Healthcare Improvement Scotland | SHTG Advice on health technologies

SHTG Recommendations
December 2024

In response to an enquiry from the Scottish Clinical Imaging Network (SCIN) National PET-CT Review Group

# FDG-PET imaging in the diagnosis of dementia

## Recommendations for NHSScotland

In people who have undergone standard assessment for dementia or mild cognitive impairment (MCI), further investigations should only be used if clarifying dementia subtype would change patient management. Based on an updated review of the evidence, either perfusion SPECT (single-photon emission CT) or FDG-PET (fluorodeoxyglucose-positron emission tomography) should be considered as a further investigation for clarifying dementia subtype in people with suspected Alzheimer's disease (AD) or frontotemporal dementia (FTD). *This finding supports the SIGN (2023) and NICE (2018) recommendations.*

Taking into account developments in diagnosis and treatments, future plans for the PET-CT service in NHSScotland should consider the provision of dementia imaging. This would help to ensure equity of access to imaging for people undergoing assessment for dementia across the UK.

*NHSScotland is required to consider the Scottish Health Technologies Group (SHTG) recommendations.*

## What were we asked to look at?

The Scottish Clinical Imaging Network (SCIN) asked us to assess the clinical and cost effectiveness of FDG-PET imaging, compared with HMPAO ($^{99m}$Tc labelled hexamethylpropyleneamine oxime)-SPECT imaging, in the diagnosis of dementia.

## Why is this important?

A clinical diagnosis of dementia is based on information from different sources. An accurate diagnosis of the subtype of dementia is important, as patients with specific subtypes follow distinct clinical courses and responses to medication. Patients undergoing assessment for dementia may benefit from functional imaging to help clarify their diagnosis. In Scotland, the patients who may benefit from functional imaging are usually offered a perfusion SPECT scan, using the radiotracer HMPAO.

The SCIN considers FDG-PET a superior imaging tool, compared with perfusion SPECT, in this patient group. They also noted that while perfusion SPECT is widely available in Scotland, access to FDG-PET for people with dementia is extremely limited. A SCIN National PET-CT Review Group is considering which clinical indications would be relevant for potential PET-CT service expansion. This SHTG Recommendation will help inform a decision on whether dementia should be included within the list of indications.

## What was our approach?

We produced an SHTG Recommendation based on a review of published evidence on the clinical and cost effectiveness of FDG-PET in the diagnosis of dementia, compared with perfusion SPECT.

## What next?

This work will inform the National PET-CT Review Group decision as to whether an FDG-PET dementia imaging service should be developed as part of a potential PET-CT service expansion in NHSScotland.

## Key points

1. In 2023, the Scottish Intercollegiate Guidelines Network (SIGN) published a guideline on the assessment, diagnosis, care and support for people with dementia and their carers. The guideline included clinical effectiveness evidence on the use of FDG-PET and SPECT, based on an evidence review conducted by the National Institute for Health and Care Excellence (NICE) in 2018.[1, 2] This SHTG Recommendation updates the clinical effectiveness evidence on FDG-PET and SPECT presented by SIGN. Consideration has also been given to cost effectiveness, organisational issues and patient issues.

   This SHTG Recommendation summarises studies on the use of FDG-PET and SPECT for predicting which people with MCI go on to develop dementia, and for differentiating between subtypes of dementia.

**Predicting the progression from MCI to dementia**

*FDG-PET*

2. For predicting progression from MCI to clinically diagnosed AD, a high-quality systematic review from 2018 (studies published between 1999 and 2017) reported that diagnostic accuracy results for FDG-PET varied across studies (sensitivity 25% to 100% and specificity 15% to 100%).[3] A systematic review from 2024, which included more up-to-date studies, reported that sensitivities in predicting progression from MCI to clinically or neuropathologically diagnosed dementia (mainly AD) ranged from 43% to 100%, and specificities from 63% to 94%.[4] The wide range of values was due to heterogeneity between studies in how images were assessed, how studies were conducted and differences in study populations.

*SPECT*

3. For predicting the progression from MCI to AD, one lower-quality systematic review with meta-analyses evaluated the accuracy of SPECT and FDG-PET (studies published between 1998 and 2006).[5] Five of the included studies were on FDG-PET and four were on SPECT. The authors reported that the sensitivity (81%) and specificity (74%) values for SPECT imaging were lower than the sensitivity (87%) and specificity (89%) values for FDG-PET. Limitations with the review mean that the results of the meta-analyses should be treated with caution.

**Differentiating subtypes of dementia**

*FDG-PET*

4. For differentiating subtypes of dementia, a high-quality systematic review from 2020 (three cohort studies published between 2007 and 2011) evaluated the accuracy of FDG-PET for distinguishing neuropathologically confirmed AD from non-AD.[6] In two studies (n=182), the median sensitivity and specificity of FDG-PET for distinguishing between AD and non-AD was 89% (range 84% to 94%) and 74% (range 73% to 74%), respectively. For distinguishing between AD and frontotemporal lobar degeneration (FTLD), one study (n=45) reported median sensitivity and specificity for FDG-PET of 97% (range 96% to 98%) and 66% (range 59% to 73%), respectively. Based on these findings, the authors concluded that FDG-PET was highly sensitive and moderately specific for diagnoses of neuropathologically confirmed AD. A systematic review from 2024 (14 studies published between 2007 and 2021) using clinically (rather than neuropathologically) diagnosed dementia subtype as the reference standard reported similar sensitivity and specificity results to the 2020 review for distinguishing between AD and non-AD or FTLD.[7]

*SPECT*

5. For differentiating subtypes of dementia, a high-quality systematic review from 2020 (three studies published between 2007 and 2011, n=205), evaluated the use of SPECT to distinguish confirmed AD (based on postmortem examination) from various non-AD neuropathologic diagnoses.[6] Median sensitivity was 63% (range 57% to 94%) and median specificity was 83% (range 76% to 92%).

**Primary studies directly comparing FDG-PET and SPECT**

6. We identified a 2020 retrospective observational study that directly compared FDG-PET with SPECT in diagnosing AD in people with MCI and dementia. The reference standard was an amyloid-PET scan.[8] The sensitivity of FDG-PET and SPECT was 76% versus 43% ($p<0.001$), while specificity was 74% versus 83% ($p=0.45$). While these findings are broadly in concordance with the results from the systematic reviews, they must be treated with caution given the study limitations.

