Forum for Evidence-Based Medicine

January/February | 2020

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Activity description	Practicing evidence-based medicine (EBM) is important in today's health care environment because this model of care offers clinicians a way to enrich quality, provide patient satisfaction, reduce costs and improve outcomes. A common implementation of EBM involves the use of clinical practice algorithms during medical decision-making to encourage optimal care. This widely recognized practice is designed to address the persistent problem of clinical practice variation with the help of actionable information at the point of care. These E-newsletters will enable health care professionals (HCPs) to put new EBM into practice.
Target audience	This activity is designed to meet the educational needs of physicians, PAs, nurses, nurse practitioners and other HCPs who have an interest in EBM.
Learning objectives	At the end of this educational activity, participants should be able to: • Explore the educational content surrounding back pain as a means to advance optimal care outcomes. • Review pharmaceutical recommendations for the management of the new oral tetracyclines; omadacycline and sarecycline. • Apply medical management principles grounded in evidence-based medicine when comparing the harms, advantages, and costs from hematuria guidelines.

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In support of improving patient care, this activity has been planned and implemented by OptumHealth Education. OptumHealth Education is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE) and the American Nurses Credentialing Center (ANCC) to provide continuing education for the health care team.

Credit designation statements

Nurses

The participant will be awarded up to 1.00 contact hour(s) of credit for attendance and completion of supplemental materials.

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The American Academy of Nurse Practitioners Certification Program (AANPCP) accepts credit from organizations accredited by the ACCME and ANCC.

Physicians

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Practical Management of Back Pain

Background and initial considerations:

Back pain is one of the most common presenting complaints to the primary care physician.[1] Over 80% of individuals will experience back pain sometime during their life.[2] In 20% to 30% of individuals, low back pain will persist at one year. This evidence-based review is intended to help guide the primary care physician through the clinical management of back pain. Subspecialty referrals, imaging, and therapies are addressed below.[3]

Step one in the evaluation of back pain is a thorough history, emphasizing the situations listed below that require urgent intervention, and physical exam, focusing on neurologic and functional impairments. Patient education should begin at the first evaluation.

Situations requiring urgent or special evaluation:

Urgent surgical evaluation is needed for less than one percent of cases seen in primary care, but these must not be missed. The relatively short list of conditions that warrant urgent evaluation include the following: active cancer, IV drug use, urinary retention, saddle anesthesia, loss of anal sphincter tone, major motor weakness, or fever.

In patients with neck pain, urgent imaging and referral is indicated for significant upper or lower extremity weakness or muscle atrophy, or other new neurologic deficits. When present, strongly consider urgent spine MRI and plain radiographic films (preferably standing) along with surgery and/or neurology referral(s).[4]

Radicular pain that is unrelenting and unresponsive to initial management should prompt the consideration of physical therapy referral. Lower back pain that has been present for more than three months should be evaluated with lumbar spine films. Imaging is primarily looking for three broad categories of pathology:

- Osteoporosis, which would prompt consideration of medical management
- Findings consistent with cancer, with referral to surgery and or oncology
- Spondylolisthesis or scoliosis, with resultant engagement of physical therapy

If imaging is normal or shows only expected degenerative changes, the clinical approach outlined below can be followed.[5]

Ongoing back pain management, practical guide:

Step two in management begins with ongoing education and reassurance accompanied by one or more of non-surgical treatment modalities. Each intervention listed in Table 1 has low to moderate levels of evidence supporting the efficacy in the treatment of low back pain. All have a low risk of adverse events.[6,7,8]

(continued on page 2)

Practical Management of Back Pain

(continued from page 1)

Table 1: Non-surgical therapies for Acute Low Back Pain (ALBP) or Chronic Low Back Pain (CLBP)

Non-surgical therapies	ALBP	CLBP
Exercise		✓
Local heat	✓	
Massage		✓
Acupuncture	✓	✓
Spinal manipulation	✓	✓
Mindfulness		✓
Tai Chi		✓
Cognitive behavioral therapy		✓
Yoga		✓
Multidisciplinary rehabilitation		✓

Shared decision making will help to identify the intervention best suited for each patient. The biggest barriers to practical implementation of these therapies is access to providers of the alternative, conservative approaches and insurance coverage.[9] Work to develop a list of providers your clinic can work with to provide these services.

Step three in management of patients with back pain is to add pharmaceutical agents. NSAIDs at the lowest effective doses are the preferred agents. Acetaminophen has been shown to not be effective in the treatment of low back pain. Tramadol for short term use can be tried when NSAIDs fail. Long-term opioid use, including tramadol, is not recommended.[10] In some circumstances, the addition of NSAIDS may appropriately be added along with the non-surgical treatments mentioned in Step Two.

Step four in management involves referral to physical therapy for active therapy and a home exercise program. Should PT not be sufficient, physiatry or conservative pain management specialty referral should be engaged. Consideration of an MRI before or after the evaluation and treatment may be indicated. The primary care physician team should track the patient's progress through these evaluations and continue to provide education and coaching to the patient.

Step five: Should PT and physiatry not resolve the pain the patient may benefit from epidural injections and/or surgical evaluation. Epidural injections tend to have only short term benefit, but may allow a bridge to recovery or to surgical intervention. Some trials have shown patients undergoing epidural steroid injections to have worse long term outcomes.[11] Specific indications for epidural injections include acute disk herniation with refractory radicular pain, degenerative disease with foraminal stenosis and refractory radicular pain, and palliative pain control in non-surgical candidates.

Surgical treatment of low back pain still lacks well designed long term outcomes studies. There is data that in carefully selected patients surgical treatment can be of benefit, particularly patients with severe lumbar spinal stenosis with refractory symptoms.[12] The utility of lumbar fusion in addition to laminectomy is in question[13] There is no dispute that surgical intervention can have frequent complications and additional surgeries with complications occurring in 10- 24% of cases.[14]

Summary: The initial history and physical exam allows selection of patients appropriate for urgent referral or for the vast majority of patients to begin conservative, non-surgical treatments. Create a network of conservative alternative therapies available to your patients. Understand the treatment philosophy and surgical options utilized by the surgeons to whom you refer and assure those practices are consistent with what is best for your patients.

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The New Oral Tetracyclines: Do they provide value?

In the last several years, two new oral tetracyclines (TCN) have been approved for use in the United States: omadacycline and sarecycline.

Omadacycline is an extended spectrum TCN with proven efficacy in treatment of community acquired pneumonia (CAP), skin and soft tissue infections (SSTI), and intra-abdominal infections (IAI).[15] It is effective for complex infections in hospitalized patients.[16] However, omadacycline may also have a role in treating CAP or SSTI in observation patients or outpatients. Of note, the omadacycline treatment arm of a CAP treatment trial exhibited increased mortality relative to other antibiotics.[17] Omadacycline is available for intravenous or oral administration, and treatment can be initiated as an infusion with a rapid change to the oral route. The economic justification for the high price of omadacycline is avoided hospital days with a more rapid transition to outpatient therapy. A treatment course of omadacycline is just under $4000.

Sarecycline is a niche TCN approved exclusively for the treatment of the inflammatory lesions of non-nodular, moderate to severe acne vulgaris in patients over nine years of age (see table).[18] Sarecycline is an expensive orally administered agent with a relatively limited therapeutic success in the treatment of acne vulgaris. There are no available data comparing outcomes in treating acne with doxycycline vs sarecycline. The yearly cost is over $10,000.

All tetracyclines, including these new agents, are bacteriostatic, meaning they prevent bacterial replication. This static activity can adversely affect the bacteriocidal activity of other antibiotics administered in conjunction with tetracyclines. For example, the addition of tetracyclines to penicillins has resulted in worse outcomes. Many tetracyclines have the potential of permanently staining developing teeth and should be avoided in children under the age of eight years. Tetracyclines all maintain activity against atypical organisms and in some instances they are the best treatment option (e.g., Rickettsia rickettsia the causative agent for Rocky Mountain Spotted Fever).

In summary, omadacycline retains the coverage common to all tetracyclines but offers greater efficacy against resistant gram negative and gram positive organisms. It has potential application in both inpatient and outpatient settings for CAP and SSTI. Currently, its high cost limits its application in the general population. Sarecycline is extremely expensive and has only modest treatment success for treatment of the inflammatory lesions of non-nodular, moderate to severe acne. Consider carefully the use of these new agents based on the reports of increased mortality associated with the use of omadacycline, treatment failures, higher cost and possible interactions with bacteriocidal agents.

Approved Indications, Efficacy and Cost of Select Tetracyclines

	Approved indications				Clinical efficacy (sensitive in vitro)					
	CAP	SSTI	IAI	Acne	Atypicals	VRE	MSSA	MRSA	RGNR	cost/day ($)
Omadacycline	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	475
Sarecycline	No	No	No	Yes	na	na	na	na	na	30
Doxycycline	Yes	Yes	No	Yes	Yes	No	Yes	No	No	4

Atypicals – refers to the broad array of organisms (eg, Parasites, Rickettsia species, Mycoplasma); VRE – Vancomycin Resistant Enterococci; MSSA – Methicillin Sensitive Staphylococcus; MRSA – Methicillin Resistant Staphylococcus; RGNR – Resistant gram-negative rods; na – not available

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Comparison of Harms, Advantages, and Costs from Hematuria Guidelines

As many as two million Americans are referred to urologists annually for a finding of gross or microscopic hematuria.[19] Although several guidelines address the clinical evaluation of urinary tract cancers when hematuria is present, [20, 21, 22, 23, 24] each guideline varies in terms of the recommended testing modalities (cystoscopy, ultrasonography, computed tomography [CT] urography) and the risk factors that warrant testing. The Table lists five guidelines, ordered from least aggressive testing recommendations (Dutch, top) to most aggressive (American Urologic Association [AUA], bottom). The Dutch guidelines, for example, recommend cystoscopy and ultrasonography as the initial evaluation for hematuria, but only in patients 50 years of age and older, whereas the AUA guidelines endorse uniform cystoscopy and CT evaluations for patients with hematuria aged 35 years and older.

Georgieva and colleagues [25] conducted a microsimulation that compared the potential advantages, harms, and costs of the five guidelines listed in the Table. The simulation used published prospective hematuria cohort studies to model data about patient age, sex, cancer risk factors (e.g., smoking status and gross hematuria), and prevalence of urinary tract cancer (bladder, renal cell carcinoma, and upper-tract urothelial carcinoma). The cohort included 100,000 hypothetical patients, ≥35 years old.

The investigators found that cancer detection rates increased in parallel with more aggressive evaluations. But aggressive evaluations, especially uniform CT imaging, also led to more radiation-induced cancers, more false-positive cancer diagnoses, more procedural complications, and higher monetary costs per evaluation. The Table provides detailed simulated cancer detection rates and potential harms and costs for each published guideline. Since the Dutch and Canadian Urologic Association guidelines do not include CT as part of the initial evaluation, no secondary cancers developed in those cohorts.

It is helpful to compare the AUA and Kaiser Permanente (KP) guidelines as these two are the most frequently used in the US. For the simulated population of 100,000 patients, the AUA guideline compared to the KP guideline would diagnose an additional 48 cancers while causing:

- 467 radiation induced cancers
- 13,000 additional false positive findings
- 3200 additional cases of contrast nephropathy
- Cost to diagnose one additional cancer close to $900,000

Additionally, the microsimulation cost calculations did not include potential downstream costs associated with further testing for patients with false-positive diagnoses or with potential incidental findings from abdominal and pelvic CT scanning. Incidental findings can be seen from abdominal and pelvic CT in up to 30% of patients.[26]

These data suggest that the routine use of CT for all cases of microscopic hematuria per the AUA guidelines is both harmful and cost-ineffective compared to the more conservative KP guideline. The approach to initial testing of patients with hematuria should incorporate both the patients' risk factors for cancer as well as potential harms from testing. Based on the results of this study, it is reasonable to not perform CT urography as an initial screening test for patients with microscopic hematuria, especially when they are at low risk of cancer.

Table. Microsimulation estimated cancer detection rates, harms, and costs associated with hematuria guideline recommendations

Guidelines	Testing recommendations	Cancer detection rates	Radiation-associated cancers (n)	False-positives (n)	Procedural complications[1]	Cost in millions, US dollars
Dutch	Cystoscopy and renal ultrasonography for patients ≥50 years	92.9%	0	6,452	7,999	$44.3
Canadian Urologic Association	Cystoscopy and renal ultrasonography for patients ≥40 years	95.1%	0	6,740	8,344	$46.2
Kaiser Permanente	Cystoscopy and renal ultrasonography only with cancer risk factors;[2] CT and cystoscopy with gross hematuria; no evaluation without risk factors	96.3%	108	9,099	9,582	$51.9
Hematuria Risk Index	Cystoscopy and renal ultrasonography with moderate cancer risk; CT and cystoscopy with high risk; no evaluation if low risk	96.7%	136	13,811	9.709	$59.8
American Urologic Association	Cystoscopy and CT for patients ≥35 years	97.7%	575	22,189	17,637	$93.9

[1]CT contrast allergy, contrast nephropathy, dysuria, urinary tract infections
[2]Smokers, male sex, ≥50 years

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Kenneth Roy Cohen, MD, FACP | *Chief Medical Officer*

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He has successfully developed and reported numerous clinical quality studies in primary care, including tobacco cessation, osteoporosis, asthma, diabetes, hypertension, and ischemic vascular disease. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He has served as Chief Medical Officer since 1995. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA | *Senior Medical Director*

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the Univ of Virginia where he played division one soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the Univ of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the Univ of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD | *Senior Clinical Practice Performance Consultant*

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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Learning objectives	At the end of this educational activity, participants should be able to: • Explore the educational content to help advance optimal care outcomes surrounding new trends in the management of coronary artery disease including CTA with fractional flow reserve. • Review pharmaceutical recommendations for triple inhaler therapy use in asthma and perioperative management of patients with atrial fibrillation on DOAC therapy. • Apply medical management for the treatment of community acquired pneumonia grounded in evidence-based medicine.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.0 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.
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New trends in the management of coronary artery disease including the use of coronary artery CTA with fractional flow reserve

When evaluating patients for the presence of cardiovascular (CV) disease in the outpatient setting, we are typically faced with one of two scenarios. The first group is asymptomatic patients at increased vascular risk and the second group is symptomatic patients with suspicious chest pain or other potential anginal equivalents.

We typically encounter the asymptomatic patient group when trying to make a determination on the need for statin and/or aspirin therapy, as for both of these a shared decision making approach is currently recommended. Also included in this category are those situations where the patient or the provider may be concerned about vascular risk in scenarios where our current CV risk calculators may be suboptimal. These include:

- Patients at younger ages with strong family histories of early vascular disease who may be at low 10-year CV risk, but high 20-year CV risk.
- Patients in the low to moderate risk range on the American Heart Association, (AHA) 10-year risk calculator for whom statin therapy may be recommended but who may wish to avoid therapy in the absence of detectable vascular disease. This includes many of our older patients in whom the 10-year risk calculator often recommends statin therapy predominantly based on the weighting of age in the CV risk formula.
- Patients with tobacco use and/or the metabolic syndrome who may otherwise not trigger statin therapy using the AHA risk calculator.

In these groups of patients, vascular plaque screening using either a coronary calcium score or carotid intima-media thickness (CIMT) can reliably detect and quantify subclinical atherosclerosis and therefore help direct therapy to the patients most likely to benefit from treatment.

A different approach is required in the group of patients with chest pain or other anginal type symptoms that suggest the possibility of coronary artery disease (CAD). Patients presenting with unstable angina need urgent cardiology referral as unstable angina may progress to a completed myocardial infarction in up to 20% of patients within the first six weeks following symptom onset. All other patients need either functional ischemia testing or anatomic testing. Until recently, virtually all patients were initially evaluated with functional testing. However, the advent of coronary artery CTA with fractional flow reserve (CCTA/FFR) is changing this algorithm.

