Patient Oriented Evidence That Matters:
2016: Important Studies That May Change Your Practice

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The amount of information in family medicine can be overwhelming for medical students and residents. Somehow, through this information jungle, learners need to be able to make cost-effective recommendations to their patients based on the best available evidence to benefit individual patients and the public health in a system with limited resources. Educators in family medicine have advocated for teaching information mastery to help tomorrow's family physicians become life-long learners.

Patient Oriented Evidence that Matters (POEMs) can help primary care physicians make cost-effective decisions and improve patient-centered care. POEMs should also be used to remove inequities in healthcare. Family physicians as information masters are the key to transforming health care.

A (very brief) introduction to information mastery:

- Usefulness= (Relevance x Validity)/Work
- Foreground and background information
- "PICO"
- POEMs vs. DOEs
- The evidence pyramid
- How do you find answers to questions? And how to you make sure important practice changers come to you even if you don't ask?
- Less is more. Become a healthy skeptic.

POEMs from the last year that could change your practice

#1) Systematic review finds limited evidence on marijuana to treat chronic noncancer pain

Clinical question: Is medical marijuana effective and safe for the management of chronic noncancer pain?
Study design: Meta-analysis (randomized controlled trials)
Funding source: Unknown/not stated **Setting**: Outpatient (any)
Synopsis: These authors searched Medline and EMBASE for randomized trials of marijuana in the treatment of chronic noncancer pain. They don't describe any attempts to identify unpublished studies or to assess the potential impact of publication bias. Although they don't say much about the mechanics of selecting which papers to include, they report that 2 authors independently assessed the methodologic quality and extracted the data. They resolved discrepancies through consensus. Ultimately, they identified 6 studies with 226 adults. Five of the studies were cross-over trials and all but one of the studies was of high methodologic quality. Two of the studies evaluated patients with HIV-associated neuropathy, 1 evaluated posttraumatic neuropathy, 2 studied mixed neuropathic conditions, and 1 evaluated patients with multiple sclerosis. Five of the studies allowed the patients to continue to take other pain medications, including opiates. The authors report significant heterogeneity in the marijuana dosing, frequency and duration of treatment, and variation in the outcomes studied. As a result, they reasonably chose not to pool data. Most of the studies lasted only a few weeks, had small numbers of patients, and had difficulty with masking. All of the studies reported statistically significant improvements in pain, but only 3 reported clinically important differences in pain severity: 46%, 52%, and 61% of marijuana users versus 18%, 24%, and 26% of the placebo takers (numbers needed to treat = 4, 4, and 3, respectively). None of the trials reported serious adverse events and all reported

neurocognitive events including feeling "high" or "stoned." None reported the munchies.
Bottom line: If these authors have found all the relevant studies, the data on marijuana for treating chronic noncancer pain are limited to a few high-quality studies that found statistically significant improvements in pain. The lack of standardized dosing and consistent outcome assessments, and the lack of effects on function and quality of life, are all significant limitations. (LOE = 1a-)
Deshpande A, Mailis-Gagnon A, Zoheiry N, Lakha SF. Efficacy and adverse effects of medical marijuana for chronic noncancer pain: systematic review of randomized controlled trials. Can Fam Physician 2015;61:e372-e381.

#2) Many patients with uncomplicated acute appendicitis do well with antibiotic therapy

Clinical question: Is antibiotic therapy a reasonable option for the treatment of uncomplicated acute appendicitis in adults?
Study design: Randomized controlled trial (single-blinded) **Funding source**: Government
Allocation: Concealed **Setting**: Inpatient (any location) with outpatient follow-up
Synopsis: The optimal management of acute uncomplicated appendicitis (ie, immediate surgery versus antibiotic therapy) remains controversial. These investigators identified 530 adults, aged 18 to 60 years, who presented to the emergency departments of 6 Finnish hospitals with uncomplicated acute appendicitis confirmed by computed tomographic scan. Exclusion criteria included the presence of an appendicolith, perforation, abscess, or suspicion of a tumor. Consenting patients were randomly assigned (concealed allocation) to either standard surgical appendectomy or antibiotic therapy (1 g intravenous ertapenem daily for 3 days followed by 7 days of oral levofloxacin, 500 mg once daily, and metronidazole, 500 mg 3 times daily). Outcomes were assessed via hospital records and telephone interviews for 1 year. Complete follow-up occurred for 83% of study participants. Using intention-to-treat analysis, of the 273 patients randomized to the surgical group, 272 (99.6%) underwent successful appendectomy. Of these, only 6% underwent laparoscopic appendectomy. Of the 256 patients available for 1-year follow-up in the antibiotic group, 186 (72.7%; 95% CI 66.8%-78.0%) did not require appendectomy; the rest underwent surgical intervention within 1 year of initial presentation. No patients in the antibiotic group developed an intra-abdominal abscess. The overall postintervention complication rate, including median length of sick leave, wound infection, pneumonia, diarrhea, incisional hernia, adhesion-related bowel obstructions, and persistent abdominal or incisional pain was significantly lower in the antibiotic group (2.8% vs 20.5%; number needed to treat to harm = 5.7; 4.2-8.4). Interestingly, the complication rate in the subgroup of patients in the antibiotic group who eventually underwent appendectomy was also significantly lower than the rate in the group who underwent initial appendectomy (7.0% vs 20.5%). There was no difference between the groups in all-cause mortality.
Bottom line: In this study--the largest randomized trial to date to examine this question--the approximately 75% of adults who presented with acute uncomplicated appendicitis and were treated initially with antibiotics did not require appendectomy. Those who underwent appendectomy after initial antibiotic treatment experienced fewer postsurgical complications than the group of patients who underwent appendectomy first. (LOE = 1b)
Salminen P, Paajanen H, Rautio T, et al. Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis. The APPAC randomized clinical trial. JAMA 2015;313(23):2340-2348.

