

Acute Chest Pain in Adults: Outpatient Evaluation

John R. McConaghy, MD; Malvika Sharma, MD; and Hiten Patel, MD

The Ohio State University Wexner Medical Center, Columbus, Ohio

Approximately 1% of primary care office visits are for chest pain, and 2% to 4% of these patients will have unstable angina or myocardial infarction. Initial evaluation is based on determining whether the patient needs to be referred to a higher level of care to rule out acute coronary syndrome (ACS). A combination of age, sex, and type of chest pain can predict the likelihood of coronary artery disease as the cause of chest pain. The Marburg Heart Score and the INTERCHEST clinical decision rule can also help estimate ACS risk. Twelve-lead electrocardiography is recommended to look for ST segment changes, new-onset left bundle branch block, presence of Q waves, and new T-wave inversions. Patients with suspicion of ACS or changes on electrocardiography should be transported immediately to the emergency department. Those at low or intermediate risk of ACS can undergo exercise stress testing, coronary computed tomography angiography, or cardiac magnetic resonance imaging. In those with low suspicion for ACS, consider other diagnoses such as chest wall pain or costochondritis, gastroesophageal reflux disease, and panic disorder or anxiety states. Other less common, but important, diagnostic considerations include acute pericarditis, pneumonia, heart failure, pulmonary embolism, and acute thoracic aortic dissection. (*Am Fam Physician*. 2020;102(12):721-727. Copyright © 2020 American Academy of Family Physicians.)

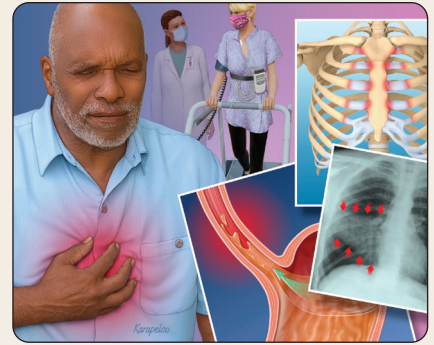


Illustration by John Karapelou

Approximately 1% of all ambulatory visits in primary care settings are for chest pain.¹ Cardiac disease is the leading cause of death in the United States, yet only 2% to 4% of patients presenting to a primary care office with chest pain will have unstable angina or an acute myocardial infarction.²⁻⁴ The most common causes of chest pain in the primary care population are chest wall pain (20% to 50%), reflux esophagitis (10% to 20%), and costochondritis (13%).² Other potential factors include pulmonary etiologies (pneumonia, pulmonary embolism [PE]), psychological etiologies (panic disorder), and nonischemic cardiovascular disorders (congestive heart failure, thoracic aortic dissection).^{2,3,5,6} No definitive diagnosis may be found in as many as 15% of patients.² Differentiating ischemic from nonischemic causes is often challenging because patients with ischemic chest pain may appear well. As such, the initial diagnostic approach should always consider a cardiac etiology for the chest pain unless other causes are apparent.⁷

Initial Evaluation

The first decision point for most physicians is to determine whether the patient needs immediate referral to the emergency department for further testing to determine whether the chest pain is an acute coronary syndrome (ACS) caused by coronary ischemia.⁷ ACS is a clinical diagnosis that includes unstable angina, ST segment elevation myocardial infarction, and non-ST segment elevation myocardial infarction. Definitions of chest pain have evolved over time. Typical chest pain or angina is a deep, poorly localized chest or arm discomfort (pain or pressure) associated with physical exertion or emotional stress and relieved with rest or sublingual nitroglycerin within five minutes.⁸ Unstable angina is new-onset angina, angina at rest, or angina that becomes more frequent, severe, or prolonged.⁹ Acute myocardial infarction is myocardial injury resulting in elevated cardiac biomarkers in the setting of acute ischemia caused by ST segment elevation myocardial infarction or non-ST segment elevation myocardial infarction.¹⁰ The impression of chest pain is often determined by a combination of clinical symptoms at the time of presentation, physical examination, initial electrocardiography (ECG), and risk factors for ACS.¹¹ Patients often do not use the term pain to describe their symptoms but frequently use other terms

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 719.

