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Original research

Impact on stable chest pain pathways of CT fractional flow reserve

Rachel A O'Leary [1] ,[1] Julie Burn [1] ,[1] Samuel G Urwin,[1] Andrew J Sims [1] ,[1,2] Anna Beattie [1] ,[3] Alan Bagnall [1] [2,4]

ABSTRACT

Objectives To evaluate the impact of introducing CT fractional flow reserve (FFR_{CT}) on stable chest pain pathways, concordance with National Institute for Health and Care Excellence (NICE) chest pain guidelines, resource usage and revascularisation of patients from a tertiary UK cardiac centre rapid access chest pain clinic (RACPC).

Methods Single-centre before and after study comparing data from electronic records and Strategic Tracing Service of all RACPC patients attending between 1 July 2017 and 31 December 2017, and 1 August 2018 and 31 January 2019.

Results Two hundred and sixty-eight and 287 patients (overall mean age 62 years, range 26–89 years, 48.3% male), were eligible for first-line CT coronary angiography (CTCA) pre-FFR_{CT} and post-FFR_{CT}, respectively. First-line CTCA use per NICE Guideline CG95 increased (50.6% pre-FFR_{CT} vs 75.7% post-FFR_{CT}, p<0.001). More patients reached pathway endpoint (revascularisation or assumed medical management) after one investigation (74.9% pre-FFR_{CT} vs 84.9% post-FFR_{CT}, p=0.005). There were fewer stress (22.8% pre-FFR_{CT} vs 7.7% post-FFR_{CT}, p<0.001) and rest (10.4% pre-FFR_{CT} vs 4.2% post-FFR_{CT}, p=0.007) myocardial perfusion scans and diagnostic-only angiograms (25.5% vs 13.7%, p<0.001). Despite fewer invasive procedures (29.3% pre-FFR_{CT} vs 17.6% post-FFR_{CT}, p=0.002), revascularisation rates remained similar (10.4% pre-FFR_{CT} vs 8.8% post-FFR_{CT}, p=0.561). Avoiding invasive investigations reduced inpatient admissions (39.0% pre-FFR_{CT} vs 24.3% post-FFR_{CT}, p<0.001). Time to revascularisation was unchanged (153.5 days pre-FFR_{CT} vs 142.0 post-FFR_{CT}, p=0.925). Unplanned hospital attendances, emergency admissions and adverse events were similar.

Conclusions FFR_{CT} adoption was associated with greater compliance with NICE guidelines, reduced invasive diagnostic angiography, planned admissions and needing more than one test to reach a pathway endpoint.

INTRODUCTION

Patients presenting with chest pain commonly require investigation to determine if they have coronary artery disease (CAD) and to plan revascularisation. Simulation software is now available to non-invasively estimate coronary fractional flow reserve from CT angiography (FFR_{CT}). FFR is the reference standard measure of the functional impact of a coronary stenosis on blood flow.[1] FFR_{CT} uses standard CT coronary angiography (CTCA)

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Fractional flow reserve CT (FFR_{CT}) facilitates the anatomical and functional assessment of coronary artery disease (CAD) using a single, non-invasive radiation exposure, which can inform clinical management decisions.

WHAT THIS STUDY ADDS

⇒ Implementation of FFR_{CT} in diagnostic pathways for stable chest pain reduced the number of diagnostic-only invasive angiograms, planned hospital admissions and need for myocardial perfusion scans. Patients were more likely to need only one diagnostic test to reach a pathway endpoint, which was achieved with no increase in time to revascularisation or adverse events.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study confirms the feasibility of National Institute for Health and Care Excellence CG95 in routine clinical practice and supports evidence that CT coronary angiography (CTCA) and FFR_{CT} is a safe alternative for guiding revascularisation decisions in patients presenting with new-onset chest pain without known CAD. Guideline adoption will likely require additional CTCA capacity but may release capacity for revascularisation by reducing the number of diagnostic-only invasive procedures.

image data to create a three-dimensional model of the coronary arteries and associated stenoses to predict this impact. FFR_{CT} analysis therefore facilitates the anatomical and functional assessment of CAD within a single, non-invasive radiation exposure and reduces the requirement for invasive angiography when employed in diagnostic pathways for stable chest pain.[2–7]

Prior to the 2016 update, the UK National Institute for Health and Care Excellence (NICE) Clinical guideline CG95 ('Recent-Onset Chest Pain of Suspected Cardiac Origin: Assessment and Diagnosis') recommended CTCA only for patients with low pretest probability of significant CAD.[8] The updated guidance recommends CTCA first line for all patients at any risk level to detect the presence of CAD if symptoms are suggestive of typical

or atypical angina, or in patients with non-anginal chest pain if ECG abnormalities are present. If CTCA shows CAD of uncertain significance or is non-diagnostic, a second-line functional investigation is recommended, such as nuclear myocardial perfusion scan (NMPS), stress echocardiography or stress MRI perfusion imaging. If results remain inconclusive, invasive coronary angiography is then offered.

In 2017, NICE published MTG32,[9] which appraised the utility of FFR$_{CT}$ for anatomical and functional assessment of CAD. A guidance update in 2021 featured economic analysis estimating a cost saving of £391 per patient for FFR$_{CT}$-based assessment pathways, potentially saving the National Health Service (NHS) >£9 million annually. In August 2018, the Newcastle on Tyne Hospitals NHS Foundation Trust (NuTH) was designated a pilot site for FFR$_{CT}$ adoption under the Innovation and Technology Payment (ITP) programme funded by NHS England. The service was made available to patients presenting to the rapid access chest pain clinic (RACPC).

This retrospective service evaluation aimed to assess the effect of introducing FFR$_{CT}$ on (1) uptake of CTCA for first-line investigation of stable chest pain, (2) requirement for other non-invasive functional tests and (3) efficiency of use of the cardiac 'cath lab' (defined by the proportion of patients undergoing invasive investigation having immediate follow-on revascularisation). The study also assessed the impact on pathway times, hospital attendances and adverse events.

METHODS
Approval
The study was registered as a service evaluation on the NuTH Clinical Effectiveness Register and jointly undertaken by the Directorates of Northern Medical Physics and Clinical Engineering, Radiology and Cardiothoracic Services.

Setting
NuTH is an NHS Trust with >2250 beds providing tertiary cardiac services to the region, performing >1600 CTCA scans and around 2800 percutaneous coronary interventions (PCIs) per year.

