Healthcare Improvement Scotland | SHTG Advice on health technologies

SHTG Adaptation 03

September 2021

In response to an enquiry from Scottish Government

HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography*

**adaptation for NHSScotland of guidance published by National Institute for Health and Care Excellence (NICE)*

Recommendations for NHSScotland

- HeartFlow fractional flow reserve computerised tomography (FFRCT) is non-invasive, safe and, by improving specificity, may improve the diagnosis of obstructive versus non-obstructive coronary artery disease (CAD) following computerised tomography-coronary angiography (CT-CA).
- HeartFlow FFRCT may be considered as an option alongside a set of complementary diagnostic tools for patients with stable, recent onset chest pain symptoms who have undergone CT-CA with adequate image quality on a 64-slice (or above) CT scanner.
    - Compared with standard care, using HeartFlow FFRCT may reduce the requirement for invasive coronary angiography (ICA) to further assess patients with CAD, though noting that the quality of supporting clinical-effectiveness evidence was limited.
    - HeartFlow FFRCT should be considered in the context of patients with reported CAD following CT-CA, patient symptoms and the introduction of guideline directed medical therapy.
    - The use of HeartFlow FFRCT should be determined in the context of the diagnostic resources and expertise available to the referring clinician. HeartFlow FFRCT may be of particular value in remote locations, when access to complementary diagnostic tools is limited.
- Use of Heartflow FFRCT has the potential to lead to cost savings, primarily driven by a reduction in referrals for ICA. There is uncertainty about the level of cost savings achievable, due to variations in clinical practice when investigating chest pain and the use of different patient management strategies.

The Scottish Health Technologies Group (SHTG) recommendation is based on guidance produced by National Institute for Health and Care Excellence (NICE) in 2017.[1] This guidance was modified following an SHTG adaptation process. NHSScotland is required to consider SHTG recommendations.

Description of the technology under consideration

HeartFlow FFRCT is a coronary physiologic simulation software that creates three-dimensional visualisations of coronary physiology from data acquired from a standard CT-CA image.* The software provides a non-invasive method of estimating fractional flow reserve (FFR). FFR is considered to be the standard of care for the functional assessment of lesion stenosis severity.[2] It is a surrogate estimate of the ratio between the maximum blood flow in a narrowed artery and the maximum blood flow in a normal artery. Currently, FFR is calculated from invasive measurement of the pressure drop across a narrowed artery during maximal hyperaemia. This requires ICA and the placement of a pressure wire in the distal coronary artery and is associated with cost and risk of adverse events.

This topic was referred to SHTG by the Scottish Government. SHTG were asked to consider the guidance produced by NICE, and whether it could be applied to NHSScotland.

*While NICE used the term coronary CT angiography (CC-TA), the term CT-CA is used here to be consistent with Scottish Intercollegiate Guidelines Network (SIGN) guidelines.

Why is this important?

Treating and preventing heart disease is a national clinical priority for Scotland, as outlined in the Heart Disease Action Plan.[3] There is a growing demand on interventional cardiac services in Scotland through a combination of increased referrals for ICA, a growth in structural heart intervention and significant pressures on cardiac catheterisation laboratories (Richard Good, Consultant Cardiologist, NHS Golden Jubilee, Personal Communication, June 2021). There are currently six sites in Scotland which conduct percutaneous coronary intervention (PCI), with over 9,000 cases in 2018/19. There were 10,352 diagnostic coronary angiographs (without angioplasty) carried out in 2017/18.[4]

Use of HeartFlow FFRCT data is intended to complement the anatomical information provided by CT-CA to aid diagnosis and management of patients with CAD and minimise the number of unnecessary invasive procedures conducted in patients who turn out to have non-flow-limiting coronary artery stenosis.

What was our approach?

We undertook an SHTG Adaptation process based on guidance produced by NICE in 2017 and updated in 2021.[1] The European Network for Health Technology Assessment (EUnetHTA) adaptation toolkit was used to assess the relevance, reliability and transferability of the NICE guidance.[5]

As part of the adaptation process, the views, perspectives and experience of topic experts were obtained via three rounds of questioning. The first draft of the SHTG Adaption was distributed to topic experts, along with a survey. The experts were asked to consider whether the NICE recommendations were appropriate for Scotland and if so, whether they should be adopted with no changes, or adapted to make them more relevant to the NHSScotland context.

