Rationale and Design of SCOT-HEART 2 Trial
CT Angiography for the Prevention of Myocardial Infarction

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Coronary artery disease continues to be the leading cause of death globally. Identifying patients who are at risk of coronary artery disease remains a public health priority. At present, the focus of cardiovascular disease prevention relies heavily on probabilistic risk scoring despite no randomized controlled trials demonstrating their efficacy. The concept of using imaging to guide preventative therapy is not new, but has previously focused on indirect measures such as carotid intima-media thickening or coronary artery calcification. In recent trials, patients found to have coronary artery disease on computed tomography (CT) coronary angiography were more likely to be started on preventative therapy and had lower rates of cardiac events. This led to the design of the SCOT-HEART 2 (Scottish Computed Tomography of the Heart 2) trial, which aims to determine whether screening with the use of CT coronary angiography is more clinically effective than cardiovascular risk scoring to guide the use of primary preventative therapies and reduce the risk of myocardial infarction. (J Am Coll Cardiol Img 2024; - - - - ) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
The Framingham Heart Study was pivotal in understanding the role of key risk factors in the development of cardiovascular disease.\(^4\) This led to the concept of risk factor identification and modification, which has become the focus of cardiovascular disease prevention, and the subsequent development of probabilistic risk scoring. Over the years, many risk-prediction tools have been developed for patients with certain diseases, different ages, and specific geographic locations throughout the world.\(^5\) Furthermore, risk-prediction tools for future cardiovascular events often focus on the medium-term (10-year) risk, which for younger patients often does not represent their true lifetime risk of cardiovascular disease.\(^6\)

At present, the American College of Cardiology and American Heart Association advocate the use of the Pooled Cohort Equation to help guide shared decision making between patients and physicians on the prevention of cardiovascular disease. A position statement acknowledging the plan to move to a more contemporary risk score (Predicting Risk of Cardiovascular Disease Events) is anticipated in the near future, but it remains to be established whether its introduction will have an impact on cardiovascular outcomes.\(^7,8\) In Europe, the European Society of Cardiology guidelines on cardiovascular disease prevention recommend the SCORE-2 risk score.\(^9\) However, all risk scores are based on retrospective observational population-level data to model an individual’s risk of cardiovascular events over a defined period of time. The health of a nation and the prevalence of disease continually change, and risk scores derived from such data will inevitably lag behind the true contemporary prevalence of disease and associated risk factors. For example, recent population health estimates have shown a reduction in blood pressure, serum cholesterol, and smoking prevalence, but a rising burden of obesity and diabetes.\(^10\) Therefore, risk-prediction models require ongoing calibration and validation to be accurate for the population in which they are being used.\(^11\)

The Pooled Cohort Equation overestimates the risk of cardiovascular disease, which leads to overtreatment with preventative therapies.\(^12,13\) But it also underestimates the risk in younger patients, especially young women and those from areas of greater socioeconomic deprivation.\(^14,15\) For example, most patients <50 years of age who have had a myocardial infarction would not have achieved a sufficient risk threshold to qualify for preventative therapy on the day before their cardiac event.\(^14\) This leaves considerable room for improvement in the identification of cardiovascular risk.

Perhaps surprisingly, the clinical application of a risk-scoring strategy has been demonstrated to be ineffective in reducing cardiovascular events.\(^16\) The reasons for this are likely multifactorial and may be due to both patient and physician factors.\(^17\) Patients feel well and often do not appreciate their own cardiovascular risk or comprehend what their calculated risk score means, and they may prefer to try lifestyle changes rather than medication with potential side-effects.\(^16,19\) Indeed, uptake of, and compliance with, preventative medications and interventions is low in those eligible for treatment, with previous population-based studies reporting that only one-third of eligible patients offered statin therapy take it.\(^20\)

From the physician’s perspective, selecting which risk score to use can be a source of confusion. Indeed, the interpretation of the results may be challenging, especially when there is no global consensus on treatment thresholds for preventative therapy.\(^21,22\) Furthermore, physicians are concerned about overtreating and medicalizing healthy individuals, and there is often a strong emphasis on statin therapy with insufficient attention to other risk and lifestyle factors, such as smoking, diet, and exercise.\(^22,23\) Finally, there are competing demands on physicians’ time, and they may not be able to give cardiovascular risk assessment and prevention the priority it requires. A recent cluster randomized controlled trial of providing financial incentives to health care providers to conduct rigorous cardiovascular risk assessments and treatment of at-risk individuals failed to demonstrate a clinically or statistically significant improvement in the primary endpoint of myocardial infarction or stroke at 5 years.\(^24\)