The RACPC assesses patients with suspected angina within 14 days of referral with capacity for approximately 1000 patients annually. Nine consultant cardiologists and one chest pain specialist nurse managed patients attending the RACPC during the study.

Inclusion and exclusion criteria
Eligible patients were ≥18 years with stable chest pain with an appointment at the RACPC in one of two recruitment periods: before the introduction of FFR$_{CT}$, 'pre-FFR$_{CT}$' between 1 July 2017 and 31 December 2017, or after FFR$_{CT}$ adoption under the ITP programme, 'post-FFR$_{CT}$' between 1 August 2018 and 31 January 2019, thus avoiding a cross-over period when FFR$_{CT}$ was used infrequently. The index appointment for each patient was the earliest appointment or earliest appointment within any 3-month period where multiple referrals were made.

Patients with previously confirmed CAD (eg, previous myocardial infarction (MI), revascularisation or angiography) were excluded from analysis as CG95 recommends first-line non-invasive functional testing in this group. Because our study was designed to examine the influence of FFR$_{CT}$ on radiological investigation pathways, patients discharged from the RACPC without radiological tests were excluded from analysis. It was

assumed such patients had non-cardiac chest pain diagnosed clinically by the attending cardiologist.

Data sources
Data were obtained retrospectively from the RACPC database for the pre-FFR$_{CT}$ and post-FFR$_{CT}$ time periods, plus 3 months prior to each, to exclude patients with index appointments before the recruitment periods. Patient-level identifiers (NHS number and local medical record number) were used to quantify healthcare encounters from local administrative data, including accident and emergency (A&E), outpatient attendances and inpatient admissions. Clinical events identified from inpatient data included acute MI, revascularisation with coronary artery bypass grafting (CABG) and invasive cath lab procedures including diagnostic angiography with or without pressure wire functional testing, and revascularisation with PCI. Patient-level identifiers were used to extract records from the radiology information system to ensure all relevant investigations were identified, including CTCA, MRI and NMPS (stress and rest) scans, intravascular ultrasound and optical coherence tomography. Investigations and events were identified using International Classification of Diseases, 10th Revision, and Office of Population Censuses and Surveys (OPCS) Classification of Interventions and Procedures codes, and standardised exam descriptions used locally (see online supplemental file). An in-house database was checked for stress echocardiography investigations. Additional data sources included the Strategic Tracing Service to identify patient deaths and the software provider's web application for FFR$_{CT}$.

All healthcare encounters and clinical event data between 1 July 2017 and 30 September 2019 were extracted. This allowed 8 months of follow-up for all patients, which was deemed appropriate for completion of related investigations.

Data cleaning
Records were excluded if duplicated, unrelated to an index appointment, or if patient identifiers were missing or invalid. Patients with known CAD were excluded if a previous inpatient episode contained relevant OPCS or ICD codes, or existing CAD was recorded at the RACPC (see online supplemental file). As the latter used a text-matching algorithm, the authors manually verified exclusions.

Definitions and outcomes
Pathway start point was defined as the date of RACPC attendance when a decision was made to refer for additional radiological investigation. Pathway endpoint was defined as either revascularisation (PCI or CABG), death or MI without revascularisation, or an assumed decision to manage medically (ie, no further investigations, procedures or adverse events recorded during follow-up).

Investigations were ordered chronologically and only the earliest instance of each considered. Times between RACPC attendance and investigations, and the pathway endpoint were calculated for each patient. Overall numbers and types (emergency/non-emergency, cardiac/non-cardiac) of inpatient and outpatient attendances, number of cardiac radiological investigations and invasive procedures were determined. Safety outcomes were frequencies of MI, death and unplanned hospital attendance.

For analysis, related investigations and procedures were grouped into 'other' non-invasive functional tests (NMPS, stress echo and stress MRI); diagnostic-only cath lab procedures
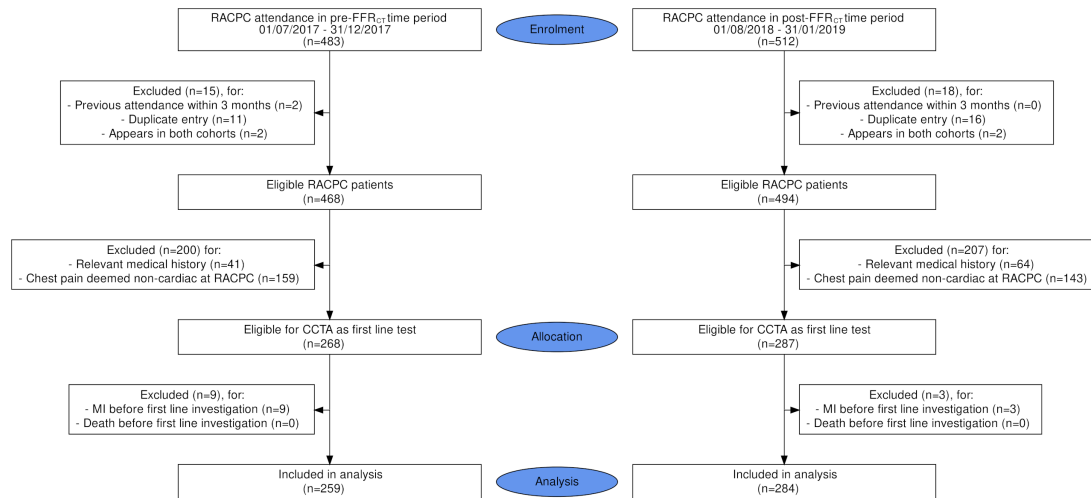
Figure 1 Recruitment flowchart for pre-FFR$_{CT}$ (left) and post-FFR$_{CT}$ (right) time periods. CTCA, CT coronary angiography; FFR$_{CT}$, CT fractional flow reserve; MI, myocardial infarction; RACPC, rapid access chest pain clinic.

(angiography or angiography plus pressure wire); and invasive revascularisation (PCI or CABG).

Statistical analysis

Analysis used 'R' statistical programming language[10] and a significance level of 0.05 using Bonferroni correction for related groups of observations. Comparisons of pre-FFR$_{CT}$ and post-FFR$_{CT}$ cohorts used Student's t-test, χ^2 test, Mann-Whitney U test or Fisher's exact test, as appropriate. Tests were two-sided. Kaplan-Meier analysis and Cox proportional hazards test were used to compare time to revascularisation events.

Patient and public involvement

This was a retrospective evaluation of standard care pathways and routinely collected data. Therefore, no patients or members of the public were directly involved.

