This is my 21st article on “Choosing Wisely” from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing “Five or Ten Things Physicians and Patients Should Know.”

I. RECOMMENDATIONS FROM THE AMERICAN SOCIETY FOR COLPOSCOPY AND CERVICAL PATHOLOGY (ASCCP)

1. Don’t perform a Pap test or HPV screening in women who have had a total hysterectomy (with removal of the cervix), if it was done for reasons other than high-grade cervical dysplasia (CIN2/3) or cancer. Vaginal cancer after hysterectomy is very rare, less likely than breast cancer in men, for which screening is not recommended. If a woman had a hysterectomy for the indication of high-grade cervical dysplasia or cancer, continued Pap testing is recommended. Vaginal assessment may also be indicated in the presence of HPV-associated vulvar cancer.1

2. Don’t do a Pap test or HPV screening in immunocompetent women under age 21. Screening of adolescents in whom cervical cancer is rare exposes them to potential harms of tests, biopsies, and procedures without proven benefit. Costs and anxiety also obviously increase.

3. Don’t do annual Pap tests or HPV screening in any immunocompetent woman with a history of negative screening. Although there is a slight risk of cancer from increasing the interval between screens, this risk is balanced by potential harm from more colposcopy prompted by HPV infection that, in most women, will clear spontaneously. Current evidence does not support a longer screening interval than three years for cervical cytology with HPV triage or for primary HPV screening with cytology triage.


5. Avoid treating CIN 1 in women under age 25. CIN 1 is the histologic manifestation of HPV infection, and like HPV infection in young women, regression rates are high.2

II. RECOMMENDATIONS FROM THE AMERICAN UROLOGICAL ASSOCIATION (AUA)

The AUA has just released its next five things physicians and patients should question. Their list is now up to 15. I will quickly summarize the first 10, then list the new ones (#11-15).

Previous Recommendations:

1. Don’t do routine bone scans in men with a low-risk of prostate cancer.

2. Don’t prescribe testosterone in men with erectile dysfunction who have normal testosterone levels.

3. Don’t order a creatinine or upper-tract imaging in men with benign prostatic hyperplasia (BPH).

4. Don’t prescribe antibiotics for asymptomatic men with an elevated PSA.

5. Don’t routinely order an ultrasound in boys with cryptorchidism.

6. Unless there are signs and symptoms of urinary tract infection, patients with indwelling or intermittent catheterization of the bladder don’t require antimicrobials.

7. Asymptomatic men with low-risk clinically localized prostate cancer should not have computed tomography (CT) scans of the pelvis.

8. Asymptomatic patients should not have synthetic vaginal mesh removed.

9. Offer PSA screening for prostate cancer only after engaging in shared decision making.

10. Microhematuria should not be diagnosed solely on the basis of the results of a urine dipstick (macroscopic urinalysis).

New Recommendations:

11. Low-risk clinically localized prostate cancer (e.g. Gleason score < 7, PSA < 10.0 ng/mL,
and tumor stage T2 or less) should not be treated without discussing active surveillance as part of the shared decision-making process. Active surveillance provides a monitored approach that can avoid some potential risks of definitive treatment while selectively providing effective treatment for more aggressive cancers that warrant intervention. The ultimate choice of treatment should be based on shared decision-making that is individualized to the patient's disease characteristics, overall health, and personal preferences.3

12. Women with uncomplicated cystitis should not be treated with fluoroquinolones if there are other oral antibiotic options. Fluoroquinolone antibiotics are associated with serious potential side effects.

13. Opioid analgesia should only be prescribed in the lowest effective dose, and fewest doses necessary to address pain expected in the immediate post-operative period. Emergence of opioid use disorder as a public health epidemic is apparent, and the appropriate use of opioid therapy should begin with adherence to a practice of minimum prescribing in terms of dose, duration, and quantity.

14. The asymptomatic patient with microhematuria should not be evaluated routinely with urine cytology or urine markers. There is insufficient evidence for routine use of these markers in asymptomatic patients with hematuria, including assays of bladder tumor antigen (BTA), nuclear matrix protein (NMP), and fluorescent in situ hybridization (FISH) to detect chromosomal alterations. These can result in a false positive that prompts unnecessary diagnostic procedures and causes psychological stress, thus outweighing the potential benefit to these patients.

15. Pediatric patients with suspected nephrolithiasis should not routinely receive computed tomography (CT). Radiation exposure from CT in children is linked to increased cancer risk; ultrasonography is sufficiently sensitive and specific as an initial imaging test. Obviously if the ultrasound is negative or indeterminate despite strong clinical suspicion, or if perioperative planning requires it, a CT is appropriate using a low-dose protocol as the next step.4

III. RECOMMENDATIONS FROM THE AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES (AASLD)

1. Patients with compensated cirrhosis and small varices without red signs, who are being treated with non-selective beta blockers for preventing a first variceal bleed, should not have a surveillance esophagogastroduodenoscopy (EGD). These patients with no increased risk of bleeding (Child Classification A, no red marks on varices), can be treated with beta blockers. If patients have cirrhosis and medium or large varices that have not bled, and they are not at the highest risk of bleeding (Child A, no red signs on varices), beta blockers are preferred, adjusted to the maximal tolerated dose. Follow-up EGD is not necessary in either of those two scenarios.

