Coronary CT angiography-guided management of patients with stable chest pain: 10-year outcomes from the SCOT-HEART randomised controlled trial in Scotland

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Summary

Background The Scottish Computed Tomography of the Heart (SCOT-HEART) trial demonstrated that management guided by coronary CT angiography (CCTA) improved the diagnosis, management, and outcome of patients with stable chest pain. We aimed to assess whether CCTA-guided care results in sustained long-term improvements in management and outcomes.

Methods SCOT-HEART was an open-label, multicentre, parallel group trial for which patients were recruited from 12 outpatient cardiology chest pain clinics across Scotland. Eligible patients were aged 18–75 years with symptoms of suspected stable angina due to coronary heart disease. Patients were randomly assigned (1:1) to standard of care plus CCTA or standard of care alone. In this prespecified 10-year analysis, prescribing data, coronary procedural interventions, and clinical outcomes were obtained through record linkage from national registries. The primary outcome was coronary heart disease death or non-fatal myocardial infarction on an intention-to-treat basis. This trial is registered at ClinicalTrials.gov (NCT01149590) and is complete.

Findings Between Nov 18, 2010, and Sept 24, 2014, 4146 patients were recruited (mean age 57 years [SD 10], 2325 [56·1%] male, 1821 [43·9%] female), with 2073 randomly assigned to standard care and CCTA and 2073 to standard care alone. After a median of 10·0 years (IQR 9·3–11·0), coronary heart disease death or non-fatal myocardial infarction was less frequent in the CCTA group compared with the standard care group (137 [6·6%] *vs* 171 [8·2%]; hazard ratio [HR] 0·79 [95% CI 0·63–0·99], p=0·044). Rates of all-cause, cardiovascular, and coronary heart disease death, and non-fatal stroke, were similar between the groups (p>0·05 for all), but non-fatal myocardial infarctions (90 [4·3%] *vs* 124 [6·0%]; HR 0·72 [0·55–0·94], p=0·017) and major adverse cardiovascular events (172 [8·3%] *vs* 214 [10·3%]; HR 0·80 [0·65–0·97], p=0·026) were less frequent in the CCTA group. Rates of coronary revascularisation procedures were similar (315 [15·2%] *vs* 318 [15·3%]; HR 1·00 [0·86–1·17], p=0·99) but preventive therapy prescribing remained more frequent in the CCTA group (831 [55·9%] of 1486 *vs* 728 [49·0%] of 1485 patients with available data; odds ratio 1·17 [95% CI 1·01–1·36], p=0·034).

Interpretation After 10 years, CCTA-guided management of patients with stable chest pain was associated with a sustained reduction in coronary heart disease death or non-fatal myocardial infarction. Identification of coronary atherosclerosis by CCTA improves long-term cardiovascular disease prevention in patients with stable chest pain.

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Introduction

Coronary artery disease remains the commonest cause of death around the world and a major source of morbidity and mortality. Non-invasive imaging offers a method to identify coronary artery disease, to improve risk stratification, and to guide patient management. Indeed, several large randomised controlled trials have provided evidence to support the use of coronary CT angiography (CCTA) for patients with stable chest pain, and CCTA is now a central part of international guidelines.[1,2] However, whether CCTA-guided care results in a sustained long-term improvement in management and outcomes is unknown.

The Scottish Computed Tomography of the Heart (SCOT-HEART) randomised controlled trial showed that in patients with suspected angina due to coronary heart disease, CCTA led to a change in diagnosis in 27% of patients, a change in investigations in 15% of patients, and a change in treatment in 23% of patients.[3] After 5 years of follow-up, this led to a reduction in the composite endpoint of coronary heart disease death or non-fatal myocardial infarction compared with standard care, with similar rates of coronary revascularisation and an increase in the use of preventive therapies.[4] However, the long-term impact of management guided by CCTA is

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See **Online** for appendix

Research in context

Evidence before this study

We searched PubMed from database inception to June 24, 2024, for randomised trials of the impact of coronary CT angiography (CCTA) on outcomes for patients with stable chest pain, using the search terms "computed tomography", "CT", "CCTA", or "CTCA", along with "coronary" or "angina pectoris". This identified 96 studies with follow-up duration ranging from 2 months to 5 years. The PROMISE trial compared CCTA with functional testing (including exercise electrocardiogram, stress echocardiogram, and nuclear stress testing) in 10 003 patients, randomly assigned in a 1:1 ratio. During 2 years of follow-up, the primary endpoint of death, myocardial infarction, hospitalisation for unstable angina, or major procedural complication occurred in 164 (3·3%) of 4996 patients in the CT group compared with 151 (3·0%) of 5006 in the functional-testing group (adjusted hazard ratio 1·04 [95% CI 0·83–1·29], p=0·75). The SCOT-HEART trial had the longest follow-up to date and showed that, after 5 years, there was a reduction in coronary heart disease death or non-fatal myocardial infarction in patients assigned to CT compared with standard care. No randomised trials have assessed outcomes beyond 5 years.

Added value of this study

The SCOT-HEART trial showed that CCTA-guided management led to a reduction in the primary endpoint of coronary heart disease death or non-fatal myocardial infarction, which extended out to 10 years of follow-up (hazard ratio 0·79 [95% CI 0·63–0·99], p=0·044). This was associated with a sustained increase in the use of preventive therapies, but similar overall rates of invasive coronary angiography and revascularisation. This is the first time that the impact of CCTA-guided management has been demonstrated in the long term; the SCOT-HEART trial had the longest follow-up to date for a randomised trial evaluating CCTA in patients with stable chest pain.