RESULTS

Study population

In total, 995 patients (483 pre-FFR$_{CT}$ and 512 post-FFR$_{CT}$) attended the RACPC. After data cleaning and exclusion of patients with known CAD, or discharge without further investigation, 268 pre-FFR$_{CT}$ and 287 post-FFR$_{CT}$ patients were eligible for CTCA first line (figure 1). The proportions of patients discharged without additional investigation were similar (pre-FFR$_{CT}$ 37.2% (n=159) vs 33.3% (n=143) post-FFR$_{CT}$, p=0.225). Of those discharged, two died and one suffered an MI in the pre-FFR$_{CT}$ cohort, and one died in the post-FFR$_{CT}$ cohort.

Patient characteristics and extent of missing data are summarised in table 1. Smoking was more prevalent in the post-FFR$_{CT}$ cohort (p=0.003). Hyperlipidaemia and hypertension were also more prevalent (p=0.0063 and 0.035, respectively), although not significantly following Bonferroni correction (Bonferroni threshold 0.0063).

After referral for investigation, 12 eligible patients (9 pre-FFR$_{CT}$ and 3 post-FFR$_{CT}$) experienced an MI before planned first-line investigations and were excluded from the main analysis. The risk of event prior to first-line investigation did not differ (9/268, 3.4% pre-FFR$_{CT}$ vs 3/287, 1.0% post-FFR$_{CT}$; p=0.08).

Investigations and pathways

The sequence and number of tests between RACPC attendance and pathway endpoint are shown in figures 2 and 3. Flow diagrams detailing a chronological breakdown of investigations and times between them are shown in online supplemental file 1.

Time from RACPC attendance to first-line investigation did not differ between cohorts (p=0.98). Median time was 52 days (IQR 35–74) pre-FFR$_{CT}$ vs 53 days (IQR 46–59) post-FFR$_{CT}$.

The proportion of patients offered CTCA as a first-line investigation increased (131/259, 50.6% pre-FFR$_{CT}$ vs 215/284, 75.7% post-FFR$_{CT}$; p<0.001).

The impact of FFR$_{CT}$ on cardiac test referral within 8 months of attendance at the RACPC is shown in table 2. After introduction of FFR$_{CT}$, more patients reached their pathway endpoint (revascularisation or assumed decision to manage medically) following one investigation (74.9% pre-FFR$_{CT}$ vs 84.9% post-FFR$_{CT}$, p=0.005; table 3).

Non-invasive cardiac investigations

After introducing FFR$_{CT}$, use of stress NMPS decreased from 22.8% to 7.7% of patients (p<0.001). Use of rest NMPS also

Table 1 Clinical characteristics of patients included in the analysis.

| Demographic	Pre-FFR$_{CT}$	Post-FFR$_{CT}$	P value
Patients, n	268*	287*	–
Male (%)	137/268 (51.1)	131/287 (45.6)	0.228
Mean age (range)	62 (35–89)	62 (26–89)	0.764†
Ever smoked (%)‡	116/261 (44.4)	167/283 (59.0)	0.003§
Hypertension (%)	112/259 (43.2)	149/283 (52.7)	0.035
Hyperlipidaemia (%)	139/252 (55.2)	184/274 (67.2)	0.006
Diabetes (%)	44/260 (16.9)	48/282 (17.0)	1
Family history (%)	123/252 (48.8)	127/270 (47.0)	0.751
Body mass index ≥30 (%)	66/159 (41.5)	95/229 (41.5)	1

*Value changes in subsequent rows due to unrecorded data or patient answering 'Don't know' when asked.
†P value calculated using t-test; all others used χ^2 test.
‡Ever smoked includes current and ex-smokers.
§Significant with Bonferroni correction applied to the group of eight observations (p<0.00625).
FFR$_{CT}$, CT fractional flow reserve .
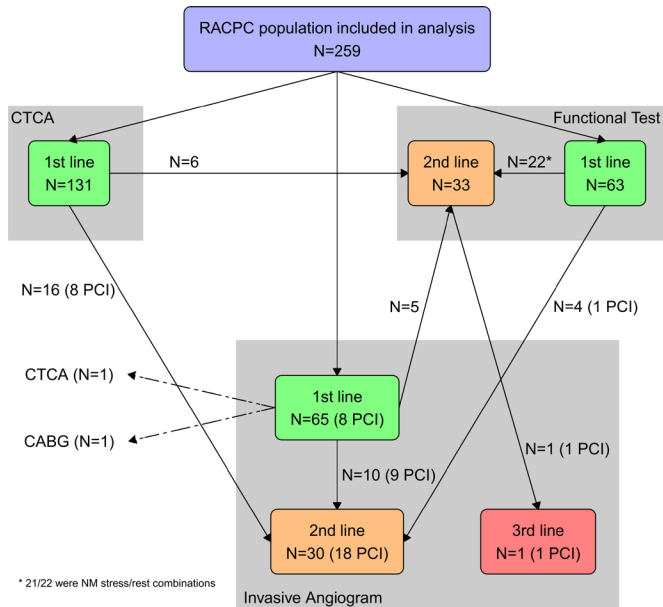
Figure 2 Pre-FFR$_{CT}$: sequence of testing between RACPC attendance and endpoint. CABG, coronary artery bypass grafting; CTCA, CT coronary angiography; FFR$_{CT}$, CT fractional flow reserve; NM, nuclear medicine; PCI, percutaneous coronary intervention; RACPC, rapid access chest pain clinic.

decreased (10.4% pre-FFR$_{CT}$ vs 4.2% post-FFR$_{CT}$), although with Bonferroni correction, this was not statistically significant (p=0.007). The use of stress cardiac MRI (cMRI) and stress echocardiography was unchanged.

