GUIDELINE WATCH
2018
Summaries and highlights of the most important new clinical guidelines to inform your practice
Dear Reader,

Clinical guidelines are increasingly important in setting practice standards and meeting quality measures, and NEJM Journal Watch wants to help you keep up with the guidelines most important to your practice. Our 90 clinician-editors regularly survey more than 250 medical journals to identify the latest critical information. As part of this effort, we evaluate a broad range of clinical guidelines in a variety of disciplines, choose those with the most clinical impact, and summarize them, highlighting key points and identifying what’s new in a feature called Guideline Watch.

This collection of Guideline Watches, published from July 2017 to June 2018, covers a range of guidelines — from the new hormone therapy position statement of the North American Menopause Society to the latest ACP recommendations on hemoglobin A1c targets for glycemic control — but the common denominator is their relevance to and implications for clinical practice. The topics in this collection span outpatient and inpatient medicine, and primary care and subspecialty perspectives. Although not every guideline will be relevant to your particular practice, we believe that you’ll find something of interest in each of them.

We hope you enjoy this compilation and find it useful for providing the best and most responsible patient care, and we invite you to interact with us at JWatch.org.

Allan S. Brett, MD
NEJM Journal Watch Editor-in-Chief
# Guideline Watch 2018

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Managing Heart Failure: A Focused Update
Frederick A. Masoudi, MD, MSPH, FACC, FAHA, reviewing Yancy CW et al. Circulation 2017 Aug 8; 136:e137.

The update addresses treatment changes for patients with either preserved or reduced systolic function.

Sponsoring Organizations: American College of Cardiology (ACC) Foundation, American Heart Association (AHA), and the Heart Failure Society of America in collaboration with American Academy of Family Physicians, American College of Chest Physicians, and International Society for Heart and Lung Transplantation

Target Audience: Cardiovascular specialists, cardiac surgeons, and primary care clinicians providing care to patients with heart failure (HF).

Background and Objective
This update of the 2013 ACC/AHA guideline is based on a review of clinical trials that were presented at national and international scientific meetings and published in the peer-reviewed literature between April 2013 and November 2016.

Key Points
1. Biomarkers: Natriuretic peptides are useful for diagnosis in patients with suspected HF or for prognosis (Class I [strong recommendations]) and might help to identify patients at risk for HF who might benefit from team-based preventive care (Class IIa [moderate recommendation]). Troponin levels at the time of hospitalization are also useful for prognostication (Class I). The value of using biomarkers in guiding therapy is not clear.

2. Renin-Angiotensin System Inhibition: This strategy is recommended to reduce morbidity and mortality in all patients with HF and reduced ejection fraction (HFrEF) and no contraindications, in addition to optimal therapy that includes beta blockers and aldosterone antagonists in those without contraindications as well as device therapy (implantable cardioverter-defibrillator cardiac resynchronization therapy, or both) in those with an indication.
   - Angiotensin-converting enzyme (ACE) inhibitors (Class I) or
   - Angiotensin receptor blockers (ARBs, Class I) or
   - Angiotensin receptor–neprilysin inhibitor (ARNI) to replace ACE inhibitors or ARBs in patients who have tolerated either agent (Class I, but with a lower level of evidence than ACE or ARB). ARNI should not be used within 36 hours of the last dose of an ACE inhibitor or in patients with angioedema (Class III [harm]).

3. Ivabradine: Consider using this drug to reduce HF hospitalizations for symptomatic HFrEF and resting heart rate ≥70 bpm in patients on optimal therapy, including a beta blocker at the maximal tolerated dose (Class IIa).

4. Therapy for HF with Preserved Ejection Fraction (HFpEF): Therapy remains largely targeted at coexisting conditions, including hypertension, coronary disease, and atrial fibrillation. Aldosterone receptor antagonists or ARBs in appropriately selected patients might reduce hospitalization risk (Class IIb [weak recommendation]). Routine nitrates or phosphodiesterase-5 inhibitors are discouraged (Class III [no benefit]).

5. Anemia and Iron Deficiency: Intravenous iron to improve health status is recommended for symptomatic patients with HF and iron deficiency (Class IIb). Erythropoietin-stimulating agents should not be used (Class III [no benefit]).

