NICE National Institute for Health and Care Excellence

Review decision - November 2025

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Contents

1 Review decision

NICE's early value assessment of CaRi-Heart for predicting cardiac risk in suspected coronary artery disease was published in March 2023.

Since its publication new evidence has become available that could have a material effect on the recommendations. So, NICE will plan a standard update of the guidance.

NICE's health technology evaluations manual details the methods and processes for guidance surveillance.

2 Current guidance

Recommendations

2.1 CaRi-Heart is not recommended for use in the NHS while further evidence is generated. It should only be used in research to predict cardiac risk in people with suspected coronary artery disease (CAD), while treatment strategies to reduce coronary inflammation and cardiac death are identified.

2.2 Further research is recommended on:

- how clinical outcomes might change for people with suspected CAD who have had CaRi-Heart testing and appropriate treatment
- how CaRi-Heart results affect clinical decision making compared with UK standard clinical practice
- the costs to the NHS of using CaRi-Heart
- how well CaRi-Heart predicts cardiac risk to validate it in a UK population; in particular, data should be generated in the following groups: women, people from different ethnic backgrounds, and people who do not have CAD identified on CT coronary angiography (CTCA).

3 New evidence

Clinical practice

NICE's guideline on cardiovascular disease: risk assessment and reduction, including lipid modification (NG238), was updated in December 2023, after CaRi-Heart was evaluated. Guideline updates that are relevant to this topic are listed here.

Statin treatment for people with and without type 2 diabetes

1.6.8 Do not rule out treatment with atorvastatin 20 mg for the primary prevention of cardiovascular disease just because the person's 10-year QRISK3 score is less than 10% if they have an informed preference for taking a statin, or there is concern that risk may be underestimated.

Lipid-lowering treatment for secondary prevention of cardiovascular disease

1.7.9 If the person is taking the maximum tolerated dose and intensity of statin but the lipid target for secondary prevention of CVD is not met, consider additional lipid-lowering treatments (see NICE's technology appraisal guidance on alirocumab, evolocumab, ezetimibe and inclisiran).

1.7.10 Consider ezetimibe in addition to the maximum tolerated intensity and dose of statin to reduce CVD risk further, even if the lipid target for secondary prevention of CVD is met.

How these recommendations might affect practice

Recommending statins to a wider population (people with QRISK scores less than 10%) is likely to lead to an increase in the use of statins. Similarly, recommending a specific lipid target for secondary prevention of CVD will likely lead to an increased use of lipid-lowering treatments. This could reduce the impact that CaRi-Heart has on clinical decision making and clinical outcomes, compared with clinical practice before the guideline update. A NICE news article reported that around 5.3 million people in England were given a NICE-recommended statin or ezetimibe by their GP to help reduce their cholesterol during 2023

to 2024. This was the largest number on record and almost 900,000 more than in 2022 to 2023.

New studies

Since HTE4 was published, the company has submitted new evidence including:

- A published study which assessed the risk profile and rates of major adverse cardiac events (MACE) and cardiac mortality in people with and without obstructive CAD (n=40,091; Chan et al. 2024a). This study was done in people who had coronary CT angiography (CCTA) as part of routine care. The aim of the study was to gather data on the level of unmet need for people without obstructive CAD.
- A prospective observational study (n=3,393; Chan et al. 2024a). The study was done in the NHS. Its aims were to:
  - evaluate the predictive value of the fat attenuation index-score (FAI-Score)
  - evaluate the performance of the AI-Risk prognostic model and related AI-Risk Classification system (CaRi-Heart)
  - assess if the technology reclassifies people's condition in a way that impacts clinical management.
- An economic evaluation of the cost effectiveness of the technology (Tsiachristas et al. 2025).
- Unpublished evidence relating to the prognostic performance of the technology among people with different demographics (Chan et al, 2024b).

Cardiac risk prediction

Considerations for HTG663

In the original assessment, the external assessment group (EAG) found 1 study that assessed the prognostic performance of CaRi-Heart for predicting cardiac death for people with suspected stable CAD (Oikonomou et al. 2021). The study was a development and validation study in a German dataset, which included 3,912 people having CTCA to assess stable CAD.

