NEJM Journal Watch

GUIDELINE WATCH 2019

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

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NEJM JOURNAL WATCH
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Dear Reader,

Clinical guidelines inform practice standards and establish quality measures. In pursuing our mission to improve patient care and foster professional development, NEJM Journal Watch seeks 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 in the last 6 months, covers a range of guidelines, from updated guidance by the Infectious Diseases Society of America on the diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza to the latest recommendations by the American College of Cardiology/American Heart Association Task Force on managing blood cholesterol. 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. 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.

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NEJM Journal Watch

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Guideline Watch 2019

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Diagnosis, Treatment, and Chemoprophylaxis of Influenza

Updated guidelines on managing seasonal influenza

Stephen G. Baum, MD, reviewing **Clin Infect Dis** 2018 Dec 19.

Sponsoring Organizations: Infectious Diseases Society of America with input from infectious-disease specialists in pediatrics and obstetrics

Target Audience: Healthcare providers who are likely to provide initial diagnosis and treatment of patients with influenza

Background and Objective

An update of diagnostic, treatment, and prophylaxis recommendations for influenza outbreaks, last published in 2009 following the emergence of pandemic novel influenza type A(H1N1).

Key Points and Recommendations

Influenza remains an infectious disease with high annual worldwide incidence and is associated with considerable morbidity, hospitalizations, and mortality, especially in high-risk populations, including those at the extremes of age, the immunocompromised, people with cardiorespiratory disease, and those who are pregnant.

- An etiologic diagnosis should be achieved, especially in high-risk patients, using one of the newer nucleic acid amplification–based rapid tests performed on specimens obtained, optimally, via nasopharyngeal swabs. These tests are most sensitive during the early phases of disease, as measured by symptom onset, and are most important if antiviral therapy decisions are to be made prior to discharge from the acute care setting to home.
- Specimens from nonrespiratory sites such as blood are not useful.
- Treatment should be initiated as soon as possible if tests are positive, regardless of vaccination status.
- A single neuraminidase inhibitor, either oral oseltamivir, inhaled zanamivir for 5 days, or single-dose intravenous peramivir, should be used.
- Combination antiviral therapy should be avoided.
- The adamantane antivirals (amantadine and rimantadine) are no longer considered useful.
- Viral resistance to the drug used should be considered if symptoms do not abate on therapy.
- Corticosteroids are not considered useful in the treatment of influenza.
- Postexposure chemoprophylaxis using oseltamivir or zanamivir should be used in the first 48 hours after exposure in settings where vaccination has not been carried out and may be continued for the entire influenza season for high-risk patients.

What's Changed

These guidelines place great emphasis on using rapid nucleic acid–based testing on properly obtained specimens to achieve a diagnosis of influenza as opposed to flu-like illness caused by other agents. They also emphasize rapid treatment or prophylaxis with anti-influenza drugs in high-risk patients regardless of vaccine status, giving tacit acknowledgement of the fact that disease has been prevalent in vaccinated persons in the past few influenza seasons.

COMMENT

These clear, evidence-based guidelines are very useful. Although they are directed at diagnosis, treatment, and chemoprophylaxis, one is struck by the lack of emphasis on vaccination as the very essence of disease prevention. This seems like a missed opportunity to drive this message home. There is also no mention of the new anti-influenza drug baloxavir marboxil (*NEJM JW Infect Dis Jan* 2019 and *N Engl J Med* 2018; 379:913). This is understandable, given the fact that the drug was approved by the FDA contemporaneously with publication of the guideline, but an addendum to the guideline describing this drug might be in order, given its apparent efficacy, unique mechanism of action, and single-dose oral regimen.

Uyeki TM et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. **Clin Infect Dis** *2018 Dec 19; [e-pub]. (https://doi.org/10.1093/cid/ciy866)*

Dr. Baum is Senior Associate Dean for Students and Professor of Medicine, Albert Einstein College of Medicine, Bronx, New York.

Guideline on Cholesterol Management: 2018 Update

Updated lipid guidelines return to LDL targets for high-risk patients, provide guidance on coronary artery calcium testing, and personalize risk assessments.

Fatima Rodriguez, MD, MPH, reviewing **J Am Coll Cardiol** 2018 Nov 10.

Sponsoring Organizations: American College of Cardiology (ACC), American Heart Association (AHA), and 10 other clinical organizations

Target Population: Patients needing primary or secondary prevention for atherosclerotic cardiovascular disease (ASCVD)

Background and Objective

The 2013 ACC/AHA prevention guidelines shifted away from LDL targets and recommended moderate- or high-intensity statin therapy for patients based on risk profiles. The 2018 updated guideline reestablishes LDL goals, incorporates new evidence on nonstatin therapies, and addresses concerns about ASCVD risk overestimation for primary prevention.

