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Systematic review of the health-economic impact of diagnostic modality selection for patients with coronary artery disease

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Introduction

- Non-invasive cardiovascular modalities [CCTA, CMR, ECG, CTA(FFR), MPI-SPECT, PET, SE] are increasingly used, either instead or alongside of invasive modalities [ICA, ICA(FFR)], in the diagnosis and management of coronary artery disease (CAD)[1,2]
- The clinical advantages of non-invasive compared to invasive modalities are recognised and increasingly established within clinical practice[3–5]
- **However, the economic consequences of non-invasive compared to invasive modality selection are not clearly defined**
- The aim of this study is to assess in a systematic review (SR) of the literature, the health-economic consequences of non-invasive relative to invasive modality selection in symptomatic individuals with low-, intermediate-, or high-risk of known (or unknown), stable or unstable CAD
- A subset of included studies that conducted head-to-head (H2H) trials is analysed here

Methodology

Systematic review question

- What is the impact of using invasive or non-invasive modalities for cardiac imaging for diagnosis and management of individuals with low-, intermediate-, or high-risk CAD or IHD*, either known or unknown, from both the economic and HRQoL perspective? (PROSPERO registration ID CRD42022384183)

Identification of studies

- Review methods followed the Centre for Research and Dissemination's (CRD) guidance on conducting systematic reviews[6]

Search strategy

- The search strategy was designed to identify studies in the UK, France, Germany, Italy, Japan, China, and the USA published in any language between 1992 and January 2023
- The search was performed on December 2nd, 2022, in the Medline and Embase, Medline In-Process, Cochrane databases and the UK National Health Service Economic Evaluation Database of Abstract of Reviews and Effects
- Backwards citation research of the included SRs from the previous 3 years and hand searches were also conducted

Data extraction

- There were two stages to data extraction: 1) an extraction of general study characteristics to best identify studies relevant to the research questions and 2) a detailed extraction of study characteristics and outcomes

Data analysis

- **H2H** studies **comparing a non-invasive to an invasive modality** were analysed
  - Invasive modalities included: invasive coronary angiography (ICA) and ICA – fractional flow reserve (ICA-FFR)
  - Non-invasive modalities included: coronary computerised tomography angiography (CCTA), cardiac magnetic resonance (CMR), stress electrocardiogram (ECG), fractional flow reserve derived from computed tomography angiography (CCTA(FFR)), myocardial perfusion imaging – single photon emission computed tomography (MPI-SPECT), positron emission tomography (PET) and stress echocardiography (SE)
- Analysis was conducted by study type (cost-effectiveness, cost and resource use, utility and mixed), by perspective (healthcare, societal and hospital), and by risk of CAD

*IHD, (ischemic heart disease), a term often used in the literature interchangeably with CAD

Results

- Of 10,089 records screened, 160 met the inclusion criteria and 23 reported H2H comparisons (Figure 1)
- H2H comparisons
  - 17 cost-effectiveness, 3 cost and resource use, 2 mixed (utilities, cost and resource use) and 1 utility
  - Patients were 50–65 years old, predominantly male (≥50%) and most had stable CAD and a low-to-intermediate risk of CAD
  - Most studies used the healthcare perspective (39%), followed by the societal perspective (22%)
  - CCTA vs. ICA was the most frequent comparison, mostly in US studies (Table 1)
- Outcomes
  - During the last decade, most studies concluded that CCTA and CMR are cost-effective and/or cost-saving compared to ICA across all risk levels. Prior to this (1999–2014) studies found CCTA more favourable than ICA in low-intermediate risk patients