Implications of all the available evidence

CCTA-guided management of patients with stable chest pain is associated with prolonged increased use of preventive therapies and both an early and a sustained long-term reduction in myocardial infarction without incurring an excess of coronary revascularisation procedures.

uncertain. The beneficial effects of a more accurate diagnosis might persist due to lifestyle modifications, the more appropriate use of preventive therapy, and access to appropriate medical services. Indeed, the beneficial effects of statin therapy persisted beyond 16 years in the Anglo-Scandinavian Cardiac Outcomes Trial Legacy study[5] and beyond 20 years in the West of Scotland Coronary Prevention Study.[6] However, coronary artery disease is a progressive condition and it is also possible that the benefits on outcomes in the SCOT-HEART trial will attenuate over the longer term, especially where the trial intervention was a single diagnostic test and the standard of care includes increased prescribing of preventive therapies as participants age. Indeed, in A Study of Cardiovascular Events in Diabetes (ASCEND),[7] the beneficial effects of aspirin appeared to be lost after 5 years of therapy. It is therefore important to ascertain whether the beneficial effects of management guided by CCTA persist after 10 years and whether there are subgroups of patients who benefit most.

In this prespecified 10-year analysis of the SCOT-HEART trial, we aimed to assess the impact of CCTA on the long-term management and outcomes of patients who presented to cardiology clinics with suspected angina due to coronary heart disease.

Methods

Study design

The SCOT-HEART trial is an open-label, multicentre, parallel group randomised controlled trial for which patients with stable chest pain attending one of 12 outpatient cardiology chest pain clinics across Scotland were recruited. The trial was approved by the South-East Scotland Research Ethics Committee (10/S1102/43). The trial protocol[8] and primary outcomes[3,4] have been published previously and the trial is registered with ClinicalTrials.gov (NCT01149590). This report describes the prespecified 10-year analysis of the SCOT-HEART trial.

Participants

Participants were recruited from dedicated cardiology chest pain clinics and provided written informed consent. Inclusion criteria were age 18–75 years and the presence of symptoms of suspected stable angina due to coronary heart disease. Exclusion criteria included the inability to give informed consent, inability to undergo CT, renal failure (serum creatinine >250 µmol/L or estimated glomerular filtration rate <30 mL/min per 1·73m²), major allergy to iodinated contrast media, known pregnancy, acute coronary syndrome within 3 months, or previous recruitment into the trial.

Data on race and ethnicity of participants were not collected. Data on sex were collected from patient health records.

Randomisation and masking

Participants in the trial were randomly assigned (1:1) to either standard care alone or standard care plus CCTA. This was performed using a web-based randomisation service which used minimisation to ensure balance for

age, sex, BMI, diabetes, history of coronary heart disease, atrial fibrillation, and baseline diagnosis of angina due to coronary heart disease. Categorisation of clinical outcomes and analysis of data were performed masked to the treatment group allocation.

Procedures

Participants underwent clinical assessment which included history, documentation of cardiovascular risk factors, and examination. Symptoms were classified according to the National Institute for Health and Care Excellence definition[9] as non-anginal chest pain or possible angina. If appropriate, participants underwent symptom-limited exercise electrocardiography using the standard Bruce protocol at the time of the index clinic attendance. Cardiovascular risk was assessed with the ASSIGN (assessing cardiovascular risk using SIGN guidelines) 10-year cardiovascular risk score.[10]

CT imaging was performed at three sites (Edinburgh, Dundee, and Glasgow) as described previously,[3,8] with either 64-detector row (Brilliance 64, Philips Medical Systems, Eindhoven, Netherlands, and Biograph mCT, Siemens, Erlangen, Germany) or 320-detector row (Aquilion ONE, Toshiba Medical Systems, Ōtawara, Japan) scanners. Participants underwent electrocardiogram-gated non-contrast CT for calcium score assessment and electrocardiogram-gated contrast-enhanced CCTA to assess the coronary arteries. Coronary artery disease was defined based on the luminal diameter as normal (<10%), non-obstructive (10–70%), or obstructive stenosis (>70% stenosis in one or more major epicardial vessel or >50% stenosis in the left main stem).

Information on clinical outcomes was obtained from Public Health Scotland via the Electronic Data Research and Innovation Service, and where required, confirmed by review of patient health records. In Scotland, all patients have a unique Community Health Index number against which all health-care data are recorded, including hospital admissions and prescriptions. In addition, linkage can be made to the statutory register of deaths held by National Records of Scotland. Follow-up was administratively censored as of May 17, 2023, for patients without an event.

Information on medication use was obtained from the Prescribing Information System, a national dataset of every prescription dispensed in the community.

Outcomes

The primary outcome of this analysis was the occurrence of coronary heart disease death or non-fatal myocardial infarction. Secondary outcomes include all-cause death, cardiovascular death, coronary heart disease death, non-fatal myocardial infarction, non-fatal stroke, coronary revascularisation, and invasive coronary angiography. ICD-10 codes were used to define outcomes (appendix pp 4–5). Major adverse cardiovascular events were defined as death from coronary heart disease, non-fatal myocardial infarction, or non-fatal stroke. Preventive therapy was defined post hoc as the use of antiplatelet or statin therapy, and a patient was classified as taking preventive therapy if they had such prescriptions dispensed 3 months before or after the start of each year of follow-up.