Based on the responses received, the draft SHTG Adaptation document was reviewed. A revised draft, along with anonymised responses to the first round of questioning, was sent back to the experts for a second round of questioning. Further changes were made to the draft based on the responses received.

Topic experts' comments are captured within the SHTG Adaptation including a detailed summary from each round of questioning. All experts' comments were available for consideration by SHTG Council to inform the final recommendations.

What next?

The SHTG Adaptation will be disseminated across NHSScotland health boards to inform the use of HeartFlow FFRCT for estimating fractional flow reserve from CT-CA in patients with CAD.

Scottish Health Technology Council considerations

The draft SHTG Adaptation was considered by the Scottish Health Technology Council on 27 July 2021. A summary of the discussion is presented as follows:

- The Council highlighted that access to CT-CA should be the focus to improve diagnosis of CAD across Scotland, and acknowledged the importance of the work by the National Planning Cardiac Imaging Group to ensure equitable access to CT-CA.
- The Council agreed that the supporting evidence for the use of HeartFlow FFRCT was of limited quality (for example non-randomised, post-hoc studies).
- The Council noted that ICA carries a risk of adverse events, and recognised the potential opportunity for HeartFlow FFRCT to reduce the need for invasive procedures.
- The Council recognised the relative cost savings opportunities from HeartFlow FFRCT in island or remote geographies, where the use of the technology may reduce the need for patients to travel long distances for further investigation of chest pain.
- The Council noted that as HeartFlow FFRCT uses information from the CT-CA scan, it negates the need for the patient to be present for the test.
- The Council acknowledged that the evidence on this topic is evolving. Scottish HeartFlow FFRCT data should be reviewed once available, particularly in relation to proposed reductions in ICA, which formed the basis of the NICE economic argument.

Reliability and transferability of the adapted guidance

The EUnetHTA health technology assessment (HTA) adaptation toolkit was used to assess the relevance, reliability and transferability of the NICE guidance.[5] The toolkit focuses on five 'domains' (or sections of an HTA report):

- The use of the technology
- Safety
- Effectiveness
- Economic evaluation
- Organisational elements

The following section 'Considerations for Scotland' describes the key issues identified through use of the toolkit.

Considerations for NHSScotland

Epidemiology and predicted volume

Although there has been a substantial reduction in the rate of death from coronary heart disease (CHD) over the last decade, it remains one of the leading causes of death in Scotland. Cancer is the leading cause of death in Scotland, followed by CHD, with CHD being the largest contributor to the overall burden of disease in 2016. In 2018/2019, the incidence of CHD in Scotland was 18,404 and in 2018, there were 6,615 deaths in Scotland where CHD was the underlying cause.[4]

A total of 4,534 CT-CA procedures were recorded in Scotland between October 2018 and September 2019.[6] NICE guidelines on stable chest pain recommend CT-CA as the first line investigation of patients with stable chest pain. A UK-wide study estimated that 28,630 CT-CAs per year would be required across Scotland if the NICE guidelines were fully implemented.[7] In Scotland, SIGN similarly recommends the use of CT-CA in the investigation of suspected stable angina.[8]

Organisational issues

The administration of HeartFlow FFRCT does not require scheduling of additional outpatient appointments as data for the HeartFlow FFRCT visualisations are taken from previously acquired CT-CA data.

Cardiac investigation of suspected angina in Scotland

In Scotland, the SIGN guideline on stable angina recommends that 'CT-CA be considered for the investigation of chest pain when stable angina is suspected, but is not clear from the history.' This is highlighted as a key clinical recommendation that should be prioritised for implementation.[8] The guideline described a number of methods of investigation which can help to confirm the presence, severity and extent of underlying CAD and guide risk stratification and management strategies. These investigations can be anatomical, such as CT-CA and ICA, or functional, such as exercise tolerance testing, stress echocardiography, stress perfusion cardiovascular magnetic resonance imaging, and myocardial perfusion scintigraphy. Which investigations the clinician chooses depends on the clinical presentation, pretest probability and prior history of CAD, and may be influenced by the local availability of these investigations and resources.

The NICE guideline on chest pain recommends CT-CA as the first-line investigation for stable angina. [9] The NICE guidance being considered for adaptation states that HeartFlow FFRCT should

be considered as an option for those patients who are offered CT-CA as recommended in the NICE guideline.

