Health Care Authority (Scherer et al, 2008) found that, in direct comparison to optical colonoscopy, CT colonography every 10 years is substantially more expensive and marginally less effective in preventing cases of cancer (47 versus 52 in a lifetime cohort of 1,000 individuals) and cancer deaths (24 versus 26). The investigators reported that only one CT colonography screening strategy is as effective as optical colonoscopy every 10 years, and that strategy is to perform CT colonography every 5 years with colonoscopy referral for polyps greater than 6 mm. For this strategy, the cost per life-year gained for CT colonography versus optical colonoscopy was \$630,700.

The USPSTF explained that CT colonography involves a wider area of examination than just the interior of the colon and that extra-colonic findings of potential clinical significance are common (7 % to 16 %). The USPSTF stated that it is not known whether the serendipitous discovery of these lesions results in better outcomes for patients and that it is possible that they result in extra follow-up testing without associated benefit. Furthermore, no studies directly addressed cancer-causing effects from CT colonography-associated radiation exposure and that it is not yet possible to quantify accurately the potential harms of extra-colonic findings or radiation exposure associated with CT colonography. The USPSTF stated that more studies are required to determine all the risks and benefits associated with CT colonography (USPSTF, 2008).

The ACG (Agrawal et al, 2005) issued recommendations to healthcare providers to begin CRC screening in African Americans at age 45 rather than 50 years. Colonoscopy is the preferred method of screening for CRC and data support the recommendation that African-Americans begin screening at a younger age because of the high incidence of CRC and a greater prevalence of proximal or right-sided polyps and cancerous lesions in this population.

In a meta-analysis of surveillance colonoscopy in individuals at risk for HNPCC, Johnson et al (2006) concluded that the best available evidence supports surveillance with complete colonoscopy to the cecum every 3 years in patients with HNPCC (B recommendation). There is no evidence to support or refute more frequent screening. Further research is needed to examine the potential harms and benefits of more frequent screening. However, given the potential for rapid progression from adenoma to carcinoma and missing lesions at colonoscopy, there is consensus that screening more frequently than every 3 years is required.

MYH is a DNA repair gene that corrects DNA base pair mismatch errors in the genetic code before replication. Mutation of the MYH gene may result in colon cancer. In this regard, the MYH gene has been found to be significantly

involved in colon cancer, both in cases where there is a clear family history of the disease, as well as in cases without any sign of a hereditary cause.

The NCCN practice guidelines on CRC screening (2006) recommends colonoscopy surveillance of asymptomatic individuals with known MYH mutations and colonoscopy screening of siblings of affected patients. Surveillance and screening is recommended beginning at age 25 to 30 years of age at 3 to 5 year intervals (the shorter intervals with advancing age). The NCCN guidelines recommend that patients with MYH-associated colorectal adenomas be managed similarly to patients with attenuated FAP. Those with small adenoma burden are surveilled with colonoscopy and complete polypectomies of all polyps. Those with dense polyposis not manageable by polypectomy are recommended surgery.

Guidelines from the NCCN (2011) recommend that persons with Cowden syndrome should consider colonoscopy, starting at age 35 years, then every 5 to 10 years or more frequently if the person is symptomatic or if polyps are found.

No current guidelines of leading medical professional organizations or Federal public health agencies recommend routine upper endoscopy screening of asymptomatic persons. Although screening upper endoscopy has been performed in conjunction with screening colonoscopy, there is no evidence-based support for this practice.

Currently, no leading medical professional organizations or Federal public health agencies recommend anal dysplasia screening. Recommendations from the Centers for Disease Control and Prevention state (Workowski and Berman, 2006): "Routine testing for anal cytological abnormalities or anal HPV infection is not recommended until more data are available on the reliability of screening methods, the safety of and response to treatment, and programmatic considerations." The Ontario Health Technology Advisory Committee (OHTAC, 2007) recently systematically reviewed the evidence for anal dysplasia screening. OHTAC "does not recommend screening of high risk individuals at this time based on the low specificity for cytological screening, inadequate evidence of effectiveness for current treatment of precancerous lesions, high recurrence rates, and no evidence that cytological screening reduces the risk of developing anal cancer."

Regarding risk factors (smoking and obesity) under consideration for more intense screening, the 2009 ACG guidelines for CRC screening (Rex et al, 2009) did not recommend that screening be initiated earlier in these groups (smokers and obese patients) at this time. The ACG recommended additional study to characterize the potential benefits, harms, and cost-effectiveness of earlier screening in these groups.