2. After an initial episode of hepatic encephalopathy with an identifiable cause, there is no need to continue treatment indefinitely. If the precipitating factors are identified and well-documented (e.g. recurrent infections, variceal bleeding), or liver function or nutritional status has improved, prophylactic therapy may be discontinued.5

3. Repeated testing of hepatitis C viral load is not necessary unless antiviral therapy is being given. Highly sensitive quantitative assays of hepatitis C RNA are appropriate at diagnosis and as part of antiviral therapy. Otherwise virologic testing does not change clinical management or outcomes.

4. Benign focal lesions in the liver should not have computed tomography or magnetic resonance imaging routinely, unless there is a major change in clinical findings or symptoms. Patients with benign focal liver lesions (other than hepatocellular adenoma) who don’t have underlying liver disease and have demonstrated clinical and radiologic stability do not need repeated imaging.

5. Prior to abdominal paracentesis or endoscopic variceal band ligation, fresh frozen plasma and platelets should not routinely be transfused. Routine tests of coagulation do not reflect bleeding risk in patients with cirrhosis, and bleeding complications with these procedures are rare.6

Top Tips

CESSATION OF ANTICOAGULANTS BEFORE ELECTIVE PROCEDURES

The American College of Cardiology (ACC) has released a 2017 consensus document with a decision pathway for managing anticoagulants and elective procedures.7 These were formulated for warfarin but their application to novel oral anticoagulants (NOACs) is included in the document.
They suggest that we ask the following five simple questions:

1. **Who?** We should know the patient’s underlying bleeding and stroke risks, complete a careful review of their medical history, medication list (including over-the-counter medications and any supplements and herbal preparations), and laboratory test results.

2. **What?** This refers to the procedure. (The guidelines are only for elective procedures.) The bleeding risk depends on the procedure and the location of the bleeding risk.

3. **When?** The INR should be checked five to seven days before the procedure. If the patient is supra-therapeutic, discontinue warfarin more than five days before the procedure. If the patient is therapeutic, discontinue the anticoagulant five days before the procedure. If the patient is sub-therapeutic, discontinue the anticoagulant three to four days before the procedure. Guidance is also offered for timing discontinuation of NOACs, with a caution that only Dabigatran has a clinically-approved reversal agent. All currently available NOACs carry a black box warning regarding their use in the setting of neuraxial anesthesia (epidural and spinal anesthesia).

4. **Why?** NOACs, with their short half-life, do not need bridging therapy. For warfarin compounds in patients with atrial fibrillation, they recommend the use of the CHA2 DS2-VASc score to assess the stroke/thrombotic risk. Bridging is considered if the score is >4, and if there is a history of prior ischemic stroke, TIA, or peripheral arterial embolism (≥3 months previously), unless there is a substantial risk of bleeding. Heparin-based parenteral agents are the first choice, unless there is a history of heparin-induced thrombocytopenia. Low molecular weight heparin should be discontinued >24 hours prior to the procedure and unfractionated heparin can be discontinued >4 hours prior to the procedure.

5. **How?** This concerns resumption of anticoagulation. It should combine answers to all previous questions such as patient and procedural bleeding and thrombotic risk, timing of resumption of anticoagulation, and consideration of whether bridging should be used while the INRs are out of the therapeutic range. Procedures that affect the pharmacokinetics of warfarin and the NOACs (e.g., ileus after abdominal surgery) should be considered when a decision about parenteral anticoagulation is being made.

**FOSTERING RESEARCH INTEGRITY**

**Editor’s note:** There has been a noticeable and worrisome increase in the number of published scientific articles that have been retracted, even from prestigious journals, mostly because they were found to report data that were unsubstantiated for various types of research misconduct, including outright fabrication.

A growing body of evidence suggests that in some fields, substantial percentages of published results are not reproducible by other investigators. The following report from the National Academies is a response to this troubling situation.

The National Academies of Sciences, Engineering, and Medicine has expressed concern about research integrity, and proposed measures to protect it. Their report—Fostering Research Integrity—can be accessed online for free of charge, or ordered from the Academies website. It also has a video of the briefing that announced the report. To bring a unified focus to addressing challenges in fostering research integrity across all disciplines and sectors, the report urges the establishment of a nonprofit, independent Research Integrity Advisory Board (RIAB). This could facilitate the exchange of information on approaches to assessing and creating environments of the highest integrity and to handling allegations of misconduct and investigations.