Key Recommendations

- For patients with established ASCVD, high-intensity statins should be used to obtain ≥50% reduction in LDL. If this is not achieved, ezetimibe could be added and then a proprotein convertase subtilisin–kexin type 9 (PCSK9) inhibitor.
- For patients with very high risk (history of major ASCVD events, older age, diabetes, hypertension, smoking, familial hypercholesterolemia [FH], kidney disease, or heart failure) and LDL levels >70 mg/dL, adding ezetimibe is reasonable, followed by a PCSK9 inhibitor.
- For patients with severe hypercholesterolemia (LDL levels, >190 mg/dL), maximally tolerated statin therapy is recommended without risk calculations. If LDL is not reduced by 50%, clinicians can reasonably add ezetimibe.
- For patients with diabetes and LDL >70 mg/dL, a moderate-intensity statin is recommended; with elevated ASCVD risk, a high-intensity statin is reasonable.
- For primary prevention, adherence to a healthy lifestyle is the cornerstone of treatment across the lifespan. Clinician-patient discussions about risk assessment and treatment should consider "ASCVD risk enhancers," such as family history, metabolic history, preeclampsia, inflammatory disease, ethnicity, and abnormal biomarkers.
- 10-year ASCVD risk scores between 7.5% and 19.9% are now considered "intermediate risk." This broad category acknowledges uncertainty in risk-calculator estimates and is intended to encourage decision-making guided by patient preferences. For patients who elect drug treatment, a moderate-intensity statin is generally recommended.
- Coronary artery calcium (CAC) measurement is helpful when decisions about statin initiation are uncertain. Withholding or postponing statin initiation is reasonable if CAC=0 and the patient lacks other high-risk features. If CAC score is ≥100, statins should be initiated.
- To monitor adherence to therapy and reduction in LDL, clinicians should check lipids 1 to 3 months after a treatment change.

COMMENT

In many respects, the 2018 guideline supports the way most of us practice by considering risk-enhancing patient factors not in ASCVD risk equations to guide shared decision-making. The guideline also endorses the importance of achieving LDL targets for high-risk groups and provides a stepwise approach to adding nonstatin therapies. CAC testing can be considered for uncertain treatment decisions. It is reasonable to withhold drug therapy when CAC scores are 0 and to provide drug therapy when scores are ≥100. Scores between 1 and 99 are less useful for refining risk.

Grundy SM et al. AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. **J Am Coll Cardiol** *2018 Nov 10; [e-pub]. (https://doi.org/10.1016/j.jacc.2018.11.003)*

Dr. Rodriguez is Assistant Professor, Division of Cardiovascular Medicine, Stanford University School of Medicine.

Primary Prevention of Cardiovascular Disease: New Guideline

Lifestyle modification and shared decision making are emphasized heavily.

Allan S. Brett, MD, reviewing **J Am Coll Cardiol** 2019 Mar 17.

Sponsoring Organizations: American College of Cardiology (ACC) and American Heart Association (AHA)

Background

A new guideline covers virtually all nonpharmacologic and pharmacologic facets of primary prevention of cardiovascular (CV) disease.

Key Points

- Lifestyle modification — including diet, exercise, and smoking cessation — is emphasized heavily, regardless of drug therapy use.
- Recommendations for lipid management duplicate the primary prevention sections of the 2018 ACC/AHA cholesterol guideline (*NEJM JW Gen Med* Feb 1 2019 and *J Am Coll Cardiol* 2018 Nov 10; [e-pub]). The new category of "intermediate" 10-year CV risk (7.5%–20%) gives clinicians leeway in individualizing decisions to prescribe statins. That broad category presumably was created, at least in part, because of concerns about the accuracy of the ACC/AHA risk calculator and potential overuse of statins in people whose risk is overestimated. Coronary calcium scoring and attention to "risk enhancers" (e.g., family history of early CV disease) are encouraged as tie-breakers in borderline cases.
- Recommendations for blood pressure treatment duplicate those of the 2017 ACC/AHA guideline on management of hypertension (*NEJM JW Gen Med* Dec 15 2017 and *J Am Coll Cardiol* 2018; 71:127). The controversial point here is recommended drug therapy starting at thresholds of 130 mm Hg (systolic) and 80 mm Hg (diastolic) for patients whose estimated 10-year CV risk exceeds 10%.
- The discussion of aspirin in primary prevention is influenced heavily by the three largely negative aspirin trials from 2018 (ARRIVE, ASPREE, and ASCEND [*NEJM JW Gen Med* Jan 1 2019]). The guideline rejects aspirin for adults older than 70 and for adults of any age "who are at increased risk of bleeding." For middle-aged adults (age range, 40–70) who are "at higher CV risk but not at increased bleeding risk, [aspirin] might be considered." In my view, the new trials don't really support even that tentative language (and the guideline does give it a weak [class IIb] recommendation).
- For patients with diabetes, recommendations for hypertension and diabetes follow those of the corresponding 2017 and 2018 guidelines cited above. The guideline does add that, in selected cases, "it may be reasonable to prescribe sodium-glucose cotransporter 2 (SGLT-2) inhibitors or glucagon-like peptide-1 receptor (GLP-1R) agonists to … reduce CV risk." However, this is a weak (IIb) recommendation, and readers should be aware that the GLP-1R agonist (liraglutide) and the two SGLT-2 inhibitors (empagliflozin and canagliflozin) that are FDA-approved for CV risk reduction showed this benefit only for secondary — not primary — prevention.
- Shared decision making between patients and clinicians is emphasized, particularly when indications are borderline for drug therapies.

