Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report [1]

Rubidium-82 PET/CT myocardial perfusion imaging for the assessment of ischaemic heart disease

What is a Topic Exploration Report?

Topic Exploration Reports are not health technology assessments. These reports provide a high-level briefing on new topics submitted to Health Technology Wales and are not based on exhaustive or systematic literature searches. Instead, they rely on a focussed scan of key resources.

What evidence is used in a Topic Exploration Report?

Priority is given to summarising the most relevant or useful evidence, rather than covering all possible evidence. Information reported is typically based on abstracts and study authors' own conclusions, rather than detailed scrutiny of full texts.

What are the aims of a Topic Exploration Report?

Topic Exploration Reports offer an overview of the available evidence on a topic and aim to highlight any uncertainties or gaps in the evidence. These reports outline the quantity and type of evidence found, but no critical appraisal or formal evidence synthesis is conducted.

How should a Topic Exploration Report be used?

Topic Exploration Reports can be used to indicate what evidence may be available for a topic, and do not provide definitive guidance on how a technology should be used. The evidence presented within the reports should be interpreted with caution.

[1] Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg
Translation of published technical HTW documents from English into Welsh

Topic exploration report number	TER686
Topic	Rubidium-82 myocardial perfusion imaging for the assessment of ischaemic heart disease
Summary of findings	Myocardial perfusion imaging (MPI) is a non-invasive test used to examine the anatomy and function of the heart. The most common technique for MPI in England and Wales is a single photon emission computed tomography (SPECT) scan. An alternative to SPECT MPI is cardiac positron emission tomography (PET). PET MPI uses dynamic imaging with radiotracers that decay with positron emission, most commonly rubidium-82. Use of rubidium-82 MPI may improve the diagnosis, risk stratification, and management of patients with suspected or known ischaemic heart disease. We identified four systematic reviews and meta-analyses of single arm studies that examined PET MPI and/or SPECT MPI for diagnosis of coronary artery disease (CAD). Pooled sensitivities for PET MPI ranged from 83% to 88% and specificities from 86% to 89%. Pooled sensitivities for SPECT MPI ranged from 69% to 83% and specificities from 77% to 85%. Two reviews examined rubidium-82 PET MPI and reported pooled sensitivities from 75% to 87% and specificities from 81% to 84%. We also identified a systematic review of economic evaluations and healthcare resource use for PET MPI vs SPECT MPI for CAD diagnosis. Seventy-one studies were identified, which varied in design, patient population and follow-up times. Economic evaluations and comparative clinical trials were limited in number. An exploratory meta-analysis of comparative studies showed that there were higher rates of early- and late-invasive coronary angiography and revascularisation for PET MPI compared with SPECT MPI, but the rate of repeat testing was lower with PET MPI. Five additional primary studies, with comparative clinical outcomes, that were published after this systematic review were also identified.

Introduction and aims

There are many different tests for the diagnosis or management of ischaemic heart disease, one of which is myocardial perfusion imaging (MPI). MPI is a non-invasive test used to examine the anatomy and function of the heart, including myocardial blood flow at rest and during exercise. The most common technique for myocardial perfusion testing in England and Wales is a single photon emission computed tomography (SPECT) scan. Radiotracers, such as Tc99m-tetrofosmin or Tc99m-MIBI, are injected into the blood stream and taken up by muscle cells in the heart. Images are taken at rest and under stress, either from exercise, or induced pharmacologically, and reconstructed to provide images of blood flow through the heart. Scans typically take three to four hours. SPECT MPI can be used to diagnose ischaemic heart disease, can assist in predicting the risk of additional coronary events, and is used to assist in planning cardiac surgery. The accuracy of SPECT MPI can vary due to issues during imaging and be difficult to interpret in certain conditions such as multivessel coronary disease and microvascular dysfunction. In addition, false positives are more likely in people with large amounts of soft tissue due to obesity, large chest muscles or large amounts of breast tissue. SPECT MPI is recommended by NICE (2016) for non-invasive functional imaging for ischaemic heart disease. The topic proposer states that Swansea Bay University Health Board performs approximately 500 SPECT MPIs annually.