**Economic evidence**

7. We did not identify any economic evidence comparing FDG-PET with SPECT imaging for the diagnosis of dementia.

**Patient issues**

8. We identified one study which included a survey of 98 people (68 with dementia and 30 controls) who had an FDG-PET and SPECT scan.[9] Results suggested that both types of scan are generally acceptable to patients, and that perceived diagnostic accuracy tended to dictate preferences for one scan over the other.

**Organisational issues**

9. The PET-CT service in NHSScotland is in high demand and expansion of the service to include dementia imaging will require infrastructure and resource investment to ensure that scanning capacity for other patients (for example, people with cancer) is not negatively affected. Existing barriers to use of PET-CT for dementia imaging include a lack of spare capacity for scans as well as the production and supply of radioisotopes.

## SHTG Council considerations

1. The Council noted that patient co-morbidities may impact on the clinical utility of FDG-PET, for example people with poorly controlled diabetes may not be suitable for a glucose-based radiotracer. In these circumstances, SPECT is an appropriate alternative.

2. Given that the current FDG-PET service is delivered from four centres in Scotland, the Council noted that some people may have to travel for PET scans and this has the potential to create inequalities in access. SPECT is widely available in Scotland.

3. Depending on how many people undergoing investigations for dementia would benefit from FDG-PET scanning, the Council acknowledged that the infrastructure and resource investment could be significant. The PET-CT service is already stretched in Scotland, with approximately 700 scans being done a month (mostly for people with cancer or suspected cancer). Based on the number of people with dementia, or suspected dementia, who are currently referred for a SPECT scan in Scotland, a clinical expert estimated that approximately 20 people per month may be eligible for FDG-PET scanning. This number may change considerably depending on developments in the diagnosis and treatment of dementia, and whether these developments impact the demand for nuclear imaging.

4. The Council agreed that the clinical-effectiveness evidence published since 2018 is limited in quality and quantity. The studies identified focused on diagnostic accuracy, and it is not clear how the addition of FDG-PET to the diagnostic pathway impacts on clinical decision-making, the treatments that patients with dementia are offered, and the outcomes for patients. The heterogeneity between the studies means that robust

conclusions are not possible. The Council also recognised the absence of cost-effectiveness evidence.

5. The Council noted that FDG-PET services for dementia are commissioned in NHS England, NHS Wales and NHS Northern Ireland. NHSScotland does not commission FDG-PET services for dementia even though the guidance in place in NHSScotland matches the guidance in the other UK nations. The Council also noted a lack of available information on the impact of FDG-PET for dementia diagnosis in other parts of the UK, either service delivery implications or patient outcomes.

6. The Council noted that the diagnosis and treatment landscape for dementia is evolving rapidly. In addition to the possible availability of disease-modifying dementia drugs in the coming years, other areas of potential development include the application of precision medicine. Given this fast-changing landscape, it is difficult to predict exactly how the demand for nuclear imaging for dementia will change in the near future.

7. The Council recognised that the experience for patients undergoing an FDG-PET or SPECT scanning may differ, but that both scans are likely to create an additional stress for people who may already feel they are in a difficult and frightening place. The Council reiterated that scans should only be used when there is a likely impact on patient management decisions.

8. Following insight from a topic expert, the Council noted:

    - there is a need for good quality evidence, particularly evidence that directly compares perfusion SPECT with FDG-PET in this patient group
    - there is a need to consider why the service in NHSScotland differs from the other UK nations
    - FDG-PET scans generally take 10 minutes, whereas SPECT scans take approximately 30 to 45 minutes
    - FDG-PET scan images are generally easier to report on, compared with SPECT scan images
    - the images produced from SPECT scanning have improved over the years as the technology advances, but we cannot be confident how image quality compares with FDG-PET image quality.

# Contents

## Definitions

**FDG** (fluorodeoxyglucose) is a radioactive tracer that is used in FDG-PET scans. It is taken up by the body in the same way as glucose. FDG-PET brain scans detect and map brain FDG uptake as an indicator of hypometabolism and neurodegeneration.

**HMPAO** ($^{99m}$Tc labelled hexamethylpropyleneamine oxime) is a radioactive tracer used in SPECT scans. HMPAO-SPECT scans detect and map cerebral perfusion as an indicator of neurodegeneration.

**PET** stands for positron emission tomography.

**PET scans** are imaging tests that are used to diagnose disease by showing the accumulation of radioactive tracers in certain parts of the body.

**Sensitivity:** the probability that a test will correctly identify a person having a disease. It is the number of true positive results divided by the total number of people tested who have the disease.[10]

**Specificity:** the probability that a test will correctly identify a person who does not a disease. It is the number of true negative results divided by the total number of people tested who do not have the disease.[10]

**SPECT** stands for single-photon emission computed tomography.

**SPECT scans** are imaging tests can be used to diagnose disease by showing the accumulation of radioactive tracers in different parts of the body.

# Introduction

Dementia is a clinical syndrome of cognitive decline that includes a range of cognitive and behavioural symptoms caused by a variety of underlying pathophysiological processes. This includes AD, vascular dementia, mixed dementia, dementia with Lewy bodies (DLB) and FTD. There is overlap between the clinical symptoms and pathophysiological processes of these diseases.[2]

## Dementia due to Alzheimer's disease

In the UK, about two thirds of people with dementia are diagnosed with AD. Memory impairment is typically the initial presenting complaint of dementia caused by AD. The characteristic course is a slow but steady decline from a previous level of cognitive functioning with impairment in additional cognitive domains emerging with disease progression. The initial stages of dementia caused by AD are often associated with mental health and behavioural symptoms such as depressed mood and apathy. Symptoms common in later stages include psychotic symptoms, irritability, aggression, confusion, abnormalities of gait and mobility, and seizures.[2]

For most people, a diagnosis of AD is made based on clinical symptoms. A definitive diagnosis of AD can only be made when the pattern of illness described above is supported by a postmortem examination demonstrating the typical supporting pathological features of amyloid plaques and neurofibrillary tangles.[2] In research centres, a diagnosis of clinical Alzheimer-type dementia is approximately 80% sensitive and 70% specific for AD confirmed on postmortem examination.[11]

## Vascular dementia

About 10 to 20% of people with dementia are diagnosed with vascular dementia. Vascular dementia is a result of significant brain parenchyma injury from cerebrovascular disease (ischaemic or haemorrhagic). The onset of cognitive deficits is temporally related to one or more vascular events. Cognitive decline is typically most prominent in the speed of information processing, complex attention and frontal-executive functioning.[2]

## Frontotemporal dementia

About 10% of people with dementia are diagnosed with FTD. FTD is a group of primary neurodegenerative disorders mainly affecting the frontal and temporal lobes. Onset is typically insidious with a gradual and worsening course. Several syndromic variants (some with an identified genetic basis or familiarity) are described that include presentations with predominantly marked personality and behavioural changes (such as executive dysfunction, apathy, deterioration of social cognition, repetitive behaviours, and dietary changes) or with predominantly language deficits (that include semantic, agrammatic/non-fluent and logopenic forms), or with a combination of these deficits. Memory function, psychomotor speed, as well as visuoperceptual and visuospatial abilities often remain relatively intact, particularly during the early stages of the disorder.[2]

Frontotemporal lobar degeneration (FTLD) is a pathological process that occurs in FTD.

