

Summaries and highlights
of the most important
new clinical guidelines
to inform your practice

Guideline Watch 2022



NEJM Journal Watch

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NEJM JOURNAL WATCH

Cardiology
General Medicine
Hospital Medicine
Infectious Diseases
Neurology
Oncology and Hematology

Dear Reader,

Clinical guidelines are used increasingly to set practice standards and quality measures. NEJM Journal Watch not only publishes summaries of the latest clinical research, but also helps you to keep up with the guidelines most important to general medical practice.

Our physician-editors regularly survey a broad range of medical journals to identify practice guidelines from a variety of disciplines. They choose clinically impactful recommendations and highlight key points, pointing out what's new and what remains unchanged. This collection of Guideline Watches is of broad relevance to clinical practice, spanning outpatient and inpatient medicine and addressing both primary care and subspecialty perspectives.

We hope you enjoy this compilation and find it useful for providing the best and most responsible patient care.

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

Guideline Watch 2022

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New Surviving Sepsis Guidelines

In this update, recommendations include using balanced crystalloid for resuscitation and steroids for persistent shock.

Patricia Kritek, MD, reviewing Crit Care Med 2021 Nov.

Sponsoring Organizations: Society of Critical Care Medicine (SCCM); European Society of Intensive Care Medicine (ESICM)

Background

This is the fourth update to these guidelines; the third update was published in 2017 (*NEJM JW Gen Med* Mar 1 2017 and *Intensive Care Med* 2017; 43:304).

Key Points

- The recommendation for an initial fluid bolus of 30 mL/kg was downgraded from a strong recommendation to a weak recommendation, based on the low quality of evidence. However, resuscitation should start immediately.
- Balanced crystalloid solution (e.g., lactated Ringer's solution) should be used (rather than normal saline) for resuscitation.
- Administration of vasopressors should be initiated via peripheral access, as opposed to waiting for placement of central venous access.
- Patients with ongoing vasopressor requirements should receive intravenous corticosteroids (this recommendation was strengthened); however, administration of intravenous vitamin C is explicitly *not* recommended.
- Adult patients who survive to discharge should have follow-up for physical, cognitive, and emotional problems associated with their admission.

COMMENT

These new guidelines highlight what has evolved in the care of patients with sepsis or septic shock in the past 5 years, while also maintaining emphasis on key principles, such as early, appropriate antibiotic administration. Many intensivists have balked at a uniform first fluid bolus for all patients because of potential deleterious effects on frail patients, including those with heart failure or kidney disease; this update reflects that concern. This change likely will be reflected in the Centers for Medicare & Medicaid Services (CMS) sepsis bundle measures in 2022. Use of steroids is associated with faster resolution of shock and shorter length of stay. Many providers have adopted the default use of balanced crystalloid solutions, as reflected in this document. Finally, the emphasis on long-term effects of critical illness is important and an area of growing focus.

Evans L et al. Executive summary: Surviving Sepsis Campaign: International guidelines for the management of sepsis and septic shock 2021. *Crit Care Med* 2021 Nov; 49:1974. (<https://doi.org/10.1097/CCM.0000000000005357>)

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2021 Update to the CHEST VTE Treatment Guidelines

Evidence published in the past 5 years supports a few new recommendations for venous thromboembolism management.

Daniel D. Dressler, MD, MSc, MHM, FACP, reviewing **Chest** 2021 Aug 2.

Sponsoring Organization: American College of Chest Physicians

Background

The ninth edition of the CHEST Clinical Practice Guidelines for managing venous thromboembolism (VTE) — published in 2012 and updated in 2016 — now has a second update, which addresses 14 clinical questions and offers 32 guidance statements for clinicians who manage patients with VTE. The 2012 guideline ([Chest 2012; 141:Suppl:e419S](#)) and the 2016 update ([NEJM JW Emerg Med Feb 2016](#) and [Chest 2016; 149:315](#)) both are publicly available.