COMMENT

The text, tables, and flow charts in this comprehensive guideline are very readable. Lifestyle modification and shared decision-making are emphasized heavily, but I believe that some of the suggestions for drug therapies are questionable. Hence, readers should pay attention to the level of evidence and strength of recommendation for each proposed intervention.

Arnett DK et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. **J Am Coll Cardiol** *2019 Mar 17; [e-pub]. (https://doi.org/10.1016/j.jacc.2019.03.010)*

Dr. Brett is Professor of Medicine and Director, Division of General Internal Medicine, University of South Carolina School of Medicine, Columbia.

Updated IDSA Guidelines for Managing Asymptomatic Bacteriuria

Screening for, or treating, asymptomatic bacteriuria is not recommended, except in pregnant patients.

Jason T. McMullan, MD, MS, FAEMS, reviewing **Clin Infect Dis** 2019 Mar 21.

Sponsoring Organization: Infectious Diseases Society of America (IDSA)

Background and Objective

Nontreatment of asymptomatic bacteriuria (ASB) is a priority in antimicrobial stewardship initiatives. This update to the 2005 IDSA guidelines incorporates new evidence and addresses additional populations, including children, patients with neutropenia, recipients of solid organ transplants, and patients undergoing nonurologic surgery.

Key Recommendations

- Screening for, and then treating, asymptomatic bacteriuria is recommended for pregnant women; 4 to 7 days of antibiotics is recommended for pregnant women with ASB.
- Screening and treatment is *not recommended* in the following populations: infants and children; healthy nonpregnant women of any age; elderly persons living independently or in a long-term care facility; patients with diabetes; renal transplant recipients >1 month after surgery; any nonrenal solid organ transplant recipients; patients with spinal cord injury; and patients with indwelling urinary catheters of any duration.
- No recommendation is made for high-risk afebrile neutropenic patients due to lack of evidence.
- Observation is preferred over antimicrobial treatment for cognitively impaired adults who experience a fall and are found to have bacteriuria without signs of infection.

COMMENT

These guidelines reinforce that the risks associated with treatment of asymptomatic bacteriuria generally outweigh the benefits, even in populations generally considered fragile. Notably, symptomatic patients are not covered by these recommendations.

Nicolle LE et al. Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America. **Clin Infect Dis** *2019 Mar 21; [e-pub]. (https://doi.org/10.1093/cid/ciy1121)*

Dr. McMullan is Director, Division of EMS and Associate Professor of Emergency Medicine, University of Cincinnati.

2019 Guidelines for Diabetes Care in the Hospital

The American Diabetes Association offers updated care standards for inpatient management of diabetes.

Daniel D. Dressler, MD, MSc, SFHM, FACP, reviewing **Diabetes Care** 2019 Jan; 42:S173.

Sponsoring Organization: American Diabetes Association (ADA)

Background

The ADA annually updates its evidence-graded recommendations; this guideline provides standards of care for hospitalized patients with diabetes or hyperglycemia.

Key Recommendations

- Initiate insulin therapy for blood glucose (BG) levels ≥180 mg/dL in most hospitalized patients, with target BG range of 140–180 mg/dL. (Evidence grade: A)
- Recommended insulin regimens for hospitalized patients with diabetes or hyperglycemia:
  - Inpatients with adequate nutritional intake: basal + prandial + correction insulin. (Evidence grade: A)
  - Inpatients with poor nutritional intake or taking nothing by mouth: basal + correction insulin. (Evidence grade: A)
  - Sliding-scale insulin alone is strongly discouraged. (Evidence grade: A)
  - When hypoglycemia (BG <70 mg/dL) occurs, insulin therapies should be reviewed and adjusted (Evidence grade: C)
- Determine glycosylated hemoglobin (HbA_{1c}) levels for all patients with diabetes or hyperglycemia (BG, >140 mg/dL) if HbA_{1c} has not recorded during the prior 3 months. (Evidence grade: B)
- Implement a systematic, individualized management plan — including structured communication to the patient and primary care clinician along with medication reconciliation — at hospital discharge. (Evidence grade: B)

COMMENT

Although targeting an inpatient BG of 140 to 180 mg/dL should maintain glycemic control while avoiding risky hypoglycemic episodes, achieving such a narrow target can be challenging. I don't make insulin adjustments in hospitalized patients if the achieved BG is between 80 and 180 mg/dL, unless levels consistently are lower than 140 mg/dL. Oral hypoglycemic agents usually are stopped during hospitalization. However, limited evidence suggests that a combination of dipeptidyl peptidase-4 inhibitors plus basal insulin might provide similar glucose control in non–intensive care inpatient settings (*Lancet Diabetes Endocrinol* 2017; 5:125).