The proportion of patients with any functional investigation (including FFR$_{CT}$) before cath lab attendance increased from 5/86 (5.8%) pre-FFR$_{CT}$, to 17/59 (28.8%) post-FFR$_{CT}$ (p<0.001).
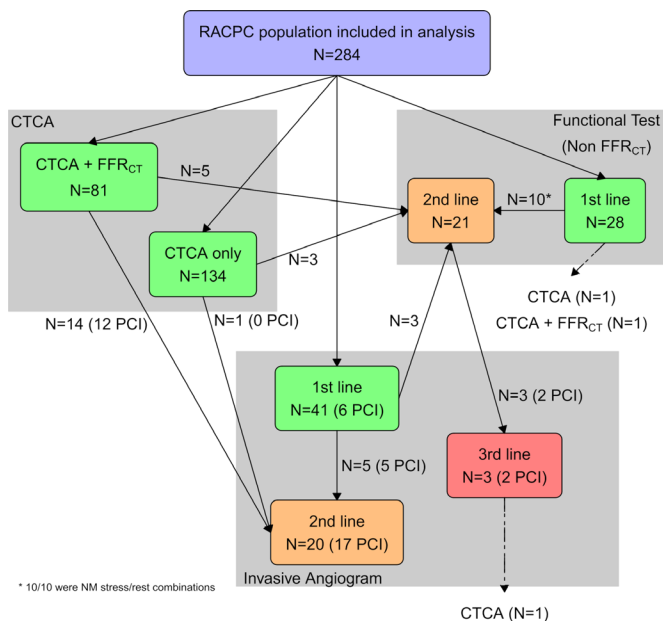
Figure 3 Post-FFR$_{CT}$; sequence of testing between RACPC attendance and endpoint. CTCA, CT coronary angiography; FFR$_{CT}$, CT fractional flow reserve; NM, nuclear medicine; PCI, percutaneous coronary intervention; RACPC, rapid access chest pain clinic.

Table 2 Cardiac test usage within 8 months of attendance at the rapid access chest pain clinic, pre-FFR$_{CT}$/post-FFR$_{CT}$ adoption

Investigation	Pre-FFR$_{CT}$ (n=259) Patients, n (%)	Post-FFR$_{CT}$ (n=284) Patients, n (%)	P value*
Invasive angiogram only	66 (25.5)	39 (13.7)	<0.001†
Invasive angiogram with pressure wire only	3 (1.2)	0 (0.0)	0.108
CTCA only	131 (50.6)	136 (47.9)	0.548
CTCA plus FFR$_{CT}$	0 (0.0)	82 (28.9)	<0.001†
Rest NMPS	27 (10.4)	12 (4.2)	0.007
Stress NMPS	59 (22.8)	22 (7.7)	<0.001†
Stress MRI	3 (1.2)	8 (2.8)	0.227
Stress echo	13 (5.0)	9 (3.2)	0.286

*P values calculated using Fisher's exact test.
†Significant with Bonferroni correction applied to the group of eight observations (p<0.00625).
CTCA, CT coronary angiography; FFR$_{CT}$, CT fractional flow reserve ; NMPS, nuclear myocardial perfusion scan.

Invasive coronary angiography and revascularisation

The overall proportion of patients undergoing diagnostic-only invasive angiography decreased significantly after introducing FFR$_{CT}$ (25.5% pre-FFR$_{CT}$ vs 13.7% post-FFR$_{CT}$, p<0.001). This reduced the overall proportion of patients requiring cath lab procedures from 86/259 (33.2%) to 59/284 (20.8%) (p=0.001).

The proportion of patients undergoing invasive coronary angiography as a first-line investigation was reduced (65/259, 25.1% pre-FFR$_{CT}$ vs 41/284, 14.4% post-FFR$_{CT}$; p=0.002), as was, non-significantly, the use of invasive coronary angiography as a second-line investigation following initial CTCA (16/131, 12.2% pre-FFR$_{CT}$ vs 15/215, 7.0% post-FFR$_{CT}$; p=0.12).

The proportion of patients revascularised remained similar between cohorts (27/259, 10.4% pre-FFR$_{CT}$ vs 25/284, 8.8% post-FFR$_{CT}$; p=0.561).

Pre-FFR$_{CT}$, the revascularisation rate was 8/16 (50.0%) among patients with first-line CTCA only before cath lab attendance. After first-line CTCA plus FFR$_{CT}$ prior to cath lab attendance, the revascularisation rate was 12/14 (85.7%), although this was not statistically significant (p=0.058).
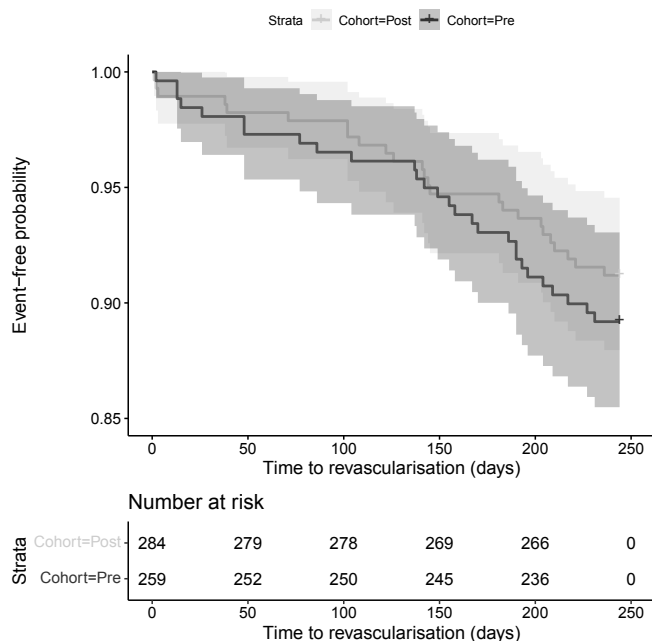
Time to revascularisation

The time taken to reach an endpoint of revascularisation was unchanged between cohorts (figure 4), with a median time of 153.5 days (maximum of 231 days) pre-FFR$_{CT}$, vs 142.0 days (maximum of 236 days) post-FFR$_{CT}$ (p=0.925).

Table 3 Number of investigations after rapid access chest pain clinic visit required to reach pathway endpoint

Investigations required to reach endpoint	Pre-FFR$_{CT}$ (n=259) Patients, n (%)	Post-FFR$_{CT}$ (n=284) Patients, n (%)	P value
1	194 (74.9)	241 (84.9)	0.014*
2	58 (22.4)	39 (13.7)	
3	7 (2.7)	4 (1.4)	

*Significant using Fisher's exact test with null hypothesis of no change in the number of investigations to reach endpoint.
FFR$_{CT}$, CT fractional flow reserve .

Figure 4 Kaplan-Meier plot comparing time to revascularisation for pre-FFR$_{CT}$ and post-FFR$_{CT}$ cohorts. The Cox proportional hazards model found no significant difference in the risk of revascularisation between cohorts. The coloured bands are 95% CIs. FFR$_{CT}$, CT fractional flow reserve.