Safety outcomes have been previously reported and included CT scan radiation dose, adverse reactions during the scan procedure, and presence of incidental findings.[3,4]

Statistical analysis

Statistical analysis was performed with R (version 4.3.2) following the same statistical analysis plan for the previous 5-year analysis with the exception of two prespecified adjustments to the ICD-10 codes (appendix p 4). All analyses were performed on an intention-to-treat basis, irrespective of whether the participant underwent scanning. Sample size was calculated for the change in 6-week diagnosis and for

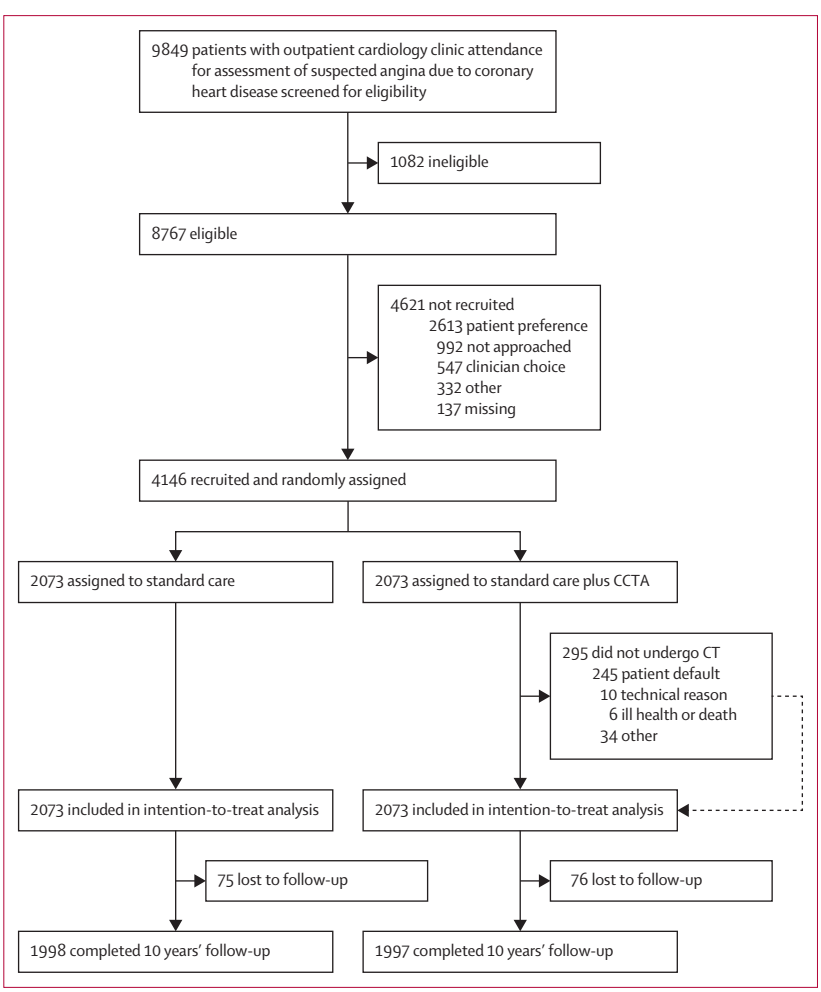

Figure 1: **Trial profile**
CCTA=coronary CT angiography.

the assessment of the primary outcome after 5 years.[8] Normally distributed data are presented as mean and SD. Data that were not normally distributed are presented as median and IQR. Clinical outcomes were assessed with Cox proportional hazards models and with Kaplan–Meier plots including log-rank tests. The proportional hazards assumption was evaluated based on Schoenfeld residuals and was satisfied for the primary outcome and all secondary outcomes, except for revascularisation. Hazard ratios (HRs) are provided with 95% CIs. For the primary outcome of coronary heart disease death or non-fatal myocardial infarction, a multivariable Cox proportional hazards model was created incorporating the variables used for baseline minimisation and in the original trial analysis. In a post-hoc sensitivity analysis, we created Cox proportional hazards models using the original ICD-10 code definitions from the 5-year analysis. Medication use at individual timepoints was compared using the χ^2 test, and as a post-hoc analysis the Cochran–Armitage test for trend was used to assess medication use across the trial. A two-sided p value less than 0·05 was considered statistically significant. Prespecified subgroup analyses were performed for the primary outcome of coronary heart disease death or non-fatal myocardial infarction. For subgroup analyses, we accounted for multiple testing by considering a two-sided p value less than 0·0125 as statistically significant.

	Standard care (n=2073)	CCTA and standard care (n=2073)	All participants (n=4146)
Sex			
Male	1163 (56·1%)	1162 (56·1%)	2325 (56·1%)
Female	910 (43·9%)	911 (43·9%)	1821 (43·9%)
Age, years	57 (10)	57 (10)	57 (10)
BMI, kg/m²	30 (6)	30 (6)	30 (6)
History of coronary heart disease	186 (9·0%)	186 (9·0%)	372 (9·0%)
History of cerebrovascular disease	48 (2·3%)	91 (4·4%)	139 (3·4%)
History of peripheral vascular disease	17 (0·8%)	36 (1·7%)	53 (1·3%)
Smoking status*			
Non-smoker	978 (47·2%)	976 (47·1%)	1954 (47·1%)
Ex-smoker	654 (31·5%)	676 (32·6%)	1330 (32·1%)
Current smoker	436 (21·0%)	419 (20·2%)	855 (20·6%)
Hypertension	683 (32·9%)	712 (34·3%)	1395 (33·6%)
Diabetes	221 (10·7%)	223 (10·8%)	444 (10·7%)
Hypercholesterolaemia	1181 (57·0%)	1229 (59·3%)	2410 (58·1%)
Family history of coronary heart disease	829 (40·0%)	887 (42·8%)	1716 (41·4%)
Anginal symptoms†			
Typical angina	725 (35·0%)	737 (35·6%)	1462 (35·3%)
Atypical angina	486 (23·4%)	502 (24·2%)	988 (23·8%)
Non-anginal chest pain	859 (41·4%)	833 (40·2%)	1692 (40·8%)
10-year cardiovascular risk, %	18 (11)	17 (12)	17 (12)

Data are n (%) or mean (SD). CCTA=coronary CT angiography. *Data were missing for five patients in the standard care group and two in the CCTA group. †Data were missing for three patients in the standard care group and one in the CCTA group.