#3) Gluten is not the culprit in many patients' symptoms

Clinical question: Can patients with nonceliac gluten sensitivity tell when they are exposed to gluten?
Study design: Cross-over trial (randomized) **Funding source**: Self-funded or unfunded
Setting: Outpatient (specialty)
Synopsis: Though the incidence in the population of celiac disease—with resulting gluten sensitivity—is approximately 0.4%, a lot of people who do not have antibodies to gluten identify symptoms when they eat gluten-containing foods. The researchers enrolled 35 patients (86% female) from a celiac disease clinic who did not have celiac disease, but were using a gluten-free diet because of self-identified gluten-related symptoms. These patients had been using a gluten-free diet for at least 6 months and reported being asymptomatic or mildly symptomatic. The participants were randomized, using a crossover design, to receive either gluten-containing flour or gluten-free flour for 10 days, followed by a 2-week washout period, and then another 10 days of the other type of flour. Only 34% (n = 12) of the participants correctly identified when they were given gluten-containing flour. These patients also had a significant increase in symptoms following the gluten challenge using the Gastrointestinal Symptoms Rating Scale. Seventeen participants (49%) believed the gluten-free flour contained gluten and they had increased symptoms during the gluten-free period. Despite the small number of patients in this study, the crossover design (in which each participant serves as his or her own control) greatly increases the statistical power. However, this group may represent a specific subtype of patient, since many patients approached to participate did not do so, either because of no interest in the study, fear of symptom recurrence, or an uncertain diagnosis.
Bottom line: Gluten may not be the cause of gastrointestinal symptoms in many patients with nonceliac gluten sensitivity. Only one-third of patients on a gluten-free diet experienced symptoms and correctly identified when they were given gluten-containing flour. Almost half (49%) of patients experienced symptoms even though they were given

gluten-free flour.
Zanini B, Basche R, Ferraresi A, et al. Randomised clinical study: gluten challenge induces symptom recurrence in only a minority of patients who meet clinical criteria for non-coeliac gluten sensitivity. Aliment Pharmacol Ther 2015;42(8):968-976.

#4) Benign thyroid nodules rarely progress to malignancy (0.3% in 5 years)

Clinical question: What is the natural history of benign thyroid nodules in adults and what is the likelihood of thyroid cancer?
Study design: Cohort (prospective) **Funding source**: Foundation
Setting: Outpatient (specialty)
Synopsis: These investigators consecutively enrolled patients who presented to 8 thyroid-disease referral centers in Italy with 1 to 4 asymptomatic thyroid nodules meeting standard criteria for benign categorization (no suspicious ultrasound findings for 59.8% or negative fine-needle aspiration results for 40.2%). Baseline assessments of the 992 patients (mean age 52.4 years; 82% women) included the measurement of serum levels of thyroid-stimulating hormone, free thyroxine, and thyroid antibodies, and evaluation by standard thyroid ultrasound. Yearly follow-up visits included repeat ultrasound examination of the thyroid and neck with examiners measuring diameters of each nodule without consulting data from previous scans. Fine-needle aspiration was performed or repeated for any suspicious findings. Complete follow-up occurred for 93% of patients at 5 years.
The size of the original nodule remained stable during follow-up for 69% of the nodules (686 patients). One or more nodules shrank spontaneously in size in 184 (18.5%), and significant growth (a 20% increase in 2 or more nodule diameters of at least 2 mm) occurred in 153 patients (15.4%), with both growth and shrinkage occurring in the same gland in 3.1% of patients. Overall, 11.1% of all nodules increased in size, with a mean change in the largest diameter of more than 4.9 mm, from a mean of 13.2 mm at baseline to 18.1 mm at the end of follow-up. Thyroid cancer was identified in only 5 of the original nodules (0.3%). Factors associated with nodule growth included the presence of multiple nodules, main nodule volumes of more than 0.2 mL, nulliparity in women, being male, and being younger than 60 years. No sonographic features nor serum thyroid-stimulating hormone levels were associated with nodule growth.
Bottom line: The development of thyroid cancer in asymptomatic, sonographically determined, or cytologically determined benign thyroid nodules is rare (0.3% in 5 years), with the majority of nodules (69%) exhibiting no significant size increase after 5 years. Factors associated with nodule growth include the presence of multiple nodules, main nodule volumes of more than 0.2 mL, nulliparity in women, being male, and being younger than 60 years. (LOE = 1b)
Durante C, Costante G, Lucisano G, et al. The natural history of benign thyroid nodules. JAMA 2015;313(9):926-935.

#5) Prednisone speeds recovery, shortens stay in patients hospitalized with CAP

Clinical question: Does adding prednisone to antibiotics improve outcomes in adults hospitalized with community-acquired pneumonia?
Study design: Randomized controlled trial (double-blinded) **Funding source:** Foundation
Allocation: Concealed **Setting:** Inpatient (any location)
Synopsis: In this Swiss study, patients admitted to the hospital with CAP randomly received 50 mg prednisone daily for 7 days (n = 402) or placebo (n = 400). Each day, a researcher unaware of treatment assignment assessed the patients' clinical status. Patients treated with prednisone reached clinical stability (at least 24 hours of stable vital signs: afebrile, no tachycardia or tachypnea, normotensive, normal mental status, no hypoxia) approximately 1.5 days faster than patients treated with placebo. The average length of stay was 1 day longer in the placebo-treated patients. The prednisone-treated patients were more likely to have hyperglycemia treated with insulin.
Bottom line: Among patients hospitalized with community-acquired pneumonia (CAP), adjunctive prednisone speeds time to recovery by 1.5 days and shortens hospital length of stay by approximately 1 day, but produces no difference in pneumonia complications at 30 days. (LOE = 1b)
Blum CA, Nigro N, Briel M, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet 2015;385(9977):1511-1518.

#6) Personalizing the experience of death in the ICU for all involved

Clinical question: Is there a way to ease the process of dying for patients in an intensive care unit and decrease the consequences of that death on patients' family members?
Study design: Qualitative **Funding source:** Government
Setting: Inpatient (ICU only)
Synopsis: These researchers invited participation of consecutive patients of a single ICU (N = 40), and their families, for whom advanced life support was withdrawn or for whom the probability of dying in the ICU was estimated to be at least 95%. The intervention consisted of sensitively asking for at least 3 wishes from the patients, family

members, or clinicians caring for the patients on how best to honor the patient. Most (82.5%) of the patients had some degree of impaired consciousness and so most of the wishes came from others. At least one family member was interviewed between 1 and 6 months and at least 3 clinicians per patient were interviewed at least 1 to 2 weeks after the patient's death. The transcripts of these interviews were appropriately analyzed by open coding followed by the development of categories (axial coding) that were then clustered into themes. The authors also collected data from family members using the Quality of End-of-Life Care-10 instrument and used writings of family members and written reflections of clinicians in their analysis. The authors defined 3 domains of this project: (1) dignifying the patient; (2) giving the family a voice; and (3) fostering clinician compassion. The 5 categories of wishes included: (1) humanizing the environment; (2) personal tributes; (3) family reconnections; (4) rituals and observances; and (5) "paying it forward" (eg, organ donation, charity donation).
Bottom line: Personalizing death in an intensive care unit (ICU) by asking dying patients, their families, and the clinicians involved in their care to make 3 wishes may provide dignity for the patient, give a voice to family members, and be valuable for clinicians. The wishes identified in this study were mostly simple and inexpensive, involving such acts as using the patient's nickname, allowing a mother to be in bed with her son as he dies, celebrating birthdays or religious ceremonies, and arranging for organ donation or volunteer work by a family member. Though studied in an ICU, asking for 3 wishes seems to be applicable to other settings as well. (LOE = 4)
Cook D, Swinton M, Toledo F, et al. Personalizing death in the intensive care unit: The 3 wishes project. A mixed-methods study. Ann Intern Med 2015;163(4):271-279.

