NICE National Institute for Health and Care Excellence

Appendix B: Stakeholder consultation comments table

2023 surveillance of NG97 Dementia: assessment, management and support for people living with dementia and their carers (2018)

Consultation dates: 4th to 17th July 2023

1. Do you agree with the proposal not to update the dementia guideline for mild cognitive impairment at this time (NICE guideline NG97)?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Dementia UK	No answer	We have nothing to add beyond the evidence NICE has already reviewed on this topic.	Thank you for your comment.
Roche Diagnostics Limited	Yes	We agree with the decision not the update the guideline presently and remain hopeful that this decision will be revisited once the identified ongoing research has been completed. We additionally wanted to flag the ongoing work being carried out by European task force to provide consensus for the diagnosis of MCI and mild dementia: Festari et al European consensus for the diagnosis of MCI and mild dementia: Preparatory phase. Alzheimers Dement. 2023 May;19(5):1729-1741. doi: 10.1002/alz.12798. Epub 2022 Oct 9. PMID: 36209379.	Thank you for your support and flagging the ongoing evidence. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review and the ongoing studies we plan to track.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

Dementia Industry Group	No	The DIG disagrees with the proposal not to update NICE guideline NG97. There is a clear need for guidelines on the investigation and follow up of mild cognitive impairment (MCI). As outlined in the recent Manchester MCI consensus5 and evidenced by the 2021 Memory Services Spotlight National Audit3, there is huge variation in how the term MCI is applied in clinical practice which results in uncertainty for patients in terms of their prognosis and inefficiency for assessment and diagnostic services. The Manchester MCI consensus describes MCI as a clinical syndrome with heterogeneous underlying pathologies and not a diagnosis in its own right. MCI mirrors dementia in this: it is a stage of brain disorder as is dementia, not a specific disease; it includes a variety of pathologies including psychopathology – as does dementia. It could be argued that if NICE are able to develop a clinical guideline for dementia knowing its caused by multiple diseases with different pathologies, causes, prognosis, and treatments then the same should apply to MCI, which could be consider earlier in the path of these diseases. Without consistent clinical use of MCI we don't know how many cases are seen in UK cognitive and memory clinics. We also know that risk reduction interventions may help to treat potentially modifiable contributions to cognition. Assessment for MCI is an ideal opportunity to highlight these modifiable risks and suggest appropriate interventions. This is not sufficiently set out in the current NICE public health guideline (NG 16, 2015). The biomarker diagnostics (amyloid PET and CSF via lumbar puncture) needed to determine if a patient has abnormal amyloid are not routinely commissioned within NHS services. This lack of capacity will need to be urgently addressed should new treatments become available. Progress with plasma biomarkers means that shortly these will be clinically validated and can offer a scalable, low-cost solution to determining those with abnormal amyloid levels. This highlights what is likely to be a	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration.

		rapidly evolving clinical pathway within MCI and mild Alzheimer's disease. For all these reasons clinical guidelines are urgently needed for MCI. If NICE believes there is insufficient evidence to change the guidelines, a clear steer on what evidence is needed must be provided as soon as possible.	
Cicely Saunders Institute of Palliative Care, Policy & Rehabilitation, King's College London	No answer	N/A	
Eisai Limited	No	No, Eisai disagrees. The dementia guideline needs to be updated for mild cognitive impairment (MCI). On 6 July 2023, the U.S. Food and Drug Administration (FDA) granted traditional approval of lecanemab (LEQEMBI®) based on data from a large, global Phase 3 trial (Clarity AD; NCT03887455). The trial population included patients with MCI or mild dementia stage of disease, (collectively referred to as early Alzheimer's disease). This makes lecanemab the first approved amyloid beta-directed antibody indicated as a disease-modifying treatment for Alzheimer's disease. Marketing authorisation applications for lecanemab are in progress with the Medicines and Healthcare products Regulatory Agency (MHRA) and European Medicines Agency (EMA). There is a clear paradigm shift in the dementia treatment pathway with other disease-modifying treatments on the horizon for people with earlier stages of Alzheimer's disease including MCI. Whilst we acknowledge a paucity of 'quality papers' on MCI, we believe this is partly attributed to the huge variation in how the term MCI is applied in clinical practice	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**

		which results in uncertainty for patients in terms of their prognosis and inefficiency for clinical assessment and diagnostic services. The biomarker diagnostics (amyloid PET and CSF via lumbar puncture) needed to determine if a patient has abnormal amyloid-beta are not routinely commissioned within NHS services. This will need to be urgently addressed should new disease-modifying treatments become available for early Alzheimer's disease. Progress with plasma biomarkers means that shortly these will be clinically validated and can offer a scalable, low-cost solution to determining those with abnormal amyloid-beta levels. This highlights what is likely to be a rapidly evolving clinical pathway within MCI and mild Alzheimer's disease. The importance of early diagnosis for patients with dementia has been clearly documented, as has the need for living well with a meaningful diagnosis.1 A review of mild cognitive impairment guidelines will support this goal. For all these reasons outlined above, NICE clinical guidelines are urgently needed for MCI. Reference: 1. Alzheimer's Society (2021). The dementia guide: Living well after your diagnosis. Accessed July 2023, available at: https://www.alzheimers.org.uk/sites/default/files/2020-03/the_dementia_guide_872.pdf	Thank you for providing references. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.
Alzheimer's Society	No	Alzheimer's Society do not agree with the proposal.	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We