ColoVantage is a plasma-based test that detects circulating methylated DNA from the SEPT9 gene which is involved in cytokinesis and cell cycle control. According to the manufacturer, case-control studies show that presence of methylated SEPT9 DNA in plasma is 58 % to 69 % sensitive for CRC detection

at a specificity of 86 % to 90 % (citing Lofton-Day et al, 2008; Grützmann et al, 2008; de Vos et al, 2009). The test is non-invasive and requires no patient preparation. The manufacturer suggests that a physician may order the test for screen-eligible patients who have previously avoided established CRC screening methods such as colonoscopy, FOBT, and fecal immunochemical tests. A patient whose ColoVantage test result is positive may be at increased risk for CRC and further evaluation should be considered. The manufacturer notes, however, that the ColoVantage test has yet to be clinically validated as a screening test. There are no evidence-based guidelines from leading medical professional organizations or public health agencies that recommend measurement of methylated Septin 9 in plasma for CRC screening.

MicroRNAs (miRNAs) are short non-coding RNA sequences that play an important role in the regulation of gene expression. They have significant regulatory functions in basic cellular processes (e.g., cell differentiation, proliferation, and apoptosis). Available evidence suggests that miRNAs may function as both tumor suppressors as well as oncogenes. The main mechanism for changes in the function of miRNAs in cancer cells is due to aberrant gene expression.

Dong and colleagues (2011) noted that recent researches have shed light on the biological importance of miRNAs in CRC genesis, progression and response to treatments. The potential utility of miRNAs in the pre-clinical stage have been explored and investigated. These researchers explored the literature and reviewed the cutting edge progress in the discovery of non-invasive plasma and fecal miRNAs for CRC early diagnosis, as well as their measurability and predictability. They also discussed the utility of miRNAs as novel prognostic and predictive markers, and their association with CRC clinical phenotypes including recurrence, metastasis and therapeutic outcomes. These investigators summarized miRNA-related single-nucleotide polymorphisms and their potential influence on sporadic CRC susceptibility and therapeutic response. The authors concluded that the use of miRNAs as biomarker for CRC is still in its infancy and need further characterization and evaluation.

Sandhu and Garzon (2011) stated that early studies have established that miRNAs are widely de-regulated in cancer and play a critical role in cancer pathogenesis. Recent research efforts are directed now towards translating these basic discoveries into novel tests or treatments that could improve the diagnosis and outcome of cancer patients. These researchers summarized the potential applications of miRNAs for cancer diagnosis, prognosis, as well as treatment; and discussed current pitfalls and future directions. The authors noted that there are still hurdles to overcome such as the development of reliable and reproducible miRNA expression assays and improvements in oligonucleotide delivery to specific tissues or cell types.

Ma et al (2012) carried out a comprehensive systematic review of published studies that compared the miRNA expression profiles between CRC tissue and paired neighboring non-cancerous colorectal tissue to determine candidate

miRNA biomarkers for CRC. A miRNA ranking system that takes the number of comparisons in agreement, total study sizes and direction of differential expression into consideration was devised and used. One of the most up-regulated miRNAs, miRNA-106a, was consistently reported to be differentially expressed in 6 studies and the 5 most down-regulated miRNAs, miR-30a-3p, miR-139, miR-145, miR-125a and miR-133a, were consistently reported to be differentially expressed in 4 studies. Moreover, these investigators further validated 5 miRNAs in a clinical setting using qRT-PCR, which demonstrated that miR-106a expression was increased, whereas the expression of miR-30a-3p, miR-145, miR-125a and miR-133a was decreased in the CRC tissues. The authors concluded that these miRNAs may be the candidates to develop a panel of biomarkers with sufficient sensitivity and specificity for the diagnosis of CRC in a clinical setting.

Wang et al (2012) stated that the recently identified class of miRNAs provided a new insight in cancer research. As members of miRNAs family, miR-34a, miR-155 and miR-200c abnormalities have been found in various types of cancer. However, the relationship between these 3 miRNAs (miR-34a, miR-155 and miR-200c) and CRC is unclear. These researchers applied stem-loop real-time PCR to quantitatively detect miR-34a, miR-155 and miR-200c expression in 109 pair-matched human CRC and the corresponding normal mucosa. MiR-34a (2.2-fold), miR-155 (2.3-fold) and miR-200c (3.1-fold) were all expressed at higher levels in CRC ($p = 0.001$, 0.005 and 0.001 , respectively). In the rectum, miR-34a and miR-200c were significantly up-regulated ($p = 0.006$ and 0.007), while the miR-155 over-expression was not statistically significant ($p = 0.083$). In the colon, the higher expression of 3 miRNAs was seen, however, without significant difference ($p > 0.05$). The investigators also found that the miR-34a expression was higher in rectal cancer having more advanced TNM stage (III + IV, $p = 0.03$). Then miR-200c expression was positively correlated with and sera CEA level of rectal cancer patients ($p = 0.04$). The authors concluded that these findings suggested that the over-expression of miR-34a, miR-155 and miR-200c may be associated with the development of CRC, meanwhile miR-34a may be involved in the development and progression of rectal cancer. They stated that more deeply and larger scale research are required to prove the correlation.