American Diabetes Association. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes — 2019. **Diabetes Care** *2019 Jan; 42:S173. (https://doi.org/10.2337/dc19-S015)*

Dr. Dressler is Director, Internal Medicine Teaching Services, Emory University Hospital; Associate Program Director, J. Willis Hurst Internal Medicine Residency Program; Professor of Medicine, Emory University School of Medicine, Atlanta.

Decompressive Surgery for Nontraumatic Subacromial Shoulder Pain?

A meta-analysis and guideline make the case for nonsurgical management.

Paul S. Mueller, MD, MPH, FACP, reviewing **BMJ** 2019 Feb 6; 364:l294.

Sponsoring Organization: BMJ Rapid Recommendations — A collaboration between the MAGIC group (http://magicproject.org/) and the BMJ

Background

Nontraumatic shoulder pain due to subacromial pain syndrome (SAPS), shoulder impingement, or rotator cuff disease that persists beyond 3 months is associated with poorer long-term recovery and disability. Nonoperative treatments for SAPS include oral analgesics, physical therapy, and corticosteroid injections. Increasing numbers of patients are undergoing surgery with arthroscopic subacromial decompression. This guideline is based on two systematic reviews and a meta-analysis of data from seven randomized controlled trials that involved 1000 participants with SAPS (mean age, 49; median symptom duration, 2 years), which showed that surgery provided no improvements in pain, function, or quality of life compared with placebo surgery or other options.

Key Points

- In two trials that involved 331 patients, researchers compared decompressive surgery with placebo surgery; decompression provided no benefit for pain, function, health-related quality of life, patient-perceived effect, or return to work at any time point from 6 months to 5 years.
- In five nonblinded trials, researchers compared exercise therapy alone with decompressive surgery plus postoperative exercise therapy. Compared with exercise therapy alone, surgery provided no benefit for pain, function, health-related quality of life, patient-perceived effect, or return to work.
- Extrapolating from data in the two placebo-controlled trials, decompressive surgery would be associated with 12 additional frozen shoulders per 1000 patients.

COMMENT

The authors make a strong recommendation against subacromial decompressive surgery for SAPS, because it provides no important benefits compared with placebo surgery or exercise therapy. Furthermore, surgery is costly and associated with complications (e.g., bleeding, infection). Clinicians should emphasize analgesics, exercise therapy, and corticosteroid injections, coupled with watchful waiting, as many patients eventually will recover without surgery. However, my colleagues and I occasionally see patients with chronic refractory subacromial symptoms who report improvement after surgery. Are these patients placebo responders, or are their orthopedists able to select a small subgroup of patients who are more likely to benefit from surgery? The answer is unclear.

Vandvik PO et al. Subacromial decompression surgery for adults with shoulder pain: A clinical practice guideline. **BMJ** *2019 Feb 6; 364:l294. (https://doi.org/10.1136/bmj.l294)*

Dr. Mueller is Chair, Division of General Internal Medicine, Professor of Medicine, Mayo Clinic College of Medicine, Rochester, MN.

Tonsillectomy in Children: An Updated Clinical Practice Guideline

Previous recommendations are strengthened, and new recommendations are offered for obstructive sleep-disordered breathing and postoperative pain control.

John D. Cowden, MD, MPH, reviewing **Otolaryngol Head Neck Surg** 2019 Feb 5.

Sponsoring Organization: American Academy of Otolaryngology–Head and Neck Surgery Foundation

Background and Objective:

Updating a 2011 guideline, a multidisciplinary group made evidence-based recommendations on the pre-, intra-, and postoperative care of children 1 to 18 years of age who are candidates for tonsillectomy.

What's Changed:

Five changed action statements, seven new action statements, and increased emphasis on patient and/or caregiver education and shared decision making

Key Points

- Strong recommendations were made *for:*
  - Watchful waiting for recurrent throat infection if <7 episodes in the last year, <5 episodes per year in the last 2 years, or <3 episodes per year in the last 3 years
  - A single intraoperative dose of intravenous dexamethasone
  - Ibuprofen and/or acetaminophen for pain control after surgery
- Strong recommendations were made *against*:
  - Prescribing or administering perioperative antibiotics
  - The use of codeine, or any medication containing codeine, after tonsillectomy
- Other recommendations addressed:
  - Factors that may indicate tonsillectomy in children who do not meet the above criteria for recurrent throat infection
  - The role of obstructive sleep-disordered breathing in tonsillectomy consideration
  - When to obtain polysomnography before tonsillectomy
  - Patient and caregiver education
  - Postoperative management, particularly related to postoperative bleeding and pain

COMMENT

In addition to supporting surgeons in their practice improvement, the recommendations in this updated guideline provide primary care clinicians with clearer guidance on thresholds for recurrent throat infection and the role of obstructive sleep-disordered breathing in considering polysomnography and referral for tonsillectomy. The new strong recommendation against postoperative codeine use is of special note.

