Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic exploration report number:	TER303
Topic:	Structural neuroimaging for diagnosis of dementia
Summary of findings:	Structural neuroimaging is the non-invasive visualisation of the anatomical structure of the brain and includes computed tomography (CT) scanning and magnetic resonance imaging (MRI). The National Institute for Health and Care Excellence (NICE) guideline NG97 (2018) included guidance on dementia diagnosis and recommended the use of structural imaging before further tests. This topic exploration report focusses on CT and MRI neuroimaging evidence published since NICE NG97. HTW researchers identified two systematic reviews that included structural MRI scans for the diagnosis of dementia, and none that reported on CT scans in this population. Only one of these systematic reviews clearly summarised diagnostic accuracy outcomes, and reported a low sensitivity and specificity of MRI for early diagnosis of dementia due to Alzheimer's disease. A retrospective primary study showed that MRI identified significantly more infarcts compared to CT, concluding that patient management would be more effected by MRI scan results; however there were many study limitations. No economic evidence was identified. In conclusion, since NICE NG97, there has limited evidence on structural neuroimaging for the diagnosis of dementia. There is some evidence to suggest that CT and MRI could be valuable tools, but there are significant study limitations and results should be interpreted with caution.

Introduction and aims

Dementia is a term used to describe a range of cognitive and behavioural symptoms that can include memory loss, problems with reasoning and communication, change in personality, and a reduction in a person's ability to carry out daily activities. The observed impairment in cognitive function may result from various neurodegenerative aetiologies and can cause severe disability. The most common types of dementia are Alzheimer's disease, vascular dementia, mixed dementia, DLB and frontotemporal dementia (NICE NG97, 2018). In 2018, dementia affected 50 million people worldwide, a figure that is predicted to increase to 152 million by 2050 (Banerjee, 2020).

Structural neuroimaging is the non-invasive visualisation of the anatomical structure of the brain that can be used to inform diagnosis of dementia. It can provide information about the shape, position, and volume of brain tissue. Structural neuroimaging techniques include CT and MRI. MRI uses magnetic fields and radio waves to form images of the brain whereas CT uses radiography (X-rays) to look at cross sections of tissue. In contrast to structural neuroimaging, functional neuroimaging measures brain activity and function, using techniques such as positron emission tomography (PET) and functional MRI (fMRI).

The focus of the topic exploration report is structural neuroimaging (CT and MRI). The topic proposer highlighted that, in Wales, there is a variation in the use of structural neuroimaging, particularly CT scans, to assist the diagnosis of dementia.

Health Technology Wales (HTW) researchers reviewed evidence on the clinical and cost-effectiveness of structural neuroimaging (CT and MRI) for the diagnosis of dementia.

Evidence overview

Guidance

We found NICE guideline (NG97) that was published in 2018 which makes recommendations on dementia assessment, management and support for people living with dementia and their carers.

One of the review questions for NG97 was ‘What are the most effective methods of diagnosing dementia and dementia subtypes in specialist dementia diagnostic services?’. NICE searched for studies with a diagnostic cross-sectional design or systematic reviews of diagnostic accuracy studies. Only one study for CT was included in the guideline and 10 studies for MRI. The outcomes included incidence of accurately identified dementia, diagnostic accuracy measures and resource and costs.

NICE NG97 (2018) recommends the use of structural neuroimaging before further tests, to rule out reversible causes of cognitive decline and to assist with subtype diagnosis, unless dementia is well established, and the subtype is clear. The guidance also states that further tests should only be considered if it would help with subtype diagnosis and also result in a change in patient management.

NICE NG97 (2018) includes initial assessment in non-specialist settings, incorporating taking patient history, physical examination and validated cognitive testing. The guidance stipulates that patients should be referred to a specialist dementia diagnostic service if reversible causes of cognitive decline have been investigated and dementia is still suspected.

NICE NG97 (2018) does refer to a number of validated criteria to guide clinical judgement when diagnosing dementia subtypes. However, the criteria give very limited direction in relation to the use and timing of CT and MRI.

Secondary Evidence

HTW researchers identified two systematic reviews since NICE NG97 that included MRI scans for the diagnosis of dementia: one in Alzheimer's disease and one in vascular cognitive impairment and dementia (VCID), an umbrella term that includes vascular dementia. We did not identify any systematic reviews published during this time period that included CT scans for the diagnosis of dementia.

A Cochrane review from Lombardi et al. (2020) included 33 studies that compared the diagnostic test accuracy of baseline structural MRI versus the clinical follow-up for the early diagnosis of Alzheimer's disease in people with mild cognitive impairment. The studies included in the review reported on different areas of the brain (total hippocampus, medial temporal lobe, lateral ventricles and total entorhinal cortex). Most of the included studies reported data on the volume of the total hippocampus (pooled mean sensitivity 0.73 (95% confidence interval (CI) 0.64 to 0.80); pooled mean specificity 0.71 (95% CI 0.65 to 0.77); 22 studies, 2209 participants). The authors concluded that structural MRI had low sensitivity and specificity if used as a stand-alone add-on test for early diagnosis of dementia due to Alzheimer's disease.

The authors noted that their findings were consistent with international guidelines which recommend structural imaging to exclude non-degenerative or surgical causes of cognitive impairment and not to diagnose dementia due to Alzheimer's disease. It should be noted that there were many study limitations identified and the authors highlighted risk of bias.