Peacock et al (2012) noted that accurate discrimination of miRNA profiles between tumor and normal mucosa in CRC allows definition of specific expression patterns of miRNAs, giving good potential as diagnostic and therapeutic targets. MicroRNAs expressed in CRC are also abundantly present and stable in stool and plasma samples; their extraction from these sources is feasible and reproducible. The ease and reliability of determining miRNA profiles in plasma or stool makes them potential molecular markers for CRC screening.

Furthermore, a guidance statement from the American College of Physicians on "Screening for colorectal cancer" (Qaseem et al, 2012) does not list miRNA as one of the tests for CRC.

Kannan et al (2013) examined the potential use of circulating miRNAs as biomarkers of CR adenomas. These investigators screened for 380 plasma-miRNAs using microfluidic array technology (Applied BioSystems) in a screening cohort of 12 healthy controls, 9 patients with CR adenomas, and 20 patients with CRC. A panel of the most dysregulated miRNAs ($p < 0.05$, False Discovery Rate: 5 %) was then validated in a blinded cohort of 26 healthy controls, 16 patients with large adenomas, and 45 patients with CRC. A panel of 8 plasma miRNAs (miR-532-3p, miR-331, miR-195, miR-17, miR-142-3p, miR-15b, miR-532, and miR-652) distinguished polyps from controls with high accuracy [area under curve (AUC) = 0.868 (95 % confidence interval [CI]: 0.76 to 0.98)]. In addition, a panel of 3 plasma miRNAs (miR-431, miR-15b, and miR-139-3p) distinguished stage IV CRC from controls with an [AUC = 0.896 (95 % CI: 0.78 to 1.0)]. Receiver-operating-characteristic curves of miRNA panels for all CRC versus controls and polyps versus all CRC showed AUC values of 0.829 (95 % CI: 0.73 to 0.93) and 0.856 (95 % CI: 0.75 to 0.97), respectively. The authors concluded that plasma miRNAs are reliable, non-invasive, and inexpensive markers for CR adenomas. They stated that this miRNA panel warrants study in larger cohorts to confirm and then increase its sensitivity and specificity. Plasma-based assays could provide better screening compliance compared to fecal occult blood or endoscopic screening.

A guidance statement from the American College of Physicians on "Screening for colorectal cancer" (Qaseem et al, 2012) stated that "The screening interval for average-risk adults older than 50 years is 10 years for colonoscopy; 5 years for flexible sigmoidoscopy, double-contrast barium enema (DCBE), and computed tomography colonography (CTC); annually for guaiac-based fecal occult blood test (gFOBT) and immunochemical-based fecal occult blood test (iFOBT); and uncertain for stool DNA (sDNA)". Furthermore, an UpToDate review on "Screening for colorectal cancer: Strategies in patients at average risk" (Fletcher, 2013) states that "A US task force representing multiple specialty societies developed consensus guidelines in 2008 that endorse two additional screening options: computed tomographic colonography (CTC) and a panel test for stool DNA (sDNA). (It should be noted that a stool DNA test, previously available, is no longer commercially available in 2012). The US Preventive Services Task Force also issued updated guidelines for colorectal cancer screening in 2008 and did not recommend barium enema, CTC or sDNA as screening options, however. Both guidelines endorse fecal occult blood testing using either a high-sensitive guaiac reagent or an immunochemical test; lower-sensitivity guaiac tests are not recommended".

The USPSTF guidelines apply to routine screening. The USPSTF have no A or B recommendations for high-risk screening. The USPSTF guidelines explain: "These recommendations apply to adults 50 years of age and older, excluding those with specific inherited syndromes (the Lynch syndrome or familial adenomatous polyposis) and those with inflammatory bowel disease. The recommendations do apply to those with first-degree relatives who have had colorectal adenomas or cancer, although for those with first-degree relatives who developed cancer at a younger age or those with multiple affected first-

degree relatives, an earlier start to screening may be reasonable (USPSTF, 2008)”.

Imperiale et al (2014) compared a non-invasive, multi-target stool DNA test with a fecal immunochemical test (FIT) in persons at average risk for CRC.