#7) Best approaches to physical diagnosis of acute red eye

Clinical question: What signs or symptoms are indicative of serious eye disease in patients with red eye or a bacterial cause in patients with presumed conjunctivitis?
Study design: Systematic review **Funding source:** Self-funded or unfunded
Setting: Various (meta-analysis)
Synopsis: The authors conducted a limited search, using only a single database (PubMed) and only selecting English-language studies that evaluated the diagnostic accuracy of the history and physical examination in adult patients with red eye. They included studies that enrolled patients with either presumed conjunctivitis who had bacterial culture or patients with red eye, all of whom eventually underwent slit-lamp examination. Two authors independently extracted the data. They did not evaluate the quality of the research. In 5 studies of 957 consecutive patients with red eye, the most useful findings that indicated serious eye disease were anisocoria (with the smaller pupil in the red eye and difference between pupil diameters >1 mm; positive likelihood ratio [LR+] = 6.5; 95% CI 2.6 - 16.3) and photophobia, elicited by direct illumination (LR+ = 8.3; 2.7 - 25.9), indirect illumination (LR+ = 28.8; 1.8 - 459), or finger-to-nose test (LR+ = 21.4; 12 - 38.2). In 3 studies of 281 patients enrolled consecutively with presumed conjunctivitis, 45% had positive bacterial cultures. No sign or symptom was particularly effective at identifying bacterial conjunctivitis, either alone or in combination. The lack of morning "glue eye," (LR+ = 0.3; 0.1 - 0.8) or failure to observe a red eye at 20 feet (LR+ = 0.2; 0 - 0.8) may be useful for ruling out a bacterial cause. None of the included studies evaluated the ability of any sign or symptom to predict response to topical antibiotic treatment.
Bottom line: Eliciting photophobia via pupillary constriction and the presence of anisocoria (>1 mm) in patients with an acute red eye are the best predictors of serious eye disease (eg, uveitis, keratitis, corneal abrasion, or scleritis) requiring prompt referral. Lack of morning eye matting is a fairly good way to rule out bacterial conjunctivitis, but no sign or symptom in this study consistently identifies a bacterial cause or response to antibiotic treatment. (LOE = 2a-)
Narayana S, McGee S. Bedside diagnosis of the 'red eye': A systematic review. Am J Med 2015;128(11):1220-1224.

#8) Hyaluronic acid = sham injections in patients with knee DJD

Clinical question: Do hyaluronic acid injections in patients with knee degenerative joint disease improve pain and function?
Study design: Meta-analysis (randomized controlled trials)
Funding source: Self-funded or unfunded **Setting**: Outpatient (specialty)
Synopsis: These authors searched multiple databases and a clinical trial registry to identify randomized trials comparing hyaluronic acid injections with control treatments in patients with knee degenerative joint disease. Studies had to include at least 30 patients in each group, include pain and function scales for which minimal clinically important differences are established, and have at least 4 weeks of follow up. The authors don't describe the process of article inclusion. Ultimately, they included 19 studies with nearly 4500 patients: 14 used sham injections as the comparator; 2 used usual care; 3 used injections combined with some other active treatment. The authors did not find any statistically significant potential for publication bias. In the studies using sham injections, hyaluronic acid was

slightly better at improving pain and function, but the improvement was not clinically important. Similarly, the improvements in double-blind trials were also not clinically significant. Among the other studies with designs at higher risk of bias, the magnitude of improvement in pain and function were really impressive. We have seen this story before: The stuff looks really effective until the studies are done correctly. In the meantime, all the placebo responders are writing testimonials about how their "lives were saved."
Bottom line: The highest quality studies, which are now fairly plentiful, show that hyaluronic acid injections are only minimally better than sham injections in improving pain and function in patients with knee degenerative joint disease.
Jevsevar D, Donnelly P, Brown GA, Cummins DS. Viscosupplementation for osteoarthritis of the knee. J Bone Joint Surg Am 2015;97(24):2047-2060.

#9) Useful signs and symptoms of severe intracranial injury after minor head trauma

Clinical question: What clinical signs and symptoms are useful in accurately diagnosing a severe intracranial injury after minor head trauma in adults?
Study design: Systematic review **Funding source**: Foundation
Setting: Various (meta-analysis)
Synopsis: Adults who appear well and have a Glasgow Coma Scale (GCS) of 13 or higher after traumatic brain injury (TBI) are defined as having minor head trauma. These investigators searched MEDLINE and the Cochrane Library, as well as pertinent references from retrieved articles, for English-language studies of adults (18 years or older) with head trauma who presented for evaluation with GCS scores ranging from 13 to 15. Inclusion criteria included diagnostic accuracy studies focusing on severe intracranial injuries requiring prompt intervention. A total of 14 studies (N = 23,079) met inclusion criteria with a severe intracranial injury prevalence of 7.1% (95% CI 6.8% - 7.4%) and a prevalence of injuries leading to death or requiring neurosurgical intervention of 0.9% (0.78% - 1.0%). The highest risk factors included pedestrians struck by motor vehicles (positive likelihood ratio [LR+] = 95% CI 3.0 - 4.3), age at least 65 years (LR+ = 2.3; 1.8 - 3.1), and age at least 60 years (LR+ = 2.2; 1.6 - 3.2). Useful symptoms included the presence of vomiting, especially at least 2 episodes (LR+ = 3.6; 3.1 - 4.1), or posttraumatic seizures (LR+ = 2.5, 1.3 - 4.3). Likelihood ratios for loss of consciousness or the presence of headache were minimally, if at all, useful for predicting adverse outcomes. Useful physical signs included features suspicious for skull fractures: visible open skull fracture, palpable depressed skull fracture, postauricular ecchymosis (Battle sign), hemotympanum, cerebrospinal fluid otorrhea, or raccoon eyes (LR+ = 16; 3.1 - 59). A GCS score of 13 (LR+ = 4.9; 2.8 - 8.5), a GCS score of less than 15 at 2 hours after injury (LR+ = 1.6 - 7.6), any decline in GCS score (LR+ range = 3.4 - 16) or a focal neurologic deficit (LR+ range = 1.9 - 7.0) also increased the likelihood of severe intracranial injury. Two clinical decision rules, including the Canadian CT Head Rule and the New Orleans Criteria, were also evaluated. The absence of all features on the Canadian CT Head Rule lower the probability of a severe injury to 0.31% (0% - 4.7%), with the corresponding absence of any of the New Orleans Criteria lowering the risk to 0.61% (0.08% - 6.0%).
Bottom line: Specific individual risk factors, clinical signs, and symptoms (see Synopsis) are useful in identifying adults with minor head trauma who are at risk of severe intracranial injury. The absence of all features of the Canadian CT Head Rule and New Orleans Criteria are also highly accurate for identifying adults at low risk of severe injury.
Easter JS, Haukoos JS, Meehan WP, Novack V, Edlow JA. Will neuroimaging reveal a severe intracranial injury in this adult with minor head trauma? The rational clinical examinations systematic review. JAMA 2015;314(24):2672-2681.

