NEJM | Clinician

Multicancer Early Detection — Ready for Prime Time?

WEEK OF October 26th

DAVID S. WEISMAN, D.O., F.A.C.P. | REVIEWING: NEW ENGLAND JOURNAL OF MEDICINE | OCTOBER 21

Clinical Takeaway: Multicancer early detection holds promise as a screening test, but long-term outcome data are needed.

Context

Early cancer detection is the goal of screening programs, but screening detects only about 15% of cancers. Recently, identifying circulating tumor DNA (cell-free DNA) has emerged as a potential tool for broad-based cancer screening using a single blood test. Results of the first randomized trial of this approach now have been published.

In the industry-sponsored NHS-Galleri trial, U.K. researchers randomized 140,000 participants (age range, 50–77) without active cancer to a proprietary cell-free DNA–based blood test or to standard care for three annual screening cycles. The primary end point was stage III or IV cancer across 12 prespecified cancer types.

Key Results

- During a median follow-up of 3.5 years, the incidence of stage III and IV cancer was similar in each group (1%).
- The incidence rate ratio for stage IV cancer (a secondary end point) after three screening rounds was 0.86, which was of borderline statistical significance, favoring the blood-test group.
- In the blood-test group, 1% of patients tested positive. Among those patients, 52% received diagnoses of cancer, and the remainder were considered to be false positives.
- In patients with confirmed cancer, the blood test correctly identified the tissue of origin in 90% of cases.

Comment

Despite the negative results, the incidence of stage IV cancer by the third cycle appeared to be marginally lower in the blood-test group and might reflect a shift toward earlier-stage diagnosis with repeat testing. Presumably, earlier cancer detection would improve patient outcomes, but this remains to be seen. The advisory panel of the U.S. FDA recently voted in favor of the Galleri blood test, but it has not been formally approved; it currently is available commercially by physician order for ≈US$1000. Cell-free DNA blood testing could change how we screen patients for cancer; however, patients and physicians who are considering this test should be aware of the above-noted false-positive rate, complexity of diagnostic testing after positive tests, and lack of evidence that benefits will outweigh harms in the long term.

Sasieni P, et al. Effect of screening with multicancer early-detection test on late-stage cancer diagnosis. N Engl J Med 2026 Oct 8; 395:1374. DOI: 10.1056/NEJMoa2505723. PubMed

More Data on a Cancer Blood Test

CHRISTOPHER W. GOODMAN, M.D. | **REVIEWING: NATURE MEDICINE | OCTOBER 21**

Clinical Takeaway: About 1% of participants had positive tests, and about half of those had cancer — but the harm–benefit balance with this test still is far from clear.

Context

Researchers in the U.K. recently reported results from a large randomized trial of a multicancer screening blood test, which is currently under review by the U.S. FDA. Here, in an industry-sponsored, observational study of the same test in the U.S., 35,000 participants (median age, 64) underwent screening during year 1. Standardized protocols, guided by a positive test's predicted cancer signal origin, were used for diagnostic testing.

Key Results

- 0.9% of participants had positive tests; 60% of those with positive tests subsequently received diagnoses of cancer.
- Among participants with positive tests, most underwent invasive testing (73%) — usually biopsy or endoscopy — and about half underwent whole-body imaging (magnetic resonance imaging, computed tomography [CT], or positron-emission tomography [PET]/CT). If targeted testing was negative, a PET/CT was performed.
- Median time to diagnostic resolution was ≈1 month for those with cancer and ≈2 months for those without cancer.

Comment

Given that patients are going to be curious about this test and that some patients might want it done despite lack of evidence on its benefit, these data can inform our discussions. About 1 in 100 tests were positive and about half of those were true positives — similar to the results from the randomized U.K. trial. However, in this study, we can see that screening comes at the cost of invasive testing, extensive (and expensive) imaging, and diagnostic uncertainty. We do not know how many of these cancers would have been discovered by other means (e.g., screening, symptoms). My advice to patients: I'm excited about a blood test for cancer, too, but let's wait until we have more data. This trial is ongoing, so we'll see results of subsequent testing rounds in future years.