Key Recommendations

- **Patients with isolated subsegmental pulmonary embolism (PE):** Rule out proximal deep venous thrombosis (e.g., with ultrasonography). If risk for recurrent VTE is low, surveillance is recommended over anticoagulation. If risk for recurrent VTE is high, anticoagulation is recommended. (*Weak recommendation, low-certainty evidence*)
- **Patients with incidentally discovered asymptomatic PE (other than isolated subsegmental PE):** Same initial and long-term anticoagulation that patients with symptomatic PE receive should be used. (*Weak recommendation, moderate-certainty evidence*)
- **Patients with cancer-associated VTE:** Direct-acting oral anticoagulants (DOACs; i.e., apixaban, edoxaban, or rivaroxaban) should be used for the treatment phase of therapy (*strong recommendation, moderate-certainty evidence*). Caveat: for patients with luminal gastrointestinal malignancies, apixaban or low-molecular-weight heparin is preferred to reduce bleeding risk.
- **Patients with antiphospholipid syndrome:** Warfarin (target international normalized ratio, 2.5) is recommended over DOAC therapy during the treatment phase for VTE. (*Weak recommendation, low-certainty evidence*)
- **Catheter-assisted mechanical thrombectomy:** Recommended for patients with PE and hypotension who also have high bleeding risk, failed systemic thrombolysis, or shock that is likely to lead to death before systemic thrombolysis can take effect. (*Weak recommendation, low-certainty evidence*)
- **Initial anticoagulation setting:** Outpatient treatment is recommended over hospitalization in patients with low-risk PE, if access to medications and outpatient care is available. (*Strong recommendation, low-certainty evidence*)
- **Treatment-phase anticoagulants:** DOACs are recommended over warfarin. (*Strong recommendation, moderate-certainty evidence*)

- **Extended-phase therapy (beyond 3 months) for VTE:** Extended anticoagulation should be offered to patients with unprovoked VTE — i.e., with no major or minor transient risk factors. Risk for recurrent VTE, risk for bleeding, and patients' values and preferences should be considered in decisions about extended anticoagulation therapy. (*Strong recommendation, moderate-certainty evidence*)
 - Low-dose apixaban or rivaroxaban is recommended over full doses of these agents. (*Weak recommendation, very low-certainty evidence*)
 - Aspirin is recommended for patients who are stopping anticoagulation. (*Weak recommendation, low-certainty evidence*)

COMMENT

Although much of the guidance in this update already is prevalent in clinical practice, some of the updated recommendations might help forge greater consistency among providers who care for patients with VTE.

Stevens SM et al. *Antithrombotic therapy for VTE disease: Second update of the CHEST Guideline and Expert Panel Report. Chest* 2021 Aug 2; [e-pub]. (<https://doi.org/10.1016/j.chest.2021.07.055>)

Dr. Dressler is Deputy Editor of *NEJM Journal Watch General Medicine* and Professor of Medicine and Co-Director of the Semmelweis Society at Emory University School of Medicine in Atlanta, Georgia.

“Clinical Care Pathway” for Nonalcoholic Fatty Liver Disease

An interdisciplinary panel has published guidance on screening, diagnosis, and management.

Allan S. Brett, MD, reviewing *Gastroenterology* 2021 Nov.

Sponsoring Organization: American Gastroenterological Association (AGA)

Background

Because the prevalence of nonalcoholic fatty liver disease (NAFLD) is high in the general population, the AGA convened a multidisciplinary panel to develop an algorithmic “clinical care pathway” for NAFLD that is appropriate for primary care clinicians.

Key Points

- Identify “at-risk” patients, who fall into these three groups: (1) type 2 diabetes; (2) two or more metabolic risk factors (i.e., central obesity, high triglycerides, low HDL cholesterol, hypertension, prediabetes); and (3) incidental finding of steatosis on imaging or high alanine or aspartate transaminase (ALT or AST) on laboratory testing.
- Screen at-risk patients for alcohol use and check ALT and AST levels (if not already completed). Patients with elevated ALT or AST should be screened for other liver diseases, especially hepatitis B and C.
- Screen noninvasively for clinically significant fibrosis, using [FIB-4](#); the FIB-4 score is derived from age, ALT and AST levels, and platelet count and can be obtained using online calculators.
- Patients with low-risk FIB-4 scores (<1.3) can be followed routinely in primary care; those with high-risk FIB-4 scores (>2.67) should be referred to a hepatologist.
- Patients with intermediate-risk FIB-4 scores (1.3–2.67) should undergo measurement of liver stiffness (e.g., using a transient elastography device such as FibroScan).
- Patients with low-risk liver stiffness (<8 kPa) can be followed routinely in primary care. Those with intermediate-risk (8–12 kPa) or high-risk (>12 kPa) stiffness should be referred to a hepatologist; however, the pathway also allows for intermediate-risk patients to be followed in primary care.
- The document includes a detailed discussion of lifestyle intervention and drug therapies for patients with NAFLD and NASH (nonalcoholic steatohepatitis). The Mediterranean diet is recommended. No drug has been FDA-approved for treating NASH, but several agents (vitamin E, pioglitazone, and glucagon-like peptide-1 [GLP-1] receptor agonists) can be considered in certain subgroups of patients.