In summary, although risk scoring can help in providing guidance to health professionals that enables them to screen individuals at risk of cardiovascular disease and start preventative therapies, the evidence to support their use is weak, with no definitive randomized controlled trials to support their routine clinical use. We suggest that a new approach is needed. A clearer and potentially more acceptable approach would be to screen for the presence of subclinical atherosclerotic cardiovascular disease rather than rely on probabilistic scores that many individuals struggle to accept and to act upon. There have been many advances in noninvasive cardiovascular imaging that could allow for a precision medicine approach, whereby early covert disease is
detected and treated before clinical manifestations of disease occur. This raises the question of whether we should screen for subclinical disease or rely on cardiovascular risk scores.

SCREENING FOR DISEASE

CORONARY ARTERY IMAGING. The concept of using imaging to guide preventative therapy is not new but has previously used surrogate markers, such as carotid arterial intimal thickening, or indirect measures, such as coronary artery calcification. To date, these studies have not demonstrated a change in outcome compared with standard care. To understand the utility of coronary artery calcium scoring in risk prediction, it is important to appreciate how coronary artery calcium is calculated. Coronary artery calcium scoring was first described by Agatston et al. in 1990, and the Agatston Score has since become the standard method of assessing overall coronary calcification. It uses contiguous 3-mm CT slices to detect calcified plaque within the coronary arterial tree that must be $\geq 130$ HU in $\geq 3$ consecutive pixels (corresponding to $>1$ mm$^3$). The area of such calcification is then multiplied by a weighting factor based on the peak attenuation within the area, and the weighted sum of all calcified plaques is presented as the total Agatston Score. It was initially developed for use in electron-beam CT scanners and not the multidetector CT scanners that was initially developed for use in electron-beam CT angiography. Clinically, this is important, because it predominantly occurs in younger patients, and those with noncalcific plaque have a higher rate of major adverse cardiovascular events. Interestingly, dense calcified plaque is inversely related to cardiovascular events, whereas widespread diffuse or spotty calcification correlates strongly with adverse events. However, coronary artery calcium scoring is relatively cheap, quick to perform and does not require the administration of intravenous contrast media, making it an attractive approach for population screening.

CLINICAL TRIALS OF CORONARY CALCIUM SCORING. There has been 1 reported randomized control trial that incorporated the use of CT coronary artery calcium scoring to guide primary prevention of cardiovascular disease: the DANCAVAS (Danish Cardiovascular Screening) trial. That study randomized asymptomatic men aged 65 to 74 years of age to undergo routine care or multimodality screening for cardiovascular disease, including coronary artery calcium scoring. It demonstrated no difference in the primary endpoint of all-cause mortality and borderline beneficial effects on the secondary outcome of myocardial infarction (HR: 0.91; 95% CI: 0.81-1.03). However, the generalizability of the study is limited because of the narrow older age range, male sex only, and high baseline use of preventive therapies, such as statins, before recruitment.

The ROBINSCA (Risk or Benefit in Screening for Cardiovascular Disease) (n = 43,447) and the CorCAL (Effectiveness of a Proactive Cardiovascular Primary Prevention Strategy, With or Without the Use of Coronary Calcium Screening, in Preventing Future Major Adverse Cardiac Events) (n = 601) trials randomized patients to primary prevention with statin and angiotensin-converting enzyme inhibitors or statin therapy alone, respectively, based on either traditional risk scoring alone or coronary artery calcium scoring. The use of coronary artery calcium scoring in both studies categorized more patients as low risk compared with probabilistic risk scoring within standard care. In both studies, this led to fewer patients starting preventative medication in the coronary artery calcium scoring arm compared with standard care. The impact of calcium scoring on cardiovascular outcomes in both studies is awaited.