Nabavizadeh N, et al. Performance and safety of a multi-cancer early detection test: The PATHFINDER 2 study. Nat Med 2026 Oct; 32:3760. DOI: 10.1038/s41591-026-04618-w. PubMed

Managing Type 1 Diabetes in Adults

OLE-PETTER R. HAMNVIK, M.B. B.CH. B.A.O., M.M.SC., M.R.C.P.I. | REVIEWING: DIABETES CARE |OCTOBER 19

An overview of the Management of Type 1 Diabetes in Adults: The Updated 2026 Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Background

The ADA and EASD last published a consensus report on type 1 diabetes in 2021. Although the ADA updates its Standards of Care report annually, the field has advanced enough to warrant a comprehensive new joint report. Diabetes self-management education and support remain foundational, both for improving health behaviors and for addressing diabetes distress. The report offers practical advice on when and how to deliver educational information and what to cover, with particular attention to nutrition, glucose management around exercise, and travel.

Key Recommendations

- Assess the cause of diabetes in all patients with new-onset diabetes, because distinguishing type 1 from type 2, monogenic, or other forms of diabetes has management implications.
- When type 1 diabetes is suspected, measure islet autoantibodies; C-peptide values also can be informative.
- Recommend continuous glucose monitoring and automated insulin delivery as the standard of care; fingerstick monitoring and multiple daily injections are alternatives.
- Because several agents approved for type 2 diabetes also might benefit people with type 1 diabetes, particularly those with kidney or cardiovascular disease, the report provides guidance on metformin, pramlintide, glucagon-like peptide-1 (GLP-1)–receptor agonists, and sodium–glucose cotransporter-2 (SGLT-2) inhibitors.
- The benefits of GLP-1 agonists and SGLT-2 inhibitors might extend to type 1 diabetes, at the cost of excess hypoglycemia if insulin is not reduced and, for SGLT-2 inhibitors, ketoacidosis.
- In people with islet autoantibodies and asymptomatic dysglycemia (stage 2), consider teplizumab to delay progression to clinical (stage 3) disease by 2 to 3 years; however, note that published data on teplizumab is mostly from studies in children.

Comment

This report captures the broad scope involved in caring for people with type 1 diabetes. Its length underscores the complexity of the disease and supports referring most, if not all, patients with type 1 diabetes to specialist care. The recommendations largely mirror the recently updated ADA Standards of Care, but the practical guidance will be useful to expert and nonexpert readers alike.

Holt RIG, et al. The management of type 1 diabetes in adults: The updated 2026 consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2026 Sep 15; [e-pub]. DOI: 10.2337/dci26-0122. PubMed

Thromboembolic and Cardiovascular Safety of Menopausal Hormone Therapy

MARIE CLAIRE O'DWYER, M.B. B.CH. B.A.O., M.P.H.
REVIEWING: BMJ
OCTOBER 20

Clinical Takeaway: Oral estradiol use was associated with small increased risks of MI, ischemic stroke, and VTE, but transdermal estradiol was not.

Context

Most of what we know about the thromboembolic and cardiovascular safety of menopausal hormone therapy (MHT) comes from older studies in which women mostly received oral conjugated equine estrogens. To estimate risks associated with contemporary estradiol-based regimens, researchers identified 40,000 women in Denmark aged 50 to 69 with a first diagnosis of venous thromboembolism (VTE), ischemic stroke, or myocardial infarction (MI), assessed their current MHT usage (at time of diagnosis), and compared it with MHT usage in age-matched controls.

Among current MHT users, 88% used oral estrogen (nearly all oral estradiol) and 73% used combination estrogen–progestin, most often with norethisterone acetate.

Key Results

- Current use of oral estrogen (alone or combined with progestin) was associated with absolute risk increases per year of 0.09% for VTE, 0.06% for ischemic stroke, and 0.03% for MI (numbers needed to harm, approximately 1100, 1700, and 3800, respectively).
- Stroke and MI risks were only increased with oral estradiol doses >1 mg/day for more than 1 year and were higher with longer use. No increased stroke or MI risk was observed for doses ≤1 mg/day, regardless of duration.
- Transdermal estradiol, irrespective of dose or treatment duration, was not associated with increased risk of any outcome.