Author disclosure: No relevant financial affiliations.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
When patients present to the primary care office with chest pain, physicians should consider age, sex, and type of chest pain to predict the likelihood that it is acute coronary syndrome caused by coronary artery disease. ¹⁵	B	Large prospective cohort study
Physicians should consider using a validated clinical decision rule such as the INTERCHEST rule or the Marburg Heart Score to stratify risk in patients with chest pain. ¹⁷⁻²⁰	B	Smaller clinical trials of validated decision rules
Twelve-lead electrocardiography should be performed on all patients in whom cardiac ischemia is suspected. The presence of ST segment changes, new-onset left bundle branch block, presence of Q waves, and new T-wave inversion increases the likelihood of acute coronary syndrome and acute myocardial infarction; these patients should be referred immediately to the emergency department. ^{21,22}	C	Clinical reviews and consensus expert opinion
Patients who have chest pain with a low to intermediate probability of coronary artery disease not requiring immediate referral to the emergency department should be evaluated for coronary artery disease with exercise stress testing, coronary computed tomography angiography, or cardiac magnetic resonance imaging. ²³⁻²⁷	B	Unblinded randomized controlled trials and clinical reviews
Patients with localized musculoskeletal pain that is reproducible by palpation or pain reproducible by palpation of the parasternal costochondral joints likely have chest wall pain or costochondritis. ^{29,30}	C	Clinical reviews and consensus expert opinion
Gastroesophageal reflux disease should be considered in patients with burning retrosternal pain, acid regurgitation, and a sour or bitter taste in the mouth. ^{31,32}	C	Clinical review and observational studies
Panic disorder and anxiety states often cause chest pain and shortness of breath; physicians should consider using a single validated screening question to confirm the diagnosis. ³⁵	B	Validation of a clinical prediction rule

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

BEST PRACTICES IN CARDIOLOGY

Recommendations from the Choosing Wisely Campaign

Recommendation	Sponsoring organization
Do not use coronary computed tomography angiography in high-risk patients presenting to the emergency department with acute chest pain.	Society of Cardiovascular Computed Tomography
Do not perform cardiac magnetic resonance imaging in patients with acute chest pain and high probability of coronary artery disease.	Society for Cardiovascular Magnetic Resonance

Source: For more information on the Choosing Wisely Campaign, see <https://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <https://www.aafp.org/afp/recommendations/search.htm>.

such as pressure, aching, discomfort, tightness, squeezing, or indigestion.¹²

A meta-analysis of studies that evaluated the role of previous chest pain in diagnosing ACS concluded that chest pain that is pleuritic, positional, or reproducible with palpation

and not related to exertion is low risk for ACS. Pain that is described as pressure (similar to that of prior myocardial infarction), worse than prior anginal pain, associated with exertion, accompanied by nausea or diaphoresis, and/or radiates to one or both arms/shoulders is higher risk for ACS.¹³

Although individual characteristics generally do not support or rule out a diagnosis, a combination of these may increase diagnostic accuracy.¹⁴ The combination of age, sex, and type of chest pain can predict the likelihood of coronary artery disease (CAD) as the cause of chest pain.¹⁵ *Table 1* outlines updated predicted pretest probabilities

of CAD in patients with chest pain based on these three factors.¹⁵ U.S. guidelines recommend that patients with a probability of less than 5% be classified as low risk and not undergo further testing.¹⁶ Those with a probability greater than 70% should undergo invasive angiography, and those

TABLE 1

Predicted Pretest Probabilities of Coronary Artery Disease in Patients with Chest Pain Based on Age, Sex, and Type of Chest Pain

Age range (years)	Men			Women		
	Typical	Atypical	Nonanginal	Typical	Atypical	Nonanginal
40 to 49	69%	38%	25%	37%	14%	8%
50 to 59	77%	49%	34%	47%	20%	12%
60 to 69	84%	59%	44%	58%	28%	17%
70 to 79	89%	69%	54%	68%	37%	24%
≥ 80	93%	77%	65%	76%	47%	32%

Information from reference 15.