As part of the SHTG Adaptation we asked Scottish experts whether they felt that HeartFlow FFRCT would alter the referral volume for other diagnostic tests. There was variability from the seven clinicians who responded:

- In line with the evidence that demonstrates a reduction in ICA following the adoption of HeartFlow FFRCT, four out of five experts with access to ICA predicted a decrease in these referrals
- One expert noted that the additional information offered by HeartFlow FFRCT would help to inform good shared decision discussions with patients
- Two experts predicted a decrease in the use of pressure wire, one of these experts noted that the assessment of microvascular disease assessment is also relevant at this point
- Two experts said they did not predict a decrease in use of pressure wire
- One expert said they had access to the exercise tolerance test and myocardial perfusion and had seen reductions in these referrals following the adoption of HeartFlow FFRCT
- One other expert predicted reductions in the exercise tolerance test and another predicted a reduction in referrals for myocardial perfusion
- One expert thought that it would change the referral rates for stress echocardiography and stress MRI
- One expert noted that they would only refer patients with established coronary disease to myocardial perfusion or stress echocardiography.

Provision of CT-CA in Scotland

HeartFlow FFRCT relies on the availability of CT-CA. A National Planning Cardiac Imaging Group was set up in 2019 following a National Planning horizon scan that identified cardiac imaging development as a key area to be progressed. An overarching objective of the group is to put together a business case for all boards in Scotland to be able to provide equitable access to CT-CA- enabled scanners (NHS National Services Scotland unpublished internal scoping report, 2019).

Although SIGN recommends CT-CA for the investigation of stable angina, the provision of CT-CA across Scotland is variable. A 2019 survey of CT-CA access in NHS boards by the Scottish Clinical Imaging Network (SCIN) highlighted several gaps in availability of CT-CA across Scotland due to a variety of factors including equipment capability and workforce. Thirteen territorial NHS boards and one national NHS board responded to the survey. Nine boards reported variable levels of CT-CA provision. Of the five NHS boards with no local CT-CA provision, three referred patients to

other NHS boards for CT-CA (NHS National Services Scotland unpublished internal scoping report, 2019).

This variation or limitation in availability of CT- CA was highlighted by six out of eight experts during the SHTG Adaptation process.

HeartFlow FFRCT referral pathway

Patient group

As part of the 2021 NICE guidance update, the number of referrals for HeartFlow FFRCT was estimated. Estimates varied from none (no access), to all CT-CAs with obstruction (due to being part of NHS Innovation and Technology Programme). One expert reported that they would refer 2–3% of patients with moderate disease (detected upon CT-CA) while another expert reported they would refer 20% of patients (including those with mild disease

In relation to the patient population referred to HeartFlow FFRCT, four of the NICE experts who used this technology said the main clinical scenario would be patients with stable chest pain and moderate or equivocal disease (detected with CT-CA). Another expert highlighted a lack of UK-wide data to determine which patient categories can benefit from using Heartflow FFRCT.

In discussions during the SHTG Adaptation process, one Scottish expert reflected the opinion of the NICE experts and suggested HeartFlow FFRCT should be considered in patients with moderate severity lesions with low and intermediate probability of CAD as part of a stratified treatment algorithm. Another Scottish expert felt that Heartflow FFRCT performs well at extremes, when there is no CAD or severe CAD, but not as well when there is indeterminate lesion severity on CT or calcified vessels. A third Scottish expert suggested that HeartFlow FFRCT is rarely needed in this pathway; they felt that asking patients about their symptoms and use of CT-CA gives most of the information required. A fourth Scottish expert noted that NICE did not account for the key roles of patient symptoms and clinical context when determining whether a patient would get ICA.

Similarly to one of the NICE experts, a Scottish expert highlighted the demonstration of an appropriate non-invasive approach for patients with well controlled symptoms on medical therapy following the results of the ISCHEMIA trial.[10] This expert also noted that in current practice, HeartFlow FFRCT may not necessarily impact on immediate decision making as not all patients with obstructive disease on CT-CA are scheduled for immediate ICA.

One Scottish expert raised the issue of the threshold for referral of CT-CA for additional HeartFlow FFRCT and suggested that there may be significant variability around when reporting clinicians felt HeartFlow FFRCT was indicated and that standardising this could be challenging.