		We think that timely and accurate diagnosis of mild cognitive impairment (MCI) should be included within the NG97 guideline. It is vital for these people to have a greater understanding of their symptoms and identify the significant percentage of people with MCI, who are at high risk of developing dementia in their lifetime. The following studies suggest that between 28.7% - 65% of people with MCI go on to develop dementia:; Six year follow-up with a 50% conversion rate to dementia. Progression of mild cognitive impairment to dementia: a challenge to current thinking | The British Journal of Psychiatry | Cambridge Core Two year follow up with a 40% conversion rate to dementia Progression of Mild Cognitive Impairment to Dementia | Stroke (ahajournals.org) Three year follow up with a 36% conversion rate to dementia Progression to Dementia or Reversion to Normal Cognition in Mild Cognitive Impairment as a Function of Late-Onset Neuropsychiatric Symptoms | Neurology Five year follow up with a 28.7% conversion rate to dementia Higher risk of progression to dementia in mild cognitive impairment cases who revert to normal - PMC (nih.gov) Diseases that cause dementia can begin in the brain years or decades before symptoms. With disease modifying treatments for Alzheimer's disease on the horizon. We need to be able to detect the people that these drugs can help, as early as possible, including those with MCI.	will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]** Thank you for highlighting evidence. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

		The lecanemab trial results showed that amyloid positive people with MCI benefited from the drug, as well as those with mild dementia. https://www.nejm.org/doi/full/10.1056/NEJMoa2212948. According to media reporting, donanemab trial results showed amyloid positive people with MCI experienced the strongest effects of the drug. https://edition.cnn.com/2023/07/17/health/second-alzheimers-drug-to-slow-disease-may-be-approved-this-year/index.html We can estimate the number of people in the UK over 60 with amyloid positive MCI may be around 435,000 people. This is 435,000 people that may be able to benefit from disease modifying treatments for Alzheimer's disease when they become available, if correctly identified. Updating the dementia guideline for mild cognitive impairment is an important step is enabling this. The 435,000 figures is based on calculations by the Alzheimer's Society using the following assumptions: Estimates suggest that 15-20% people over 60 have mild cognitive impairment https://pubmed.ncbi.nlm.nih.gov/27042901/. The UK 2021 census reports that the over 60 population of the UK is 14.5 million. 15% of 14.5 million = 2,175,000 as the number of people in UK with MCI over 60 Data from a US study suggests that one fifth of people with MCI may be amyloid positive Assessing the Preparedness of the U.S. Health Care System Infrastructure for	

		an Alzheimer's Treatment | RAND . 20% of 2,175,000 = 435,000 as the number of people in the UK with amyloid positive MCI The National Institute on Aging and the Alzheimer's Association have convened workgroups of academics and clinicians to draft a new framework of guidelines for new clinical criteria to define Alzheimer's disease. These diagnostic guidelines cover the whole continuum of Alzheimer's disease, from people who don't have symptoms but carry a gene which is highly likely to cause AD in the future, to mild cognitive impairment caused by Alzheimer's disease and finally to dementia symptoms caused by Alzheimer's disease. The core principles of the guidance state that Alzheimer's disease should be defined biologically using the presence of core biomarkers like amyloid and tau within the brain, rather than defined by clinical symptoms. They also state that the Alzheimer's disease continuum starts with the appearance of amyloid and tau pathology, when a person is still asymptomatic. This would include people who do not have symptoms and as the disease progresses, will include people living with mild cognitive impairment who also have amyloid and tau pathology in their brains. This represents a shift in scientific approaches to defining who is living with a disease like Alzheimer's disease and incorporates people who have mild cognitive impairment and Alzheimer's disease pathology, where the pathology is most likely to be the cause of their symptoms and who will likely progress to develop Alzheimer's	