Mitchell RB et al. Clinical practice guideline: Tonsillectomy in children (update). **Otolaryngol Head Neck Surg** *2019 Feb 5; [e-pub]. (https://doi.org/10.1177/0194599818801757)*

Dr. Cowden is Medical Director, Office of Equity and Diversity, Children's Mercy Kansas City; Professor of Pediatrics, University of Missouri — Kansas City School of Medicine.

New ACP Guidance Statement: Breast Cancer Screening in Average-Risk Women

The ACP Clinical Guidelines Committee discourages screening in women younger than 50 and recommends biennial mammograms in women aged 50 to 74.

Andrew M. Kaunitz, MD, reviewing **Ann Intern Med** 2019 Apr 9.

Sponsoring Organization: American College of Physicians (ACP)

Background

Recommendations for breast cancer screening in asymptomatic average-risk women vary regarding frequency, age to start and stop, and whether clinical breast examination (CBE) is useful. To develop this guidance statement, the ACP Clinical Guidelines Committee reviewed seven relevant guidelines from U.S. and Canadian professional organizations and the WHO.

Key Points

- For women aged 40 to 49, clinicians should review the pros and cons of mammography before age 50, taking into account patients' preferences. Screening harms outweigh benefits for most women in this age group.
- Clinicians should offer biennial mammograms for women aged 50 to 74.
- Clinicians should discontinue screening in women aged ≥75 or those with life expectancy ≤10 years.
- Regardless of a woman's age, CBE is not a useful approach to screening.

COMMENT

The ACP committee noted that, in general, the magnitude of reduction in breast cancer mortality associated with mammography screening is small, a point it believes most guidelines did not emphasize. The guidance statement also points out that most guidelines did not demonstrate any reduction among women aged 39 to 49 (the group that received the least benefit from screening with respect to deaths prevented). Screening in this age group likewise did not reduce the incidence of advanced breast cancer. Regardless of women's age, mammography did not reduce all-cause mortality. In most women aged 40 to 49, screening's harms (overdiagnosis, overtreatment, false-positive results, unnecessary diagnostic testing and biopsies) outweighed its benefits. More-frequent screening was associated with greater harm, and outcomes of annual mammography did not clearly differ from those of longer intervals.

Breast cancer screening remains a fraught subject. While this ACP guidance is targeted to average-risk women, many who are not at excess risk actually perceive their risk as high. I agree with the editorialists that providing clear evidence-based guidance about breast cancer screening (as this statement does) is easier than implementing it, particularly within the time constraints of a well-woman visit.

Qaseem A et al. Screening for breast cancer in average-risk women: A guidance statement from the American College of Physicians. **Ann Intern Med** *2019 Apr 9; [e-pub]. (https://doi.org/10.7326/M18-2147)*

Elmore JG and Lee CI. A guide to a guidance statement on screening guidelines. **Ann Intern Med** *2019 Apr 9; [e-pub]. (https://doi.org/10.7326/M19-0726)*

Dr. Kaunitz is University of Florida Research Foundation Professor and Associate Chair, Department of Obstetrics and Gynecology, University of Florida College of Medicine — Jacksonville.

New Perinatal HIV Guidelines Make Substantial Changes

New information and unexpected uncertainties on optimal antiretroviral therapy during pregnancy course through the new guidelines.

Rajesh T. Gandhi, MD, reviewing **Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission**.

Sponsoring Organization: Department of Health and Human Services (DHHS)

Target Audience: Infectious disease specialists, obstetricians, and other clinicians caring for people with HIV

Background and Objective

Approximately 5000 women with HIV give birth each year in the U.S. Comprehensive care, including antiretroviral therapy (ART) during pregnancy, improves maternal outcomes and prevents HIV transmission to the infant. Based on new antiviral safety and pharmacokinetic information, the DHHS has made substantial changes to the perinatal HIV guidelines, last updated in 2017.