COMMENT

This “care pathway” document is worthwhile reading for primary care clinicians. Its 8 pages (excluding references) include easy-to-follow algorithms and concise, clearly written discussions of the rationale for each step. For areas of uncertainty, the authors allow for shared decision-making that incorporates patient preferences. One point not mentioned is that consultation with a hepatologist might not be readily available in certain geographic areas.

*Kanwal F et al. Clinical care pathway for the risk stratification and management of patients with nonalcoholic fatty liver disease. **Gastroenterology** 2021 Nov; 161:1657. (<https://doi.org/10.1053/j.gastro.2021.07.049>)*

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Acute Diverticulitis: Two New Guidelines

The American College of Physicians weighs in on diagnosis, treatment, and postepisode management.

Allan S. Brett, MD, reviewing *Ann Intern Med* 2022 Jan 18.

Sponsoring Organization: American College of Physicians (ACP)

Background

The ACP has published two new clinical guidelines on diverticulitis. One addresses diagnosis and management, and the other addresses colonoscopy after episodes of diverticulitis and interventions to prevention recurrence. The guidelines refer exclusively to acute left-sided diverticulitis.

Key Recommendations

- Computed tomography (CT) is recommended for patients with suspected diverticulitis “when there is diagnostic uncertainty,” but the authors don’t explain fully what should count as diagnostic certainty.
- Immunocompetent, relatively healthy patients with uncomplicated diverticulitis who have no evidence of systemic inflammatory response can be managed as outpatients. According to results of several randomized trials, such patients do not routinely require antibiotic therapy.
- On occasion, the first manifestation of colorectal cancer is a clinical episode that appears to be acute diverticulitis; in most of these cases, the presentation mimics *complicated* left-sided diverticulitis (i.e., associated with abscess, phlegmon, fistula, obstruction, bleeding, or perforation). Thus, colonoscopy is recommended in patients who receive clinical diagnoses of complicated left-sided diverticulitis, unless they have recently undergone colonoscopy; the procedure should be done a minimum of 6 to 8 weeks after symptoms resolve. The ACP does not recommend colonoscopy for those with *uncomplicated* diverticulitis.
- Elective surgery should be discussed with patients who have frequently recurring diverticulitis (i.e., ≥3 episodes within 2 years) or those with persistent “smoldering” episodes (i.e., lasting >3 months). The authors advocate for shared decision making according to patient preferences.
- The ACP found no evidence to support any pharmacologic or dietary intervention to prevent recurrence of diverticulitis.

COMMENT

These recommendations generally are sensible, although virtually all of them are rated as “conditional” — a label indicating “appreciable uncertainty” about the balance of benefit, burden, and risk. It is interesting to compare these recommendations with those in a 2021 Clinical Practice Update from the American Gastroenterological Association (AGA; [NEJM JW Gen Med Apr 1 2021](#) and *Gastroenterology* 2021; 160:906). Both groups endorse selective management of uncomplicated diverticulitis without antibiotics. But unlike the ACP, the AGA recommends (1) CT scanning routinely for patients who have never had an imaging-confirmed diagnosis of acute diverticulitis, and (2) colonoscopy after a first episode of uncomplicated diverticulitis. I generally favor the AGA approach for CT (given that diagnostic error is not uncommon), but I believe that the ACP’s recommendation to omit colonoscopy after mild, uncomplicated cases is reasonable.

Qaseem A et al. Colonoscopy for diagnostic evaluation and interventions to prevent recurrence after acute left-sided colonic diverticulitis: A clinical guideline from the American College of Physicians. **Ann Intern Med** 2022 Jan 18; [e-pub]. (<https://doi.org/10.7326/M21-2711>)

Balk EM et al. Diagnostic imaging and medical management of acute left-sided colonic diverticulitis: A systematic review. **Ann Intern Med** 2022 Jan 18; [e-pub]. (<https://doi.org/10.7326/M21-1645>)

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Updated Coronary Revascularization Guideline

New focus areas are multidisciplinary decision making, reduction of health disparities, and limitations of revascularization in managing coronary disease.

Stephen P. Vampola, MD, reviewing **Circulation** 2022 Jan 18.

Sponsoring Organizations: American College of Cardiology (ACC), American Heart Association (AHA), and Society for Cardiovascular Angiography and Interventions (SCAI)

Background and Objective

Because of evolving evidence regarding revascularization for obstructive coronary artery disease (CAD), the ACC, AHA, and SCAI have updated 2011 and 2105 guidelines for percutaneous coronary intervention (PCI) and a 2011 coronary artery bypass grafting (CABG) guideline.