The results of the study showed that it was better at predicting risk than a risk model based on traditional clinical risk factors. These include smoking, hypercholesterolaemia, hypertension, diabetes, Duke Activity Status Index, presence of high-risk plaque features, and epicardial adipose tissue volume. The committee agreed that, based on the results of Oikonomou et al. (2021), CaRi-Heart was likely to improve risk prediction for cardiac death.

The comparator used in the CaRi-Heart study did not reflect UK clinical practice, which limits the generalisability of the study. The committee said that the comparator for future studies should include assessing CTCA images alongside clinical risk factors, and that QRISK3 should be used in the 'no CAD' group. It recommended external validation of CaRi-Heart in a UK setting and that data should be collected to demonstrate prognostic performance in people who do not have CAD identified on CTCA.

In the original assessment some data was presented that suggests the prognostic performance of CaRi-Heart is consistent by groups including age, sex, CAD status (obstructive and non-obstructive) and ethnicity. The committee said that ongoing validation of CaRi-Heart should include groups by sex, age, ethnicity, socioeconomic status and CAD status if possible.

New evidence

A prospective nested cohort of 3,393 people in the UK evaluated the prognostic value of FAI-Score and the performance of the AI-Risk algorithm (Chan et al. 2024a). CaRi-Heart analyses CCTA scans then generates the FAI-Score and uses an AI-Risk algorithm to assess the risk for each patient. The FAI-Score provides an estimate of the inflammation in the coronary arteries. The AI-Risk algorithm is an AI-assisted prognostic algorithm that incorporates the FAI-Score of 3 coronary arteries, the coronary atherosclerotic burden and traditional risk factors. The AI-Risk algorithm classifies people into very high risk (≥10% 8-year risk for fatal cardiac events), high risk (5% to <10%), and low or medium risk (<5%) categories.

In the study the AI-Risk algorithm output was analysed as a continuous variable and as a categorical variable. Both outputs predicted cardiac death and MACE in the overall population, as well as in people without obstructive CAD. The algorithm appeared to overestimate risk in people with obstructive CAD.

The company submitted an unpublished abstract with results on the performance of the AI-Risk algorithm in people from different demographic and socioeconomic backgrounds

(Chan et al. 2024b). The results are confidential and so cannot be reported here.

Clinical decision making

Considerations for HTG663

The EAG found no evidence on how CaRi-Heart analysis changes risk assessment or clinical decision making for people with suspected CAD who have a CTCA. The Oikonomou study presented data on how risk groups (low, medium and high risk) changed when a CaRi-Heart score was used, compared with a clinical risk score. But the clinical experts said that the clinical risk score used in the study was not used in UK clinical practice. So, it was still uncertain how using CaRi-Heart would affect the outcome of a risk assessment compared with CTCA. The committee concluded that it was currently uncertain how CaRi-Heart influences risk assessment but that the ongoing study would likely address this.

The committee discussed the treatments available for people identified with no CAD (low risk), non-obstructive CAD (medium risk) and obstructive CAD (high risk) after a CTCA and how these might change with the introduction of CaRi-Heart. It noted that the company's suggestions included starting statins in the low-risk group, increasing the intensity of statins in the medium-risk group, and introducing other anti-inflammatory medicines such as colchicine in the high-risk group.

For the low-risk group, the clinical experts said there is good evidence on the effectiveness of starting and intensifying statins. So, it said that treatment strategies for people with no CAD or non-obstructive CAD may be clearer. For the high-risk group, colchicine is not licensed or recommended in the UK for this indication. The clinical experts discussed treatments that may be more widely used in the future, such as PCSK9 inhibitors and inclisiran. But they said that higher quality evidence is needed to show that these treatments could reduce cardiac events and mortality in this population, because they were expensive.

The committee concluded that further evidence is needed on how CaRi-Heart affects clinical decision making and clinical management compared with UK standard clinical practice (CTCA alongside clinical risk assessment). It noted that QRISK3 should be included as a comparator for people who have no CAD identified on CTCA.

New evidence

A prospective real-world evaluation exercise was done to understand the impact of CaRi-Heart reports on clinical decision making in the UK (Chan et al. 2024a). This was done in 4 NHS trusts:

- Oxford University Hospitals NHS Foundation Trust
- Milton Keynes University Hospital NHS Foundation Trust
- University Hospitals of Leicester NHS Trust
- The Royal Wolverhampton NHS Trust.

