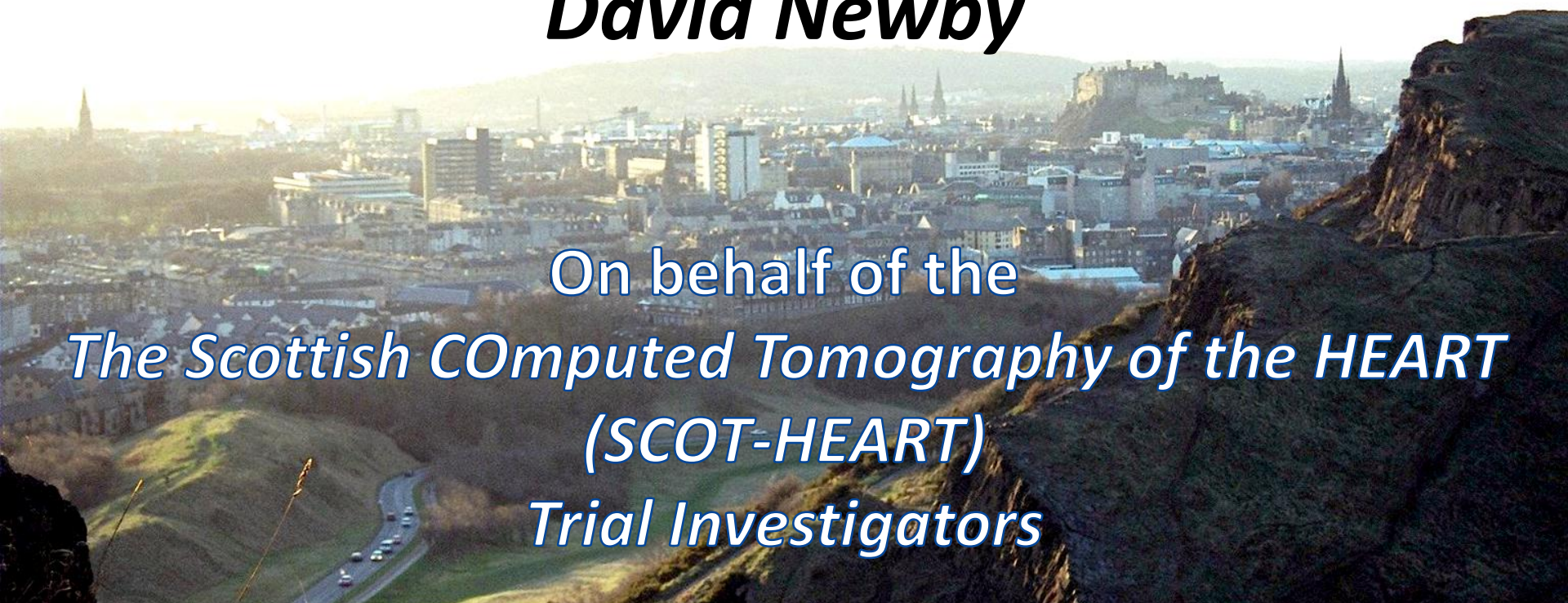
Computed Tomography Coronary Angiography in Patients with Suspected Angina due to Coronary Heart Disease

David Newby

On behalf of the

The Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial Investigators



Declarations

Funder

- **Chief Scientist Office, Scotland, UK (CZH/4/588)**
- **Supplementary awards from Edinburgh and Lothian Health Foundation and the Heart Diseases Research Fund**

Sponsors

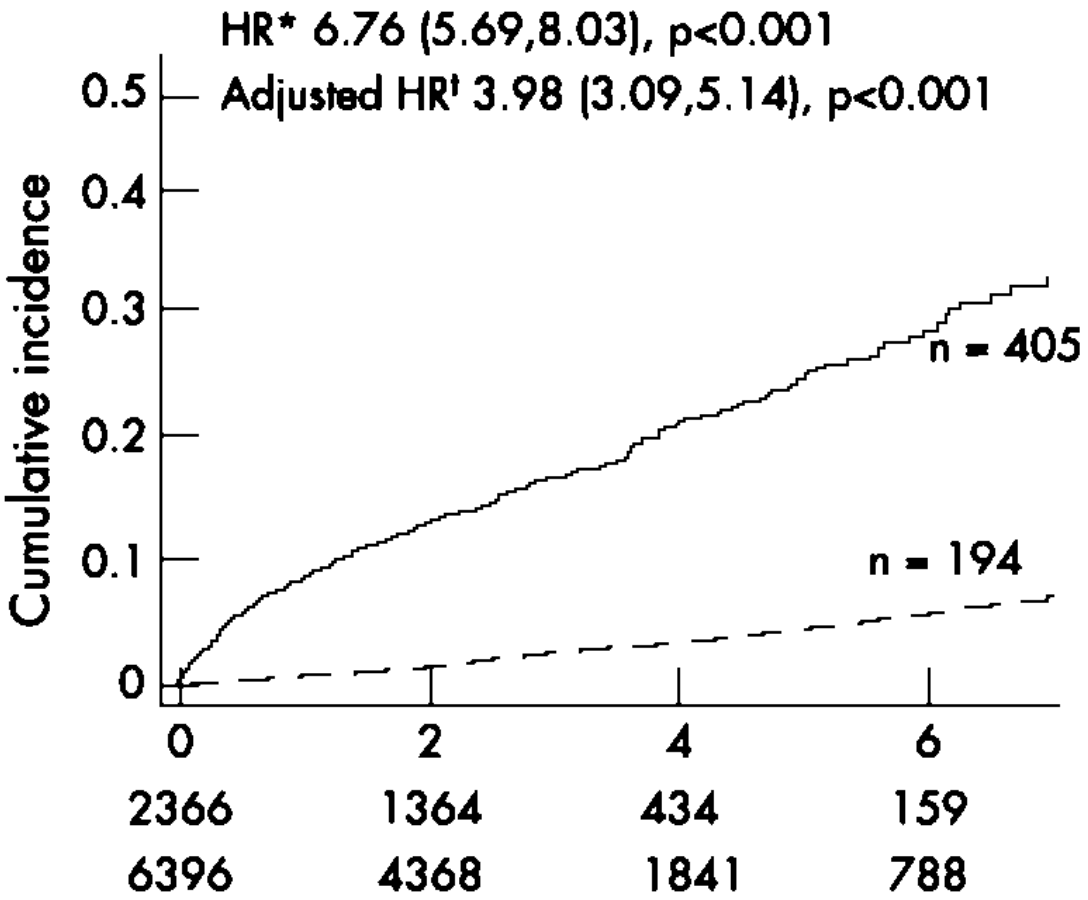
- **University of Edinburgh and NHS Lothian**

Conflicts of Interest

- **DEN, EvB, GMcK and GR have undertaken consultancy for one or more of the following companies: Toshiba, Bracco, Bayer-Schering, GE Healthcare and Guerbet**

Clinic Assessment of Patients with Suspected Angina due to CHD

Fatal and Non-fatal Myocardial Infarction



Angina due to Coronary Heart Disease

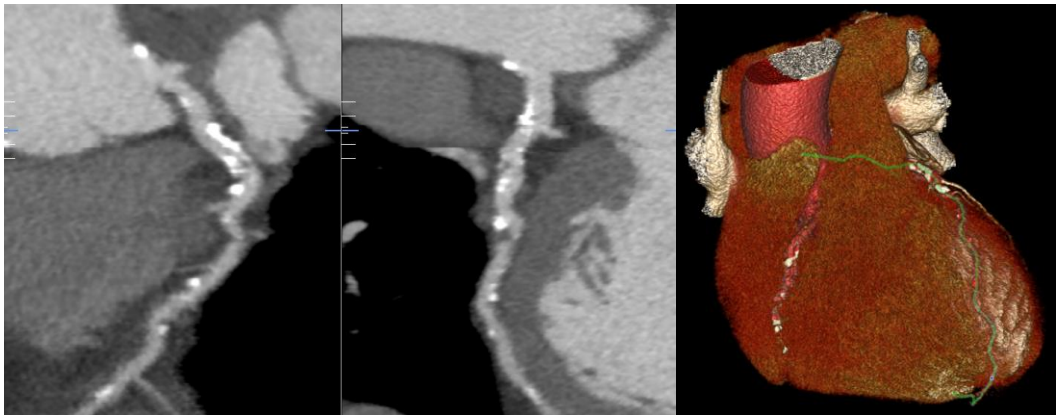
Non-cardiac Chest Pain

Sekhri *et al*. *Heart* 2007;93:458–463

Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

First trial to assess the clinical impact of the addition of CTCA in patients presenting with suspected angina due to coronary heart disease in the Cardiology clinic