Key Recommendations

- Clinical indications should be used — regardless of sex, race, or ethnicity — to guide treatment decisions in CAD and reduce disparities in treatment.
- A multidisciplinary “Heart Team” approach should be utilized for CAD patients who might benefit from CABG or when the optimal strategy is unclear. This includes most patients with multivessel CAD, left main disease, and diabetes, among others.
- Left main disease should be revascularized. CABG is recommended over PCI when high-complexity CAD is present. PCI is reasonable in selected patients if equivalent revascularization is possible.
- Diabetic patients with multivessel CAD involving the left anterior descending artery should undergo CABG instead of PCI.
- In selected patients with stable CAD, aspirin may be safely stopped in favor of P2Y12 monotherapy after 1 to 3 months.
- Radial artery access is recommended for patients undergoing PCI.
- In ST-segment elevation myocardial infarction patients, treatment of severe nonculprit lesions is recommended, typically as a staged procedure. This should not be done at the time of primary PCI for patients in cardiogenic shock.
- Radial artery should be used as conduit for the second most important graft during CABG.

COMMENT

This updated guideline incorporates recent evidence and shows a greater recognition of both the nuances and limitations of coronary revascularization. Due to the complex decision making involved, the guideline appropriately emphasizes a multidisciplinary “Heart Team” approach to selecting optimal strategies for individual patients while also deemphasizing the role of revascularization in stable ischemic heart disease.

Lawton JS et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. **Circulation** 2022 Jan 18; 145:e18. (<https://doi.org/10.1161/CIR.0000000000001038>)

Lawton JS et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. **Circulation** 2022 Jan 18; 145:e4. (<https://doi.org/10.1161/CIR.0000000000001039>)

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Update on GERD Management

A new guideline on diagnosing and treating gastroesophageal reflux disease

Allan S. Brett, MD, reviewing *Am J Gastroenterol* 2022 Jan.

Sponsoring Organization: American College of Gastroenterology (ACG)

Background

This document updates an ACG guideline from 2013 ([NEJM JW Gastroenterol May 2013](#) and *Am J Gastroenterol* 2013; 108:308). The guideline encompasses 30 pages and includes 39 recommendations covering all aspects of diagnosis and treatment. In this summary, I've chosen to highlight several points of particular relevance for primary care clinicians.

Key Points

- An empirical 8-week trial of a proton-pump inhibitor (PPI), given once daily, is recommended for a patient who has classic heartburn and regurgitation but no alarm symptoms. A good clinical response to PPIs is considered an adequate (although not perfect) diagnostic test for gastroesophageal reflux disease (GERD). The authors emphasize that many nonresponders to PPIs have not taken the drugs correctly: PPIs should be taken 30 to 60 minutes before a meal, because they bind to proton pumps that have been stimulated by meals.
- PPI nonresponders, and PPI responders whose symptoms return after an 8-week PPI course, should be evaluated for objective evidence of GERD. Endoscopy should be done after 2 to 4 weeks off PPIs (to maximize the chance to document esophagitis). If endoscopy is normal, ambulatory pH monitoring (off treatment) is the next step.
- The authors encourage intermittent or “on-demand” (rather than indefinite) PPI therapy in patients with no history of high-grade esophagitis or Barrett esophagus. A patient who requires ongoing PPI therapy for symptom control should use the lowest effective dose. Although there are statistical associations between long-term PPI therapy and various purported “complications,” a causal relation is doubtful for most of them.
- Although scientific evidence to support favorable effects of diet and lifestyle modification on GERD generally is weak, the authors recommend several — in particular, weight loss, smoking cessation, and avoiding eating before bedtime. Elevating the head of the bed or sleeping on a wedge, and sleeping preferentially on the left side, also are recommended ([NEJM JW Gen Med Mar 15 2022](#) and *Am J Gastroenterol* 2022; 117:346).
- GERD is thought to contribute to various extraesophageal symptoms, including chronic cough, hoarseness, and laryngitis; however, a causal relation often is unclear in any given patient. For patients with extraesophageal symptoms — but no heartburn or regurgitation — the authors argue against empirical PPI therapy unless reflux is documented by objective testing.
- For refractory GERD, recommendations vary depending on the extent of previous diagnostic evaluation. Some patients will respond to twice-daily PPIs or as-needed addition of a histamine-2 (H₂)-receptor antagonist at bedtime. However, clinicians should be vigilant for alternative conditions with symptoms that might be mistaken for GERD (e.g., achalasia). Pros and cons of surgical approaches to GERD also are discussed.