## Dementia due to Lewy body disease

About 5% of people with dementia are diagnosed with DLB. The precise cause is unknown but involves abnormal alpha-synuclein protein folding and aggregation with Lewy body formation primarily in the cortex and brainstem. Onset is insidious with attentional and executive functioning deficits typically reported as the initial presenting complaint, often accompanied by visual hallucinations and symptoms of rapid eye movement sleep behaviour disorder. Hallucinations in other sensory modalities, depressive symptoms and delusions may also be present. Spontaneous onset of Parkinsonism within approximately 1 year of the onset of cognitive symptoms is characteristic of the disease.[2]

## Other types of dementia

Other types of dementia include dementia due to psychoactive substances (including medications), or other diseases, behavioural or psychological disturbances. Dementia may also be due to an unknown or unspecified cause.

Mixed dementia includes dementia presenting with both Alzheimer's and vascular pathology or other nonvascular aetiologies contributing to the dementia.[2]

## Mild cognitive impairment

A diagnosis of MCI is often given in the early stages of dementia. There is a broad range of symptoms associated with MCI, including impact on mental processes (for example, attention and memory) and behavioural changes (for example, apathy, anxiety or irritability). It is difficult for clinicians to associate these symptoms with a single condition in the early stages.[2]

MCI is a precursor to dementia, with approximately 8–15% of people with MCI developing dementia each year, compared with 1–2% of older people without MCI.[2, 5]

## Diagnosis of dementia

The diagnosis of dementia is a clinical diagnosis, based on information from different sources. An accurate diagnosis of dementia subtype is important, as each has a different response to various medications, as well as distinct clinical courses, prognoses and mortality rates.[7]

In November 2023, SIGN published a clinical guideline on the assessment, diagnosis, care and support for people with dementia and their carers.[2] The guideline states that a diagnosis of dementia should be made following an appropriate clinical assessment by a clinician with knowledge of dementia (alongside appropriate neurological examination and cognitive testing). The guideline states that blood tests should be undertaken to exclude reversible causes of cognitive decline if these have not already been addressed. The guideline also states that neuropsychology testing can be considered if it is unclear:

- whether the person has cognitive impairment
- whether the cognitive impairment is caused by dementia, or

- what the correct subtype diagnosis is.[1, 2]

Following this comprehensive assessment for dementia, the guideline states that further investigations can be considered to help rule out other causes in people presenting with cognitive decline, or help diagnose dementia subtype in those with a diagnosis of dementia.[2] The guideline makes the following recommendation:[1]

*Offer structural imaging to rule out reversible causes of cognitive decline and to assist with subtype diagnosis, unless dementia is well established and the subtype is clear.*

*Only consider further tests if:*

- *it would help to diagnose dementia subtype and*
- *knowing more about the dementia subtype would change management.*

With regard to further testing, SIGN includes the following recommendation for diagnosing AD:

*If the diagnosis is uncertain and Alzheimer's disease is suspected, consider either:*

- *FDG-PET (fluorodeoxyglucose-positron emission tomography-CT), or perfusion SPECT (single-photon emission CT) if FDG-PET is unavailable*

  ***or***

- *examining cerebrospinal fluid for:*
  - *either total tau or total tau and phosphorylated-tau 181 and*
  - *either amyloid beta 1-42 or amyloid beta 1-42 and amyloid beta 1-40.*

*If a diagnosis cannot be made after one of these tests, consider using the other one.*

For the other dementia subtypes, SIGN references the NICE guidance from 2018:[1, 2]

- If dementia subtype is uncertain and **frontotemporal dementia is suspected**, use either FDG-PET or perfusion SPECT. Do not rule out frontotemporal dementia based solely on the results of structural, perfusion or metabolic imaging tests.
- If dementia subtype is uncertain and **vascular dementia is suspected**, use MRI. If MRI is unavailable or contraindicated, use CT. Do not diagnose vascular dementia based solely on vascular lesion burden. Be aware that young-onset vascular dementia has a genetic cause in some people.
- If a diagnosis is uncertain and **Lewy body dementia is suspected**, use $^{123}$I-FP-CIT SPECT. If $^{123}$I-FP-CIT SPECT is unavailable, consider $^{123}$I-MIBG cardiac scintigraphy. Do not rule out dementia with Lewy bodies based solely on normal results of the above investigations.

## A changing context

The SIGN guideline acknowledges that while perfusion SPECT is widely available in NHSScotland, access to FDG-PET for dementia diagnoses remains extremely limited. PET-CT services are currently delivered via five PET-CT scanners across four regional PET-CT centres. FDG can be produced onsite in NHS Grampian and NHS Greater Glasgow and Clyde. The PET-CT service is currently used mainly for diagnosing cancer or suspected cancer. Based on national data from 2024, approximately 700 PET-CT scans are done per month in Scotland.[12] The current target waiting time in Scotland is 14 days from referral to scan with a 3-day target from scan to report. This target is often breached because of issues with scanning capacity and radiopharmaceutical supply issues.[13]

PET-CT service provision is currently being considered by SCIN, to help inform national strategic discussions on service expansion. As PET-CT scanning is already at capacity, increasing the use of the existing service to include FDG-PET dementia imaging would impact on current service delivery. Any increase in use of PET-CT imaging for dementia may potentially reduce the workload of nuclear medicine departments if this leads to a reduction in demand for SPECT scans.

The development of new disease-modifying dementia treatments may increase the number of people who require functional imaging for an accurate diagnosis. For example, the new monoclonal antibody therapies (donanemab and lecanemab) being reviewed by the Scottish Medicines Consortium and NICE. These treatments for AD directly target amyloid plaques in the brain and may slow disease progression. If these drugs are approved for use, this may change the demand for PET scanning. It is possible that these drugs will only be prescribed if amyloid plaques can be confirmed, either by examining cerebral spinal fluid (via lumbar puncture) or by a different type of PET scanning which detects amyloid plaques. While it is unclear how the dementia diagnosis and treatment landscape will develop, foresight and planning are essential to minimise disruption and delay to the service and to ensure that patients have access to appropriate treatments at the right time.