Hospitalisation and adverse events

The proportion of patients with ≥1 planned inpatient admissions reduced from 39.0% pre-FFR$_{CT}$ to 24.3% post-FFR$_{CT}$ (p<0.001) due to fewer elective invasive angiography procedures. Unplanned hospital attendances did not differ with 5.8% of pre-FFR$_{CT}$ patients attending A&E at least once for cardiovascular reasons, compared with 4.9% of post-FFR$_{CT}$ patients (p=0.705). Both cohorts had similar rates of ≥1 emergency admissions (6.9% pre-FFR$_{CT}$ vs 7.7% post-FFR$_{CT}$, p=0.745), table 4.

Of patients completing first-line investigations, there were no deaths and one MI in the pre-FFR$_{CT}$ cohort, and one death and two MIs post-FFR$_{CT}$. All MIs were treated with revascularisation, and the death in the post-FFR$_{CT}$ cohort occurred following revascularisation.

DISCUSSION
Summary of findings

We assessed RACPC diagnostic pathways and concordance with NICE Guideline CG95[8] before and after introducing FFR$_{CT}$ at a large NHS tertiary cardiac centre. FFR$_{CT}$ adoption was associated with improved compliance through increased CTCA as a first-line investigation and reduced use of some alternative functional tests. Elective inpatient admissions were reduced, as were the number of diagnostic-only invasive angiography procedures. The proportion of patients having percutaneous revascularisation after an invasive angiogram increased. The overall proportion of patients with stable chest pain requiring revascularisation was unchanged. Unplanned hospital admissions were not increased.

Within a single non-invasive test, FFR$_{CT}$ provides anatomical and functional information based on the modelled impact of epicardial stenoses. It does not identify patients with chest pain and evidence of ischaemia in the absence of fixed epicardial stenosis, such as those with microvascular dysfunction or vasospastic angina who may require alternative invasive or non-invasive assessment.

NICE economic modelling estimates potential cost savings of £391 per patient compared with alternative stable chest pain pathways,[9] though this saving may only be achieved in those otherwise undergoing invasive angiography. Despite reduced use of invasive coronary angiography and other diagnostic modalities, similar to that observed in our own study, cost savings were not substantiated in the large UK randomised Fractional Flow Reserve Derived From Computed Tomography Coronary Angiography in the Assessment and Management of Stable Chest Pain (FORECAST) trial.[7] Of note, first-line CTCA use was higher (63%) in the standard care arm of FORECAST compared with our pre-FFR$_{CT}$ cohort (51%), which may reflect local differences in guideline adoption, service provision or the influence of trial participation.

In common with previous studies,[2–7] we observed fewer patients undergoing invasive, diagnostic-only angiography. Despite performing fewer invasive angiograms, revascularisation rates were similar between cohorts, with no increase in adverse events. This suggests that patients received the interventions they needed when triaged using FFR$_{CT}$, while avoiding the associated risks of invasive angiography. Our data and those of other studies[4 11] support the concept that patients with prior positive FFR$_{CT}$ results are more likely to undergo immediate follow-on PCI if referred for invasive assessment. Prioritising cath lab use for revascularisation (rather than diagnosis) is important to minimise revascularisation waiting times for those with proven stable CAD with symptoms inadequately controlled with medical therapy. This may release capacity for urgent or emergency angiography in patients with unstable coronary syndromes. Shifting towards cath lab usage for revascularisation will be particularly important to manage the backlog of patients awaiting PCI following the COVID-19 pandemic.

We observed reduced use of nuclear stress tests, previously our most used functional test. With resource constraints, this has important implications for service planning and may alleviate waiting times for nuclear investigations for other conditions. Reduced use of nuclear stress tests may particularly benefit patients as an abnormal scan requires a second resting test on a

Table 4 Hospital attendance for cardiovascular emergency or elective treatment within 8 months of rapid access chest pain clinic attendance

Type of attendance	Pre-FFR$_{CT}$ (n=259) Patients, n (%)	Post-FFR$_{CT}$ (n=284) Patients, n (%)	P value*
A&E attendance	15 (5.8)	14 (4.9)	0.705
Inpatient admission (elective)	101 (39.0)	69 (24.3)	<0.001†
Inpatient admission (for reasons other than angiography or revascularisation)	33 (12.7)	28 (9.9)	0.341
Inpatient admission (emergency)	18 (6.9)	22 (7.7)	0.745
Outpatient appointment	256 (98.8)	282 (99.3)	0.673

*P values calculated using Fisher's exact test.
†Significant with Bonferroni correction applied to the group of five observations (p<0.01)
A&E, accident and emergency; FFR$_{CT}$, CT fractional flow reserve.

separate visit. Therefore, FFR_{CT} reduces not only total patient visits but also patient exposure to ionising radiation. The potential reduction in radiation exposure associated with FFR_{CT} is quantified elsewhere.[5][12] Despite differences in study design, we found our decreased reliance on diagnostic cath lab procedures and non-FFR_{CT} functional tests to be concordant with other studies[7] and NHS hospitals.[13] However, it is challenging to disaggregate the influence of increased CTCA use alone, compared with CTCA plus selective FFR_{CT}.

FFR_{CT} analysis is available within 12 hours, potentially enabling communication of diagnostic and treatment decisions to patients within a day of their CTCA. Conversely, pathways that 'layer' diagnostic tests (eg, CTCA followed by functional testing with stress cMRI, stress echocardiography or NMPS) typically have additive waiting times, potentially taking longer to reach diagnosis. Although we saw no difference in adverse events while patients awaited investigation, longer waiting times may prolong anxiety for patients and may delay return to work, travel or investigation of alternative causes of symptoms.

There was no significant difference in either the overall time patients spent on pathways or the median number of hospital attendances and procedures. However, this disguised changes in how attendances and investigation types were distributed. There was greater reliance on invasive testing earlier in the pathway before adopting FFR_{CT}, with more patients undergoing first-line invasive coronary angiography. Changes in pathway time may also have been masked because waiting times for clinic review or elective revascularisation procedures did not change. We found a greater proportion of patients reached pathway endpoint after one test, which may be important for patient satisfaction and planning new 'one-stop-shop' services for diagnosis and management of new-onset stable chest pain.

Strengths and limitations

Our study is from a large UK NHS Trust and provides a comprehensive picture of all cardiac investigation modalities and hospital settings used to assess and diagnose stable chest pain. The work was retrospective and therefore reflects a 'real-world' change in pathways, without the influence of trial participation, although as an uncontrolled study, there were potential confounders.

