COMMENTARY

Rahul Aggarwal, MD
Heart and Vascular Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Ron Blankstein, MD
Heart and Vascular Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Deepak L. Bhatt, MD, MPH, MBA
Director, Mount Sinai Fuster Heart Hospital, New York, NY; Dr. Valentin Fuster Professor of Cardiovascular Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; Member, Writing Committee, 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

The PRECISE trial: How should patients with chest pain be tested?

Patients who present with chest pain pose a dilemma. As clinicians, we do not want to miss true cases of obstructive coronary artery disease, but chest pain is a nonspecific symptom and many patients with chest pain have no cardiac disease. We cannot take every patient with chest pain to the catheterization laboratory for the gold-standard test, coronary angiography—there are not enough catheterization labs in the world, it would be prohibitively expensive, and we might harm more patients than we help. Therefore, we apply clinical judgment and noninvasive cardiac tests to decide who goes to the catheterization lab.

Clinical guidelines recommend noninvasive cardiac testing in patients who have an intermediate or high pretest probability of having obstructive coronary artery disease and, conversely, say it is reasonable to *not* test patients who are at low risk of it.[1,2]

Determining that a patient is at low risk is challenging, but several scoring systems have been devised. As the latest example, and most relevant to our discussion here, the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE)[3] investigators retrospectively analyzed data from a clinical trial (more about this below) and developed a "minimal risk score" for patients who are having chest pain, to identify those who are actually at low cardiac risk and don't need to undergo cardiac testing.This score is based on 10 clinical variables: age, sex, race or ethnicity, hypertension, hyperlipidemia, diabetes, smoking history, family history of coronary artery disease, unrelated symptoms with physical or mental stress, and high-density lipoprotein cholesterol level.[3] The score assigns a probability of being at minimal cardiac risk, with higher scores indicating lower risk. In the development cohort, the decile with the lowest risk had a mean probability of no risk of 0.54, and 65.6% had normal computed tomography (CT) angiography.[3] The risk score's performance for discrimination was modest, with a C statistic of 0.730, though this was in the cohort in which the risk score was developed and so may overestimate performance. Validation studies did suggest the score could be combined with clinical judgment to help identify patients with low cardiac risk.[4,5] A study also suggested that the risk score overestimated the probability of patients being low risk, indicating that the score assigned them a higher probability of safety than actually observed.[6] As such, studies to evaluate the safety of its use, such as the Prospective Randomized Trial of the Optimal Evaluation of Cardiac Symptoms and Revascularization (PRECISE) trial[7] (further discussion to follow), provide important information on the clinical safety of the risk score.

Another issue in evaluation of chest pain is which noninvasive test to use: the options are functional (stress) testing or anatomic testing with CT angiography, depending on the clinical situation.[1,8,9] CT can also be used to measure the fractional flow reserve, which is a measurement of the flow in distal segments of the coronary artery relative to maximal flow in proximal segments. When used in patients undergoing CT angiography, the addition of CT fractional flow reserve can decrease the rate of unnecessary cardiac catheterizations.[10]

The PRECISE trial[7] sought to answer 2 questions:

- Could the PROMISE minimal risk score identify individuals with symptoms suggesting coronary artery disease who actually were at low risk and could safely forego testing?
- Could a strategy of CT angiography with selective measurement of CT-based fractional flow reserve be beneficial compared with standard testing?

