



## CHOOSING WISELY III AND OTHER TOP TIPS

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This is my third report in this Journal on the “Choosing Wisely” initiative from The Board of Internal Medicine Foundation.<sup>1,2</sup> Each specialty group has or will be developing “Five Things Physicians and Patients Should Question.” Other “Top Tips” are included after the Choosing Wisely items.

The Choosing Wisely items covered in this article complete the recommendations from The American Society of Clinical Oncology, The American Gastroenterological Association, and The American College of Radiology.

### AMERICAN COLLEGE OF RADIOLOGY RECOMMENDATIONS

1. Patients being evaluated for headache who do not have any clinical neurological findings that suggest structural disease, or risk factors such as multiple family members with brain tumors, are not likely to require an imaging study, as it probably will not change their management or improve their outcomes. Those with a significant likelihood for structural disease obviously require immediate attention and are detected by clinical screens that have been validated in many settings. Incidental imaging findings lead to additional medical procedures and expenses that do not improve patient well-being. Many studies and clinical practice guidelines concur.
2. For suspected pulmonary embolism, don’t image without moderate or high probability of positive findings. This was covered in my article in the last *JLGH*.<sup>2</sup>
3. How many times have we all felt that we had ordered a preoperative or admission chest x-ray that was not indicated? This item of Choosing Wisely states that we can avoid admission or preoperative chest x-rays for ambulatory patients with an unremarkable history and physical exam. Only 2% of such images lead to a change in management. Obviously a chest radiograph is reasonable if acute cardiopulmonary disease is suspected or there is a history of chronic stable cardiopulmonary disease

in a patient older than 70 who has not had chest radiography within 6 months. The American College of Physicians also lists this as number 5 in their list of items that physicians and patients should question. It is obviously thought of highly by these two groups.<sup>4</sup>

4. For the evaluation for suspected appendicitis in children, computed tomography (CT) should not be contemplated until after an ultrasound has been considered as an option. In experienced hands, ultrasound is nearly as good as a CT in the pediatric population; it obviously will reduce radiation exposure; and it is cost-effective. If the results of the ultrasound are equivocal, it may be followed by CT. The reported sensitivity and specificity are 94%.
5. Clinically inconsequential adnexal cysts don’t require follow-up imaging. Hemorrhagic cysts and simple cysts in women of reproductive age are almost always physiologic. Small simple cysts in postmenopausal women are common and are likewise inconsequential. Ovarian cancer, while typically cystic, does not arise in these benign-appearing cysts. After a quality ultrasound in women of reproductive age, don’t recommend follow-up for classic corpus luteum or simple cysts under 5 cm in greatest diameter. Use 1 cm as a threshold for follow-up imaging of a simple cyst in postmenopausal women.

### AMERICAN GASTROENTEROLOGICAL ASSOCIATION RECOMMENDATIONS

1. Long-term acid suppression therapy with proton pump inhibitors (PPIs) or histamine 2 receptor antagonists should be titrated down to the lowest effective dose needed to achieve therapeutic goals for treatment of patients with gastroesophageal reflux disease. The main risk associated with reducing or discontinuing acid suppression therapy is an increased symptom burden. The decision regarding the need for maintenance therapy is driven by the impact of the remaining symptoms