An alternative to SPECT for MPI is cardiac positron emission tomography (PET). Cardiac PET MPI uses dynamic imaging with radiotracers that decay with positron emission, most commonly rubidium-82, although 13-N-ammonia may also be used. Images are taken at rest and under pharmacologically induced stress. Cardiac PET was used only as a research tool until the 1990s due to high costs. The first clinical PET centre was established in the UK in 1992. Technological advances over the last 30 years have made the technique more accessible and there has been a major increase in the number of PET scanners for clinical use. Rubidium-82 PET/CT imaging combines PET with computed tomography (CT), adding detailed anatomic information to the functional information provided by the PET scan and is currently the only routinely available non-invasive imaging technique capable of quantifying myocardial blood flow at rest and stress. Rubidium-82 PET/CT MPI takes around 30 to 45 mins, results in lower radiation exposure, and produces higher quality images than SPECT MPI. The technology may improve the diagnosis, risk stratification, and management of patients with suspected or known ischaemic heart disease, including patients with microvascular dysfunction, and ischaemia with non-obstructive coronary arteries.

At present, rubidium-82 PET/CT scans are available in larger tertiary centres in London and Manchester. A permanent specialised PET/CT centre is currently under construction at Singleton Hospital, Swansea Bay University Health Board, to provide an oncology PET/CT service. The centre is expected to open in February 2027. In addition to the oncology PET/CT service, there will be capacity to open a Mid/South Wales Cardiac PET/CT MPI service through the Nuclear Cardiology Department in Swansea, supported by Nuclear Medicine services. It is estimated that the cardiac PET/CT service would be able to provide access to approximately 30 to 40 cardiac patients per week for the whole of Wales. Oncology PET/CT scans do not use rubidium-82 so a Sr82/Rb82 generator will need to be purchased for cardiac scans, and there are some training needs for radiologists in infusion of rubidium-82, physicists to provide quality assurance, and cardiologists for image analysis, although the topic proposer has indicated that the training needs are not high.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of rubidium-82 PET/CT MPI for the assessment of ischaemic heart disease in comparison with SPECT MPI. The topic proposer told us that Cardiac PET and Cardiac PET/CT are terms used interchangeably in the literature for the same diagnostic test.

Introduction and aims

Due to the amount of literature identified for diagnostic accuracy, we have only summarised evidence from systematic reviews conducted within the last 10 years. For primary studies we prioritised studies that reported on clinical outcomes, such as rates of angiography, and diagnostic accuracy studies in populations of interest.

Evidence overview

Health technology assessment and clinical guidelines

We did not identify any health technology assessments, but cardiac PET/CT, including rubidium-82 PET/CT, is endorsed for use by international clinical guidelines. Two reviews of clinical guidelines for cardiac PET/CT were identified.

Alwan et al. (2025) conducted a review examining clinical practice guidelines to assess how cardiac PET was included in recommendations from the American College of Cardiology/American Heart Association, the European Society of Cardiology, the International Society for Heart and Lung Transplantation and in multi-society consensus statements up to December 2024. No results were reported in the abstract.

Besson et al. (2024) conducted a review aiming to evaluate the level of evidence included in guidelines for hybrid nuclear cardiovascular imaging, including SPECT/CT, PET/CT and PET/MRI. Searches were conducted up to August 2023. 76 clinical guidelines published between 2013 and 2023 were identified. The review did not summarise the recommendations.