Using NHS numbers and national datasets permitted identification of all patient deaths, although cause of death information was not available. RACPC patients undergo subsequent investigations at our hospital, and our records, combined with manual review of coded events, enabled identification of all encounters. We could not, however, identify additional investigations or emergency admissions at other hospitals. Exclusion of patients ineligible for CTCA under CG95 was achieved using local data and clinical history, although CAD events recorded outside of NuTH would rely on patient recall. However, it is likely that missed exclusions would occur proportionally across both cohorts and would not, therefore, alter our results.

The two cohorts differed significantly in certain clinical characteristics, with higher proportions of hyperlipidaemia, hypertension and smoking in the post-FFR_{CT} cohort. There were no changes in RACPC referral criteria during the study, and it is unlikely that these factors would have affected investigation choices. However, we could not determine the factors influencing first-line or second-line investigation choices. Patients with persistent symptoms and non-obstructive CAD on CTCA or FFR_{CT} may have undergone functional assessment for identification of ischaemia in the context of normal coronary arteries (eg, due to microvascular dysfunction) or because the physician

suspected a false-negative result. Increased awareness of non-obstructive causes of ischaemic chest pain may have influenced second-line referral patterns.

Data relating to symptoms in the RACPC dataset were recorded as a free-text summary rather than a standardised scale and so were unsuitable for analysis, and no information on quality of life was available.

Similar results may not be realised in smaller hospitals or those without the necessary high-quality cardiac CT service capacity or compliance with information governance standards. The implications of the latter were presented in NICE shared learning from Liverpool Heart & Chest Hospital NHS Foundation Trust[14] and from Bath Hospital.[13]

CONCLUSIONS

Introduction of FFR_{CT} was associated with greater compliance with NICE CG95, reduction in invasive diagnostic coronary angiography, planned hospital admissions and need for more than one diagnostic test to reach a stable CAD pathway endpoint.

ORCID iDs
Rachel A O'Leary http://orcid.org/0000-0003-2544-9827
Julie Burn http://orcid.org/0000-0002-2300-2725
Andrew J Sims http://orcid.org/0000-0002-9553-7278
Anna Beattie http://orcid.org/0000-0001-7723-8760
Alan Bagnall http://orcid.org/0000-0003-0683-851X

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Supplementary material

Exclusions

Free-text RACPC history exclusions for known existing CAD

The following regular expressions were used to exclude patients with known existing CAD based on the free-text history recorded at the RACPC.

"(?<!failed)PCI|DES|CABG|(?<!renal) stent|oronary artery bypass|ngioplasty| single vessel"

Identifies patients with mention of:

- PCI (not failed); OR
- DES (drug eluting stent); OR
- CABG; OR
- stent (not renal); OR
- oronary artery bypass (missing first letter to account for case sensitivity if term appears at start of sentence); OR
- ngioplasty (missing first letter to account for case sensitivity if term appears at start of sentence); OR
- single vessel (single vessel disease, would only be mentioned in this context)

"MI|Mi"

Identifies patients with mention of:

- MI (myocardial infarction); OR
- Mi (missed capitalisation of the "i")

These exclusions were checked manually to ensure instances including a patient name (i.e. "Miss [surname]") were not incorrectly flagged for exclusion, and were truly indicative of an MI.

ICD10 exclusions for known existing CAD

The following ICD10 codes were identified as being relevant for the exclusion of patients with known existing CAD previously seen as inpatients in our cohorts.

Code	Description
I200	Unstable angina
I252	Old myocardial infarction
I219	Acute myocardial infarction, unspecified
I214	Acute subendocardial myocardial infarction
I211	Acute transmural myocardial infarction of inferior wall
I212	Acute transmural myocardial infarction of other sites
I210	Acute transmural myocardial infarction of anterior wall
I255	Ischaemic cardiomyopathy
I213	Acute transmural myocardial infarction of unspecified site
I253	Aneurysm of heart
I248	Other forms of acute ischaemic heart disease
I201	Angina pectoris with documented spasm
I249	Acute ischaemic heart disease, unspecified

I229	Subsequent myocardial infarction of unspecified site
I240	Coronary thrombosis not resulting in myocardial infarction

OPCS exclusions for known existing CAD

The following OPCS codes were identified as being relevant for the exclusion of patients with known existing CAD previously seen as inpatients in our cohorts.

Code	Description
K404	Saphenous vein graft replacement of four or more coronary arteries
K453	Anastomosis of mammary artery to left anterior descending coronary artery
K751	Percutaneous transluminal balloon angioplasty and insertion of 1-2 drug-eluting stents into coronary artery
K752	Percutaneous transluminal balloon angioplasty and insertion of 3 or more drug-eluting stents into coronary artery
K491	Percutaneous transluminal balloon angioplasty of one coronary artery
K503	Percutaneous transluminal injection of therapeutic substance into coronary artery NEC
K753	Percutaneous transluminal balloon angioplasty and insertion of 1-2 stents into coronary artery
K402	Saphenous vein graft replacement of two coronary arteries
K411	Autograft replacement of one coronary artery NEC
K498	Other specified transluminal balloon angioplasty of coronary artery
K518	Other specified diagnostic transluminal operations on coronary artery
K403	Saphenous vein graft replacement of three coronary arteries
K493	Percutaneous transluminal balloon angioplasty of bypass graft of coronary artery
K512	Intravascular ultrasound of coronary artery

Identification of diagnoses and investigations

A&E cardiovascular diagnoses

The following conditions were identified as being relevant for the classification of A&E attendances being for cardiovascular reasons.

Description
ACS - Acute coronary syndrome
Acute chest pain
Angina
Angina of effort
Cardiac chest pain
Chest pain
Chest pain at rest
Chest tightness
Ischaemic heart disease
NSTEMI - Non-ST segment elevation MI
Unstable angina

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Inpatient admission for cardiovascular reasons

The following ICD10 codes were identified as being relevant for the classification of inpatient admissions being for cardiovascular reasons.

Code	Description
Ix	All codes beginning with 'I' are cardiovascular
R00x	Abnormalities of heart beat Tachycardia, unspecified Bradycardia, unspecified Palpitations Other and unspecified abnormalities of heart beat
R01x	Cardiac murmurs and other cardiac sounds Benign and innocent cardiac murmurs Cardiac murmur, unspecified Other cardiac sounds
R03x	Abnormal blood-pressure reading, without diagnosis Elevated blood-pressure reading, without diagnosis of hypertension Nonspecific low blood-pressure reading
R060	Dyspnoea
R071	Chest pain on breathing
R073	Other chest pain
R074	Chest pain, unspecified
R098	Other specified symptoms and signs involving the circulatory and respiratory systems
R55	Syncope and collapse
R570	Cardiogenic shock
R931	Abnormal findings on diagnostic imaging of heart and coronary circulation
R943	Abnormal results of cardiovascular function studies

Inpatient procedures

The following OPCS codes were identified as classifying procedures relevant to the study, carried out on an inpatient basis.