with a probability of 5% to 70% should undergo noninvasive testing.¹⁶ European guidelines use cutoffs of 15% and 85%, respectively.¹⁵

Validated clinical decision rules can help determine whether chest pain is caused by CAD. One systematic review found that the validated Marburg Heart Score is better than clinical judgment alone for predicting whether chest pain is cardiac in origin.^{17,18} Table 2 outlines the scoring for this clinical rule and presents the probability of CAD as the cause of chest pain for pretest probabilities of 2%, 10%, and 20%.¹⁸

The INTERCHEST clinical decision rule is a second validated decision rule that can predict the presence or absence of CAD in patients who present with chest pain in the primary care setting (Table 3).^{19,20} Patients with a score of less than 2 have only a 2% chance of having CAD, whereas 43% of patients with a score of 2 or more have CAD, making the test useful for ruling out CAD as a cause of the patient's chest pain.²⁰

Because history alone usually cannot determine whether a patient is actively experiencing cardiac ischemia, a 12-lead ECG should be performed on all patients in whom cardiac ischemia is suspected.²¹ ECG findings that increase the likelihood of ACS include ST segment elevation, new-onset left bundle branch block, presence of Q waves, or new T-wave inversions.²² Similar ECG findings may be observed in non-ACS conditions, including acute pericarditis and left ventricular hypertrophy. Patients with suspicion of ACS based on clinical presentation (history, physical examination, risk factors) with changes seen on ECG should be transported immediately to the emergency department.¹⁶

For patients with chest pain not requiring immediate referral who have a low to intermediate pretest probability of CAD, exercise stress testing should be considered.²³ Adding myocardial perfusion or echocardiography to the stress test increases test accuracy with a negative predictive value for acute myocardial infarction and cardiac death of 98%.²⁴ Evaluating with coronary computed tomography angiography (CCTA) decreases the number of nonfatal acute

myocardial infarctions²⁵ and is moderately more accurate than stress ECG in ruling out CAD in patients with chest pain (positive likelihood ratio [LR+] = 5.62; negative likelihood ratio [LR-] = 0.05).²⁶ As a result, CCTA is becoming a first-line test for patients presenting with chest pain in the emergency department and should be a con-

sideration for family physicians evaluating and managing patients with stable chest pain in the office. Cardiac magnetic resonance imaging may be useful in the evaluation of typical angina. For the evaluation of acute chest pain, cardiac magnetic resonance imaging is comparable to angiography in mortality at one year; however, it results in less need

TABLE 2

Marburg Heart Score to Predict CAD as a Cause of Chest Pain

Component	Points
Sex/age (women ≥ 65 years; men ≥ 55 years)	1
Known clinical vascular disease (CAD, occlusive vascular disease, cerebrovascular disease)	1
Increased pain with exercise	1
Pain not elicited with palpation of chest wall	1
Patient assumes pain is of cardiac origin	1

Prevalence of CAD as cause of chest pain given overall population risk of:

Score	Likelihood ratio	2%	10%	20%
0 to 1 point	0.04	0.1	0.4	0.9
2 to 3 points	0.92	1.8	9.3	18.8
4 to 5 points	11.2	18.6	55.5	73.7

MDCalc Marburg Heart Score calculator: <https://www.mdcalc.com/marburg-heart-score-mhs>

CAD = coronary artery disease.

Adapted with permission from Haasenritter J, Bösner S, Vaucher P, et al. Ruling out coronary heart disease in primary care: external validation of a clinical prediction rule. *Br J Gen Pract.* 2012;62(599):e416.

TABLE 3

INTERCHEST Rule for Predicting CAD as the Etiology of Chest Pain

Clinical predictor	Points	Risk group	CAD/total (%)
Pain reproduced by palpating chest wall	-1	Low risk (-1 to 0)	1/295 (0.3)
Men ≥ 55 years or women ≥ 65 years	+1	Moderate risk (1 to 2)	17/245 (6.9)
Physician initially suspected a serious condition	+1	High risk (3+)	67/104 (64.4)
Chest discomfort feels like pressure	+1		
Chest pain related to effort	+1		
History of CAD	+1		
Total:			

MDCalc INTERCHEST calculator: <https://www.mdcalc.com/interchest-clinical-prediction-rule-chest-pain-primary-care>

CAD = coronary artery disease.