6. Hypertension: Recommended optimal levels (Class I) are <130/80 mm Hg for those at risk for HF (stage A) or systolic <130 mm Hg in patients with HFrEF or HFpEF.

7. Sleep-Disordered Breathing: Screening (Class IIa) and treatment of obstructive sleep apnea (Class IIb) to reduce sleepiness are recommended. Adaptive servo-ventilation in patients with central sleep apnea should be avoided (Class III [harm]).
What's Changed
This update includes new recommendations on substituting ARNI for ACE or ARB in HFrEF and selective use of ivabradine in optimally managed patients with HFrEF, plus a modest recommendation for aldosterone antagonists for HFpEF. The dos and don’ts for treating coexisting conditions integrate data from other randomized trials.

Dr. Masoudi was a member of the writing committee for this guideline update.


Reaffirmation of HT’s efficacy for managing vasomotor symptoms and genitourinary syndrome of menopause.

Sponsoring Organization: The North American Menopause Society (NAMS)

Target Population: Women’s healthcare providers

Background and Objective
Moderate to severe vasomotor symptoms (VMS) affect a high percentage of peri- and postmenopausal women. VMS may persist for many years, negatively affecting quality of life. Genitourinary syndrome of menopause (GSM) is also highly prevalent and may become more bothersome as women age. Using an evidence-based approach, an advisory panel of >20 experts updated the hormone therapy (HT) guidelines of the NAMS. Highlights include the following important clinical points.

Key Recommendations

Vasomotor Symptoms
- Systemic HT is the most effective treatment for VMS.
- Systemic HT has the most favorable benefit-risk ratio in women who are aged <60 or within 10 years of the onset of menopause. This ratio is optimal in women who do not have a uterus and are eligible for estrogen monotherapy.
- For women aged ≥60 or >10 years from the onset of menopause, the benefit-risk ratio of HT is less favorable because of the greater absolute risk for coronary heart disease, stroke, venous thromboembolism, and dementia.
- No evidence supports the routine discontinuation of HT at a specific age (e.g., 65).
- For systemic HT, type, dose, duration, and route of administration should be individualized; shared decision making is recommended.
- When prescribing systemic estrogen for women with an intact uterus, progestin or bazedoxifene is also recommended to prevent the development of endometrial hyperplasia or cancer.

Genitourinary Syndrome of Menopause
- For women with isolated moderate to severe GSM who experience insufficient symptom relief with non-prescription lubricants and moisturizers, low-dose vaginal HT is recommended. This option has a superior benefit-risk ratio compared with systemic HT.
- When using low-dose vaginal HT, progestin treatment to protect the endometrium is not necessary. If vaginal bleeding occurs, appropriate evaluation of the endometrium should be performed.
- Premature Ovarian Insufficiency (POI)
- For women with POI, HT is recommended until at least the median age of menopause, (i.e., age 52).

Bone Loss
- Women with osteoporosis should be offered medical therapy to reduce risk for fracture.
• For women aged <60 or within 10 years of the onset of menopause, HT may be considered a primary therapy for preventing additional bone loss and fracture. Other treatment options include bone-specific medications such as bisphosphonates.

**COMMENT**

The 2017 NAMS position statement reaffirms that HT is an effective treatment for both VMS and GSM. For management of VMS, my first-line HT regimen is a transdermal estradiol 0.037-mg patch plus a progestin taken either cyclically or continuously if the woman has a uterus. For women who do not have a uterus, I prescribe estrogen without progestin. Some observational evidence indicates that transdermal estradiol is associated with lower risk for venous thromboembolism compared with standard doses of oral estradiol. For GSM, my first-line HT option is a 10-µg vaginal estradiol tablet twice weekly. The FDA should remove or revise the current warning label for topical low-dose vaginal hormone products.

Andrew Kaunitz, MD, Editor-in-Chief of *NEJM Journal Watch Women's Health*, served on the NAMS advisory panel but had no role in the selection or editing of this Guideline Watch.