- **Diagnosis (Primary Endpoint)**
- **Investigations**
- **Treatments**
- **Outcomes**



Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Diagnosis: Primary Endpoint

Diagnosis of Coronary Heart Disease

Diagnosis of Angina due to Coronary Heart Disease

- **Yes**
- **Probable**
- **Unlikely**
- **No**

Certainty:
Yes/No *versus* Probable/Unlikely

Frequency:
Yes/Probable *versus* Unlikely/No

Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Entry Criteria

Inclusion Criteria

- Age 18-75 years
- Suspected angina due to coronary heart disease

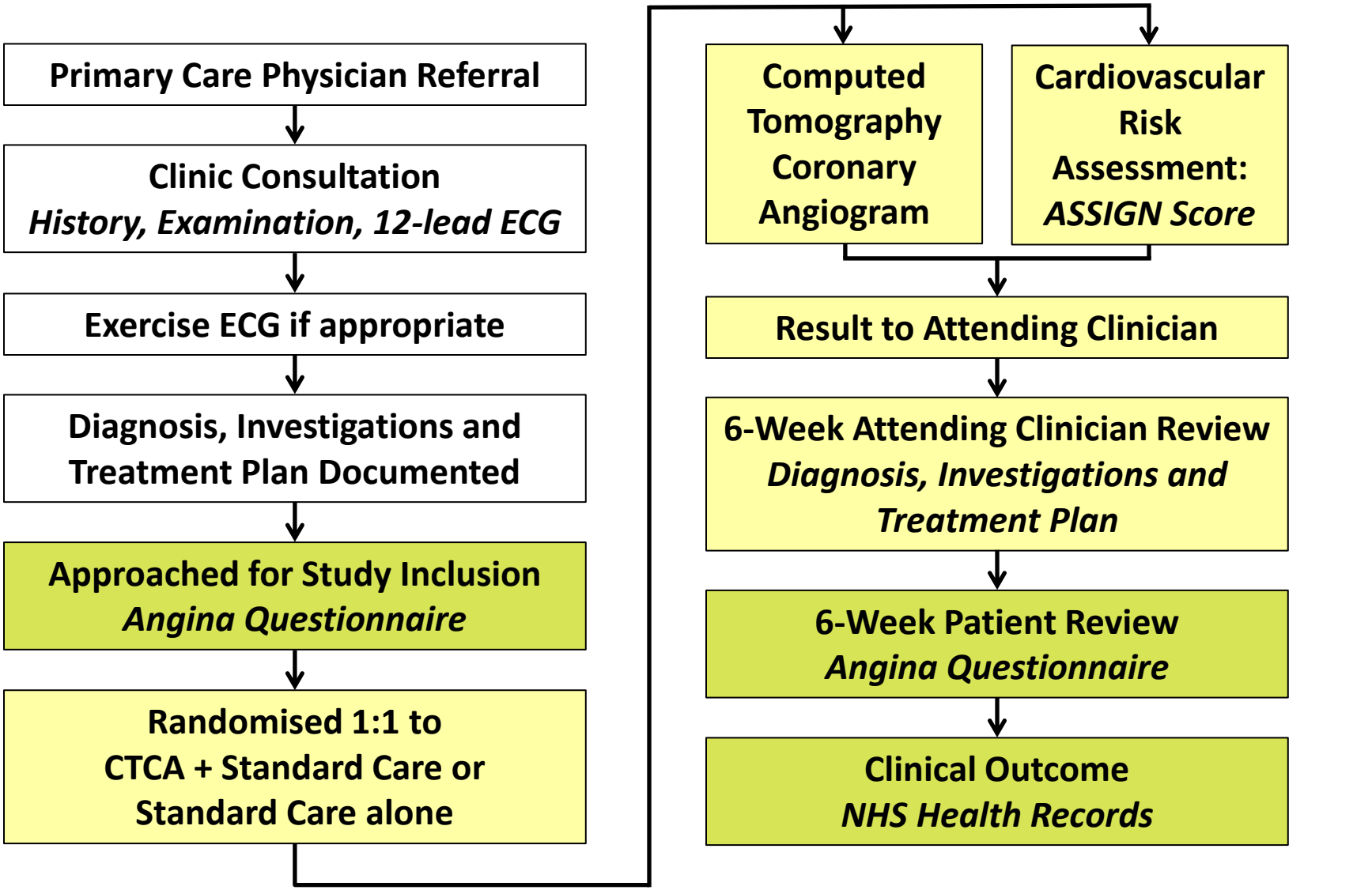
Exclusion Criteria

- Inability to undergo CT scanning
- Renal failure (estimated GFR <30 mL/min)
- Allergy to contrast media
- Pregnancy
- Acute coronary syndrome within 3 months
- Previous recruitment to the trial

No restriction according to:

- **Obesity (65 kg/m^2)**
- **Calcium score (9015 AU)**
- **Arrhythmia (AF)**

The SCOT-HEART Trial
Study Protocol



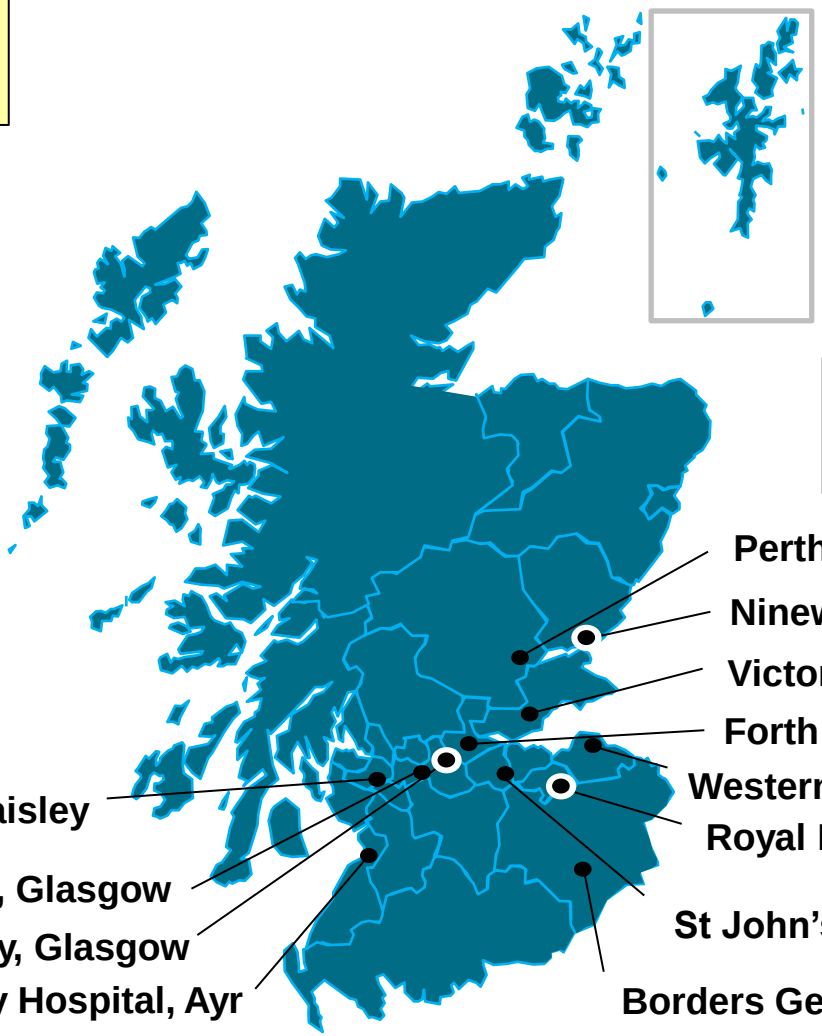
Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Trial Centers