Code	Description
K634	Coronary arteriography using two catheters
K635	Coronary arteriography using single catheter
K636	Coronary arteriography NEC
K49x	Percutaneous transluminal balloon angioplasty of one coronary artery Percutaneous transluminal balloon angioplasty of multiple coronary arteries Percutaneous transluminal balloon angioplasty of bypass graft of coronary artery Percutaneous transluminal cutting balloon angioplasty of coronary artery Other specified transluminal balloon angioplasty of coronary artery Unspecified transluminal balloon angioplasty of coronary artery
K501	Percutaneous transluminal laser coronary angioplasty
K75x	Percutaneous transluminal balloon angioplasty and insertion of 1-2 drug-eluting stents into coronary artery Percutaneous transluminal balloon angioplasty and insertion of 3 or more drug-eluting stents into coronary artery Percutaneous transluminal balloon angioplasty and insertion of 1-2 stents into coronary artery Percutaneous transluminal balloon angioplasty and insertion of 3 or more stents into

	coronary artery NEC Other specified percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery Unspecified percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery
K40x	Saphenous vein graft replacement of one coronary artery Saphenous vein graft replacement of two coronary arteries Saphenous vein graft replacement of three coronary arteries Saphenous vein graft replacement of four or more coronary arteries Other specified saphenous vein graft replacement of coronary artery Unspecified saphenous vein graft replacement of coronary artery
K41x	Autograft replacement of one coronary artery NEC Autograft replacement of two coronary arteries NEC Autograft replacement of three coronary arteries NEC Autograft replacement of four or more coronary arteries NEC Other specified other autograft replacement of coronary artery Unspecified other autograft replacement of coronary artery
K42x	Allograft replacement of one coronary artery Allograft replacement of two coronary arteries Allograft replacement of three coronary arteries Allograft replacement of four or more coronary arteries Other specified allograft replacement of coronary artery Unspecified allograft replacement of coronary artery
K43x	Prosthetic replacement of one coronary artery Prosthetic replacement of two coronary arteries Prosthetic replacement of three coronary arteries Prosthetic replacement of four or more coronary arteries Other specified prosthetic replacement of coronary artery Unspecified prosthetic replacement of coronary artery
K44x	Replacement of coronary arteries using multiple methods Revision of replacement of coronary artery Other specified other replacement of coronary artery Unspecified other replacement of coronary artery

Inpatient events

The following ICD10 codes were identified as classifying events relevant to the study, occurring on an inpatient basis.

Code	Description
I21x	Acute myocardial infarction Acute transmural myocardial infarction of anterior wall Acute transmural myocardial infarction of inferior wall Acute transmural myocardial infarction of other sites Acute transmural myocardial infarction of unspecified site Acute subendocardial myocardial infarction Acute myocardial infarction, unspecified
I22x	Subsequent myocardial infarction Subsequent myocardial infarction of anterior wall Subsequent myocardial infarction of inferior wall Subsequent myocardial infarction of other sites

	Subsequent myocardial infarction of unspecified site

Radiology Information System – procedures

The following exam names were identified as classifying relevant investigations, as recorded in the RIS dataset.

| Procedure	Exam Name
CTCA	CT Cardiac Angiogram Coronary
CTCA	CT Cardiac Cor Artery Calcium Scoring
CTCA	CT Cardiac Gated Function With Contrast
Stress NMPS	NM Mps Tf Stress Gated
Rest NMPS	NM Mps Tf Rest Gated
Angiography	Cardiac Angio Coronaries
Angiography	Cardiac Angio Lt Ventricle and Cor A
Pressure wire	Cardiac Pressure Wire and Cath Insertion
PCI	Primary Pc coronary intervention
PCI	Cardiac Angio Coronary Stent
PCI	Cardiac Pressure Wire and Pci
MRI	MRI Card Morphology Func With Contrast
MRI	MRI Card Morph Func Velocity Stress Cont
MRI	MRI Card Morph Func Velocity With Cont
MRI	MRI Card Morphology Function Velocity
IVUS	Intravascular Ultrasound
OCT	OCT Coronary artery Fluoro guided Right
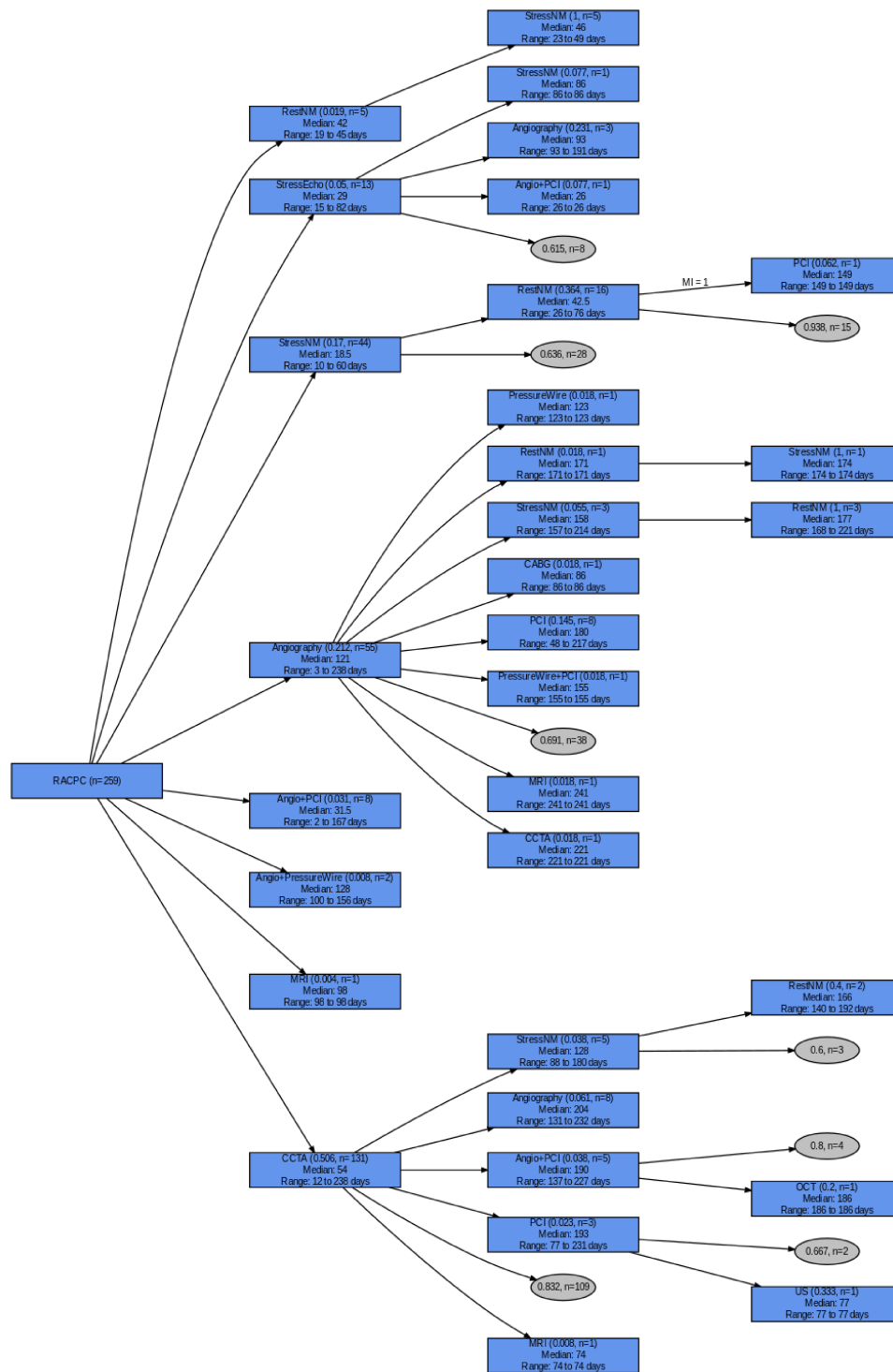
Figure S1. Pre-fractional flow reserve computed tomography (FFR_CT); chronological breakdown of investigations between Rapid Access Chest Pain Clinic (RACPC) attendance and endpoint.