New Multisociety Hypertension Guideline Is Released

Karol E. Watson, MD, PhD, FACC, and Allan S. Brett, MD, reviewing Whelton PK et al. J Am Coll Cardiol 2017 Nov 13; [e-pub].

The guideline lowers thresholds for categorizing people as having hypertension and for prescribing drug therapy.

**Sponsoring Organizations:** American College of Cardiology (ACC), American Heart Association (AHA), and nine other organizations

**Target Audience:** All clinicians

**Background**

In 2003, the National Institutes of Health (NIH) issued its last guideline on hypertension (Seventh Joint National Committee [JNC7]; NEJM JW Gen Med Jun 15 2003 and JAMA 2003; 289:2560). In 2014, the JNC8 guideline — written by an expert panel no longer affiliated with NIH — was published (NEJM JW Gen Med Jan 15 2014 and JAMA 2014; 311:507). Now, the ACC and AHA have issued a new guideline, intended to be the U.S. standard of care.

**Key Recommendations**

- Newly defined categories are "elevated blood pressure (BP)" (systolic BP, 120–129 mm Hg and diastolic BP, <80 mm Hg); stage 1 hypertension (systolic BP, 130–139 mm Hg or diastolic BP, 80–89 mm Hg), and stage 2 hypertension (systolic BP, ≥140 mm Hg or diastolic BP, ≥90 mm Hg).

- For people with elevated BP (but not hypertension), lifestyle modification is recommended.

- For people with stage 1 hypertension who have known atherosclerotic cardiovascular disease (CVD) or 10-year cardiovascular risk ≥10% (according to the ACC/AHA calculator (http://www.cvriskcalculator.com), which also is used for cholesterol management), both lifestyle modification and drug therapy are recommended. Stage 1 patients with <10% 10-year risk should pursue lifestyle modification only.

- All people with stage 2 hypertension should receive medication (in addition to lifestyle modification).

- The treatment goal for everyone is <130/80 mm Hg.

**COMMENT — NEJM JOURNAL WATCH GENERAL MEDICINE**

This guideline is a 194-page document (currently online) that addresses a broad spectrum of topics, including BP measurement, secondary hypertension, and managing hypertension in patients with comorbidities. But the big changes — heavily influenced by results of the SPRINT study (NEJM JW Gen Med Dec 15 2015 and N Engl J Med 2015; 373:2103) — are those in the bulleted list above.

First, the new categories will label many more people as having elevated BP or frank hypertension. In JNC7, systolic thresholds for so-called prehypertension, stage 1 hypertension, and stage 2 hypertension were 120 mm Hg, 140 mm Hg, and 160 mm Hg, respectively; diastolic thresholds were 80 mm Hg, 90 mm Hg, and 100 mm Hg, respectively. The downstream consequences of telling people with BP of 120/70 mm Hg that their BP is "elevated" are unknown.

Second, in the new guideline, hypertension treatment is based on both BP thresholds and 10-year overall CV risk. Younger and middle-aged people without other substantial risk factors who are labeled as having stage 1 hypertension (130–139/80–89 mm Hg) generally will have estimated 10-year CVD risk <10%, and lifestyle modification (but not drug therapy) will be recommended for them. However, nearly all older people with BP in this range will be candidates for drug therapy, because the risk calculator gives them 10-year CV risk >10% based on age alone.

(Comment continued on next page)
Consider, for example, a healthy white 65-year-old male nonsmoker with a BP of 130/80 mm Hg, total cholesterol level of 160 mg/dL, HDL cholesterol of 60 mg/dL, LDL cholesterol of 80 mg/dL, and fasting blood glucose of 80 mg/dL — all favorable numbers. The calculator estimates his 10-year CV risk to be 10.1%, making him eligible for BP-lowering medication under the new guideline. To my knowledge, no compelling evidence exists to support drug therapy for this person, and, keep in mind, several studies have suggested that the ACC/AHA risk calculator overestimates risk in certain populations. In addition, a recent guideline from the American College of Physicians and the American Academy of Family Physicians (NEJM JW Gen Med Apr 15 2017 and Ann Intern Med 2017; 166:430) recommends — as did JNC8 — a systolic BP treatment threshold of 150 mm Hg for average-risk older people (age, ≥60).

