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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 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.

Accreditation statement



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Credit designation statements

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

Nurse practitioners

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

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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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A certificate of attendance will be provided to learners upon completion of activity requirements, enabling participants to register with licensing boards or associations that have not been pre-approved for credits. To apply for credit types not listed above, participants should use the procedure established by the specific organization with which they wish to obtain 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 trial¹ 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 study² 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.

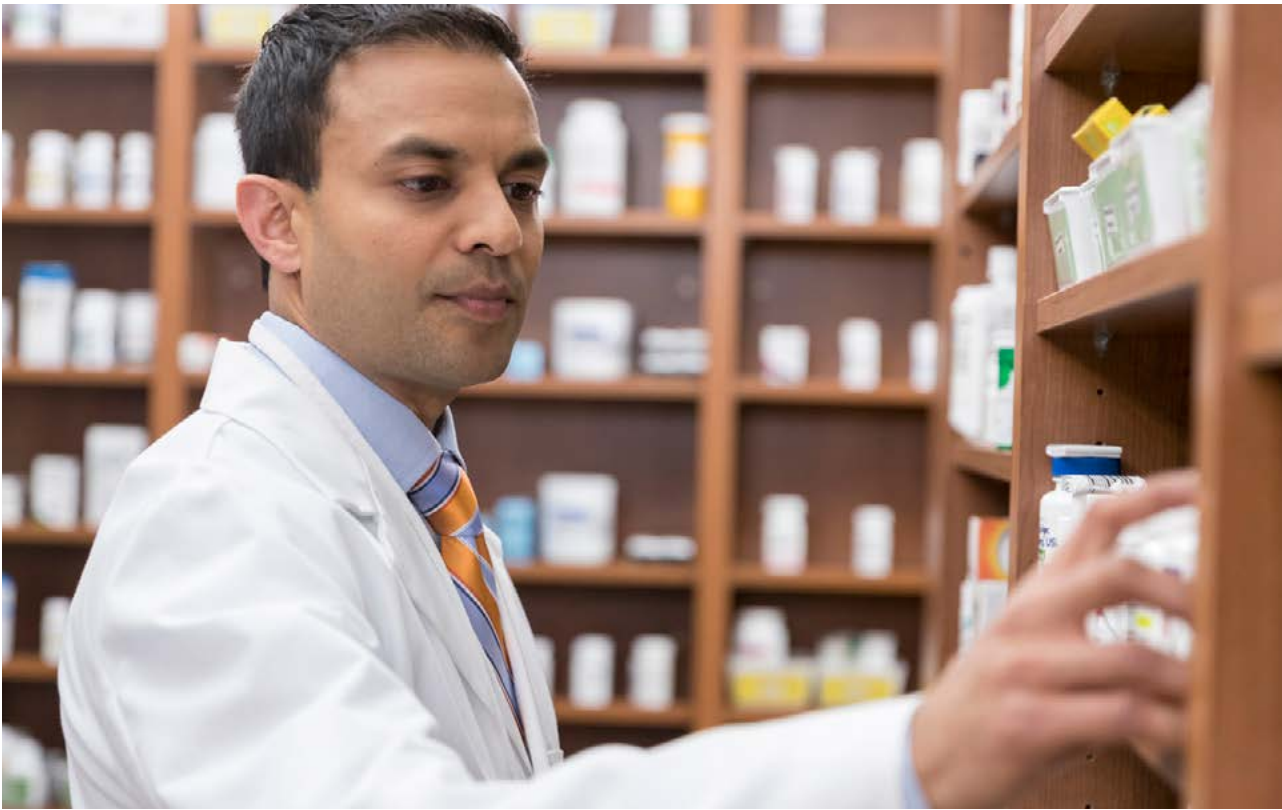
Beginning 27 years ago, four large, high quality randomized trials encompassing close to 10,000 patients have been published.^{4,5} They all asked the question of whether coronary interventions done as a result of routine ischemia testing improve cardiovascular outcomes in stable CAD. The results

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 beclomethasone (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.

6. Virchow, J. C., Kuna, P., Paggiaro, P., Papi, A., Singh, D., Corre, S., . . . Canonica, G. (2019). Single inhaler extrafine triple therapy in uncontrolled asthma (TRIMARAN and TRIGGER): Two double-blind, parallel-group, randomised, controlled phase 3 trials. *The Lancet*, 394(10210), 1737-1749. doi:10.1016/S0140-6736(19)32215-9

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 study⁷ 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:

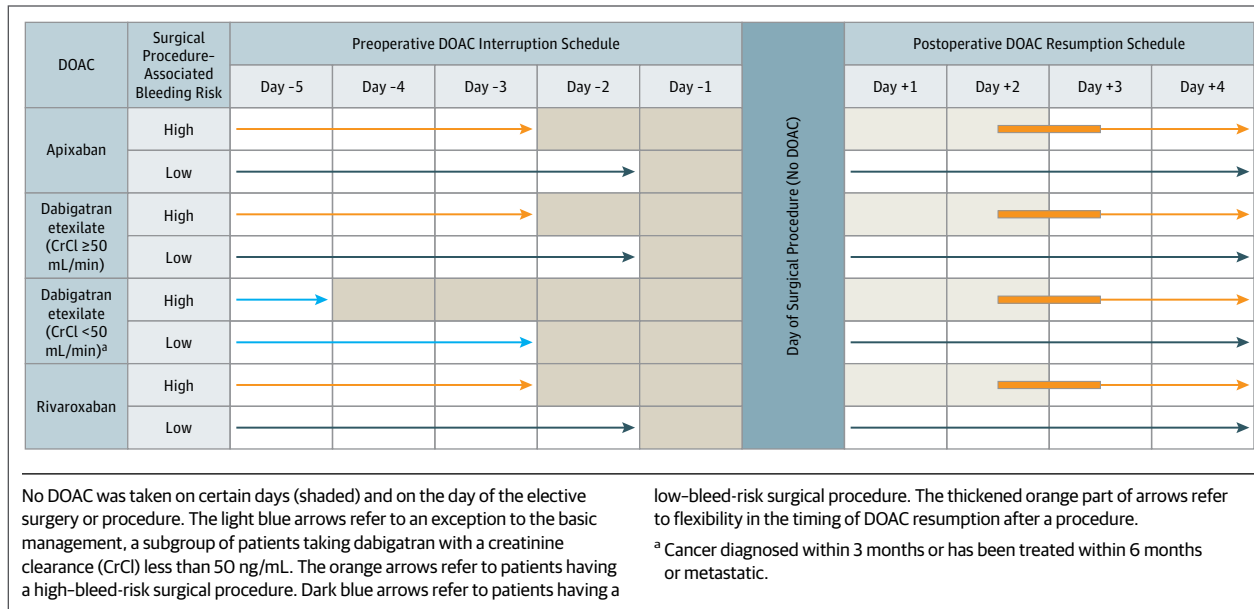
1. The specific DOAC used
2. High versus low bleeding risk of the procedure
3. The creatinine clearance level for dabigatran

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



7. Douketis, J. D., Spyropoulos, A. C., & Duncan, J. (2019). Perioperative management of patients with atrial fibrillation receiving a direct oral anticoagulant. *JAMA*, 179(11), 1469-1478. doi:10.1001/jamainternmed.2019.2431

8. chulman, S., Carrier, M., Lee, A. Y., Shivakumar, S., Blostein, M., Spencer, F. A., . . . Douketis, J. D. (2015). Perioperative management of Dabigatran: A prospective cohort study. *Circulation*, 132(3), 167-173. doi:10.1161/CIRCULATIONAHA.115.015688



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.

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. pneumoniae* 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.

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*

+ Amoxicillin 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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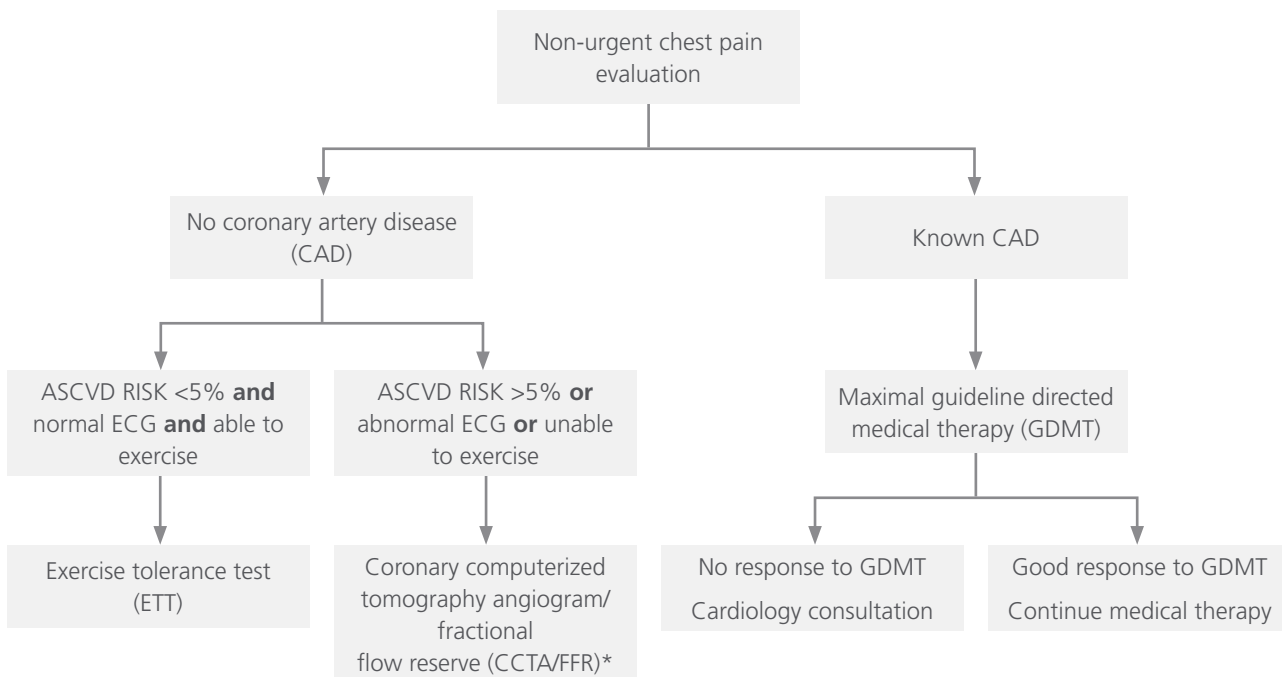
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This information is for informational purposes and should only be used by trained clinicians to aid in improving diagnosis, detection and/or clinically appropriate treatment; this information is not a substitute for clinical decision-making and should not be used to make individualized diagnostic or treatment decisions for specific patients.

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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17. Coronary angioplasty versus medical therapy for angina: The second Randomised Intervention Treatment of Angina (RITA-2) trial. (1997). *The Lancet*, 350(9076), 461-468. doi:10.1016/S0140-6736(97)07298-X

18. Parisi, A. F., Folland, E. D., & Hartigan, P. (1992). A comparison of angioplasty with medical therapy in the treatment of a single-vessel coronary artery disease. Veterans Affairs ACME Investigators. *NEJM*, 326(1), 10-16. doi:10.1056/NEJM199201023260102