This is my 29th article on Choosing Wisely from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing “Five, Ten, or Fifteen Things that Physicians and Patients Should Know.”

I. RECOMMENDATIONS OF THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS (ACOG).

The American College of Obstetricians and Gynecologists now has 10 things physicians and patients should question. We have previously covered the first five,1 which I will just list without comment, and then add the five new additions.

1. Inductions of labor or cesarean deliveries that are elective and are not medically indicated should not be scheduled until after 39 weeks, 0 days gestational age.

2. Elective, non-medically indicated inductions of labor between 39 weeks, 0 days and 41 weeks, 0 days should not be scheduled unless the cervix is deemed favorable.

3. Annual Pap test screening of cervical cytology should not be done routinely in women 30-65 years of age, as it has not been shown to offer advantages over screening at three-year intervals.

4. Patients who have had mild cervical dysplasia of less than two years duration should not be treated.

5. Screening for ovarian cancer in asymptomatic women at average risk is not indicated, as there is only fair evidence that such screening with serum CA-125 level and/or trans-vaginal ultrasound can detect ovarian cancer at an earlier stage than it can be detected without screening.

6. Robotic-assisted laparoscopic surgery for benign gynecologic disease should be avoided when it is feasible to use a conventional laparoscopic or vaginal approach. The latter two approaches are comparable with respect to perioperative outcomes, intraoperative complications, length of hospital stay, and rate of conversion to open surgery. Robotic-assisted laparoscopic surgery has similar or longer operating times and higher associated costs.

7. Prenatal ultrasounds should not be performed for non-medical purposes, such as solely to create keepsake videos or photographs. The U.S. Food and Drug Administration considers keepsake imaging as an unapproved use of a medical device.2

8. Asymptomatic hospitalized patients with a hemoglobin level >7-8 grams should not be routinely transfused. Multiple factors need to be considered for these decisions, including the patient’s clinical status and oxygen delivery ability.

9. Don’t perform pelvic ultrasounds to screen for ovarian cancer in average risk women. The age-adjusted incidence is 13 cases per 100,000 women. A positive predictive value of screening for ovarian cancer is low, and most women with a positive screening test will have a false-positive result.3

10. During pregnancy, activity restriction or bedrest is not routinely recommended for any indication. These have been commonly recommended for a variety of conditions in pregnancy, but information to date does not show an improvement in birth outcome with the use of bedrest or activity restrictions. These do show an increase in loss of muscle conditioning and in thromboembolic disease.

II. RECOMMENDATIONS OF AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION AND CANADIAN BLOOD AND MARROW TRANSPLANT GROUP

1. In patients with aplastic anemia, peripheral blood stem cells should not be routinely used when a suitable bone marrow donor is available, due to a higher risk of graft-versus-host disease. While faster engraftment with filgrastim-mobilized peripheral blood stem cells results in quicker recovery of peripheral blood counts compared to bone marrow in patients with aplastic anemia, the higher rate of
graft-versus-host disease may be detrimental.

2. For the initial treatment of graft-versus-host disease, don’t use methylprednisolone greater than 2 mg/kg/day (or equivalent). Higher doses than 2 mg/kg/day have shown no advantage, and the higher doses increase risks of corticosteroid-related toxicity.

3. For standard umbilical cord blood transplantation, don’t routinely use two cord blood units when a single unit of adequate size is available, recognizing that higher cell doses are preferred when using units with greater HLA mismatch. Graft-versus-host disease may be more frequent after double-cord blood transplantation. Similar outcomes after single-unit and double-unit umbilical cord transplantation are demonstrated in randomized trials.

4. For matched unrelated donor transplantation using myeloablative conditioning and standard graft-versus-host disease prevention regimens, don’t routinely use peripheral blood stem cells when a suitable bone marrow donor is available. Peripheral blood stem cells may be considered in cases with substantial recipient/donor size discrepancy, donor preference, and for malignant diseases with high risk of graft failure.

5. Adult hematopoietic cell transplantation recipients should not routinely receive immunoglobulin replacement in the absence of recurrent infections, regardless of their IgG levels. Meta-analyses of controlled trials conclude that immunoglobulin replacement offers no advantage for infection prevention and overall survival, may predispose to a higher risk of hepatic sinusoidal obstruction syndrome and venous thromboembolism, and may impair the efficacy of post-transplant vaccinations.

III. RECOMMENDATIONS OF AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS (AANS) AND CONGRESS OF NEUROLOGICAL SURGEONS (CNS)

1. After severe traumatic brain injury, steroids should not be administered. They are not recommended for improving outcomes or reducing intracranial pressure in patients with traumatic brain injury. High dose steroid administration may increase the risk of complications and may produce increased mortality.

2. Patients with non-specific acute low back pain without red flags should not receive imaging of the spine (plain radiographs, magnetic resonance imaging, computed tomography [CT], or other advanced imaging). Such studies are unnecessary during the early phase of symptoms, unless red flags indicate that early imaging of the spine is required. These can include neurological deficits such as weakness or numbness, any bowel or bladder dysfunction, fever, history of cancer, history of intravenous drug use, immunosuppression, steroid use, history of osteoporosis, or worsening symptoms.