The SCOT-HEART trial[1] was one of the initial large comparison trials of stress testing versus CCTA for the evaluation of suspected CAD. The two-year follow-up showed that CCTA resulted in an increase in early catheterization rate without improved CV outcomes. Recently however, the five-year follow-up results were published and showed that the catheterization rate at the end of five years was equivalent in both arms, but the mortality was reduced in the CCTA group at 2.3% compared to 3.9% in the stress testing group. Moreover, with the addition of FFR, the landscape evolves even further. CCTA initially was unable to differentiate functionally significant stenoses from stenoses that did not limit coronary artery blood flow and therefore were not functionally significant. New software allows an accurate estimation of the pressure gradient across a stenotic artery and therefore can determine functionally significant from non-significant stenoses. This allows for a marked reduction

(continued on page 2)

New trends in the management of coronary artery disease including the use of coronary artery CTA with fractional flow reserve *(continued from page 1)*

in the need for cardiac catheterization in the group of patients who do not have a functionally significant stenosis. The PLATFORM study[2] looked at ischemia testing versus CCTA/FFR to guide cardiac catheterization. In the ischemia testing group, 73% of subsequent catheterizations were found to have no coronary stenoses greater than 50% which were therefore considered negative catheterizations. In contrast, only 12% met this criteria in the CCTA/FFR group. Using CCTA/FFR compared to ischemia testing therefore resulted in a 61% reduction in cardiac catheterization rates with an attendant decreased cost of care and reduced procedural risks to our patients.

Additionally, although routine treadmill stress testing is cost effective and still has a role in the evaluation of chest pain, the majority of stress tests today are done with nuclear imaging. Nationally, over 70% of stress tests are done with nuclear imaging, at an average cost of about $1,800. CCTA, when compared to a nuclear stress test, is about a third the cost and has a lower radiation exposure. When evaluating the combined benefits of lower radiation exposure, significant lower cost of testing, and a marked decrease in unnecessary cardiac catheterizations, the rationale for the use of CCTA/FFR becomes clear. Ideal patients for CCTA/FFR are:

- Moderate to high risk patients (>5% 10-year CV risk) in normal sinus rhythm (rate controlled atrial fibrillation is acceptable). Oral beta blockers are used the evening before and morning of the CCTA to bring the resting heart rate to around 65 to improve the image capture.
- Adequate renal function to allow the use of contrast
- No contrast allergy (or management of such)
- Patients should not have had a prior coronary stent or bypass procedure as these procedures lessen the accuracy of the CCTA. Coronary artery calcium scores over 1,000 may also limit the ability to interpret the CCTA due to image interference from the heavy vascular calcium burden.

The last area to discuss in our review of CAD management is the role of routine ischemia testing in patients with stable CAD. This is timely due to the recent publication of the Ischemia Trial.[3] It has long been observed that when high quality research conflicts with current revenue generating procedures such as nuclear stress testing and elective angioplasty and stenting, the studies are often dismissed as methodologically flawed and for many providers the results do not change practice patterns. Such is the case with routine ischemia testing in stable CAD.

Beginning 27 years ago, four large, high quality randomized trials encompassing close to 10,000 patients have been published.[4,5] They all asked the question of whether coronary interventions done as a result of routine ischemia testing improve cardiovascular outcomes in stable CAD. The results of the four trials have been strikingly consistent. For the subset of patients with significant enough CAD that they have regular exertional angina, the frequency of angina symptoms is diminished with elective coronary intervention. However, all four trials showed no improvements in the rate of myocardial infarction or mortality from coronary artery disease. This is easy to understand knowing the different physiologies of unstable coronary syndromes as opposed to stable CAD. Unstable angina is due to plaque disruption and thrombosis and is therefore best treated urgently with coronary artery revascularization. On the other hand, stable exertional angina is most often due to stable atherosclerotic plaque and these types of plaques progress to unstable angina or myocardial infarction at a rate of only ~3% per year. Moreover, routine stress testing does not predict who these 3% of patients might be since it doesn't have the ability to determine who will develop plaque disruption with subsequent thrombosis. Therefore routine ischemia testing results in an increase in procedural interventions with increased risks and cost of care, but without subsequent improvements in CV outcomes.

Overall, these data strongly support an algorithm incorporating CCTA/FFR for the evaluation of appropriate patients presenting with symptoms suspicious for CAD. The literature cited above does not support routine ischemia testing in patients with stable CAD.

For more information, see "Highlights", p. 7.

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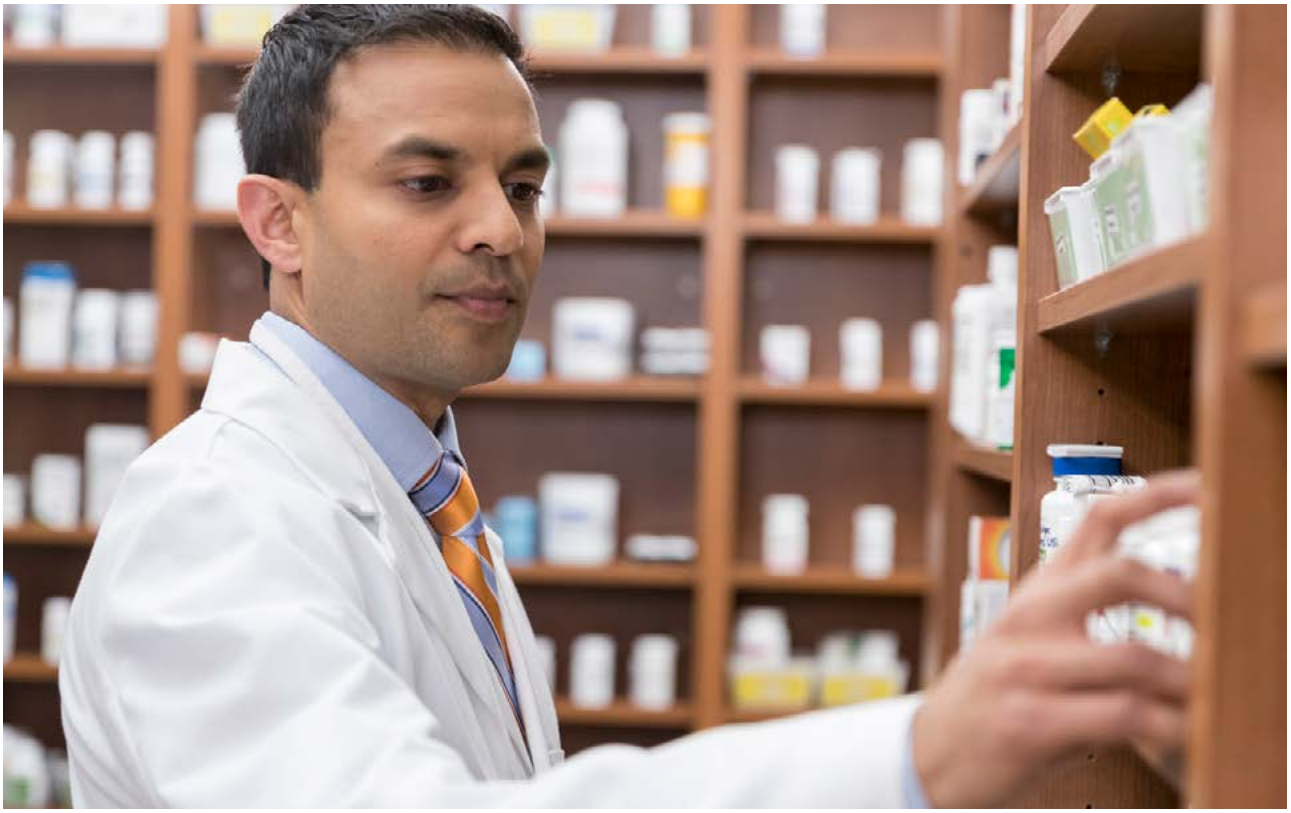

Triple inhaler therapy for moderate to severe asthma

Triple inhaler therapy is the use of a long acting beta agonist (LABA), a long-acting muscarinic antagonist (LAMA), and an inhaled corticosteroid (ICS) in a single inhaler. The use of triple inhaler therapy for chronic obstructive pulmonary disease (COPD) was discussed in the Sept/Oct 2018 Forum newsletter.

The findings of the two large COPD trials (IMPACT and TRIBUTE) showed small improvements in measured outcomes which were of questionable real world impact or cost effectiveness. For example, in the TRIBUTE study, a patient with severe COPD would need to be treated for ten years with triple therapy compared to LABA/LAMA therapy to prevent a single exacerbation. There was no difference in the rate of moderate to severe exacerbations and no difference in time to first exacerbation. In COPD, triple inhaler therapy is best reserved for the subset of patients with severe disease and frequent exacerbations on dual inhaler therapy; however, this will be a small population of patients.

TRIMARIN and TRIGGER are two new trials looking at triple inhaler therapy in patients with asthma.[6] The studies focused on the population with uncontrolled asthma despite LABA/ICS therapy and at least one exacerbation in the prior year. Together over 2500 patients were randomized to LABA/ICS versus triple inhaler therapy. The differences between the two studies being the dose of inhaled beclamethasone (100 mcg BID in TRIMARIN vs. 200 mcg BID in TRIGGER) and a third arm in TRIGGER treated with LABA/ICS plus one dose daily of ipratropium. As in the COPD trials, the overall benefits were small. The pre dose improvement in FEV-1 ranged from 57 to 73 ml compared to LABA/ICS treatment. Triple therapy was associated with an absolute 4% reduction in severe exacerbations yearly, and there was a 7-week increase in time to first exacerbation. Asthma symptom control did not differ in the low dose ICS study and only to a small degree in the high dose ICS study. With the availability of a generic Advair (Wixela) whose cost should drop over the next year, the difference in cost between Wixela and the more expensive triple inhalers triple inhaler therapy will likely be in the range of $4,000 yearly. Triple inhaler therapy in asthma will likely be cost effective for patients who continue to have frequent exacerbations on LABA/ICS therapy or those who might be controlled on triple inhaler therapy in lieu of the much more expensive biologic therapies.

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Perioperative management of patients with atrial fibrillation on direct oral anticoagulant (DOAC) therapy

Every year, one in six patients with atrial fibrillation (AF) will require perioperative management. Optimal anticoagulant management of these patients is uncertain. There are no data that these patients benefit from heparin bridging but the timing of perioperative dose interruption has not been well studied. The PAUSE study[7] looked at over 3,000 patients on apixaban, dabigatran, or rivaroxaban who were scheduled for elective surgeries. The following three variables were used to create a dosing algorithm:

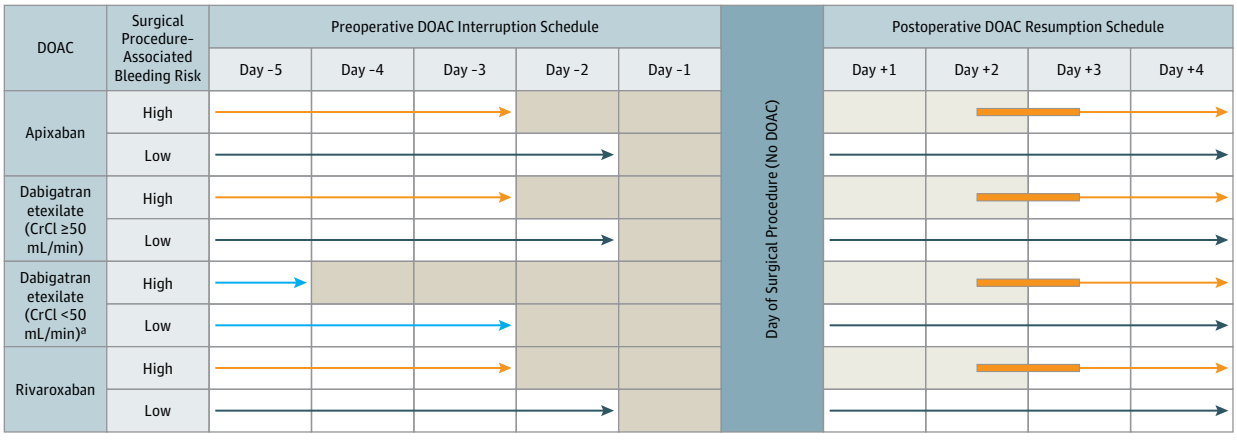
1. The specific DOAC used
2. High versus low bleeding risk of the procedure
3. The creatinine clearance level for dabigatran

The algorithm was designed such that over 90% of patients would have an undetectable or minimal residual DOAC level at the time of the surgery. The endpoints were the 30-day rates of major bleeding or arterial thromboembolism. Using the protocol as outlined in the below table in the patients who adhered to the protocol, the following results were obtained.

Outcomes	DOAC Cohort		
	Apixaban (Eliquis)	Dabigatran (Pradaxa)	Rivaroxaban (Xarelto)
Major Bleeding Rate	1.2%	1.0%	1.69%
Arterial Thromboembolism Rate	0.19%	0.50%	0.42%

Among the 832 patients with high bleeding risk procedures who had anticoagulation levels measured, 98.8% had undetectable or minimal residual DOAC levels. These results met the pre-specified goals of a less than 2% risk of major bleeding and a less than 1.5% risk of thromboembolism with one exception. Although the major bleeding rate with rivaroxaban was 1.69%, the confidence interval was 0-2.53% and therefore overlapped with the upper end of the goal. With respect to other data looking at perioperative management of DOAC therapy, a single study evaluating only dabigatran was published but the algorithm is more complex and the outcomes similar.[8] Interestingly, with respect to the bleeding risks with rivaroxaban, this was reviewed in the May/June 2019 Forum. **Of three large observational studies looking at the bleeding rates with apixaban compared to rivaroxaban, all three showed an approximate 50% lower bleeding risk with apixaban. This is of increased significance as apixaban will be the first generic DOAC and should be available in 2020.**

Dosage interruption schedule for the PAUSE study.[7]



No DOAC was taken on certain days (shaded) and on the day of the elective surgery or procedure. The light blue arrows refer to an exception to the basic management, a subgroup of patients taking dabigatran with a creatinine clearance (CrCl) less than 50 ng/mL. The orange arrows refer to patients having a high-bleed-risk surgical procedure. Dark blue arrows refer to patients having a low-bleed-risk surgical procedure. The thickened orange part of arrows refer to flexibility in the timing of DOAC resumption after a procedure.

[a] Cancer diagnosed within 3 months or has been treated within 6 months or metastatic.

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New guideline for the treatment of community-acquired pneumonia

Community-acquired pneumonia (CAP) is one of the leading causes of morbidity and mortality in adults. The incidence increases with age with up to 164 cases per 10,000,over age 79. Roughly one-third of patients hospitalized with pneumonia will die within one year.[9,10]

The American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) recently updated the guidelines covering treatment of CAP.[11] This review will summarize the key recommendations for treatment of adults without known immune deficiencies in an ambulatory setting. This will not address infectious pathogens associated with travel or with HIV infection, chemotherapy, or organ transplantation.

The most common causative agents of CAP include; *Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Staphylococcus aureus, Legionella species, Chlamydia pneumoniae, and Moraxella catarrhalis.*

Often CAP can be diagnosed clinically without a chest x-ray in the ambulatory setting. Sputum cultures and blood cultures are no longer recommended as part of routine outpatient care (see Table 1). Testing for Legionella antigen is reserved for severe CAP or in cases where it would aid in understanding an outbreak epidemiologically and diagnostic use of pneumococcal antigen is not recommended. Procalcitonin should not be relied on to indicate the need for antibiotics, and it is not recommended in the diagnostic workup of CAP. Increasingly viral infections are recognized as causative agents. Influenza testing using a rapid influenza molecular assay (i.e., nucleic acid amplification) is recommended when influenza is present in the community.