The DNA test includes quantitative molecular assays for KRAS mutations, aberrant NDRG4 and BMP3 methylation, and β -actin, plus a hemoglobin immunoassay. Results were generated with the use of a logistic-regression algorithm, with values of 183 or more considered to be positive. Fecal immunochemical test values of more than 100 ng of hemoglobin per milliliter of buffer were considered to be positive. Tests were processed independently of colonoscopic findings. Of the 9,989 participants who could be evaluated, 65 (0.7 %) had CRC and 757 (7.6 %) had advanced pre-cancerous lesions (advanced adenomas or sessile serrated polyps measuring greater than or equal to 1 cm in the greatest dimension) on colonoscopy. The sensitivity for detecting CRC was 92.3 % with DNA testing and 73.8 % with FIT ($p = 0.002$). The sensitivity for detecting advanced pre-cancerous lesions was 42.4 % with DNA testing and 23.8 % with FIT ($p < 0.001$). The rate of detection of polyps with high-grade dysplasia was 69.2 % with DNA testing and 46.2 % with FIT ($p = 0.004$); the rates of detection of serrated sessile polyps measuring 1 cm or more were 42.4 % and 5.1 %, respectively ($p < 0.001$). Specificities with DNA testing and FIT were 86.6 % and 94.9 %, respectively, among participants with non-advanced or negative findings ($p < 0.001$) and 89.8 % and 96.4 %, respectively, among those with negative results on colonoscopy ($p < 0.001$).

The numbers of persons who would need to be screened to detect 1 cancer were 154 with colonoscopy, 166 with DNA testing, and 208 with FIT. The authors concluded that in asymptomatic persons at average risk for CRC, multi-target stool DNA testing detected significantly more cancers than did FIT but had more false-positive results.

In an editorial that accompanied the afore-mentioned study, Robertson and Dominitz (2014) stated that “The new multitarget stool DNA test is clearly an improvement over its predecessors, and the results of this study will help to inform the current effort of the U.S. Preventive Services Task Force to reevaluate screening tests. Comparative-effectiveness studies are now needed to clarify the role of stool DNA testing with respect to programmatic screening with other test options. Only through a better understanding of other key factors, such as the screening interval, adherence, cost, and diagnostic evaluation of positive results, can we determine the appropriate place for stool DNA testing on the screening menu”.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

45330

45331

45332

45333

45334

45335

45337

45338

45339

45378

45379

45380

45381

45382

45383

45384

45385

74270

74280

82270

82272

82274

CPT codes not covered for indications listed in the CPB:

87620

87621

87622

Other CPT codes related to the CPB:

81201 - 81203

81201 - 81203

81292 - 81294

81295 - 81297

81298 - 81300

81317 - 81319

88271 - 88275

HCPCS codes covered if selection criteria are met:

G0104	Colorectal cancer screening; flexible sigmoidoscopy
G0105	Colorectal cancer screening; colonoscopy on individual at high risk
G0106	Colorectal cancer screening; alternative to G0104, screening sigmoidoscopy, barium enema
G0120	Colorectal cancer screening; alternative to G0105, screening colonoscopy, barium enema
G0121	Colorectal cancer screening; colonoscopy on individual not meeting criteria for high risk
G0122	Colorectal cancer screening; barium enema

HCPCS codes not covered for indications listed in the CPB:

S3890	DNA analysis, fecal, for colorectal cancer screening [e.g., Cologuard, ColoSure, PreGen-Plus]
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ICD-9 codes covered if selection criteria are met:

153.0 - 154.9	Malignant neoplasm of colon, rectum, rectosigmoid junction and anus
209.11 - 209.17	Malignant carcinoid tumors of the appendix, large intestine, and rectum
209.50 - 209.57	Benign carcinoid tumors of the appendix, large intestine, and rectum
211.3	Benign neoplasm of colon
211.4	Benign neoplasm of rectum and anal canal
280.0	Iron deficiency anemia secondary to blood loss (chronic)
280.9	Iron deficiency anemia, unspecified
285.1	Acute posthemorrhagic anemia
556.0 - 558.9	Non-infectious enteritis and colitis
562.10 - 562.13	Diverticula of colon
564.00 - 564.09	Constipation
569.0	Anal and rectal polyp
569.3	Hemorrhage of rectum and anus
578.1	Blood in stool
759.6	Other congenital hamartoses, NEC [Cowden syndrome]
792.1	Non-specific abnormal findings in stool contents
V10.05	Personal history of malignant neoplasm of large intestine

V10.06	Personal history of malignant neoplasm of rectum, rectosigmoid junction, and anus.
V12.72	Personal history of colonic polyps
V16.0	Family history of malignant neoplasm of gastrointestinal tract (first degree relative-sibling, parent, child)
V18.51	Family history, colonic polyps
V76.41	Special screening for malignant neoplasms of rectum
V76.50	Special screening for malignant neoplasms of intestine, unspecified
V76.51	Special screening for malignant neoplasms of colon
V84.09	Genetic susceptibility to other malignant neoplasm

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

079.4	Human papillomavirus [HPV]
796.70 - 796.79	Abnormal cytologic smear of anus and anal HPV
V73.81	Special screening examination for human papillomavirus (HPV)

Other ICD-9 codes related to the CPB:

278.00	Obesity, unspecified
278.01	Morbid Obesity
278.02	Overweight
305.1	Tobacco use disorder
V15.82	History of tobacco use
V85.4	Body Mass Index 40 and over, adult

The above policy is based on the following references:

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Multitarget Stool DNA Testing for Colorectal-Cancer Screening

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ABSTRACT

BACKGROUND

An accurate, noninvasive test could improve the effectiveness of colorectal-cancer screening.