CT CORONARY ANGIOGRAPHY. There are currently no guideline recommendations for the role of CT coronary angiography in guiding primary prevention, reflecting an absence of randomized controlled trial evidence for this indication. CT coronary angiography has several advantages over other imaging modalities as it allows for the detection of both atherosclerotic plaque and the severity of coronary artery stenoses.
The absence of any coronary artery plaque confers a favorable prognosis for patients, with the future risk of myocardial infarction in the years following CT coronary angiography being exceptionally low. Crucially, CT coronary angiography provides more detailed assessment of coronary plaque composition, allowing the detection of both calcified and noncalcified plaque as well as identification of plaque features associated with adverse outcomes. In particular, the burden of quantitatively assessed low-attenuation plaque, a marker of the lipid-rich necrotic core, demonstrates powerful prognostic information beyond CT calcium scoring and stenosis assessment. However, CT coronary angiography is
more complex to perform than calcium scoring, requiring the administration of intravenous contrast media, heart-rate limiting medications, and sublingual nitrate.

**CLINICAL TRIALS OF CT CORONARY ANGIOGRAPHY.** The FACTOR-64 (Screening for Asymptomatic Obstructive Coronary Artery Disease Among High-Risk Diabetic Patients Using CT Angiography, Following Core 64) trial is currently the only randomized control trial to evaluate the role of CT coronary angiography in primary prevention. It recruited 900 patients with type 1 or type 2 diabetes mellitus who had no history of coronary, cerebrovascular, or peripheral arterial disease and randomized them to either standard care or CT coronary angiography. The study showed no demonstrable benefit of CT coronary angiography guided therapy on death, nonfatal myocardial infarction, or unstable angina hospitalization at 4 years. There was minimal impact on cardiovascular risk factors: CT coronary angiography-guided therapy led to no improvement in glycated hemoglobin, blood pressure, or triglyceride concentrations, and only minimal reductions in low-density lipoprotein (2.1 mg/dL [0.06 mmol/L]) and increases in high-density lipoprotein (0.8 mg/dL [0.02 mmol/L]) cholesterol concentrations. This reflected the excellent baseline control of cardiovascular risk factors in the standard care group with little room to improve patient treatment or care with the addition of CT coronary angiography.

The SCOT-HEART (Scottish Computed Tomography of the Heart) trial recruited 4,146 symptomatic patients who were referred to a cardiology clinic for the assessment of stable chest pain. In that trial, 75% of participants did not have obstructive coronary artery disease, although nonobstructive coronary artery disease was common, occurring in 38% of patients in the CT coronary angiography arm of the study. Those participants often had cardiovascular risk factors, and they were more likely to be started on preventative therapy than those in the standard care arm. This resulted in halving of the 5-year event rates of fatal or nonfatal myocardial infarction. Whether this can be extrapolated to asymptomatic at-risk individuals is unclear, and that is the focus of the SCOT-HEART 2 Trial. The study showed no demonstrable benefit of CT coronary angiography-guided therapy on death, nonfatal myocardial infarction, or unstable angina hospitalization at 4 years. There was minimal impact on cardiovascular risk factors: CT coronary angiography-guided therapy led to no improvement in glycated hemoglobin, blood pressure, or triglyceride concentrations, and only minimal reductions in low-density lipoprotein (2.1 mg/dL [0.06 mmol/L]) and increases in high-density lipoprotein (0.8 mg/dL [0.02 mmol/L]) cholesterol concentrations. This reflected the excellent baseline control of cardiovascular risk factors in the standard care group with little room to improve patient treatment or care with the addition of CT coronary angiography.

The SCOT-HEART 2 Trial Rationale and Design

![Eligibility Criteria for the SCOT-HEART 2 Trial](image)