Table 1: Recommendations for test / interventions[12]

Test / intervention	Site of care / severity	
	Ambulatory setting	Inpatient setting
Gram Stain and sputum culture	NR	SC
Blood culture	NR	SC
Legionella antigen	SC	SC
Pneumococcal antigen	NR	NR
Procalcitonin	NR	NR
Corticosteroids	NR	NR

NR= Not recommended
SC= Recommended only in special circumstances

Treatment options for CAP are listed in Table 2. Macrolides should not be used as monotherapy unless local pneumococcal resistance is low. In the United States *S. pneumonia* resistance in excess of 30% has been documented.[13] Two important risk factors for CAP caused by MRSA or Pseudomonas species include prior identification of those pathogens in the respiratory tract or recent hospitalization with antibiotic exposure. These risk factors may prompt broader coverage and often hospital admission.

Table 2: Antibiotic Regimens for Community Acquired Pneumonia[14]

Modifying condition	Standard Regimen
No comorbidities or risk for MRSA or Pseudomonas aeruginosa (no recent hospitalizations or isolates from respiratory tract of either of these pathogens)	Amoxicillin or Doxycycline or Macrolide (if local resistance is <25%)+
With comorbidities (chronic heart, lung liver or renal disease; diabetes; alcoholism; malignancy or asplenia)	Amoxicillin/clavulanate or cephalosporin and macrolide or doxycycline## Or Monotherapy with a respiratory fluoroquinolone*

+ Amoxacillin 1 gram three times daily, doxycycline 100 mg twice daily, azithromycin 500 mg day 1 then 250 mg daily, clarithromycin 500 mg twice daily or extend release 1000 mg daily.
##Amoxicillin/clavulanate 500 mg/125 mg three times daily, amoxicillin/clavulanate 875 mg/125 mg twice daily, 2,000 mg/125 mg twice daily, cefpodoxime 200 mg twice daily, or cefuroxime 500 mg twice daily; AND azithromycin 500 mg on first day then 250 mg daily, clarithromycin 500 mg twice daily, clarithromycin ER 1,000 mg daily, or doxycycline 100 mg twice daily.
*Levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily.

Positive results from influenza testing should be treated. Antiviral treatment is most effective when initiated within 48 hours of symptom onset. However, some small clinical benefit is likely to occur when antivirals are initiated within 5 days. As many as 30% of influenza infections can be accompanied by bacterial infections. The most common bacteria accompanying viral infections are *S. aureus, S. pneumoniae, H.influenzae,* and group A *Streptococcus*. The same antibiotic regimens suggested in Table 2 can be used to cover suspected co-infection.

The duration of antibiotic coverage for ambulatory patients treated for CAP should be guided by clinical recovery and stability. Multiple trials have demonstrated antibiotic courses of five to seven days to be sufficient.[15] Particularly when treating with fluoroquinolones, 5-day treatment courses are preferred due to the potential for peripheral and central nervous system toxicity, tendinopathy, and aortopathy with use of this drug class. These complications occur with increased frequency in the elderly.

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Kenneth Roy Cohen, MD, FACP | *Chief Medical Officer*

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He has successfully developed and reported numerous clinical quality studies in primary care, including tobacco cessation, osteoporosis, asthma, diabetes, hypertension, and ischemic vascular disease. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He has served as Chief Medical Officer since 1995. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA | *Senior Medical Director*

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the University of Virginia where he played Division 1 soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the University of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the University of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD | *Senior Clinical Practice Performance Consultant*

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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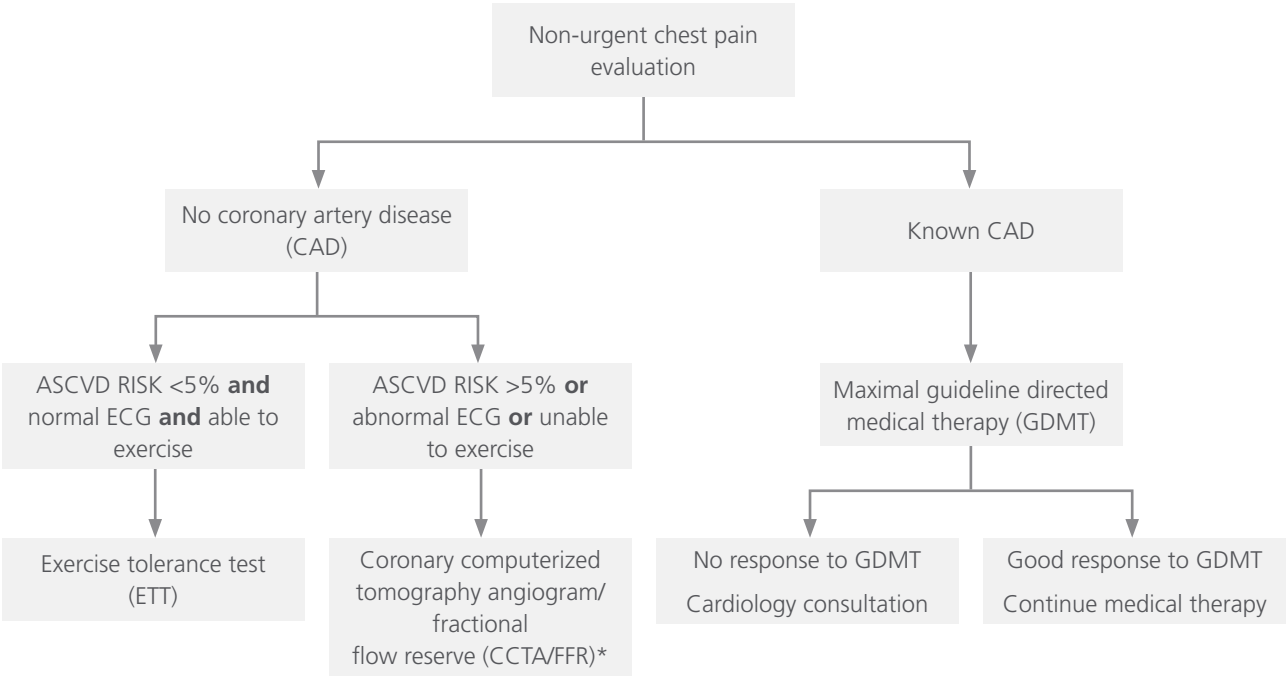
Below is the algorithm currently being deployed in the CCTA/FFR pilot at New West Physicians. We hope to scale this across OptumCare and groups wishing to move forward with CCTA/FFR can use this algorithm.

Of note, Great Britain's National Health Service has removed the option of nuclear stress testing and replaced it with CCTA as the initial test in patients without a prior stent or bypass surgery.[16,17,18]

Non-urgent chest pain evaluation — New West Physicians pilot



*Consider a stress ECHO or nuclear stress test for patients with renal insufficiency, contrast allergy or inability to tolerate beta-blockers.

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Target audience	This activity is designed to meet the educational needs of physicians, PAs, nurses, nurse practitioners and other HCPs who have an interest in EBM.
Learning objectives	At the end of this educational activity, participants should be able to: • Utilize the five-step, "PLACE" process in order to better communicate with individuals and enhance the shared-decision making process. • Review pharmaceutical recommendations for dual antiplatelet therapy following a percutaneous coronary intervention (PCI) and management of acute gout. • Apply a shared-decision making process that includes the low benefit/harm calculus when considering mammography, especially for women ≥75 years. • Assess non-invasive testing, including Wells rule and D-dimer testing, when evaluating individuals for pulmonary embolus.

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Improving the clinical encounter by fostering presence and connection with patients

This article differs from prior Forum articles which have been focused on optimizing the quality and efficiency of our care through the use of evidence-based medicine. However, there is a burgeoning literature on the value of connection and compassion in improving patient outcomes and clinician wellbeing. A JAMA "Special Communication"[1] summarized this literature and presented it as a five-step process. The article was comprehensive in scope and therefore this review will be a summary of the article and its attached references to all of the below-mentioned studies.

Step 1 – Prepare with intention.

There are two components to this process.

First, we intuitively understand that the quality of our visit is improved when we enter an exam room armed with a quick review of our patient's chart. A brief glance at the problem list, medication list, and when important, the most recent labs and the last note's assessment/plan will generally suffice for the majority of patient interactions. This process can be done in about one minute and improves the efficiency of the visit. Thus, it may often be time-saving while simultaneously improving the clinical outcome and the patient's perception of the value of the visit. This can be supplemented by any new significant information gleaned by our medical assistants following their rooming of the patient. Additionally, many of us document important social context (family, sports, hobbies and interests, etc.) within the EHR and, particularly in the setting of the comprehensive exam, reviewing this information just before the visit can foster the social connection necessary to maximize the visit experience for both patient and clinician.

The second component involves taking a moment to set the intention for the visit. It is easy to overlook this step during a hectic clinic session but it serves an important function for both the patient and the clinician. The stress level of a clinic session often escalates as the competing pressures of time and work volume build up. A momentary pause prior to entering the exam room can help deescalate this pressure in real time. Two practices that have been shown to be beneficial are setting the visit intention during hand washing and/or pausing for three deep breaths prior to entering the exam room. These techniques fall into the realm of mindfulness-based stress reduction (MBSR) and a recent review of 81 studies has shown that they improve clinician anxiety, depression and stress. Our patients are acutely aware of the energy we bring with us into the exam room. These

techniques require no training, take very little time, and help to create a holding environment for the visit that is palpable to patients.

Step 2 – Listen intently and completely.

This also has two components.

The first is known to all of us — avoiding interruptions. This has been well studied and when uninterrupted, patients complete their opening monologs more quickly. Nonetheless, studies have also shown that the average time until a physician interrupts a patient is 11 seconds. Uninterrupted patients provide more medical information, have reduced anxiety, and greater satisfaction with the encounter. One study had the MA hand the provider a reminder note not to interrupt the patient just before entering the room, and this improved provider listening skills.

The second component of this is more subtle but equally important. It is listening with one's whole body. This involves receptive body language in which the provider uses nonverbal behaviors that facilitate communication. The most important of these is sitting down. Data shows that this conveys to patients that the provider is not rushed. It can also increase the perception of visit length and attentiveness of the provider. In addition, the patient and provider are at the same height removing much of the hierarchy that can dampen effective patient/physician communication. Another component of this is maintaining an open body position and orienting oneself towards the patient. Careful positioning of the screen and keyboard so that the patient may see the screen has shown to enhance the quality of the visit.

Step 3 – Agree on what matters most.

This begins with an open-ended question asking the patient what brings them to the clinic for the visit. Understanding this from the patient's perspective is at the core of patient-centered care and sets the stage for a meaningful patient/provider interaction. It allows the provider to incorporate the patient's concerns into their narrative, and helps set the

(continued on page 2)

(continued from page 1)

agenda for the visit (unless they tell you they are here to review their list of 10 immediate concerns!). Collaborative agenda-setting helps remove the last minute, "Oh, by the way," and can improve the efficiency of the visit. There are data that show using pre-visit questionnaires done in the waiting room, can also improve the efficiency of the visit and the patient's perceived value of the interaction.

Step 4 – Connect with the patient's story.

This involves forging a connection by asking a patient about their sociocultural background and life circumstances. This step is often unnecessary with established patients, and this ongoing connection may account for the observed phenomenon that providers with long-established patient panels usually fare better in patient satisfaction surveys than newer providers. This shared connection also improves provider satisfaction with the encounter and helps prevent burnout. When medical students are asked to look at the world through the patient's eyes and walk through the world in the patient's shoes, they receive higher satisfaction ratings from standardized patients. There is a highly recommended short video produced by the Cleveland Clinic that brings light to the importance of this aspect of care.

Video:
The Heart of Compassion

This practice also includes acknowledging patients' efforts in self-management in a genuine and positive manner. Provider positivity has been associated with positive patient health outcomes, including improved medication adherence, successful weight loss and tobacco cessation. A study conducted in the United Kingdom showed that this practice of connection with a patient's story, can reduce the number of clinic visits in high-utilizing patients.

Step 5 – Explore emotional cues.

This practice is innate in some individuals and improves with experience in others. It involves being sensitive to a patient's voice, facial expression and body language. It also includes actively eliciting patient emotions through specific questions such as "How are you feeling about this?", as well as reflecting perceptions of a patient's emotions with comments such as, "I can see that this is affecting you deeply." There is a large body of evidence correlating a clinician's ability to perceive a patient's emotions with positive patient outcomes; including shorter, less severe illness, adherence to the treatment regimen and improved patient satisfaction.

For some individuals, these skills are innate or learned from earlier life experiences. For others, it may be somewhat more difficult to master and thus require mentoring, shadowing or patient role-play to effect changes in practice style and patient interaction. There are self-administered learning formats which have shown efficacy. Other patient interactions of demonstrated benefit include humor and vulnerability, connecting with family members in the exam room, taking a moment to establish a social connection prior to addressing the medical issues, and good use of eye contact.

We are all challenged daily by time pressures and work volume; and while all of the above may appear to extend the visit, this has not proven to be the case. Most of us have had the experience of working with both a calm, centered provider and a more frenetic and less focused provider. Most resonate with the improved patient interactions in the former scenario. The challenge is being mindful of the difference and willing to work to implement these straightforward changes in our day-to-day practice.

Call to action: Thinking about your patient interactions and focusing on one or two of the above would be a good place to start.

Dual antiplatelet therapy following a percutaneous coronary intervention (PCI) for an acute coronary syndrome – clopidogrel versus ticagrelor (Brilinta)

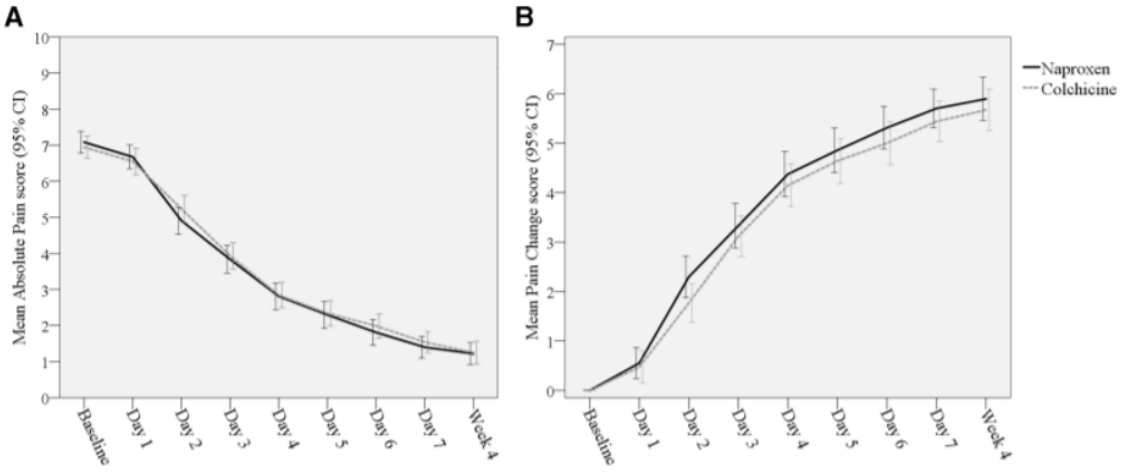
Dual antiplatelet therapy (DAPT) is recommended for up to one year following an acute coronary syndrome (ACS). Since publication of the PLATO trial,[2] some guidelines have recommended ticagrelor over clopidogrel based on a small improvement in outcomes seen in that trial. Ticagrelor showed a 1.1% reduction in myocardial infarction and vascular death, compared to clopidogrel. There was no difference in stent thrombosis. Ticagrelor had a higher risk of major bleeding, and a higher risk of intracranial bleeding, with overall bleeding 1.5% above that seen with clopidogrel.