#10) SBP of 120 instead of 140 in nondiabetic, high-risk elderly leads to significant benefits and some harms (SPRINT)

Clinical question: Is there a net benefit to a systolic blood pressure target of 120 mm Hg compared with 140 mm Hg in patients without diabetes who are at high risk of cardiovascular disease?
Study design: Randomized controlled trial (single-blinded) **Funding source:** Government
Allocation: Uncertain **Setting:** Outpatient (any)
Synopsis: Previous trials of more aggressive blood pressure targets in high-risk patients have either shown no benefit, or in some cases a benefit limited to only one of many possible clinical outcomes (eg, hemorrhagic stroke only). This study identified patients 50 years and older with a baseline systolic blood pressure between 130 mm Hg and 180 mm Hg and no history of diabetes mellitus or stroke. All were at increased risk of cardiovascular complications based on at least one of the following: cardiovascular disease, chronic kidney disease (glomerular filtration rate [GFR] = 20 mL/min to 60 mL/min); 10-year cardiovascular risk of 15% or more based on the Framingham risk score, or at least 75 years old. Only outcome assessors were masked to the treatment assignment; patients and their physicians were not. Details regarding allocation concealment were not provided, but the groups

were balanced with regard to demographics, baseline blood pressure, and cardiovascular risk factors. Of 14,692 patients screened for eligibility, 9361 were randomized to either a systolic blood pressure target of 120 mm Hg or 140 mm Hg. The mean age of participants was 68 years, 56% were current or former smokers, 30% were non-Hispanic black, and 11% were Hispanic. The most common reasons for exclusion prior to randomization were lack of cardiovascular risk, out-of-range systolic blood pressure, or were the use of too many blood pressure medications. The protocol for the 120 mm Hg group specified beginning with 2- or 3-drug therapy with a combination of a thiazide diuretic, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and/or a calcium channel blocker; those in the 140 mm Hg group were converted from their usual drug to an equivalent in the formulary. The formulary included a broad range of medications, including most of the drugs most commonly prescribed in the United States. The exception was that hydrochlorothiazide was only available in combination with triamterene at a dose of 50 mg; chlorthalidone, furosemide, spironolactone, and amiloride were the other diuretics. Drugs were added from the formulary as needed to achieve blood pressure targets. The average number of agents used in the 120 mm Hg group was 2.7, with 32% of patients requiring 3 drugs and 24% of patients requiring 4 or more drugs. In the 140 mm Hg group, the average number of medications was 1.8, only 17% of patients required 3 drugs, and 7% required 4 or more. Clinical outcomes and adverse events were adjudicated by a committee masked to treatment assignment. Analysis was by intention to treat, and the mean blood pressures achieved in the 2 groups were 121 mm Hg and 136 mm Hg. Although the study originally planned a 5-year follow-up, it was halted after 3.3 years on the basis of positive findings in an interim analysis. The intensive treatment group was less likely to die from any cause (3.3% vs 4.5%; P = .003; number needed to treat [NNT] = 83 over 3.3 years), less likely to die from a cardiovascular cause (0.8% vs 1.4%; P = .005; NNT = 167 over 3.3 years), and less likely to develop heart failure (1.3% vs 2.1%; P = .002; NNT = 125 over 3.3 years). There were no significant differences in the likelihood of myocardial infarction, acute coronary syndrome, or stroke. Among the patients with chronic kidney disease at baseline (n = 2646), there was no difference in the likelihood of end-stage renal disease or a 50% or higher reduction in GFR. Among those without chronic kidney disease, there was a small increase in the likelihood of a 30% or greater decline in GFR (3.8% vs 1.1%; P = .001; NNT = 37 over 3.3 years). The benefits became apparent after 2 to 3 years of therapy based on the Kaplan-Meier curves. Looking at a composite outcome of myocardial infarction, acute coronary syndrome, stroke, heart failure, or cardiovascular death, benefits appeared to be somewhat greater among patients older than 75 years and for men. Although there were clear benefits, there were also harms. Serious adverse events were defined as fatal or life-threatening, resulting in disability, or requiring hospitalization. Episodes of hypotension (2.4% vs 1.4%), syncope (2.3% vs 1.7%), electrolyte abnormality (3.1% vs 2.3%), and acute kidney injury or acute renal failure (4.1% vs 2.5%) were all significantly more common in the intensive therapy group.
Bottom line: In this group of older patients (mean age = 68 years) who do not have diabetes but are at high risk of cardiovascular disease, a more aggressive systolic blood pressure target of 120 mm Hg instead of 140 mm Hg led to benefits (lower all-cause mortality, lower cardiovascular mortality, less heart failure), but also some harms (more serious episodes of hypotension, electrolyte abnormality, syncope, and acute kidney injury). Patients in the intensive therapy group took an average of one additional drug to achieve this target. The decision to pursue this more aggressive target should be guided by how well the patient fits the profile of patients in this study (ie, no diabetes, older than 50 years, high risk of cardiovascular disease) and how well the additional therapy is tolerated. (LOE = 1b)
The SPRINT Research Group, Wright JT Jr, Williamson JD, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373(22):2103-2116.