* It is an indicator of the deterioration of the moral standards of society, and — by extension — the scientific community, that since 1955 there has been a real Journal of Irreproducible Results, positioned as the scientific community’s counterpart to Mad Magazine. It is much less visible and active now than it was during the decades of the ’70s-’80s when I subscribed briefly. It published irreverent, often wacky spoofs of scientific research, with titles like “American Pi,” “A Double Blind Efficacy Trial of Placebos, Extra Strength Placebos, and Generic Placebos,” and “Using Infinite Loops to Compute an Approximate Value of Infinity.” The only time any of this good-natured nonsense was taken seriously, it seems, was by a captured Al Qaeda terrorist, whose possessions revealed a typically fanciful article from the Journal titled “How to Make a Nuclear Bomb.” We can only hope that the investigation of this “leaked” document by our military was quickly aborted!

For more information, simply Google the Journal’s name; it still has a website and a Wikipedia entry. Sadly, the Journal’s title is no longer so obviously humorous.
The report states:

• Scientific societies and journals should develop clear authorship standards based on the principle that those listed as authors have made a significant intellectual contribution.
• Researchers should routinely disclose all statistical tests carried out, including negative findings.
• Research sponsors, publishers, and federal funding agencies should ensure that the information needed for knowledgeable persons to reproduce the reported results is made available at the time of publication or as soon as possible after that.
• Research institutions and federal agencies should ensure that good faith whistleblowers—those who raise concerns about the integrity of research—are protected, and their concerns are addressed in a fair, thorough, and timely manner.
• Detrimental practices should be understood to include not only actions of individual researchers, but also irresponsible or abusive actions by research institutions and journals.
• Practices that have until now been categorized as "questionable—for example, misleading use of statistics that fall short of falsification or failure to retain research data—should be recognized as "detrimental" practices.
• New forms of detrimental research practices are appearing, such as predatory journals that do little or no editorial review or quality control of papers, while charging authors substantial fees.
• While a certain level of irreproducibility due to unknown variables or errors is a normal part of research, detrimental research practices play a role, including inappropriate use of statistics, after-the-fact fitting of hypotheses to previously collected data, or falsification of data.

TREATMENTS FOR CHRONIC LYME DISEASE ARE UNPROVEN AND POTENTIALLY HARMFUL

Unproven treatments for patients given the diagnosis of “chronic Lyme disease” can cause serious adverse events, including death. This report from the CDC described five patients treated with long courses of IV antibiotics or immunoglobulins who show the range of possible complications. Adverse events included septic shock, serious bacterial infection, osteomyelitis, paraspinal abscess, and clostridium difficile colitis. One of the patients died from septic shock attributed to catheter-associated bacteremia.

Chronic Lyme disease is a nonspecific diagnosis applied by some practitioners to patients with various symptoms such as fatigue, generalized pain, and neurologic disorders. Treatments for this presumed condition are unproven and not recommended.

Since many of these patients have experienced significant debility from their symptoms and have not found relief after consultation with conventional medical practitioners, they seek treatment from practitioners who identify themselves as Lyme disease specialists (“Lyme literate” doctors), or from complementary and alternative medicine clinics where they receive a diagnosis of chronic Lyme disease. These patients are then given various treatments for which there is often no evidence of effectiveness, including extended courses of antibiotics (lasting months to years), IV infusions of hydrogen peroxide, immunoglobulin therapy, hyperbaric oxygen therapy, electromagnetic frequency treatments, garlic supplements, colloidal silver, and stem cell transplants. At least five randomized, placebo-controlled studies have shown that, in particular, prolonged courses of IV antibiotics do not substantially improve long-term outcome for patients with this diagnosis.

A related article from the New England Journal of Medicine reported 17 patients with recurrent erythema migrans (EM) due to strains of Borrelia burgdorferi that were different between the first and second episodes. The most common initial symptom was EM, a target-like lesion, and some patients, despite appropriate antibiotic treatment, experienced another episode of EM.

Molecular typing of the isolated strains of the B. burgdorferi, including analysis of the gene governing an outer-surface protein, revealed that all the paired EM episodes were associated with different strains of Borrelia. All repeat episodes were due to reinfection rather than relapse. All patients were treated with standard courses of antibiotics during each episode, with subsequent resolution of lesions. Thus, these were not instances of chronic Lyme disease.

RECOMMENDATION AGAINST SCREENING PELVIC EXAMS

The American Academy of Family Practice (AAFP) is recommending against doing a screening pelvic exam in adult women who are asymptomatic and not pregnant. This is going a step further than the United States Preventive Services Task Force (USPSTF), which in March said the evidence was insufficient to decide on the balance of benefits and
harms. The AAFP, however, now recommends against screening pelvic exams, given the low likelihood of benefit, and the increased risk of potential harm from invasive testing and unnecessary treatment. The USPSTF’s recommendation on pelvic exams was not about screening or preventing a specific disease, but instead was evaluating the benefits of the procedure to reduce overall morbidity and mortality. The AAFP focused on those gynecologic conditions that caused the majority of morbidity and mortality in women: malignancy and pelvic inflammatory disease. This AAFP recommendation is consistent with its earlier endorsement of the American College of Physicians (ACP) recommendation against pelvic screening exams. The ACP’s guidance was based on evidence that pelvic exams are not an effective screening test for malignancy, STDs, or pelvic inflammatory disease.

REFERENCES


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