- on the patient's quality of life rather than as a disease control measure. Possible long-term theoretical risks of PPIs include decreased levels of vitamin B12, iron and/or magnesium; decreased bone density; an increase in gut infections, primarily *Clostridium difficile* colitis or pneumonia; an increase in gastrointestinal neoplasms; and changes in absorption of other medications.<sup>6</sup>
2. Don't repeat colorectal cancer screening by any method for 10 years after a high-quality colonoscopy is negative in an average-risk individual. Screening colonoscopy should begin at age 50 for adults without increased risk of colorectal cancer and be repeated every 10 years if negative. The risk of cancer is low for 10 years after failure to detect neoplasia in this population.
  3. Don't repeat colonoscopy for at least 5 years for patients who have one or two small (less than 1 cm) adenomatous polyps without high-grade dysplasia, completely removed via a high-quality colonoscopy. Published guidelines provide recommendations that patients with one or two small tubular adenomas with low-grade dysplasia have surveillance colonoscopy five to ten years after an initial polypectomy. Precise timing within this interval should be based on other clinical factors such as prior colonoscopy findings, family history, and preferences of the patient and judgment of the physician.
  4. In patients with Barrett's esophagus, who undergo a second endoscopy that confirms the absence of dysplasia on biopsy, a follow-up surveillance examination should not be performed in less than three years. In patients with Barrett's without dysplasia the risk of cancer is very low. In these patients, it is safe to recheck for dysplasia no more than every three years because of the slow potential for cellular changes.
  5. For patients with functional abdominal pain syndrome (as per ROME III criteria), CT scans should not be repeated unless there is a major change in clinical findings or symptoms. Aside from the significant cost of this procedure, there is a small increase in cancer risk from x-ray exposure. An abdominal CT gives one the equivalent of up to three years of natural background radiation.

#### **AMERICAN SOCIETY OF CLINICAL ONCOLOGY RECOMMENDATIONS**

As we look forward with great anticipation to the new Ann B. Barshinger Cancer Center at the Suburban Outpatient Pavilion, it is very appropriate to

include the Choosing Wisely items from the American Society of Clinical Oncology.

1. For patients with solid tumors, don't use cancer-directed therapy if they have the following characteristics: have a low performance status (3 or 4); had no benefit from prior evidence-based interventions, are not eligible for a clinical trial; and have no strong evidence supporting the clinical value of further anti-cancer treatment. Studies have shown that cancer directed treatments are likely to be ineffective in solid tumor patients who meet the above criteria. There are exceptions, including patients with functional limitations due to other conditions that result in a low performance status, or with disease characteristics such as mutations that suggest a high likelihood of response to therapy. Appropriate palliative and supportive care should be implemented in patients in this first category.
2. In the staging of early prostate cancer at low risk for metastasis, don't perform PET, CT, or radionuclide bone scans. Evidence does not support the use of these scans for staging of newly diagnosed low-grade carcinoma for prostate (Stage T1c/T2a, prostate-specific antigen (PSA) less than 10 ng/mL, Gleason score ≤ to 6) with low-risk of distant metastasis. Imaging in these cases may lead to harm through unnecessary invasive procedures, over-treatment, unnecessary radiation exposure, and misdiagnosis.<sup>7</sup>
3. In the staging of early breast cancer at low risk for metastasis, don't perform PET, CT, or radionuclide bone scans. There is lack of evidence demonstrating a benefit for these scans in asymptomatic individuals with newly identified ductal carcinoma in situ (DCIS), or clinical stage I or II disease. This could potentially lead to harm as described in number 2 above.
4. Don't perform surveillance testing (biomarkers) or imaging with PET, CT, or radionuclide bone scans for asymptomatic individuals who have been treated for breast cancer with curative intent. Surveillance testing has been shown to have clinical value for certain cancers such as colorectal cancer. However, for breast cancer that has been treated with curative intent, several studies have shown there is no benefit from routine imaging or serial serum tumor markers in asymptomatic patients. False positive tests can lead to harm as in number 2 above.

5. Don't use white cell stimulating factors for primary prevention of febrile neutropenia in patients with less than 20% risk for this complication. These guidelines recommend using white cell stimulating factors when the risk of febrile neutropenia secondary to a recommended chemotherapy regimen, is approximately 20%, and equally effective treatment programs that do not require white cell stimulating factors are unavailable. Exceptions can be made if the patient is at high risk for this complication such as due to age, medical history, or disease characteristics.<sup>8</sup>

For our non-physician readers, it is important to mention that the foregoing items are provided solely for informational purposes and are not intended as a substitute for consultation with a medical professional. Patients with any specific questions about the items on this list or their individual situation should consult their physician.