#11) Back-up culture not needed for negative rapid strep test results

Clinical question: Do negative "rapid strep" test results need to be confirmed by culture?
Study design: Meta-analysis (other) **Funding source:** Self-funded or unfunded
Setting: Various (meta-analysis)
Synopsis: The investigators searched MEDLINE and EMBASE to identify 48 studies that compared rapid antigen tests for group A streptococcus with throat culture, the gold standard. They limited their search to English-language studies, but searched bibliographies of identified studies and previous reviews. Two investigators assessed all studies for quality. Studies were performed throughout the world and used 6 different testing methods (latex agglutination, ELISA, and so forth). Overall, the sensitivity of all rapid antigen tests was 86% (95% CI 83% - 88%) and specificity was 96% (94% - 97%). Results were similar when limited to studies performed in children. Molecular techniques (DNA probes, polymerase chain reaction methods) were slightly better, though these tests have a turnaround time of 1 hour to 3 hours.
Bottom line: Although rheumatic heart disease due to group A streptococcal infection has all but disappeared in wealthy countries (Lancet 2012;379:953-964), some countries still go to great lengths to test for Streptococcal throat infections -- I'm talking to you, United States. As a result, we spend more than $8 million per each additional case of rheumatic heart disease prevented (Prev Med 2002;35(3):250 -257).This meta-analysis found that the rapid antigen tests widely in use are very effective in both identifying and excluding strep. Overall, the sensitivity of these tests is 86% and specificity is 96%, both overall and in children. The authors of this analysis argue that this sensitivity is high enough -- and the likelihood of rheumatic heart disease is low enough -- to drop the long-held practice of confirming

negative antigen test results with culture. Maybe one day we'll retire strep testing; until then, maybe we can get rid of cultures. Show this paper to your local micro lab director. (LOE = 1a)
Lean WL, Arnup S, Canchin M, Steer AC. Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis. Pediatrics 2014;134(4);771-781.

#12) PubMed: Early introduction of peanuts reduces peanut allergy in high risk children

BACKGROUND: The prevalence of peanut allergy among children in Western countries has doubled in the past 10 years, and peanut allergy is becoming apparent in Africa and Asia. We evaluated strategies of peanut consumption and avoidance to determine which strategy is most effective in preventing the development of peanut allergy in infants at high risk for the allergy.
METHODS: We randomly assigned 640 infants with severe eczema, egg allergy, or both to consume or avoid peanuts until 60 months of age. Participants, who were at least 4 months but younger than 11 months of age at randomization, were assigned to separate study cohorts on the basis of preexisting sensitivity to peanut extract, which was determined with the use of a skin-prick test--one consisting of participants with no measurable wheal after testing and the other consisting of those with a wheal measuring 1 to 4 mm in diameter. The primary outcome, which was assessed independently in each cohort, was the proportion of participants with peanut allergy at 60 months of age.
RESULTS: Among the 530 infants in the intention-to-treat population who initially had negative results on the skin-prick test, the prevalence of peanut allergy at 60 months of age was 13.7% in the avoidance group and 1.9% in the consumption group (P<0.001). Among the 98 participants in the intention-to-treat population who initially had positive test results, the prevalence of peanut allergy was 35.3% in the avoidance group and 10.6% in the consumption group (P=0.004). There was no significant between-group difference in the incidence of serious adverse events. Increases in levels of peanut-specific IgG4 antibody occurred predominantly in the consumption group; a greater percentage of participants in the avoidance group had elevated titers of peanut-specific IgE antibody. A larger wheal on the skin-prick test and a lower ratio of peanut-specific IgG4:IgE were associated with peanut allergy.
CONCLUSIONS: The early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk for this allergy and modulated immune responses to peanuts. (Funded by the National Institute of Allergy and Infectious Diseases and others; ClinicalTrials.gov number, NCT00329784.)
Du Toit G, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med. 2015 Feb 26;372(9):803-13.
This is practice changing.

In June 2015, the American Academy of Pediatrics endorses and accepts as its policy, the "Consensus Communication on Early Peanut Introduction and the Prevention of Peanut Allergy in High-Risk Infants." ***Pediatrics Sept 2015;136(3).***

The purpose of this brief communication is to highlight emerging evidence to existing guidelines regarding potential benefits of supporting early, rather than delayed, peanut introduction during the period of complementary food introduction in infants. Interim guidance regarding early peanut introduction Based on data generated in the LEAP trial and existing guidelines, the following interim guidance is suggested to assist the clinical decision making of health care providers: There is now scientific evidence (Level 1 evidence from a randomized controlled trial) that health care providers should recommend introducing peanut-containing products into the diets of "high-risk" infants early on in life (between 4 and 11 months of age) in countries where peanut allergy is prevalent because delaying the introduction of peanut can be associated with an increased risk of peanut allergy.

#13) Several methods to help children learn to swallow medicines

Clinical question: What can be done to help children swallow solid medicine?
Study design: Systematic review **Funding source:** Foundation
Setting: Various (meta-analysis)
Synopsis: Okay, so philanthropies are not lining up to support research on how to teach children to swallow tables or capsules; as a result the studies are small and of low quality. This systematic review had its limitations, searching only one database (PubMed) for English-language articles published between December 1986 and December 2013. These authors included any type of evaluation; there were no randomized controlled trials and the largest study enrolled 67 children. Only one study had a patient-oriented outcome, demonstrating improved CD4 counts in children with HIV who were taught to swallow antivirals. Successful methods to try in children include: a spray lubricant designed to coat the throat (Pill Glide); cut-to-size candy (gummy worms) for practice, increasing the size until it reaches the size of the capsule or tablet; patient instructions; a specialized pill cup; and head posture training aimed at finding the head position that makes swallowing easier.

Bottom line: Several mechanisms can be used to help children overcome the psychological barrier of swallowing a hard capsule or tablet, though I suspect these methods are lucky charms more than anything physiologic. You can use a "magic spray" to coat the throat (Pill Glide); practice with small, soft candies that can be swallowed whole; give extensive patient instructions; use a specialized pill-swallowing cup; or teach head posture that's purported to increase esophageal diameter. No research has compared the effectiveness of these approaches, so suggest any or all of them. (LOE = 2a-)
Patel A, Jacobsen L, Jhaveri R, Bradford KK. Effectiveness of pediatric pill swallowing interventions: A systematic review. Pediatrics 2015;135(5):883-889.