Figure 1: PRISMA flow diagram

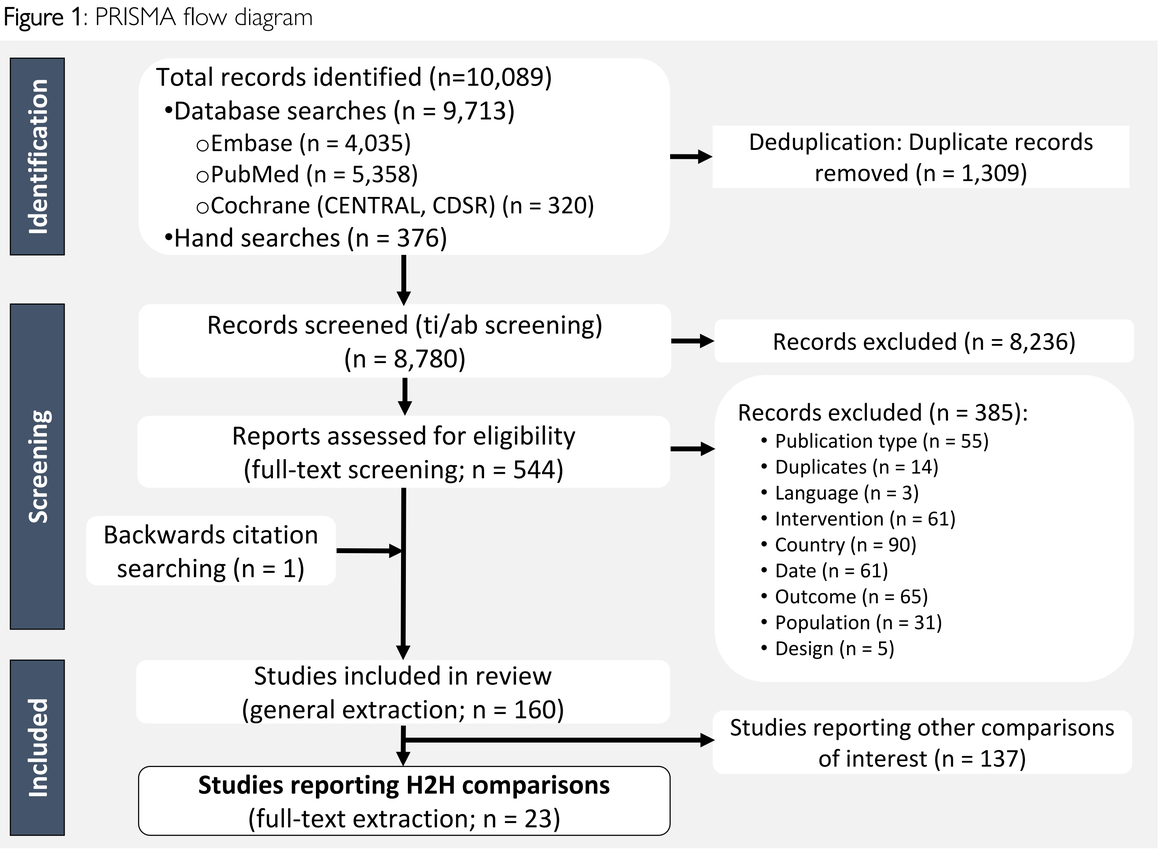


Table 1: Included H2H studies by type and region*

Comparisons	Cost-effectiveness studies (n=17)	Cost and resource use studies (n=3)	Utility and mixed studies (n=3)
CCTA (FFR_{CTA}) vs ICA	US n=7; UK/DE n=2; JP n=1	US n=2; DE n=1	US/EU/DE n=1
MPI – SPECT vs ICA	US n=5; UK n=3; EU/JP n=1	US n=1	-
Stress echo vs ICA	US n=5; UK n=3; EU/DE n=1	-	-
CMR vs ICA	UK n=3; DE/US n=2; EU n=1	-	-
Exercise ECG vs ICA	US n=3; DE n=1	-	-
PET vs ICA	EU n=1	-	-

The European flags show studies with data from different European countries, including those of interest to the SR.

Cost-effectiveness results

For low-to-intermediate risk patients:

- 68% and 100% of comparisons showed that **non-invasive modalities are cost saving** versus invasive modalities for the US and UK, respectively (Figures 2 and 3)
- Incremental impact on QALYs was generally minimal and mixed. While all figures for CCTA, CMR and MPI-SPECT fell between +/-0.1 QALYs, some stress ECG and stress echo results showed larger decrements (Figures 2 and 3)
  - This is expected as the modalities are analysed as diagnostic modalities, not treatment modalities
- 74% and 75% of comparisons showed a **non-invasive modality to be cost effective vs. ICA** at a willingness to pay (WTP) threshold of $100,000/QALY and £30,000/QALY for the US and UK, respectively (Figures 2 and 3)
- These results were **true for the US and UK, irrespective of the economic perspective taken**
- The main drivers of cost-effectiveness were cost savings

Figure 2: The cost-effectiveness plane of reported incremental cost and QALY. Studies from the US