Comment

When counseling patients about MHT, the choice of drug, dose, duration, and delivery route all matter. Given previous studies suggested lower VTE risk with transdermal estradiol, I have favored it over oral formulations in older adults or those with higher VTE risk, and these results strengthen the case that transdermal estradiol is likely safer. Nevertheless, both formulations are guideline-based options, and these results will help me counsel patients considering hormone therapy.

Berggreen J, et al. Contemporary menopausal hormone therapy and thrombotic disease: Nationwide nested case-control study. BMJ 2026 Sep 23; 394:e100688 (https://www.bmj.com/content/394/bmj-2026-100688). PubMed

Fructose and Hypertension: The Source Matters

CLEMENT D. LEE, M.D., M.SC.
REVIEWING: CIRCULATION
OCTOBER 20

Clinical Takeaway: Higher intake of sugar-sweetened beverages and 100% fruit juice, but not whole fruit, was associated with higher hypertension risk.

Context

Fructose has been linked to obesity and adverse cardiovascular outcomes, particularly when consumed in sugar-sweetened beverages like soda and sports drinks. The potential cardiovascular risks of fructose in whole fruits and 100% fruit juices remain controversial. To examine associations between different fructose sources and incident hypertension, researchers followed 26,000 children (ages 9–16 at enrollment; mean age, 12) into adulthood for up to 25 years, surveying them every 1 to 4 years.

Key Results

- During follow-up, 6% of participants were diagnosed with hypertension.
- Total fructose consumption was not associated with an elevated risk of hypertension, but findings differed by source:
    - Sugar-sweetened beverages: Higher intake was associated with hypertension, with risk increasing by 14% for each additional daily serving.
    - 100% fruit juice: Higher intake (particularly of orange juice) was also associated with hypertension, with risk increasing by 20% for each additional daily serving of orange juice.
    - Whole fruits: Overall consumption was not associated with hypertension risk.
- Modeling replacement of one daily serving of sugar-sweetened beverages or fruit juice with one serving of whole fruit was associated with a 22% and 19% reduction in hypertension risk, respectively.

Comment

Parents have asked me whether certain fruits like grapes and mangos (both included in this study) should be avoided because of their sugar content. I can now answer with more confidence that the answer is likely no. Increasingly, we are finding that replacing sodas and fruit juices with actual fruit has cardiovascular benefits. After all, it is an apple a day — not 100% apple juice — that keeps the doctor away.

Nguyen M, et al. Consumption of fructose-containing food and beverage sources in childhood through to adulthood and risk of hypertension: A prospective cohort study. Circulation 2026 Aug 18; 154:612. DOI: 10.1161/CIRCULATIONAHA.125.077666. PubMed

Migraine Prevention in Adults: Updated AAN/AHS Guideline

NEJM Clinician

WEEK OF October 19th

TESHAMAE MONTEITH, M.D. AND CHRISTOPHER W. GOODMAN, M.D.
REVIEWING: NEUROLOGY

Clinical Takeaway: The latest recommendations support the use of CGRP inhibitors, propranolol, topiramate, and valproate as first line, with onabotulinumtoxinA also recommended for chronic migraine.

An overview of Pharmacologic Treatment for Migraine Prevention in Adults Practice Guideline Recommendations: Report of the AAN Guidelines Subcommittee and the American Headache Society (2026)

Background

The American Academy of Neurology (AAN) and American Headache Society (AHS) have updated their 2012 guideline on migraine prevention in adults. To develop their latest recommendations, they conducted a systematic review of over 200 randomized, controlled studies published through mid-2024.