COMMENT

Much of this guideline is worthwhile for nongastroenterologists. One discrepancy between these recommendations and typical primary care practice is notable: If a patient with no alarm symptoms and good response to a PPI stops the drug after several months and symptoms relapse, primary care clinicians often resume PPI therapy, without further evaluation. For such patients, this guideline recommends endoscopy to identify complications that merit indefinite PPI therapy (i.e., erosive esophagitis or Barret esophagus) and to identify alternative diagnoses (e.g., eosinophilic esophagitis).

Katz PO et al. ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol 2022 Jan; 117:27. (<https://doi.org/10.14309/ajg.0000000000001538>)

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Recommendations for Managing Venous Thromboembolism Related to Orthopedic Surgery

International experts have collaborated to produce a comprehensive guideline.

Allan S. Brett, MD, reviewing *J Bone Joint Surg Am* 2022 Mar 16.

Sponsoring Organization: International Consensus Meeting on Venous Thromboembolism (ICM-VTE)

Background

A group of 600 international experts have issued a new set of guidelines that address virtually all aspects of venous thromboembolism (VTE) related to orthopedic surgery. The 328-page report, with scores of recommendations, is divided into 10 topics (general, hip/knee, foot/ankle, hand/wrist, shoulder/elbow, spine, oncology, pediatrics, sports, and trauma).

Key Points and Recommendations

Here we present selected points, drawn from the “general” and “hip/knee” sections, that might be of interest to nonorthopedists who comanage elective surgical patients with orthopedists.

- A history of VTE is a well-known risk factor for postoperative VTE. However, presence of varicose veins and a history of unprovoked superficial venous thrombosis also are risk factors for VTE in lower-limb orthopedic surgery.
- Because scoring systems for VTE risk stratification generally have not been validated in large orthopedic surgery populations, they are not reliable for such patients.
- Although VTE prophylaxis lowers the incidence of postoperative VTE generally, no strong evidence shows that it lowers the incidence of fatal pulmonary embolism.
- The recommended duration of posthospital VTE prophylaxis after hip or knee arthroplasty is 14 to 35 days. Aspirin is the optimal choice, accounting for efficacy, safety, ease of administration, and cost-effectiveness.
- Intermittent compression devices lower the incidence of VTE after hip or knee arthroplasty, but the authors don't specify precisely when such devices should be used in addition to (or as a substitute for) chemoprophylaxis, and they acknowledge that adherence is low after patients leave the hospital.
- For patients with postoperative isolated distal deep venous thrombosis, it is acceptable either to monitor the thrombus (with a follow-up ultrasound in 1 week) or to institute full anticoagulation.
- Taking a nonsteroidal anti-inflammatory drug (NSAID) at the same time as aspirin can negate aspirin's antiplatelet effect. If a patient is receiving postoperative VTE prophylaxis with aspirin plus an NSAID for pain, aspirin should be taken 2 hours before the NSAID (and not with, or immediately after, the NSAID).

COMMENT

The points listed above only scratch the surface of this lengthy publication. Clinicians who comanage these patients with orthopedic surgeons can access [the full set of documents on the journal's website](#).

ICM-VTE General Delegates. Recommendations from the ICM-VTE: General. J Bone Joint Surg Am 2022 Mar 16; 104:Suppl 1:4. (<https://doi.org/10.2106/JBJS.21.01531>)

ICM-VTE Hip & Knee Delegates. Recommendations from the ICM-VTE: Hip & Knee. J Bone Joint Surg Am 2022 Mar 16; 104:Suppl 1:180. (<https://doi.org/10.2106/JBJS.21.01529>)

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Updated Comprehensive Heart Failure Guideline

Changes from previous guidelines include more-aggressive treatment with SGLT-2 inhibitors and ARNIs, including SGLT-2 inhibitor use in heart failure with preserved ejection fraction.

Mark S. Link, MD, reviewing *J Am Coll Cardiol* 2022 Apr 1.

Sponsoring Organizations: American Heart Association, American College of Cardiology, and the Heart Failure Society of America

Background and Objective

This comprehensive guideline updates and consolidates a 2013 multisociety guideline on management of heart failure (HF) and a 2017 update. Recommendations encompass prevention, evaluation, and treatment in patients with heart failure from stages A (at risk for HF) to D (advanced HF).