PRECISE DESIGN: USUAL VS 'PRECISION' TESTING

PRECISE was conducted in patients with stable symptoms that suggested coronary artery disease but who did

doi:10.3949/ccjm.91a.24024

TABLE 1
PRECISE trial at a glance

	Precision strategy (n = 1,057)	Usual-testing strategy (n = 1,046)
Intervention	Risk stratification using PROMISE minimal risk score: if score was > 0.46, then further testing was deferred unless patients had known vascular calcifications or atherosclerosis Cardiac testing with CT angiography: if 30% to 90% stenosis was present, then CT fractional flow reserve was added	Physician-guided decision-making: options included deferred testing, stress testing, or cardiac catheterization
Patients who had cardiac testing, n (%)	883 (83.5)[a]	978 (93.5)[a]
Initial cardiac testing, %		
CT angiography	48	< 1
CT angiography + CT fractional flow reserve	31	< 1
Cardiac catheterization	< 1	10
Single-photon emission computed tomography-positron emission tomography	2	32
Stress echocardiography	2	30
Treadmill electrocardiography	1	11
Stress cardiac magnetic resonance imaging	< 1	10
No test	16	7
Patients who had cardiac catheterization, n (%)	135 (12.8)[a]	177 (16.9)[a]
Patients with primary composite endpoint (death, nonfatal myocardial infarction, or cardiac catheterization without obstructive coronary artery disease), n (%)	44 (4.2)[a]	118 (11.3)[a]
Death or nonfatal myocardial infarction	18 (1.7)	12 (1.1)
Cardiac catheterization without obstructive coronary artery disease	27 (2.6)[a]	107 (10.2)[a]
Patients who had revascularization, n (%)	97 (9.2)[a]	54 (5.2)[a]

[a]Statistically significant difference.

CT = computed tomography; PRECISE = Prospective Randomized Trial of the Optimal Evaluation of Cardiac Symptoms and Revascularization; PROMISE = Prospective Multicenter Imaging Study for Evaluation of Chest Pain

Based on information from reference 7.

not have a history of it. Those with contraindications to CT angiography or who had been tested for coronary artery disease within the past year were excluded.[7]

Patients were randomized in a 1-to-1 ratio to either a usual testing strategy—a standard cardiac diagnostic approach based on the clinician's judgment, with options including deferred testing, functional testing, or cardiac catheterization—or to a "precision strategy" (**Table 1**).[7]

Patients in the precision strategy group were first evaluated for cardiac risk by the PROMISE minimal risk score.[3] Patients at low risk (defined as a score > 0.46) were deferred from subsequent cardiac testing unless they had atherosclerosis on prior imaging such as chest CT, in which case they underwent CT angiography anyway, as did patients with higher-risk (lower PROMISE scores). Patients with 30% to 90% stenosis on CT angiography also underwent CT fractional

flow reserve testing to assist in the decision whether to proceed with cardiac catheterization.[7] Of note, the chest pain guideline suggests selectively measuring CT fractional flow reserve in patients who have 40% to 90% stenosis—a slightly more stringent threshold.[1]

The primary composite outcome was death or nonfatal myocardial infarction within 1 year or needless cardiac catheterization, ie, that found no trace of obstructive coronary artery disease.

PRECISE FINDINGS

The PRECISE trial enrolled 2,103 patients in North America and Europe.[7] The mean age was 58 years, about half of the patients were women, and about 85% identified as non-Hispanic White. The primary presenting complaint, present in about 80% of the cohort, was chest pain; 10% of the patients had dyspnea on exertion.

Fewer patients in the precision-testing group compared with the usual-testing group underwent subsequent testing (83.5% vs 93.5%, $P < .001$) (**Table 1**).[7] A total of 20.2% of the patients in the precision group were determined to be at minimal risk by the PROMISE minimal risk score, though only 64.4% of these patients were actually deferred from testing. In the usual-testing group, 32% of the patients underwent nuclear stress testing, 30% underwent stress echocardiography, 11% underwent exercise electrocardiography, 10% underwent stress cardiac magnetic resonance imaging, 10% underwent cardiac catheterization, and 7% had no further testing.