Key Recommendations

- The authors encourage clinicians to consider patient priorities (e.g., tolerability and cost) and relevant comorbidities (e.g., hypertension) when choosing among medication options.
- For episodic migraine (<15 headache days/month), first-line medications include propranolol, topiramate, valproate, and the following calcitonin gene–related peptide (CGRP) inhibitors: atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab.
- Second-line medications include amitriptyline, flunarizine, metoprolol, pizotifen, rimegepant, and telmisartan.
- For chronic migraine (≥15 headache days/month for >3 months, with migraine features on ≥8 days), first-line medications include topiramate, valproate, onabotulinumtoxinA, and the CGRP inhibitors listed above.
- If long-term safety is a priority, consider propranolol, topiramate, and onabotulinumtoxinA.
- In pregnant patients or patients who **may** become pregnant, valproate and topiramate are teratogenic and should be avoided. For these patients, the authors endorse nonpharmacological options and medications recommended by the American College of Obstetricians and Gynecologists, which include nifedipine, propranolol, metoprolol, and onabotulinumtoxinA (chronic migraine only).
- For hypertensive patients, consider use of enalapril, nifedipine, and telmisartan.

Potrebic S, et al. Pharmacologic treatment for migraine prevention in adults practice guideline recommendations: Report of the AAN Guidelines Subcommittee and the American Headache Society. Neurology 2026 Oct 13; 107:e214881. DOI: 10.1212/WNL.0000000000214881. PubMed

Managing Infective Endocarditis: An Update

GEORGE SAKOULAS, M.D. | **REVIEWING: CIRCULATION | OCTOBER 2**

Clinical Takeaway: The latest AHA guidance addresses recent advances in treatment, such as partial oral antibiotic therapy in stabilized patients.

An overview of Infective Endocarditis: Diagnosis, Antibiotic Therapy, and Management: A Scientific Statement from the American Heart Association (2026)

Background

This latest scientific statement on infective endocarditis (IE) from the American Heart Association (AHA) emphasizes a multidisciplinary approach and incorporates advances in diagnosis and therapy since the last iteration in 2015 — such as non–culture-based pathogen identification, partial oral antibiotic therapy in stabilized patients, and long-acting injectable lipoglycopeptide therapy.

Key Points

- Transesophageal echocardiography (TEE) has lower sensitivity for diagnosing suspected IE in the setting of transcatheter aortic valve replacement (TAVR); therefore, consider multimodality imaging.
- Utilize molecular diagnostics (e.g., cell-free DNA assays) in cases of negative blood or valve-tissue culture.
- Brain MRI (but not chest/abdomen/pelvis computed tomography imaging) is considered reasonable in neurologically asymptomatic patients before cardiac surgery.
- Transition to oral therapy can be considered after ≥10 days of IV therapy under these criteria: surgical indications ruled out by TEE; no fever for at least 3 days; 75% minimum drop from peak C-reactive protein value; and white blood cell count <15,000/mm3. Patients with body-mass index >40 kg/m2 or compliance concerns are not candidates for oral therapy.
- Dalbavancin 1500 mg followed by repeat dose at day 8 or 15 is considered an alternative to oral therapy in methicillin-resistant Staphylococcus aureus (MRSA) native valve endocarditis. Oritavancin 1200 mg on day 1 and day 8 is also offered as a consideration for methicillin-susceptible S. aureus (MSSA) native valve endocarditis.
- In patients with Enterococcus faecalis endocarditis, colonoscopy is reasonable to rule out colonic malignancy.
- A post-therapy echocardiogram is encouraged for comparison to imaging done during hospitalization.
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Comment

This is a practical, thorough guide for all clinicians who manage patients with endocarditis. Although aminoglycosides are still appearing in guidance documents, including this one, personally, I abandoned their use several years ago in favor of other combinatorial regimens. Challenging cases of bacterial endocarditis warrant discussion with endocarditis experts including a multidisciplinary team.

DeSimone DC, et al. Infective endocarditis: diagnosis, antibiotic therapy, and management: A scientific statement from the American Heart Association. Circulation 2026 Sep 8; [e-pub]. DOI: 10.1161/CIR.0000000000001466. PubMed

Should We Continue Anticoagulation after Atrial Fibrillation Ablation?

MARK S. LINK, M.D.
REVIEWING: JOURNAL OF THE AMERICAN HEART ASSOCIATION
OCTOBER 14

Clinical Takeaway: Patients in a registry who had discontinued anticoagulation by 6 months were no more likely to have ischemic events and were less likely to bleed.