## The use of FDG-PET imaging for dementia in other parts of the UK

NHS England and NHS Wales commissions FDG-PET scans for the ‘evaluation of memory loss/neurological signs suggestive of dementia and differentiation of types of dementia in selected patients’.[14, 15]

Northern Ireland commissions FDG-PET scans for dementia in accordance with NICE guidance from 2018.[1] The FDG-PET service for dementia is centralised in Belfast and provides for Northern Ireland’s five health and social care trusts.

# Research question:

What is the clinical and cost effectiveness of FDG-PET scanning in dementia diagnoses, compared with perfusion SPECT?

## Literature search

A systematic search of the literature was carried out between 15-18 April 2024 to identify systematic reviews, health technology assessments and other evidence-based reports. Medline, Embase, Centre for Reviews and Dissemination (CRD) and Cochrane databases were searched for systematic reviews and meta-analyses. The primary literature was systematically searched between 22-24 April 2024 to identify economics articles, using the following databases: Medline, Embase and NHS Economic Evaluation Database (EED). Key websites were searched for guidelines, policy documents, clinical summaries and economic reports.

A further systematic search was carried out between 17-24 June 2024 to identify primary literature using the Medline, Embase and PsycINFO databases. Specific patient issues filters were included as part of the search.

Results were limited to English language publications and from 2018 onwards, except for the patient issues search which had no date limit applied. Concepts used in all searches included: dementia, Alzheimer's, FDG-PET imaging. A full list of resources searched, and terms used are available on request.

## Health technology description

PET and SPECT are both types of nuclear imaging, using radioactive tracers to create images of the inside of the body. PET and SPECT scans use different radioactive tracers and produce different kinds of images.

### FDG-PET

PET scans produce detailed 3-dimensional images. While PET scans can be used for different indications they are most commonly used to detect cancer. Radioactive tracers are usually given to patients via an injection. PET scanners detect the radiation given off by the radioactive tracer as it collects in different parts of the body.[16]

Different types of radioactive tracers can be used. Most PET scans use FDG which is taken up by glucose-using cells. By analysing areas where the FDG accumulates it is possible to work out how certain body functions are working.

In people with dementia or suspected dementia, an FDG-PET scan measures the concentration of glucose in the brain. FDG-PET detects specific patterns of hypometabolism (reduced glucose consumption) in the brain and can be used for both early and differential diagnosis in patients with MCI and dementia.

### SPECT

SPECT imaging also produces 3-dimensional images. SPECT imaging can be used with different tracers to study physiological processes, including cerebral perfusion. Patients are given a radioactive

tracer (normally via injection), and a gamma camera detects the radiation given off. SPECT scans are most commonly used to take images of the heart, brain and bones.

In people with suspected dementia, a cerebral perfusion SPECT scan is used to show if there is any altered blood flow through the brain. As each type of dementia is associated with different patterns of blood flow, these scans may be used in differential diagnosis.[17] In Scotland, the radioactive tracer most commonly used for dementia diagnosis is HMPAO.

SPECT scanners and radioactive tracers tend to cost less and be more readily available than PET scanners and radioactive tracers.[2] PET offers a higher spatial resolution compared to SPECT, and so produces higher quality images.[18]

## Epidemiology

An estimated 90,000 people are living with dementia in Scotland, including approximately 3,000 people under the age of 65 with young-onset dementia. The estimated annual incidence of diagnosed dementia is 20,000.[2]

Non-modifiable risks for dementia are age and family history. Many of the risk factors for dementia are associated with socioeconomic disparities. The 14 most important potentially modifiable risk factors for dementia are: less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, low social contact, excessive alcohol consumption, traumatic brain injury, air pollution, untreated vision loss and high low-density lipoprotein (LDL) cholesterol.[2, 19]

Health inequalities persist into old age, and as the population in Scotland ages, it is likely that the number of people with a dementia diagnosis will rise, and social patterning in dementia may become more apparent.[20] The prevalence of dementia is greater in women (67% of people with dementia are women) and in people with learning disabilities. Public Health Scotland states that, in general, the prevalence rate for dementia does not appear to vary based on ethnicity, though vascular dementia and early-onset dementia may be more prevalent in some 'black and ethnic minority communities' (a more specific description of the people this applies to was not given).[20]

The current cost of dementia care to the UK is £26 billion, including informal care, social care and healthcare. It has been estimated that delaying the onset of dementia by 5 years in each individual, would save £21.2 billion a year by 2050.[2]

# Clinical effectiveness

## Systematic reviews

We identified six systematic reviews (in seven publications) that were published after the 2018 NICE guidance on the use of FDG-PET and/or SPECT imaging in the diagnosis of dementia.[3-7, 11, 21] The results of the systematic reviews are summarised in *Table 1* and discussed below. None of the systematic reviews directly compared FDG-PET to SPECT, so the results for each are reported separately. For each imaging modality, the accuracy results for predicting progression from MCI to dementia, and for differential diagnosis, have been presented.

**FDG-PET for predicting progression from MCI to dementia**

Three systematic reviews evaluated the diagnostic accuracy of FDG-PET in predicting progression from MCI to dementia.[3-5]

The oldest, by Smailagic *et al.* (2018), was methodologically robust and well reported.[3] It aimed to evaluate the accuracy of FDG-PET for detecting people with MCI at baseline who would clinically convert to AD dementia at follow-up. Dementia types other than AD were not included. The review updated a Cochrane review from 2014, which had concluded there was insufficient evidence to support the routine use of FDG-PET in people with MCI. The literature search was limited to studies published between 2013 and 2017. The twenty studies identified were combined with the studies in the original Cochrane review (n=16), giving a total of 36 studies. The results were reported narratively in the review because heterogeneity across the studies prevented meta-analyses.

Smailagic *et al.* noted that the included studies had methodological limitations, with most at risk of bias that threatened the validity of their results. They included 24 studies in an exploratory analysis, which assessed the accuracy of FDG-PET for predicting conversion from MCI to clinically diagnosed AD dementia. As several studies were based on the same cohort of patients only one study per cohort was included in the analysis to avoid double counting of patients. Diagnostic accuracy results varied substantially across the 24 studies (sensitivity values ranged from 25% to 100%, and specificity values ranged from 15% to 100%).

Smailagic *et al.* also presented the results according to the analytical method used for FDG-PET. All 24 studies used quantitative/semi-quantitative methods, with 18 using computer aided visual read metrics (for example, single case statistical parametric mapping or sc-SPM). There was evidence of higher and more consistent accuracy results in six out of eight studies using sc-SPM, with sensitivity and specificity values of 80% and above. Four of these studies were published after the Cochrane review and sensitivity values ranged from 77% to 100%, and specificity from 74% to 100%.