The precision-testing group had a lower rate of the primary composite outcome (4.2% vs 11.3%, unadjusted hazard ratio [HR] 0.35, 95% confidence interval [CI] 0.25–0.50). However, the difference was primarily driven by fewer unnecessary cardiac catheterizations (2.6% vs 10.2%, HR 0.24, 95% CI 0.16–0.36). By 1 year, 18 patients (1.7%) in the precision-testing group had died or had a nonfatal myocardial infarction, compared with 12 patients (1.1%) in the usual-testing group, but the difference was not statistically significant (HR 1.52, 95% CI 0.73–3.15).[7]

Also at 1 year, more patients in the precision group (vs usual testing) were using antiplatelet medications (35.7% vs 27.1%, $P < .001$) and cholesterol-lowering medications (50.0% vs 41.8%, $P < .001$).[7]

IMPLICATIONS

In the PRECISE trial, patients who underwent testing according to the precision strategy were less likely to undergo unnecessary cardiac catheterizations than those with a usual testing strategy. The rates of death or nonfatal myocardial infarction were not statistically significantly different between the precision- and usual-testing groups; however, the study was not powered to detect differences in these clinical outcomes over a 1-year period, as evidenced by low event rates. Indeed, prior studies that demonstrated a benefit of more aggressive preventive therapies in terms of preventing death or myocardial infarction required longer follow-up and more patients.[9] Though the clinical outcomes (death or nonfatal myocardial infarction) and the efficiency outcome (unnecessary cardiac catheterization) were combined into a single outcome, the results were driven by the reduction in unnecessary cardiac catheterizations.

The original PROMISE trial compared functional stress testing (electrocardiography- or imaging-based) and anatomic testing with CT angiography and found no significant difference in cardiovascular outcomes with either approach, although the composite outcome used in PROMISE also included hospitalization for unstable angina and procedural complications. Nevertheless, more patients in the CT angiography group went on to undergo cardiac catheterization, and fewer of them did so unnecessarily, indicating that they had a lower rate of cardiac catheterization without obstructive coronary artery disease.[8]

Notably, the Scottish Computed Tomography of the Heart (SCOT-HEART) trial,[9] which randomized patients with stable chest pain to standard care vs standard care and CT angiography, observed a higher rate of cardiac catheterizations initially but not by 5 years with CT angiography.

Because PROMISE indicated potentially higher rates of cardiac catheterization in those undergoing CT angiography, the use of fractional flow reserve as part of the precision strategy may provide a way to decrease unnecessary cardiac catheterizations among patients with stable cardiac symptoms who undergo CT angiography. PRECISE provides evidence that using this strategy with CT angiography can help identify patients with low cardiac risk who can safely be deferred from subsequent testing and provide clinical parity with a typical physician-driven risk stratification approach.

PROMISE MINIMAL RISK SCORE

Almost one-third of the patients in the precision- strategy group who were identified as being at low risk still underwent CT angiography. Presumably, their physicians used clinical judgment to identify patients who were incorrectly categorized as being at low risk, though some of these patients may have been stratified as higher

risk based on vascular calcifications or atherosclerosis on imaging or by having worrisome symptoms. A prespecified secondary analysis of PRECISE demonstrated that 96% of those who underwent subsequent testing despite being at low risk by the PROMISE minimal risk score had negative testing for obstructive coronary artery disease or ischemia.[11]

These findings highlight challenges that are inherent to using risk scores that are aimed to reduce testing. Notably, physicians who are interested in pursuing testing will often do so, even when advised that such testing can be deferred. Similarly, a registry-based analysis showed that 17% of patients referred for cardiac catheterization were actually at low risk based on the PROMISE minimal risk score, suggesting that too many people are undergoing cardiac catheterization.[4]

IS THE PRECISION STRATEGY SAFE?

An important question is the safety of the precision strategy compared with the usual strategy. The rate of death or nonfatal myocardial infarction was not statistically significantly different between the 2 groups, although at 1 year there was a numerically higher rate of these clinical outcomes in the precision-strategy group (1.7% vs 1.1%, HR 1.52, 95% CI 0.73–3.15).[7] These were attributed to periprocedural myocardial infarctions and type 2 myocardial infarction events. The event rates were low, so determining whether there is a real difference will require further study and monitoring. If anything, one might expect that the precision strategy would have resulted in a lower rate of death or nonfatal myocardial infarction, as prior studies have shown that the use of CT angiography is associated with a reduction in such events.[9,12] Overall, the precision strategy appears safe, but long-term monitoring will be needed.