Adapted with permission from Sox HC, Aerts M, Haasenritter J. Applying a clinical decision rule for CAD in primary care to select a diagnostic test and interpret the results [Point-of-Care Guide]. *Am Fam Physician*. 2019;99(9):585, with additional information from reference 19.

for invasive angiography and fewer subsequent revascularization procedures.²⁷ Cost is a barrier to the use of CCTA and cardiac magnetic resonance imaging. According to Healthcare Bluebook, the cost of an exercise stress test is \$171, whereas the price of CCTA is \$667 and cardiac magnetic resonance imaging angiography is \$1,075.²⁸ Consideration should also be given to the harms of radiation and contrast exposure from CCTA.

Other Diagnostic Considerations

If the initial evaluation indicates that ACS is less likely or the diagnostic evaluation for ACS in higher-risk patients is negative, other non-ACS conditions that may cause symptoms similar to coronary ischemia should be considered (Table 4). Understanding the presentation of these common conditions with the clinical impression will help lead to a correct diagnosis.

CHEST WALL PAIN

Chest wall pain is the most common cause of chest pain in the outpatient setting, accounting for 33% to 50% of chest pain.²⁹ One prospective cohort study identified four clinical factors that predict a final diagnosis of chest wall pain in patients presenting to the primary care office with chest

pain: localized muscle tension, stinging pain, pain reproducible by palpation, and the absence of a cough. In a study population with a prevalence of chest wall pain of 47%, patients with at least two of these findings had a 77% likelihood of chest wall pain as the cause of their discomfort (LR+ = 3.02), and those with none or one of the findings had only an 18% likelihood (LR- = 0.47).²⁹

COSTOCHONDRITIS

Often considered a subset of chest wall pain, costochondritis is a self-limited condition characterized by pain that is reproducible with palpation in the parasternal costochondral joints. Costochondritis is a clinical diagnosis and does not require specific diagnostic testing in the absence of concomitant cardiopulmonary symptoms or risk factors.³⁰

GASTROESOPHAGEAL REFLUX DISEASE

Classic symptoms of gastroesophageal reflux disease (GERD) include a burning retrosternal pain, acid regurgitation, and a sour or bitter taste in the mouth.^{31,32} There are no useful physical examination maneuvers or standard tests to establish the diagnosis or to support or rule it out. A one-week trial of a high-dose proton pump inhibitor is modestly sensitive and specific for GERD, with a 50% reduction in reflux symptoms being moderately accurate for a final diagnosis of GERD (LR+ = 5.5; LR- = 0.24).³³ ACS symptoms can often be mistaken for those of GERD; if clinical suspicion is high for ACS, an ECG should be obtained.

Panic Disorder and Anxiety State

Panic disorder and anxiety states are common. One in four people with a panic attack will have chest pain and

TABLE 4

Nonischemic Causes of Chest Pain

Cardiac	Musculoskeletal
Acute aortic dissection	Chest wall pain
Heart failure	Costochondritis
Pericarditis	Psychological
Gastrointestinal	Panic attack
Gastroesophageal reflux disease	Pulmonary
	Pneumonia
	Pulmonary embolism

shortness of breath.³⁴ Yet, concomitant panic disorder and chest pain are often not recognized, leading to more testing, follow-up, and higher costs of care.³⁴ A moderately accurate assessment for detecting panic disorder is had by asking the following validated screening question: “In the past four weeks, have you had an anxiety attack (suddenly feeling fear or panic)?” This question is good at supporting a diagnosis of panic disorder when patients answer yes (LR+ = 4.2) and is good at ruling it out when the answer is no (LR- = 0.09).³⁵

Less Common, but Important, Diagnostic Considerations

PERICARDITIS

Pericarditis manifests as a clinical triad of pleuritic chest pain, a pericardial friction rub, and diffuse ECG ST-T-wave changes often preceded by a viral illness.³⁶ Acute pericarditis should be considered in patients presenting with new-onset chest pain that increases with inspiration or when reclining and is lessened by leaning forward.³⁶ ECG usually demonstrates diffuse ST segment elevation and PR interval depression.