What's Changed

More-aggressive use of sodium–glucose cotransporter-2 (SGLT-2) and angiotensin receptor–neprilysin inhibitors (ARNIs) is recommended, including use of SGLT-2 inhibitors for HF with preserved ejection fraction. Atrial fibrillation (AF) management is more fully addressed with anticoagulation and a rhythm control strategy.

Key Points

- Many millions of individuals in the U.S. are in stage-A HF, including those with high blood pressure, obesity, and diabetes. Treatment of these risk factors should be aggressive. In patients with diabetes, use SGLT-2 inhibitors. Healthy lifestyles are also useful in preventing HF in stage-A patients.
- For stage-B HF (pre-HF with no signs or symptoms of HF, but with evidence of structural heart disease or elevated pressures) with reduced left ventricular ejection fraction (LVEF), treat with angiotensin-converting–enzyme (ACE) inhibitors or angiotensin-receptor blockers and beta-blockers to prevent the development of symptomatic HF. Implantable cardioverter-defibrillators (ICDs) are recommended for those who qualify according to standard guidelines. Do not use nondihydropyridine calcium channel blockers.
- Patients with stage-C HF (symptomatic) should receive care from a multidisciplinary team. Medical therapy should include the agents used in stage-B disease but also SGLT-2 inhibitors for those with symptomatic HF with reduced ejection fraction, regardless of presence of diabetes. Mineral corticoid receptor antagonists are also useful, and ARNIs are recommended. Titrate guideline-directed medical therapy upward to achieve target doses shown to be effective in randomized, controlled trials (RCTs). Use diuretics as needed.
- For stage-D HF, use pharmacologic therapies as above and, additionally, implantable cardiac devices, such as ICDs and cardiac resynchronization therapy. Consider advanced therapies (e.g., left ventricular assist device, heart transplant). Treat cardiac amyloid.
- Use ICDs in patients with genetic arrhythmic cardiomyopathies with high-risk features for sudden death and LVEF <45%.
- AF management should increasingly follow a rhythm control strategy with ablation for those in whom it is appropriate.

COMMENT

The recommendations in this comprehensive guideline, incorporating the latest data from RCTs, will be the standard of care for many years. In putting them into practice, I plan to treat more aggressively with SGLT-2 inhibitors and ARNIs and will attempt AF rhythm control strategies sooner.

Heidenreich PA et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure. *J Am Coll Cardiol* 2022 Apr 1; [e-pub]. (<https://doi.org/10.1016/j.jacc.2021.12.012>)

Dr. Link is Deputy Editor of *NEJM Journal Watch Cardiology* and Professor of Medicine and Director of Cardiac Electrophysiology at UT Southwestern Medical Center in Dallas. Dr. Link was a member of the writing committee for this guideline.

Deprescribing Proton-Pump Inhibitors

Practical advice for discontinuing these medications in ambulatory patients

Molly S. Brett, MD, reviewing *Gastroenterology* 2022 Apr.

Sponsoring Organization: American Gastroenterological Association

Background

Proton-pump inhibitors (PPIs) are consistently among the top 10 medications prescribed in the U.S. Although indications for long-term use are limited, many patients continue to take these medications for years or even decades. This clinical practice update — geared toward generalists — offers considerations for discontinuing PPIs safely.

Recommendations

Note that these recommendations are based on expert opinion, supported by literature review, and thus do not include evidence grades.

- Primary care providers should review and document indications for ongoing PPI use regularly. The only definite indications for chronic use (>8 weeks) are complicated gastroesophageal reflux disease (e.g., severe erosive esophagitis, peptic stricture), Barrett esophagus, eosinophilic esophagitis, Zollinger-Ellison syndrome, gastroprotection in high-risk users of nonsteroidal anti-inflammatory drugs, and possibly idiopathic pulmonary fibrosis.
- In most other patients, deprescribing can be considered after assessing risk for gastrointestinal (GI) bleeding. The authors specifically caution against discontinuing PPIs in patients on multiple blood thinners or with prior GI bleeding.
- Clinicians should prepare patients for the possibility of rebound acid hypersecretion, which can last for weeks. PPIs can be tapered or stopped abruptly — in either case, patients might have some rebound symptoms that can be managed with on-demand PPIs, histamine-2 blockers, or antacids.
- Most patients who take twice-daily or double-dose PPIs can be stepped down to standard, once-daily dosing; minimal evidence supports higher doses.
- The authors assert that PPIs should be stopped due to lack of indication rather than concern for adverse effects: Although observational studies have stirred concern about a variety of PPI-related adverse events, no serious adverse effects have been demonstrated in randomized trials.