**FIGURE 1** Eligibility Criteria for the SCOT-HEART 2 Trial

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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<tr>
<td>≥40 and ≤70 years of age</td>
<td>Inability to give informed consent</td>
</tr>
<tr>
<td>Resident in Scotland</td>
<td>Inability or unwilling to undergo CT coronary angiography</td>
</tr>
<tr>
<td>At least one risk factor for coronary artery disease:</td>
<td>Pregnant or breastfeeding</td>
</tr>
<tr>
<td>1. Hypertension</td>
<td>Known coronary artery disease or other major atherosclerotic cardiovascular disease</td>
</tr>
<tr>
<td>2. Hypercholesterolemia</td>
<td>Previous invasive or non-invasive coronary angiography within the last 5 years</td>
</tr>
<tr>
<td>3. Current or recent smoking habit</td>
<td>eGFR &lt;30mL/min/1.73m²</td>
</tr>
<tr>
<td>4. Diabetes mellitus</td>
<td>Known familial hypercholesterolaemia or other inherited lipid disorder requiring lipid lowering therapy</td>
</tr>
<tr>
<td>5. Family history of cardiovascular disease</td>
<td>Intolerance of all statins</td>
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<tr>
<td>6. Chronic kidney disease stage III (eGFR 30-59mL/min)</td>
<td>Lipid lowering therapy for &gt;2 years</td>
</tr>
<tr>
<td>7. Systemic inflammatory condition (Rheumatoid arthritis, systemic lupus erythematosus)</td>
<td>CT = computed tomography; eGFR = estimated glomerular filtration rate; SCOT-HEART 2 = Scottish Computed Tomography of the Heart 2.</td>
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**RATIONALE FOR CT CORONARY ANGIOGRAPHY VS CT CORONARY ARTERY CALCIUM SCORING.** When selecting a test for cardiovascular screening, the principles outlined by Wilson and Jungner need to be considered. CT coronary artery calcium scoring is relatively inexpensive ($48-$246), and acquisition of images and interpretation can be readily performed. Although coronary artery calcification signifies the presence of coronary artery disease, the converse is not true. Up to 1 in 6 patients with a coronary artery calcium score of zero have noncalcified coronary artery plaque, and this is particularly important for individuals aged 40 to 60 years. Furthermore, the coronary artery calcium score does not indicate the level of stenosis or the extent or distribution of disease.

CT coronary angiography detects coronary artery plaque along its evolutionary spectrum, regardless of whether calcium is present or not. It not only characterizes the presence or absence of disease, but provides information on the severity of stenosis and extent and distribution of disease. Patients with nonobstructive and nonextensive disease have a lower risk of future myocardial infarction than those with obstructive or extensive disease. This in turn could allow for more intensive preventative therapy and lifestyle modification in patients at higher risk. Whether this tiered approach to primary prevention
would result in a difference regarding cardiovascular outcomes needs to be established.

The selection of CT coronary angiography over CT coronary artery calcium scoring is based on its greater sensitivity for the detection of coronary artery disease, its better characterization of coronary artery disease severity, and the selection of treatment intensity depending on disease severity. The higher costs ($311-$737) and complexity of CT coronary angiography do need to be balanced against its superior performance. However, CT coronary angiography is the best and most accurate approach to assess coronary artery disease noninvasively and therefore the most appropriate to establish whether an imaging-based screening approach is superior to cardiovascular risk scores. The SCOT-HEART 2 trial aims to address this question. However, it has not been designed to determine the effectiveness of CT coronary angiography compared with CT coronary artery calcium scoring in cardiovascular screening to guide primary prevention. It will require future studies to address that specific question.

THE SCOT-HEART 2 TRIAL

STUDY DESIGN. The SCOT-HEART 2 trial is a prospective open-label parallel-group randomized controlled trial that will compare cardiovascular risk scoring and screening for coronary artery disease with CT coronary angiography to guide primary prevention recommendations (Central Illustration).

STUDY OBJECTIVES. The primary objective of the trial is to determine whether screening for coronary artery disease with CT coronary angiography is more clinically effective than cardiovascular risk scoring in guiding primary prevention recommendations.

PATIENT POPULATION. The study aims to recruit at least 6,000 participants from across Scotland. Participants are being identified through their primary care providers and sent an invitation letter to participate in the trial. Participants can also directly refer themselves to be considered for the trial through an online portal. All participants are assessed for their potential eligibility before being invited for their initial study visit and subsequent randomization (Figure 1). All participants must be asymptomatic and have at least 1 risk factor for cardiovascular disease to be eligible for enrolment in the trial (Figure 1). We will record a participant’s age at randomization, sex, ethnicity, Scottish Index of Multiple Deprivation (an area-based measure of socioeconomic deprivation within Scotland),50 presence of hypertension, hypercholesterolemia, diabetes, smoking status, and baseline cardiovascular risk score. We will record the use of lipid-lowering drugs at baseline. Participants will complete a health, economic, and lifestyle questionnaire at baseline.