#14) Watch-and-wait strategy may be appropriate for candy lodged in the nose of children

Clinical question: How long does it take candy (sweets) to dissolve in the human nose?
Study design: Case series **Funding source:** Self-funded or unfunded
Setting: Outpatient (specialty)
Synopsis: In what probably started as a dare on what must have been a slow afternoon in the ENT clinic, one author placed 5 different candies, one at a time, into his nose underneath the inferior turbinate (the most common site of nasal foreign bodies in children). There was no mention of how the candies were chosen (probably a convenience sample of what was in a nearby vending machine) or how the order of placement was determined. The patient was not masked. The other author performed rhinoscopy every 5 minutes until the foreign body could no longer be seen and the foreign body sensation was gone. Boom! Study done. The 5 hard sugar candies—Fizzers, Tic Tac, Smarties, Skittles, Polo mints (like LifeSavers in the United States)— dissolved in less than hour, the rate roughly proportional to their size. The authors point out that a child's nares is smaller than an adults and results may vary. Still, a watch-and-wait approach might be the way to go with this type of foreign body.
Bottom line: This is one of those delicious (pun intended) medical facts that 2 researchers took the time—probably an afternoon—to investigate. Sugar candies such as Tic Tac, Fizzers, Smarties, and others will dissolve in the nose in less than an hour. Although unknown foreign bodies still need to be investigated and removed from the nose, it may be prudent to let this type of candy dissolve in situ rather than trying to remove it. (LOE = 4)
Leopard DC, Williams RG. Nasal foreign bodies: A sweet experiment. Clin Otolaryngol 2015;40(5): 420-421.

#15) Genetic test results that identify increased risk do not change behavior

Clinical question: Does genetic testing for disease risk motivate people to change their behavior?
Study design: Meta-analysis (randomized controlled trials) **Funding source:** Government
Setting: Various (meta-analysis)
Synopsis: These researchers identified 18 studies by searching 5 databases, including the Cochrane Register, as well as by performing citation searches. The studies were randomized or quasi-randomized controlled trials of adults receiving personalized DNA-based risk estimates for which a behavior change might reduce risk. In other words, people at increased risk of disease-for example, smokers or patients with a family history of melanoma-underwent DNA analysis and were told if they had an increased risk based on a personalized risk estimate. Most of the studies were of low quality (which typically favors treatment) and may have been too small to find small differences. Two authors selected studies for inclusion and abstracted the data. The studies were homogeneous. Overall, communicating specific risk did not change behavior. Telling smokers that they are at increased risk of lung cancer, based on their genetic makeup, did not induce them to quit smoking. Similarly, people told they are at risk of melanoma did not use more sunscreen; patients at risk for developing diabetes, obesity, cardiovascular disease, hypertension, or Alzheimer disease did not change their diet or physical activity; and patients at particular risk of alcohol use disorder did not change their drinking.
Bottom line: If you forgot for a moment that humans are irrational beings, here's yet another reminder. Patients informed, via genetic test results, that they were at increased risk for disease did not subsequently alter their behaviors: for example, people at increased risk of diabetes or hypertension were no more likely to change their diet or increase their physical activity. So, you can forget the fancy tests as motivators of behavior change. (LOE = 1a-)
Hollands GJ, French DP, Griffin SJ, et al. The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis. BMJ 2016;352:i1102.

#16) Behavioral interventions reduce inappropriate antibiotic prescribing for acute respiratory tract infections

Clinical question: Do behavioral interventions reduce rates of inappropriate antibiotic prescribing for acute respiratory tract infections in primary care?
Study design: Randomized controlled trial (nonblinded) **Funding source:** Government

Allocation: Uncertain **Setting:** Outpatient (primary care)
Synopsis: Clinical guidelines encourage avoiding antibiotics for infections when treatment is of minimal, if any, benefit. However, inappropriate antibiotic prescribing for acute respiratory tract infections persists. These investigators invited 49 practices in Massachusetts and California (N = 243 clinicians) to receive various combinations of behavioral interventions aimed at reducing inappropriate antibiotic prescribing. The first intervention used automated alternative treatment suggestions when providers attempted to prescribe antibiotics for antibiotic-inappropriate diagnoses. A second intervention required providers to text an "antibiotic justification note" that became a permanent part of the medical record. The third intervention distributed periodic emails to participating providers labeling them as either a "top performer" or "not a top performer" by comparing their antibiotic prescribing behavior with their peers'. Providers included internists (60%), nurse practitioners/physician assistants (19%), and family physicians (13%). The study excluded patients with chronic medical conditions that necessitate more frequent antibiotic prescriptions for acute respiratory tract infections (eg, emphysema). Practices were randomized to receive 0, 1, 2, or all 3 interventions for 18 months and no cases were lost to follow-up. Not surprisingly, the control group significantly decreased inappropriate antibiotic prescribing rates (11% absolute reduction) during the study period. This is known as the Hawthorne effect: changing your behavior simply because you know you're being observed. Both the accountable justification and peer comparison interventions significantly decreased antibiotic prescribing rates compared with the control group (-7.0% and -5.2%, respectively). However, the suggested alternatives intervention did not significantly reduce antibiotic prescribing rates compared with control. The latter result is disheartening but consistent with prior findings about influencing clinical decision making: Information alone rarely changes behavior. The most powerful influence continues to be peer pressure and the desire to conform
Bottom line: Requiring clinicians to justify antibiotic prescribing in the permanent electronic health record and to undergo periodic peer comparisons of prescribing rates are both effective interventions for reducing inappropriate antibiotic prescribing for acute respiratory tract infections. Helpful reminders and suggested treatment alternatives do not reduce inappropriate prescribing rates. Information alone rarely changes behavior, but the desire to conform with our peers can be very persuasive. (LOE = 1b-)
Meeker D, Linder JA, Fox CR, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices. JAMA 2016;315(6):562-570.