COMMENT

This guideline empowers generalists to discontinue PPIs for most patients who do not have one of the few indications for chronic use. The authors emphasize that concern for adverse events should *not* prompt deprescribing in patients with valid indications for PPI therapy, and they cite the reassuring safety outcomes in randomized trials in which patients were followed for as long as 3 years ([NEJM JW Gen Med Sep 15 2019](#) and *Gastroenterology* 2019; 157:682). However, many of my patients have been taking PPIs for much longer than 3 years, and we still don't know whether many years of chronic use might confer small risks for adverse effects, such as gastric cancer ([NEJM JW Gen Med Feb 15 2022](#) and *Gut* 2022; 71:16).

Targownik LE et al. AGA clinical practice update on de-prescribing of proton pump inhibitors: Expert review. **Gastroenterology** 2022 Apr; 162:1334. (<https://doi.org/10.1053/j.gastro.2021.12.247>)

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The Pendulum Swings Away from Aspirin for Primary Prevention of Cardiovascular Disease

The USPSTF suggests — but does not strongly recommend — considering aspirin use for certain high-risk, middle-aged people.

Thomas L. Schwenk, MD and Allan S. Brett, MD, reviewing *JAMA* 2022 Apr 26.

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

Background

The potential value of aspirin for primary prevention of cardiovascular disease (CVD) first appeared in a 1989 recommendation by the USPSTF. During the years since 1989 (Table), subsequent iterations of the USPSTF guideline have varied in strength of recommendation, target age groups, and approach to balancing CVD benefit against bleeding risk. The Task Force broadened and strengthened its recommendation in 2009 and then weakened it in 2016. The pendulum now has swung further away from routine use of aspirin in the 2022 update that reflects results of three major randomized trials, published in 2018, that involved mostly older patients at moderate-to-high risk for CVD — ASPREE, ASCEND, and ARRIVE ([NEJM JW Gen Med Oct 15 2018](#) and *N Engl J Med* 2018; 379:1509; [NEJM JW Gen Med Oct 1 2018](#) and *N Engl J Med* 2018; 379:1529; and [NEJM JW Gen Med Oct 1 2018](#) and *Lancet* 2018; 392:1036).

Key Recommendations

- For middle-aged patients (age range, 40–59) with a 10-year risk for CVD $\geq 10\%$, the net benefit of aspirin use is small, but patients at low risk for bleeding might wish to consider initiating it (C recommendation).
- The USPSTF recommends against the initiation of aspirin use in older patients (age, ≥ 60 ; D recommendation).

COMMENT

In 13 years, the USPSTF has moved from a strong recommendation for aspirin use for primary prevention of CVD in a wide swath of adult patients to a weak recommendation for selective use only in patients at high risk for CVD and at low risk for bleeding (after a detailed shared decision-making discussion). One reason for this shift is the decline in absolute baseline risk for CVD due to the widespread application of other preventive strategies (i.e., antihypertensives, statins, and smoking cessation), leading to a smaller window of opportunity for benefit from aspirin, whereas risk for harm from bleeding has remained the same.

In an accompanying editorial in *JAMA*, Dr. Brett discusses additional points. First, the recommendation statements only address initiating aspirin; the guideline does not directly address the issue of stopping aspirin therapy in patients when they reach the age of 60 or stopping it in longstanding aspirin users who now are presenting in their 60s or 70s. Although it makes intuitive sense to do so if one accepts the USPSTF position that net benefit disappears beyond age 60, stopping a preventive strategy once started is a different psychological decision than never starting it in the first place. The second issue is that the Task Force recommendation depends heavily on risk stratification derived

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from [the American College of Cardiology/American Heart Association CVD risk calculator](#) that overpredicts risk in some populations. The seemingly objective, but actually imprecise, nature of the risk calculator presents significant challenges to both clinicians and patients in having productive shared decision-making discussions.

A close reading of the full USPSTF recommendation statement — and the evidence review that accompanies it — will provide helpful guidance for the patient-clinician discussions that inevitably will result from release of this recommendation.

Davidson KW et al. Aspirin use to prevent cardiovascular disease. *JAMA* 2022 Apr 26; 327:1577. (<https://doi.org/10.1001/jama.2022.4983>)

Guirguis-Blake JM et al. Aspirin use to prevent cardiovascular disease and colorectal cancer: Updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2022 Apr 26; 327:1585. (<https://doi.org/10.1001/jama.2022.3337>)

Brett AS. Should patients take aspirin for primary cardiovascular prevention? Updated recommendations from the US Preventive Services Task Force. *JAMA* 2022 Apr 26; 327:1552. (<https://doi.org/10.1001/jama.2022.2460>)

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USPSTF Reaffirms Its Recommendation Against Screening for Chronic Obstructive Pulmonary Disease

The U.S. Preventive Services Task Force found no new evidence and continues to focus on reducing harm from tobacco use.