Complete Health Record Data Capture

One National Healthcare Provider

12 Centers Across Scotland



Perth Royal Infirmary, Perth

Ninewells, Dundee

Victoria Hospital, Kirkcaldy

Forth Valley Hospital, Larbert

Western General Hospital, Edinburgh

Royal Infirmary, Edinburgh

St John's Hospital, Livingston

Borders General Hospital, Melrose

Royal Alexandra Hospital, Paisley

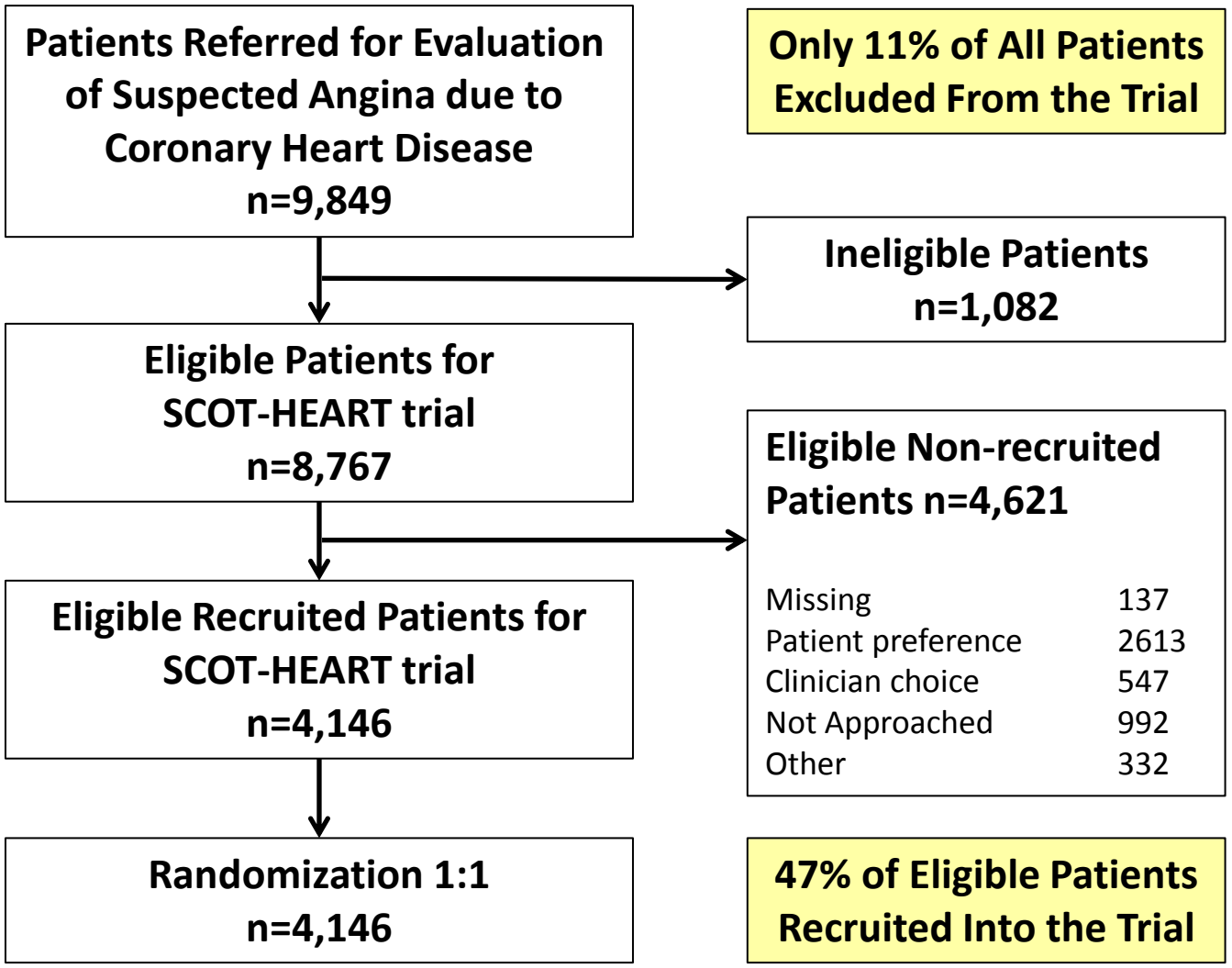
Western Infirmary, Glasgow

Glasgow Royal Infirmary, Glasgow

University Hospital, Ayr

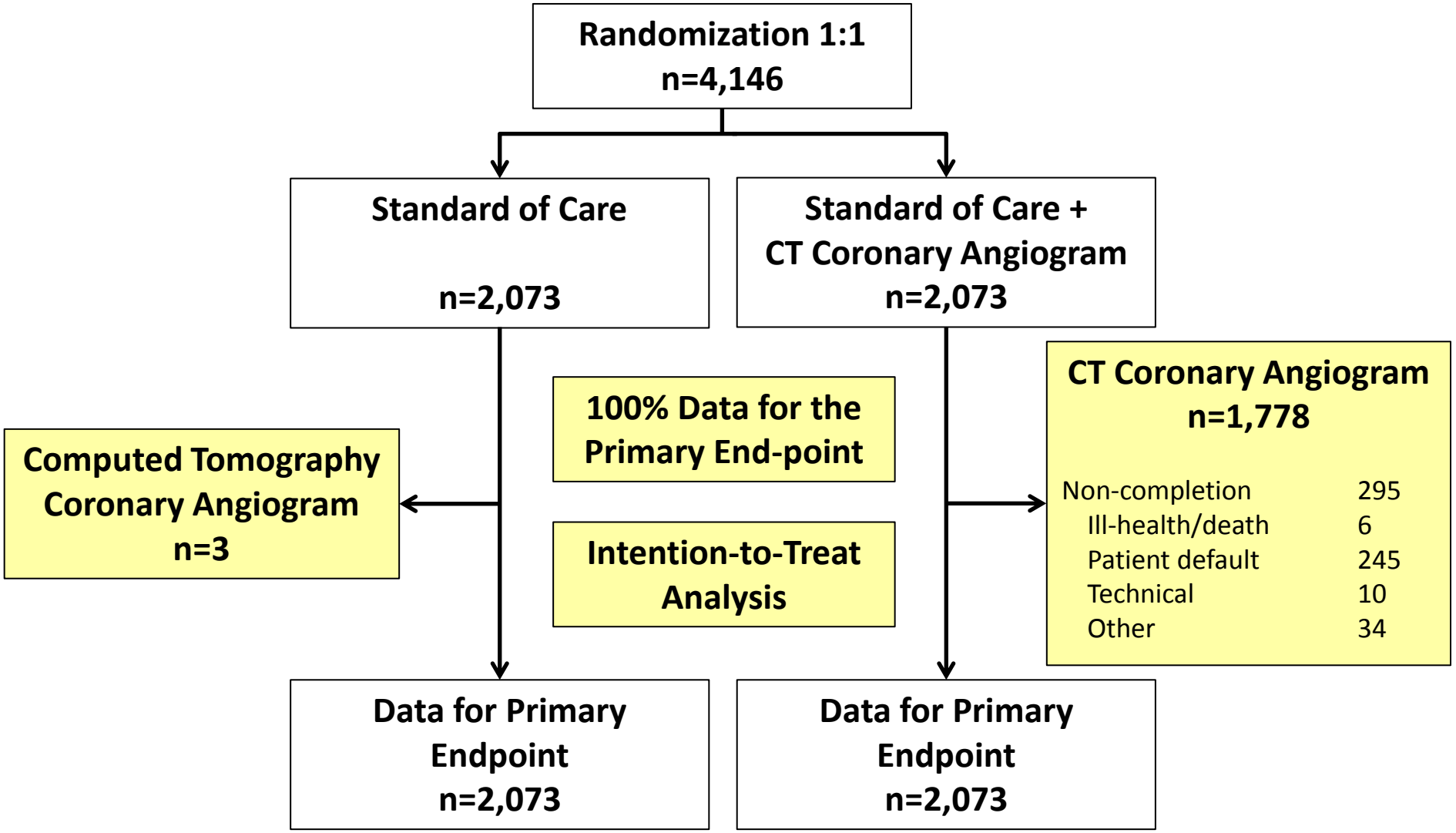
Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Trial Population



Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial

Trial Population

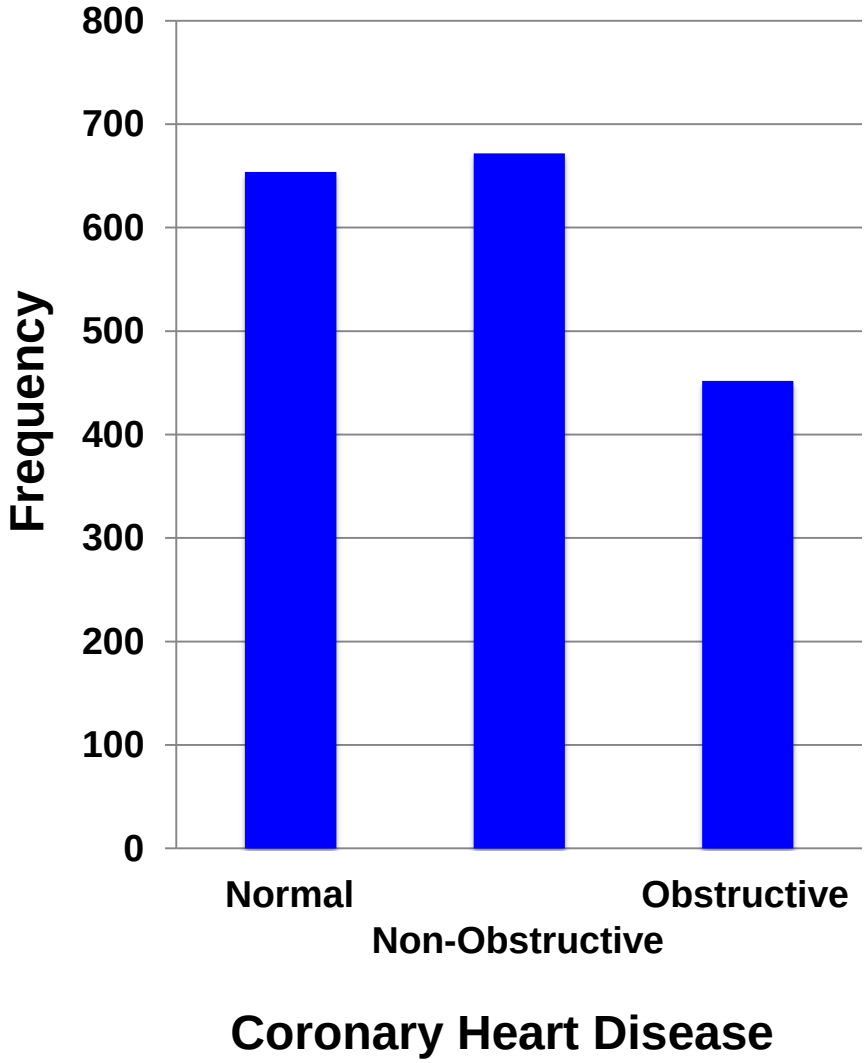


	All Participants	Standard Care + CTCA	Standard Care
Number	4146 (100%)	2073 (50%)	2073 (50%)
Male	2325 (56%)	1162 (56%)	1163 (56%)
Age (years)	57±10	57±10	57±10
Body-mass Index (kg/m^2)	30±6	30±6	30±6
Atrial Fibrillation	84 (2%)	42 (2%)	42 (2%)
Prior Coronary Heart Disease	372 (9%)	186 (9%)	186 (9%)
Prior Cerebrovascular Disease	139 (3%)	91 (4%)	48 (2%)
Prior Peripheral Vascular Disease	53 (1%)	36 (2%)	17 (1%)
Current or Ex-smoker	2185 (53%)	1095 (53%)	1090 (53%)
Hypertension	1395 (34%)	712 (34%)	683 (33%)
Diabetes Mellitus	444 (11%)	223 (11%)	221 (11%)
Hypercholesterolemia	2176 (53%)	1099 (53%)	1077 (52%)
Family History	1716 (41%)	887 (43%)	829 (40%)
Serum Total Cholesterol (mg/dL)	206±46	206±47	206±44
Serum High-density Lipoprotein Cholesterol (mg/dL)	51±16	51±16	51±16

		All Participants	Standard Care + CTCA	Standard Care
Anginal Symptoms	**Typical**	1462 (35%)	737 (36%)	725 (35%)
	Atypical	988 (24%)	502 (24%)	486 (23%)
	Non-anginal	1692 (41%)	833 (40%)	859 (41%)
Electrocardiogram	**Normal**	3492 (84%)	1757 (85%)	1735 (84%)
	Abnormal	608 (15%)	292 (14%)	316 (15%)
Stress Electrocardiogram				
	Performed	3517 (85%)	1764 (85%)	1753 (85%)
	Normal	2188 (62%)	1103 (63%)	1085 (62%)
	Inconclusive	566 (16%)	284 (16%)	282 (16%)
	Abnormal	529 (15%)	264 (15%)	265 (15%)
Further Investigation		1315 (32%)	633 (31%)	682 (33%)
Stress Imaging	**Radionuclide**	389 (9%)	176 (9%)	213 (10%)
	Other	30 (1%)	16 (1%)	14 (1%)
Invasive Coronary Angiography		515 (12%)	255 (12%)	260 (13%)
Baseline Diagnosis	**Coronary Heart Disease**	1938 (47%)	982 (47%)	956 (46%)
	Angina due to CHD	1485 (36%)	742 (36%)	743 (36%)
Predicted 10-year Coronary Heart Disease Risk		17±12%	18±11%	17±12%

CT Coronary Angiography

Prevalence of Coronary Heart Disease



Clinicians Reporting CTCA

Diagnosis of Angina due to CHD

- **Certainty**

RR 3.76 [95% CI, 3.61-3.89]

- **Frequency**

RR 0.78 [95% CI, 0.70-0.86]

CT Coronary Angiography Safety

Adverse Reactions & Radiation Dose

	Frequency
Contrast Reactions	13 (0.7%)
Contrast Extravasation	7 (0.4%)
Vasovagal Reaction	4 (0.2%)
Headache	4 (0.2%)
Other	3 (0.2%)
TOTAL	31 (1.7%)

Median Radiation Dose: 4.1 mSv (Interquartile Range 3.0-5.6)

Dose-length Product: 291 mGy.cm (Interquartile Range 216-397)

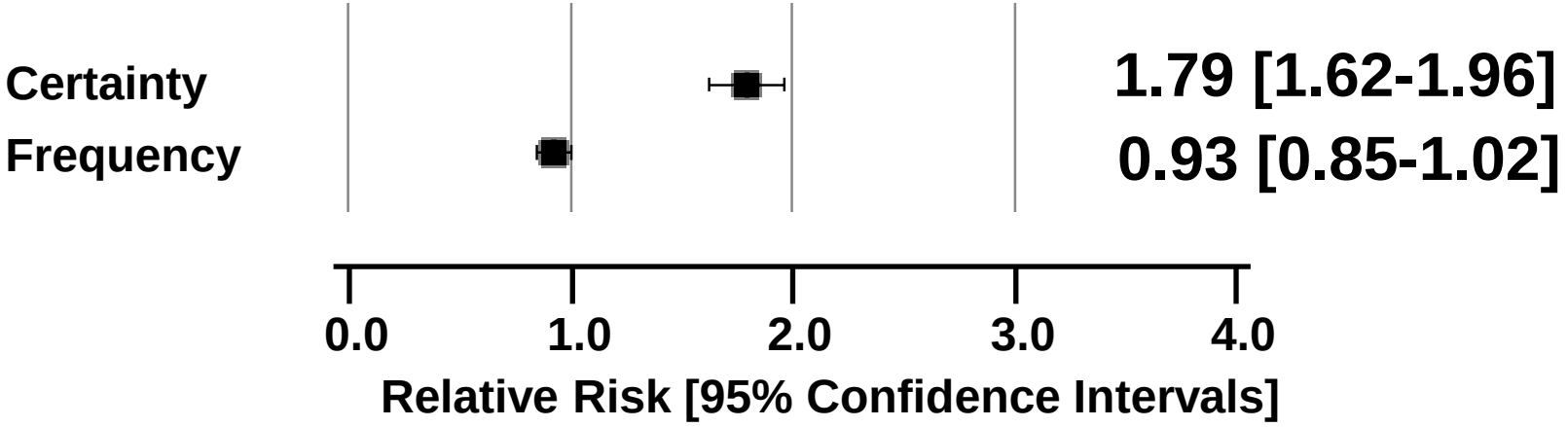
37% Radiation Dose Attributable to Coronary Artery Calcium Score

CT Coronary Angiography: Diagnosis
Baseline Compared to 6 Weeks

Overall Changes in Diagnosis: 25% *versus* 1%, P<0.001

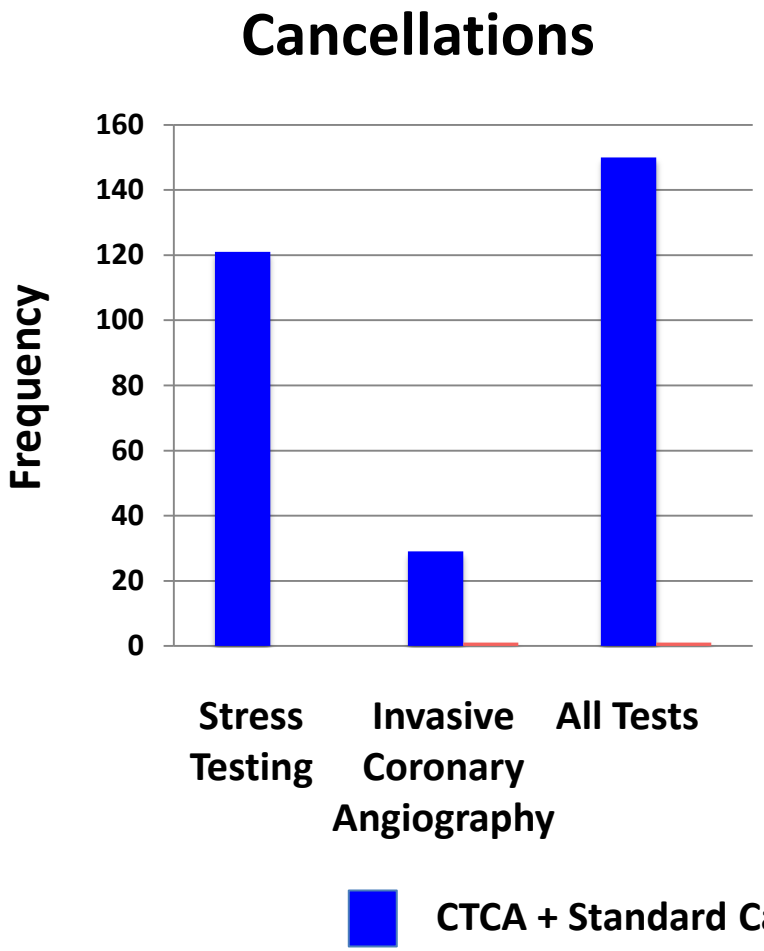
Attending Clinician: Diagnosis of Coronary Heart Disease