METHODS

We compared a noninvasive, multitarget stool DNA test with a fecal immunochemical test (FIT) in persons at average risk for colorectal cancer. The DNA test includes quantitative molecular assays for *KRAS* mutations, aberrant *NDRG4* and *BMP3* methylation, and β -actin, plus a hemoglobin immunoassay. Results were generated with the use of a logistic-regression algorithm, with values of 183 or more considered to be positive. FIT values of more than 100 ng of hemoglobin per milliliter of buffer were considered to be positive. Tests were processed independently of colonoscopic findings.

RESULTS

Of the 9989 participants who could be evaluated, 65 (0.7%) had colorectal cancer and 757 (7.6%) had advanced precancerous lesions (advanced adenomas or sessile serrated polyps measuring ≥ 1 cm in the greatest dimension) on colonoscopy. The sensitivity for detecting colorectal cancer was 92.3% with DNA testing and 73.8% with FIT ($P=0.002$). The sensitivity for detecting advanced precancerous lesions was 42.4% with DNA testing and 23.8% with FIT ($P<0.001$). The rate of detection of polyps with high-grade dysplasia was 69.2% with DNA testing and 46.2% with FIT ($P=0.004$); the rates of detection of serrated sessile polyps measuring 1 cm or more were 42.4% and 5.1%, respectively ($P<0.001$). Specificities with DNA testing and FIT were 86.6% and 94.9%, respectively, among participants with nonadvanced or negative findings ($P<0.001$) and 89.8% and 96.4%, respectively, among those with negative results on colonoscopy ($P<0.001$). The numbers of persons who would need to be screened to detect one cancer were 154 with colonoscopy, 166 with DNA testing, and 208 with FIT.

CONCLUSIONS

In asymptomatic persons at average risk for colorectal cancer, multitarget stool DNA testing detected significantly more cancers than did FIT but had more false positive results. (Funded by Exact Sciences; ClinicalTrials.gov number, NCT01397747.)

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American College of Gastroenterology Guidelines for Colorectal Cancer Screening 2008

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This document is the first update of the American College of Gastroenterology (ACG) colorectal cancer (CRC) screening recommendations since 2000. The CRC screening tests are now grouped into cancer prevention tests and cancer detection tests. Colonoscopy every 10 years, beginning at age 50, remains the preferred CRC screening strategy. It is recognized that colonoscopy is not available in every clinical setting because of economic limitations. It is also realized that not all eligible persons are willing to undergo colonoscopy for screening purposes. In these cases, patients should be offered an alternative CRC prevention test (flexible sigmoidoscopy every 5–10 years, or a computed tomography (CT) colonography every 5 years) or a cancer detection test (fecal immunochemical test for blood, FIT).

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INTRODUCTION

The members of the writing committee carried out a systematic literature review and developed the updated guideline recommendation document. Only peer-reviewed English language articles were included. The criteria used for evaluation of studies and assessment of the category of evidence and strength of recommendation are shown in **Table 1** (1). These guidelines have also been reviewed and approved by the Practice Parameters Committee of the American College of Gastroenterology (ACG) and by the ACG Board of Trustees.

The ACG is an organization of more than 10,000 clinical gastroenterologists and related health professionals. In 2000, the ACG issued colorectal cancer (CRC) screening recommendations that endorsed colonoscopy every 10 years, beginning at age 50, as the preferred CRC screening strategy (2). The ACG was the first organization to recommend colonoscopy as the preferred strategy for the CRC screening; and the American Society for Gastrointestinal Endoscopy (3) and National Comprehensive Cancer Network (4) subsequently endorsed this recommendation.

Other guidelines for CRC screening often utilize an approach called the “menu of options.” In this approach, multiple options for screening are presented which differ with regard to their effectiveness, risk, and degree of invasiveness (and, therefore, potentially their acceptability to patients). The menu-of-options approach was first formalized by the “GI consortium” in May 1997 (5), endorsed by the American Cancer Society in 1997 (6), revised by the US Multisociety Task Force in 2003 (7), and

revised by a joint committee of the US Multisociety Task Force, the American Cancer Society, and the American College of Radiology in 2008 (8). The ACG participated in and endorsed the menu-of-options approach in 1997, 2003, and 2008. The ACG continues to endorse the menu-of-options approach as appropriate to CRC screening. Publication of this guideline does not rescind the ACG’s endorsement of the joint guideline (8). New recommendations, which differ from the earlier ACG guideline, are highlighted in **Table 2**. The rationale for a separate ACG screening guideline is discussed below.