Context

Patients with atrial fibrillation (AF) who discontinued anticoagulants 1 year after ablation had better outcomes than those who continued the drugs in both the ALONE-AF trial and the OCEAN trial. To provide more data on the risks of discontinuing oral anticoagulation after ablation, researchers analyzed a prospective registry, including more than 13,600 patients who had no AF recurrence for 3 months after ablation.

Key Results

- As of 6 months after ablation, about 11,000 of the patients had discontinued oral anticoagulation while more than 2600 continued. Patients with higher stroke risk (CHA2Ds2-Va score) were more likely to continue anticoagulation.
- During a median 4 years of follow-up, continued oral anticoagulation at 6 months was not significantly associated with reduced risk of thromboembolism even for patients considered at high risk of thromboembolism (CHA2Ds2-Va ≥3).
- Continued anticoagulation was associated with a significantly higher risk of nonmajor bleeding (adjusted hazard ratio, 1.8) and with significantly higher major bleeding among those with high stroke risk (aHR, 2.3; unadjusted absolute risks, 0.6 with vs. 0.26 without continued anticoagulation).

Comment

Although the findings of this prospective registry analysis are not definitive, as there may have been selection bias surrounding who stayed on anticoagulation, they are in line with the prior randomized controlled trials. The message: discontinuation of anticoagulation after a successful ablation for AF is reasonable after 6 to 12 months. However, I remained concerned about patients with very high stroke-risk scores (≥5), few of whom are likely to have been in the cohort that discontinued anticoagulation in this study. For these patients, we still need a real discussion about the risk and benefits of continuing anticoagulation.

Ren L, et al. Thromboembolism and bleeding risks in atrial fibrillation: Outcomes of oral anticoagulation after catheter ablation. J Am Heart Assoc 2026 Oct 6; 15:e047527. DOI: 10.1161/JAHA.125.047527. PubMed

Medetomidine in the Illicit Fentanyl Supply: Recognizing Overdose and Withdrawal

REBEKAH ROLLSTON, M.D., M.P.H. | **REVIEWING: JOURNAL OF MEDICAL TOXICOLOGY | OCTOBER 9**

Clinical Takeaway: This drug can complicate opioid overdose, causing profound, prolonged sedation that persists despite naloxone.

Context

Medetomidine, a potent alpha-2 adrenergic agonist used in veterinary medicine, has emerged as an adulterant in the illicit fentanyl supply. Because this drug's effects differ from those of opioids alone, clinicians may not recognize medetomidine intoxication and withdrawal. Two recent studies characterize these clinical presentations.

Key Results

In a retrospective study of opioid overdoses in Chicago in 2024, researchers described clinical outcomes for 12 patients with laboratory-confirmed medetomidine exposure.

- All 12 had persistent altered mental status despite naloxone.
- Seven required respiratory support, including three who were intubated; five required ICU care.
- Among those admitted, median hospital stay was 3.5 days.

In another study, 16 hospitalized patients with opioid use disorder and confirmed recent medetomidine exposure were interviewed about their experiences with the drug. They described:

- Profound sedation and loss of consciousness, with increased vulnerability to injury, robbery, and assault
- Withdrawal that was more severe than what they had previously experienced with fentanyl alone or fentanyl–xylazine

Comment

These data support what those of us in addiction care have seen recently: Medetomidine can complicate fentanyl overdose. Since medetomidine isn't detected on routine toxicology testing, clinicians must recognize possible exposure based on clinical presentation and local trends; confirmation requires specialized toxicology testing. Two potential signs of exposure are respiratory depression and profound sedation that doesn't respond to naloxone. In addition, patients might recognize atypical withdrawal symptoms or know that medetomidine is in the local drug supply. When medetomidine intoxication or withdrawal is suspected, patients may need prolonged supportive care and alpha-2 agonist treatment (e.g., clonidine and dexmedetomidine).