STUDY INTERVENTION. Patients will be randomized 1:1 to primary prevention recommendations guided by routine care with cardiovascular risk scoring (ASSIGN score) or by CT coronary angiography.51

FIGURE 2 Definition of Normal, Nonobstructive, and Obstructive Coronary Artery Disease in the SCOT-HEART 2 Trial

<table>
<thead>
<tr>
<th>Definition of Coronary Artery Disease</th>
<th>Normal</th>
<th>Non-obstructive disease</th>
<th>Obstructive disease</th>
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<tr>
<td>No evidence of coronary artery plaque in any major epicardial artery or &lt;10% plaque stenosis by luminal cross sectional area</td>
<td>Atherosclerotic plaque stenosis &lt;70% by luminal cross sectional area but &gt;10% stenosis in at least one major epicardial artery</td>
<td>Plaque stenosis ≥70% by luminal cross sectional area in at least one major epicardial artery or ≥50% stenosis of the left main stem</td>
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Abbreviation as in Figure 1.
**STANDARD CARE.** All patients within the study will have their ASSIGN 10-year cardiovascular risk score calculated. This is a cardiovascular risk score that has been validated in and calibrated for the Scottish population and currently guides treatment decisions across Scotland. In patients randomized to receive standard care, their ASSIGN score will guide treatment recommendations. Patients and their primary care physician will receive their calculated score and recommendation from the study. Patients with a 10-year cardiovascular risk predicted at $10\%$ will have a recommendation to adhere to a healthy lifestyle and to consider statin therapy. For patients who have a 10-year cardiovascular risk score calculated at $<10\%$, only adherence to a healthy lifestyle will be recommended.

**CT CORONARY ANGIOGRAPHY.** Participants who are randomized to CT coronary angiography will undergo a noncontrast electrocardiography-gated CT scan to measure the CT coronary artery calcium score before having an electrocardiography-gated contrast-enhanced CT coronary angiogram during suspended respiration, with the use of a 64- or more multi-detector CT scanner according to international guidelines. Participants who are randomized to CT coronary angiography will have their treatment recommendations based on the result of their CT findings (Figure 2). The CT coronary artery calcium score will not be reported to the research team or clinicians but will inform comparisons with the CT coronary angiography findings.

Participants who have no evidence of coronary artery disease will receive lifestyle recommendations only. Participants who have nonobstructive coronary artery disease ($<70\%$ cross-sectional luminal stenosis) will receive lifestyle advice and a recommendation to start 75 mg aspirin (or clopidogrel if intolerant to aspirin) and lipid-lowering therapy (20 mg atorvastatin). Participants with obstructive coronary artery disease (cross-sectional luminal stenosis $>70\%$) will receive lifestyle recommendations, 75 mg aspirin (or clopidogrel if intolerant to aspirin) and high-dose statin therapy (80 mg atorvastatin) and will be reviewed in the cardiology clinic.

**OUTCOMES AND CLINICAL FOLLOW-UP.** The primary outcome of the study is the composite of coronary heart disease death or non-fatal myocardial infarction (Figure 3). The main secondary outcomes are coronary heart disease death, nonfatal myocardial infarction, fatal myocardial infarction, all-cause death, noncardiovascular death, fatal stroke, nonfatal stroke, major bleeding, invasive coronary angiography, percutaneous coronary intervention, and coronary artery bypass surgery.

Patients will be followed for a period of 5 years. All outcomes will be obtained through the electronic Data Research and Innovation Service and the General Register Office. Health economic and lifestyle questionnaires will be sent to all study participants at 6 months. This will explore health care-related quality of life (HRQOL) (EQ-5D-5L) and use of National Health Service resources. The first 3,000 participants recruited will receive a further HRQOL questionnaire 2 years after randomization.

**ADDITIONAL ANALYSES.** We will compare the proportion of patients who receive a recommendation for...
primary prevention, those with an ASSIGN 10-year cardiovascular risk score $\geq$10%, and those with evidence of coronary artery disease on CT coronary angiography. In addition, we will perform a sub-analysis comparing primary and secondary outcomes for patients who were and were not recommended primary prevention in each arm, those with an ASSIGN 10-year cardiovascular risk score <10% and $\geq$10%, and those with and without coronary artery disease on CT coronary angiography. We will assess the cost of treatment, the proportion of patients filling prescriptions for primary prevention, and the reported adherence to recommended primary-prevention therapies.

**SAMPLE SIZE AND POWER.** The SCOT-HEART 2 trial will likely have a low overall event rate, which is common to primary prevention trials. In a CT coronary angiography substudy of the Copenhagen General Population Study, the composite endpoint of myocardial infarction or all-cause death was 2.7% (260/9,533) after 3.5 years of follow-up. In the nonanginal chest pain group of the SCOT-HEART trial, we observed a 5-year event rate of 2.5% (18/735), with treatment and effect sizes equating to HRs from 0.45 to 0.65 across all subgroups with differing levels of risk. In the SCOT-HEART 2 trial, we will randomize 6,000 participants, which will give 90% power at a 5% level of significance to detect treatment effects across a range of HRs (corresponding to observing aggregates of around 90, 116, 142, 169, and 196 events) for 5-year primary outcome rates of 2.0%, 2.5%, 3.0%, 3.5%, or 4.0%, respectively. Where insufficient events have accrued, extending follow-up can be undertaken at minimal cost.