		disease in the future. This is an important distinction, as both lecanemab and donanemab have shown evidence of slowing down how quickly Alzheimer's disease gets worse in both people living with mild cognitive impairment and Alzheimer's disease. A new approach to MCI and Alzheimer's Disease would bring the condition into line with diabetes, where a guideline on preventing Type 2 diabetes amongst people at high risk is already well established. In light of both the international direction of travel towards a biological model and evidence of the benefits of treating amyloid positive MCI patients, we urge NICE to revisit the decision to review NG97 with a view to including of MCI within the guideline.	
London Dementia Clinical Network	Yes	We agree with NICE's proposal not to update the dementia guideline for MCI at this time. Although we feel that people with MCI should be followed up at least annually (either in primary or secondary care) to check if they have progressed to dementia (or reverted to normal cognition) and to review potentially treatable risk factors such as hearing loss and depression, we are not aware of any research that would support this advice. Therefore, any such recommendation would have to be made on the basis of consensus rather than evidence and would likely be a "consider" recommendation. We think it unlikely that putting together a guideline committee simply to create soft consensus recommendations would be the best use of NICE's resources. There are other ways of promoting best practice in MCI e.g., through the NHS England regional dementia clinical networks. Furthermore, we are unaware of any evidence-based interventions for people with MCI. Although a lot of interventions, including pharmacological, lifestyle and multi-component interventions have been trialled in MCI, results remain inconclusive, with nothing that would reach the threshold to be strongly recommended in a NICE	Thank you for providing your comments and your support. We agree that unfortunately at this time there is insufficient evidence to expand the scope of the dementia guideline to include MCI. We are tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is also aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**

		guideline. Finally, although the 2018 guideline considered the role of biomarkers only in the diagnosis of dementia and did not look at MCI, we do not believe that recommending biomarker-based diagnosis in MCI is a priority, particularly as there is no currently licensed or NICE-approved treatment for MCI that requires biomarker-based diagnosis.	
NHS England	No	This will be a great missed opportunity to miss out on including MCI from the dementia guidelines in this update NG97. Everybody including patients and their families are very much engaged with the development of new drugs in the form of Disease Modifying Therapies (DMT) and the most prominent molecules that are being used are Monoclonal antibodies. The two molecules Aducanumab and Lecanemab have been given approval by the FDA in the United States to be used for Early Alzheimer's disease or MCI or Prodromal Alzheimer's dementia. The third molecule of the same category is Donanumab which the company has finished the Trailblazer trial and in the process of applying to FDA for approval and it is very likely that this molecule as well will be given approval. In the last 20 years or so we did not have any approved molecules for dementia and MCI and this is a great opportunity to add MCI into the dementia guidelines so that in the coming future medications will be licenced and trialled in this particular group of patients. If this is not placed in the guidelines the fear is that there will be no emphasis on this and UK will be left behind compared to many similar countries in having access to these new medication. There is a need for sophistication and advancements in the use of imaging and biomarker evaluation is subtyping of not only dementia but also MCI. As these molecules will be licenced only for MCI due to AD there is a requirement of diagnosing patients with cause of MCI. This needs Amyloid PET scanning and also other CSF and plasma biomarkers to be used for assessment and subtyping. This needs training of staff and	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**

		professionals to do this and will take a substantial amount of time to do this once the meds are approved here in the UK. Currently there is no MCI register or MCI follow up is very patchy as there is no mechanism in NICE to have clear pathway but in the future we need to have this as number of patients will start to ask about the new medication and its use in MCI. Services being stretched in MAS teams mean that any new including should be backed up by new funding as well. This cannot be absorbed by the existing CMHTs for older adult or MAS case loads. Currently we have been discussing 3 molecules which have completed phase 4 trials and two approved by FDA but there are many more in the pipeline which are targeting amyloid pathology but also Tau pathology, Inflammation and Synaptic plasticity etc. These are some innovative mechanisms which have been studied Alzheimer's dementia. All these medications are being licenced for Early onset AD or MCI due to AD and this should prompt to include MCI to NICE guidelines. The evidence for this is overwhelming in terms of all the clinical trial across the world pointing to the introduction of the meds at the MCI level. There is also the counter argument that MCI conversions to dementia are not significantly higher and range between 15-20% in one year but looking at the literature this is quite misleading as up until now there is no real research looking at the subtyping of MCI from pathology perspective.	
Eli Lilly and Company	No	Eli Lilly and Company (Lilly) UK do not agree with the proposal not to update the dementia guideline for mild cognitive impairment. An expert consensus meeting in 2021 identified that mild cognitive impairment (MCI) is a clinical syndrome with heterogeneous underlying pathologies, rather than a diagnosis in its own right and that guidance is required on the use of biomarker confirmation in MCI (Dunne et al. 2021). MCI due to Alzheimer's Disease (AD) with biomarker confirmation is an important stage within the AD continuum (Aisen et al. 2017). It is crucial that guidelines are updated to include MCI so that clinicians,	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration.