Referring clinician

Experts were asked who should make the decision about whether the CT-CA scans should be sent for additional HeartFlow FFRCT analysis (referring cardiologist or reporting radiologist or cardiologist). Four of the eight experts who responded said the reporting radiologist or cardiologist, two experts said the referring cardiologist and two suggested either the referring cardiologist or the reporting radiologist or cardiologist depending on the local set-up and within a multi-disciplinary team context. One expert commented that while the reporting team would understand the quality of the scan and the likely additive information from HeartFlow FFRCT, it is the referring cardiologist that makes the management decision.

Training

Contributing experts in the NICE guidance noted that while no specific HeartFlow FFRCT training was required, they were aware that using CT-CA requires training, following instructions and standards, and the procurement and use of required facilities. There was consensus among five NICE experts that obtaining high quality images required training. Scottish experts were asked whether they would need training or education in order to make management decisions based on Heartflow FFRCT reports. Four experts felt they would not need further training, one added that the referring clinician may do if they were a non-interventional cardiologist. One expert with experience in HeartFlow FFRCT said the interpretation had so far been relatively straightforward with support from the reporting radiologist. Another expert thought they would need additional training though experience would develop with time and exposure.

Use of the technology in Scotland

Current use

An ongoing pilot project, funded by the Modernising Patient Pathways Programme, has introduced HeartFlow FFRCT to NHS Western Isles to facilitate the triage of diagnostic coronary angiography and as a further diagnostic option to the current NHS Western Isles pathway for the diagnosis of patients with stable CAD. The project began in December 2020 and will complete when 40 scans have been sent for analysis (Debra Vickers, Nurse Consultant Cardiology, Jane MacDonald, Radiology Manager, NHS Western Isles, Personal Communication, February 2021). HeartFlow FFRCT has also been used in the FORECAST trial in NHS Lothian which recruited 93 patients between January 2019 and July 2019 (Nick Cruden, Consultant Cardiologist, NHS Lothian, Personal Communication, May 2021).

Two Scottish experts highlighted that the value from HeartFlow FFRCT may be in remote and rural settings where access to cardiology expertise or onsite cardiac catheterisation facilities, to ascertain if disease is likely to be flow-limiting or not, is limited. Establishing this would in turn reduce the number of patients with normal arteries or minimal disease being referred for invasive assessment at regional centres.

Barriers to adoption in Scotland

Scottish experts were asked to identify barriers to the adoption of the NICE guidance in NHSScotland. The following issues were raised: potential of insufficient or under-utilised equipment required to support HeartFlow FFRCT (two mentions), lack of a properly trained workforce (one mention), potential for poor acceptance of a new technique that may change practice (two mentions) and extent of calcific CAD in population and cost (one mention).

Experts in the NICE guidance highlighted that up to 25% of CT-CA scans in clinical trials were not suitable for HeartFlow FFRCT analysis. This was echoed by two Scottish clinicians. One estimated 30–50% of scans were rejected, the other suggested that achieving adequate scan quality to permit analysis was a potential barrier to adoption.

One Scottish expert shared their experience on the importance of the CT-CA quality. During their participation in a HeartFlow FFRCT trial they reported a proportion of scans were rejected by Heartflow FFRCT because of stair-step and motion artefacts. They observed that careful attention to heart rate control and scan acquisition was required.

Of the six clinical experts in the NICE 2021 update who contributed opinion, four had either had direct involvement in the use of HeartFlow FFRCT or had referred patients for its use.
The NICE experts cited low availability, few referrals, costly information technology (IT) infrastructure requirements and delays in integration with the picture archiving and communication system (PACS) as some of the reasons that limit the use of HeartFlow FFRCT. Four out of the six experts felt that evidence from recent trials (notably the FORECAST and ISCHEMIA trials) meant that the recommendations by NICE should be updated. They also questioned the cost compared to other modalities. One expert highlighted the recent ISCHEMIA trial which suggested that patients with stable CAD can be managed safely by conservative care, without the need for ischaemia testing or invasive management and so makes the indication for HeartFlow FFRCT questionable.

Heartflow FFRCT evidence base: NICE medical technologies guidance 2017 (MTG32) and 2021 update

Within their 2021 update, NICE took into account changes to the HeartfFlow FFRCT technology, clinical environment and evidence base, and concluded that the original recommendations held. The evidence review supported the diagnostic performance, prognostic performance and reported improved clinical outcomes for patients. HeartFlow FFRCT remained cost-saving and to a greater extent than the original cost model. The review decision document included details of the updated literature search and the clinical opinion that was gathered as part of the update.