Key Points

- Maternal HIV testing should be performed as early as possible during pregnancy. If negative, testing should be repeated during the third trimester for those at increased risk for acquisition.
- For couples in which one partner has HIV and the other does not, sexual intercourse without a condom limited to 2–3 days before and the day of ovulation is a way to conceive that carries "effectively no risk" of HIV transmission as long as the person with HIV is on ART and has achieved sustained virologic suppression.
- Regardless of CD4 cell count, ART should be started as early as possible during pregnancy or, even better, before conception.
- Preferred regimens include two nucleoside reverse transcriptase inhibitors — either abacavir/lamivudine or tenofovir disoproxil fumarate with lamivudine or emtricitabine — plus an integrase inhibitor (raltegravir twice daily or dolutegravir; but see caveats below regarding when not to use dolutegravir) or a boosted protease inhibitor (darunavir/ritonavir twice daily or atazanavir/ritonavir). Two-drug regimens are not recommended during pregnancy.
- In a surveillance study in Botswana, neural tube defects were reported in 4 infants born among >500 women who conceived while on dolutegravir, a rate higher than in offspring of women receiving other antiretroviral medications.

What's Changed

- Because of concerns about a possible increased risk for neural tube defects, while more data are gathered (expected in 2019), dolutegravir is not recommended during the first trimester or in women who are trying to conceive. Dolutegravir is a preferred medication in the second and third trimesters based on substantial experience with no signal for safety problems during those periods.
- Due to concerns about inadequate levels during pregnancy, elvitegravir/cobicistat, darunavir/cobicistat, and atazanavir/cobicistat should not be used during pregnancy.
- Data with bictegravir or doravirine are insufficient to recommend their use during pregnancy.
- Tenofovir alafenamide exposures appear to be adequate, but data are not yet sufficient to recommend initiation during pregnancy.

COMMENT

These guidelines provide much-needed assistance in caring for women with HIV before, during, and after pregnancy. To inform optimal care, however, more studies on the safety of specific medications, like dolutegravir and newer agents, around the time of conception and during early pregnancy are desperately needed. In the meantime, we should do our part by prospectively reporting pregnancy exposures and outcomes of individuals receiving ART to the Antiretroviral Pregnancy Registry. We owe our patients nothing less.

Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in transmission in the United States. Downloaded Jan 4, 2019. (http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf)

Dr. Gandhi is Professor of Medicine, Harvard Medical School; Director, HIV Clinical Services and Education, Massachusetts General Hospital, Boston. Dr. Gandhi is a member of the Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents.

New Guidance for Preventing Peripartum Depression

The USPSTF recommends that pregnant and postpartum women be screened for excess risk for depression and referred for appropriate counseling.

Robert L. Barbieri, MD, reviewing **JAMA** 2019 Feb 12; 321:580; 588; 550, and other sources.

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

Target Audience: Women's healthcare providers

Background

Peripartum depression affects up to one in seven new mothers in the U.S. Prior guidelines have recommended screening for depression during and after pregnancy (e.g., *Pediatrics* 2010; 126:1032, *Obstet Gynecol* 2015; 125:1268, *JAMA* 2016; 315:380), and such screening is now widely practiced; however, seamless referral for evaluation and treatment of screen-positive mothers remains a challenge. Now, in a shift toward a population-based public health strategy, the USPSTF has extended its recommendation from screening for a disease — depression — to screening for associated risk factors and implementing preventive measures.

Key Points

- The task force recommends that clinicians provide or refer pregnant and postpartum patients at excess risk for perinatal depression to counseling interventions (B recommendation)
- Acknowledging the lack of a validated screening tool for identifying at-risk women, the task force notes that women with at least one of the following factors are at increased risk for perinatal depression:
  - History of depression
  - Current depressive symptoms not meeting the threshold for screening positive for depression
  - Low income
  - Adolescence
  - Single parenthood
  - Recent intimate partner violence
  - Anxiety
  - Recent significant negative life events.
- Counseling or psychotherapeutic interventions can reduce the likelihood of onset of perinatal depression.
- Mixed or limited evidence support other interventions, including physical activity, education, pharmacotherapy, dietary supplements, and health system interventions.

COMMENT

Editorialists note that most high-quality studies of interventions to prevent perinatal depression have focused on women with elevated depressive symptoms or a personal history of depression; accordingly (and given the substantial challenges of full implementation), initial changes to practice should focus on these two groups, which can be identified with the Edinburgh Postnatal Depression Scale, and two questions about history of depression ("Before this pregnancy, did you ever have a period of 2 weeks or more when you felt particularly miserable or depressed?" and "If so, did being depressed interfere with your ability to get things done or your relationships with friends and family or did it lead you to seek professional help?") Other editorialists point out that the U.S. is the only industrialized country without a federal paid maternity leave law; paid parental leave represents an important policy change that would significantly advance maternal and child health.

Although this recommendation has the potential to change practice dramatically, considerable time will be required. It took many years to adopt universal screening for perinatal depression itself; now, it will take a concerted effort to accelerate implementation of screening for the causative factors.