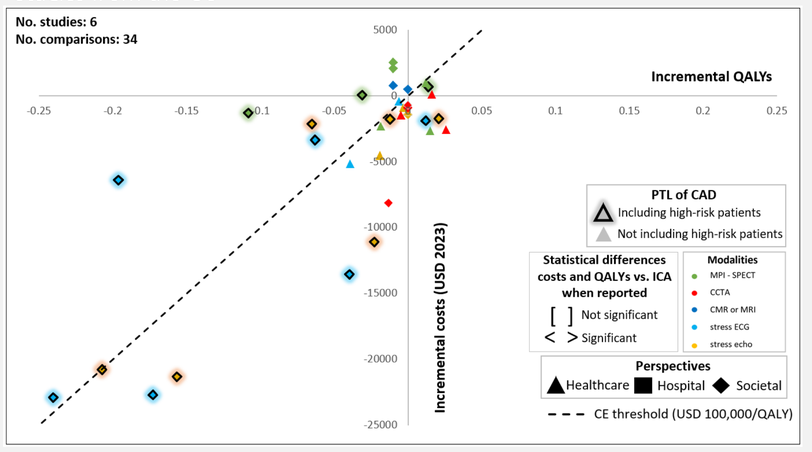
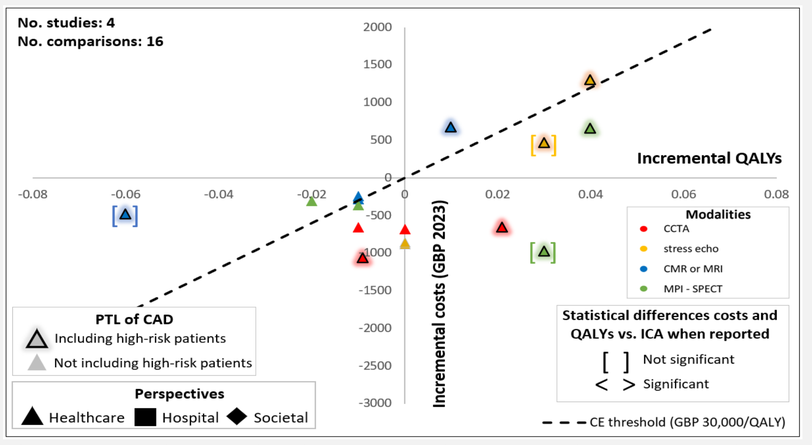


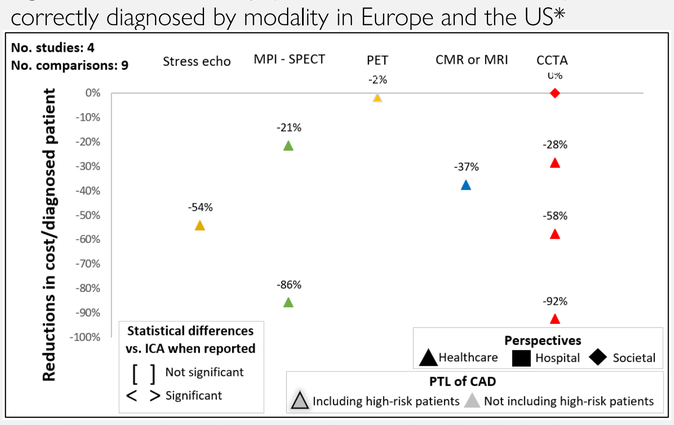
Figure 3: The cost-effectiveness plane of reported incremental cost and QALY. Studies from the UK*



*For UK patients, authors provided mixed results on costs and QALY outcomes when comparing ICA and CMR, mainly due to the limited data available at the time of the analyses.[7,8]

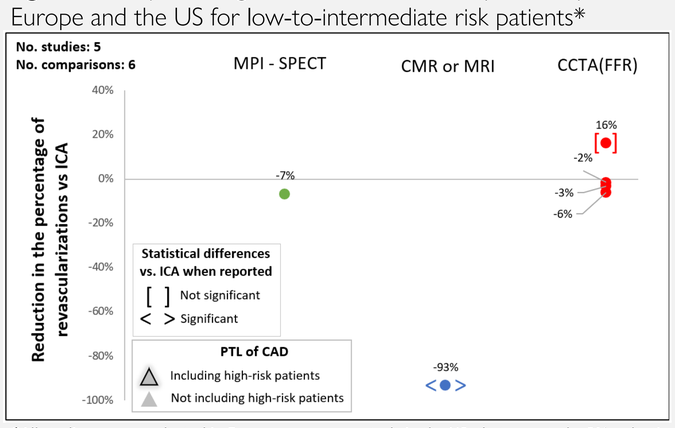
Cost-savings and reductions in resource use

Figure 4: The cost-savings per low-to-intermediate risk patient correctly diagnosed by modality in Europe and the US*



*All studies were conducted in Europe except for one study conducted in the US, demonstrating cost savings of 86% for MPI - SPECT and 92% for CCTA.