Abbreviations: CTCA, computed tomography coronary angiography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; NM, nuclear medicine; MRI, magnetic resonance imaging; OCT, optical coherence tomography; US, ultrasound.
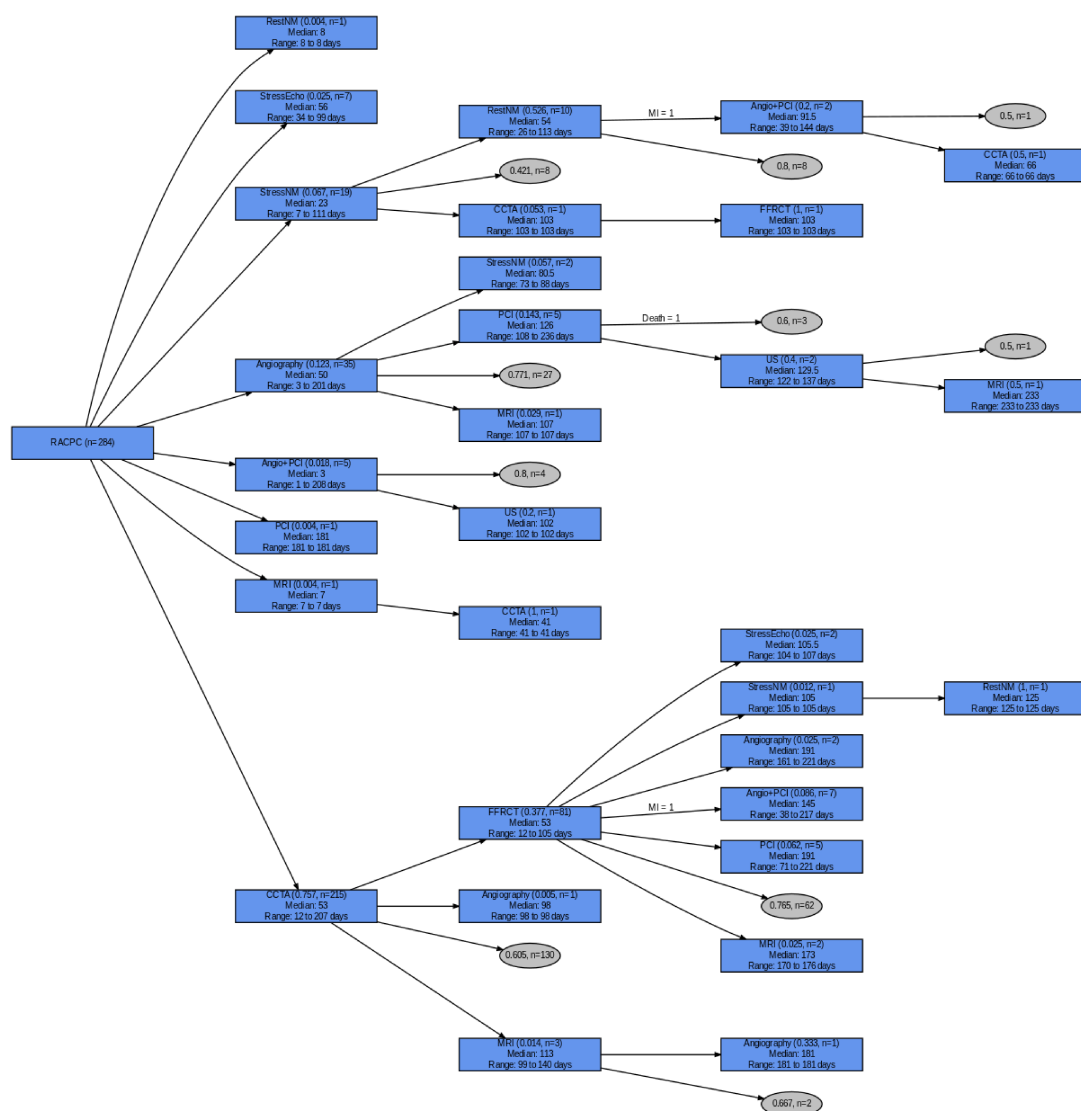
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Figure S2. Post-fractional flow reserve computed tomography (FFR$_{CT}$); chronological breakdown of investigations between Rapid Access Chest Pain Clinic (RACPC) attendance and endpoint.

Abbreviations: CTCA, computed tomography coronary angiography; PCI, percutaneous coronary intervention; NM, nuclear medicine; MRI, magnetic resonance imaging; US, ultrasound.