3. In children with mild head injuries, don’t routinely obtain a CT scan. Mild traumatic brain injury is defined as a temporary loss of neurological function resulting from a blunt blow to the head or an acceleration/deceleration injury. More severe injury may be predicted in patients younger than 2 years with a persistent altered mental status, nonfrontal scalp hematoma, loss of consciousness for five seconds or more, severe injury mechanism, palpable skull fracture, or abnormal behavior according to the parent. In those over age 2, prolonged abnormal mental status, any loss of consciousness, history of vomiting, severe injury mechanism, clinical signs of basal skull fracture, or severe headache may also necessitate CT imaging. Any patient with a traumatic head injury that has any neurologic deficit should also be imaged if no other cause can be determined.

4. Don’t routinely screen asymptomatic patients without a family or personal history of brain aneurysms, subarachnoid hemorrhage (SAH), or genetic disorders that may predispose to aneurysm formation. Family history of aneurysmal SAH increases the individual’s risk of harboring an aneurysm.

5. In patients with ischemic stroke, don’t routinely use seizure prophylaxis. Patients who suffer a seizure after a stroke may need seizure treatment, but otherwise there is no evidence that using prophylactic antiepileptic drugs prevents seizures.

**Top Tips**

CUMULATIVE INCIDENCE OF WEST NILE VIRUS INFECTION IN CONTINENTAL UNITED STATES, 1999-2016

Using reported case data from ArboNET* and

* ArboNET is a national arboviral surveillance system managed by CDC and state health departments.
previous seroprevalence data stratified by age and sex, this study conservatively estimates that approximately 7 million people in the United States have been infected with West Nile Virus (WNV) since its introduction into the United States in 1999. There is an obvious need for public health interventions and improved surveillance.

WNV is a mosquito-transmitted flavivirus that infects humans and has become endemic across the continental United States. Large outbreaks occur throughout the country with seasonal outbreaks annually. Infection is commonly asymptomatic. A general febrile illness occurs in about 20% of the population with WNV, and less than 1% progress to neuro-invasive disease, which might include encephalitis, meningitis, and acute flaccid paralysis.

WNV infection can cause permanent sequelae including physical, neurological, and cognitive disabilities, as well as renal impairment and ocular damage. Initial and long-term cost can exceed $700,000 per patient in the United States.

As the cumulative incidence continues to climb, the statistics provide additional support for the economic benefit of insecticide and vaccine, especially in the Midwest, Southwest, and West. Nearly 98% of the U.S. population remains vulnerable to WNV infection.

HISTORY OF FEVER AT HOME IN YOUNG INFANTS WHO ARE CURRENTLY AFEBRILE

Prior studies have suggested that a caregiver report of fever in a young infant who is afebrile on presentation to the emergency department warrants further evaluation for bacterial infection. In this multicenter, prospective cohort study of over 1,200 infants (60 days of age or younger) who were afebrile on examination in the emergency room but had a history of fever at home, the risks of bactere mia and meningitis (1.5 and 0.6% respectively) were substantial and not significantly different from the risk of infection in almost 2,600 young infants who were febrile in the emergency room. This study provides further support for the approach of evaluating infants with a history of fever according to their age and clinical findings, regardless of their temperature when they present clinically.8

PRINCIPAL CONTROVERSIES IN VACCINE SAFETY IN THE UNITED STATES 9

This article discusses concerns about vaccine safety that can lead to decreased acceptance of vaccines and resurgence of vaccine-preventable diseases. The main current controversies about the safety of vaccines are not supported by the available biological and epidemiological evidence. It includes the following items: MMR vaccine and autism; Thimerosal, a mercury-based vaccine preservative, and the risk of neurodevelopmental disorders; vaccine-induced Guillain-Barré Syndrome (GBS); vaccine-induced autoimmune diseases; safety of HPV vaccine; aluminum adjuvant-induced autoimmune diseases and other disorders; and too many vaccines given early in life predisposing children to health and developmental problems.

The biological and epidemiological evidence does not support any of the above vaccine safety concerns, except for a possible small increase in risk of GBS following influenza vaccination. However, the magnitude of that increase is less than the risk of GBS following influenza itself.

Speculation that MMR vaccine causes autism is among the most damaging controversies in vaccine safety. As is well known, the suggestion that MMR vaccine might cause autism was first raised in 1998 in Lancet by A.J. Wakefield. Although the article was ultimately retracted by the journal because of improprieties in subject recruitment and financial conflicts of interest, the doubts that it raised have lingered. It no doubt is one of the main reasons that we are seeing an outbreak of measles in the world today. The evidence is strong that MMR vaccine does not cause autism.

The mercury-containing preservative, thimerosal, has also been feared to possibly increase the risk of autism. The evidence is strong that thimerosal in vaccines does not increase the risk of autism or other neurodevelopmental disorders. MMR vaccine has never contained thimerosal.