IS ANATOMIC TESTING SUPERIOR TO FUNCTIONAL TESTING?

When interpreting the PRECISE trial, physicians need to account for the trial having 2 separate interventions that were randomized.

The first intervention was the risk-stratification approach. The usual-testing group was managed exclusively according to their physicians' clinical judgment as to whether they needed subsequent testing, whereas the precision group was managed using the PROMISE minimal risk score, vascular calcifications, atherosclerosis on prior imaging, and clinical judgment.

The second intervention was the type of testing. The usual-testing group underwent functional testing, with options for a variety of testing modalities, or cardiac catheterization. The precision group underwent anatomic testing with CT angiography, followed by selective use of CT fractional flow reserve.

Thus, it is difficult to directly compare the impact of CT angiography vs usual testing. Because the design tested 2 different strategies, it is unclear how each intervention contributed to the improvements in reducing unnecessary cardiac catheterizations.

Understanding the impact of measuring CT fractional flow reserve on the results is also important. PROMISE did not use CT fractional flow reserve in the original study, though a retrospective study observed that it improved the identification of those at risk for adverse cardiovascular outcomes.[13] CT fractional flow reserve has been shown in several registries to identify patients at low risk who can safely forego testing.[14–16]

OPTIMIZING MEDICAL THERAPY

Significantly more patients in the precision-testing group were prescribed antiplatelet and lipid-lowering drugs. Similar findings were observed in SCOT-HEART.[9] This is important, as optimal medical therapy improves cardiac outcomes.[17,18]

A reason that more patients got these needed drugs may be that they underwent CT angiography. Earlier studies also found higher rates of medical therapy after CT angiography.[19] Why would this be? First, CT angiography can detect nonobstructive plaque, which would prompt the physician to prescribe medical therapy.[19,20] Also, with CT angiography, patients can see the plaque for themselves on the images and therefore may be more motivated to adhere to medical therapy, and physicians may be better able to risk-stratify patients and also to educate patients about their risk.[21]

Additional studies are needed to understand how the use of CT angiography can lead to meaningful improvements in cardiovascular outcomes by increasing the use of medical therapies. Importantly, PROMISE and SCOT-HEART were trials that did not provide much guidance to physicians (or patients) with respect to how to intensify medical therapy. In fact, these trials were conducted before we had robust data on the importance of treating nonobstructive plaque. In contrast, reporting the amount of plaque and specific management recommendations based on these findings are now standards of care.[22]

PRECISE WAS PROMISING

PRECISE demonstrated that incorporating the PROMISE minimal risk score in evaluating patients

with worrisome symptoms, along with CT angiography with selective measuring of CT fractional flow reserve, can be an effective strategy to approach evaluation for coronary artery disease and minimize unnecessary cardiac catheterizations. PRECISE was not powered to evaluate the rates of death or myocardial infarction, so monitoring these events will be important. Further studies comparing CT angiography with functional testing are required to better define the benefits of CT fractional flow reserve in avoiding unnecessary cardiac catheterizations—and to test the benefits of CT angiography imaging in guiding medical therapy—but the PRECISE results are very promising.

DISCLOSURES

Dr. Aggarwal has disclosed serving as a research collaborator for Amarin, Lexicon, and Novartis; receiving research funding support from Bristol Meyers Squibb-Pfizer Alliance; serving as a research principal investigator for Bristol Meyers Squibb-Pfizer Alliance; and prior consulting for Lexicon.

Dr. Blankstein has disclosed consulting for Amgen, Caristo, HeartFlow, Novartis, and Star Therapeutics; conducting institutional research for Amgen; serving as research principal investigator for Nanox AI; and serving as research site principal investigator for Novartis.