Attending Clinician: Diagnosis of Angina due to CHD (Primary End-point)



CTCA and Investigations
Baseline Compared to 6 Weeks

Overall Changes in Investigations: 15% *versus* 1%, P<0.001

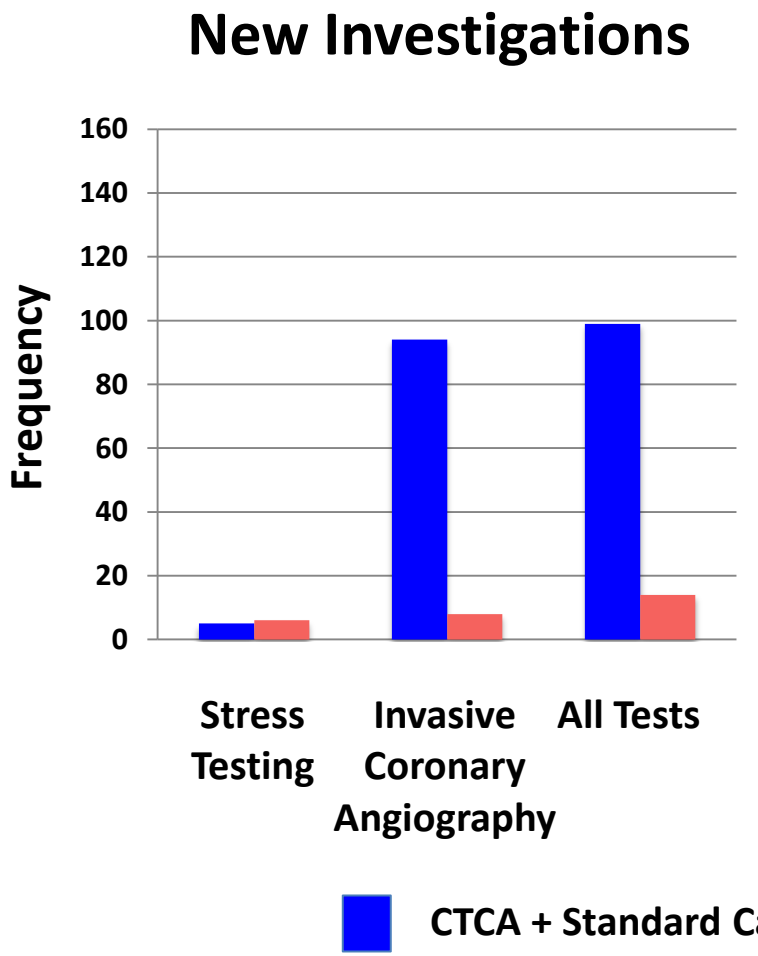


CTCA Report in those with cancelled Invasive Coronary Angiogram:

Normal	**15 (52%)**
Non-obstructive	**9 (31%)**
Obstructive	**5 (17%)**

CTCA and Investigations
Baseline Compared to 6 Weeks

Overall Changes in Investigations: 15% *versus* 1%, P<0.001



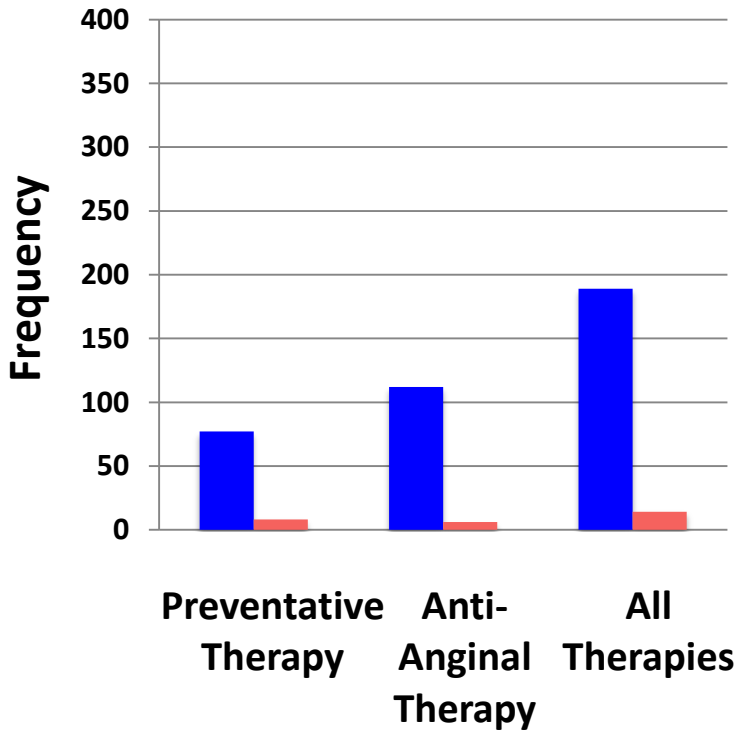
CTCA Report in those with new Invasive Coronary Angiogram:

Normal	**0 (0%)**
Non-obstructive	**11 (12%)**
Obstructive	**79 (88%)**

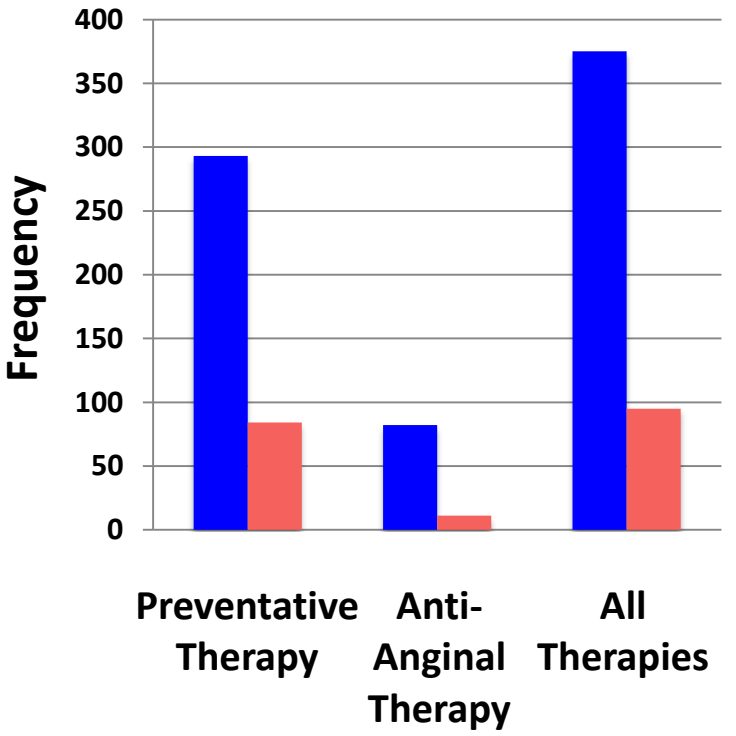
CTCA and Medical Therapy
Baseline Compared to 6 Weeks