In addition, the topic proposer highlighted that the Royal College of Radiologists published guidance on populations and circumstances when rubidium-82 PET/CT should be preferred to SPECT (Dizdarevic et al. 2022):

1. Previous poor quality SPECT images; Equivocal other functional imaging or CT coronary angiography; Functional imaging results discordant with clinical assessment or coronary angiogram findings
2. Body characteristics where artefacts are likely to affect image quality, e.g., in high BMI patients
3. High-risk patients, for example with significant coronary artery disease (CAD) on coronary angiogram, cardiac transplant vasculopathy or severe left ventricular dysfunction
4. Young patients with established CAD or those with suspected CAD who cannot undergo non radiation functional imaging to exclude ischaemia
5. Patients in whom myocardial blood flow would be helpful to exclude multi-vessel disease causing ischaemia or patients with suspected microvascular dysfunction
6. In selected patients with coronary anomalies, congenital disease post-surgery and Kawasaki's disease

Secondary evidence

We did not identify any systematic reviews where direct comparisons were made between rubidium-82 PET and SPECT or SPECT/CT. We did identify four systematic reviews examining diagnostic accuracy, with searches undertaken in the last 10 years. All reviews conducted single arm meta-analyses and compared methods using exploratory analyses. This means that participant characteristics and methodology may vary between methods. It is likely that there is overlap in the included studies across the reviews. The reviews are presented in reverse order for search dates.

Evidence overview

Xu et al. (2021) conducted a systematic review and meta-analysis comparing cardiac magnetic resonance (CMR), SPECT and cardiac PET for myocardial perfusion imaging for the diagnosis of coronary artery disease (CAD). Searches were conducted up to July 2020. A total of 203 studies were identified of which 134 were conducted with SPECT and 25 with PET. The reference standard used in all studies were invasive tests, either fractional flow reserve (FFR) or invasive coronary angiography (CA). The pooled sensitivities were 83% for SPECT and 85% for PET ($p = 0.109$). Pooled specificities were 77% for SPECT and 86% for PET ($p < 0.01$). Subgroup analysis was undertaken for different radiotracers. For SPECT, 21 studies used Tc99m-tetrofosmin, pooled sensitivity was 76% and pooled specificity was 80%. 53 studies used Tc99m-MIBI and pooled sensitivity was 84% and pooled specificity was 80%. For PET, 15 studies used rubidium-82 and pooled sensitivity was 87% and pooled specificity was 84%.

Alenezi et al. (2023) conducted a systematic review comparing Tc99m-MIBI SPECT with rubidium-82 PET for the diagnosis of CAD. Searches were conducted up to June 2019. Eighteen studies were included. The authors report that, for Tc99m-MIBI, mean sensitivity for diagnosis of CAD was 84% compared with 75% for rubidium-82-PET and mean specificity was 75% for Tc99m-MIBI compared with 81% for rubidium-82-PET. The accuracy of diagnosis was affected by the radiotracers and pharmacological stress agents used and authors concluded that 99mTc-MIBI-SPECT with adenosine as a stress agent was to be preferred for diagnosing CAD. However, only two studies were included that used rubidium-82-PET, and there are no details given about the methods used to derive the mean sensitivities and specificities and methods of comparison.

Yang et al. (2019) conducted a systematic review and meta-analysis comparing diagnostic accuracy of stress MPI between CMR, SPECT and PET for the diagnosis of CAD, with FFR as the reference standard. Searches were conducted up to July 2018. Twenty-eight studies were included, 13 with SPECT and 5 with PET. The pooled sensitivities were 69% for SPECT and 83% for PET and pooled specificities were 85% for SPECT and 89% for PET. No subgroup analysis was undertaken for different radiotracers, and it was not clear which ones were used.

Pontone et al. (2020) conducted a similar systematic review of non-invasive tests, with FFR as the reference standard. Searches were conducted up to March 2017. Seventy-seven studies were included, 19 with SPECT and 5 with PET. Diagnostic test accuracy was presented at both vessel-based and patient-based levels. For vessel-based analysis, the pooled sensitivities were 64% for SPECT and 85% for PET and pooled specificities were 82% for SPECT and 87% for PET. For patient-based analysis, the pooled sensitivities were 71% for SPECT and 88% for PET and pooled specificities were 79% for SPECT and 86% for PET. No subgroup analysis was undertaken for different radiotracers, and it was not clear which ones were used.