Smailagic *et al.* highlighted the need for robust prospective longitudinal cohort studies with longer follow-up of 5 years at least. They note that these studies should define a specific threshold for FDG-PET biomarker at baseline and then prospectively assess its predictive accuracy. They also discuss the issue of accuracy being highly influenced by the analytical approach used and the need for the initial promising results for sc-SPM to be confirmed in future studies. They concluded that further work

needs to be completed before FDG-PET as a single test can be widely recommended as a routine diagnostic test for conversion from MCI to AD dementia in clinical practice.

A second systematic review by Cotta Ramusino *et al.* was published in 2024.[4] This review was of reasonable quality, and evaluated the diagnostic accuracy of various molecular imaging techniques (including FDG-PET) in predicting progression from MCI to dementia (AD, DLB or FTD). The review only included studies of at least 50 patients with MCI, that had a follow-up of at least 3 years and recorded progression to a clinical diagnosis of dementia during follow-up or diagnosis on pathology as the reference standard. The literature search was limited to evidence published between 2017 and 2022 and so updates the review by Smailagic *et al*. The other imaging techniques evaluated in the review were amyloid-PET, tau-PET, dopamine transporter imaging and cardiac scintigraphy. As these are beyond the scope of this SHTG Recommendation the results have not been included.

In evaluating FDG-PET, Cotta Ramusino *et al.* included 25 studies including 6,803 people with MCI, who were followed for a mean of 51 months. The review authors noted a high risk of bias regarding patient selection, with most studies including patients non-consecutively. The FDG-PET assessments were primarily semi-quantitative (21 studies), although combined assessments (a visual interpretation of the semi-quantitative output) were also used (four studies). The sensitivity values in predicting progression from MCI to dementia (mainly AD) reported in the studies ranged from 43% to 100%, and specificity values ranged from 63% to 94%. While these ranges are narrower than those reported by Smailagic *et al.* (2018), they still show that the accuracy figures reported in the literature are variable, making it difficult to reach confident conclusions.

Cotta Ramusino *et al.* concluded that their 2024 review confirms the findings of their previous review, that is, that FDG-PET and amyloid-PET (results not reported here as amyloid-PET is out with our scope) are the most accurate molecular imaging biomarkers in predicting MCI conversion to dementia, in particular AD. Similarly to Smailagic *et al.*, they acknowledge the wide variability in diagnostic accuracy (especially sensitivity) of FDG-PET in predicting progression from MCI to dementia and suggest that this is because of heterogeneity in the study populations as well as different methods of image assessment.

A third systematic review, by Zhu *et al.* (2022)[5] evaluated the use of FDG-PET imaging in predicting the progression to AD in people with MCI. The review does not add to the results reported by Smailagic *et al.* and Cotta Ramusino *et al*. Zhu *et al.* included five studies on FDG-PET, four of which were included in the review by Smailagic *et al*. They combined their results in meta-analyses, but methodological limitations of the review mean that these should be treated with caution. The review results are summarised in *Table 1* for information.

**FDG-PET for differential diagnosis**

Three systematic reviews evaluated the use of FDG-PET in differentiating subtypes of dementia.[4, 6, 7]

The best evidence comes from a high-quality systematic review by Fink *et al.*[6] on the accuracy of brain imaging and cerebrospinal fluid (CSF) biomarkers for distinguishing neuropathologically-confirmed AD from non-AD (no AD pathology, DLB or FTLD) in people with dementia. The authors

only included diagnostic accuracy studies that were rated as having a low or medium risk of bias. Fink *et al.* included studies published between 2007 and 2011.

In evaluating the accuracy of FDG-PET for neuropathologically-confirmed AD, Fink *et al.* included three cohort studies (n=227), two retrospective and one prospective. The studies used visual and quantitative scoring systems and criteria for positive scans. For AD versus non-AD, in two studies (n=182), median sensitivity and specificity of FDG-PET was 89% (range 84% to 94%) and 74% (range 73% to 74%), respectively. For AD versus FTLD, a retrospective cohort study with a medium risk of bias evaluated 45 people who had FDG-PET scans and in whom postmortem examination later showed either AD or FTLD. Median sensitivity and specificity for FDG-PET was 97% (range 96% to 98%) and 66% (range 59% to 73%), respectively. When the reviewers in the study used clinical evaluation to predict AD versus FTLD neuropathology, sensitivity was 85% and specificity was 65%. When clinical evaluation and FDG-PET were used together, sensitivity was 98% and specificity was 71%.

Based on these findings, the authors concluded that FDG-PET was highly sensitive and moderately specific for neuropathologically confirmed AD. They also noted that FDG-PET may increase accuracy in differentiating neuropathologically confirmed AD from non-AD dementia when added to clinical evaluation.

A second systematic review, by Na *et al.* (2024) examined the effectiveness of FDG-PET in differentiating the subtypes of dementia (AD, DLB, FTD) for precise treatment and management.[7] The literature search included 14 studies (one of which was included by Fink *et al.*) published between 2007 and 2015, except for one study published in 2021. The results were combined in meta-analyses. Most studies used case-control designs and images were assessed using visual and quantitative methods. The reference standard was the clinical diagnosis of each dementia subtype.

For AD versus FTD, the review authors included seven case-control studies. Mean sensitivity was 96% (95% CI 88% to 98%) and specificity was 84% (95% CI 70% to 92%). Heterogeneity was high for both analyses, with $I^2$ values (a statistical measure of heterogeneity) being 87.7% for sensitivity and 66.2% for specificity.

For AD versus DLB, the review authors combined five results, which were reported in four case-control studies. Mean sensitivity was 93% (95% CI 88% to 98%) and specificity was 92% (95% CI 70% to 92%). Heterogeneity was high for both analyses, with $I^2$ values of 82.5% for sensitivity and 81.5% for specificity.

For AD versus non-AD dementias, the review authors combined the results from four studies (three case-control and one prospective cohort). Mean sensitivity was 86% (95% CI 80% to 91%) and specificity was 88% (95% CI 80% to 91%). Heterogeneity was moderate for both analyses, with $I^2$ values of 50.0% for sensitivity and 47.9% for specificity. The non-AD group included conditions such as FTLD, DLB, depression, unspecified dementia, Creutzfeldt-Jakob disease and mixed dementia.