In the new guideline, the authors discuss accurate measurement of BP in the office and encourage home or ambulatory monitoring to identify white-coat hypertension. Unfortunately, proper office measurement (e.g., seated position for at least 5 minutes in a quiet and relaxed setting, proper positioning of the arm, repeat measurements after several minutes in some cases) is the exception and not the rule in most primary care practices. BP lability is common with both office-based and home readings, making it difficult to say, “your blood pressure is X” (a single number that represents the patient’s “true” BP).

I’m not going to change my practice until I weigh responses to this guideline from a broad range of experts. In the end, initiating drug therapy in patients with BPs near treatment thresholds should reflect shared decision making between clinicians and patients. — Allan S. Brett, MD

COMMENT — NEJM JOURNAL WATCH CARDIOLOGY

The new hypertension guidelines have the potential to improve cardiovascular outcomes by shining a bright light on the dangers of even modest BP elevations and encouraging lifestyle management. These guidelines now label many more Americans as having hypertension, but this should be seen not as a mandate for more drug treatment but as a call to action for lifestyle changes and, if necessary, drug therapy.

— Karol E. Watson, MD, PhD, FACC

Managing Seasonal Allergic Rhinitis with Medications


*Updated guidelines from the 2017 Joint Task Force on Practice Parameters recommend initial treatment with an intranasal corticosteroid alone.*

**Sponsoring Organizations:** American Academy of Allergy, Asthma, and Immunology (AAAAI); American College of Allergy, Asthma, and Immunology (ACAAI)

**Target Audience:** Primary care providers, otolaryngologists, allergists, and pulmonologists

**Background** Seasonal allergic rhinitis affects as many as 14% of adults in the U.S. Most patients either self-treat or see primary care clinicians; only a minority of patients see allergists. Patients and physicians alike often express confusion about the best medication or combination of medications to use. This update of a 2008 guideline from the AAAAI and ACAAI provides specific guidance on pharmacologic treatment for seasonal allergic rhinitis, including for initial therapy.

**Key Recommendations**

- For initial treatment in adolescents and adults (age, ≥12), monotherapy with an intranasal corticosteroid is preferred; combining it with an oral antihistamine confers no additional benefit.
- For initial treatment in patients older than 14, an intranasal corticosteroid should be chosen over a leukotriene-receptor antagonist such as montelukast.
- For moderate-to-severe allergic rhinitis, adding an intranasal antihistamine to an intranasal corticosteroid can be beneficial.

**COMMENT**

Patients tend to prefer oral medications over nasal sprays, but if an intranasal corticosteroid is used regularly, it is the most effective medication for addressing all allergic rhinitis symptoms, with no need to add an oral antihistamine. However, because many patients seem to feel better while taking oral antihistamines, I suggest using them only as needed and stressing daily use of their nasal steroid. For patients with mild nasal symptoms (especially mild itching, rhinorrhea, or sneezing) or systemic itching or urticaria, an oral antihistamine is appropriate first-line therapy. For patients whose allergic rhinitis is not controlled adequately with intranasal corticosteroids alone or who have severe symptoms and want quicker onset of action, intranasal antihistamines such as azelastine can be added to their nasal steroid, albeit at the expense of dysgeusia.

Pharmacological Treatment of Patients with Alcohol Use Disorder


Approaches for treating this highly prevalent disorder may include naltrexone and acamprosate and, in specific circumstances, topiramate, gabapentin, and disulfiram.

Sponsoring Organization: American Psychiatric Association (APA)

Target Audience: Prescribing providers in primary care, psychiatry, and addiction-treatment settings

Target Population: Individuals with alcohol use disorder (AUD)

Background and Objective: This evidence-based guideline provides recommendations regarding AUD pharmacologic treatments; several are FDA-approved for treating AUD (naltrexone, acamprosate, disulfiram [Antabuse]). The guidelines focus on helping individuals reduce or stop their use of alcohol (not on treating withdrawal).

Key Points

The guidelines are categorized by whether benefits of treatment outweigh harms and by the level of evidence.