## TOP TIPS

### AMERICAN ACADEMY OF NEUROLOGY GUIDELINE: USE STEROIDS FOR BELL'S PALSY

The annual incidence of Bell Palsy is 20/100,000. The characteristic facial paresis in most cases resolves with or without treatment, but as many as 30% of patients do not recover full facial function. This guideline is an update of that issued in 2001. The authors limited their discussion in this study to class I and II studies that had the highest levels of evidence. Improvement with the use of steroids was associated with a number needed to treat (NNT) of 6 to 8.

Adding an antiviral agent to steroids has a low probability of improving a patient's function over taking steroids alone. The authors did state that large randomized trials would need to be conducted with or without antivirals to help in determining whether the addition of antivirals to steroid treatment results in a modest benefit. They also said that all patients with Bell's Palsy need not take steroids. If a patient has brittle diabetes, morbid obesity, osteopenia or osteoporosis, or a prior history of steroid intolerance, individual circumstances should figure into the decision.<sup>9</sup>

### RESUSCITATION ONLY WITH CHEST COMPRESSIONS DOUBLED SURVIVAL IN OUT-OF-HOSPITAL CARDIAC ARREST

This report shows that adoption of chest-compressions-only resuscitation instead of traditional cardiopulmonary resuscitation (CPR) for bystander

intervention in out-of-hospital cardiac arrest dramatically improved survival rates in Arizona and other regions of the U.S. The authors state that this new method, cardio-cerebral resuscitation (CCR), should now replace CPR.<sup>10</sup> They feel the heart and the brain need the resuscitation and not the lungs. They explain that for the first 10 minutes after cardiac arrest the blood is still well oxygenated, so respiratory help is not necessary and it takes the focus away from life-saving chest compressions. However, if a victim has a respiratory arrest such as drowning or drug overdose, mouth-to-mouth resuscitation is needed.

Only one in four patients who have a witnessed cardiac arrest actually receives CPR. It is thought that bystanders do not perform CPR because they are reluctant to give mouth-to-mouth resuscitation to a stranger. The average time taken to give 2 breaths is 16 seconds, much longer than the 2 seconds recommended.

They admitted that they did not have any randomized control trials but they felt that survival rates from out-of-hospital cardiac arrest were so low that they needed to do something to improve them. The change to chest compressions only is now being taken up around the world. It has already been adopted in many Asian countries and The American Heart Association has now changed its recommendations to favor this approach.

In Arizona, a third level has been added and they are now advising that if patients come in with a pulse, having been resuscitated but still being in a coma, they are cooled down quickly to 33°C for 24 hours and then taken to the cath lab. Most cardiac arrests in adults are caused by a blocked coronary artery. Lancaster General Health has been using therapeutic hypothermia for cardiac arrest for some time, and this approach was described by Tom Shuman and Dr. Roy Small in the last issue of *JLGH*.<sup>11</sup>

### NEW DIABETES GUIDELINES

The American Diabetes Association (ADA) Clinical Practice Recommendations 2013 is published as a supplement to the January issue of *Diabetes Care*.<sup>12</sup>

For those with Type 1 or Type 2 diabetes who take multiple daily doses of insulin or use an insulin pump for therapy, the previous recommendations have been to perform glucose self-monitoring three or more times daily. The most recent advice for patients on intensive therapy with insulin is for testing at least before meals, occasionally after eating, at bedtime, before exercise or critical tasks such as driving, when low blood glucose is suspected, and after treating low blood glucose to

insure therapeutic levels. This recommendation gives the patient more options depending on the situation. Blood glucose monitoring is really not useful if it is not being acted upon.

Another revision of the standards includes a new recommendation for hepatitis B vaccination of patients with diabetes. Hopefully insurance plans are picking up on this revision and paying for it. It has been found that diabetics have a higher incidence of hepatitis B than non-diabetics.