Rationale for a preferred strategy

As in 2000, the ACG recommends that clinicians have access to a “preferred” strategy for making CRC screening recommendations, as an alternative to the “menu of options” approach, if warranted by the performance characteristics of one of the tests. The ACG recommends colonoscopy every 10 years based on the evidence of colonoscopy effectiveness, cost-effectiveness, and acceptance by patients. A “preferred” strategy simplifies and shortens discussions with patients and could also increase the likelihood that screening is offered to patients. One randomized trial showed that patients were more likely to undergo screening with the “preferred” strategy approach compared with the “menu of options” (9). Another study found no improvement in screening rates when multiple options were presented (10). Maintaining simplicity in guidelines may have value, in that recent evidence has suggested that practi-

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Diagnostic value of stool DNA testing for multiple markers of colorectal cancer and advanced adenoma: A meta-analysis

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H Yang, B-Q Xia, B Jiang, et al. Diagnostic value of stool DNA testing for multiple markers of colorectal cancer and advanced adenoma: A meta-analysis. *Can J Gastroenterol* 2013;27(8): 467-475.

BACKGROUND AND OBJECTIVES: The diagnostic value of stool DNA (sDNA) testing for colorectal neoplasms remains controversial. To compensate for the lack of large-scale unbiased population studies, a meta-analysis was performed to evaluate the diagnostic value of sDNA testing for multiple markers of colorectal cancer (CRC) and advanced adenoma.

METHODS: The PubMed, Science Direct, Biosis Review, Cochrane Library and Embase databases were systematically searched in January 2012 without time restriction. Meta-analysis was performed using a random-effects model using sensitivity, specificity, diagnostic OR (DOR), summary ROC curves, area under the curve (AUC), and 95% CIs as effect measures. Heterogeneity was measured using the χ^2 test and Q statistic; subgroup analysis was also conducted.

RESULTS: A total of 20 studies comprising 5876 individuals were eligible. There was no heterogeneity for CRC, but adenoma and advanced adenoma harboured considerable heterogeneity influenced by risk classification and various detection markers. Stratification analysis according to risk classification showed that multiple markers had a high DOR for the high-risk subgroups of both CRC (sensitivity 0.759 [95% CI 0.711 to 0.804]; specificity 0.883 [95% CI 0.846 to 0.913]; AUC 0.906) and advanced adenoma (sensitivity 0.683 [95% CI 0.584 to 0.771]; specificity 0.918 [95% CI 0.866 to 0.954]; AUC 0.946) but not for the average-risk subgroups of either. In the methylation subgroup, sDNA testing had significantly higher DOR for CRC (sensitivity 0.753 [95% CI 0.685 to 0.812]; specificity 0.913 [95% CI 0.860 to 0.950]; AUC 0.918) and advanced adenoma (sensitivity 0.623 [95% CI 0.527 to 0.712]; specificity 0.926 [95% CI 0.882 to 0.958]; AUC 0.910) compared with the mutation subgroup. There was no significant heterogeneity among studies for subgroup analysis.

CONCLUSION: sDNA testing for multiple markers had strong diagnostic significance for CRC and advanced adenoma in high-risk subjects. Methylation markers had more diagnostic value than mutation markers.

Key Words: Adenoma; Colorectal cancer; Diagnosis; Meta-analysis; Stool DNA test

Colorectal cancer (CRC) is the third leading cause of cancer death worldwide. Small but steady decreases in CRC mortality have been achieved, in part, by early detection through population-based screening programs (1). Further expansion of screening programs based on the traditional diagnostic methods of CRC and adenoma has been hindered by technique-related limitations, including the

La valeur diagnostique du test d'ADN fécal pour déceler des marqueurs multiples de cancer colorectal et d'adénome avancé : une méta-analyse

HISTORIQUE ET OBJECTIFS : La valeur diagnostique du test d'ADN fécal (ADNf) pour dépister les néoplasmes colorectaux demeure controversée. Pour compenser l'absence d'études en population à vaste échelle non biaisées, les chercheurs ont mené une méta-analyse afin d'évaluer la valeur diagnostique du test d'ADNf pour déceler des marqueurs multiples du cancer colorectal (CCR) et de l'adénome avancé.