• Recommendations (benefits clearly outweigh harms)
  – Evaluate patients for comorbid substance use and psychiatric disorders, and elicit patients’ treatment goals and preferences during the assessment.
  – Offer naltrexone or acamprosate to patients with moderate-to-severe AUD (ms-AUD) who have a goal of abstinence or reducing alcohol consumption.
  – Offer naltrexone to patients with ms-AUD and co-occurring opioid use disorder who wish to abstain from opioids.
  – Avoid acamprosate if there is severe renal impairment.
  – Avoid naltrexone if there is acute hepatitis, hepatic failure, or ongoing opioid use.
  – Avoid benzodiazepines and antidepressants unless treating alcohol withdrawal or a comorbid disorder.
  – Avoid pharmacological treatments in pregnant or breast-feeding women.

• Suggestions (benefits outweigh harms, but the balance is less clear)
  – Topiramate or gabapentin can be offered to ms-AUD patients who have a goal of abstinence or reducing alcohol use.
  – Disulfiram can be offered to ms-AUD patients who wish to achieve abstinence.

COMMENT

A systematic review and meta-analysis (JAMA 2014; 311:1889) formed the basis for the guidelines. Expansions beyond this earlier publication occur in the suggestions regarding gabapentin (because of new data) and disulfiram (because of a newer meta-analysis with open-label trials plus a study using supervised medication delivery). The guidelines did not distinguish between depot and oral naltrexone because head-to-head studies have not been published.

Most of the medication studies used to develop these guidelines provided evidence-based psychosocial interventions concurrently, which should be considered first-line AUD treatments.
Joel Yager, MD, an Associate Editor of NEJM Journal Watch Psychiatry, was an author of these guidelines but had no role in the selection or editing of this Guideline Watch.


Updated Guidelines for the Early Management of Patients with Acute Ischemic Stroke

Anthony S. Kim, MD, reviewing Powers WJ et al. Stroke 2018 Jan 24; [e-pub].

A new extended time window for mechanical thrombectomy and a focus on targeted cost-effective diagnostic testing are included in this long-anticipated update.

Sponsoring Organization: American Heart Association/American Stroke Association

Target Population: Adult patients with acute arterial ischemic stroke

Background and Objective: To provide comprehensive evidence-based recommendations for acute stroke management, using a new format and grading system to rate the strength and the quality of evidence for each recommendation.

Key Points

Important new recommendations are as follows:

- **Expanded Time Window for Mechanical Thrombectomy**: The DAWN and DEFUSE 3 studies selected patients for mechanical thrombectomy within an extended time window based on a combination of clinical and imaging-based criteria. Based on these studies, mechanical thrombectomy is recommended for acute-stroke patients with anterior circulation large vessel occlusion (LVO) who meet either DAWN or DEFUSE-3 eligibility criteria within 6 to 16 hours (I, A) and is reasonable for DAWN-eligible patients within 6 to 24 hours of being observed to be normal (IIa, B-Randomized).

- **Vascular Imaging**: Because identifying candidates for endovascular therapy requires identifying a target LVO early on, intracranial vascular imaging is recommended during the initial imaging evaluation for patients who otherwise meet criteria for endovascular therapy (I, A). For expediency, performing computed tomographic angiography (CTA) before obtaining serum creatinine is reasonable for patients without a history of renal impairment (IIa, B-Nonrandomized), but vascular imaging should not delay administration of intravenous alteplase if indicated.

- **Perfusion Imaging**: Since DAWN and DEFUSE 3 relied on multimodal imaging for patient selection, CT perfusion, diffusion-weighted-MRI, or magnetic resonance perfusion is recommended, provided that this information is used to strictly apply the eligibility criteria from these studies to select patients for mechanical thrombectomy in the 6- to 24-hour time window (I, A). However, additional imaging beyond CT/CTA or MRI/MR angiography (MRA) is not recommended for selecting patients for mechanical thrombectomy <6 hours (III: No benefit, B-Randomized). Multimodal CT and MRI, including perfusion imaging, should not delay administration of intravenous alteplase. (III: Harm, B-Nonrandomized)

- **Routine Diagnostic Testing**: Routine cholesterol testing (III: No benefit, B-Randomized), sleep apnea screening (III: No benefit, B-Randomized), brain MRI (III: No benefit, B-Nonrandomized), intracranial CTA or MRA (III: No benefit, A), echocardiography (III: No benefit, B-Nonrandomized), and MRI to exclude cerebral microbleeds before IV alteplase (III: No benefit, B-Nonrandomized) are not recommended.