Those of us who have been practicing the patient-centered care recommendations will be interested in the next guideline change: the ADA is now calling for a less stringent systolic blood pressure target of 140 mm Hg instead of 130 mm Hg. There is evidence that there is not a great deal of additional value in keeping the BP < 130 mm Hg, but there is an increased risk for hypotension and other adverse events. Furthermore, pushing the blood pressure under 130 mm Hg did not show any evidence of decreased mortality or myocardial infarction, but was associated with a small reduction in the risk of stroke. The previous target of less than 130 mm Hg had not been derived from randomized controlled clinical trials but from observational studies. The new recommendations do say that a target below 130 mm Hg might be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden. They point out that controlling the blood pressure to below 140 mm Hg is a very important threshold. Interestingly there are no new studies, only meta-analyses.

#### STUDIES TO INTERPRET WITH CAUTION

Evaluation of studies that appear to indicate very large treatment effects of medical interventions illustrates the important principle of regression to the mean.<sup>13</sup> Case reports and case series often demonstrate dramatic effects of new approaches to treating an illness and frequently they are followed by small studies that show great promise. But large controlled trials do not necessarily confirm the initial impressions that generated the headlines. In this study, the authors recommend that most studies with large effects should be viewed with skepticism because many have spurious findings or contain substantial overestimations.

The authors evaluated the frequency and features of very large effects in medical research by utilizing the Cochran Database of Systematic Reviews, and

examining binary outcomes with very large effects (odds ratio [OR],  $\geq 5$ ). Significant large effects typically appeared in small trials with median number of events of 18 in the first trial, and 15 in subsequent trials. Of the very large effects observed in the first and subsequent published trials, 90% and 98%, respectively, became smaller in meta-analyses that included other trials. The median OR declined from 11.8 to 4.2 for the first trials and from 10.0 to 2.6 for subsequent trials. They concluded that most large treatment effects emerged from small studies, and when subsequent trials are performed, the effect sizes become much smaller showing that well-validated large effects are uncommon.

#### GRAPEFRUIT (AND OTHER CITRUS FRUIT) DRUG INTERACTIONS

Dr. Larry Carroll recently brought this item to my attention.<sup>14</sup> I know the Florida Citrus Lobby will target us for this, but Dr. Carroll and I feel it's an important reminder.

At the present time there are 85 drugs that can interact with grapefruit! This has dramatically increased in the last 4 years. Grapefruits are not the only citrus fruit that is implicated; others include Seville oranges often used to make marmalade. Limes and pomelos also contain the active ingredients (furanocoumarins). One published case report has suggested that pomegranate may increase the potency of certain drugs. The list includes many drugs that we use every day such as some of the statins: atorvastatin, lovastatin, and simvastatin. Others include certain antibiotics, anti-cancer drugs, some heart drugs, synthetic opiates, drugs treating overactive bladder, psychiatric drugs, immunosuppressant medications such as cyclosporine, some AIDS drugs, certain birth control pills, as well as estrogens. The interaction can also cause less action from drugs like plavix®. There are obviously too many interactions to fully delineate here.

Normally these drugs are metabolized in the GI tract, with relatively little being absorbed because enzyme CYP3A4 deactivates them. But grapefruit and some other fruits contain furanocoumarins that inhibit the enzyme, and without it the gut absorbs much more of the drug and the blood levels rise dramatically. There is a case report, for example, of a patient who could only tolerate grapefruit juice when experiencing nausea and vomiting from migraine attacks. The patient was taking verapamil to help prevent the migraines, and was found to

have blood levels that were five times a safe level. Another example: a patient who drank a 7 ounce glass of grapefruit juice once a day for 3 days had a 330% greater concentration of simvastatin in the blood compared with taking it with water, which put the patient at risk for potentially life-threatening rhabdomyolysis.

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It is possible to see this effect even if the medication is taken 12 hours before consuming grapefruit or grapefruit juice.

The bottom line: if you have a patient taking oral medication who likes these fruits, check to see if their drugs interact with grapefruit, grapefruit juice, or the other fruits listed above.

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