We identified two systematic reviews that may be partially relevant to address the clinical effectiveness of neuroimaging to diagnose dementia. Frantellizzi et al. (2020) aimed to s to explore the state of the art and future perspective of non-invasive diagnostics of VCID and presented the key conclusions/results in narrative format. Ferreira (2020) reviews studies using multivariate analysis on structural neuroimaging data (MRI or CT) in DLB patients. Fuller assessment of these review as part of fuller appraisal is required to ascertain if it includes relevant primary evidence.

Primary evidence

HTW researchers identified one comparative study published after NICE NG97 that included CT and MRI for the diagnosis of dementia.

Kaltoft et al. (2019) carried out a retrospective study (78 participants) where structural (CT and MRI) and functional (fluorodeoxyglucose-PET-MRI) imaging scans were evaluated and classified by a memory clinic expert. MRI identified significantly more infarcts (areas of dead tissue) compared to CT, demonstrating one or more infarcts in 28 patients compared to nine patients using CT ($p<0.001$). In seven of the nine patients with infarcts on CT, MRI demonstrated additional infarcts. Furthermore, in all cases with influence on patient management, the change of management was related to additional vascular pathology on MRI, and not CT. These findings are in line with older studies showing that MRI is more sensitive for detection of vascular pathology compared to CT.

This small, retrospective study has a number of limitations, including the fact that MRI was not performed at the same time as CT, and lesions could have developed or progressed between the two scans. However, the frequency of additional infarcts was not related to whether MRI was performed before or after CT. The authors noted that in some cases, the additional finding made on MRI may in retrospect also be identified on CT. Furthermore, CT was performed on a variety of scanners and a higher diagnostic sensitivity may have been achieved if all CT scanners were of the highest standard. Finally, given the lack of diagnostic gold standard, long-term follow up would have been useful to consider diagnostic accuracy.

Economic evidence

No economic evidence was found since NICE NG97. HTW notes that scanner acquisition costs and the cost of scans would be higher for MRI than CT in NHS Wales.

Ongoing Research

HTW researchers did not identify any ongoing research within the scope of this topic exploration.

Areas of uncertainty

There was a lack of evidence on structural neuroimaging for the diagnosis of dementia since NICE NG97. We identified gaps in the evidence for patient management and downstream outcomes. Whilst there was some evidence to suggest that CT and MRI could be valuable tools, there were significant study limitations.

No systematic reviews were identified on the use of CT scans for the diagnosis of dementia and limited conclusions can be drawn from the evidence that was identified. There was no cost-effectiveness evidence identified for structural neuroimaging (CT or MRI) in dementia diagnosis.

We identified evidence evaluating diagnosis of dementia versus not dementia, as well as evidence diagnosis between different dementia subtypes. It is uncertain if the PICO would require refining going forward to focus on dementia diagnosis or dementia subtype diagnosis.

Literature search results

Health Technology Assessments and Guidance

Dementia: assessment, management and support for people living with dementia and their carers. NICE guideline [NG97] Published: 20 June 2018 https://www.nice.org.uk/guidance/ng97

Guidance in progress for Dementia (2023) that will include diagnosis and assessment. https://www.sign.ac.uk/our-guidelines/dementia/

Evidence reviews and economic evaluations

Frantellizzi V, Pani A, Ricci M, et al. (2020). Neuroimaging in vascular cognitive impairment and dementia: A systematic review. Journal of Alzheimer's disease: JAD. 73(4): 1279-94. https://doi.org/10.3233/jad-191046

Lombardi G, Crescioli G, Cavedo E, et al (2020). Structural magnetic resonance imaging for the early diagnosis of dementia due to Alzheimer's disease in people with mild cognitive impairment. Cochrane. 3: CD009628. https://doi.org/10.1002/14651858.cd009628.pub2

Atri A. (2019). The Alzheimer's Disease Clinical Spectrum: Diagnosis and Management. Medical Clinics of North America. 103(2): 263-93. doi: https://doi.org/10.1016/j.mcna.2018.10.009

Arvanitakis Z, Shah RC, Bennett DA. (2019). Diagnosis and Management of Dementia: Review. JAMA. 322(16): 1589-99. https://dx.doi.org/10.1001%2Fjama.2019.4782

Ferreira D. (2020). Structural imaging in dementia with Lewy bodies: the potential of multivariate data analysis. Psychiatry Research: Neuroimaging. 306: 111180. doi: https://doi.org/10.1016/j.pscychresns.2020.111180

Khan S, Barve KH, Kumar MS. (2020). Recent Advancements in Pathogenesis, Diagnostics and Treatment of Alzheimer's Disease. Current neuropharmacology. 18(11): 1106-25. https://dx.doi.org/10.2174%2F1570159X18666200528142429

Individual studies

Kaltoft NS, Marner L, Larsen VA, et al (2019) Hybrid FDG PET/MRI vs. FDG PET and CT in patients with suspected dementia - A comparison of diagnostic yield and propagated influence on clinical diagnosis and patient management. PLoS ONE.14(5): e0216409 https://doi.org/10.1371/journal.pone.0216409

Ongoing research

We did not identify any ongoing secondary evidence.

Date of search:	July 2021
Concepts used:	Alzheimer's Disease (AD), Computerised Tomography (CT), Dementia, Dementia with Lewy Bodies (DLB), Frontotemporal Dementia, Magnetic Resonance Imaging (MRI), Neuroimaging, Structural Imaging, Vascular Dementia, Vascular cognitive impairment and dementia (VCID)