For FTLD versus non-FTLD, the review authors identified two case-control and one cohort study and reported on their results narratively. In one study, 100 patients with uncertain dementia type were

classified into FTLD, AD and DLB using FDG-PET and a sensitivity of 82% and specificity of 90% was reported. A second study used FDG-PET to differentiate FTLD from Creutzfeldt-Jakob disease, vascular dementia, mixed dementia, posterior cortical atrophy and AD and reported a sensitivity of 89% and a specificity of 100%. The final study analysed behavioural variant FTLD differentiation from vascular cognitive impairment, other dementias, AD, DLB and major psychiatric disorders using FDG-PET and showed a sensitivity of 70% and a specificity of 93%.

The authors conclude that FDG-PET, while not a standalone diagnostic tool, exhibits high sensitivity and specificity in differentiating dementia subtypes. While this review was well conducted, the authors did not explore the high levels of heterogeneity.

The third review, by Cotta Ramusino *et al.,* included nine cross-sectional studies which evaluated the diagnostic accuracy of FDG-PET in detecting the cause of neurocognitive disorders.[4] Clinical or biomarker-based diagnosis was used as the reference standard. Five studies assessed FDG-PET accuracy in detecting AD co-pathology in people with DLB and reported sensitivity values ranged from 56% to 94%, and specificity values from 51% to 100%. Cotta Ramusino *et al.* stratified these results according to FDG-PET assessment method and semi-quantitative procedures achieved higher accuracy values than visual qualitative assessment. Based on the remaining four studies, the authors concluded that FDG-PET was slightly less accurate in differentiating FTLD from AD, psychiatric, or other cognitively impaired conditions (sensitivity 8% to 100%; specificity 48% to 100%). The wide-ranging results reported in this study limit the conclusions that can be drawn, and highlights the heterogeneity in the evidence.

**SPECT – predicting progression from MCI to dementia**

A systematic review with meta-analyses by Zhu *et al.* (2022) evaluated the use of FDG-PET, SPECT and MRI imaging in predicting the progression to AD in people with MCI.[5] The authors identified five studies on FDG-PET (summarised in *Table 1*), and four on SPECT. All studies were published between 1998 and 2006 with limited detail, for example number of patients, provided. The authors report moderate to high statistical heterogeneity in their analyses but do not explore this further. The meta-analyses for SPECT found that sensitivity was 80.5% (95% CI 78.3% to 90.12%) and heterogeneity was moderate ($I^2$=63.1%). Specificity was 74.3% (95% CI 61.3% to 78.5%) and heterogeneity was moderate ($I^2$=71.9%).

The review authors conclude that the sensitivity and specificity of FDG-PET imaging were significantly higher than those of SPECT (and MRI imaging, results not included here). Given the limitations of the review, these results need to be treated with caution.

**SPECT – use in differential diagnosis**

Two systematic reviews evaluated the use of SPECT in differentiating subtypes of dementia.[6, 21]

The best evidence comes from Fink *et al.,* who included a research question on the accuracy of brain imaging and CSF biomarkers for distinguishing neuropathologically-confirmed AD from non-AD (no AD pathology, DLB or FTLD) in people with dementia.[6] The authors only included diagnostic accuracy

studies that were rated as having a low or medium risk of bias. The included studies on FDG-PET and SPECT were published between 2007 and 2011.

In evaluating the accuracy of HMPAO-SPECT for neuropathologically confirmed AD, Fink *et al.* included two retrospective cohort studies and two prospective cohort studies (n=232). Definition of a positive scan for AD varied across the studies but was based on prevalent regional hypoperfusion (most commonly in temporal or parietal lobes). Three studies (n=205) used SPECT to distinguish confirmed AD (based on postmortem examination) from various non-AD neuropathologic diagnoses. Median sensitivity was 63% (range 57% to 94%) and median specificity was 83% (range 76% to 92%). Fink *et al.* also noted that clinical information combined with SPECT appeared to have higher specificity but lower sensitivity for confirmed AD (based on postmortem examination), compared with clinical information alone.

A second, lower quality, systematic review (Athanasio *et al.,* 2024) investigated the diagnostic accuracy of brain SPECT in distinguishing FTD from AD and other dementias, and in differentiating FTD variants.[21] The authors included 35 studies, including 3,142 participants (1,029 with FTD). One of the studies was included in the review by Fink *et al.* Most of the included studies were published before 2007. The authors do not appear to have formally appraised the included studies, and none appear to have been excluded based on quality.

The review authors identified 17 studies that investigated the use of SPECT to differentiate FTD from AD but noted that only five of the studies reported diagnostic accuracy values. The sensitivity and the specificity for the differential diagnosis of FTD versus AD ranged from 56% to 88% and from 51% to 93%, respectively. With regard to the differentiation between FTD subtypes, only two studies were included and limited conclusions were drawn. The authors conclude that 'perfusion SPECT seems to provide a valuable tool in the differential diagnosis of FTD when FDG-PET is not available. SPECT is recommended only for selected cases of difficult differential diagnosis…more research is warranted'.

*Table 1: Summary of systematic reviews evaluating FDG-PET or HMPAO-SPECT*

| Reference | Included studies | Study characteristics | Main results | Quality considerations |
|---|---|---|---|---|
| **FDG-PET – predicting progression from MCI to dementia** | | | | |
| Cotta Ramusino *et al.* (2024)[4] | 25 | 6,803 people with MCI<br>Longitudinal prospective studies<br>Follow-up: 51 months (range 24-120 months)<br>Diagnosis at follow-up:<br>- AD 2,572<br>- FTLD 8<br>- LBD 92<br>- Vascular Dementia 12<br>- Conversion diagnosis not further specified 180<br>- MCI non-converter 3,989 | **Sensitivity:** range 43% to 100%<br>**Specificity:** range 63% to 94% | The systematic review is reasonably well conducted and reported. The literature search was limited by date (2017-2022), and only in Medline (although they ran a check in Embase). They evaluated the quality of the included studies, and note bias, particularly with regard to patient selection. |
| Zhu *et al.* (2022)[5] | five | All studies were case-control designs. Included studies appeared only to include AD, rather than other types of dementia. | **Sensitivity:** 87.2% (95% CI 81.3% to 92.1%), $I^2$=65.9%<br>**Specificity:** 89.35% (95% CI 77.6% to 91.8%), $I^2$=56.8% | This systematic review has some limitations.<br><br>Insufficient details were provided from included studies, all of which were published between 1998 and 2006. |
| Smailagic *et al.* (2018)[3] | 36 (24 in the main analysis) | The included studies had methodological limitations, with most at risk of bias that threatens the validity of their results. Studies were focused on conversion to AD rather than other types of dementia. | Across 24 studies<br>**Sensitivity** values ranged from 25% to 100%<br>**Specificity** values ranged from 15% to 100%<br><br>In four studies that used sc-SPM as a metric<br>**Sensitivity** values ranged from 77% to 100%<br>**Specificity** values ranged from 74% to 100% | This high-quality systematic review is comprehensive and well reported. The included studies were published between 1999 and 2017. |