Dr. Bhatt has disclosed the following: Advisory Board: Boehringer Ingelheim, Cardax, CellProthera, Cereno Scientific, Elsevier, Janssen, Level Ex, Merck, Myokardia, NirvaMed, Novartis, Novo Nordisk, PLx Pharma, PhaseBio, Stasys; Ownership interest (stock, stock options in a publicly owned company): AngioWave, Bristol-Myers Squibb, DRS. LINQ, High Enroll; Board of Directors: AHA New York City, Boston VA Research Institute, Bristol-Myers Squibb, DRS.LINQ, High Enroll, Society of Cardiovascular Patient Care, TobeSoft; Consulting: Broadview Ventures, Cowen & Company, GlaxoSmithKline, HIMS, Piper Sandler, SFJ, Youngene; Royalties: Elsevier (textbooks); Unfunded Research: FlowCo, Takeda; Advisor or Review Panel Participant: Medscape Cardiology, Novo Nordisk, PLx Pharma, Regado; Data Monitoring Committees: Acesion Pharma, Assistance Publique-Hôpitaux de Paris, Cleveland Clinic (including for the ExCEED trial, funded by Edwards), Contego Medical (Chair, PERFORMANCE 2), Duke Clinical Research Institute, Javelin (CAPTURE-2), Mayo Clinic, Mount Sinai School of Medicine, Novartis, Population Health Research Institute, Rutgers University (for MINT trial); Research funding: Abbott, Afimmune, Aker Biomarine, Alnylam, Amarin, Astra Zeneca, Beren, Boehringer Ingelheim, Cereno Scientific, Chiesi USA, CinCor, Cleerly, Eisai, Ethicon, Faraday Pharmaceuticals, Forest Laboratories, Fractyl Laboratories, Garmin, HLS Therapeutics, Idorsia Pharmaceuticals, Ironwood Pharmaceuticals, Ischemix, Janssen, Javelin, Lilly, Medtronic, Moderna, Myokardia, NirvaMed, Novartis, Otsuka Pharmaceuticals, Owkin, PLx Pharma, Pfizer, PhaseBio, Recardio, Regeneron, Reid Hoffman Foundation, Roche, Sanofi, Stasys, Synaptic, The Medicines Company; Youngene; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee; Trustee; Chair, ACTION Registry Steering Committee), American Heart Association (Inaugural Chair, American Heart Association Quality Oversight Committee), work related to clopidogrel litigation (Sanofi/Bristol-Myers Squibb), Assistance Publique-Hôpitaux de Paris (DSMB Chair), Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring; data monitoring committee chair for PORTICO funded by St. Jude, now Abbott), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial and CME steering committees), *Clinical Cardiology* (Deputy Editor), Elsevier (Elsevier Practice Update Cardiology), Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor in Chief, *Journal of Invasive Cardiology*), Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo, and for the ABILITY-DM trial, funded by Concept Medical), K2P (co-chair, interdisciplinary curriculum), Level Ex, MJH Life Sciences, McKinsey (Cardiovascular advisory board), Medtelligence/ReachMD (CME steering committee), Oakstone CME (Course Director, Comprehensive Review of Interventional Cardiology), Slack Publishing (Chief Medical Editor, Cardiology Today's Intervention), VA CART Research and Publications Committee (Chair), WebMD (CME steering committees), Wiley Publishing Company (steering committee); Research: steering committee for 89Bio Inc, chair and principal investigator for Amarin (for REDUCE-IT), co-principal investigator, co-chair, or executive committee for Astra Zeneca (co-principal investigator for SAVOR-TIMI 53, co-chair and co-principal investigator for THEMIS and THEMIS PCI, executive committee for PEGASUS-TIMI 54, executive committee for DECLARE-TIMI 58), site co-investigator and DSMB Chair for Boston Scientific (PEITHO trial), site co-investigator for Biotronik; site co-investigator for CSI; co-primary investigator and co-chair for Chiesi USA (CHAMPION PHOENIX), principal investigator for Eisai, site co-investigator for Endotronix (PROACTIVE-HF), co-principal investigator for Ethicon (STAMPEDE), Clinical Events Committee Chair for Forest Laboratories (ASCENT COPD), principal investigator for Ischemix, chair for Lexicon (SCORED, and SOLOIST), co- principal investigator for Medtronic (SYMPLICITY trial), chair and principal investigator for PhaseBio (REVERSE IT), site co-investigator for Philips, principal investigator for Roche, chair for Sanofi (SCORED and SOLOIST), site investigator for SpectraWAVE, site co-investigator for St Jude Medical (now Abbott), site co-investigator for Svelte, co-principal investigator and co-chair for The Medicines Company (CHAMPION PLATFORM, CHAMPION PCI, CHAMPION PHOENIX), site investigator for Vascular Solutions.

