Institution: The University of Edinburgh		
Unit of Assessment: 1		
Title of case study: E: Computed Tomography Coronary Angiography improves diagnosis, management and outcome for patients with stable chest pain		
Period when the underpinning research was undertaken: 2010-2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
David Newby	BHF Duke of Edinburgh Chair of Cardiology	2000 – present
Michelle Williams	Senior Lecturer	2009 – present
Anoop Shah	Clinical Lecturer in Cardiology	2011 – present
Philip Adamson	Senior Clinical Research Fellow in Cardiology	2014 – present
Marc Dweck	Personal Chair of Clinical Cardiology	2009 – present
Nick Mills	Personal Chair of Cardiology	2003 – present
Stephanie Lewis	Personal Chair of Medical Statistics	1997 – present
John Norrie	Chair of Medical Statistics & Trial Methodology	2016 – present
Edwin van Beek	SINAPSE Chair of Clinical Radiology	2009 – present
Period when the claimed impact occurred: 2016 – 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Underpinning Research: The UoE-led SCOT-HEART randomised controlled trial showed that using computed tomography coronary angiography (CTCA) rather than the previous standard care (diagnostic scores) to manage patients with stable chest pain and suspected coronary artery disease leads to a 40% reduction in the rate of death from CAD or non-fatal myocardial infarction.

Significance and Reach of Impact: CTCA is recommended as a first-line diagnostic tool for patients with stable chest pain in clinical guidelines from UK's National Institute for Health and Care Excellence (NICE; 2016) and the European Society of Cardiologists (2019); both cite SCOT-HEART results as evidence in favour of CTCA.

Rates of CTCA use in England have doubled between 2016 and 2018, with 223,740 patients benefitting in that time. This rate of use is preventing approximately 660 myocardial infarctions per year. A global survey showed that CTCA is the commonest test for patients with suspected coronary artery disease in 110 imaging centres from 37 countries across the world.

NICE estimates that implementation of its guideline results in annual savings of GBP16,000,000 for the NHS, through CTCA being the lowest-cost testing strategy for a correct diagnosis of coronary artery disease and reducing further adverse cardiac events.

2. Underpinning research

The Challenge: How to diagnose stable chest pain accurately

Angina due to coronary artery disease (CAD) is one of several causes of stable chest pain. It is therefore paramount that patients presenting with this symptom receive an accurate and timely diagnosis to guide appropriate investigations and therapeutic interventions, as untreated CAD can lead to myocardial infarction (MI). Although clinical assessment is often successful at identifying cases of CAD, many patients are still misdiagnosed with 1/3 of MIs in patients who initially presented with stable chest pain occurring in those who had previously been diagnosed as having a non-cardiac cause.

The gold standard for establishing the presence, location and severity of CAD has historically been invasive coronary angiography (ICA). However, this technique is costly and associated with a small but significant risk of morbidity and mortality. Non-invasive imaging techniques to detect CAD include CTCA, exercise electrocardiogram, single positron emission computed tomography (SPECT), positron emission tomography (PET) and magnetic resonance imaging

(MRI). Of these, CTCA has the best sensitivity (98%) and specificity (87%) for the detection of obstructive CAD, but historically was not widely used in this indication, as its clinical utility in this patient group had not been systematically studied.

SCOT-HEART clinical trial tested the usefulness of CTCA in diagnosing chest pain

UoE researchers designed and conducted the SCOT-HEART randomised controlled trial to determine the clinical usefulness and cost-effectiveness of CTCA in the diagnosis of stable chest pain. Conducted between 2010 and 2014 at 12 clinics across Scotland, SCOT-HEART recruited 4,146 patients with stable chest pain possibly due to CAD, who had been referred by a primary-care physician to a rapid-access chest pain clinic.

CTCA enables clinicians to make a more accurate diagnosis of CAD

The SCOT-HEART trial demonstrated that using CTCA results in more accurate diagnosis of CAD, chiefly through identifying more genuine cases of CAD, but also through correctly diagnosing non-cardiac chest pain [3.1]. Attending clinicians reported that use of CTCA increased the certainty (Relative risk (RR) 2.56 [95% confidence interval (CI) 2.33–2.79], p<0·001) and frequency (RR 1.09 [95% CI, 1.02–1.17], p=0·017) of the diagnosis of CAD. Overall, diagnosis of CAD changed in 25% of participants assigned to CTCA, compared with 1% in patients assigned to standard care alone (the diagnostic score ASSIGN; p<0·001 for both) [3.1; 3.2].

More accurate diagnoses result in better targeted use of therapies

The changes in diagnosis led to changes in the medications recommended to 1 in 4 patients, including both increased use of aspirin and statin therapies and decreased use of antianginal therapies [3.2]. In addition, during the first year of the SCOT-HEART trial, 21% more patients in the CTCA group were referred for a coronary revascularisation procedure to treat blocked arteries, reflecting that more patients were identified to have CAD and to require the procedure. However, beyond 1 year, patients in the CTCA group had lower rates of coronary revascularisation (41% reduction, p=0.015) [3.3]. This indicates that 1) the undetected cases of CAD in the standard care group had additional and avoidable cardiac events, and 2) correctly diagnosed and appropriately treated cases in the CTCA group were protected from further downstream events.