MÉTHODOLOGIE : Les chercheurs ont fouillé les bases de données PubMed, Science Direct, Biosis Review, Bibliothèque Cochrane et Embase de manière systématique en janvier 2012, sans restriction dans le temps. Ils ont effectué une méta-analyse au moyen d'un modèle à effets aléatoires dont les mesures d'effet étaient la sensibilité, la spécificité, le RRR diagnostique (RRRD), les courbes ROC sommaires, l'aire sous la courbe (ASC), et les 95 % IC. Ils ont mesuré l'hétérogénéité au moyen du test χ^2 et de la statistique Q, et ont effectué une analyse de sous-groupe.

RÉSULTATS : Au total, 20 études menées auprès de 5 876 personnes étaient admissibles. Il n'y avait pas d'hétérogénéité en cas de CCR, mais l'adénome et l'adénome avancé recelaient une importante hétérogénéité influencée par la classification du risque et divers marqueurs de détection. L'analyse de stratification d'après la classification du risque a révélé que de multiples marqueurs présentaient un RRRD élevé dans les sous-groupes à haut risque de CCR (sensibilité de 0,759 [95 % IC 0,711 à 0,804], spécificité de 0,883 [95 % IC de 0,846 à 0,913], ASC de 0,906) et d'adénome avancé (sensibilité de 0,683 [95 % IC de 0,584 à 0,771], spécificité de 0,918 [95 % IC de 0,866 à 0,954], ASC de 0,946), mais pas dans les sous-groupes à risque moyen de l'un ou de l'autre. Dans le sous-groupe de méthylation, le test d'ADNf présentait un RRRD considérablement plus élevé de CCR (sensibilité de 0,753 [95 % IC de 0,685 à 0,812], spécificité de 0,913 [95 % IC de 0,860 à 0,950], ASC de 0,918) et d'adénome avancé (sensibilité de 0,623 [95 % IC de 0,527 à 0,712], spécificité de 0,926 [95 % IC de 0,882 à 0,958], ASC de 0,910) que le sous-groupe de mutation. Il n'y avait pas d'hétérogénéité significative entre les études pour l'analyse de sous-groupe.

CONCLUSION : Le test d'ADNf pour déceler de multiples marqueurs avait une forte signification diagnostique de CCR et d'adénome avancé chez les sujets à haut risque. Les marqueurs de méthylation avaient une plus forte valeur diagnostique que les marqueurs de mutation.

requirement of a visibly detectable lesion, risk of complications, costs and low patient compliance for endoscopy. Thus, the patient-preferred screening method is the fecal occult blood test (FOBT). While the non-invasive nature of this method promotes patient compliance for initial screening, its dependence on the 'bleeding phenotype' and occult bleeding in CRC, regardless of stage, has low sensitivity for accurate

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ICD-9	Diagnosis Description	Current file	Recommended Placement
521.40	Pathological resorption, unspecified	ANCILLARY CODES	Non-Covered List
521.41	Pathological resorption, internal	EXCLUDED FILE	654
521.42	Pathological resorption, external	EXCLUDED FILE	654
521.49	Other pathological resorption	EXCLUDED FILE	654
521.5	Hypercementosis	ANCILLARY CODES	654
523.00	Acute gingivitis, plaque induced	ANCILLARY CODES	222 DENTAL CONDITIONS (EG. PERIODONTAL DISEASE)
523.01	Acute gingivitis, non-plaque induced	ANCILLARY CODES	222
523.10	Chronic gingivitis, plaque induced	ANCILLARY CODES	222
523.11	Chronic gingivitis, non-plaque induced	ANCILLARY CODES	222
523.20	Gingival recession, unspecified	ANCILLARY CODES	222
523.21	Gingival recession, minimal	ANCILLARY CODES	222
523.22	Gingival recession, moderate	ANCILLARY CODES	222
523.23	Gingival recession, severe	ANCILLARY CODES	222
523.24	Gingival recession, localized	ANCILLARY CODES	222
523.25	Gingival recession, generalized	ANCILLARY CODES	222
523.30	Aggressive periodontitis, unspecified	ANCILLARY CODES	222
523.31	Aggressive periodontitis, localized	ANCILLARY CODES	222
523.32	Aggressive periodontitis, generalized	ANCILLARY CODES	222
523.33	Acute periodontitis	ANCILLARY CODES	222
523.40	Chronic periodontitis, unspecified	ANCILLARY CODES	222
523.41	Chronic periodontitis, localized	ANCILLARY CODES	222
523.42	Chronic periodontitis, generalized	ANCILLARY CODES	222
523.5	Periodontosis	ANCILLARY CODES	222
523.6	Accretions on teeth	ANCILLARY CODES	654
523.8	Other specified periodontal diseases	ANCILLARY CODES	222
523.9	Unspecified gingival and periodontal disease	ANCILLARY CODES	222
524.32	Excessive spacing of teeth	ANCILLARY CODES	626 DENTAL CONDITIONS (EG. MALOCCLUSION)
525.0	Exfoliation of teeth due to systemic causes	ANCILLARY CODES	655 DENTAL CONDITIONS WHERE TREATMENT RESULTS IN MARGINAL IMPROVEMENT
525.10	Acquired absence of teeth, unspecified	EXCLUDED FILE	457 DENTAL CONDITIONS (EG. MISSING TEETH, PROSTHESIS FAILURE)
525.11	Loss of teeth due to trauma	EXCLUDED FILE	457
525.12	Loss of teeth due to periodontal disease	EXCLUDED FILE	457
525.13	Loss of teeth due to caries	EXCLUDED FILE	457
525.19	Other loss of teeth	EXCLUDED FILE	457
525.61	Open restoration margins	EXCLUDED FILE	347 DENTAL CONDITIONS (EG. CARIES, FRACTURED TOOTH)
525.62	Unrepairable overhanging of dental restorative materials	EXCLUDED FILE	347
525.63	Fractured dental restorative material without loss of material	EXCLUDED FILE	347
525.64	Fractured dental restorative material with loss of material	EXCLUDED FILE	347
525.65	Contour of existing restoration of tooth biologically incompatible with oral health	EXCLUDED FILE	347
525.66	Allergy to existing dental restorative material	EXCLUDED FILE	347
525.8	Other specified disorders of the teeth and supporting structures	ANCILLARY CODES	655
526.61	Perforation of root canal space	EXCLUDED FILE	655
526.62	Endodontic overfill	EXCLUDED FILE	655
526.63	Endodontic underfill	EXCLUDED FILE	655
526.69	Other periradicular pathology associated with previous endodontic treatment	EXCLUDED FILE	655