REFERENCES

1. **Writing Committee Members, Gulati M, Levy PD, et al.** 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Cardiovasc Comput Tomogr 2022; 16(1): 54–122. doi:10.1016/j.jcct.2021.11.009
2. **Koskinas KC.** Appropriate use of non-invasive testing for diagnosis of stable coronary artery disease. E-J Cardiol Pract 2014; 12(19).
3. **Fordyce CB, Douglas PS, Roberts RS, et al.** Identification of patients with stable chest pain deriving minimal value from noninvasive testing: the PROMISE minimal-risk tool, a secondary analysis of a randomized clinical trial [published correction appears in JAMA Cardiol 2018; 3(12):1256]. JAMA Cardio 2017; 2(4):400–408. doi:10.1001/jamacardio.2016.5501
4. **Nanna MG, Wang TY, Chiswell K, et al.** Estimating the real-world performance of the PROMISE minimal-risk tool. Am Heart J 2021; 239:100–109. doi:10.1016/j.ahj.2021.05.016
5. **Rasmussen LD, Fordyce CB, Nissen L, et al.** The PROMISE minimal risk score improves risk classification of symptomatic patients with suspected CAD. JACC Cardiovasc Imaging 2022; 15(8):1442–1454. doi:10.1016/j.jcmg.2022.03.009
6. **Adamson PD, Fordyce CB, McAllister DA, Udelson JE, Douglas PS, Newby DE.** Identification of patients with stable chest pain deriving minimal value from coronary computed tomography angiography: an external validation of the PROMISE minimal-risk tool. Int J Cardiol 2018; 252:31–34. doi:10.1016/j.ijcard.2017.09.033
7. **Douglas PS, Nanna MG, Kelsey MD, et al.** Comparison of an initial risk-based testing strategy vs usual testing in stable symptomatic patients with suspected coronary artery disease: the PRECISE randomized clinical trial. JAMA Cardiol 2023; 8(10):904–914. doi:10.1001/jamacardio.2023.2595
8. **Douglas PS, Hoffmann U, Patel MR, et al.** Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med 2015; 372(14):1291–1300. doi:10.1056/NEJMoa1415516