COMMENT

The diligence required to implement effective systems of care to disseminate these recommendations into widespread clinical practice, and the discipline required to fill the gaps in the evidence base that are highlighted by this new recommendation grading system, ensure that this particularly consequential update will reverberate for years to come.
Type 2 Diabetes Glycosylated Hemoglobin Targets: ACP Guidance Statement

Daniel D. Dressler, MD, MSc, SFHM, FACP, reviewing Qaseem A et al. Ann Intern Med 2018 Mar 6; [e-pub].

Reviewers for the American College of Physicians integrate HbA\textsubscript{1c} target recommendations from multiple guidelines that have been published since 2013.

Sponsoring Organization: American College of Physicians (ACP)

Target Audience: Primary care clinicians, endocrinologists, and hospitalists

Background

Reviewers for the ACP have critically evaluated six recently published guidelines — from the Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE), the American Diabetes Association (ADA), the Institute for Clinical Systems Improvement (ICSI), the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the U.S. Department of Veterans Affairs and Department of Defense (VA/DoD). They offer summary guidance in using glycosylated hemoglobin (HbA\textsubscript{1c}) targets in managing nonpregnant adults with type 2 diabetes.

Key Recommendations

- Personalize goals for glycemic control based on benefits and risks of pharmacotherapy, patient’s preferences, patient’s overall health and life expectancy, and cost and burden of treatment (e.g., number of medications, ability to adhere).
- HbA\textsubscript{1c} goal should be between 7% and 8% for most patients.
- Deintensify pharmacologic therapies when HbA\textsubscript{1c} levels are <6.5%.
- For patients with life expectancies <10 years — due to age ≥80, residence in a nursing home, or chronic debilitating conditions — treat to minimize symptoms related to hyperglycemia and avoid targeting a specific HbA\textsubscript{1c} goal.

COMMENT

Five major clinical trials in which intensive versus less-intensive type 2 diabetes control were evaluated have been published during the past 2 decades. The 2008 ACCORD trial was stopped early when its intensive-therapy arm was associated with higher mortality than its conservative-management arm (number needed to harm, 100; NEJM JW Gen Med Jul 1 2008 and N Engl J Med 2008; 358:2545); the ADVANCE trial (NEJM JW Gen Med Jul 1 2008 and N Engl J Med 2008; 358:2460), the two UKPDS trials (NEJM JW Gen Med Nov 1 1998 and Lancet 1998; 352:837), and the VADT trial (NEJM JW Gen Med Jan 15 2009 and N Engl J Med 2009; 360:129) did not demonstrate macrovascular benefits, showed only marginal or surrogate benefits in microvascular outcomes (e.g., less albuminuria, less retinal photocoagulation interventions), and revealed excess morbidity (e.g., severe hypoglycemic episodes). The ACP offers reasonable and conservative guidance on HbA\textsubscript{1c} targets for managing type 2 diabetes. However, because most study patients were older, a more aggressive approach might be appropriate in younger patients with few comorbid conditions — they might reap microvascular benefits from decades of tighter control.

**Clostridium difficile** Infection Guidelines with New Diagnosis, Treatment, and Pediatric Recommendations


*Metronidazole is no longer recommended as first-line treatment for adults; nucleic acid testing alone is discouraged unless institutional guidelines limit the collection of specimens to those at increased risk for CDI.*

**Sponsoring Organization:** Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

**Target Audience:** Infectious diseases physicians, gastroenterologists, hospitalists, clinical pharmacists, clinical microbiologists, and infection preventionists

**Background and Objective**

Since publication of the previous *Clostridium difficile* infection (CDI) guidelines in 2010, knowledge regarding epidemiology, testing, and treatment of CDI has progressed considerably. The new guidelines incorporate these advances. Pediatric populations are now covered by these recommendations as well.