PNEUMONIA

Common symptoms of pneumonia include fever, chills, productive cough, and pleuritic chest pain.³⁷ Egophony (LR+ = 8.6), dullness to percussion of the posterior thorax (LR+ = 4.3), and respiratory rate greater than 20 breaths per minute (LR+ = 3.5) are suggestive of pneumonia.³⁸ Normal temperature, heart rate, and respiratory rate with a normal pulmonary examination rules out pneumonia (LR- = 0.10).³⁹ Chest radiography can assist in the diagnosis of pneumonia; however, a Cochrane review suggests that routine chest radiography does not affect outcomes in patients who present with signs of lower respiratory tract infection.⁴⁰

HEART FAILURE

Most patients with heart failure present with dyspnea on exertion, although some will present with chest pain.⁴¹ Clinical impression is predictive of heart failure (LR+ = 9.9; LR- = 0.65), as is pulmonary edema on chest radiography (LR+ = 11.0).⁴¹ Patients with acute dyspnea and one or more of the MICE criteria (Male sex, history of myocardial Infarction, basal lung Creptitations, and ankle Edema) likely have heart failure and should be evaluated with echocardiography.^{42,43}

PULMONARY EMBOLISM

Diagnosing PE in the office is challenging because its presentation is highly variable. Although dyspnea, tachycardia, and/or chest pain are present in 97% of those

diagnosed with PE, no single clinical feature effectively supports or rules out its diagnosis.⁴⁴ Risk of PE can be estimated by using a validated clinical decision rule, such as the Wells criteria (Table 5).⁴⁵ Patients at moderate or higher risk should undergo additional testing with a D-dimer assay, ventilation-perfusion scan, or helical computed tomography of the pulmonary arteries.⁴⁵ The Pulmonary Embolism Rule-out Criteria were developed to specifically rule out PE in the primary care setting.⁴⁶ Patients meeting all eight criteria (50 years or younger, heart rate less than 100 beats per minute, oxygen saturation greater than 94%, no unilateral leg swelling, no hemoptysis, no surgery or trauma within four weeks, no previous deep venous thrombosis or PE, no oral hormone use) have a less than 1% likelihood of PE and thus do not need D-dimer testing or imaging.^{46,47}

ACUTE THORACIC AORTIC DISSECTION

Patients with acute thoracic aortic dissection may present with chest or back pain.⁴⁸ History and physical examination

TABLE 5

Wells Clinical Prediction Rule for PE

Criteria	Points	
Signs or symptoms of DVT (leg swelling or pain with palpation of deep vein)	3	
Diagnosis of PE is more likely than an alternative diagnosis	3	
Heart rate > 100 beats per minute	1.5	
Immobilization (bed rest > 3 days) or surgery in past 4 weeks	1.5	
History of PE or DVT	1.5	
Hemoptysis	1	
Active malignancy (or cancer treatment stopped in past 6 months)	1	
Total points	Risk of PE	Probability of PE (overall probability = 9.2%)
0 to 1 point	Low	1.3
2 to 6 points	Moderate	16.2
More than 6 points	High	37.5

MDCalc Wells calculator: <https://www.mdcalc.com/wells-criteria-pulmonary-embolism>

DVT = deep venous thrombosis; PE = pulmonary embolism.

Information from reference 45.

are only modestly useful for supporting or ruling out the diagnosis; acute chest or back pain and a pulse differential in the upper extremities modestly increases the likelihood of an acute thoracic aortic dissection (LR+ = 5.3).⁴⁹ Clinical suspicion for thoracic dissection warrants immediate referral to the emergency department.

This article updates previous articles on this topic by McConaghy and Oza⁵⁰ and Cayley.⁵¹

Data Sources: A PubMed search was completed using the key terms chest pain, chest pain evaluation, diagnosis, clinical decision rule, differential diagnosis, acute coronary syndrome, and angina. The search included meta-analyses, reviews, randomized controlled trials, point-of-care guides, and clinical trials. We also searched the Cochrane Database of Systematic Reviews, the National Guideline Clearinghouse, Essential Evidence Plus, Database of Abstracts of Reviews of Effects, and Agency for Healthcare Research and Quality Evidence Reports. Search date: literature search was completed on several occasions; last date was October 11, 2020.