Gressick K, et al. Clinical presentation of medetomidine-involved opioid overdoses—Chicago, 2024. J Med Toxicol 2026 Oct; 22:423. DOI: 10.1007/s13181-026-01148-2. PubMed
Pressimone C, et al. Medetomidine exposure in a shifting drug landscape: Insights from patient experiences. Ann Intern Med 2026 Sep 15; [e-pub]. DOI: 10.7326/ANNALS-26-02480. PubMed

Consensus Statement on Managing S. aureus Bacteremia

NEJM Clinician
WEEK OF October 12th

GEORGE SAKOULAS, M.D. | REVIEWING: INFECTIOUS DISEASES SOCIETY OF AMERICA | OCTOBER 2

Clinical Takeaway: A more practical risk-stratification strategy from IDSA/ESCMID replaces the conventional “complicated” versus “uncomplicated” designations.

An overview of the IDSA/ESCMID 2026 Consensus Statements on Staphylococcus aureus Bacteremia: Risk Stratification, Diagnostic Evaluation, and Management of Adults and Children

Background

For managing patients with Staphylococcus aureus bacteremia (SaB), clinicians at the bedside need practical guidelines. This updated consensus statement (the first of an anticipated series by the Infectious Diseases Society of America and the European Society of Clinical Microbiology and Infectious Diseases) focuses on the risk stratification and diagnostic evaluation of children and adults with S. aureus bacteremia, addressing seven clinical questions.

Key Recommendations

- For adults with SAB, stratify evaluation based on key risk factors (community-onset infection, persistent positive blood cultures for ≥48 hours, presence of an intracardiac device) and additional risk factors (predisposing cardiac valve conditions, injection drug use, endovascular graft, unknown focus, 2 or more noncontiguous infection sites, signs of emboli, SaB within the previous 90 days).
- Order follow-up blood cultures 48 hours after the first positive set, and repeat cultures every 24 to 48 hours until negative to document clearance.
- Obtain a transthoracic echocardiogram (TTE) for all adults with SaB, prolonged bacteremia, or evidence of possible endocarditis.
- Obtain a transesophageal echocardiogram (TEE) after negative TTE for all adults with SaB and an intracardiac device (e.g., pacemaker, prosthetic valve), predisposing valvular disease, persistent positive blood cultures ≥48 hours after the first positive culture, embolic events, or multiple foci of infection.
- Use whole-body imaging, such as computed tomography or positron emission tomography (PET), for adults at risk of metastatic or deep-seated infection who have an undefined primary focus of infection.
- In low-risk patients with SaB, after evaluation rules out deep-seated infection, 14 days of antibiotics can be used.
- For patients who have positive blood cultures for ≥48 hours, look carefully for deep-seated or metastatic infection foci and consider >14 days of antibiotics.

- The day of blood culture clearance should be the start time for calculating treatment duration in most cases.

Comment

These updated guidelines eliminate the largely academic SaB designations of “complicated” versus “uncomplicated,” while reinforcing the established need for great diagnostic respect, particularly if the patient has had prior SaB or valvular disease or has cardiac or vascular biomedical devices. This statement and prior studies frequently mention PET scans, yet they are impossible to obtain for most clinicians in the U.S. and cost thousands of dollars, exceeding the cost of weeks of antibiotic therapy. One high-risk condition not mentioned that I pay particular attention to is thrombocytopenia with poor platelet function (e.g., in renal disease, including dialysis). Overall, I am cautious about considering shorter therapy (e.g., 14 days) and strongly recommend longer therapy for those who have positive blood cultures for ≥48 hours, because discerning low-risk SaB is challenging.

Liu C et al. IDSA/ESCMID 2026 consensus statements on Staphylococcus aureus bacteremia: Risk stratification, diagnostic evaluation, and management of adults and children. Infectious Diseases Society of America. 2026 Sep 9; [e-pub]. (https://www.idsociety.org/practice-guideline/staphylococcus-aureus-bacteremia)

Alternative Guidance on Dyslipidemia

CHRISTOPHER W. GOODMAN, M.D. | **REVIEWING: ANNALS OF INTERNAL MEDICINE | SEPTEMBER 24**

Clinical Takeaway: The VA/DoD dyslipidemia guideline differs in significant ways from the ACC/AHA guideline, highlighting room for interpretation of the clinical evidence.