A recent study in JAMA IM[3] looked at all discharges following PCI for an ACS from one Canadian province over a 4 year period, encompassing over 11,000 patients. The comparison was between clopidogrel which was prescribed in 7100 patients and ticagrelor which was prescribed in 3100 patients. After multivariable adjustment, there were no significant differences in major cardiovascular events, recurrent ACS, or revascularization between the two groups. The major bleeding rate following multivariable adjustment was 1.5 times as high with ticagrelor compared to clopidogrel (7% vs. 4.9%), driven by a gastrointestinal bleeding rate which was twice as high. Dyspnea, a common side effect with ticagrelor use, resulted in a higher rate of ER evaluation (3.1 vs 1.2%).

It is possible that the lower rates of stent thrombosis with the second generation stents may have negated the benefits seen in the PLATO trial, where patients received bare metal or first generation drug eluting stents. However, as would be expected, the increased bleeding risk of ticagrelor over clopidogrel persisted in this trial, as did the higher incidence of dyspnea, which resulted in twice the number of ER evaluations for this complaint. The current yearly cost of ticagrelor is $5500, compared to $600 for clopidogrel.

Management of acute gout – naproxen versus colchicine

Many of the trials evaluating NSAID therapy for acute gout used either indomethacin or diclofenac, two of the most toxic NSAID's. Whereas high dose colchicine is effective for acute gout, it is poorly tolerated due to diarrhea. Low dose colchicine is better tolerated but not well studied. Naproxen, one of the safest NSAID's has never been directly compared to low dose colchicine in the management of acute gout. A randomized pragmatic trial enrolling 400 patients from primary care practices across England compared the two drugs.[4] Patients were randomized to colchicine 0.5 mg three times daily for 4 days or naproxen, 750 mg initial dose followed by 250 mg three times daily for up to one week. As seen below, the magnitude of pain relief was identical for both treatment arms, however the temporal relief curves favored naproxen for slightly earlier pain relief. In each treatment arm, 67% of patients had complete pain resolution at 7 days and 75% of patients had complete pain relief at 4 weeks. In the colchicine arm there was a 5% higher recurrence rate and a 6% higher rate of return visits to the PCP. Additionally, in the colchicine group, 20% more patients required additional analgesia, split equally between acetaminophen and codeine. Even with low dose colchicine, 46% of patients had diarrhea. Overall, in the absence of a contraindication to NSAID therapy, naproxen should be preferred over colchicine for acute gout based on a moderate benefit beyond that conferred by colchicine with a better safety profile. A prior study[5] compared prednisone 35 mg daily for 5 days to naproxen 500 mg twice daily for 5 days and showed equivalence. Initial therapy for acute gout should therefore be either prednisone or naproxen, with colchicine considered a second tier therapy.



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Should women continue screening mammography beyond 75 years of age?

Clinical trials have demonstrated that screening mammography reduces mortality from breast cancer among women who begin screening between 50–69 years of age and continue for 10 years or more.[6] Unfortunately, few women over 70 years of age were included in these trials. An estimated 52% of women ≥75 years have had mammography within the past two years,[7] yet it is not known whether screening mammography in older women effectively reduces breast cancer mortality.

Since a randomized trial of screening mammography is not feasible, investigators conducted a population-based cohort study to estimate the effect of breast cancer screening in Medicare beneficiaries aged 70–84 years.[8] Women were included if they met age criteria, had a life expectancy of at least 10 years, had no previous breast cancer diagnosis, and underwent screening mammography. Based on Medicare data from 2000 to 2008, women were categorized as either "stop screening" (no further screening after baseline) or "continue screening," and these cohorts were compared for breast cancer mortality.

Among women aged 70–74 years, the estimated 8-year risk of breast cancer death was 2.7 (CI, 1.8-3.7) deaths per 1,000 women in the "continue screening" cohort and 3.7 (CI, 2.7-5) deaths per 1,000 women in the "stop screening" cohort, with an estimated difference of 1 death per 1,000 women, favoring screening. In contrast, no differences in breast cancer mortality were seen between cohorts aged 75–84 years. An estimated 3.8 (CI, 2.7-5.1) cancer deaths per 1,000 were seen in the "continue screening" cohort, and an estimated 3.7 (CI, 3-4.6) deaths per 1,000 were seen in the "stop screening" cohort.

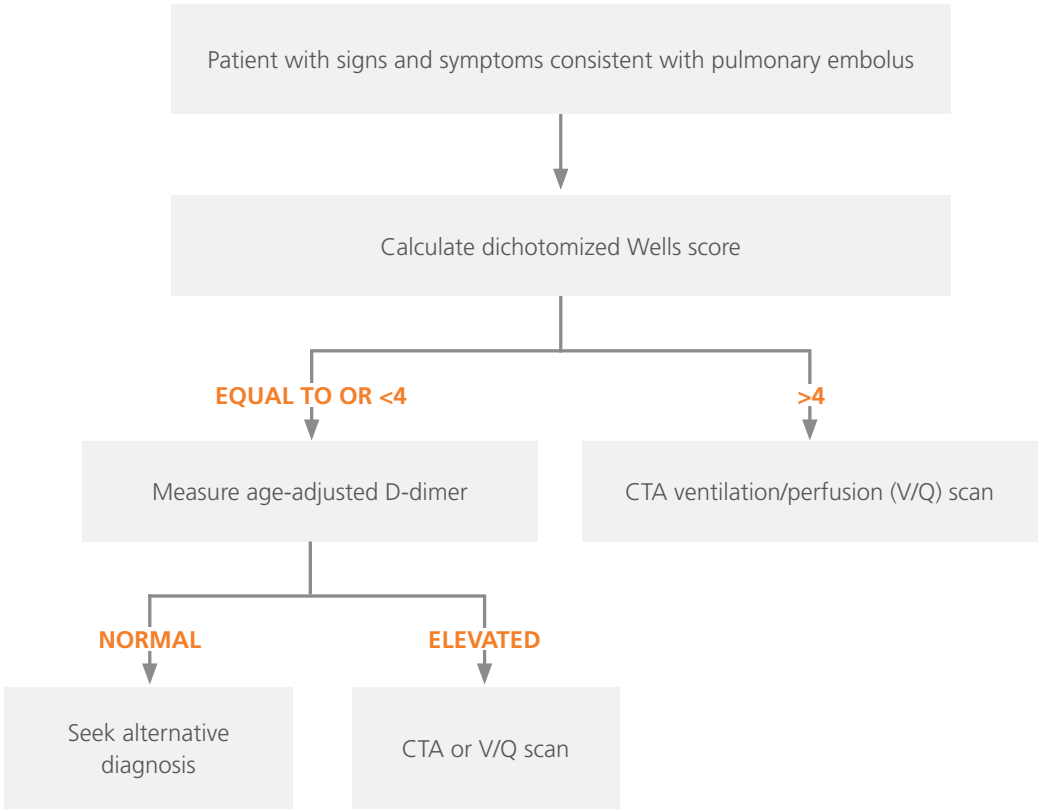
Based on these results, continuing screening mammography past age 75 years does not appear to change cancer-specific mortality over the following 8-year period. The authors reasonably hypothesize that the lack of benefit from screening stems from the multiple competing causes of death that overtake breast cancer mortality as age increases.[9] Since screening mammography is not without potential harms (e.g., discomfort from testing, distress from positive results, overdiagnosis and overtreatment), clinicians should use shared-decision making that includes the low benefit/harm calculus before recommending screening mammography in women ≥75 years of age.

Wells Rule and D-dimer testing to r/o pulmonary embolus

Non-invasive testing is underutilized in the evaluation of suspected pulmonary embolus. Since only about 20% of patients presenting with possible PE actually have the diagnosis, CTA as the first diagnostic step is often inappropriate in patients who are at low risk. 61% of all CTAs ordered for the evaluation of possible PE are done in low-risk patients and therefore could have been avoided. Reliance on CTA often results in unnecessary radiation and dye exposure, ER utilization and downstream procedures and costs related to incidental findings on the CTA. The Wells score was devised to quickly categorize the risk in any given patient based on their presenting symptoms. The "dichotomized," or simplified Wells score reduced the categories to only two: a score of 4 or less, or a score of greater than 4.

To increase the sensitivity of the Wells score, the D-dimer level is added to further triage the low-risk group. The normal level of D-dimer increases with age and there is a new algorithm using age-dependent D-dimer.[10] Imaging can be safely withheld in an additional 5% of patients by applying an age-adjusted D-dimer positivity threshold, defined as a patient's age multiplied by 10 μg L–1 for those aged >50 years. This age adjustment increases the specificity of D-dimer testing in elderly patients. The age adjustment is simple to use and is now fully described in the text that accompanies the report from the commercial laboratories. The combination of a "dichotomized" Wells score of 4 or less and a negative age adjusted D-dimer excludes PE with a high reliability of 99.1%.[11]

The algorithm using the "dichotomized" Wells rule and age-adjusted D-dimer should be used prior to considering a CTA to evaluate for suspected pulmonary embolism.



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Kenneth Roy Cohen, MD, FACP | *Chief Medical Officer*

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He has successfully developed and reported numerous clinical quality studies in primary care, including tobacco cessation, osteoporosis, asthma, diabetes, hypertension, and ischemic vascular disease. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He has served as Chief Medical Officer since 1995. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA | *Senior Medical Director*

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the University of Virginia where he played Division 1 soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the University of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the University of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD | *Senior Clinical Practice Performance Consultant*

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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Activity description	Practicing evidence-based medicine (EBM) is important in today's health care environment because this model of care offers clinicians a way to enrich quality, provide patient satisfaction, reduce costs and improve outcomes. A common implementation of EBM involves the use of clinical practice algorithms during medical decision-making to encourage optimal care. This widely recognized practice is designed to address the persistent problem of clinical practice variation with the help of actionable information at the point of care. These E-newsletters will enable health care professionals (HCPs) to put new EBM into practice.
Target audience	This activity is designed to meet the educational needs of physicians, PAs, nurses, nurse practitioners and other HCPs who have an interest in EBM.
Learning objectives	At the end of this educational activity, participants should be able to: • Explore the educational content surrounding the use of IV iodinated contrast in chronic kidney disorder (CKD) from radiology and nephrology. • Review pharmaceutical recommendations for the management of perioperative gabapentinoids linked with respiratory complications and the effectiveness of behavioral therapy for men with symptoms of overactive bladder. • Apply medical management principles grounded in evidence-based medicine regarding CPAP versus standard of care in mild obstructive sleep apnea and review of echocardiogram in the diagnosis of syncope in patients with normal heart exams and ECG.

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Use of IV-iodinated contrast in CKD — New joint consensus statement from radiology and nephrology[1]

Use of IV contrast is an important area where clinical practice has lagged behind the evidence and has created barriers to optimal patient care. Historical data suggesting that IV contrast caused acute kidney injury (AKI) was confounded as these studies were usually done in ill patients seen in the ER or the hospital with many other potential causes for AKI being present. High quality recent data has dispelled the fear that IV contrast poses a significant risk for AKI but latent bias has persisted and prevented new practice algorithms from being deployed. Earlier this year, the American College of Radiology and the National Kidney Foundation released a joint statement on the use of IV contrast in patients with kidney disease and serves as the basis for this review. All studies referenced below can be found in the joint statement.

To clarify the above situations where acute illness, dehydration, use of nephrotoxic drugs, etc. are the likely cause of AKI around the time of IV contrast administration, this clinical picture has been labelled **contrast associated** AKI (CA-AKI). This is to specifically highlight that in these situations, the contrast is not felt to be contributory to the AKI. On the other hand, the rare circumstances where IV contrast, if felt to be the etiology, are termed **contrast induced** AKI (CI-AKI). The consensus statement asked a series of relevant questions and followed with evidence-based answers. Throughout the statement, CA-AKI is differentiated from CI-AKI since the kidney injury in the former is not felt to be related to IV contrast. The most important questions are as follows:

What Is the risk of CA-AKI and CI-AKI in patients who have stage 1 through 4 CKD?

- The risk of CA-AKI ranges from 5% at an eGFR >60 mL/min up to 30% for an eGFR <30mL/min. This risk is much higher than the risk of CI-AKI because it includes any and all causes of AKI coincident to contrast media administration, even though the contrast is not felt to be etiologic to the AKI.
- The risk of CI-AKI is substantially less than that of CA-AKI. However, the actual risk has not been consistently quantified in patients with severe pre-existing kidney disease. Importantly, several large controlled observational studies have shown no evidence of CI-AKI regardless of CKD stage, whereas others found evidence of CI-AKI only in patients with severely reduced kidney function. In such studies, the risk of CI-AKI has been estimated to be near 0% at eGFR greater than or equal to 45, 0%–2% at eGFR of 30–44, and 0%–17% at eGFR <30 mL/min.

What other major patient-related factors increase the risk of CA-AKI or CI-AKI?

- **CA-AKI.** Multiple patient-related risk factors have been associated with CA-AKI. The primary risk factor is a baseline reduced eGFR, with some studies finding an additive risk of CA-AKI from diabetes mellitus. Additional risk factors include nephrotoxic agents and exposures, hypotension, hypovolemia, albuminuria, and impaired kidney perfusion (e.g., congestive heart failure.) Although multiple myeloma has long been considered a risk factor for CA-AKI, this is not supported by more recent literature.
- **CI-AKI.** Few studies have linked patient-related risk factors with CI-AKI. In studies that did find evidence of CI-AKI, the primary risk factor was a baseline, reduced eGFR. No other factors that increase CI-AKI risk beyond eGFR alone have been confirmed in well-controlled studies of intravenous media.

Are there clinically relevant differences in CA-AKI and CI-AKI risk for patients with reduced kidney function with intravenous iodinated low-osmolality contrast media compared with intravenous iodinated iso-osmolality contrast media?

The simple answer for both categories is that there are no relevant differences in risk related to the osmolality of the contrast agent.

Which patients should undergo IV saline prophylaxis to prevent AKI prior to intravenous iodinated contrast media administration?

Prophylaxis is indicated for patients who have had a recent history AKI or a baseline eGFR less than 30 mL/min. However, the evidence supporting this statement is based on data for the general prevention of CA-AKI rather than CI-AKI specifically. Prophylaxis is not indicated for the general population of patients with stable eGFR greater than or equal to 30 mL/min. This eGFR threshold should not be adjusted solely based on concomitant diabetes mellitus. In an observational study of 1,112 patients with stable eGFR of 30–44 mL/min, diabetes mellitus did not independently increase risk of CI-AKI in patients undergoing contrast-enhanced CT. When prophylaxis is indicated, isotonic volume expansion with normal saline is the preferred method.

Should serum creatinine/eGFR screening be used to identify patients at risk for CI-AKI prior to IV contrast?

Routine screening of renal function is not recommended in the consensus statement. Rather, the consensus statement recommends screening based on eGFR to be used to identify patients who may be at increased risk of CI-AKI. A personal history of kidney disease (e.g., CKD, remote AKI, kidney surgery, kidney ablation, albuminuria) is the most useful clinical issue to suggest the need for kidney function measurement. It seems prudent to verify renal function with eGFR within the prior 30 days of test ordering for these patients. Diabetes

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mellitus is an optional factor for screening, although not supported by current data. Patient age and the presence of hypertension, both treated and untreated, are of uncertain utility as independent triggers for kidney function assessment during radiology point of care. They are sensitive indicators and confer a large false-positive rate to the identification of patients with eGFR <30 mL/min. Patients who do have an eGFR <30 mL/min should prompt consideration by the referring provider and radiologist to discuss the risks and benefits of contrast media administration.

Should intravenous iodinated contrast media be withheld in patients with CKD Stages 4 and 5 not undergoing hemodialysis?

Patients with CKD Stages 4 or 5 (eGFRs of 15–29 mL/min) who are not undergoing maintenance hemodialysis are at potential risk of CI-AKI. The number needed to harm from contrast media administration has been calculated in well-controlled observational studies to be as low as six and as high as infinity (i.e., no harm). If contrast media administration is required for a life-threatening diagnosis, then it should not be withheld based on kidney function.

Should any of the above recommendations be altered in patients receiving certain nephrotoxic medications or undergoing chemotherapy, especially if they have normal kidney function?