**Key Points**

- The guidelines recommend two possible testing strategies:
  1. If institutional agreements limit testing to patients with ≥3 unformed stools over 24 hours, not on laxatives, and lacking another explanation for the diarrhea, use either nucleic acid testing (NAT) or a multistep approach using some combination of antigen testing, NAT testing, and toxin testing.
  2. If no institutional guidelines are in place (and thus specimens with a lower probability of having CDI are routinely obtained), NAT alone is considered to have too high a false-positive rate; a multistep approach using stool toxin testing is preferred. Due to high colonization rates, do not routinely test children younger than 1 year old, and test those aged 1 to 2 years only after excluding other causes of diarrhea.

- For a first CDI episode, treat orally with a 10-day course of either vancomycin or fidaxomicin rather than metronidazole. For a first recurrence after a course of vancomycin, options include a 10-day course of fidaxomicin or an extended tapered and pulsed course of vancomycin. For patients with more than one recurrence, options include 10 days of vancomycin followed by rifaximin (400 mg three times a day for 20 days). For patients with multiple recurrences, fecal microbiota transplantation (FMT) is recommended.

- No recommendations are made regarding probiotic use or whether CDI treatment should be extended if continued antibiotics are required in patients with histories of recurrent CDI.

**COMMENT**

Much has changed in the CDI world since 2010. The new guidelines are a needed update reflecting the growing role of FMT in patients with multiple recurrences of CDI and minimizing the role of metronidazole in adult CDI treatment. The two options for testing will, it is hoped, encourage hospital stakeholders to create local criteria discouraging the overtesting of patients with low clinical suspicion of CDI.

USPSTF Shifts to a Neutral Position on Prostate-Specific Antigen Screening


The U.S. Preventive Services Task Force advises discussions of potential benefits and harms with middle-aged men who are interested in screening.

Sponsoring Organization: U.S. Preventive Services Task Force (USPSTF)

Target Audience: Primary care clinicians

Background
The USPSTF has updated its 2012 Grade D recommendation against prostate-specific antigen (PSA) screening for prostate cancer (NEJM JW Gen Med Jul 1 2012 and Ann Intern Med 2012; 157:120). This publication is the final version of the draft statement, released in 2017, that received substantial publicity (NEJM JW Gen Med May 15 2017). Public comment and research that has been published since the draft release did not result in any changes.

Key Recommendations
- For middle-aged men (age range, 55–69), the USPSTF now recommends that clinicians discuss the potential benefits and harms of screening; decisions to undergo PSA screening should be individualized (Grade C recommendation).
- The USPSTF recommends against PSA screening for older men (age, ≥70; Grade D recommendation).

COMMENT
This shift from a negative to a relatively neutral position on PSA screening in middle-aged men reflects an interpretation that benefits and harms of screening now are balanced more evenly. This view was influenced by more- positive 13-year follow-up data from the European Randomized Study of Screening for Prostate Cancer (ERSPC; NEJM JW Gen Med Sep 15 2014 and Lancet 2014; 384:2027) and by an increasing trend toward active surveillance rather than aggressive treatment in men with low-grade cancers (generally defined as a Gleason score ≤6). Editorialists predict that PSA screening rates will rise, based on a shared decision-making approach, reversing a substantial decline after the USPSTF’s 2012 negative recommendation. However, despite the statistically positive result of the European trial, all-cause mortality was not different between screened and control groups, and only slightly more than 1 prostate cancer death per 1000 men screened was prevented during 13 years of follow-up. The absolute benefit still is very small, and false-positive screenings are common, leading to excess biopsies, overdiagnosis, and complications from overtreatment.


Testosterone Therapy: An Update

Allan S. Brett, MD, reviewing Bhasin S et al. J Clin Endocrinol Metab 2018 May 1; 103:1715.

A new Endocrine Society guideline reviews diagnosis and management of hypogonadism.