The Authors

JOHN R. MCCONAGHY, MD, is a professor of family and community medicine, department vice chair, and the associate director of the Family Medicine Residency Program at The Ohio State University Wexner Medical Center, Columbus.

MALVIKA SHARMA, MD, is a resident in the Family Medicine Residency Program at The Ohio State University Wexner Medical Center.

HITEN PATEL, MD, is an ultrasound fellow in the Family Medicine Residency Program at The Ohio State University Wexner Medical Center. At the time the article was written, Dr. Patel was chief resident.

Address correspondence to John R. McConaghy, MD, The Ohio State University Wexner Medical Center, 2231 N High St., Columbus, OH 43201 (email: john.mcconaghy@osumc.edu). Reprints are not available from the authors.

References

- Rui P, Okeyode T. National ambulatory medical care survey: 2016 national summary tables. Accessed December 28, 2019. https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2016_namcs_web_tables.pdf
- Klinkman MS, Stevens D, Gorenflo DW. Episodes of care for chest pain: a preliminary report from MIRNET. Michigan Research Network. *J Fam Pract.* 1994;38(4):345-352.
- Will JC, Loustalot F, Hong Y. National trends in visits to physician offices and outpatient clinics for angina 1995 to 2010. *Circ Cardiovasc Qual Outcomes.* 2014;7(1):110-117.
- Heron M. Deaths: leading causes for 2017. National Vital Statistics Reports. National Center for Health Statistics. June 24, 2019. Accessed January 8, 2020. https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_06-508.pdf
- Svavarsdóttir AE, Jónasson MR, Gudmundsson GH, et al. Chest pain in family practice. Diagnosis and long-term outcome in a community setting [published correction appears in *Can Fam Physician.* 1996;42:1672]. *Can Fam Physician.* 1996;42:1122-1128.
- Ebell MH. Evaluation of chest pain in primary care patients. *Am Fam Physician.* 2011;83(5):603-605. Accessed September 15, 2020. <https://www.aafp.org/afp/2011/0301/p603.html>
- Kontos MC, Diercks DB, Kirk JD. Emergency department and office-based evaluation of patients with chest pain. *Mayo Clin Proc.* 2010;85(3):284-299.
- Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update of the guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines [published corrections appear in *Circulation.* 2011;124(12):e337-e340 and *Circulation.* 2011;123(22):e625-e626]. *Circulation.* 2011;123(18):2022-2060.
- Braunwald E. Unstable angina. A classification. *Circulation.* 1989;80(2):410-414.
- Thygesen K, Alpert JS, Jaffe AS, et al.; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol.* 2018;72(18):2231-2264.
- National Clinical Guideline Centre for Acute and Chronic Conditions (UK). Chest Pain of Recent Onset: Assessment and Diagnosis. NICE clinical guideline no. 95. Royal College of Physicians; 2010.
- Rouan GW, Lee TH, Cook EF, et al. Clinical characteristics and outcome of acute myocardial infarction in patients with initially normal or non-specific electrocardiograms (a report from the Multicenter Chest Pain Study). *Am J Cardiol.* 1989;64(18):1087-1092.
- Swap CJ, Nagurny JT. Value and limitations of chest pain history in the evaluation of patients with suspected acute coronary syndromes [published correction appears in *JAMA.* 2006;295(19):2250]. *JAMA.* 2005;294(20):2623-2629.
- Bösner S, Becker A, Abu Hani M, et al. Accuracy of symptoms and signs for coronary heart disease assessed in primary care. *Br J Gen Pract.* 2010;60(575):e246-e257.
- Bittencourt MS, Hulten E, Polonsky TS, et al. European Society of Cardiology—recommended coronary artery disease consortium pretest probability scores more accurately predict obstructive coronary disease and cardiovascular events than the Diamond and Forrester score: the Partners Registry [published correction appears in *Circulation.* 2018;138(5):e80]. *Circulation.* 2016;134(3):201-211.
- Amsterdam EA, Wenger NK, Brindis RG, et al.; ACC/AHA Task Force members. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published correction appears in *Circulation.* 2014;130(25):e433-e434]. *Circulation.* 2014;130(25):e344-e426.
- Harskamp RE, Laeven SC, Himmelreich JCI, et al. Chest pain in general practice: a systematic review of prediction rules. *BMJ Open.* 2019;9(2):e027081.
- Haasenritter J, Bösner S, Vaucher P, et al. Ruling out coronary heart disease in primary care: external validation of a clinical prediction rule. *Br J Gen Pract.* 2012;62(599):e415-e421.
- Aerts M, Minalu G, Bösner S, et al.; International Working Group on Chest Pain in Primary Care (INTERCHEST). Pooled individual patient data from five countries were used to derive a clinical prediction rule for coronary artery disease in primary care. *J Clin Epidemiol.* 2017;81:120-128.
- Sox HC, Aerts M, Haasenritter J. Applying a clinical decision rule for CAD in primary care to select a diagnostic test and interpret the