In general, the above recommendations should not be altered in patients receiving nephrotoxic medications or undergoing chemotherapy. This is especially true for patients who have normal eGFR or mild-to-moderate reductions in eGFR because they are not considered at risk, regardless of the drug(s) prescribed, and therefore do not need eGFR screening prior to contrast administration. However, monitoring eGFR in patients receiving nephrotoxic medications (e.g., aminoglycosides) or undergoing chemotherapy is important before, during, and after treatment to identify incident nephrotoxicity (CA-AKI).

Is there a role for withholding certain medications prior to intravenous iodinated contrast media administration to decrease the risk of kidney injury?

Metformin does not increase the risk of CA-AKI or CI-AKI. Metformin should only be withheld in patients with eGFR <30 mL/min. This is already an FDA guideline for metformin use and therefore not relevant assuming metformin is used in the appropriate patient population with an eGFR >30 mL/min. Also, in patients with an eGFR>30 mL/min, it is not necessary to withhold nonessential potentially nephrotoxic medications (e.g., nonsteroidal anti-inflammatory drugs, diuretics, aminoglycosides, amphotericin, platins, zoledronate, methotrexate). Whether to withhold renin-angiotensin-aldosterone system inhibitors (RAASi) is controversial. A meta-analysis of 12 studies and 4,493 patients found no difference in risk of CA-AKI between patients receiving and patients not receiving RAASi. On the other hand, given the lack of strong evidence demonstrating that continuing RAASi is beneficial, one option would be to withhold RAASi in patients at risk for CA-AKI for at least 48 hours before elective contrast-enhanced CT to avoid the potential for hypotension and hyperkalemia should CA-AKI develop.

In summary

At many practices nationwide it is still a standard of care to avoid IV contrast in patients with an eGFR between 30–60 mL/min. Additionally, many radiologists still request recent renal function monitoring in the absence of an indication, despite this new consensus statement. It is time to advance our clinical practice to match contemporary evidence-based guidelines. The risk of administering modern intravenous iodinated contrast media in patients with reduced kidney function has been overstated. This is primarily because of the conflation of contrast-associated acute kidney injury (CA-AKI) with contrast-induced acute kidney injury (CI-AKI) in uncontrolled studies. In certain high-risk circumstances, IV saline prophylaxis may be considered in patients with an eGFR of 30–44 mL/min at the discretion of the ordering clinician. The presence of a solitary kidney should not independently influence decision making regarding the risk of CI-AKI. In the setting of a recent AKI or if the eGFR is <30 mL/min, nephrotoxic medications should be withheld by the referring clinician, and volume expansion is recommended. Aside from the above considerations, when medically indicated, historical concerns over the potential renal toxicity of IV contrast should not alter contemporary evidence-based decision making. This is particularly relevant as we begin to replace nuclear stress testing with coronary CTA. A summary of these recommendations is provided in the table below.

Table: Summary of major ACR-NKF consensus statements on use of intravenous iodinated contrast media in patients with kidney disease

1. The terms CA-AKI or CI-AKI are recommended for use in clinical practice due to the large proportion of AKI events correlated with, but not necessarily caused by, contrast media administration.
2. The risk of CI-AKI from intravenous iodinated contrast media is lower than previously thought. Necessary contrast material–enhanced CT without a suitable alternative should not be avoided solely on the basis of CI-AKI risk.
3. CI-AKI risk should be determined primarily by using baseline CKD stage and AKI. Patients at high risk include those with recent AKI and those with eGFR ≤30 mL/min.
4. Kidney function screening is only indicated to identify patients at high risk for CI-AKI. Personal history of kidney disease (CKD, remote AKI, kidney surgery or ablation) is the strongest risk factor indicating the need for kidney function assessment.
5. Prophylaxis with intravenous normal saline is indicated for patients not undergoing dialysis who have eGFR ≤30 mL/min/1.73 m2 or a recent AKI. In individual high-risk circumstances, prophylaxis may be considered in patients with eGFR of 30–44 mL/min at the discretion of the ordering clinician.
6. Prophylaxis is not indicated for patients with stable eGFR greater than or equal to 45 mL/min.
7. The presence of a solitary kidney should not independently influence decision-making regarding the risk of CI-AKI.
8. When feasible, nephrotoxic medications should be withheld by the referring clinician in patients at high risk for CA-AKI.

1. Davenport MS, Perazella MA, Yee J, et al. Use of intravenous iodinated contrast media in patients with kidney disease: Consensus statements from the American College of Radiology and the National Kidney Foundation. *Radiology.* 2020;294(3):660-668. doi:10.1148/radiol.2019192094.

Perioperative gabapentinoids are associated with respiratory complications and do not decrease postoperative opioid use. They are now being used in a wide range of non-evidence-based scenarios.

Gabapentinoids are being used increasingly for osteoarthritis (OA) pain and chronic spinal radicular pain, both without an evidence base of support. A 2017 study[2] of acute and chronic sciatica looked at over 200 patients randomized to pregabalin up to 600 mg daily versus placebo for 8 weeks. Patients were then evaluated at 8 and 52 weeks. No significant between-group differences were observed with respect to the primary outcome of radicular pain reduction or any secondary outcome at either week 8 or week 52. A total of 227 adverse events were reported in the pregabalin group with only half that number in the placebo group. Dizziness was the most common, present in 40% of the pregabalin group. With respect to osteoarthritis, a British study[3] noted that prescriptions for gabapentinoids increased over 15-fold for OA from 2000 to 2015. Gabapentinoids are not even mentioned as a therapeutic option in the 2019 American College of Rheumatology osteoarthritis management guideline. Gabapentiniods are indicated for diabetic and postherpetic neuralgia, neuropathic pain post spinal cord injury and fibromyalgia. Given the paucity of evidence for other diagnoses and the very high incidence of side effects, they are not recommended for off-label use.

Gabapentinoids (gabapentin and pregabalin) are now being increasingly prescribed as part of perioperative pain-control protocols with an aim to reduce post-operative opioid use. However, the evidence to support this strategy is suboptimal with some data suggesting an increased risk of respiratory depression. Ohnuma and colleagues[4] assessed the dose-dependent effects of gabapentinoids on opioid consumption and pulmonary complications following total hip or knee replacement surgery. Using an existing database, the investigators identified 858,306 patients who underwent total hip or knee arthroplasty. Of those patients, 11% received gabapentin and 10.2% received pregabalin. Dosing for gabapentin was stratified into five groups, ranging from none to >1,050 mg per day, and dosing for pregabalin was stratified into four groups, ranging from none to >250 mg per day.

Receipt of gabapentin or pregabalin at any dose was associated with increased odds of respiratory complications. Compared to no exposure to gabapentinoids, gabapentin dosing >1,050 mg per day led to an odds ratio of 1.51 for respiratory complications; pregabalin dosing >250 mg per day led to an odds ratio of 1.81. Additionally, neither gabapentin nor pregabalin exposure reduced opioid consumption or decrease hospital length of stay.

Unless and until evidence of a beneficial effect of the perioperative use of this drug class has been established, they should not routinely be used in perioperative pain management. This is of concern as their use is becoming widespread in the United States. We can now add perioperative pain management to the list of indications for which gabapentinoids are ineffective. Gabapentiniods are only indicated for diabetic and postherpetic neuralgia, neuropathic pain post spinal cord injury and fibromyalgia. Once again, given the paucity of evidence for other diagnoses and the very high incidence of side effects, they are not recommended for off label use.

Behavioral therapy is effective, alone or combined with drug therapy, for men with symptoms of overactive bladder

The drug classes that treat overactive bladder symptoms include α-adrenergic receptor antagonists and antimuscarinic agents. In women, drug therapy combined with behavioral therapy is more effective than drug therapy alone. The effects of combined (drug plus behavioral) therapy for men, however, are not well understood. Burgio and colleagues[5] compared combined therapy versus individual drug or behavioral therapy among men with symptoms of overactive bladder.

In a multi-center clinical trial, 204 men (≥40 years of age) with urinary urgency and ≥9 voids per 24 hours were randomized to six weeks of behavioral therapy alone, drug therapy alone, or combined therapy. Drug therapy included sustained-release tolterodine (4 mg) plus tamsulosin (0.4 mg). After the initial six weeks, all groups were given combined therapy for an additional six weeks. Seven-day bladder diaries were completed before and after each treatment stage. The average number of voids per 24 hours decreased in all three treatment groups. Voiding frequencies were significantly lower in those who received combined therapy compared to those who received drug therapy alone, but not lower than those who received behavioral therapy alone. At 12 weeks, after all groups had received combined therapy, improvements in average voids were seen in all groups compared to baseline.

In elderly patients, potent anticholinergic therapies such as tolterodine have been shown to increase risk of dementia by 65%[6] and are discontinued by most patients within one year due to lack of effect or intolerable side effects[7]. Accordingly, behavioral therapy is optimal in treating men with overactive bladder symptoms. If a stepped approach in treatment is taken, consider starting with behavioral therapy and adding medications later for persistent symptoms. In all patients being treated with drugs for overactive bladder, deprescribing is an important part of management if drug response is suboptimal or side effects outweigh the benefit of treatment. http://www.camurology.org.uk/wp-content/uploads/pelvic-floor-exercises-male-27.pdf

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CPAP versus standard of care in mild OSA

The evidence-based management of obstructive sleep apnea (OSA) was reviewed in the July/August 2019 edition of the Forum. It was then noted that when looking at the populations that served as the asymptomatic controls in multiple OSA studies, the apnea hypopnea index (AHI) increased with age. That meta-analysis in Lancet Respiratory Medicine[8] looked at over 5,200 healthy individuals who served as controls in sleep research studies and reported the sleep parameters derived from overnight polysomnography. At the age range from 18–64 years, the average AHI remained below 5 per hour, which is consistent with our definition of a normal AHI on our sleep study reports. However, in the age range of 65–80 years, the average AHI was 15, and over age 80, the average AHI was 30. There are good data that in patients with significant symptomatic OSA, treatment improves daytime sleepiness and fatigue, snoring and quality of life. Data, however, are lacking in the subset of patients with only mild OSA. Documenting improved outcomes in this group of patients is particularly important given the very high prevalence of sleep-disordered breathing with advancing age.

A recent study in The Lancet Respiratory Medicine[9] looked at the results of continuous positive airway pressure (CPAP) treatment in a population of patients with mild OSA. This was a multicenter, randomized trial that enrolled 233 patients between ages 18–80, with symptomatic but mild OSA (AHI 5–15). All patients had been referred to NHS sleep centers based on typical symptoms of OSA with an average Epworth Sleepiness Scale (ESS) score of 10, and all were studied using the ApneaLink home sleep study device. Patients were then randomized to sleep hygiene counseling versus an auto titrating CPAP unit and treated for three months. The outcomes favored CPAP therapy compared to the standard of care group, with a 10-point improvement in the SF-36 score. Most of the improvements were seen in the mental health components of the score, as opposed to the physical health components. There was also a modest improvement in the ESS score from 10 down to 7, with no ESS score change in the standard of care group. Compliance with CPAP use averaged four hours per night, a number that is consistent across multiple trials of CPAP therapy. At the end of the three months, 81% of the patients randomized to CPAP therapy chose to continue treatment.

This well-done trial confirms the benefit of CPAP treatment in patients with symptomatic, but mild OSA. It is important to note that although the AHI results fell into the mild category, the average ESS score of ten suggests that these patients scored in the "moderately symptomatic" range.

Also discussed in the prior Forum article were the data looking at CV risk and OSA. It is established that the other significant risks associated with OSA include an increased incidence of hypertension, and associated risks of cardiovascular disease and sleep related dysrhythmias. It is important to recognize however, that the data demonstrating a reduction of these risks through treatment of OSA is far more limited. There are data looking at hypertension control, and treatment of OSA has been associated with a small 4 mmHg improvement in systolic BP. However, there are not data showing reductions in cardiovascular risk with OSA treatment. Two important studies have looked at this.

- The first was a randomized trial of four years duration in 725 non-sleepy individuals with an AHI>20 and showed no reduction in the incidence of hypertension or cardiovascular events.[10]
- The second study was more compelling. It looked at a group of 2,700 patients with known CAD or stroke and moderate to severe OSA. The primary composite end point was death from cardiovascular causes, myocardial infarction, stroke or hospitalization for unstable angina, heart failure or transient ischemic attack. Patients were randomized to usual care or CPAP therapy and after 3.7 years, there was no reduction in CV events or improvement in mortality in the CPAP group.[11]

Examining this data in its totality suggests that treatment of OSA should be based upon symptoms and not coexistent disease. The United States Preventive Services Task Force (USPSTF) recently recognized this when it recommended against population screening for OSA in asymptomatic individuals. The important information added by this most recent study is that the subgroup of patients with significant symptoms but an only mildly abnormal AHI, are deserving of a trial of auto titrating CPAP therapy with continued treatment if symptomatic improvement is noted.

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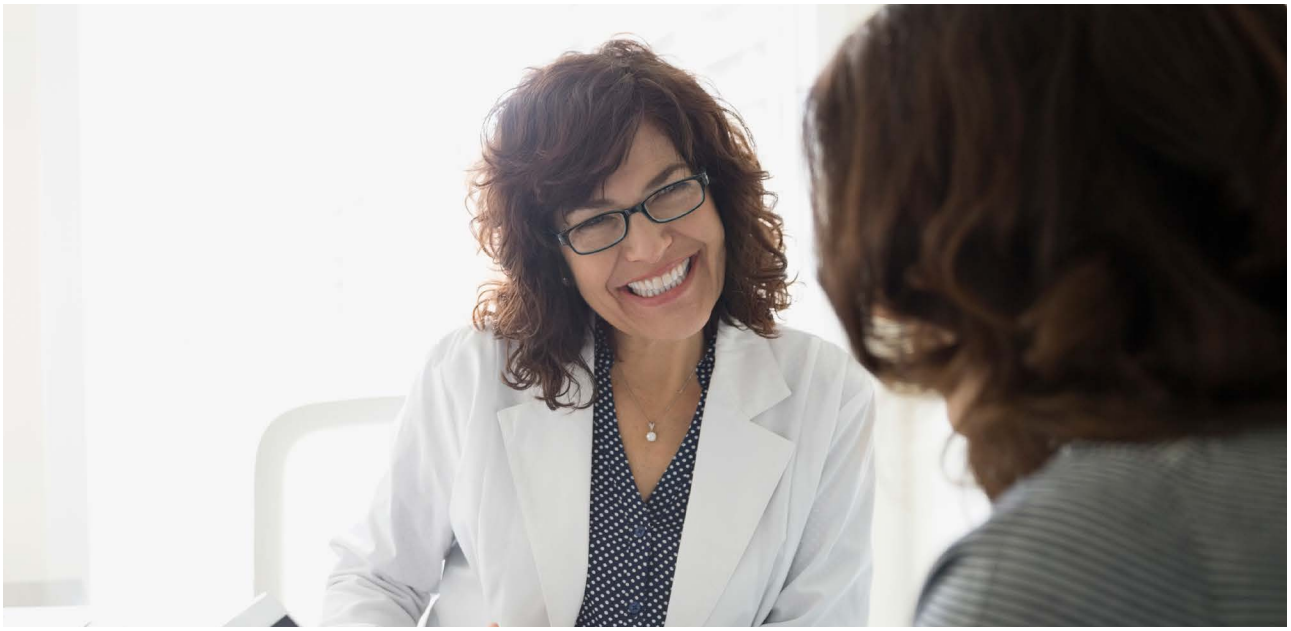

Is the echocardiogram of any value in the diagnosis of syncope in patients with a normal heart exam and ECG?