Thomas L. Schwenk, MD, reviewing *JAMA* 2022 May 10.

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

Background

Despite a 2016 recommendation against screening for chronic obstructive pulmonary disease (COPD), the USPSTF recognizes the substantial morbidity and mortality burdens of COPD (particularly in women and minority patients). The Task Force now has revisited this issue to determine if any new evidence would support a change in its 2016 D recommendation (*NEJM JW Gen Med May 15 2016* and *JAMA* 2016; 315:1372). The target population of this recommendation is asymptomatic adults who do not recognize or report respiratory symptoms, such as a chronic cough, sputum production, or difficulty breathing. The recommendation does not apply to patients at especially high risk for COPD, including those with α -1-antitrypsin deficiency or occupational toxin exposures.

Recommendation

The Task Force continues to recommend *against* screening for COPD (D recommendation).

COMMENT

The USPSTF requires substantial new and robust evidence to overturn their previous strongly established recommendation. They found no new studies of sufficient quality or power that directly assessed the potential benefits of screening on morbidity, mortality, or health-related quality of life to justify a change in the previous recommendation. No new evidence showed harms from screening, but the opportunity costs of screening and the lack of benefit led to the D recommendation. Clinicians should continue to focus their efforts on reducing tobacco use through lower rates of smoking initiation and higher rates of cessation.

Mangione CM et al. Screening for chronic obstructive pulmonary disease: US Preventive Services Task Force reaffirmation recommendation statement. *JAMA* 2022 May 10; 327:1806. (<https://doi.org/10.1001/jama.2022.5692>)

Webber EM et al. Screening for chronic obstructive pulmonary disease: Updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2022 May 10; 327:1812. (<https://doi.org/10.1001/jama.2022.4708>)

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USPSTF Updates Recommendations on Routine Vitamin and Mineral Supplements

The U.S. Preventive Services Task Force found inadequate evidence to make recommendations about most vitamins and minerals for primary disease prevention.

Thomas L. Schwenk, MD, reviewing *JAMA* 2022 Jun 21.

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

Background

Because more than half of U.S. adults use at least one multivitamin, mineral, or other nutrient supplement, the USPSTF updated its 2014 recommendation regarding vitamin and mineral supplementation, based on a review of more than 50 studies that have been published since 2014 ([NEJM JW Gen Med Jun 1 2014](#) and *Ann Intern Med* 2014; 160:558). The recommendations apply to community-dwelling, nonpregnant adults and do not apply to children, pregnant women, or people who are chronically ill or have known nutritional deficiencies.

Recommendations

- The Task Force found no benefit and likely harm from use of β -carotene and lack of either benefit or harm from use of vitamin E, leading to a recommendation against use of either one for preventing cardiovascular disease or cancer (D recommendation).
- They found insufficient evidence to make a recommendation for or against use of multivitamins or other nutrients (except β -carotene or vitamin E) for preventing cardiovascular disease or cancer (I statement).

COMMENT

These recommendations by the USPSTF are identical to the 2014 version, despite the large number of new studies published since then. Many patients ask about multivitamins and other nutrient supplements, and many clinicians recommend supplements, based on the assumption that they can't hurt and might help (except for the known excess risk for lung cancer with β -carotene use). In these clinical encounters, I would focus mainly on counseling against use of supplements that are proven to be harmful and then transition to a more general discussion of a healthy lifestyle.

US Preventive Services Task Force. *Vitamin, mineral, and multivitamin supplementation to prevent cardiovascular disease and cancer: US Preventive Services Task Force recommendation statement.* *JAMA* 2022 Jun 21; 327:2326. (<https://doi.org/10.1001/jama.2022.8970>)

O'Connor EA et al. *Vitamin and mineral supplements for the primary prevention of cardiovascular disease and cancer: Updated evidence report and systematic review for the US Preventive Services Task Force.* *JAMA* 2022 Jun 21; 327:2334. (<https://doi.org/10.1001/jama.2021.15650>)

Jia J et al. *Multivitamins and supplements — Benign prevention or potentially harmful distraction?* *JAMA* 2022 Jun 21; 327:2294. (<https://doi.org/10.1001/jama.2022.9167>)

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