Table 1: **Baseline characteristics of the study population**

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Participants were recruited between Nov 18, 2010, and Sept 24, 2014. Of the 9849 patients who were referred to the outpatient cardiology chest patient clinics, 8767 were eligible and 4146 patients were recruited into the study. Of these, 2073 were randomly assigned to the standard of

	Standard care (n=2073)	CCTA and standard care (n=2073)	HR (95% CI)	p value
Primary outcome				
Coronary heart disease death or non-fatal myocardial infarction	171 (8·2%)	137 (6·6%)	0·79 (0·63–0·99)	0·044
Secondary outcomes				
All-cause death	166 (8·0%)	168 (8·1%)	1·01 (0·82–1·25)	0·93
Coronary heart disease death	62 (3·0%)	60 (2·9%)	0·97 (0·68–1·38)	0·85
Cardiovascular death	89 (4·3%)	85 (4·1%)	0·95 (0·71–1·28)	0·75
Non-fatal myocardial infarction	124 (6·0%)	90 (4·3%)	0·72 (0·55–0·94)	0·017
Non-fatal ischaemic stroke	52 (2·5%)	40 (1·9%)	0·77 (0·51–1·16)	0·21
Major adverse cardiovascular events*	214 (10·3%)	172 (8·3%)	0·80 (0·65–0·97)	0·026
Procedures				
Invasive coronary angiography	575 (27·7%)	554 (26·7%)	0·96 (0·86–1·08)	0·55
Coronary revascularisation	318 (15·3%)	315 (15·2%)	1·00 (0·86–1·17)	0·99
Percutaneous coronary intervention	255 (12·3%)	249 (12·0%)	0·98 (0·83–1·17)	0·86
Coronary artery bypass grafting	73 (3·5%)	80 (3·9%)	1·10 (0·80–1·51)	0·56

CCTA=coronary CT angiography. HR=hazard ratio. *Coronary heart disease death, non-fatal myocardial infarction, or non-fatal stroke.

Table 2: **Clinical outcomes at 10 years**

care alone, and 2073 to CCTA plus standard of care (figure 1).

Across the trial, 2325 (56·1%) participants were male and 1821 (43·9%) female, mean age was 57 years (SD 10) and the mean 10-year cardiovascular risk score was 17% (SD 12; table 1). Among the 1778 who underwent CCTA, the median coronary artery calcium score was 20 Agatston units (IQR 0–230), and normal coronary arteries were identified in 654 (36·7%), non-obstructive coronary artery disease in 672 (37·7%), and obstructive coronary artery disease in 425 (23·9%).

At 10 years, 151 participants were no longer registered in Scotland (3·6%; 76 in the CCTA group and 75 in the standard care group), giving complete follow-up in 3995 (96·4%) participants. After a median of 10·0 years (IQR 9·3–11·0), the primary outcome of coronary artery disease death or non-fatal myocardial infarction remained less frequent in the CCTA group compared with the standard care group (137 [6·6%] *vs* 171 [8·2%], respectively; HR 0·79 [95% CI 0·63–0·99], p=0·044; table 2, figure 2). There was a reduction in non-fatal myocardial infarction (90 [4·3%] *vs* 124 [6·0%]; HR 0·72 [0·55–0·94], p=0·017; appendix p 7). There were no differences in all-cause, cardiovascular, or coronary heart disease deaths, or non-fatal ischaemic stroke (table 2, appendix p 7). Major adverse cardiovascular events (combination of death from coronary artery disease, non-fatal myocardial infarction, or non-fatal stroke) were also reduced in patients whose management was guided by CCTA (172 [8·3%] *vs* 214 [10%]; HR 0·80 [0·65–0·97]; table 2). In a post-hoc sensitivity analysis, similar findings were identified using the original ICD-10 code definitions from the 5-year analysis[4] (table 3, appendix p 8).

At 10 years, there was no difference in the use of invasive coronary angiography between patients who were assigned to CCTA compared with those allocated to standard care alone (554 [26·7%] *vs* 575 [27·7%]; HR 0·96 [95% CI 0·86–1·08]; figure 3A, table 2). There was also no difference in the 10-year rates of coronary revascularisation (315 [15·1%] *vs* 318 [15·3%]; HR 1·00 [0·86–1·17]; figure 3B, table 2). This included similar rates of percutaneous coronary intervention and coronary artery bypass grafting (table 2). Of the patients who had invasive coronary angiography, 249 (44·9%) of 554 in the CCTA group and 265 (46·1%) of 575 in the standard care group did not undergo revascularisation.

In year 10, prescriptions for preventive therapies continued to be higher in patients assigned to CCTA compared with those assigned to standard care alone (831 [55·9%] of 1486 *vs* 728 [49·0%] of 1485 patients with available data; odds ratio 1·17 [95% CI 1·01–1·36], p=0·034). The use of aspirin, antiplatelet, and statin therapy was higher in patients assigned to CCTA than those in the standard care group throughout the follow-up period (appendix p 9). In post-hoc analyses, use of preventive therapies increased in both groups with time (trend: p<0·0001 for CCTA group and p=0·030 for standard care group), with an apparent slight attenuation in the differential rates of prescribing over time (figure 3C).