We also identified a systematic review and exploratory meta-analysis of clinical outcomes for PET MPI vs SPECT MPI for CAD diagnosis (Ferko et al. 2024). Seventy-one studies were identified, but the review found comparative clinical trials were limited in number and in reported outcomes. The meta-analysis showed that there were higher rates of early- and late-invasive coronary angiography and revascularisation for PET MPI compared with SPECT MPI, but the rate of repeat testing was lower with PET MPI. The rate of acute myocardial infarction may have been lower with PET MPI. Studies varied in design, patient population and follow-up times.

Primary evidence

Evidence overview

We identified five comparative primary studies that were not included in Ferko et al. (2024) that included clinical outcomes and one diagnostic accuracy study in people with severe obesity (one of the populations of interest for PET MPI).

Tabaja et al. (2026) conducted a retrospective propensity matched study in 33,822 adults without previous coronary revascularisation who underwent PET or SPECT MPI to examine rates of invasive coronary angiography and percutaneous coronary intervention within 90 days. At 90 days, coronary angiography occurred less frequently after PET vs SPECT (6.0% vs 6.8%; risk ratio [RR]: 0.89, 95% confidence interval [CI] 0.82 to 0.97, p=0.005) and percutaneous coronary intervention was more frequent (0.9% vs 0.4%; RR: 2.0, 95% CI: 1.51 to 2.65; p<0.001). The authors suggest that the findings indicate that PET may improve selection of patients for invasive evaluation and improve efficiency.

Huck et al. (2024) conducted a retrospective propensity matched study in patients with obesity, diabetes, or chronic kidney disease without known CAD who were referred for PET, exercise SPECT, or pharmacologic SPECT MPI to examine whether PET-identified impaired myocardial flow reserve provides additional value for risk stratification. Follow-up was over a median 6.4-years. A normal PET identified low-risk patients, and abnormal PET identified high-risk patients with cardiometabolic disease. Those with normal pharmacologic SPECT remained moderate-risk compared to normal PET (p < 0.001). The authors conclude that PET with myocardial flow reserve can detect non-obstructive CAD and more accurately stratify low-risk and higher-risk patients.

Pelletier-Galarneau et al. (2024) conducted a retrospective study using claims and electronic health records data from the US to compare healthcare resource use after different cardiac imaging procedures. Data from 2.5 million US patients were analysed. In patients with suspected CAD diagnosed within three months of the cardiac imaging procedure, 25% to 37% of patients who received PET MPI needed additional healthcare resources compared with 40% to 49% of patients who received SPECT MPI. Patients who received PET MPI were reported as experiencing fewer acute cardiac events (5.3% to 9.4% compared with 9.5% to 13.2% for SPECT MPI) and lower rates of invasive coronary angiography (15.4% to 24.2% compared with 31.3% to 38.2% for SPECT MPI).

Patel et al. (2019) conducted a single centre randomised controlled trial (RCT) in 322 participants with known CAD and suspected ischemia who were randomised to PET MPI or SPECT MPI. Participants were followed for 12 months, and the primary endpoint was diagnostic failure, defined as unnecessary angiography or an additional non-invasive test within 60 days of the MPI. Diagnostic failure within 60 days occurred in 3 (1.9%) patients in the PET group and 4 (2.5%) in the SPECT group (p = 0.70). There was no evidence for a difference between the groups in rates of coronary angiography, coronary revascularisation, or health status at three, six and 12 months of follow-up.

Merhige et al. (2007) conducted an observational study in 2,159 patients who received rubidium-82-PET MPI, comparing them with two control groups, matched for a pretest likelihood of CAD, who received SPECT-MPI. One was an internal control group of 102 patients and the other an external control group of 5,826 patients. Outcomes were the frequency of diagnostic arteriography, revascularisation, costs, and clinical outcomes at one year. Arteriography rates were 0.34 and 0.31 for the external and internal control SPECT groups and 0.13 for rubidium-82-PET group (p < 0.0001). Revascularisation rates were 0.06 for the PET group, 0.13 for the external SPECT group (p<0.0001) and 0.11 for the internal SPECT group (p < 0.01), with a cost savings of 30% noted for PET patients. There was no evidence for a difference in cardiac death or myocardial infarction at one year follow-up.