CTCA reduces the rate of cardiovascular events by 40% in 5 years

The correctly targeted medications and procedures resulted in markedly improved clinical outcomes for patients: 5-year follow-up data showed that death from CAD or non-fatal MI was substantially reduced in patients who underwent CTCA, occurring in 48 patients (2.3%) in the CTCA group versus 81 patients (3.9%) in the standard care group (p=0.004) [3.2]. This was the first time that an imaging test had been unequivocally shown to improve patient outcomes and to lead to a major long-term reduction in the risk of MI.

Undergoing CTCA also benefits patients who do *not* have CAD, as it provides confidence to clinicians to rule out disease, and thus removes the need for unnecessary investigations or preventative medications; CTCA was associated with cancellation of 121 functional stress tests and 29 ICAs, and clinicians were more likely to recommend cancellation of preventative therapies when the patients had undergone CTCA than if they had not (77 versus 8, p <0.0001) [3.3; 3.4].

3. References to the research

[3.1] The Scottish Computed Tomography of the HEART (SCOT-HEART) Trial Investigators. Computed tomography coronary angiography in patients with suspected angina due to coronary heart disease. *Lancet* 2015;385:2383-2391. doi: 10.1016/S0140-6736(15)60291-4

[3.2] The SCOT-HEART investigators 2018, 'Coronary CT Angiography and 5-Year Risk of Myocardial Infarction' *The New England Journal of Medicine*: 379(10):924-933. doi: 10.1056/NEJMoa1805971

[3.3] Williams MC, Hunter A, Shah A, Assi V, Lewis S, Smith J, Berry C, Boon NA, Clark E, Flather M, Forbes J, McLean S, Roditi G, van Beek EJR, Timmis AD, Newby DE on behalf of the Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial Investigators. Use of coronary computed tomographic angiography to guide management of patients with coronary disease. *J Am Coll Cardiol.* 2016;67:1759-1768. doi: 10.1016/j.jacc.2016.02.026

[3.4] Adamson PD, Williams MC, Dweck MR, Mills NL, Boon NA [... incl Newby DE] and Berry C on behalf of SCOT-HEART Investigators. Guiding therapy by coronary CT angiography improves outcomes in patients with stable chest pain. *Journal of the American College of Cardiology*, 2019:74(16):2058-70. doi: 10.1016/j.jacc.2019.07.085

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4. Details of the impact

Impact on clinical guidelines

The NICE Clinical Guideline for the assessment and diagnosis of chest pain of recent onset (CG95) was updated in 2016, and now recommends CTCA as the first-line testing strategy in patients with stable chest pain [5.1a]. Further investigations are only recommended when CTCA results are inconclusive. The draft for consultation refers to the SCOT-HEART trial 22 times, and it was 1 of only 3 randomised controlled trials listed in evidence for review question 1 ("In people with stable chest pain of suspected cardiac origin, what is the accuracy, clinical utility and cost-effectiveness of non-invasive diagnostic tests, invasive diagnostic tests and calcium scoring?"). The SCOT-HEART trial is described in detail in both the evidence summary [p. 26; 5.1b] and evidence tables in Appendix G [p. 359–362; 5.1b]. The NICE guideline CG95 was reviewed in September 2019 and no new evidence was identified which would have changed the recommendations [5.1c].

The European Society of Cardiologists (ESC) updated its guidelines in 2019, and now also recommends CTCA as the initial test to diagnose stable chest pain [5.2]. This updated version elevates CTCA from a Class IIb recommendation ("may be considered") to a Class I recommendation ("is recommended or is indicated"), and specifically highlights SCOT-HEART as evidence in favour of CTCA [5.2] as well as citing 4 UoE papers.

Impact on clinical practice

United Kingdom

Since the update to NICE CG95 in 2016, the use of CTCA has more than doubled in the UK, while use of other cardiac imaging methods has remained stable. These trends can be seen in electronic imaging records held by NHS Digital (**Figure 1** below): from 2016 onwards: there was a sharp upturn in the average annual growth of CTCA scans performed in England, from 21.9 ± 52.8 tests per 100,000 people per year before the CG95 update, to 52.8 ± 79.1 tests per 100,000 people per year after the update, $p<0.001$) [5.3].