The analysis was done in 744 people having CCTA as part of clinical care for diagnosis of CAD during 2021 to 2022. The study took place before NG238 was updated in December 2023. Local teams decided on the clinical management, based on current standard-care data, including QRISK3, and the choices were recorded. The CaRi-Heart reports (containing FAI-Score and CaRi-Heart risk metrics) were then provided to the same healthcare professionals, who were asked to record how the additional information provided in the CaRi-Heart report had changed their clinical decisions.

The additional information provided by CaRi-Heart led to changes of management recommendations for 45% of people in the study. Changes included initiation of statin treatment (24%), increase in statin dosage (13%) and starting additional treatments beyond statins (8%). Additional treatments beyond statins included aspirin (2.4%), colchicine (8.3%) or icosapent ethyl (0.4%). The 8% of people in the study who were already on the maximum dose of statins had changes in clinical decision making that are not recommended by NICE.

Clinical outcomes

Considerations for HTG663

During development of HTG663, no evidence was found on how CaRi-Heart affects patient outcomes such as cardiac mortality and morbidity. The EAG found no studies on targeting treatments using any measure of coronary inflammation. The committee noted that there is evidence that shows statins may benefit everyone, regardless of CAD status. Because changes to the guidelines mean that statins can be prescribed more widely, it is

expected that this would impact the extent to which CaRi-Heart influences treatment options.

The committee recommended further research to address the uncertainty around clinical outcomes for people with suspected CAD having CTCA for chest pain who have had CaRi-Heart testing. The committee said that a clinical outcome study using CaRi-Heart to determine a treatment strategy, with people followed up for long enough to observe a reduction in cardiac events or death would be ideal. But because this may be difficult it agreed that a linked-evidence approach would be acceptable.

New evidence

There is no direct evidence on how cardiac risk prediction and changes in clinical decision making following a CaRi-Heart test impact on clinical outcomes. The company used a linked-evidence approach to develop a cost-effectiveness model.

Costs and cost effectiveness

Considerations for HTG663

No evidence was identified on the costs or cost effectiveness of CaRi-Heart. The committee heard that there was no evidence on how CaRi-Heart might affect resource use because of changes in treatments or the potential reduction in cardiac events. The committee recommended that data is collected on the costs associated with using CaRi-Heart, including implementation costs, training costs, and impact on costs and resource use later in the treatment pathway.

New evidence

A new study reports a decision analytic model that compares AI-Risk assessment with CaRi-Heart plus standard care versus standard care alone over a lifetime time horizon (Tsiachristas et al. 2025). The model used data from:

- the long-term cohort study, to inform transition probabilities between disease states (n=3,393; Chan et al. 2024a)
- the prospective real-world evaluation survey on the impact of CaRi-Heart on current clinical practice (n=744; Chan et al. 2024a)

- an existing meta-analysis to establish the effect size of statins on different cardiovascular outcomes in different risk groups (Cholesterol Treatment Trialists' Collaborators 2012).

The meta-analysis results were used to inform the effect of statins in people in different risk categories. It is uncertain whether the effect of statins would be the same in people identified:

- as having low to medium, high or very high risk by CaRi-Heart
- in the 5 risk categories defined in the meta-analysis.

The base-case economic analysis uses costs for CaRi-Heart of £300, £500 and £700 per scan. Implementing CaRi-Heart in routine clinical practice and assuming full compliance with treatment reduced the number of cardiovascular events when modelled over a lifetime horizon. The model results suggested an 11% reduction in myocardial infarction, 4% reduction in stroke, 4% reduction in heart failure events and 12% reduction in cardiac mortality when using CaRi-Heart. These reductions resulted in an increase in quality-adjusted life years (QALYs) of 0.21. The incremental cost-effectiveness ratios (ICERs) are presented in table 1.

Table 1 Base-case results for AI-Risk with standard care versus standard care alone

Cost of CaRi-Heart per scan	Incremental healthcare costs (difference in mean cost of CaRi-Heart versus mean cost of standard care, (95% CI))	ICER (per QALY gained; assuming QALY gain of 0.21)
£300	£293 (281 to 304)	£1,371
£500	£493 (481 to 504)	£2,307
£700	£693 (680 to 705)	£3,244

Abbreviations: CI, confidence interval; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

To test the robustness of the results, 5 different scenarios analyses were done:

- full compliance with NG238 in the standard-care arm (prior to the update in December 2023)
- providing colchicine alongside statins to patients with a very high risk

- implementation of AI-Risk only in people without obstructive CAD
- assuming a 50% lower statin effect on MACE
- reducing the change in AI-Risk classification by 50%.