As part of this SHTG Adaptation, the evidence for HeartFlow FFRCT in reducing ICA was found to be limited. Many of the studies cited in the NICE guidance were either poorly designed to

determine the effect of HeartFlow FFRCT over and above CT-CA alone, or of limited quality (for example, non-randomised, post-hoc studies).

FORECAST trial

The FORECAST trial is a recent large (n=1,400 adults with stable chest pain) randomised controlled trial (RCT) from the United Kingdom (UK). The FORECAST trial compared CT-CA and HeartFlow FFRCT with the routine clinical pathway on resource utilisation at 9 months. Patients with a coronary stenosis of >40% in at least one major epicardial vessel of stentable/graftable diameter were referred to HeartFlow FFRCT. In the intervention arm, 31.5% of patients had HeartFlow FFRCT. In the intervention arm 479 (68.5%) patients did not receive HeartFlow FFRCT for the following reasons: 415 had no lesions >40%, 39 had no analysable images and 25 did not have CT-CA. At 9 months, there was a 14% lower level of ICA in the intervention arm compared with the reference group (p=0.02). The mean costs for the intervention arm were £1,605.50 and £1,491.46 for the reference group, with no significant difference (p=0.962). The FORECAST trail concluded that HeartFlow FFRCT does not lead to cost savings, which challenges the recommendations of the NICE guidance. FORECAST did not compare the outcomes of HeartFlow FFRCT plus CT-CA with those of CT-CA alone. NICE noted that the FORECAST trial is unpublished and while preliminary evidence was available from a conference presentation,[5] they were not able to assess the risk of bias. They noted the importance of reviewing the published paper before concluding on the impact of available evidence.

Funding of studies

The NICE guidance noted that 'Most of the major studies were funded by HeartFlow and the independent studies had either a small sample size or their researchers had received funding or support from HeartFlow that potentially could cause conflicts of interest and bias.' No other issues relating to relevance, reliability and transferability of the NICE guidance were identified.

Cost considerations in Scotland

The NICE Heartflow economic model

As part of the NICE 2021 updated guidance on HeartFlow FFRCT, a decision-tree model based on the NICE clinical guideline on the assessment and diagnosis of recent onset chest pain of suspected cardiac origin was assessed.[9] Two strategies were compared in the model: Using CT-CA to inform treatment of stable angina; versus using Heartflow FFRCT after a positive CT-CA result to inform treatment. The costs associated with each strategy over a 1 year time horizon were compared. The model structure is illustrated in *Figure 1* below. In both arms an uncertain CT-CA result leads to further functional imaging (SPECT, MRI, or ECHO). Uncertain functional imaging

results lead to an ICA. Treatment for patients with stable angina is either PCI or optimal medical therapy. Use of HeartFlow FFRCT led to a reduction in the proportion of patients referred to ICA. Results of the cost model showed that Heartflow FFRCT was associated with cost savings of £391 per patient.