Overall Changes in Treatments: 23% *versus* 5%, P<0.001

Cancellations



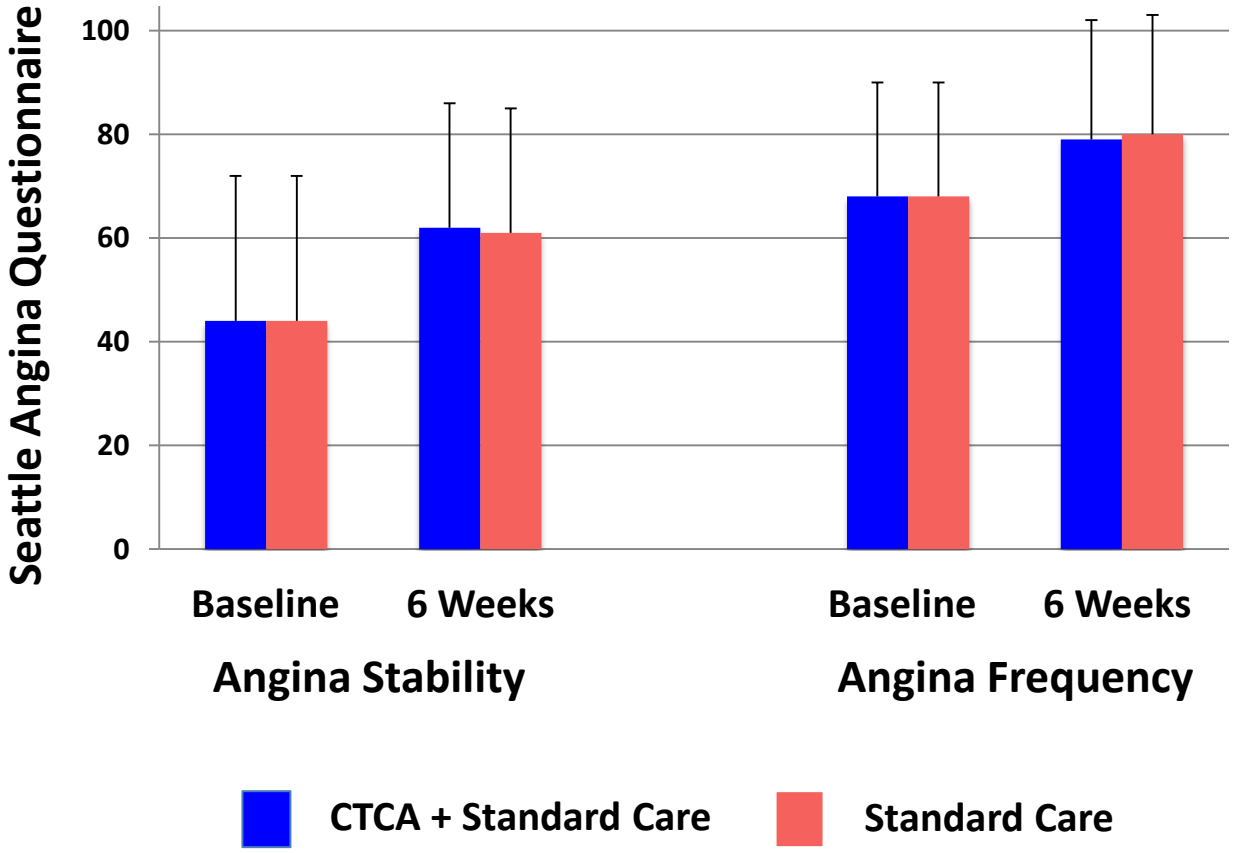
New Treatments



CTCA + Standard Care Standard Care

CTCA and Symptoms
Baseline Compared to 6 Weeks

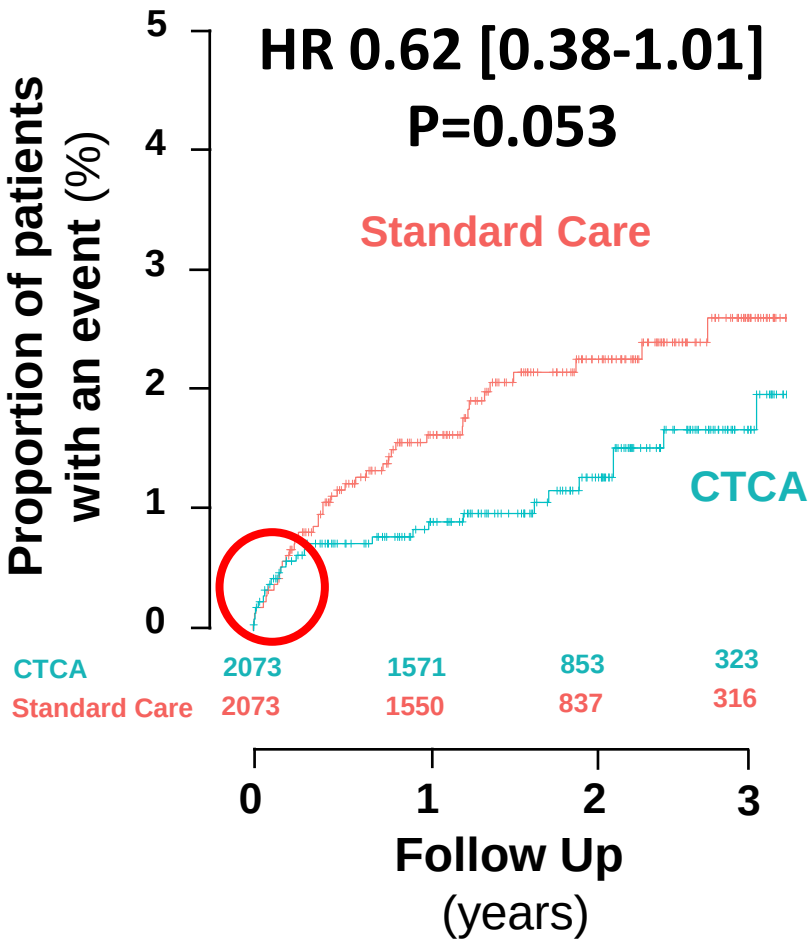
No Overall Change in Symptoms at 6 Weeks
Overall Treatment Satisfaction High (92/100) in Both Groups