ACUTE CHEST PAIN

- results [Point-of-Care Guide]. *Am Fam Physician*. 2019;99(9):584-586. Accessed September 15, 2020. <https://www.aafp.org/afp/2019/0501/p584.html>
21. Thygesen K, Alpert JS, Jaffe AS, et al.; Joint ESC/ACC/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. *Circulation*. 2012;126(16):2020-2035.
 22. Rude RE, Poole WK, Muller JE, et al. Electrocardiographic and clinical criteria for recognition of acute myocardial infarction based on analysis of 3,697 patients. *Am J Cardiol*. 1983;52(8):936-942.
 23. Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines) [published correction appears in *J Am Coll Cardiol*. 2006;48(8):1731]. *J Am Coll Cardiol*. 2002;40(8):1531-1540.
 24. Metz LD, Beattie M, Hom R, et al. The prognostic value of normal exercise myocardial perfusion imaging and exercise echocardiography: a meta-analysis. *J Am Coll Cardiol*. 2007;49(2):227-237.
 25. Newby DE, Adamson PD, Berry C, et al.; SCOT-HEART Investigators. Coronary CT angiography and 5-year risk of myocardial infarction. *N Engl J Med*. 2018;379(10):924-933.
 26. Yin X, Wang J, Zheng W, et al. Diagnostic performance of coronary computed tomography angiography versus exercise electrocardiography for coronary artery disease: a systematic review and meta-analysis. *J Thorac Dis*. 2016;8(7):1688-1696.
 27. Nagel E, Greenwood JP, McCann GP, et al.; MR-INFORM Investigators. Magnetic resonance perfusion or fractional flow reserve in coronary disease. *N Engl J Med*. 2019;380(25):2418-2428.
 28. Healthcare bluebook. Accessed May 7, 2020. <https://www.healthcarebluebook.com/>
 29. Bösner S, Becker A, Abu Hani M, et al. Chest wall syndrome in primary care patients with chest pain: presentation, associated features and diagnosis. *Fam Pract*. 2010;27(4):363-369.
 30. Disla E, Rhim HR, Reddy A, et al. Costochondritis. A prospective analysis in an emergency department setting. *Arch Intern Med*. 1994;154(21):2466-2469.
 31. Zimmerman J. Validation of a brief inventory for diagnosis and monitoring of symptomatic gastro-oesophageal reflux. *Scand J Gastroenterol*. 2004;39(3):212-216.
 32. Mousavi S, Tosi J, Eskandarian R, et al. Role of clinical presentation in diagnosing reflux-related non-cardiac chest pain. *J Gastroenterol Hepatol*. 2007;22(2):218-221.
 33. Wang WH, Huang JQ, Zheng GF, et al. Is proton pump inhibitor testing an effective approach to diagnose gastroesophageal reflux disease in patients with noncardiac chest pain?: a meta-analysis. *Arch Intern Med*. 2005;165(11):1222-1228.
 34. Huffman JC, Pollack MH, Stern TA. Panic disorder and chest pain: mechanisms, morbidity, and management. *Prim Care Companion J Clin Psychiatry*. 2002;4(2):54-62.
 35. Löwe B, Gräfe K, Zipfel S, et al. Detecting panic disorder in medical and psychosomatic outpatients: comparative validation of the Hospital Anxiety and Depression Scale, the Patient Health Questionnaire, a screening question, and physicians' diagnosis. *J Psychosom Res*. 2003;55(6):515-519.