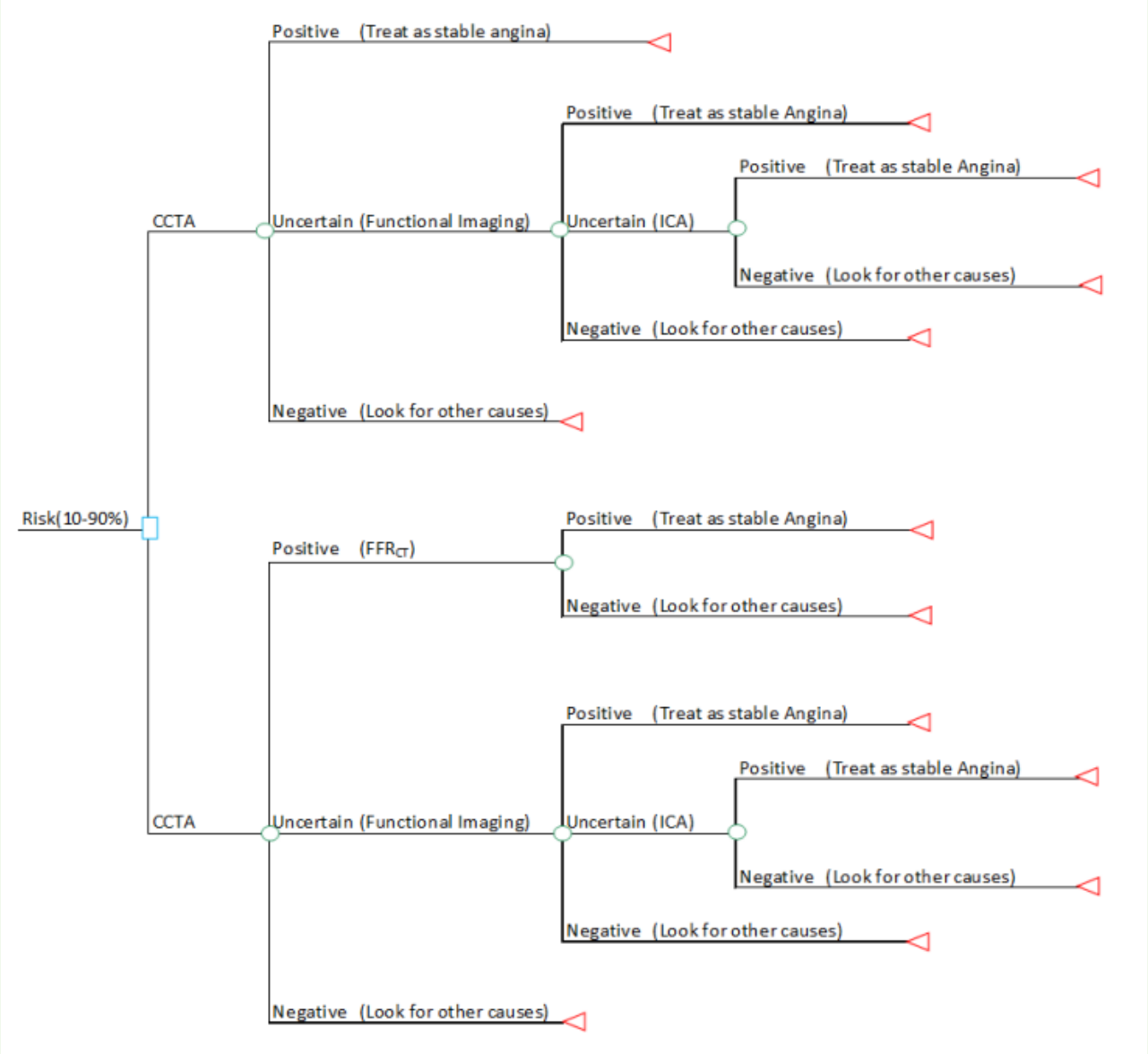

Figure 1: Decision-tree model comparing CT-CA with CT-CA plus HeartFlow FFRCT to inform treatment of stable angina

Transferability to Scotland

The results of the NICE economic model are unlikely to apply to the Scottish context. There are several discrepancies with respect to costs and patient management in Scotland which cast doubt on whether the predicted cost savings may be realised.

- Test and procedure costs in the NICE model were based on NHS reference costs tariffs which do not include data from Scotland. Reliable Scottish costs for procedures, particularly for ICA and CT-CA, could not be obtained.
- Whilst the model broadly reflects SIGN and NICE guidelines, Scottish experts indicated that there could be significant variability in the pathway when investigating chest pain. The patient pathway in Scotland is contingent on many factors including the availability of functional tests and CT-CA. It is not possible for us to estimate the impact of this variability, but it would have an effect on the economic model for HeartFlow FFRCT.
- The Scottish experts highlighted further areas of uncertainty in relation to the model assumptions. For example, the model suggests that all initial management decisions are contingent on the patient having FFR<0.80 in a major epicardial vessel which does not reflect clinical practice. There are also questions about the appropriate threshold and time point for a FFRCT referral, for example, whether it should be undertaken for all patients with CT-CAs showing 30–90% stenosis or just those with uncertain significance.
- The savings estimated in the NICE model were based on an ICA cost of £2,369 per patient as the average cost of an ICA across all types of stay. With the exception of remote or rural populations where an overnight stay is necessary, nearly all patients undergoing ICA in Scotland would be day cases. The average cost of ICA for day cases only is £1,379. This reduces the level of cost savings estimated by the model to £189 per patient.
- ICA offers further advantages in relation to epicardial and microcirculatory assessment which are not accounted for in the NICE cost model.
- Scottish experts were asked whether the NICE estimate of a 51% decrease in the number of ICAs in patients with a positive CT-CA was realistic. Of the seven experts who responded, two were unable to comment, two said yes and three said no. One expert noted that the adoption of HeartFlow FFRCT has reduced the number of patients being sent from their island board to Glasgow for ICA from 16 patients, to eight. One expert who said no, thought that the model was too simple. Another believed that the 20% reduction seen in the FORECAST trial was more realistic. The third expert thought it was a significant overestimation and added that if HeartFlow FFRCT were to be used according to the NICE guidance, the population would be small.