Syncope is estimated to account for 3% of all emergency room visits and up to 6% of hospital admissions. Lifetime prevalence of syncope is estimated to be 42%. Researchers at Abington Jefferson Hospital designed a retrospective chart review of patients admitted with syncope. They sought to understand the value of a transthoracic echocardiogram (TTE) in the setting of a normal physical exam and normal electrocardiogram (ECG).[12]

Researchers retrospectively reviewed charts of adult patients presenting with hospital admission for syncope over a two-year period. The review included 369 patients, of which 139 met all inclusion criteria.

Abnormal ECG defined	Abnormal TTE defined
• Abnormal axis • Ischemic changes • Conduction blocks including first degree, second degree, third degree blocks • Bi-fascicular blocks • Abnormal QTc • Left bundle branch block	• Ejection fraction <45% • Valvular abnormalities • Ventricular hypertrophy • Outflow tract obstruction • Pericardial effusion • Pulmonary hypertension

Of patients with an abnormal physical examination, 36% had an abnormal echocardiogram. In contrast, less than 1% of patients (1 of 120) with a normal physical exam had an abnormal echocardiogram. With respect to ECG abnormalities, the findings were similar. An abnormal echocardiogram was present in 23% of patients with an abnormal ECG, but in only 2% of patients with a normal ECG. A similar study[13] looked only at the value of the ECG in predicting an abnormal echocardiogram in patients presenting with syncope. Of 468 patients in the study, 210 (45%) had a normal ECG and underwent echocardiography. Excluding three patients with known severe aortic stenosis, only 4% had abnormal echocardiogram findings which were nondiagnostic and not related to the cause of syncope. Finally, a prospective observational study[14] showed that in 155 patients with unexplained syncope, routine echocardiography showed no abnormalities that established the cause of the syncope. Echocardiography was normal or nonrelevant in all patients with a negative cardiac history and a normal ECG.

The diagnostic value of the echocardiogram in patients presenting with syncope has been well studied with consistent findings over time. The use of an echocardiogram in the evaluation of syncope is not indicated in the presence of a normal physical examination of the heart and a normal ECG. It is highly overutilized in this setting.

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Kenneth Roy Cohen, MD, FACP | *Chief Medical Officer*

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He has successfully developed and reported numerous clinical quality studies in primary care, including tobacco cessation, osteoporosis, asthma, diabetes, hypertension, and ischemic vascular disease. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He has served as Chief Medical Officer since 1995. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA | *Senior Medical Director*

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the University of Virginia where he played Division 1 soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the University of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the University of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD | *Senior Clinical Practice Performance Consultant*

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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Activity description	Practicing evidence-based medicine (EBM) is important in today's health care environment because this model of care offers clinicians a way to enrich quality, provide patient satisfaction, reduce costs and improve outcomes. A common implementation of EBM involves the use of clinical practice algorithms during medical decision-making to encourage optimal care. This widely recognized practice is designed to address the persistent problem of clinical practice variation with the help of actionable information at the point of care. These e-newsletters will enable health care professionals (HCPs) to put new EBM into practice.
Target audience	This activity is designed to meet the educational needs of physicians, PAs, nurses, nurse practitioners and other HCPs who have an interest in EBM.
Learning objectives	At the end of this educational activity participants should be able to: • Discuss colorectal cancer screening and colon polyp surveillance in order to promote optimal outcomes. • Review recommendations for the optimal use of triple inhaler therapy for chronic obstructive pulmonary disease (COPD). • Illustrate the positive and negative health aspects of caffeine. • Apply medical management principles grounded in evidence-based medicine regarding treatment options for intermediate-risk prostate cancer (IRPC). • Compare physical therapy versus steroid injection for knee osteoarthritis.

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Please note, by claiming ABIM points, you authorize OptumHealth Education to share your attendance information with the ABIM.

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Colorectal cancer screening and colon polyp surveillance

Colorectal cancer (CRC) screening update

Most providers continue to view colonoscopy as the "gold standard" for CRC screening. This assumes that most, if not all CRCs can be avoided with a screening colonoscopy program. Interestingly, there has never been a prospective randomized trial demonstrating a reduction in CRC mortality with colonoscopy screening. There are multiple observational and cohort studies which have suggested a reduction in both the incidence and mortality of colonoscopic CRC screening. However, it is the magnitude of this reduction that is often not well understood. For example, based on a comprehensive literature review, the U.S. Preventive Services Task Force (USPSTF) estimated that 57% of CRC deaths can be avoided with colonoscopy, compared to 52% with yearly fecal immunochemical test (FIT) or stool DNA testing (Figure 3).[1]

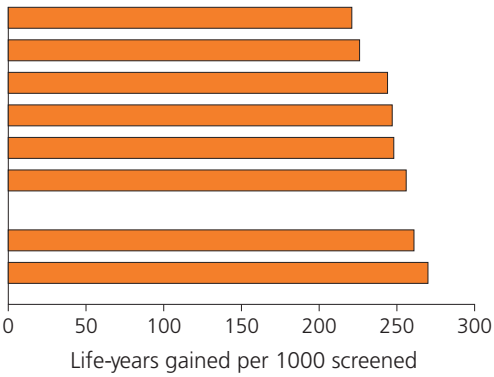
Since these results are similar, patients should make preference-based decisions. New West Physicians recently completed a pilot looking at an unbiased shared decision-making tool to help patients choose their preferred test, while at the same time increasing overall screening rates. Patients were presented with the tool that incorporated the above data, as well as the false positive and negative rates and complication rates of the three screening options. Surprisingly, only 27% of the patients chose colonoscopy. The USPSTF guideline is currently under revision, but the 2016 guideline lists all three of the above as acceptable screening options (along with the others we rarely use such as flexible sigmoidoscopy with FIT, and CT colonography). Based on the results of the pilot at New West, we are launching a phase II pilot which will enroll 10,000 patients to see if the results are consistent with phase I in a much larger patient population. This pilot will also use an updated shared decision-making tool which is a professionally produced interactive video that can be pushed to patients when they are making a decision around CRC screening.

The cost-effectiveness of the screening modality is also important to consider when screening large segments of the population. Stool FIT is clearly the most cost-effective and many countries around the globe screen with FIT and reserve colonoscopy for positive FIT tests. A recent meta-analysis of over 120,000 patients showed that the sensitivity of stool FIT was 91% for the detection of cancer.[2] Stool DNA (Cologuard) has variable reimbursement but the cost is ~$500 in many health plans. At this cost, whether or not it is cost-effective is a function of what the costs are for a colonoscopy in any given market. At a frequency of every three years, the stool DNA cost equivalent over the ten-year span of the colonoscopy interval would be ~$1,650. Colonoscopy reimbursement (anesthesia, GI and facility combined) in most commercial health plans is well above this, and therefore stool DNA would be cost-effective. For our Medicare markets, this will be a market-specific calculation as the cost-effectiveness will vary with the colonoscopy reimbursement. It could vary from cost-effective to cost-neutral to cost-ineffective in different markets. If the cost of the stool DNA test is reduced significantly, it would become cost-effective in all markets.

Figure 3. Benefits, harms, and burden of colorectal screening strategies over a lifetime

A Benefit: Life-years gained per 1000 individuals screened

Screening method and frequency	Model estimates, life-years gained per 1000 screened		
	Middle	Low	High
Flexible sigmoidoscopy every 5 years	221	181	227
FIT-DNA every 3 years	226	215	250
FIT every year[a]	244	231	260
HSgFOBT every year	247	232	261
CT colonography every 5 years[b]	248	226	265
Flexible sigmoidoscopy every 10 years plus FIT every year[a]	256	246	270
FIT-DNA every year	261	246	271
Colonoscopy every 10 years[a]	270	248	275



(continued on page 2)

EDUCATIONAL FORUM

Colon polyp surveillance update

One of the concerns with colonoscopy is the high rate of detection of unimportant polyps, including hyperplastic polyps and small tubular adenomas. Over the past decade, the detection of small tubular adenomas has increased such that they are currently found on over a third of all colonoscopies. These patients are then placed on an accelerated surveillance regimen, typically at five years. There is no evidence base to support a reduction in colorectal cancer (CRC) rates using this approach, and these patients are therefore exposed to the risks and costs of colonoscopies that may not be indicated. Earlier this year, the U.S. Multi-Society Task Force on CRC updated their polyp surveillance guidelines.[3] That document, as well as a recent European Society of GI Endoscopy update,[4] form the basis for the following recommendations.

As noted, there are multiple large cohort studies that have estimated the percent reduction in CRC incidence with screening colonoscopy. The largest looked at over 1.3 million individuals and estimated the reduction in incidence on long-term follow-up at 66%. Because the reductions in risk and mortality extend for a long period of time following a colonoscopy that did not reveal CRC (up to 10–15 years), the important question which needs to be addressed is how often is repeat colonoscopy indicated in patients with one or two small tubular adenomas, as this is the most frequent abnormality found on colonoscopy. These adenomas are referred to as "non-advanced adenomas." Interestingly, in several studies that examined future CRC risk in these patients, it was found to be the same or up to 32% lower than the general population. This reduced risk is likely because these individuals have had a colonoscopic exam that did not reveal a CRC or advanced adenoma, and therefore this may selectively represent a "lower risk population." The updated U.S. guidelines therefore states that:

"New evidence suggests that most adenoma patients (such as those with 1–2 small adenomas) are at lower than average risk for subsequent CRC than the general population after baseline polypectomy."

Nonetheless, despite the above statement of equal to or lower than average risk, the consensus guideline then goes on to state that:

"For patients with 1–2 tubular adenomas <10 mm in size completely removed at a high-quality examination, we recommend repeat colonoscopy in 7–10 years (strong recommendation, moderate quality of evidence). We suggest that physicians may reevaluate patients previously recommended an interval shorter than 7–10 years and reasonably choose to provide an updated recommendation for follow-up between 7 and 10 years after the prior examination that diagnosed 1–2 adenomas, <10 mm."

It thus appears we have finally gotten over the hurdle of every five-year surveillance in these individuals and we should no longer be recommending this for our patients with 1–2 small adenomas. Unfortunately, when considering a recommendation for 10-year rather than seven-year surveillance, the guideline states:

"We considered a recommendation of 10 years alone rather than a range of 7- to 10-year follow-up after removal of 1–2 adenomas, <10 mm in size, given that evidence supports that these patients are at lower than average risk for CRC. The 7- to 10-year range was chosen because of ongoing uncertainty regarding whether the observed lower than average risk for CRC could be reduced further by exposure to surveillance, and also because we cannot rule out the possibility that exposure to surveillance colonoscopy in some studies contributed to the low risk of CRC observed in these patients."

In this author's opinion, taking a group of patients with a lower than average risk of CRC and subjecting them to more intense surveillance in hopes of further reducing risk is highly unlikely to be cost-effective and has the potential to cause harm from unnecessary colonoscopies. These resources would likely be better utilized to increase the screening rate in non-screened individuals. Interestingly, in contrast to the U.S. guideline, the European guideline recommends a return to a 10-year interval for patients who are found to have 1–4 small adenomas, <10 mm in size, or one sessile serrated polyp <10 mm in size, irrespective of histology unless high grade dysplasia is present. The more conservative European guideline is based on a 13-year follow-up study of 16,000 post-polypectomy patients showing that those with three or more nonadvanced adenomas had no increased risk of CRC incidence compared to those without adenomas.[5] Based upon the literature as well as the 7–10 year accepted range in the new U.S. guideline, we should feel comfortable recommending 10-year surveillance in our patients with 1–2 small adenomas.

Another area of confusion for many providers is the appropriate surveillance interval for patients who are found to have advanced adenomas on their baseline colonoscopy. In these individuals the confusion arises as surveillance can range from one year up to five years, and is based on size, number and histologic appearance of the polyp, as well as whether the resection was intact or piecemeal. The surveillance of high-risk adenomas is another area where the evidence lags behind the recommendations. There is a large European trial of polyp surveillance well under way which may help answer many of the outstanding questions. Fortunately, the new U.S. guideline has simplified follow-up of these patients and the link to the follow-up algorithm of high-risk adenomas is included with this article. The follow-up of serrated polyps is unfortunately still complex and is also included in the algorithm.

Algorithm link:
https://journals.lww.com/ajg/_layouts/15/oaks.journals/ImageView.aspx?k=ajg:2020:03000:00019&i=F1&year=2020&issue=03000&article=00019&type=Fulltext

Triple inhaler therapy for COPD — optimal use

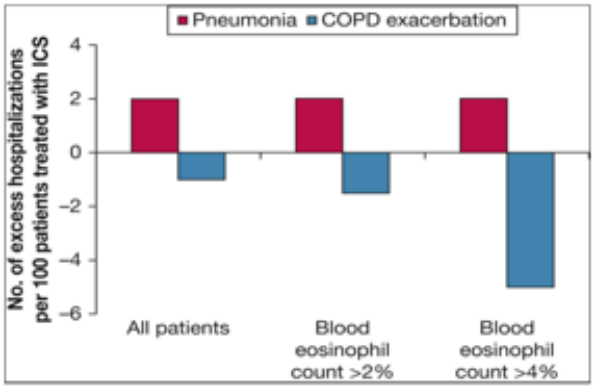
It is estimated that only 30% of COPD patients on triple inhaler therapy meet the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for use. In an observational study, UK investigators looked at dual inhaler therapy (LABA/LAMA) versus triple inhaler therapy (LABA/LAMA/ICS) in a primary care data base.[6] A cohort of 7,000 patients on triple therapy was propensity matched to 2,000 patients on dual therapy. Using a moderate to severe exacerbation definition as one requiring hospitalization or systemic corticosteroid therapy, the yearly rate was approximately 45% in each group. It has been consistently demonstrated in COPD inhaler trials that the use of inhaled corticosteroids increases the rate of bacterial pneumonia. This was once again observed in this trial with 4% of the triple inhaler group requiring hospitalization for bacterial pneumonia, compared to 2% of the dual inhaler group. On the other hand, in the over 2,400 patients with either frequent exacerbations or eosinophilia, triple therapy was associated with significantly fewer exacerbations than dual therapy. The GOLD guidelines recommend the consideration of triple inhaler therapy for the subset of patients with:

- Asthmatic COPD
- Eosinophilia
  - For patients with one exacerbation per year, ICS recommended if the blood eosinophil level is >300 per microliter.
  - For patients with two or more exacerbations per year, ICS is recommended if the blood eosinophil count is >100 per microliter.

When triple inhaler therapy is confined to this subpopulation of COPD patients, the frequency reduction in moderate to severe exacerbations outpaces the increase in bacterial pneumonia for an absolute benefit to the patient, as reflected in the table below. Inappropriate utilization of ICS therapy in patients with COPD is associated with greater harm than benefit, and adherence to the GOLD guidelines is recommended.