#17) Expectant management after PPROM is beneficial for newborns

Clinical question: Among women with preterm pre-labor rupture of membranes close to term, what are the risks for newborns of immediate delivery versus expectant management?
Study design: Randomized controlled trial (nonblinded) **Funding source:** Government
Allocation: Concealed **Setting:** Inpatient (any location) with outpatient follow-up
Synopsis: In this study including 65 centers in 11 countries women with PPROM at 34 weeks' to 36 6/7 weeks' gestation (N = 1838) who were not in labor were randomized to expectant management or immediate delivery. Women who were in labor or had chorioamnionitis, meconium staining, or any other contraindication to continue pregnancy were excluded. Presence of group B Strep colonization was not an exclusion criterion. Women in the immediate delivery group had delivery scheduled as soon as possible (usually within 24 hours). Women in the expectant management group continued pregnancy until term, until spontaneous labor occurred, or until there was any indication for delivery. The use of antibiotics, laboratory testing, and other management was per usual hospital protocol. Neonatal sepsis was carefully defined and adjudicated by masked assessment. Almost all women were managed according to the group to which they were assigned, and the groups were well balanced along numerous variables. Neonatal sepsis was the primary outcome analyzed and occurred in 2% of newborns in the immediate delivery group versus 3% of the expectant management group (relative risk [RR] 0.8; 95% CI 0.5-1.3; P = .37). Sepsis rates did not differ according to baseline vaginal culture positivity for any organism, including group B Strep.There were three deaths in each group. Newborns in the immediate delivery group had less favorable outcomes for respiratory distress (RR 1.6; 1.1-2.3), any mechanical ventilation (RR 1.4; 1.0-1.8), and spent more time in NICU (median 4 days vs 2 days; P < .0001).
Bottom line: Among women with preterm premature rupture of membranes (PPROM) at 34 weeks' to 36 6/7 weeks' gestation who were were randomized to receive expectant management or immediate delivery, there was no statistically significant difference in the incidence of neonatal sepsis. Newborns from the immediate delivery group had increased incidence of respiratory distress and mechanical ventilation, and spent more time in the neonatal intensive care unit (NICU). (LOE = 1b)
Morris JM, Roberts CL, Bowen JR, et al, for the PPROMT Collaboration. Immediate delivery compared with expectant management after preterm pre-labour rupture of membranes close to term (PPROMT trial): a randomized trial. Lancet 2016;387(10017):444-451.

#18) No survival advantage to PCI over optimal medical therapy after 12 years (COURAGE)

Clinical question: Does a percutaneous coronary intervention, when added to optimal medical therapy, improve survival in patients with stable coronary artery disease?
Study design: Randomized controlled trial (single-blinded) **Funding source:** Government
Allocation: Uncertain **Setting:** Outpatient (any)
Synopsis: The original COURAGE trial identified 2287 adults with chronic stable angina, defined as typical ECG findings and symptoms accompanied by at least a 70% stenosis of one coronary artery. Most had class II or class III angina that had been diagnosed a mean of 2 years previously; approximately two-thirds had multivessel disease. The patients were randomized to receive a percutaneous coronary intervention (chosen by their cardiologist) plus optimal medical therapy, or optimal medical therapy alone. Medical therapy had targets of 70 mg/dL for low-density lipoprotein cholesterol and 130/85 for blood pressure. The original study had a median follow-up of 4.6 years and found no difference in clinical outcomes between groups. At the time of enrollment, where not forbidden by human subjects committees (Canada and some non-VA hospitals), patients were asked for their Social Security number so mortality could be tracked over the long term. Social Security numbers were obtained for slightly more than half of the patients in each original study group (613 in the PCI group and 598 in the medical therapy group). The extended follow-up period was a median of 11.9 years, and the researchers found no difference in all-cause mortality between the 2 groups (24% vs 25%).
Bottom line: This extended follow-up of the largest trial comparing percutaneous coronary intervention (PCI) with medical therapy still found no survival advantage of PCI plus optimal medical therapy over optimal medical therapy alone. (LOE = 1b)
Sedlis SP, Hartigan P, Teo KK, et al, for the COURAGE Trial Investigators. Effect of PCI on long-term survival in patients with stable ischemic heart disease. N Engl J Med 2015;373(20):1937-1946.

#19) More nuanced guidelines for lipid lowering to prevent CV disease

Clinical question: For the primary and secondary prevention of cardiovascular disease, how should risk be assessed and what should be done about elevated lipid levels?
Study design: Practice guideline **Funding source:** Government
Setting: Various (guideline)
Synopsis: This guideline was developed by 2 government agencies tasked with providing health care for active duty military personnel and veterans. The guideline was based on a systematic review of the literature; the authors graded the evidence and the strength of their recommendations using the GRADE system. The panel members were free of conflicts of interest. From primary prevention, calculate 10-year CVD risk using a risk calculator (weak recommendation). The authors suggest 3 cutoffs: less than 6% risk of CVD: there's no evidence of benefit with treatment; 6% to 12% risk: there's limited evidence of benefit with treatment; greater than 12%: there's a 20% to 30% decrease in risk with treatment (weak recommendation). Treat most patients at the highest risk but allow patients at lower risk levels to weigh possible benefit versus possible risk; for example, muscle symptoms and a small risk of diabetes (weak recommendation). Use a moderate, fixed-dose statin; that is, don't continue to check lipid levels and adjust dosing (strong recommendation). For secondary prevention, also use a moderate, fixed-dose statin (strong recommendation). In some patients -- those with recurrent cardiac events or who have multiple uncontrolled risk factors -- consider using higher doses, weighing questionable benefits against a slightly higher risk of developing diabetes (weak recommendation).
Bottom line: The authors of this guideline give a more nuanced and less aggressive approach to lipid lowering than other groups. For the primary prevention of cardiovascular disease (CVD), check blood pressure and lipids (nonfasting is fine) to calculate the 10-year CVD risk. If greater than 12%, treat; if 12% or less, discuss treatment with the patient. Pick a moderate-dose statin and don't check lipid levels again. For secondary prevention, use moderate-dose statins and titrate to a higher dose only in a few, high-risk patients. Again, don't titrate based on lipid levels. (LOE = 5)
Downs JR, O'Malley PG. Management of dyslipidemia for cardiovascular disease risk reduction: Synopsis of the 2014 U.S. Department of Veterans Affairs and U.S. Department of Defense clinical practice guideline. Ann Intern Med 2015;163(4):291-297.