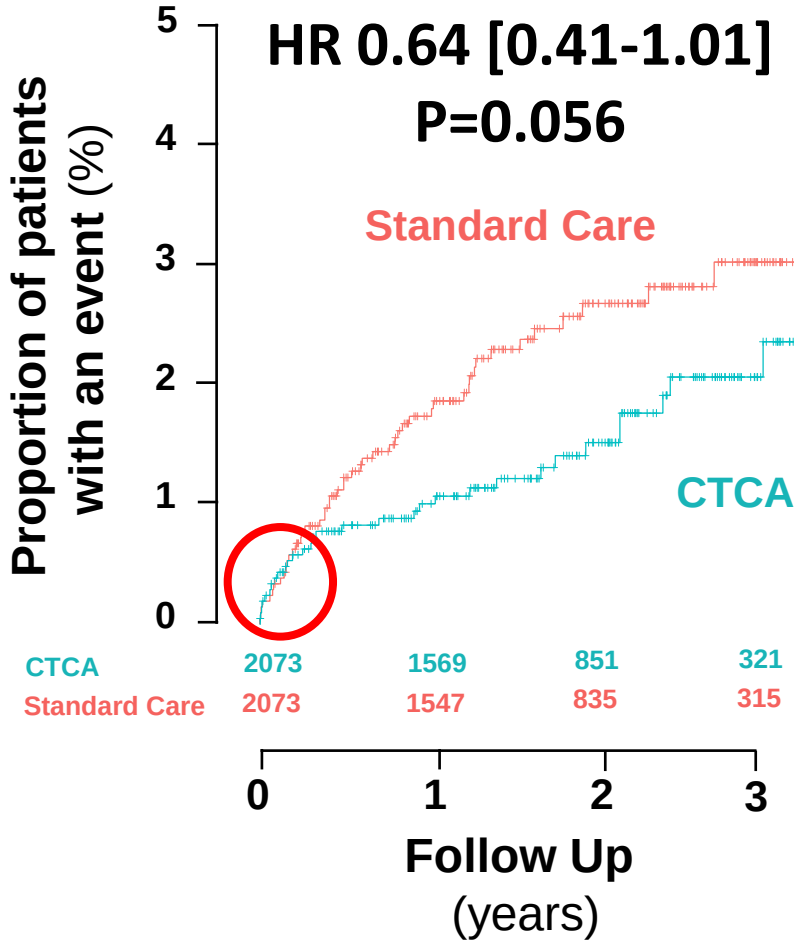
CTCA and Clinical Outcome

1.7 Years of Follow-up

Fatal and Non-Fatal MI



CHD Death, Non-Fatal MI and Non-fatal Stroke

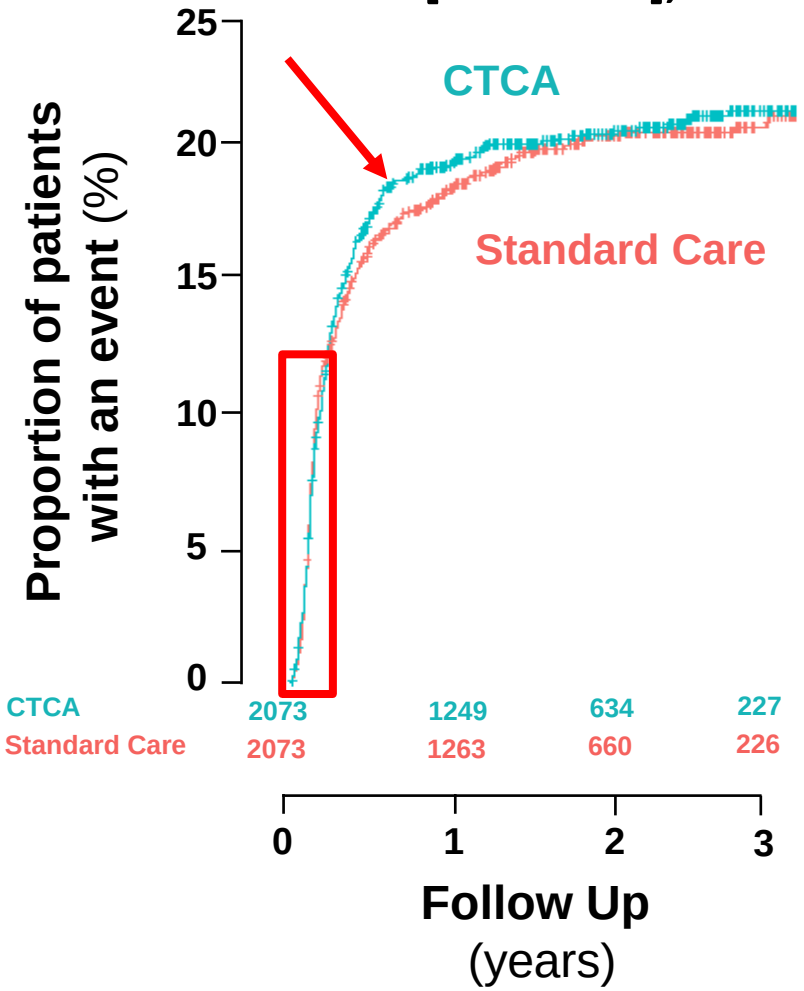


CTCA and Clinical Outcome

Coronary Angiography & Revascularisation

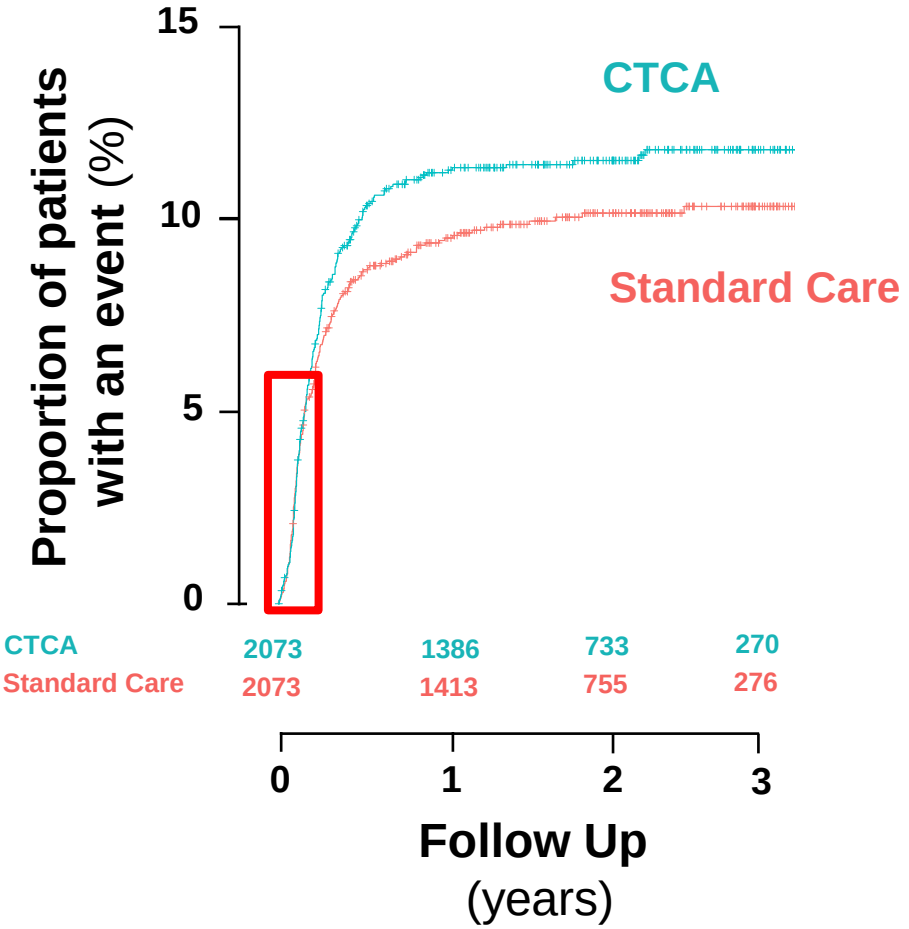
Coronary Angiography

HR 1.06 [0.92-1.21], P=0.451



Coronary Revascularisation

HR 1.20 [0.99-1.45], P=0.061

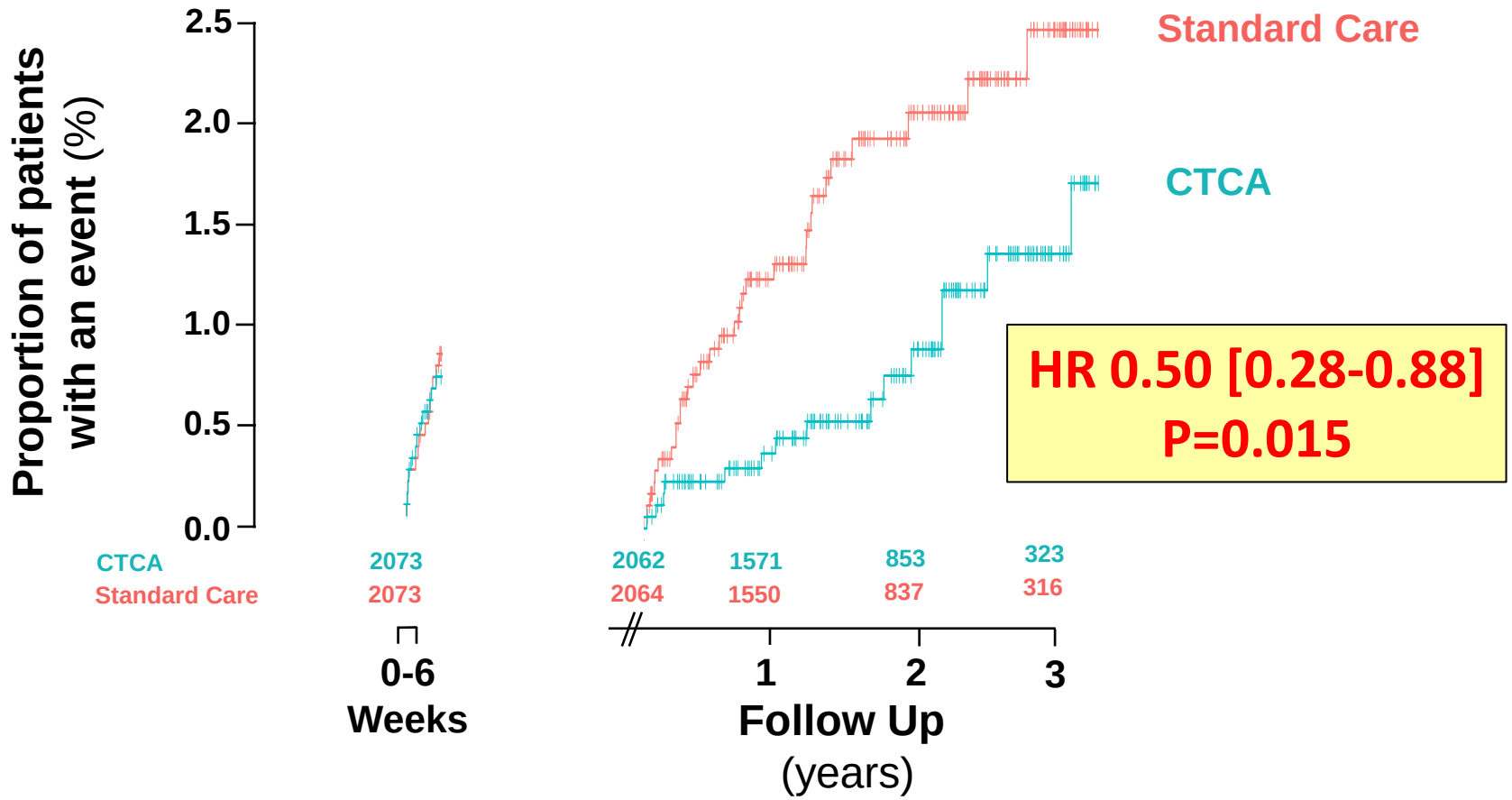


Fatal and Non-fatal MI

Post-hoc 6-Week Landmark Analysis

Diagnostic Delay

Implementation of CTCA Findings



Conclusions

In patients presenting with suspected angina due to coronary heart disease, the addition of computed tomography coronary angiography