| Reference | Included studies | Study characteristics | Main results | Quality considerations |
|---|---|---|---|---|
| **FDG-PET – use in differential diagnosis** | | | | |
| Cotta Ramusino *et al.* (2024)[4] | nine | 679 people with different diagnostic conditions<br>Cross-sectional studies<br>Diagnosis:<br>- AD 255<br>- FTLD 128<br>- LBD 245<br>- healthy controls 51 | **Five studies assessed FDG-PET accuracy in detecting AD co-pathology in DLB**<br>Sensitivities ranged from 56% to 94%<br>Specificities ranged from 51% to 100%.<br><br>FDG-PET was slightly less accurate in differentiating frontotemporal lobe degeneration from Alzheimer's disease, psychiatric, or other cognitively impaired conditions (sensitivity 8% to 100%; specificity 48% to 100%). | The systematic review is reasonably well conducted and reported. The literature search was limited by date (2017-2022), and only in Medline (although they ran a check in Embase). They evaluated the quality of the included studies, and note bias, particularly with regard to patient selection.<br><br>For this analysis, they used cross-sectional studies (rather than longitudinal). |
| Na *et al.* (2024)[7] | 14 | 12 case-control studies and two cohort studies<br>FDG-PET were analysed with visual and quantitative assessments | **AD versus FTD**<br>Seven studies<br>Sensitivity: 96% (95% CI 88% to 98%), $I^2$=87.7%<br>Specificity: 84% (95% CI 70% to 92%), $I^2$=66.18%<br>**AD versus DLB**<br>Five studies<br>Sensitivity: 93% (95% CI 88% to 98%), $I^2$=82.47%<br>Specificity: 84% (95% CI 70% to 92%), $I^2$=81.51% | This systematic review is of reasonable quality, including a comprehensive literature search, clear inclusion criteria and quality appraisal of the included studies. The included studies were published between 2007 and 2021<br><br>The results have been combined in meta-analyses, with significant heterogeneity reported. The authors do not explore or discuss this heterogeneity. This |

| Reference | Included studies | Study characteristics | Main results | Quality considerations |
|---|---|---|---|---|
| | | | **AD versus non-AD dementias**<br>Four studies<br>Sensitivity: 86% (95% CI 80% to 91%), $I^2$ = 50%<br>Specificity: 88% (95% CI 80% to 91%), $I^2$=47.9% | heterogeneity means the results need to be treated with caution. |
| Fink *et al.* (2020)[6, 11] | Three | Three cohort studies (n=227), two retrospective and one prospective<br><br>The studies used visual and quantitative scoring systems and criteria for positive scans. | **AD versus non-AD dementias**<br>Based on two studies (n=182)<br>median sensitivity 89% (range 84% to 94%)<br>median specificity 74% (range 73% to 74%)<br>**AD versus FTLD**<br>Based on one study (n=45)<br>Median sensitivity 97% (range 96% to 98%)<br>Median specificity 66% (range 59% to 73%) | The systematic review is high quality. The studies were published between 2007 and 2011. The review authors limited inclusion to studies that had a moderate or low risk of bias, although note that they were mostly retrospective and susceptible to selection bias, and that applicability may be limited for healthier patients and those earlier in their disease course. |
| **SPECT – predicting progression from MCI to dementia** | | | | |
| Zhu *et al.* (2022)[5] | Four | All studies were case-control designs<br>Included studies appeared only to include AD, rather than other types of dementia. | **SPECT:**<br>**Sensitivity:** 80.5% (95% CI 78.3% to 90.12%), $I^2$=63.1%<br>**Specificity:** 74.3% (95% CI 61.3% to 78.5%), $I^2$=71.9% | This systematic review has some limitations.<br><br>Insufficient details were provided from included studies, all of which were published between 1998 and 2006. |

| Reference | Included studies | Study characteristics | Main results | Quality considerations |
|---|---|---|---|---|
| **SPECT – use in differential diagnosis** | | | | |
| Athanasio *et al.* (2024)[21] | 35 | Most of the included studies were published before 2007. Most studies used HMPAO. | **FTD versus AD**<br>Based on five studies<br>Sensitivity ranged from 56% to 88%<br>Specificity ranged from 51% to 93% | The included studies do not appear to be formally appraised, and there do not appear to have been any studies excluded based on quality. This systematic review has some limitations, but it is a comprehensive overview of the existing literature, and the conclusions are fair and reasonable based on the evidence presented. |
| Fink *et al.* (2020)[6, 11] | Four | Two retrospective cohort studies and two prospective cohort studies (n=232). Definition of a positive HMPAO-SCAN for AD varied across the studies, but was based on prevalent regional hypoperfusion (most commonly in temporal or parietal lobes). | **AD versus non-AD dementias**<br>Based on three studies (n=205)<br>Median sensitivity: 63% (range 57% to 94%)<br>median specificity: 83% (range 76% to 92%) | The systematic review is high quality. The review authors limited inclusion to studies that had a moderate or low risk of bias. |

### Primary studies

We identified one primary study that directly compared FDG-PET and SPECT in the assessment of people with suspected AD.

The study by Nadebaum *et al.* (2020) was retrospective and included 126 participants (56% had MCI and 44% had dementia).[8] All participants had a SPECT scan (HMPAO or a different radioactive tracer called ethyl cysteinate dimer, ECD) and an FDG-PET scan as part of their diagnostic assessment, and then underwent an amyloid-PET scan. The results of the amyloid-PET scan were used as the reference standard. Trans-axial slices and Neurostat 3D-SSP analyses of FDG-PET and SPECT scans were reviewed by five nuclear medicine clinicians blinded to all other data. The clinicians reported on their most likely diagnosis and their diagnostic confidence.

Clinicians reported high diagnostic confidence in 83% of FDG-PET scans compared with 67% for SPECT (p=0.001). The receiver operating characteristic curve in diagnosing AD was 0.71 for FDG-PET and 0.61 for SPECT (p=0.02). The sensitivity of FDG-PET and SPECT was 76% versus 43% (p<0.001), while specificity was 74% versus 83% (p=0.45). The authors concluded that FDG-PET was more accurate in differentiating AD from non-AD than SPECT, largely because of the higher sensitivity values.