ICS use in COPD guided by eosinophil percentage

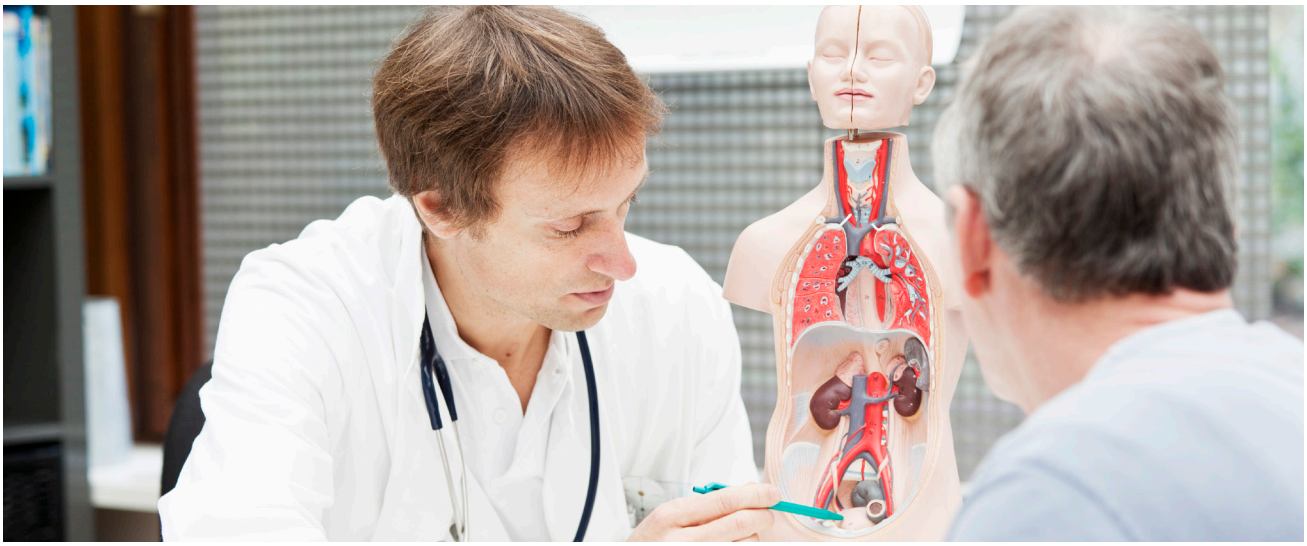
http://dx.doi.org/10.1016/j.chest.2017.05.020



Caffeine and health

A common patient discussion for most of us surrounds the health risks of caffeine. A recent review in the ***New England Journal of Medicine*** reviewed the positive and negative health aspects of caffeine, and merits review as caffeine is arguably the most frequently ingested drug in the world.[7] In terms of positive effects, caffeine has been demonstrated to reduce fatigue, increase alertness and reduce reaction time. These benefits have led to improved performance in distance driving, working an assembly line, etc. Caffeine also increases the effect of commonly used analgesics. With respect to adverse effects, it can reduce sleep efficiency and quality and increase anxiety. All of these effects vary widely from person to person due to large variations in individual metabolism. There is a well-recognized caffeine withdrawal syndrome consisting of headache, fatigue, depressed mood and occasional flu-like symptoms which can last for two to nine days. Caffeine can be toxic and even lethal in very high doses, but this is usually from misuse of supplements, as it would take about 75 cups of coffee to reach a toxic serum level.

Another common area of discussion is the interplay of caffeine and chronic diseases. Most of these observations come from population studies which are subject to the usual confounding. In terms of cardiovascular disease, there is a short-term modest blood pressure increase, but tolerance develops within a week of regular consumption and blood pressure levels then return to normal. The risk of sustained hypertension is not not increased by daily caffeine use. Cholesterol levels are increased by cafestrol in coffee, but only with consumption of unfiltered coffee. Cafestrol levels are highest in boiled and French press coffee, moderate in espresso style drinks, and minimal in filtered coffee. High consumption of unfiltered coffee (six cups of French press coffee daily) can raise LDL cholesterol by as much as 18 mg/dl. This level of cholesterol elevation could contribute to an increased risk of cardiovascular (CV) disease. Studies of consumption of up to six cups daily of filtered coffee, however, have not been associated with an increase in MI or stroke rates even in high-risk populations. In fact, at consumption levels of 3–5 cups daily, a reduced risk of CV events has been observed. There is not an association between coffee consumption and atrial fibrillation. Interestingly, both caffeinated and decaffeinated coffee consumption at moderate levels has been associated with a decreased risk of Type 2 diabetes. There are no associations between caffeine ingestion and an increased incidence of cancers. There is a mild protective effect for multiple cancers including skin, breast, prostate, endometrial and hepatic cancers. In terms of GI effects, caffeine can worsen esophageal reflux but does not have a clear relation to either dyspepsia or peptic ulcer disease. Caffeine has a beneficial effect on reducing gallstones and seems to also have a protective effect against hepatic cirrhosis. Neurologically, although there is no protective effect against Alzheimer's disease, there is a strong protective effect against Parkinson's disease. With respect to pregnancy, there are some data that caffeine in moderate to high doses may reduce fetal growth rates and increase the rate of pregnancy loss. Lastly, there are consistent international data that all-cause mortality is reduced with consumption of both caffeinated and decaffeinated coffee. Because there are some adverse effects to caffeine ingestion, recommendations are to limit caffeine to 400 mg daily, or 200 mg for pregnant and lactating women. Click the link to view a good infographic summary (Figure 2): **https://www.nejm.org/doi/10.1056/NEJMra1816604**



Comparative treatment options for intermediate-risk prostate cancer (IRPC)

Historically, treatment options for prostate cancer include radical prostatectomy (RP) and external beam radiation therapy (EBRT). Classically, recurrence with RP occurred at the surgical margins while recurrence associated with EBRT arose in the central portion, the site of origin of the cancer. Most recently, promising results have been noted with brachytherapy (percutaneous placement of radioactive seeds within the prostate). Brachytherapy seems to offer better cure at both the margins of the tumor and at its point of origin. Initially, brachytherapy was only offered in combination with EBRT.[8] More recently for intermediate-risk prostate cancer the addition of EBRT was shown to add no benefit.[9] Researchers at Kaiser Permanente compared treatment outcomes in 1,503 patients with intermediate-risk prostate cancer over 10 years resulting from RP, EBRT or brachytherapy.[10] Patients were studied retrospectively using a propensity score matching system. Patient characteristics and treatment outcomes are summarized in the table below. As can be seen from the data, in this study EBRT and brachytherapy were equally effective.

Importantly, there were no significant differences in metastases-free or prostate cancer-specific survival between the three treatment options after adjustment for age and comorbidities. Brachytherapy showed improvements in biochemical markers of prostate cancer. This study adds to growing information suggesting that intermediate-risk prostate cancer can effectively be treated with brachytherapy alone. This is important, as many of our patients may prefer brachytherapy and it is not often provided as an option. The advantages are that treatment is usually complete in two visits at a cost that can be as much as 50% lower than EBRT. Androgen-suppression therapy does not provide added benefit when added to brachytherapy, whereas androgen-suppression therapy does add benefit when used along with EBRT. In terms of the toxicity of the treatment, this also favors brachytherapy. The authors of the Kaiser paper also point out that the current higher reimbursement favors intensity-modulated radiation therapy and therefore fewer patients may be directed to brachytherapy.[11] Providers should strongly consider recommending brachytherapy as one option for their patients with intermediate-risk prostate cancer. It is prudent to identify a high-quality provider of brachytherapy in each geography and have that practice be available to our patients.

Parameter	Treatment modality		
	Radical prostatectomy	External beam RT	Brachytherapy
Patient number	819	574	110
Therapy	Surgery	Median dose 75.3 Gray	Iodine-125
Follow-up (years)	10	9.6	9.8
Use of androgen suppression Rx (%)	0.6	59	12.7
Added external RT (%)	0	0	14
No biochemical failure Amer Urologic Assoc (%)	57.1	N/A	N/A
No biochemical failure Phoenix criteria (%)	N/A	57	80.2
Overall survival	85.5	75.5	78.3
Prostate Ca-free survival	96.6	96.2	95.4

Rx= adjunctive therapy; RT= radiation therapy

Physical therapy versus intraarticular steroid injection for treatment of knee osteoarthritis

Both physical therapy and glucocorticoid intraarticular knee injections confer clinical benefit for the treatment of knee osteoarthritis pain and function. A recently published study in the *New England Journal of Medicine* compared the two treatment modalities in a randomized clinical trial.[12] Patients with osteoarthritis in one or both knees were randomly assigned to receive a glucocorticoid injection (triamcinolone acetate, 40 mg, plus lidocaine) or undergo physical therapy. Patients in the glucocorticoid cohort could receive up to three injections during the one-year trial period; those in the physical therapy cohort could undergo up to eight sessions in the first four- to six-week period plus up to three additional sessions at the time of the four-month and nine-month reassessments. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were used as the primary outcome, with higher scores (up to 240) indicating worse pain, function and stiffness. Additional measures were used for secondary outcomes.

Data for at least three study time points were available for 78 patients in each group and analyzed. The mean patient age was 56 years. Patients who received physical therapy had significantly lower WOMAC scores at one year than those who received glucocorticoid injections, 37.0±30.7 versus 55.8±53.8, p=0.008. Ninety percent of the physical therapy patients and 74% of the cortisone injection patients had clinically significant improvement in pain. Secondary outcome analyses demonstrated that patients who received physical therapy had a median score of "quite a bit better" on the global rating of change scale compared to the glucocorticoid injection group median score of "moderately better." Patients in the physical therapy group also performed better on the alternate step test and timed up and go test.

Although improvements were seen among most patients in both cohorts, patients who underwent physical therapy had less pain and less functional disability at one year than patients who received glucocorticoid injections. Discussing treatment options with patients, physical therapy appears to be superior, but glucocorticoid injections could be offered to those patients who do not have an initial response to physical therapy.

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Kenneth Roy Cohen, MD, FACP

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He served as Chief Medical Officer from 1995 - 2020. He now serves as the Executive Director of Clinical Research for UHG R&D and Senior National Medical Director for OptumCare. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the University of Virginia where he played Division 1 soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the University of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the University of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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Target audience	This activity is designed to meet the educational needs of physicians, PAs, nurses, nurse practitioners and other HCPs who have an interest in EBM.
Learning objectives	At the end of this educational activity participants should be able to: • Explore the educational content surrounding preoperative cardiac evaluation and management to promote optimal care outcomes. • Review recommendations for apixaban as the optimal choice in treating nonvalvular atrial fibrillation. • Discuss the risk and benefits of bisphosphonate use to prevent osteoporotic fractures. • Apply medical management principles grounded in evidence-based medicine regarding the benefits of pulmonary rehabilitation for COPD and follow-up monitoring of patients with asymptomatic intracranial stenosis.

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Preoperative cardiac evaluation and management

Optimal perioperative cardiac management continues to evolve. A recent JAMA review highlighted the relevant literature for both preoperative assessment and perioperative management.[1] This review was supplemented with additional new studies where appropriate. Approximately half of the patients undergoing elective surgery have cardiovascular risk factors and about a quarter have a prior history of atherosclerotic cardiovascular disease. Across all noncardiac surgeries on U.S. adults, the overall combined rate of perioperative death, myocardial infarction, or stroke is 3%. The goals of the preoperative assessment and perioperative management are to reduce this risk.

Evaluation of potential coronary artery disease. There are five scenarios where the patient's underlying condition causes the perioperative risk to be very high. Therefore, in these situations, nonemergent surgery should be held pending consultation with cardiology. These include:

- Acute coronary syndrome
- Acutely decompensated heart failure
- Severe aortic stenosis
- Unstable tachyarrhythmia or bradyrhythmia requiring immediate therapy
- Recent placement of a coronary artery stent

Assuming none of these to be present, the preoperative evaluation then moves to looking at the risk of major adverse cardiac events (MACE) as a function of the type of surgery being performed. These can be divided into three categories:

- Low-risk procedures (MACE risk of <1%), including ophthalmologic surgery, cosmetic surgery, arthroscopic surgery and mastectomy
- Intermediate-risk procedures (MACE risk of 1–3%), including orthopedic, GU/GYN, ENT, general abdominal and neurosurgical procedures
- High-risk procedures (>5% MACE risk), including vascular, thoracic and transplant surgeries

Low-risk procedures. Patients undergoing low-risk procedures do not require a preoperative evaluation or an ECG. A recent study of unnecessary ECGs prior to cataract surgery showed that as a result of the pre-op ECG being performed, these patients incurred additional downstream costs of consultation and testing that averaged $1,700 per patient and had no positive impact on outcomes.[2] The excess cost to Medicare was $35 million.

Intermediate- and high-risk procedures. For intermediate- and high-risk procedures, the next question becomes whether there is a role for preoperative ischemia testing. To start, the revised cardiac risk index (RCRI) should be calculated. Using the RCRI, one point is assigned for each of the following: ischemic heart disease, cerebrovascular disease, heart failure, insulin-dependent diabetes, chronic kidney disease (serum creatinine level ≥2.0 mg/dL), and high-risk surgery (intraperitoneal, intrathoracic, or vascular). Those with a score of zero have a very low perioperative risk of MACE and may proceed to surgery. For those with a score above zero, patients who are able to walk up a hill or climb two flights of stairs (4 METS of activity) without cardiopulmonary symptoms do not require ischemia testing and may proceed to surgery. In patients who have poor functional capacity and can't achieve this level of exertion, it is controversial as to whether to perform ischemia testing. The controversy stems from the fact that coronary revascularization prior to surgery in patients with abnormal ischemia tests has not been shown to improve perioperative MACE rates. Additionally, a recent study looked at over 36,000 patients with an RCRI score of one or higher who had a stress test prior to elective knee surgery and compared them to matched controls who did not undergo stress testing. The perioperative MI and cardiac death rates in both groups were statistically identical.[3] Routine coronary revascularization is not recommended before noncardiac surgery to reduce perioperative MACE. Thus, the reason to consider ischemia testing is if an abnormal outcome would change the decision to have the surgery, or materially change the perioperative medical or surgical management of the patient. For this group of patients, ischemia testing may be considered, and cardiology consultation obtained. Coronary computed tomography angiography (CCTA) alone is not recommended as a replacement for ischemia testing but CCTA with fractional flow reserve (FFR) could be considered as an alternative to ischemia testing in this setting.

Preoperative echocardiogram. The evaluation of left ventricular function is not routinely indicated. It should be reserved for suspected moderate to severe valvular disease in patients who have new signs or symptoms or have not had their valvular disease assessed within the past year. Treatment of severe valvular disease should be considered prior to elective surgery.

Preoperative measurement of BNP levels. This is an area of emerging interest as there have been several studies correlating postoperative MACE with preoperative BNP levels. A recent study prospectively looked at pre-op NT–proBNP levels in over 10,000 patients in nine countries.[4] Providers caring for these patients were blinded to the levels. Patients with elevated levels were placed into three groups and had the following rates of the primary endpoint of perioperative vascular death or MI:

- 100–200 pcg/ml: 12%
- 200-1,500 pcg/ml: 20.8%
- >1,500 pcg/ml: 37.5%

(continued on page 3)

(continued from page 2)

A similar meta-analysis of individual patient data from 18 prospective observational studies looked at preoperative BNP levels greater than 92 pg/mL or NT–proBNP levels greater than 300 pg/mL. These elevations were associated with increased risk of death or myocardial infarction at 30 days (21.8% in those with elevated levels versus 4.9% in patients with BNP below these levels).[5] The Canadian guidelines now recommend preoperative BNP measurement in patients in three circumstances: over age 65, having an elevated RCRI, or having a history of CAD. This has not been adopted by the AHA/ACC guidelines. Pending revision of the U.S. guidelines, where might pre-op BNP levels be useful in changing management? On average, patients age 75 or older have a 9.5% perioperative mortality and this is not always communicated prior to surgery. One potential application of preoperative BNP measurement would be in elective surgery for those patients at high CV risk and in the frail or elderly. Identification of BNP levels which would predict a much higher perioperative mortality rate can be discussed with the patient and used to help inform their decisions around their desire for elective surgery.

Beta blocker and ACE/ARB use perioperatively. Although there are theoretical advantageous effects to the perioperative use of these drug classes, randomized controlled trials have failed to demonstrate benefits with their use, and in fact have shown an increase incidence of adverse outcomes including stroke, MI and mortality. This is likely related to the fact that these adverse perioperative outcomes are strongly associated with intraoperative hypotension and all three of these drug classes increase this risk. It is possible that initiation of beta blocker therapy one week or more preoperatively may minimize the risk of intraoperative hypotension and maintain the potential benefits. However, this has yet to be demonstrated in randomized trials.