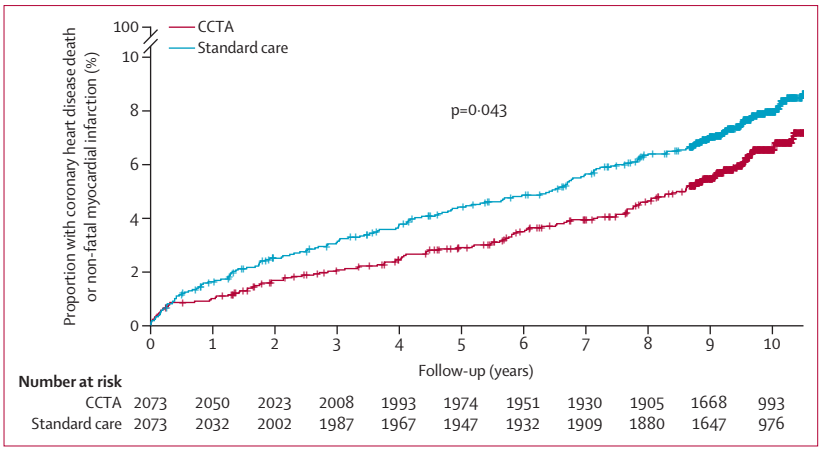

Figure 2: **Cumulative incidence for the primary outcome of coronary heart disease death and non-fatal myocardial infarction**
P value indicates the log-rank test. CCTA=coronary CT angiography.

	Standard care (n=2073)	CCTA and standard care (n=2073)	HR (95% CI)	p value
Non-fatal myocardial infarction	129 (6·2%)	95 (4·6%)	0·73 (0·56–0·95)	0·019
Coronary heart disease death	19 (0·9%)	21 (1·0%)	1·10 (0·59–2·05)	0·760
Coronary heart disease death or non-fatal myocardial infarction	141 (6·8%)	111 (5·4%)	0·78 (0·61–1·00)	0·049

CCTA=coronary CT angiography. HR=hazard ratio.

Table 3: **Post-hoc sensitivity analysis of clinical outcomes at 10 years using ICD-10 codes for myocardial infarction of I21, I22, I249, and I25.6, and for coronary heart disease death of I21, I22, I249, I25.6, and I46**

Across different subgroups, there was no evidence of interaction for the primary outcome (appendix p 11). Female participants appeared to have a more pronounced relative risk reduction in the primary outcome with CCTA compared with male participants, but this was not statistically significant ($p_{interaction}$=0·10). In a multivariable model, age, male sex, diabetes, and history of coronary heart disease were all predictors of the primary outcome (appendix p 6).

Discussion

In patients with stable chest pain, management guided by CCTA was associated with a sustained reduction in death from coronary heart disease or non-fatal myocardial infarction at 10 years, which appeared to be predominantly due to the prevention of non-fatal myocardial infarction. These improvements occurred despite no difference in the use of invasive coronary angiography or coronary revascularisation, although the use of preventive therapies remained higher in those with CCTA-guided management even after 10 years of follow-up. These findings have important

implications for the diagnosis and long-term prevention of coronary artery disease and myocardial infarction.