Summary of survey responses

Full details of the questions asked in each round, and the anonymised responses received, can be obtained from SHTG on request.

First round of questioning

Eleven experts were invited to respond; eight experts responded to the first round of survey questions and an additional two experts gave comments. There was representation from general practice, cardiology, radiology and public health. The experts came from the following boards: NHS Western Isles, NHS Lothian, NHS Borders, NHS Greater Glasgow and Clyde and NHS Highland.

Responses to the rounds of questioning took into account the 2017 and 2021 update version of the NICE guidance.

The results from the first round of questioning are summarised as follows:

- Five experts stated that they either agreed or strongly agreed with the recommendations within the guidance produced by NICE. Two experts strongly disagreed and one expert was undecided. Of those who agreed, reasons included:
    - the benefits with respect to patient journey and addressing the green agenda
    - supporting decision making
    - potential cost savings
    - potential reduction in radiation exposure
    - correlation with invasive FFR
    - good diagnostic accuracy of HeartFlow
    - determining the functional significance of stenosis, and
    - rapid availability of results.

  For those who disagreed, concerns were lack of clinical benefit over and above existing pathways, the NICE interpretation of cost-effectiveness data, and its applicability to Scotland. The expert who was undecided highlighted the results from the ISCHEMIA and FORECAST trials which at the point of review, were not included in the NICE guidance. The May 2021 NICE update discussed these trials.
- Five experts agreed or strongly agreed that the guidance produced by NICE was an accurate interpretation of the evidence base. Two experts disagreed or strongly disagreed and one expert was undecided. Of those who agreed, reasons included the reduction in ICA rates without a significant reduction in overall revascularisation rates and the clinical safety of a negative HeartFlow FFRCT. For those who disagreed, concerns were around the correlation

between invasive FFR and HeartFlow FFRCT, performance compared to other non-invasive CT tests, the selective patient population and the lack of trials comparing CT-CA with CT-CA plus HeartFlow FFRCT. The expert who was undecided highlighted the updated evidence which is now included in the NICE 2021 update.

- Six experts agreed that guidance for NHSScotland should support the use of HeartFlow FFRCT to identify obstructive versus non-obstructive coronary artery disease from CT-CA. Two experts disagreed. Of the six that agreed, three said it should be implemented in its entirety in NHS Scotland and three said it should be adapted. Suggestions for changes to the SHTG Adaptation included: that HeartFlow FFRCT should not be done at the expense of widening access to CT-CA scanning, there should be a limited number of HeartFlow FFRCT analyses available for request, and its use should be considered in the evaluation of moderate severity lesions. Of the two that disagreed, reasons included that HeartFlow FFRCT often does not work and it is of limited value (especially given the cost and the large volume of CT-CA scans that are rejected by HeartFlow FFRCT), and concerns over the volume and quality of the evidence comparing HeratFlow FFRCT with CT-CA alone.
- In addition, one expert noted that while HeartFlow FFRCT is helpful, there was surprise at the extent of the original NICE endorsement and it should not be prioritised over expanding access to CT-CA in Scotland.
- One expert questioned the NICE recommendation that 'Using HeartFlow FFRCT may avoid the need for … revascularisation'. Following further consideration of this statement, we chose not to include it in our recommendations. The study NICE used as evidence to support this statement was published prior to the guidance that CT-CA should be used as the first line investigation and so may be outdated. Further, key for the use of HeartFlow is the avoidance of ICA showing non-obstructive coronary disease.

