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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: <ul style="list-style-type: none"> • 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.

Accreditation statement



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

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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 bradyarrhythmia 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 (intraabdominal, 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)

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.

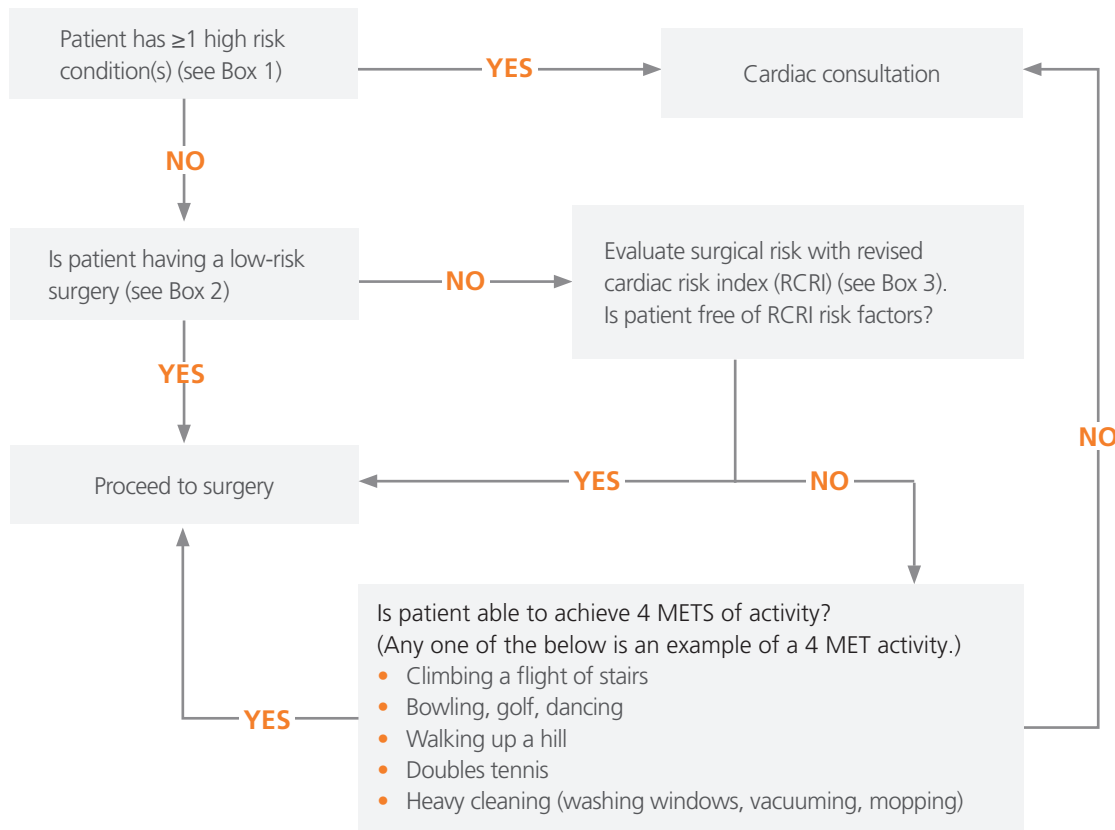
Perioperative anticoagulation. Patients with nonvalvular atrial fibrillation do not require bridging anticoagulation. This also holds true for most patients on long-term anticoagulation for recurrent deep venous thrombosis or pulmonary embolus. In a trial of 1,884 patients with nonvalvular atrial fibrillation 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.

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 valvular stenosis 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 CHA₂DS₂-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 $\geq 50\%$ 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.

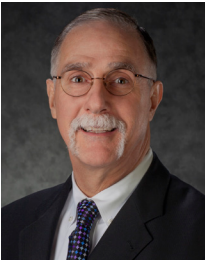
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Kenneth Roy Cohen, MD, FACP

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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