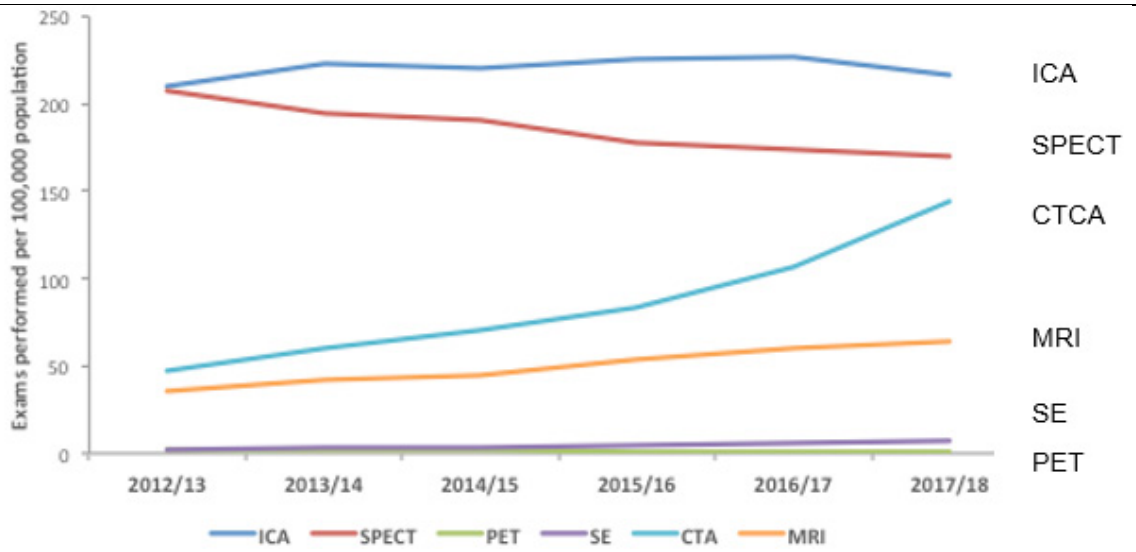

Figure 1. England-wide numbers of examinations performed for the investigation of CAD by method, 2012–2018 [5.3]. (Acronyms are defined in section 2)

A **global survey** of uptake of the ESC guidelines, conducted by the European Association of Cardiovascular Imaging Scientific Initiatives Committee in 2020, revealed that in 110 imaging centres in 37 countries across the world, CTCA was the most commonly used non-invasive diagnostic test, with 31% of respondents using it as the principal test for diagnosing CAD (compared with 15% stress echocardiography, 12% exercise electrocardiogram, 5% SPECT or PET and 4% MRI). Only 1% of centres proceeded directly to ICA [5.4].

Impact on health & welfare

The improved diagnostic accuracy offered by CTCA saves lives of patients with CAD, as evidenced by SCOT-HEART, which showed that patients who had undergone CTCA were 41% less likely to die from CAD or experience non-fatal MI than those who had not.

The real-life impact of this can be projected as follows: based on the data from the national imaging records [5.3], 51–52 CTCA scans are required to prevent 1 MI in 5 years; thus, the 53 CTCAs per 100,000 population performed per year since 2016 prevented 1 MI per 100,000 population per year. Scaling this up to the UK population of 66,000,000 people, this rate of use of CTCA is preventing approximately 660 MIs per year.

Economic impact

A health economic analysis was undertaken as part of the 2016 update to NICE CG95 to determine the cost-effectiveness of the various testing strategies for diagnosing stable chest pain [5.1b]. This compared the average proportion of correct diagnoses (effectiveness) and the costs of each testing strategy (from NHS Reference Costs: CTCA GBP122.11, exercise test GBP271.31, SPECT GBP367.29, MRI GBP515, ICA GBP1,684.71). This analysis found that a first-line testing strategy using CTCA has the lowest cost per correct diagnosis of CAD [5.5].

Furthermore, a NICE report on the resource impact of implementing CG95 [5.6] estimated that the recommended change in diagnostic tests performed would lead to annual savings increasing year-on year from GBP1,132,000 in 2016–17 to GBP16,974,000 by 2020–21 through better targeted use of NHS resources and reducing future adverse cardiac events.

Use of CTCA also results in cost-savings outside the UK. An independent randomised controlled trial run in the USA and South Korea found that when patients were triaged by CTCA rather than being directly referred to ICA, total diagnostic costs per patient were 57% lower (an average of USD2,755 [GBP2,105; 01-21] in the direct referral group versus USD1,183 [GBP902; 01-21] in the CTCA-triaged group) with no difference in clinical outcomes [5.7].

5. Sources to corroborate the impact

[5.1] NICE update 2016
a. NICE guideline 95, 2016 update (recommendation on p. 17–18)
b. The draft for consultation (cost-effectiveness analysis p. 551 –552).
c. NICE guideline 95 review in September 2019

[5.2] European Society of Cardiologists Guidelines, 2019, p. 17, 18, 20

[5.3] National Trends in Coronary Artery Disease Imaging: Abstract of data presented at ESC Congress in September 2019; citation: European Heart Journal (2019) 40 (Supplement), 1304

[5.4] European Association of Cardiovascular Imaging survey: Bularga et al. 2020 doi: 10.1093/ehjci/jeaa300

[5.5] NICE Guideline update review: Moss et al. 2017 *Curr Cardiovasc Imaging Rep* doi: 10.1007/s12410-017-9412-6

[5.6] NICE resource impact report 2016

[5.7] CONSERVE trial: Chang et al. 2018 *Journal of the American College of Cardiology: Cardiovascular Imaging* doi: 10.1016/j.jcmg.2018.09.018