Second round of questioning

Seven experts out of the original 10 responded to the second round of questioning. The key results from the second round of questioning are summarised as follows:

- We asked the experts whether they had used HeartFlow FFRCT and if so, whether it was within a clinical trial or within clinical practice. Seven people responded, and one had not used it. Of the six that had, two had used it within a clinical trial and four within their clinical practice.
- Three experts agreed with the re-drafted 'Recommendations for NHSScotland'. The only changes made to the recommendations were those made by NICE following the publication of their 2021 update. Three experts partially agreed and one expert disagreed. Reasons for incomplete agreement included the imminent publication of the FORECAST trial which might show HeartFlow FFRCT not to be cost-saving (mentioned by three experts), use of English data in the NICE economic model, and the ISCHEMIA trial which questions the use of diagnostic tests. One expert noted that clinicians need to consider when HeartFlow FFRCT

should be requested; the expert argued that the clinician should consider the information from CT-CA together with an assessment of the patient's symptoms both before and after the introduction of antianginal therapy. Another expert disagreed, feeling that there is not sufficient clinical evidence of benefit over CT-CA to justify its use. FORECAST and ISCHEMIA trials are described in the document. The recommendation for Scotland was amended to reflect some of these concerns.

- We asked experts how the adoption of HeartFlow would alter their referral volume for other diagnostic tests. Results are included in the main body of the document (Cardiac investigation of suspected angina in Scotland).
- We asked the experts whether they thought the pathway from the NICE economic model would reflect clinical practice in Scotland if HeartFlow FFRCT was introduced. Of the seven experts who responded, one felt unable to comment as they didn't work in a clinical setting, two agreed that it would broadly reflect clinical practice and one expert noted that their department did not see a role of Heartflow FFRCT in their clinical practice. The remaining three experts said that the pathways were more complex. Suggested differences in clinical practice compared to the model pathway included that in clinical practice, functional imaging may remain part of the decision tree if negative CT-CA and clinical suspicion is high, the threshold and time point for referral would be considered, and microcirculatory assessment may still be required, as well as the evaluation of ongoing patient symptoms. One expert thought that HeartFlow FFRCT performed least well in the crucial area of FFR 0.75 to 0.85 and further, for example a patient with an FFR of 0.83 and ongoing symptoms on medical treatment would need ICA. Responses are reflected in the main body of the document (Cost considerations in Scotland).
- We asked whether experts thought that the average cost of ICA across all types of stay (£2,369) or for day case (£1,379) that were acquired from NHS reference costs, and which do not include data from Scotland, would be close to Scottish costs. Two experts were unable to comment. One expert said the cost of their ICA was £2,500, and three experts said they would be day rates but did not comment on whether the cost would be similar in Scotland. Another expert noted there may be greater cost saving for remote or rural populations.
- We asked whether experts thought that the average cost of CT-CA across all types of stay (£290) or for day case (£164), that were acquired from NHS reference costs and which do not include data from Scotland, would be close to Scottish costs. Of the six experts that responded, one was unable to comment. One expert said they thought the cost may be closer to £290, another expert felt it would be nearer £164. Three experts said they would be day rates but did not comment on whether the cost would be similar in Scotland.
- We asked the experts whether they thought the 51% estimate in ICA reduction quoted in the NICE economic model was realistic. Responses are captured in the main body of the document (Cost considerations in Scotland).
- The recommendations for Scotland were changed to reflect the Scottish experts' comments.

Third round of questioning

Six experts responded to the third round of questioning. The key results from the third round of questioning are summarised as follows:

- We asked the experts whether they agreed with proposed changes to the Recommendations for Scotland. The wording was amended to reflect the clinical opinion and evidence base. The amended recommendations highlighted that HeartFlow FFRCT was one potential option, the effect on revascularisation rates was removed, the context in which it should be considered was added and NHS England figures were removed from the cost savings recommendation. Five experts responded to this question. One expert suggested a minor wording change to the first recommendation, and reiterated their position on HeartFlow FFRCT; that there is no additional clinical benefit over existing practice and the cost-effectiveness data is limited. The other four experts were in agreement with all recommendations with the exception of the cost-effectiveness recommendation. Based on the limited evidence and opinion of some experts within the group over the three survey rounds, the following was added to the recommendations: 'Evidence of a clinical benefit with HeartFlow FFRCT over CT-CA alone is of limited quality.'
- Two experts commented on the cost-effectiveness recommendation. One expert raised a concern over an assumption made based on results of the unpublished FORECAST trial. The wording was changed to reflect the uncertainty around the outcome.
- One expert suggested that HeartFlow FFRCT may reduce waiting times for assessment of flow limitation compared to existing alternatives. This would allow earlier decision making and appropriate management, reduce anxiety for the patient and may reduce re-presentation of the patient to health services while waiting for definitive diagnosis. HeartFlow FFRCT may also reduce the impact of assessment on the NHS staff as analysis is performed by a third party.

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