US Preventive Services Task Force. Interventions to prevent perinatal depression: US Preventive Services Task Force Recommendation Statement. **JAMA** *2019 Feb 12; 321:580. (https://doi.org/10.1001/jama.2019.0007)*

O'Connor E et al. Interventions to prevent perinatal depression: Evidence report and systematic review for the US Preventive Services Task Force. **JAMA** *2019 Feb 12; 321:588. (https://doi.org/10.1001/jama.2018.20865)*

Freeman MP. Perinatal depression: Recommendations for prevention and the challenges of implementation. **JAMA** *2019 Feb 12; 321:550. (https://doi.org/10.1001/jama.2018.21247)*

Felder JN. Implementing the USPSTF recommendations on prevention of perinatal depression— Opportunities and challenges. **JAMA Intern Med** *2019 Feb 12; [e-pub]. (https://doi.org/10.1001/jamainternmed.2018.7729)*

Avalos LA. Preventing perinatal depression to improve maternal and child health—A health care imperative. **JAMA Pediatr** *2019 Feb 12; [e-pub]. (https://doi.org/10.1001/jamapediatrics.2018.5491)*

Wisner KL et al. Attention to prevention—Can we stop perinatal depression before it starts? **JAMA Psychiatry** *2019 Feb 12; [e-pub]. (https://doi.org/10.1001/jamapsychiatry.2018.4085)*

Dr. Barbieri is Kate Macy Ladd Professor and Chair, Department of Obstetrics, Gynecology, and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston.

Management of High-Risk Infantile Hemangiomas: A Clinical Guideline

Once high-risk hemangiomas are identified, infants should receive propranolol therapy or, alternatively, surgery for severe complications to the airway or orbit.

F. Bruder Stapleton, MD, reviewing **Pediatrics** 2019 Jan; 143:e20183475.

Sponsoring Organization: American Academy of Pediatrics (AAP)

Background and Objective

Most infantile hemangiomas (IHs) are benign and transient, requiring only observation. However, some may be serious, due to size or location, possibly leading to residual scarring or even acute respiratory or hemorrhagic complications. A multidisciplinary subcommittee of the AAP has created a new practice guideline for management of high-risk IH based on recent studies.

Key Points

- Growth of superficial IHs is most rapid between ages 1 and 3 months and typically concludes by age 5 months.
- A "high-risk" IH that might require early treatment is one with potential for causing life-threatening complications (airway obstruction, bleeding, congestive heart failure, severe hypothyroidism), functional impairment (ocular restriction, feeding interference), ulceration, or permanent scarring.
- Infants identified with a high-risk IH should receive early referral to a hemangioma specialist (by age 1 month).
- The preferred treatment for high-risk IH is oral propranolol at a dose of 2–3 mg/kg/day for 6 months, given 2–3 times daily. To avoid hypoglycemia, administer doses during or after feedings and hold doses if the infant is not hungry or is vomiting.
- Surgical interventions usually can be delayed unless an IH causes serious risks to the airway or orbit, or the IH ulcerates. Late surgery (i.e., at age 3 to 5 years) may be needed for residual skin changes.
- Topical timolol may be helpful in some small superficial IHs.
- In most cases, imaging is not required. However, ultrasonography is recommended when a hepatic IH is suspected by the presence of ≥5 IHs. Also, segmented IHs on the upper body (PHACE syndrome) or on the lower body (LUMBAR syndrome) require investigation, usually via magnetic resonance imaging, to determine if boney or other internal abnormalities coexist.

COMMENT

This comprehensive clinical guideline offers helpful recommendations and counters the past practice of taking a wait-and-see approach before referral of IH to a specialist.

Krowchuk DP et al. Clinical practice guideline for the management of infantile hemangiomas. **Pediatrics** *2019 Jan; 143:e20183475. (https://doi.org/10.1542/peds.2018-3475)*

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2019 U.S. Adult Immunization Schedule

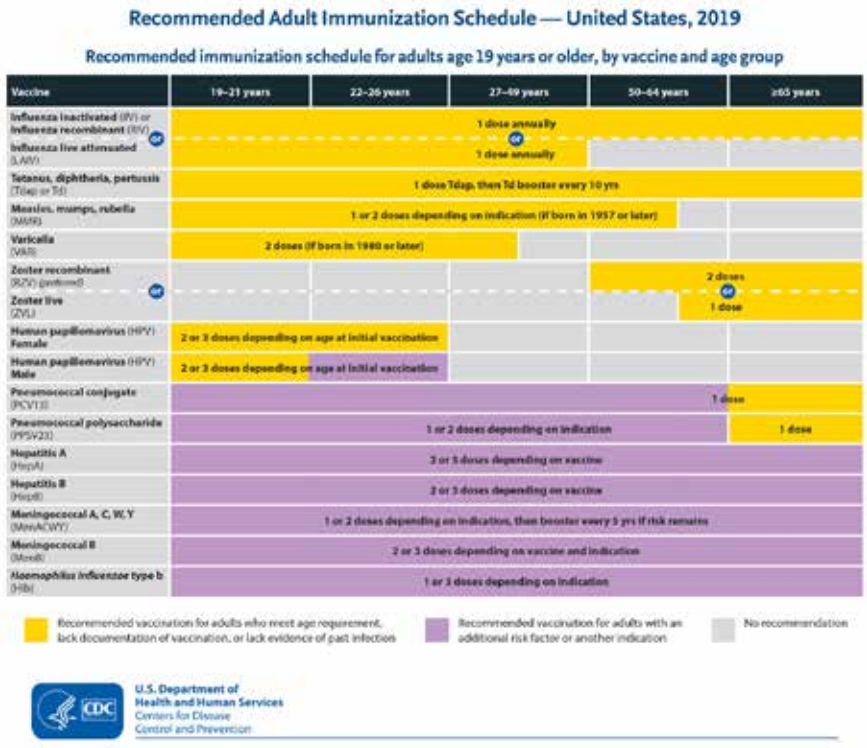
The biggest changes in this annual publication are welcome improvements to graphics.