 36. Imazio M, Gaita F, LeWinter M. Evaluation and treatment of pericarditis: a systematic review [published corrections appear in *JAMA*. 2016;315(1):90 and *JAMA*. 2015;314(18):1978]. *JAMA*. 2015;314(14):1498-1506.
 37. Kaysin A, Viera AJ. Community-acquired pneumonia in adults: diagnosis and management [published correction appears in *Am Fam Physician*. 2017;95(7):414]. *Am Fam Physician*. 2016;94(9):698-706. Accessed September 15, 2020. <https://www.aafp.org/afp/2016/1101/p698>
 38. Htun TP, Sun Y, Chua HL, et al. Clinical features for diagnosis of pneumonia among adults in primary care setting: a systematic and meta-review. *Sci Rep*. 2019;9(1):7600.
 39. Marchello CS, Ebell MH, Dale AP, et al. Signs and symptoms that rule out community-acquired pneumonia in outpatient adults: a systematic review and meta-analysis. *J Am Board Fam Med*. 2019;32(2):234-247.
 40. Cao AMY, Choy JP, Mohanakrishnan LN, et al. Chest radiographs for acute lower respiratory tract infections. *Cochrane Database Syst Rev*. 2013;(12):CD009119.
 41. Wang CS, FitzGerald JM, Schulzer M, et al. Does this dyspneic patient in the emergency department have congestive heart failure? *JAMA*. 2005;294(15):1944-1956.
 42. Ebell MH. Diagnosis of heart failure with reduced ejection fraction [Point-of-Care Guide]. *Am Fam Physician*. 2020;101(4):230-232. Accessed April 8, 2020. <https://www.aafp.org/afp/2020/0215/p230.html>
 43. Roalfe AK, Mant J, Doust JA, et al. Development and initial validation of a simple clinical decision tool to predict the presence of heart failure in primary care: the MICE (male, infarction, crepitations, edema) rule. *Eur J Heart Fail*. 2012;14(9):1000-1008.
 44. West J, Goodacre S, Sampson F. The value of clinical features in the diagnosis of acute pulmonary embolism: systematic review and meta-analysis. *QJM*. 2007;100(12):763-769.
 45. Wells PS, Anderson DR, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. *Ann Intern Med*. 2001;135(2):98-107.
 46. Singh B, Parsaik AK, Agarwal D, et al. Diagnostic accuracy of pulmonary embolism rule-out criteria: a systematic review and meta-analysis. *Ann Emerg Med*. 2012;59(6):517-520.e1-4.
 47. Kline JA, Webb WB, Jones AE, et al. Impact of a rapid rule-out protocol for pulmonary embolism on the rate of screening, missed cases, and pulmonary vascular imaging in an urban US emergency department. *Ann Emerg Med*. 2004;44(5):490-502.
 48. Klompas M. Does this patient have an acute thoracic aortic dissection? *JAMA*. 2002;287(17):2262-2272.
 49. Ohle R, Kareemi HK, Wells G, et al. Clinical examination for acute aortic dissection: a systematic review and meta-analysis. *Acad Emerg Med*. 2018;25(4):397-412.
 50. McConaghy JR, Oza RS. Outpatient diagnosis of acute chest pain in adults. *Am Fam Physician*. 2013;87(3):177-182. Accessed September 15, 2020. <https://www.aafp.org/afp/2013/0201/p177.html>
 51. Cayley WE Jr. Diagnosing the cause of chest pain. *Am Fam Physician*. 2005;72(10):2012-2021. Accessed September 18, 2020. <https://www.aafp.org/afp/2005/1115/p2012.html>