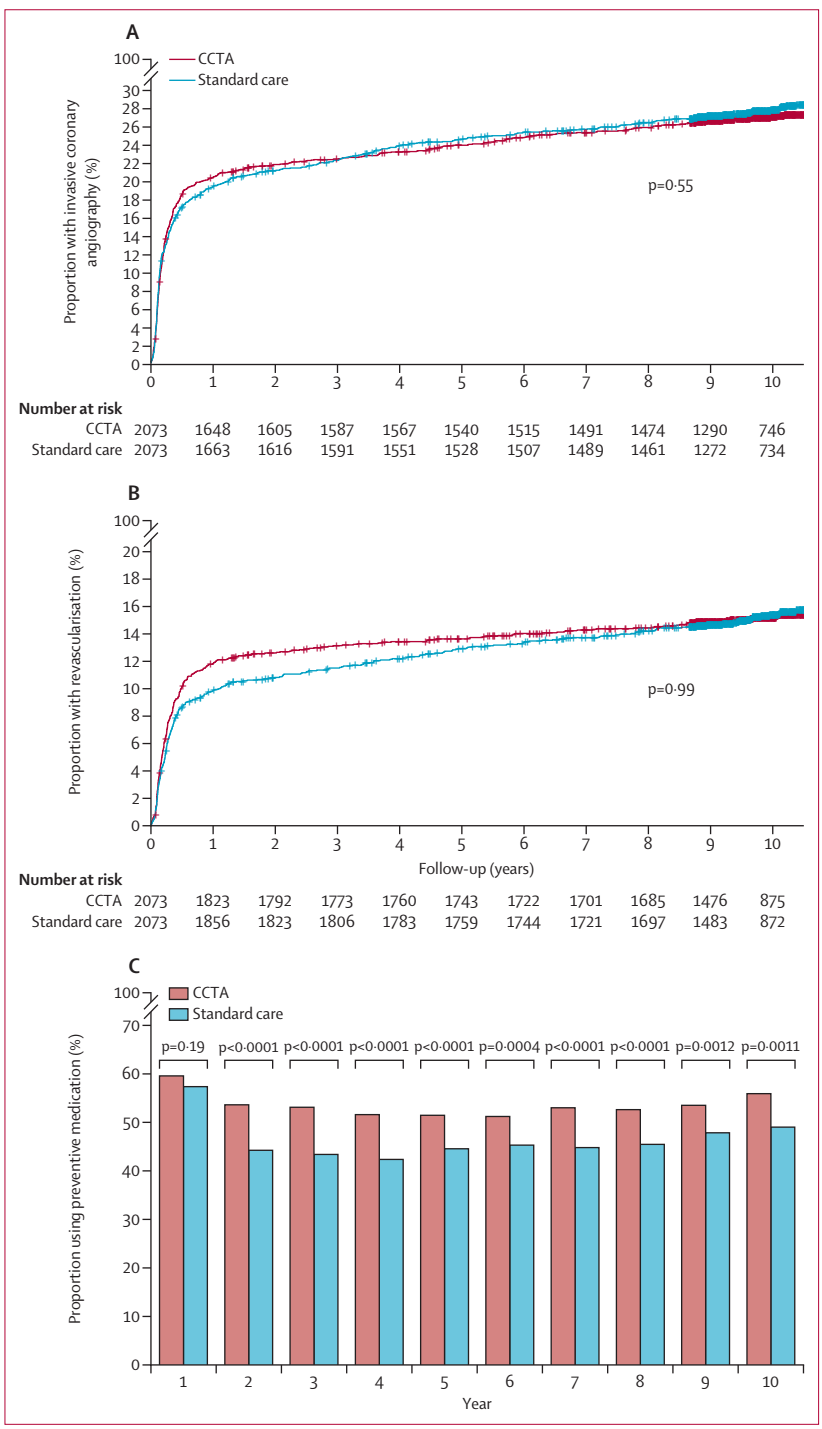

Figure 3: **Cumulative incidence for (A) invasive coronary angiography and (B) coronary revascularisation, and (C) frequency of preventive medication use**

P values in the cumulative incidence plots (A, B) indicate the log-rank test. Panel C shows the preventive medication use in the CCTA group versus the standard care group in the first 3 months of each timepoint, starting from trial recruitment. Comparisons in frequency of medication use between groups were assessed with the χ^2 test. CCTA=coronary CT angiography.

To date, most randomised controlled trials of CCTA-guided care in patients with stable chest pain have only assessed clinical outcomes up to 2–5 years of follow-up,[3,4,11] with a median follow-up of 2 years.[12] In the current analysis, we have now shown that the previously reported beneficial effects of CCTA in reducing rates of coronary heart disease death or non-fatal myocardial infarction extend out to 10 years of follow-up, the longest follow-up of any CCTA trial to date. These extended and sustained benefits appear to be primarily driven by a reduction in the rate of non-fatal myocardial infarction, suggesting that the principal benefit of CCTA is driven by the prevention of coronary artery disease progression and atherothrombotic events.

There were initial concerns that CCTA would lead to an increase in the use of invasive coronary angiography and coronary revascularisation. Indeed, this was reported in the early follow-up period (1–2 years) of both the SCOT-HEART and Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trials.[3,11] This result likely reflects the identification of unrecognised coronary artery disease that triggered further invasive investigation and coronary revascularisation in these symptomatic patients. However, our long-term follow-up data show that this early increase is not sustained, and the subsequent rates of invasive coronary angiography and coronary revascularisation after 1 year are lower,[13,14] resulting in similar overall 10-year rates of invasive coronary angiography and coronary revascularisation. This finding would indicate that CCTA led to more appropriate early use of revascularisation in patients who were more likely to derive benefit from it and reduced the subsequent need for further intervention beyond this initial excess of invasive evaluation and intervention.[13]

We had previously reported that patients in the CCTA group were more likely to be prescribed preventive medications compared with those in the standard care group.[4,14] Others have also highlighted that knowledge of the presence of coronary artery disease on CCTA improves medication acceptance and adherence.[15] We have now shown that this difference in prescribing patterns extends to 10 years. Previous randomised studies have often not assessed the long-term use of cardiovascular medications due to the challenges of data collection. An important advantage of the SCOT-HEART trial is the use of nationally coded health-care datasets for long-term follow-up and the fact that Scotland provides free prescriptions which are recorded in a national database. This prolonged adherence to preventive therapy likely underpins the persistent beneficial effects of CCTA-guided management in preventing myocardial infarction. Moreover, there was a trend for slight increases in prescribing rates across both groups with time, which likely reflects the increasing age and cardiovascular risk of the study

population. However, more detailed information on the mechanisms underlying improved outcomes in these patients is required and will be assessed in ongoing trials.[16]

We explored whether certain subgroups had greater long-term benefits. Although we did not find any definitive evidence of benefit in any subgroup, it is interesting to note that the point estimates for benefit were generally greater in lower-risk groups, perhaps reflecting the identification of previously undetected disease in participants who had been ascribed a lower risk of cardiovascular disease. This was particularly notable for women, who do have a different risk profile to men.[17] Indeed, cardiovascular risk scores underestimate disease in females,[18] and the use of preventive medications in primary care is lower in women.[19] In the SCOT-HEART trial, we have previously shown that women have quantitatively less coronary artery plaque, but those who subsequently experienced myocardial infarction had plaque burdens comparable to those in men.[20] Interestingly, there appears to be a 10-year delay in the development of coronary artery disease in women compared with men, as seen on CCTA in the Swedish Cardiopulmonary Bioimage Study (SCAPIS)[21] of 25 182 asymptomatic individuals, and in the CAC Consortium registry of 63 215 asymptomatic individuals.[22] This observation suggests that CCTA-guided preventive intervention might have greater long-term beneficial effects in lower-risk groups, such as women.