**DISCUSSION**

The debate continues as to whether we should consider population screening for coronary heart disease with CT coronary angiography or undertake cardiovascular risk scoring (Figure 4). There are theoretical benefits for both approaches, but currently neither has a strong evidence base. We have already highlighted the shortcomings of a risk score-based approach, but will a screening approach with CT coronary angiography be more beneficial? The potential hazards of screening need to be considered. First, although patients may welcome screening, the finding of coronary disease may cause undue alarm and concern. It can also have implications for some forms of employment and insurance premiums. For cancer screening program, the vast majority of those screened are given the “all-clear,” whereas coronary artery disease will be present in at least one-half of middle-aged individuals. Second, there are the consequences of incidental findings and the potential for unnecessary further downstream testing. Third, there are the hazards of ionizing radiation exposure and the rare risk of anaphylaxis or renal impairment from contrast media. Finally, a reassuring normal CT coronary angiogram may lead to adverse lifestyle changes leading to health problems later in life, and younger patients may require subsequent repeated screening scans to estimate future risk.

It is important to assess everyone’s quality of life, especially in asymptomatic individuals being considered for preventative therapies. In the first SCOT-HEART trial of patients with stable chest pain symptoms, CT coronary angiography was associated with a smaller improvement in quality of life compared with standard care. This appears to be a consequence of the finding of nonobstructive coronary artery disease, whereby patients were not given a cause for their symptoms but needed further medication for the incidental finding of coronary artery disease. Conversely, patients who were found to have normal coronary arteries had the biggest improvements in quality of life. It will be important to understand the effect of CT coronary angiography on quality of life in individuals undergoing health screening in the absence of symptoms.
The benefits of screening are potentially important. First, this leads to a personalized approach where overtreatment or undertreatment is avoided (Figure 5). This may also lead to better engagement of individuals in lifestyle intervention and acceptance of preventative therapies for those with proven coronary artery disease. Moreover, this may enable better targeting of antiplatelet therapies for the prevention of coronary thrombosis. Recent primary prevention trials of antiplatelet therapy have highlighted that beneficial reductions in atherothrombotic events are counterbalanced by the increased hazard of major bleeding events. This has led to a reluctance to prescribe antiplatelet therapy for the primary prevention of atherosclerotic cardiovascular disease. However, because risk scores overestimate risk, many of the individuals treated with antiplatelet therapy do not have underlying atherosclerotic disease and will have the hazards without the potential benefit from such therapy. A screening approach with the use of CT coronary angiography would avoid this imbalance, facilitating a more targeted approach that may allow for the benefits to outweigh the small hazard of major bleeding. This will be addressed in

**FIGURE 5** Case Examples of Patients Enrolled in the SCOT-HEART 2 Trial

(A) Case example 1: A patient identified as low risk by ASSIGN Score who was found to have nonobstructive coronary artery disease in the proximal left anterior descending coronary artery (LAD). (B) Case example 2: A patient identified as high risk of future cardiovascular events by ASSIGN Score who had normal coronary arteries. (C) Case example 3: A patient identified as intermediate risk of future cardiovascular events was found to have obstructive disease affecting his left main stem and left anterior descending coronary artery. Abbreviations as in Figure 1.
The SCOT-HEART 2 Trial Rationale and Design

**HIGHLIGHTS**

- Cardiovascular death is rising, and the current strategy of probabilistic risk scoring is failing.
- CT coronary angiography allows enhanced risk stratification and tailoring of preventative therapy.
- Whether this screening strategy improves outcomes is yet to be determined.

the SCOT-HEART 2 trial, which has therefore been highlighted as a potential guideline-informing trial by the National Institute for Clinical Excellence.29

Over the coming years, several trials will report to establish the role of CT coronary angiography in delivering cost-effective primary prevention strategies to prevent the devastating consequences of myocardial infarction. There are potential risks and benefits for the patient, the physician, and health care providers with all strategies, and it will be important to quantify them to determine whether screening for coronary artery disease delivers on the promise of personalized medicine and better targeted preventative therapies.

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