Figure 5: The percentage of revascularisations by modality in Europe and the US for low-to-intermediate risk patients*



*All studies were conducted in Europe, except one study in the US, that reported a 2% reduction in revascularizations for CCTA and a 7% reduction for MPI-SPECT.[12]

For correctly diagnosed low-intermediate risk patients:

- All non-invasive modalities, particularly CCTA and CMR, showed **lower total costs** per patient vs. ICA
- **Cost-savings ranged between 2–92% per patient** when using non-invasive rather than invasive modalities (Figure 4)
- **Cost-savings were driven by the cost of the tests and the use of fewer resources** when using non-invasive modalities vs. ICA[9,10]
  - Non-invasive modalities mostly **reduce unnecessary revascularisations** compared to ICA (Figure 5)
  - **The strongest effect is reported for CMR, with a reduction in revascularisations by 93%** compared to ICA, which, together with the reduction in resource use, led to a reduction in costs[11]
  - In Europe, **CCTA(FFR) reduced the length of hospital stays** (days) compared to ICA (by 34% and 47%)[13,14,15]

Utility results

- The single, small (n=30) utility study showed no statistically significant difference between the disutility associated with CCTA and ICA, with a trend towards more disutility for ICA[16]

Conclusions

- Overall, non-invasive modalities were cost-saving vs. ICA in CAD diagnosis in low-to-intermediate risk patients, while no clear trend on QALYs was observed for CCTA, CMR and MPI-SPECT; this was consistent across healthcare and societal perspectives
- Cost-savings per low-to-intermediate risk patient correctly diagnosed were between 2–92% per patient, and were driven by the cost of the tests and the use of fewer resources:
  - CCTA is the non-invasive modality that showed the shortest hospital stays and highest cost savings compared to ICA

Abbreviations: ACS, acute coronary syndrome; CAD, coronary artery disease; CCTA, coronary computerised tomography angiography; CE, cost-effectiveness; CMR, cardiac magnetic resonance; CRD, Centre for Research and Dissemination's; ECG, electrocardiogram, CCTA(FFR), fractional flow reserve derived from computed tomography angiography; HRQoL, health related quality of life; H2H, head-to-head; ICA, invasive coronary angiography; ICA(FFR), invasive coronary angiography – fractional flow reserve; MI, myocardial infarction; MPI-SPECT, myocardial perfusion imaging – single photon emission computed tomography; PET, position emission tomography; PRISMA, preferred reporting items for systematic reviews and meta-analyses; PTL, pre-test likelihood; SE, stress echocardiography; SR, systematic review; QALY, quality-adjusted life year; TI/abs, title/abstract; WTP, willingness to pay

References [1]Knuuti et al. European Heart Journal, 2020, 41(3), 407-77. [2]Writing committee members et al. Journal of the American College of Cardiology, 2021, 78(22), 187-285. [3]Achenbach et al.. European Heart Journal Cardiovasc Imaging, 2022, 23(4), 465-475. [4]Douglas et al. The New England Journal of medicine, 2015, 372(14), 1291-1300. [5]Williams et al. Journal of the American College of Cardiology, 2016, 67(15), 1759-1768. [6]Centre for Reviews and Dissemination & Akers, J. 2009 Systematic reviews : CRD's guidance for undertaking reviews in health care: York : CRD, University of York, 2009., Available at: http://www.york.ac.uk/crd/SysRev/!SSL!/WebHelp/SysRev3.htm). [7]Sharples et al. Health Technology Assessment – Southampton, 2007, 11(49). [8]Thom et al. BMJ, 2014, 4(2), e003419. [9]Dorenkamp M et al. Heart, 2012, 98(6):460-7. [10]Dewey M, et al. European radiology, 2007, 17:1301-9.). [11]Genders et al. Annals of internal medicine, 2015, 162(7), 474-84 . [12]Ge Y, et al. Cardiovascular Imaging. 2020 Jul 1;13(7):1505-17. [13]Colleran et al. Open heart, 2017, 4(1), e000526. [14]Douglas et al. Journal of the American college of cardiology, 2016, 68(5), 435-45. [15]Dewey et al. BMJ, 2016, 355(544). [16]Sadigh G et al. Academic Radiology, 2013, 20(9):1091-8.

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