Sponsoring Organization: Endocrine Society

Background

In 2010, the Endocrine Society published a guideline on testosterone (T) therapy (NEJM JW Gen Med Aug 1 2010 and J Clin Endocrinol Metab 2010; 95:2536). The society now has published an update, with “hypogonadism” substituting for “androgen deficiency” in the title.

The guideline makes the following recommendations:

• Diagnose hypogonadism in men with symptoms and signs of T deficiency and “unequivocally and consistently low” T levels. Symptoms are divided into “specific” or “suggestive” (mostly sexual-related) and “nonspecific” (e.g., decreased energy). Two fasting T measurements on separate mornings are recommended, given day-to-day variability in T levels. Diagnoses usually can be based on total T levels, but free T levels are indicated in certain clinical scenarios.

• In men with unequivocal hypogonadism, distinguish between primary (testicular) and secondary (hypothalamic–pituitary) causes.

• Do not screen men “routinely” for hypogonadism.

• Do not prescribe T therapy routinely to older men (age, >65) with low T levels. However, in those with “suggestive” symptoms of T deficiency and consistently low T levels, offer T therapy individually after discussing potential benefits and risks. The recent “TTrials” (NEJM JW Gen Med Mar 15 2016 and N Engl J Med 2016; 374:611) suggested that potential benefits are limited mainly to improved sexual function in men with sexual symptoms.

COMMENT

This 2018 guideline is similar to the 2010 version. Although some recommendations now have more supportive evidence, some of the language remains tentative (e.g., advice to not do certain things “routinely”; symptoms classified as “suggestive”). This reflects lingering uncertainty about who to evaluate, who to label as androgen-deficient, and who to treat — particularly among middle-aged and older men with nonspecific symptoms or signs. For clinicians who prescribe T therapy, the guideline comprehensively reviews the various T formulations, absolute and relative contraindications to T therapy, and how to monitor treatment.

Update on Screening for Osteoporosis to Prevent Fractures


The U.S. Preventive Services Task Force expands clinical risk assessment in postmenopausal women younger than 65.

Sponsoring Organization: U.S. Preventive Services Task Force (USPSTF)

Target Audience: All clinicians

Background
The heavy clinical, functional, and economic burden of osteoporotic fractures, particularly hip fractures, caused the USPSTF to revisit its 2011 recommendation on screening for osteoporosis (Ann Intern Med 2011; 154:356). This guideline focuses on postmenopausal women without osteoporotic fractures or known risks for osteoporosis or falls.

Recommendations
- Bone-density testing should be performed in older women (age, ≥65) to prevent osteoporotic fractures (B recommendation).
- Younger postmenopausal women (age, <65) at high risk for osteoporosis based on traditional risk factors (i.e., smoking, excess alcohol use, low body weight) should undergo bone-density testing if excess risk is noted on any of several validated clinical risk assessment tools (e.g., Simple Calculated Osteoporosis Risk Estimation [SCORE], Osteoporosis Risk Assessment Instrument [ORAI], Osteoporosis Self-Assessment Tool [OST], Fracture Risk Assessment Tool [FRAX]) (B recommendation).
- Evidence is insufficient to make a recommendation regarding screening for osteoporosis in men (I statement).

COMMENT
The USPSTF emphasizes that this guideline applies only to patients without prior osteoporotic fractures or any risk for secondary osteoporosis, including taking medications such as corticosteroids or aromatase inhibitors. The major change in this guideline from the 2011 version is expansion of clinical risk assessment to include several validated instruments and deemphasis of the FRAX instrument (recommended in 2011), because several of its components do not apply to this population. The USPSTF makes no specific recommendation about repeated testing but mentions evidence showing that repeated testing (as long as 8 years after baseline) had no value. The Task Force’s inability to make a recommendation on the value of screening in men is an important evidence gap. The full guideline contains considerable additional valuable information on clinical risk assessment and approaches to prevention and treatment of osteoporosis.


SCORE, ORAI, OST, and FRAX calculators are available free of charge at https://viajwat.ch/2LrdDsC, https://viajwat.ch/2mOjYQi, https://viajwat.ch/2v9ZTaI, and https://viajwat.ch/2OnLYH4, respectively.
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