#20) Perioperative bridging anticoagulation unhelpful for invasive procedures

Clinical question: Does bridging anticoagulation during invasive procedures improve outcomes in patients with atrial fibrillation who take warfarin?
Study design: Randomized controlled trial (double-blinded) **Funding source:** Government

Setting: Inpatient (any location)
Synopsis: The evidence for bridging anticoagulation is looking increasingly questionable, with a recent registry-based study finding worse outcomes with bridging (http://www.essentialevidenceplus.com/content/poem/170602). This study provides the best evidence to date. A total of 1884 adults with chronic atrial fibrillation and at least one CHADS2 risk factor were randomized to bridging anticoagulation with dalteparin or to placebo. Patients with a mechanical heart valve, recent stroke or embolism, impaired renal function, or thrombocytepenia were excluded, as were patients undergoing cardiac, intracranial, or intraspinal surgery. All participants had received warfarin for at least 3 months and had an INR between 2.0 and 3.0. The protocol for bridging was as follows: (1) stop warfarin 5 days before the procedure, (2) start dalteparin or placebo 3 days before the procedure, (3) stop the study drug 1 day before the procedure, (4) restart warfarin 12 hours to 36 hours after the procedure, and (5) restart the study drug 12 hours to 72 hours after the procedure (based on bleeding risk) and continue it until the INR is therapeutic. The mean age of patients was 72 years, and the mean CHADS2 score was 2.3 (range = 1 - 6). Basically, the bridging group had their time without anticoagulation minimized, while the placebo group was without anticoagulation for approximately 10 days (2 to 3 days before the procedure and a mean of 8 days after). Most of the procedures were classified as low bleeding risk. At 30 days, the risk of arterial thromboembolism did not differ between groups (2 strokes and 2 transient ischemic attacks in the placebo group, and 3 strokes in the bridging group). The risk of major bleeding was significantly higher in the bridging group (3.2% vs 1.3%; P = .01; number needed to treat to harm [NNTH] = 53). There was no difference between groups in the likelihood of death, myocardial infarction, deep vein thrombosis, or pulmonary embolism. Minor bleeding was also more common in the bridging group (20.9% vs 12.0%; P < .001; NNTH = 11).
Bottom line: Bridging anticoagulation worsens outcomes for patients with atrial fibrillation who undergo an elective invasive procedure, resulting in more episodes of major bleeding and no difference in the rate of stroke or venous thromboembolism. Most of the patients in the study had a CHADS2 score of 1 (23%), 2 (40%), 3 (24%), or 4 (10%). The patients were largely undergoing minor surgical procedures with low bleeding risk and patients at very high risk for thromboembolism or stroke were not represented in this study. (LOE = 1b)
Douketis JD, Spyropoulos AC, Kaatz S, et al, for the BRIDGE Investigators. Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med 2015;373(9):823-833.

#21) Don't trust industry-sponsored head-to-head trials

Clinical question: What are the outcomes of head-to-head trials?
Study design: Systematic review **Funding source:** Unknown/not stated
Setting: Various (meta-analysis)
Synopsis: This team of researchers randomly selected 50% of the 20,088 randomized trials published in 2011. From these, they subsequently selected those trials that evaluated direct comparisons of 2 or more drugs, biologics, or medical devices for effectiveness or safety. They excluded placebo-controlled trials and those with fewer than 100 participants. Four of the authors independently extracted the data and resolved discrepancies by discussion. Ultimately, they included 319 trials with a median of 300 patients per study. Approximately 20% of the studies came from each of the United States, western Europe, and Asia and 30% were international. Not surprising, given their prevalence, approximately half the studies addressed cardiovascular disorders, cancer, infectious diseases, or diabetes. All of the studies compared drugs (90%) and biologics (10%). Approximately 25% of the studies were noninferiority trials and nearly 75% of the studies had favorable results. More than half (182) were sponsored by industry and approximately one fourth were sponsored by nonprofit organizations. In spite of a yeoman's effort by the research team, the funding source was not identifiable in approximately 16% of the studies. Approximately 33% of the studies had at least one author with specific industry affiliations and 58% had at least one author reporting a conflict of interest. Of the nearly 300,000 patients in all the studies, 82% were in industry-sponsored studies. Only 23 of the industry-sponsored studies had 2 or more sponsors. Industry-sponsored trials were more likely to be international, registered, and use noninferiority designs ("our drug is at least as good as the competition") and were 3 times more likely to have favorable results than nonindustry-sponsored studies. A total of 55 of the 57 noninferiority trials sponsored by industry had favorable results. One of the key foundations of the responsible conduct of research is the principle of equipoise. In other words, before exposing patients to the potential harms of a study, there ought to be a reasonable doubt as to the study's outcome. This study, one of several, suggests that much of the existing research, especially that funded by industry, is not really research but thinly veiled marketing.
Bottom line: More often than not, head-to-head trials of drugs and biologics tend to have favorable outcomes, especially those that are industry-sponsored and use a noninferiority design. (LOE = 1a-)
Flacco ME, Manzoli L, Boccia S, et al. Head-to-head randomized trials are mostly industry sponsored and almost always favor the industry sponsor. J Clin Epidemiol 2015;68(7):811-820.

#22) ACP: Do not screen low-risk adults for cardiac disease

Clinical question: When should adults be screened for cardiac diseases?
Study design: Practice guideline **Funding source:** Foundation

Setting: Various (guideline)
Synopsis: This statement from the ACP is based on a systematic review and recommendations from the United States Preventive Services Task Force and on guidelines and standards developed by the American College of Cardiology. The guidelines apply to screening (ie, testing for disease in asymptomatic individuals) in patients with a 10-year heart disease risk of less than either 7.5% or 10% (the cutoff is under debate). Risk can be calculated using the Framingham calculator in Essential Evidence Plus or at: http://cvdrisk.nhlbi.nih.gov/calculator.asp). In these patients, there is no evidence showing that screening improves clinical outcomes. Given the low prevalence of heart disease in these patients, this screening will produce many false-positive results and expose patients to risks of additional testing. Both true positives and false positives may also result in labeling and denial of insurance. Also, the out-of-pocket cost for an uninsured patient is an estimated $500USD to $3000USD for a simple ECG, which is outrageous for a service that is typically reimbursed at approximately $35USD by insurance companies in the United States.
Bottom line: Citing low yield, ineffectiveness in preventing patient outcomes, and high cost, the American College of Physicians (ACP) recommends against resting electrocardiography (ECG) or stress ECG, stress echocardiography, or stress myocardial perfusion imaging for asymptomatic, low-risk adults. In these patients, the risks of labeling and downstream harm outweigh the benefits. (LOE = 5)
Chou R, for the High Value Care Task Force of the American College of Physicians. Cardiac screening with electrocardiography, stress echocardiography, or myocardial perfusion imaging: advice for high-value care from the American College of Physicians. Ann Intern Med 2015;162(6):438-447.