Evidence overview

Harnett et al. (2019) conducted a retrospective study in 108 patients with a body mass index of >40kg/m^2 (defined as severe obesity) who underwent angiography and either Tc99m-tetrofosmin SPECT or rubidium-82 PET within the previous six months to compare the performance of SPECT and PET. Scans were classified as definitely normal or abnormal in 83% of PET vs 61% of SPECT scans ($p < 0.01$). The abstract reported that PET demonstrated a higher diagnostic accuracy and normalcy rate and had higher specificity.

Economic evaluations

Ferko et al. (2024) included a systematic review of economic evaluations and healthcare resource use for PET MPI vs SPECT MPI for CAD diagnosis. Economic evaluations were limited in number and in reported outcomes. Only one economic evaluation linked diagnostic performance to resource use. Details of economic synthesis were not reported in the abstract.

Areas of uncertainty

- Limited direct comparative diagnostic accuracy evidence identified for PET MPI vs SPECT MPI.
- Not all studies included in the reviews used rubidium-82 PET and it was not always clear which radiotracers were used in studies evaluating clinical outcomes.
- Limited evidence found in the populations and circumstances highlighted by the Royal College of Radiographers as being indications for PET MPI or PET/CT MPI use.

Literature search results

Health technology assessments and guidance

Alwan M, El Yaman A, Sayed A, et al. (2025). Cardiac positron emission tomography/Computed tomography (PET/CT) in current cardiology guidelines. J Nucl Cardiol. 48: 102231. doi: https://doi.org/10.1016/j.nuclcard.2025.102231

Besson FL, Treglia G, Bucerius J, et al. (2024). A systematic review for the evidence of recommendations and guidelines in hybrid nuclear cardiovascular imaging. Eur J Nucl Med Mol Imaging. 51(8): 2247-59. doi: https://doi.org/10.1007/s00259-024-06597-x

Dizdarevic S, Scarsbrook A, Barrington S. (2022). Evidence-based indications For The Use Of PET-CT In The United Kingdom. Royal College of Radiologists. Available at: https://www.rcr.ac.uk/media/esmdhcjd/rcr-publications_evidence-based-indications-for-the-use-of-pet-ct-in-the-united-kingdom-2022_july-2022.pdf [Accessed 4 August 2026].

Evidence reviews and economic evaluations

Alenezi MM, Majrashi NA, Sharif H, et al. (2023). A systemic review of rubidium-82 PET contrasted with 99mTc-MIBI SPECT for imaging coronary artery disease. Medicine. 102(10): e33068. doi: https://dx.doi.org/10.1097/MD.0000000000033068

Ferko N, Priest S, Almuallem L, et al. (2024). Economic and healthcare resource utilization assessments of pet imaging in coronary artery disease diagnosis: a systematic review and discussion of opportunities for future economic evaluations. J Med Econ. 27(1): 715-29. doi: https://dx.doi.org/10.1080/13696998.2024.2345507

Pontone G, Guaricci AI, Palmer SC, et al. (2020). Diagnostic performance of non-invasive imaging for stable coronary artery disease: a meta-analysis. Int J Cardiol. 300(1): 276-81. doi: https://dx.doi.org/10.1016/j.ijcard.2019.10.046

Xu J, Cai F, Geng C, et al. (2021). Diagnostic performance of CMR, SPECT, and PET imaging for the identification of coronary artery disease: a meta-analysis. Front Cardiovasc Med. 8: 621389. doi: https://dx.doi.org/10.3389/fcvm.2021.621389