We found no demonstrable effects on all-cause or coronary heart disease mortality and the improvement in the primary outcome was predominantly driven by reductions in non-fatal myocardial infarction. This finding is consistent with many contemporary randomised controlled trials evaluating novel interventions or therapies for coronary heart disease, including those assessing coronary intervention as well as preventive therapies.[7,23,24] This perhaps reflects the effectiveness of current cardiovascular therapy making it increasingly challenging to demonstrate a mortality benefit. In the SCOT-HEART trial, all participants were receiving ongoing long-term care as demonstrated by the high frequency of preventive therapy prescribing over the 10-year follow-up period. Given this engagement, it is perhaps unsurprising that we could not detect a mortality benefit, especially given the overall event rate and a study population that included nearly 40% of participants who had normal coronary arteries.

Both all-cause and coronary heart disease deaths increased between years 5 and 10 of follow-up, consistent with the ageing trial population. The rate of all-cause mortality was more than double that of coronary heart disease mortality, which likely reflects the fact that over a third of trial participants had normal coronary arteries, only a quarter had obstructive coronary artery disease, and cardiovascular preventive therapies were given in nearly two-thirds of those at risk. The differential rate of all-cause and coronary heart disease mortality is consistent with previous trials of preventive therapies in at-risk populations that also included patients with angina pectoris.[25] The increase in coronary heart disease deaths between the 5-year and 10-year analyses also reflects our broadening of the definition of coronary heart disease deaths, as well as the fact that over a third of the trial population were diagnosed with angina pectoris[3] and two-thirds were diagnosed with coronary artery disease on CCTA. For people dying in the community, it would perhaps be unsurprising if coronary artery disease was the registered primary cause of death in many of the trial participants. Non-fatal myocardial infarction might therefore be a more robust diagnosis that is less susceptible to misclassification, and perhaps reflects why it appears to have been the main driver for the difference in the primary endpoint.

Our study has some limitations which we should acknowledge. First, outcomes and medication use were defined based on nationally coded data and there was no independent clinical endpoint adjudication. Coding of hospital episodes was performed independent of the study team and this approach has previously been shown to provide similar results to independent adjudication of cardiovascular endpoints in several other clinical trials.[26–28] Moreover, the diagnosis of coronary artery disease was higher in patients allocated to CCTA,[3] which would be anticipated to lead to overestimation of coronary events in this trial group, meaning our findings are likely to be conservative. However, as this was an open-label trial, we cannot exclude the possibility of ascertainment bias, particularly for the primary and secondary outcomes. Second, a small number of patients would be lost to follow-up if they had emigrated or been admitted to hospital outside of Scotland, although we still had detailed follow-up data in over 96% of the trial population. Third, subsequent crossover of clinical evaluations and investigations (including invasive or non-invasive coronary angiography) might have influenced patient management during the 10 years of follow-up and could have attenuated the differential effects of the trial intervention. Fourth, we have accounted for multiple testing in subgroup analyses but not in other analyses. Fifth, the management of patients with stable coronary artery disease has changed over the past 10 years, partly in response to the results of the SCOT-HEART trial. In particular, the number of patients who undergo invasive coronary angiography might be lower in contemporary practice, especially given the findings of the Diagnostic Imaging Strategies for Patients with Stable Chest Pain and Intermediate Risk of Coronary Artery Disease (DISCHARGE) trial.[29] Patients in the standard care group might have subsequently undergone CCTA since their initial inclusion in our trial, which could have attenuated the effect size reported

here. In addition, CT technology continues to evolve, and this analysis was performed before the advent of the latest generation of photon-counting CT scanners. Finally, the cardiovascular risk score overestimated the 10-year cardiovascular event rate of the study population. This likely reflects the high use of preventive therapies in the trial population, which will modify this risk, as well as the overestimation of cardiovascular risk in contemporary populations, which has been well documented.

In conclusion, we have shown that CCTA-guided management is associated with a beneficial long-term impact on patient care. After 10 years of follow-up, CCTA-guided management continued to be associated with reduction in the rates of coronary heart disease death or non-fatal myocardial infarction and sustained increases in the use of preventive therapies.

Contributors

The SCOT-HEART Investigators contributed to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work. The writing group were involved in drafting the manuscript and revising it. MCW and DEN accessed and verified the underlying data reported in the manuscript. DEN is the guarantor of the study. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

MCW has given talks for Canon Medical Systems, Siemens Healthineers, GE Healthcare, and Novartis, and performed consultancy for FEOPS and Canon Medical Systems. NLM has received honoraria from Abbott Diagnostics, Roche Diagnostics, and Siemens Healthineers. CB is employed by the University of Glasgow, which holds consultancy and research agreements for his work with Abbott Vascular, AstraZeneca, Boehringer Ingelheim, CorFlow, Coroventis, HeartFlow, Menarini, Merck, Novartis, Siemens Healthcare, Xylocor, Zoll, and Valo Health. PDA has given talks for Novartis, performed consultancy for Edwards Lifesciences, and received travel support from Medtronic. ASVS has received honoraria from Abbott Diagnostics. All other authors declare no competing interests.

Data sharing

Long-term follow up of the SCOT-HEART trial makes use of several routine electronic health-care data sources that are only accessible by approved individuals who have undertaken the necessary governance training. Where possible, data will be shared upon reasonable request to the Chief Investigator, DEN (d.e.newby@ed.ac.uk), under a data sharing agreement.

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References

1 Gulati M, Levy PD, Mukherjee D, 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. *Circulation* 2021; **144:** e368–454.