Vaccines have also been feared to cause a variety of chronic autoimmune diseases, but numerous studies have confirmed that vaccines do not increase the risk of chronic disease of possible autoimmune origin.

HPV vaccine has received considerable media attention associated with reports of a variety of adverse events, many of which may have an autoimmune etiology. Again, the evidence from several studies supports the safety of HPV vaccine.

Aluminum salts have been safely used in vaccines as an adjuvant to boost the immune response.
since the 1930s. They are currently used in vaccines such as Hepatitis A, Hepatitis B, diphtheria-tetanus, Hemophilus influenza type B (Hib), and pneumococcal vaccines, but they are not used in the live viral vaccines, such as measles, mumps, rubella, varicella, and rotavirus. A study that evaluated the incidence of autoimmune disease in more than 18,000 patients who received subcutaneous allergen-specific immunotherapy containing large quantities of injected aluminum adjuvants found that patients receiving injected aluminum had a lower incidence of autoimmune disease compared with controls. Current evidence supports the safety of aluminum adjuvants in vaccines.

Today’s routine childhood immunization schedule in the United States includes 10 vaccines against 14 diseases; children in the first few years of life can receive as many as 26 vaccine injections and as many as five injections at one time. The immune system of infants is perfectly capable of handling the number of antigens in vaccines, and studies have not found increased risks of adverse health outcomes related to the number of vaccines or vaccine antigens received early in life.

UNNECESSARY ANTIBIOTICS LINKED TO NEARLY 70,000 YEARLY EMERGENCY ROOM (ER) VISITS

These data are from the CDC, and they write, “antibiotics are among the most commonly prescribed medications for children: however, at least one third of pediatric antibiotic prescriptions are unnecessary.”

To further investigate short-term antibiotic-related harms, the researchers estimated frequencies and rates of ER visits for antibiotic Adverse Drug Events (ADEs) in children, using adverse event data from the National Electronic Injury Surveillance system—Cooperative Adverse Drug Event Surveillance (ADEs) project, as well as data on retail pharmacy dispensing from QuintilesIMS. Using data from 6,542 surveillance cases, they estimated that between 2011 and 2015 there were 69,464 ER visits per year for antibiotic ADEs among children aged 19 years and younger. Of these, 40.7% involved children aged 2 years or younger, and 86.1% of these were for allergic problems. Amoxicillin was the most commonly implicated antibiotic among children aged 9 years or less. When they accounted for dispensed prescriptions, the rates of ER visits for antibiotic ADEs declined with increasing age for all antibiotics except sulfamethoxazole-trimethoprin. Amoxicillin had the highest rate of ER visits for antibiotic ADEs among children aged 2 years or less, whereas sulfamethoxazole-trimethoprin resulted in the highest rate among children aged 10-19 years.

They concluded that antibiotic ADEs lead to many ER visits, particularly among young children. Communicating the risks of antibiotic ADEs could help reduce unnecessary prescribing. Efforts could target pediatric patients who are at the greatest risk of harm.

NUMBER NEEDED TO TREAT (NNT)

Effective communication of clinical trial results to patients and clinicians is a requirement for appropriate application in clinical practice. Since its first description 30 years ago, the NNT has become an important means to express the magnitude of benefit conferred by a therapy. The NNT may be defined as the number of patients who need to be treated with one therapy versus another, for one additional patient to have the desired outcome.

When a clinical trial is completed, the fraction of patients who experienced the desired outcome is reported for the active and control groups. The NNT is derived by dividing 100 by the difference between the percentage response of the treatment group and that of the control group.

The concept of NNT may be applied to many types of outcomes in both therapeutic and diagnostic studies. It is intuitively understandable by patients and clinicians. It is also quantitative, facilitating decision-making when selecting among available therapeutic strategies. Other well-established indices for treatment effect are not well suited for this purpose. For example, a statistically significant P value conveys statistical rather than clinical significance. Risk ratios and odds ratios convey the relative, rather than the absolute, differences and outcomes with treatments.

The NNT aligns more closely with the patient’s perspective because the patient will often be making a particular treatment decision only once (“my chance of benefit is 1 in X”).

Despite its several advantages, the NNT metric does have important limitations, and helpful alternative metrics are available that indicate the magnitude of a treatment’s effect. First, the NNT combines two proportions (the fraction of a treatment’s success in each treatment group) into a single number, which
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sacrifices information. A second limitation is that it can be challenging to compare and integrate different NNTs because their values are expressed as fractions with different denominators.

The limitations of the NNT are:

- Randomized clinical trial results fully specify NNT values only for binary outcomes (such as the occurrence of an infection, rash, or death), but not for ordinal or continuous outcomes (such as reduced pain or degree of stability);
- It reflects the number, not the importance of events;
- It does not convey the financial costs and benefits of treatments;
- It only expresses the magnitudes of effect expected for a prototypical patient, reflecting the aggregate characteristics of the population enrolled in a particular clinical trial.

REFERENCES


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