Liver Elastoplasty

Issue: MED report on non-invasive liver tests was just released. This topic was reviewed as part of the 2015 CPT code review. In the initial review, HERC staff recommended that this test be placed on the Non-Covered List, pending an expected MED report. The MED report has just been published.

MED report highlights:

- 1) Literature
 - a. One additional systematic review not included in the HERC staff review was identified in the MED report, but was rated poor quality with high risk of bias (Poynard et al., 2011).
- 2) Policies
 - a. Additional private payer policies were reviewed, and none were found to cover liver elastoplasty.
- 3) Findings
 - a. Liver elastoplasty was found to be accurate for diagnosing cirrhosis (late-stage) but not early or intermediate fibrosis.
 - b. Good quality guidelines are consistent with the evidence and recommend against using non-invasive tests to diagnose early or intermediate stages of fibrosis (METAVIR Stage F1 to F3 or equivalent), but note that these tests are reliable to identify cirrhosis (METAVIR Stage F4).
 - c. No evidence was found about effect on patient health outcomes from using fibrosis stage to guide treatment decisions.
 - d. No evidence on harms was identified for liver elastoplasty.
- 4) Policy considerations
 - a. Considerations for coverage include availability of imaging equipment, costs of patented blood tests, clinical characteristics of patients, consequences of misclassification.
 - b. Liver biopsy is considerably more expensive than liver elastoplasty, with much higher complication rates
 - c. A recent, good-quality cost-effectiveness analysis concluded that treating all patients with HCV without first determining fibrosis stage was the most cost-effective strategy from a United Kingdom (U.K.) National Health Service perspective, even when including newer, more expensive treatments in the analysis. The applicability of this analysis to the U.S. healthcare system is limited, however, because of differences in treatment costs and other healthcare system factors.
 - i. If stage of fibrosis does not guide treatment, then this test does not have clinical utility
 - ii. If the goal is to identify treatment for only those patients with advanced stages of HCV (i.e. those with cirrhosis of the liver), the evidence shows that non-invasive tests are a reasonable alternative to liver biopsy.
- 5) MED call discussion highlights:

- a. Hard to be competent to do scan—need to complete about 100 patient scans to be considered competent
- b. Scan not available in many areas in Oregon (available only at OHSU currently)
- c. About a 50% sensitivity for test (miss ½ of patients)
- d. Even if stage of fibrosis does not guide medication treatment, fibrosis stage should guide surveillance for complications such as liver cancer

HERC staff recommendation:

- 1) No change to 2015 CPT code review recommendation for Non-Covered List
 - a. Rapidly evolving field, should be re-reviewed in near future to see if clinical utility is clarified
 - b. Alternative option (not staff recommended): consider placement of liver elastoplasty (CPT 91200) on line 338 ALCOHOLIC FATTY LIVER OR ALCOHOLIC HEPATITIS, CIRRHOSIS OF LIVER with a guideline to be determined