2 Vrints C, Andreotti F, Koskinas KC, et al. 2024 ESC Guidelines for the management of chronic coronary syndromes. *Eur Heart J* 2024; **45:** 3415–537.

3 SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. *Lancet* 2015; **385:** 2383–91.

4 Newby DE, Adamson PD, Berry C, et al. Coronary CT angiography and 5-year risk of myocardial infarction. *N Engl J Med* 2018; **379:** 924–33.

5 Gupta A, Mackay J, Whitehouse A, et al. Long-term mortality after blood pressure-lowering and lipid-lowering treatment in patients with hypertension in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Legacy study: 16-year follow-up results of a randomised factorial trial. *Lancet* 2018; **392:** 1127–37.

6 Ford I, Murray H, McCowan C, Packard CJ. Long-term safety and efficacy of lowering low-density lipoprotein cholesterol with statin therapy: 20-year follow-up of West Of Scotland Coronary Prevention Study. *Circulation* 2016; **133:** 1073–80.

7 Bowman L, Mafham M, Wallendszus K, et al. Effects of aspirin for primary prevention in persons with diabetes mellitus. *N Engl J Med* 2018; **379:** 1529–39.

8 Newby DE, Williams MC, Flapan AD, et al. Role of multidetector computed tomography in the diagnosis and management of patients attending the rapid access chest pain clinic, The Scottish computed tomography of the heart (SCOT-HEART) trial: study protocol for randomized controlled trial. *Trials* 2012; **13:** 184.

9 NICE. Chest pain of recent onset: assessment and diagnosis. NICE, 2016.

10 Woodward M, Brindle P, Tunstall-Pedoe H. Adding social deprivation and family history to cardiovascular risk assessment: the ASSIGN score from the Scottish Heart Health Extended Cohort (SHHEC). *Heart* 2007; **93:** 172–76.

11 Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med* 2015; **372:** 1291–300.

12 Bittencourt MS, Hulten EA, Murthy VL, et al. Clinical outcomes after evaluation of stable chest pain by coronary computed tomographic angiography versus usual care: a meta-analysis. *Circ Cardiovasc Imaging* 2016; **9:** e004419.

13 Adamson PD, Williams MC, Dweck MR, et al. Guiding therapy by coronary CT angiography improves outcomes in patients with stable chest pain. *J Am Coll Cardiol* 2019; **74:** 2058–70.

14 Adamson PD, Newby DE. The SCOT-HEART Trial. What we observed and what we learned. *J Cardiovasc Comput Tomogr* 2019; **13:** 54–58.

15 Feger S, Elzenbeck L, Rieckmann N, et al. Effect of computed tomography versus invasive coronary angiography on statin adherence: a randomized controlled trial. *JACC Cardiovasc Imaging* 2021; **14:** 1480–83.

16 McDermott M, Meah MN, Khaing P, et al. Rationale and design of SCOT-HEART 2 trial: CT angiography for the prevention of myocardial infarction. *JACC Cardiovasc Imaging* 2024; **17:** 1101–12.

17 Mangion K, Adamson PD, Williams MC, et al. Sex associations and computed tomography coronary angiography-guided management in patients with stable chest pain. *Eur Heart J* 2020; **41:** 1337–45.

18 Michos ED, Nasir K, Braunstein JB, et al. Framingham risk equation underestimates subclinical atherosclerosis risk in asymptomatic women. *Atherosclerosis* 2006; **184:** 201–06.

19 Zhao M, Woodward M, Vaartjes I, et al. Sex differences in cardiovascular medication prescription in primary care: a systematic review and meta-analysis. *J Am Heart Assoc* 2020; **9:** e014742.

20 Williams MC, Kwiecinski J, Doris M, et al. Sex-specific computed tomography coronary plaque characterization and risk of myocardial infarction. *JACC Cardiovasc Imaging* 2021; **14:** 1804–14.

21 Bergström G, Persson M, Adiels M, et al. Prevalence of subclinical coronary artery atherosclerosis in the general population. *Circulation* 2021; **144:** 916–29.

22 Shaw LJ, Min JK, Nasir K, et al. Sex differences in calcified plaque and long-term cardiovascular mortality: observations from the CAC Consortium. *Eur Heart J* 2018; **39:** 3727–35.

23 Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017; **376:** 1713–22.

24 Mehta SR, Wood DA, Storey RF, et al. Complete revascularization with multivessel PCI for myocardial infarction. *N Engl J Med* 2019; **381:** 1411–21.

25 Ford I, Murray H, Packard CJ, Shepherd J, Macfarlane PW, Cobbe SM. Long-term follow-up of the West of Scotland Coronary Prevention Study. *N Engl J Med* 2007; **357:** 1477–86.

26 Barry SJE, Dinnett E, Kean S, Gaw A, Ford I. Are routinely collected NHS administrative records suitable for endpoint identification in clinical trials? Evidence from the West of Scotland Coronary Prevention Study. *PLoS One* 2013; **8:** e75379.

27 Harper C, Mafham M, Herrington W, et al. Reliability of major bleeding events in UK routine data versus clinical trial adjudicated follow-up data. *Heart* 2023; **109:** 1467–72.

28 Meah MN, Denvir MA, Mills NL, Norrie J, Newby DE. Clinical endpoint adjudication. *Lancet* 2020; **395:** 1878–82.

29 Maurovich-Horvat P, Bosserdt M, Kofoed KF, et al. CT or invasive coronary angiography in stable chest pain. *N Engl J Med* 2022; **386:** 1591–602.