9. **SCOT-HEART Investigators, Newby DE, Adamson PD, et al.** Coronary CT angiography and 5-year risk of myocardial infarction. N Engl J Med 2018; 379(10):924–933. doi:10.1056/NEJMoa1805971
10. **Douglas PS, Pontone G, Hlatky MA, et al.** Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFR(CT): outcome and resource impacts study. Eur Heart J 2015; 36(47):3359–3367. doi:10.1093/eurheartj/ehv444
11. **Udelson JE, Kelsey MD, Nanna MG, et al.** Deferred testing in stable outpatients with suspected coronary artery disease: a prespecified secondary analysis of the PRECISE randomized clinical trial. JAMA Cardiol 2023; 8(10):915–924. doi:10.1001/jamacardio.2023.2614
12. **Sharma A, Coles A, Sekaran NK, et al.** Stress testing versus CT angiography in patients with diabetes and suspected coronary artery disease. J Am Coll Cardiol 2019; 73(8):893–902. doi:10.1016/j.jacc.2018.11.056
13. **Lu MT, Ferencik M, Roberts RS, et al.** Noninvasive FFR derived from coronary CT angiography: management and outcomes in the PROMISE trial. JACC Cardiovasc Imaging 2017; 10(11):1350–1358. doi:10.1016/j.jcmg.2016.11.024
14. **Rabbat MG, Lakshmanan S, Benjamin MM, et al.** Benefit of icosapent ethyl on coronary physiology assessed by computed tomography angiography fractional flow reserve: EVAPORATE-FFRCT. Eur Heart J Cardiovasc Imaging 2023; 24(7):866–873. doi:10.1093/ehjci/jead063
15. **Freeman AM, Raman SV, Aggarwal M, et al.** Integrating coronary atherosclerosis burden and progression with coronary artery disease risk factors to guide therapeutic decision making [published correction appears in Am J Med 2023; 136(7):720–721]. Am J Med 2023; 136(3):260–269.e7. doi:10.1016/j.amjmed.2022.10.021
16. **Patel MR, Nørgaard BL, Fairbairn TA, et al.** 1-year impact on medical practice and clinical outcomes of FFRCT: the ADVANCE registry. JACC Cardiovasc Imaging 2020; 13(1 Pt 1):97–105. doi:10.1016/j.jcmg.2019.03.003
17. **Iqbal J, Zhang YJ, Holmes DR, et al.** Optimal medical therapy improves clinical outcomes in patients undergoing revascularization with percutaneous coronary intervention or coronary artery bypass grafting: insights from the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial at the 5-year follow-up. Circulation 2015; 131(14):1269–1277. doi:10.1161/CIRCULATIONAHA.114.013042
18. **Lee K, Han S, Lee M, et al.** Evidence-based optimal medical therapy and mortality in patients with acute myocardial infarction after percutaneous coronary intervention. J Am Heart Assoc 2023; 12(10):e024370. doi:10.1161/JAHA.121.024370
19. **Generoso G, Agarwal V, Shaw LJ, Cardoso R, Blankstein R, Bittencourt MS.** Changes in use of preventive medications after assessment of chest pain by coronary computed tomography angiography: a meta-analysis. J Cardiovasc Comput Tomogr 2024; 18(3):233–242. doi:10.1016/j.jcct.2024.01.006
20. **Sandhu AT, Rodriguez F, Ngo S, et al.** Incidental coronary artery calcium: opportunistic screening of previous nongated chest computed tomography scans to improve statin rates (NOTIFY-1 Project). Circulation 2023; 147(9):703–714. doi:10.1161/CIRCULATIONAHA.122.062746
21. **Nurmohamed NS, van Rosendael AR, Danad I, et al.** Atherosclerosis evaluation and cardiovascular risk estimation using coronary computed tomography angiography [published correction appears in Eur Heart J 2024; 45(26):2332]. Eur Heart J 2024; 45(20):1783–1800. doi:10.1093/eurheartj/ehae190
22. **Cury RC, Leipsic J, Abbara S, et al.** CAD-RADS™ 2.0—2022 Coronary Artery Disease—Reporting and Data System: an expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Cardiology (ACC), the American College of Radiology (ACR) and the North America Society of Cardiovascular Imaging (NASCI). J Am Coll Radiol 2022; 19(11): 1185–1212. doi:10.1016/j.jacr.2022.09.012

Address: *Deepak L. Bhatt, MD, MPH, MBA, Director, Mount Sinai Fuster Heart Hospital and Dr. Valentin Fuster Professor of Cardiovascular Medicine, Icahn School of Medicine at Mount Sinai, 1 Gustave Levy Place, Box 1030, New York, NY 10029; DLBhattMD@post.Harvard.edu*