- **Clarifies the diagnosis: 1 in 4**
- **Increases the diagnosis of CHD but appears to reduce the diagnosis of angina due to CHD**
- **Alters subsequent investigations: 1 in 6**
- **Changes treatments: 1 in 4**
- **Does not affect immediate anginal symptoms**
- **Appears to increase coronary revascularisation and reduce fatal and non-fatal myocardial infarction**

Chief Investigator: Prof David Newby. **Trial Research Fellows:** Dr Michelle Williams, Dr Amanda Hunter, Dr Tania Pawade, Dr Anoop Shah.
Grant Applicants: Prof David Newby (Principal Applicant), Dr Andrew Flapan, Prof John Forbes, Dr Allister Hargreaves, Prof Stephen Leslie, Dr Steff Lewis, Dr Graham McKillop, Dr Scott McLean, Dr John Reid, Dr James Spratt, Dr Neal Uren.
Trial Steering Committee: Prof Adam Timmis (Chair), Prof Colin Berry, Dr Nicholas Boon, Mrs Liz Clark, Dr Peter Craig, Dr Tom Barlow, Dr Marcus Flather, Prof John Forbes, Dr Steff Lewis, Dr Chiara McCormack, Dr Scott McLean, Prof David Newby, Dr Giles Roditi, Prof Edwin van Beek, Dr Michelle Williams, Dr Amanda Hunter, Mrs Susan Shepherd, Ms Marise Bucukoglu.
Edinburgh Clinical Trials Unit: Dr Steff Lewis, Dr Valentina Assi, Dr Richard Parker, Miss Ashma Krishan, Dr Chiara McCormack, Mrs Fiona Wee, Mr Anthony Wackett, Mr Allan Walker, Miss Lynsey Milne, Ms Kat Oatey.
Royal Infirmary of Edinburgh, Edinburgh: Ms Barbara Allen, Prof Edwin van Beek, Dr Miles Behan, Miss Danielle Bertram, Mr David Brian, Ms Amy Cowan, Dr Nicholas Cruden, Dr Martin Denvir, Dr Marc Dweck, Ms Laura Flint, Dr Andrew Flapan, Miss Samantha Fyfe, Dr Neil Grubb, Mrs Collette Keanie, Dr Chris Lang, Dr Tom MacGillivray, Dr David MacLachlan, Miss Margaret MacLeod, Dr Saeed Mirsadraee, Mrs Avril Morrison, Dr Nicholas Mills, Dr David Northridge, Mrs Alyson Phillips, Miss Laura Queripel, Dr John Reid, Dr Neal Uren, Dr Nicholas Weir
St John's Hospital, Livingston; Dr Ashok Jacob, Mrs Fiona Bett, Mrs Frances Divers, Ms Katie Fairley, Ms Edith Keegan, Ms Tricia White, Ms Julia Fowler
University Hospital, Ayr: Dr John Gemmill, Dr James McGowan, Mrs Margo Henry
Victoria Hospital, Kirkcaldy: Dr Mark Francis, Mr Dennis Sandeman Ms Lorraine Dinnel
Western General Hospital, Edinburgh: Prof David Newby Dr Peter Bloomfield, Dr Martin Denvir, Dr Peter Henriksen, Dr Donald MacLeod, Mrs Avril Morrison
Western Infirmary, Glasgow & Institute of Cardiovascular & Medical Sciences, University of Glasgow: Prof Colin Berry, Dr Kenneth Mangion, Dr Ify Mordi, Dr Giles Roditi, Dr Nikolaos Tzemos, Dr Eugene Connolly, Mrs Heather Boylan, Mrs Ammani Brown, Ms Lesley Farrell, Mrs Alison Frood, Ms Caroline Glover, Mrs Janet Johnstone, Mrs Tracey Steedman, Mrs Kirsten Lanaghan, Mrs Deborah McGlynn, Ms Lorraine McGregor, Ms Evonne McLennan, Ms Laura Murdoch, Miss Victoria Paterson, Ms Fiona Teyhan, Ms Marion Teenan, Ms Rosie Woodward
Borders General Hospital, Melrose: Dr Paul Neary Mrs Gillian Donaldson, Mr Terry Fairbairn, Mrs Marlene Fotheringham, Mrs Fiona Hall.
Forth Valley Royal Hospital, Larbert: Dr Allister Hargreaves, Dr James Spratt, Dr Stephen Glen, Ms Sarah Perkins, Ms Fiona Taylor Mrs Louisa Cram, Ms Catherine Beveridge, Ms Avril Cairns, Ms Frances Dougherty
Glasgow Royal Infirmary: Dr Hany Eteiba, Dr Alan Rae, Ms Kate Robb, Ms Wenda Crawford, Ms Patricia Clarkin, Ms Elizabeth Lennon
Ninewells Hospital, Dundee: Prof. Graeme Houston, Prof Stuart Pringle, Dr Prasad Guntur Ramkumar, Dr Thiru Sudarshan, Dr Yvonne Fogarty, Ms Dawn Barrie, Ms Kim Bissett, Dr Adelle Dawson, Mr Scott Dundas, Mrs Deborah Letham, Ms Linda O'Neill, Mrs Valerie Ritchie.
Perth Royal Infirmary, Perth: Dr Hamish Dougall
Royal Alexandra Hospital, Paisley: Dr Faheem Ahmed, Dr Alistair Cormack, Dr Iain Findlay, Dr Stuart Hood, Dr Clare Murphy, Dr Eileen Peat, Ms Lynne McCabe, Ms Margaret McCubbin.

THE LANCET

CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open label, parallel group multicentre trial

The SCOT-HEART Investigators*

Summary

Background The benefit of CT coronary angiography (CTCA) in patients presenting with stable chest pain has not been systematically studied. We aimed to assess the effect of CTCA on the diagnosis, management, and outcome of patients referred to the cardiology clinic with suspected angina due to coronary heart disease.

Methods In this prospective open-label, parallel group multicentre trial, we recruited patients aged 18–75 years referred for the assessment of suspected angina due to coronary heart disease from 12 cardiology chest pain clinics across Scotland. We randomly assigned (1:1) participants to standard care plus CTCA or standard care alone. Randomisation was done with a web-based service to ensure allocation concealment. The primary endpoint was certainty of the diagnosis of angina secondary to coronary heart disease at 6 weeks. All analyses were intention-to-treat, and patients were analysed in the group they were allocated to, irrespective of compliance with scanning. This study is registered with ClinicalTrials.gov, number NCT01149590.

Findings Between Nov 18, 2010, and Sept 24, 2014, we randomly assigned 4146 (42%) of 9849 patients who had been referred for assessment of suspected angina due to coronary heart disease. 47% of participants had a baseline clinic diagnosis of coronary heart disease and 36% had angina due to coronary heart disease. At 6 weeks, CTCA reclassified the diagnosis of coronary heart disease in 558 (27%) patients and the diagnosis of angina due to coronary heart disease in 481 (23%) patients (standard care 22 [1%] and 23 [1%]; p<0·0001). Although both the certainty (relative risk [RR] 2·56, 95% CI 2·33–2·79; p<0·0001) and frequency of coronary heart disease increased (1·09, 1·02–1·17; p=0·0172), the certainty increased (1·79, 1·62–1·96; p<0·0001) and frequency seemed to decrease (0·93, 0·85–1·02; p=0·1289) for the diagnosis of angina due to coronary heart disease. This changed planned investigations (15% *vs* 1%; p<0·0001) and treatments (23% *vs* 5%; p<0·0001) but did not affect 6-week symptom severity or subsequent admittances to hospital for chest pain. After 1·7 years, CTCA was associated with a 38% reduction in fatal and non-fatal myocardial infarction (26 *vs* 42, HR 0·62, 95% CI 0·38–1·01; p=0·0527), but this was not significant.

Interpretation In patients with suspected angina due to coronary heart disease, CTCA clarifies the diagnosis, enables targeting of interventions, and might reduce the future risk of myocardial infarction.

Funding The Chief Scientist Office of the Scottish Government Health and Social Care Directorates (CZH/4/588) funded the trial with supplementary awards from Edinburgh and Lothian's Health Foundation Trust and the Heart Diseases Research Fund.

Published Online
March 15, 2015
http://dx.doi.org/10.1016/S0140-6736(15)60293-0

See Online/Comment
http://dx.doi.org/10.1016/S0140-6736(15)60463-9

*Members listed at end of report.

Correspondence to:
Prof David Newby, Centre for Cardiovascular Science, Chancellor's Building, Edinburgh EH16 4SA, Scotland
d.e.newby@ed.ac.uk