There are limitations with this study. The study was retrospective and it is not clear why the included people had both a SPECT and an FDG-PET scan. If people had an FDG-PET scan because the SPECT scan had not been clear, that might result in the difference in diagnostic accuracy being over-estimated. In addition the study reported a delay between the SPECT and FDG-PET scans, of up to 12 months in some cases, which may have contributed to the difference in diagnostic accuracy between scans.[22]

## Patient aspects

Undergoing an assessment for dementia is likely to be stressful and frightening for people and their carers. For this reason, SIGN states that any further tests over and above a standard comprehensive assessment should only be considered if they would change management. NICE notes that any additional tests for dementia subtype should be carried out sequentially. While this may increase the time to diagnosis, it will minimise the number of potentially stressful tests that people are exposed to.

Although FDG-PET and perfusion SPECT are both nuclear medicine scans, the experience for patients and carers for each will be different. With FDG-PET scans, patients must fast and have their glucose checked prior to scanning. Usually carers cannot stay in the room because of the exposure to a higher level of radiation. With SPECT scans, there is no need to fast, and carers are able to stay with the patient during the scan.

FDG-PET scans will not be suitable for some groups of people, for example people with poorly controlled diabetes, due to the use of the glucose-based radioactive tracer. The time taken for an FDG-PET scan is shorter than SPECT, which may impact on patients' preferences.

We identified one study which compared whether people with suspected dementia and their carers preferred FDG-PET scans or SPECT scans.[9] This was part of a larger study, which investigated the diagnostic utility of FDG-PET and SPECT in distinguishing between people with AD and DLB and normal controls. Study participants, and their carers, were asked to complete questionnaires immediately after their scan and pulse rate data was collected during the scans.

The study included 38 people with AD, 30 people with DLB and 30 people from a healthy control group. Everybody in the study received both FDG-PET and SPECT.[9] The authors concluded that the two types of scans were equally acceptable to the majority of people with dementia, their carers and to the control group. Some carers preferred SPECT, probably because they were able to stay and support their relative or companion. Importantly, even where a preference for one scan was expressed, the perceived diagnostic accuracy of the scan over-ruled any initial preferences suggesting that this was more important than other scan characteristics. For most patients pulse rate data was no different during brain imaging than when completing questionnaires in their own home.

In preparing this report we sought input from organisations that represent people with dementia and their carers. We received comments from a carer organisation, tide (together in dementia everyday). They noted that elements of the FDG-PET scans (such as fasting, having glucose checked and not having carers present) are likely to be an additional stress for people who are already in a difficult position. They also noted that people may have to travel long distances in order to access FDG-PET scans. For this reason, they suggested that FDG-PET scans should only be used when the clinical and management benefits are clear (Personal Communication, Ruth Eley, Director and Chair, tide, 13 August 2024).

## Organisational issues

In NHSScotland, PET-CT services are currently delivered via four regional PET-CT centres.

Any development to the PET-CT service in NHSScotland will require infrastructure and resource investment, including workforce and radioisotope production. FDG is produced onsite in NHS Grampian and NHS Greater Glasgow and Clyde. NHS Tayside and NHS Lothian have their FDG supplied via a commercial supplier based in NHS England.

As part of our peer review process, we asked what the barriers were to the implementation of an FDG-PET service for people with dementia. The main barriers identified included the production and supply of radioisotopes and machine scanning capacity. Reducing or removing both barriers will require infrastructure development and appropriate staffing.

Implementation of an FDG-PET service for people with dementia should not impact negatively on capacity for other services (notably, for people with cancer).

The PET CT service in Scotland is currently delivered regionally which means that many people must travel substantial distances for their scans. The practicalities of this for people who may be more frail than the general population, or who have greater levels of cognitive impairment, needs to be considered.

## Cost effectiveness

No economic evidence was identified comparing FDG-PET versus SPECT imaging for the diagnosis of dementia.

Indicative capital and construction costs associated with acquiring each technology are outlined in *Table 2*. These figures do not include service implementation or staffing costs.

Given the substantially higher acquisition cost of FDG-PET and its presumed greater clinical utility over SPECT, it is likely that future economic evaluations might find the cost effectiveness of FDG-PET to be situated in the north-east domain of the cost-effectiveness plane, that is, costlier but more effective than comparator technologies.

*Table 2: Estimated acquisition costs of technologies*

| | FDG-PET | SPECT |
|---|---|---|
| Scanner<br>(Cost varies by configuration) | £1.9 million to £2.3 million | £500k to £530k |
| Service costs (per annum) | £100k to £115k | £57k to £62k |
| FDG injector | £69k to £160k<br>maintenance: £5k to £14k | N/A |
| Construction/Turnkey costs<br>(varies by project and ventilation requirements) | £400k to £1.0 million | £120k to £250k |

## Conclusion

This SHTG Recommendation is based on an updated review of the evidence, published since 2018, on the use of FDG-PET scans and perfusion SPECT scans in dementia diagnosis. The evidence we identified either evaluated the use of FDG-PET or SPECT in predicting the progression of MCI to dementia, or in differential diagnosis. The clinical evidence base is heterogeneous and limited in quality, and our review highlighted fewer studies on SPECT than FDG-PET. The research studies tended to exclude people who are older, frailer or have more comorbidities. This means that the value of FDG-PET and SPECT imaging may be different in the 'real-life' dementia population.

In summary, the body of evidence suggests that FDG-PET scans demonstrate greater diagnostic accuracy compared with SPECT scans in people undergoing assessment for dementia or MCI, although the heterogeneity and variation in results between studies means that robust conclusions are not possible.

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### Healthcare Improvement Scotland development team

- Mr Guy Berg, Senior Health Economist
- Ms Joanna Kelly (lead author), Health Services Researcher
- Ms Charis Miller, Health Information Scientist
- Ms Tammy Nicol, Senior Project Officer
- Mr James Stewart, Programme Manager
- Ms Kym Stewart, Project Officer

### SHTG Evidence Review Team

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- Mr Edward Clifton, SHTG Unit Head, Healthcare Improvement Scotland
- Ms Claire Fernie, Public Partner, Healthcare Improvement Scotland
- Dr Claudia Geue, Senior Lecturer in Health Economics and Health Technology Assessment, University of Glasgow
- Dr Moray Nairn, Programme Manager, Scottish Intercollegiate Guidelines Network (SIGN), Healthcare Improvement Scotland
- Dr Neil Smart, SHTG Council Chair, Healthcare Improvement Scotland, and Consultant Anaesthetist, NHS Greater Glasgow and Clyde

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