Perioperative anticoagulation. Patients with nonvalvular atrial fibrillation do not require bridging anticoagulation. This also holds true for most patients on long-term anticoagulation for recurrent deep venous thrombosis or pulmonary embolus. In a trial of 1,884 patients with nonvalvular atrial fibrillation randomly assigned to either perioperative bridging therapy with low-molecular weight heparin or placebo, the incidence of arterial thromboembolism was not different between the groups, but perioperative bleeding was increased in the bridging group.[6]

In a study of 3,640 patients with atrial fibrillation taking a direct oral anticoagulant, stopping use of the oral anticoagulant one to two days prior to a procedure with a low bleeding risk (e.g., eye surgeries or dental procedures) and two to four days before a procedure with a high bleeding risk (e.g., orthopedic surgeries or vascular surgeries) without perioperative bridging therapy was associated with low rates of arterial thromboembolism (0.33%).[7] Patients with mechanical mitral and certain mechanical aortic valves do require bridging anticoagulation with heparin. Lastly, unless the risk of coronary ischemia is significant, routine use of aspirin perioperatively is also not recommended due to an increase in bleeding risk without an improvement in MACE.

Patients with prior coronary stenting procedures. We are commonly faced with a decision around the timing of elective surgery post coronary stent. Individuals requiring surgery within one year after PCI are at increased risk of perioperative events compared with those without coronary stents (8.9% vs. 1.5%).[8] Specific factors increasing the event rates include time from stent placement, the type of stent, the specific thrombotic risk of the surgery and the timing of discontinuation of antiplatelet therapy. Due to the complexity of this decision, the timing of surgery should be determined in consultation with cardiology. Guidelines suggest that elective surgery be delayed at least 30 days post bare metal stent placement and one-year post drug eluting stent (DES) placement. However, new data suggest that elective surgery may be safe three to six months post DES placement.

In summary, the goal of a preoperative evaluation is not to "clear" the patient for surgery. Rather it is to use an evidence-based approach to quantitate the specific risks to the patient based upon their medical conditions and the type of surgery that is planned. These risks should then be communicated to the patient in a shared decision-making approach. This approach should outline any preoperative testing that is indicated, as well as how this testing could impact perioperative management in order to reduce the perioperative risks. Please reference the Preoperative CV Risk Evaluation algorithm which summarizes the above approach on the next page.

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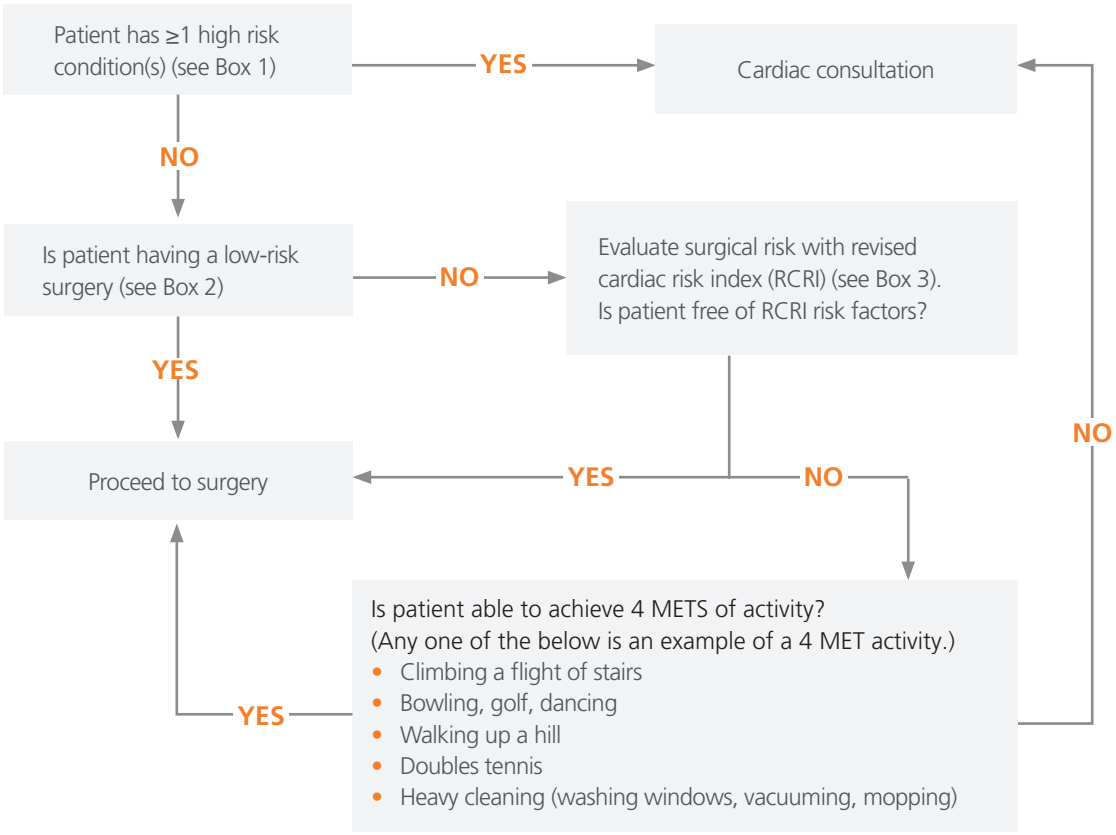
Preoperative cardiac surgical risk assessment: non-cardiac surgery



Box 1: Examples of high-risk surgical conditions

- Cardiac implantable device
- Congenital heart disease
- Decompensated heart failure
- High-grade arrhythmias
- Moderate or greater valvularstenosis or regurgitation (particularly aortic)
- Moderate or severe pulmonary hypertension
- Unstable angina or MI within 60 days

Box 2: Examples of low-risk surgical procedures

- Arthroscopic procedures
- Dermatology procedure
- Ophthalmologic surgery
- Partial mastectomy
- Simple mastectomy (complete breast)

Box 3: Revised cardiac risk index

- High-risk site (any vascular, intraperitoneal, or intrathoracic site)
- History of ischemic heart disease
- Previous myocardial infarction or a positive exercise test
- Current complaint of chest pain considered to be secondary to myocardial ischemia
- Use of nitrate therapy
- ECG with pathological Q waves
- Coronary revascularization procedures (DO NOT COUNT unless at least one other criterion for ischemic heart disease is present)
- History of heart failure
- History of cerebrovascular disease
- Diabetes requiring insulin therapy
- Preoperative serum creatinine >2 mg/dl

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Apixaban versus rivaroxaban: Safety and efficacy analysis in patients with nonvalvular atrial fibrillation

Of the four available direct-acting oral anticoagulants (DOAC), apixaban and rivaroxaban are the two most frequently prescribed. Several observational trials dating back to 2012 have suggested that apixaban is more efficacious and has a better safety profile compared to rivaroxaban. Added to this body of evidence is a new study which looked at over 90,000 patients in a single commercial health plan database spanning seven years.[9] Overall, the apixaban group had a slightly higher comorbidity burden. After propensity matching, the stroke and systemic embolism rate was lower in the apixaban group compared with the rivaroxaban group (6.6 events compared with 8.0 events per 1,000 patient years). In the group over 70 years of age, the stroke/systemic embolism rate for apixaban-treated patients was 8.3 compared to 10.5 in those treated with rivaroxaban. At the same time, the major bleeding risk in apixaban-treated patients was 12.9 per 1,000 patient years compared with 21.9 with rivaroxaban. This reduced rate included both lower rates of gastrointestinal and intracranial bleeding.

The potential reason for the improved outcomes with apixaban may be related to its twice- rather than once-daily dosing. Anti-factor Xa activity can be used as a surrogate for the therapeutic effect of these drugs. The twice-daily dosing of apixaban allows for more stable blood levels. There is a lower peak anti-factor Xa activity possibly contributing to the lower relative bleeding risk, as well as a higher trough level possibly accounting for the relative reduction in stroke and systemic embolism. This study now adds to the available evidence suggesting improved outcomes with apixaban compared to rivaroxaban. Pending the results of an ongoing randomized head-to-head trial, apixaban should be considered the preferred agent.

Continued bisphosphonate use warranted: Reduced fracture risk outweighs increase in atypical fractures

Researchers at Kaiser reviewed the records of more than one million women over 50 years of age and followed 196,129 women with bisphosphonate treatment histories from 2007 to 2017.[10] There was a clear increased risk of atypical fracture (atypical fragility fractures in the subtrochanteric region and along the femoral diaphysis) in women on bisphosphonates (see Table 1).

Table 1. Bisphosphonates atypical fracture risk

Exposure to bisphosphonates	Atypical fracture risk (hazard ratio)	95% Confidence interval
Less than 3 months	1.0	NA
3 years to less than 5 years	8.86	2.79–28.2
More than 8 years	43.51	13.7–138.1

This risk has been appreciated and reported in a number of studies. The risk for these atypical fractures is increased in Asians vs. Whites. However — and importantly — the reduction in risk for osteoporotic fractures of the hip and other locations far outweighed the increase in risk of atypical fractures. Even with the increased risk of atypical fractures in Asians, the highest risk subgroup, the benefits of bisphosphonates remain clear (see Table 2).

Table 2. Number of bisphosphonate-associated atypical fractures vs. clinical fractures prevented

Patient group	Bisphosphonate-associated atypical fracture	Hip fractures prevented	Clinical fractures prevented
	Associated with 5 years duration of bisphosphonate treatment (per 10,000 women)		
Asian	38	174	524
White	8	286	859
Hispanic	1	194	576

This study emphasizes the importance of understanding both the risk and benefit of bisphosphonate use to prevent osteoporotic fractures and supports the continued use of bisphosphonates in the treatment of osteoporosis in women. It also very importantly highlights the association of prolonged bisphosphonate use with an increase in the incidence of atypical fractures. The atypical fracture rate increased fivefold in those on bisphosphonate therapy for greater than eight years compared to those on treatment for three to five years. This underscores the appropriateness of a bisphosphonate holiday in most women to minimize the risk of atypical femur fractures while maintaining the therapeutic effect of decreasing fragility fractures.

Shared decision-making tool for anticoagulation

Atrial fibrillation (AF) is associated with increased risk of systemic embolism and stroke. The use of anticoagulation reduces the risk of stroke by about 65% among patients with non-valvular AF. Yet nearly half of patients with AF do not start anticoagulation or do not remain compliant.[11] A major 2014 guideline addressing the management of AF issued a class I recommendation for the use of shared decision-making (SDM) to individualize the benefits and harms of anticoagulant treatment for patients at risk of stroke.[12] Although SDM tools have been developed, rigorous evaluation of the tools is lacking. A recently published study compared several quality and outcome measures between patients with AF who were randomly selected to receive the SDM intervention about anticoagulation and control patients who received standard care (discussions without the SDM tool).[13]

The clinical trial was conducted at several locations including emergency and inpatient hospital departments, primary care clinics and cardiology clinics. All participating clinicians had experience discussing the use of anticoagulation for AF. Eligible patients were diagnosed with nonvalvular AF, were at high risk of a thromboembolic event based on CHA_2DS_2-VASc score and were literate. Survey items about the discussions were completed by patients and clinicians. Patient involvement in decision-making was assessed by video recording of the encounter and use of the Observing Patient Involvement in Decision-Making (OPTION) scale.

Among 942 patients recruited, 463 were randomized to the SDM intervention and 459 to standard care. Patient reports were similar between groups for survey items about clinicians showing respect, listening carefully and using terms that were easy to understand. Patients recommended the communication approach with and without SDM similarly (90.9% versus 89.9%). Decisional conflict, assessed from the Decisional Conflict Scale, was similarly low in both groups; patient–clinician concordance about treatment selection was similarly high in both groups. Clinicians were more satisfied with the encounters where SDM was used and more likely to recommend the SDM approach to others. Patients were more involved in decision-making when SDM was used. Yet, the encounter durations with and without SDM did not differ, with mean 32±16 minutes versus 31±17 minutes.

Thus, an SDM tool about anticoagulation may improve clinician satisfaction, better engage patients in the decision-making process, and does not necessarily prolong the encounter duration. Some study limitations were present. The nature of the intervention precluded clinician blinding, which may have affected how clinicians interacted with patients and how they rated their own satisfaction with SDM. Selection bias also may be present, including the participation of clinicians based on experience with these discussions and the possibility of selective enrollment of patients by clinicians.

Pulmonary rehabilitation in Medicare beneficiaries decreases mortality

Researchers used Medicare claims data to study 197,376 patients hospitalized for COPD exacerbations in the United States in 2014.[14] Patients who began pulmonary rehabilitation within 90 days of discharge (1.5%) had a 7.3% mortality rate at one year. Patients not undergoing pulmonary rehabilitation or beginning rehabilitation more than 90 days after discharge had a one-year mortality rate of 19.6%. The absolute lower risk of death resulting from initiation of pulmonary rehabilitation within 90 days of hospitalization was 12.3%. Authors did acknowledge that patients receiving rehabilitation had fewer comorbidities, a lower frailty index, were younger and lived nearer to a rehabilitation facility. Authors attempted to account for these differences using a propensity-matched cohort but acknowledged potential unaccounted for confounding factors. Another recent meta-analysis of 13 studies (801 patients) similarly showed the benefits of early pulmonary rehabilitation following hospital discharge (relative mortality risk 0.58).[15]

Remarkably, only 1.5% of patients with COPD hospitalizations in this study participated in pulmonary rehabilitation. In an accompanying editorial, three reasons are suggested for this contradiction: 1) providers failing to encourage or order pulmonary rehabilitation at discharge; 2) failure likely resulting from the lack of financial or quality incentives and/or a lack of awareness of patients and providers of the benefit of pulmonary rehabilitation; and 3) consistently under-resourced pulmonary rehabilitation programs.[16]

With noninvasive ventilation and continuous oxygen therapy in severely hypoxic patients, the only treatments to show a survival benefit in COPD, the benefits of pulmonary rehabilitation post hospital discharge should be welcomed by clinicians and patients. This study should serve as an important notice to clinicians, patients, health plans and payors of the benefits of early pulmonary rehabilitation for patients with COPD following an exacerbation.

Asymptomatic intracranial artery stenoses are common and confer relatively low stroke risk

Although intracranial artery stenosis is a leading cause of stroke, little is known about the prevalence or the prognosis of intracranial stenoses that are found incidentally and are asymptomatic. A recent population-based study addressed these gaps in knowledge.[17] Investigators recruited patients who had a transient ischemic attack (TIA) or minor stroke and underwent vascular imaging by magnetic resonance angiography (MRA), computed tomography angiography (CTA), or transcranial Doppler. Significant stenosis was defined as ≥50% of the vessel luminal diameter. If the intracranial artery stenosis corresponded with the TIA clinical presentation or the parenchymal stroke, it was labeled symptomatic, whereas asymptomatic stenoses were unrelated to any clinical events or parenchymal evidence of stroke. Stenoses of the carotid artery bifurcations were also evaluated. Follow-up was done at 1, 6, 12, 24, 60, and 120 months.

Of the 1,368 patients eligible for the study, 426 intracranial stenoses were identified in 260 patients. Of these, 58 patients (4.2%) had only symptomatic stenoses; 155 (11.3%) had only asymptomatic stenoses; and 47 (3.4%) had both symptomatic and asymptomatic stenoses. The prevalence of asymptomatic stenoses increased with age: 4.8% among patients younger than 70 years and 34.6% among patients 90 years of age and older. Additionally, asymptomatic intracranial stenosis was more common than asymptomatic carotid artery (extracranial) stenosis in this cohort (14.8% versus 7.2%).

Among patients with only asymptomatic intracranial stenoses, 506 patient-years of follow-up led to detection of eight recurrent strokes. However, only three strokes occurred in the stenotic artery distributions, for an annualized stroke rate from asymptomatic intracranial stenoses of 0.6%. The major morbidity with surgery for intracranial stenosis is as high as 5%, or close to tenfold higher than the annual stroke rate with medical management.

In summary, asymptomatic intracranial arterial stenoses are common, especially among older aged patients, and confer relatively low stroke risk. Based on these results, when an intracranial arterial stenosis is found on neuroimaging and is unrelated to the clinical presentation or stroke distribution, the patient can be counseled about the low stroke risk, and the clinician can avoid follow-up imaging to monitor the asymptomatic lesion. The treatment should be guideline-directed medical therapy.

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