Yang K, Yu SQ, Lu MJ, et al. (2019). Comparison of diagnostic accuracy of stress myocardial perfusion imaging for detecting hemodynamically significant coronary artery disease between cardiac magnetic resonance and nuclear medical imaging: a meta-analysis. Int J Cardiol. 293: 278-85. doi: https://dx.doi.org/10.1016/j.ijcard.2019.06.054

Individual studies

Harnett DT, Hazra S, Maze R, et al. (2019). Clinical performance of Rb-82 myocardial perfusion PET and Tc-99m-based SPECT in patients with extreme obesity. J Nucl Cardiol. 26(1): 275-83. doi: https://doi.org/10.1007/s12350-017-0855-6

Huck DM, Divakaran S, Weber B, et al. (2024). Comparative effectiveness of positron emission tomography and single-photon emission computed tomography myocardial perfusion imaging for predicting risk in patients with cardiometabolic disease. J Nucl Cardiol. 40: 101908. doi: https://doi.org/10.1016/j.nuclcard.2024.101908

Merhige ME, Breen WJ, Shelton V, et al. (2007). Impact of myocardial perfusion imaging with PET and (82)Rb on downstream invasive procedure utilization, costs, and outcomes in coronary disease management. J Nucl Med. 48(7): 1069-76. doi: https://doi.org/10.2967/jnumed.106.038323

Patel KK, Al Badarin F, Chan PS, et al. (2019). Randomized Comparison of Clinical Effectiveness of Pharmacologic SPECT and PET MPI in Symptomatic CAD Patients. JACC Cardiovasc Imaging. 12(9): 1821-31. doi: https://doi.org/10.1016/j.jcmg.2019.04.020

Pelletier-Galarneau M, Cabra A, Szabo E, et al. (2024). Real-world evidence study on the impact of SPECT MPI, PET MPI, cCTA and stress echocardiography on downstream healthcare utilisation in patients with coronary artery disease in the US. BMC Cardiovascular Disorders. 24(1): 543. doi: https://doi.org/10.1186/s12872-024-04225-y

Tabaja C, Motairek I, Abadie B, et al. (2026). Downstream invasive coronary procedures following PET Versus SPECT myocardial perfusion imaging: a propensity-matched analysis. Eur J Nucl Med Mol Imaging. doi: https://doi.org/10.1007/s00259-026-08062-3
Ongoing research
Only considered RCTs with clinical outcomes using rubidium-82 PET and no evidence was identified
Background
NICE. (2016). Recent-onset chest pain of suspected cardiac origin: assessment and diagnosis. NICE clinical guideline [CG95]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/cg95 [Accessed 11 August 2026].

Date of search	August 2026
Concepts used	Rubidium-82 PET/CT; Cardiac PET/CT; hybrid PET/CT Myocardial Perfusion Imaging/scintigraphy; cardiac nuclear imaging

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	**What is the clinical and cost effectiveness of rubidium-82 PET/CT MPI or rubidium-82 PET MPI for the assessment of ischaemic heart disease in comparison with SPECT or SPECT/CT MPI?**

	Inclusion criteria	Exclusion criteria
Population	Adults with established or suspected coronary artery disease and one of the following indications for rubidium-82 PET MPI: 1. previous poor quality SPECT images; 2. High BMI patients 3. High-risk patients, 4. Young patients with established CAD or those with suspected CAD 5. Needing exclusion of multi-vessel disease causing ischaemia or with suspected microvascular dysfunction 6. With coronary anomalies, congenital disease post-surgery and Kawasaki's disease	
Intervention	Rubidium-82 PET MPI or rubidium-82 PET/CT MPI	Cardiac PET with other radiotracers
Comparison/ Comparators	SPECT or SPECT/CT MPI	

	Inclusion criteria	Exclusion criteria
Outcome measures	Rates of angiography, revascularisation and other coronary interventions Test related adverse events Health related QoL Resource use Economic outcomes	

Proposed speciality	**Cardiovascular system**