The sensitivity analyses gave ICERs ranging from £1,837 to £6,592 per QALY gained, assuming that the test cost £700.

In 2023 to 2024, during which NG238 was updated, almost 900,000 more people were given a NICE-recommended statin or ezetimibe by their GP to help reduce their cholesterol than in 2022 to 2023. This may result in increased ICERs for CaRi-Heart because of a reduced clinical benefit compared with current practice.

The budget impact of implementing the AI-Risk model (at £700 per scan) was estimated over 5 years, assuming annual changes in uptake of AI-Risk in the NHS at 2%, 5%, 10%, 15% and 20% (see table 2).

Table 2 Budget impact of adopting CaRi-Heart in the NHS over 5 years

Year	Percentage national uptake, %	Cost, £
1	2	2,821,971
2	5	7,076,651
3	10	14,182,648
4	15	21,992,618
5	20	30,169,955

4 Summary of new evidence and implications for review

Table 3 Summary of new evidence and implications for review

Area	Recommendation	New evidence
Prognostic ability	How well CaRi-Heart predicts cardiac risk in a UK population, especially in the following groups: • women • people from different ethnic backgrounds • people who do not have CAD identified on CTCA.	The AI-Risk algorithm predicted cardiac death and MACE in the whole cohort and for people without obstructive CAD. AI-Risk appeared to overestimate risk in people with obstructive CAD. AUC results indicate that adding AI-Risk to QRISK3 and CAD-RADS 2.0 improved its prognostic ability for cardiac mortality and MACE. The confidential results on the prognostic performance of the AI-Risk algorithm in people from different demographic and socioeconomic backgrounds are available from Chan et al. (2024b).
Clinical decision making	How CaRi-Heart results affect clinical decision making compared with UK standard clinical practice	In a real-world study, using CaRi-Heart results led to changes in clinical management in 45% of people, which included: • initiation of statin treatment for 24% of people • increase in statin dosage for 13% of people • initiation of additional treatments beyond statins for 8% of people.

Area	Recommendation	New evidence
Clinical outcomes	How clinical outcomes might change for people with suspected CAD who have had CaRi-Heart testing and appropriate treatment	There is no direct evidence on how this could result in changes to clinical outcomes. Linked-evidence modelling has been used to establish the effect size of statins on different cardiovascular outcomes in different risk groups.
Costs	The costs to the NHS of using CaRi-Heart	A model was developed to compare AI-Risk in addition to standard care versus standard care over a person's lifetime. Using linked-evidence modelling, a simulation of 5,000 people after implementing CaRi-Heart estimated a reduction in events of: • myocardial infarction (11%) • stroke (4%) • heart failure (4%) • cardiac death (12%). ICERs were calculated using 3 different costs for AI-Risk: £300, £500 and £700 per scan. ICERs were £1,371, £2,307 and £3,244, respectively. The budget impact over 5 years was calculated assuming £700 per scan and gradual uptake up to 20% by year 5. This came to £30,169,955 for year 5.

Abbreviations: AUC, area under the curve; CAD, coronary artery disease; CTCA, CT coronary angiography; ICER, incremental cost-effectiveness ratio; MACE, major adverse cardiac events.

5 Implementation

The technology is being used in private practice and is also being piloted at 5 NHS sites.

6 Equality issues

Potential equality issues were identified during the assessment, including:

- Angina and CAD may have a substantial and long-term adverse effect on a person's ability to carry out normal day-to-day activities. People with these conditions may be classified as having a disability and so may be protected under the Equality Act 2010.
- People with certain conditions, such as diabetes, may be at higher risk of developing CAD. These people may be protected under the disability provision of the Equality Act 2010.
- CAD is more common in men than in women, but women are often underdiagnosed.
- CAD is more common in older people and people who live in deprived areas.
- People from some ethnic minority backgrounds, particularly African and South Asian groups, are more likely to have higher rates of CAD than White British and East Asian groups.
- Variation in access to CTCA in the NHS could result in inequity of access to the technology.

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7 References

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