Background

The U.S. Department of Veterans Affairs and Department of Defense (VA/DoD) released their new guideline on dyslipidemia online in 2025, and a summary was published recently in Annals of Internal Medicine. The guideline explicitly is intended for adults "who are eligible for care in the VA and/or DOD healthcare systems." However, readers who don't practice in the VA/DoD systems will still find it instructive, especially with respect to areas in which it differs from the recent dyslipidemia guideline from the American College of Cardiology and American Heart Association (ACC/AHA). Here we outline notable differences, focusing on primary prevention.

Key Differences

Cardiac Biomarkers and Risk Stratification

- The VA/DoD weakly endorses use of lipoprotein(a) "at least once" in a person's lifetime for risk stratification, whereas the ACC/AHA encourages use of other biomarkers (apolipoprotein B, hs-CRP) in addition to lipoprotein(a).
- The VA/DoD notes a lack of prospective randomized trial evidence for cardiac biomarkers.

Primary Prevention Treatment Thresholds

- The VA/DoD weakly recommends a moderate-intensity statin for individuals with 10-year atherosclerotic cardiovascular disease risk of 5%–10% whereas the ACC/AHA strongly recommends treatment for this group.
- The VA/DoD provides no recommendation for statin treatment in the 3%–5% risk range ("borderline risk"), noting limited clinical trial data; in contrast, the ACC/AHA weakly recommends statins for this group.

"Treat to Target" versus Fixed-Dose Strategy

- The VA/DoD endorses a fixed-dose approach to statin treatment but encourages clinical judgment in deciding whether to use LDL treatment goals; in contrast, the ACC/AHA specifies LDL targets.

Comment

These differences largely reflect different approaches to handling gradations in the strength of the clinical evidence: The VA/DoD took a strict approach, making fewer, more well-substantiated statements, and the ACC/AHA took a more expansive approach, making a broader set of recommendations, at times based on weaker data. In the end, the differences serve as a good reminder that guidelines are just that — recommendations that necessitate clinical judgment at the point of care.

Arnold MJ, et al. A synopsis of the 2025 U.S. Department of Veterans Affairs and U.S. Department of Defense clinical practice guideline for lipid management for cardiovascular disease risk reduction. Ann Intern Med 2026 Sep 15; [e-pub]. DOI: 10.7326/ANNALS-26-01374. PubMed

Exercise and Bone Density: Does Modality Matter?

SARAH E. POST, M.D. | **REVIEWING: BMJ |OCTOBER 7**

Clinical Takeaway: Brisk walking or jogging was the most effective option in this meta-analysis.

Context

Exercise is widely recommended for patients with low bone density and osteoporosis, but specific guidance on modality and quantity is based mostly on expert opinion. To assess how different forms of exercise affect bone mineral density (BMD) among adults aged 40 and older, investigators performed a network meta-analysis of 124 randomized trials involving 18,000 participants. Most trials lasted 6 to 12 months.

Key Results

- Brisk walking or jogging was the most effective form of exercise, improving BMD at all three sites measured: lumbar spine, total hip, and femoral neck. Combined aerobic–resistance exercise led to similar improvements for spine and femoral neck BMD but not total hip BMD.
- The other exercise programs evaluated (resistance training, mixed aerobic exercises, whole body vibration, and mind–body exercises like tai chi) generally had smaller effects on BMD, with benefits limited to only one or two sites.
- Clinically meaningful BMD improvements generally occurred at around 600 metabolic equivalent–minutes per week, which is about 2 to 3 hours of brisk walking or jogging.
- No type of exercise was associated with increased fracture risk.

Comment

Brisk walking or jogging is accessible for most patients and easy to recommend, so I'm glad to see that it may be particularly effective for improving bone density. We still don't know for sure whether these increases in BMD lead to lower fracture risk, but harm is unlikely, and exercise has many other known benefits. Some sedentary patients feel hesitant about starting to exercise; I'd recommend starting with brief periods of brisk walking every day and gradually building toward a goal of 2 to 3 hours weekly.

Lu C, et al. Effect of exercise on bone health in middle aged and older adults: Hierarchical network meta-analysis of randomised trials. BMJ 2026 Sep 9; 394:e100561. DOI: 10.1136/bmj-2026-100561. PubMed