Abigail Zuger, MD, reviewing **Ann Intern Med** 2019 Feb 5; 170:182.

Sponsoring Organization: CDC/Advisory Committee on Immunization Practices (ACIP)

Background

The 2019 update to the ACIP immunization schedule for adults (age, ≥19) includes a few scientific changes and a few design changes intended to make an increasingly complicated algorithm a little easier for clinicians to master. (see graphic) We have reprinted the age-specific recommended immunization table.



What's Changed?

- The live attenuated influenza vaccine (LAIV, FluMist) is back. This preparation was banned from the last two flu seasons for lack of efficacy but once again is an acceptable vaccination option. It should not be given to immunocompromised people, to pregnant women, or to anyone in close contact with severely immunocompromised people. Adults with diabetes or substantial heart, liver, or renal disease probably should receive another preparation.
- A new recombinant hepatitis B vaccine (Heplisav-B; Dynavax) can be dosed only twice, thanks to its novel adjuvant, rather than the usual three-dose schedule used for older preparations. Ideally, clinicians should use a single manufacturer's preparation for an individual patient's hepatitis B vaccinations but, in a pinch, a dose of the new preparation can be substituted for a dose of an older one.
- Because of recent outbreaks of hepatitis A in homeless populations, homelessness has been added to other clinical indications for routine hepatitis A vaccination.

- Consultations with visual designers and several different focus groups of healthcare providers have led to changes in the content and appearance of the schedule. The document now includes a set of instructions, fonts have been enlarged for clarity, and a few colors have been added to illustrate some clinical situations.

COMMENT

The new vaccine schedule doesn't look all that different from the old one, but the changes to the font have made a complicated document considerably easier to navigate, and the brief set of instructions is remarkably helpful.

Kim DK and Hunter P. Recommended adult immunization schedule, United States, 2019. **Ann Intern Med** *2019 Feb 5; 170:182. (https://doi.org/10.7326/M18-3600)*

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Childhood and Adolescent Immunization Schedule: 2019 Update

The CDC's Advisory Committee on Immunization Practices provides clarification on administration of several vaccines.

Deborah Lehman, MD, reviewing **Pediatrics** 2019 Feb 5.

Sponsoring Organizations: American Academy of Pediatrics (AAP), Centers for Disease Control and Prevention (CDC), American Academy of Family Physicians, American College of Obstetricians and Gynecologists

Target Audience: Pediatric primary care providers

Background:

The 2019 childhood immunization schedule has been updated and is available on the AAP website (https://redbook.solutions.aap.org/SS/Immunization_Schedules.aspx) and the CDC website (http://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html). As in previous years, the CDC also publishes a parent-friendly schedule as well as an adult schedule (http://www.cdc.gov/vaccines/schedules/index.html).

What's Changed:

- Early administration of hepatitis A vaccine and measles, mumps, rubella vaccine to children aged 6 to 11 months prior to international travel is noted.
- The influenza recommendations now include live attenuated influenza vaccine as well as information about administering vaccine to egg-allergic children.
- A separate table indicates vaccines recommended for children with specific medical conditions, including pregnancy.
- For recommendations about vaccine administration during an outbreak, providers are now referred to local health departments for guidance.
- This year's catch-up schedule includes the recommendation that children who received vaccination for diphtheria, tetanus, and acellular pertussis (either DTaP or Tdap vaccine) between ages 7 and 10 years should receive Tdap again at age 11 to 12 years.

COMMENT

The 2019 immunization schedule is similar in content to last year's schedule but includes clarification about the administration of several vaccines. Routine vaccination protects against 15 different childhood diseases that in the prevaccine era were responsible for many tragic outcomes and premature deaths. We are all charged with the responsibility of keeping the memory of these diseases alive so that the remarkable successes of this complex and growing vaccine schedule are celebrated.

AAP Committee on Infectious Diseases. Recommended childhood and adolescent immunization schedules: United States, 2019. **Pediatrics** *2019 Feb 5; [e-pub]. (https://doi.org/10.1542/peds.2019-0065)*

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