		patients, and family members have clarity on the recommended management of their condition within this stage of disease. It is imperative that the guidance update consider that biomarker testing should be recommended to understand the underlying cause of MCI to ensure patients receive an accurate diagnosis and can be managed appropriately. As stated in the consultation document, not all patients with MCI will go on to develop a form of dementia. However, research suggests that in MCI patients with confirmation of presence of AD biomarkers, the three-year progression rate was 59% compared with 4% in patients with no abnormal AD biomarkers (Vos et al. 2015). Therefore, early and accurate of patients with MCI due to AD with biomarker confirmation is key to providing a high quality of care and allows patients and families to understand their cognitive decline and plan more effectively for the future. Early diagnosis of MCI due to AD is likely to alter the treatment approach and contribute to improved patient outcomes by allowing adjustments to lifestyle factors and awareness of available pharmacological and non-pharmacological management options upon progression to later stages of disease. Ongoing technology appraisals include patients with MCI due to AD within the relevant population. Providing clarity regarding the recommended management of these patients in current clinical practice would be of value to submitting companies, external assessment groups, NICE technical team, and NICE technology appraisal committee members involved in these appraisals. The guideline should be updated in parallel with these technology appraisals or directly afterwards once availability of treatment options are understood.	NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
British Geriatrics Society	No	Mild cognitive impairment (MCI) is a significant and growing concern for both public and clinicians in identifying early / prodromal stages of dementia and in ensuring access to disease modifying treatments and clinical interventions which would reduce	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as

		risk of further deterioration and avoidable complications. As such guidelines for MCI are necessary to help with early and accurate identification. It should be noted that the current dementia guideline is extensive and currently does not include mild cognitive impairment (MCI) but there is a risk of it being lost within these guidelines. As indicated by studies to date there may be multiple factors contributing to MCI which may or may not progress to Alzheimer's dementia but we are also concerned that other dementias are not considered adequately. For example, recent research criteria for prodromal features for Dementia with Lewy bodies includes MCI, delirium and psychiatric features see: https://n.neurology.org/content/94/17/743.abstract Specific guidelines for MCI would be supportive of ensuring inclusion of other features which may be otherwise neglected in clinical settings: https://journals.sagepub.com/doi/abs/10.1177/08919887211023586 It is proposed that there should either be a separate guideline on MCI OR Each condition (i.e. Alzheimer's disease; Lewy body dementia; including Dementia with Lewy bodes and Parkinson's disease dementia; Fronto-temporal dementia; etc), should have its own guideline which could then include the early/ prodromal stages to support more accurate diagnosis.	soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]** Thank you for providing references. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.
Alzheimer's Research UK	No	In principle we disagree with the proposal not to update the dementia guideline, as we believe there is a clear need for guidelines on the investigation and follow up of mild cognitive impairment (MCI). As outlined in the recent Manchester MCI consensus (Mild Cognitive Impairment: the Manchester consensus | Age and Ageing | Oxford Academic (oup.com)) and evidenced by the 2021 Memory Services Spotlight National Audit (https://www.rcpsych.ac.uk/docs/default-source/improving-	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through

		care/ccqi/national-clinical-audits/national-audit-of-dementia/round-5/final-1608-nad-mas-national-report-2021.pdf?sfvrsn=dc5b5d40_8) there is huge variation in how the term MCI is applied in clinical practice which results in uncertainty for patients in terms of their prognosis and inefficiency for assessment and diagnostic services. We recognise that defining MCI is challenging and that not all people with MCI will develop dementia. The Manchester MCI consensus describes MCI as a clinical syndrome with heterogeneous underlying pathologies and not a diagnosis in its own right. MCI mirrors dementia in this: it is a stage of brain disorder as is dementia, not a specific disease; it includes a variety of pathologies including psychopathology – as does dementia. It could be argued that if NICE are able to develop a clinical guideline for dementia knowing its caused by multiple diseases with different pathologies, causes, prognosis, and treatments then the same should apply to MCI, which could be consider earlier in the path of these diseases. Without consistent clinical use of MCI we don't know how many cases are seen in UK cognitive and memory clinics. We also know that risk reduction interventions may help to treat potentially modifiable contributions to cognition. Assessment for MCI is an ideal opportunity to highlight these modifiable risks and suggest appropriate interventions. This is not sufficiently set out in the current NICE public health guideline (NG 16, 2015). With new disease modifying treatments for Alzheimer's disease and MCI due to Alzheimer's disease under, or soon to be under, regulatory review with MHRA, the clinical pathway is likely to change significantly in the next 18 months. The recent approval by the FDA in the USA for lecanemab states it should be used in patients	the new NICE Prioritisation board that is being set up for further consideration. Thank you for providing evidence. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**

		with mild cognitive impairment due to dementia, we should expect a similar eligible population should it be approved in the UK. For the first approved diseased modifying drugs, there will be significant demand for more accurate and early diagnosis of the diseases that cause dementia and a need to identify those people with MCI due to Alzheimer's disease at the right stage. At the moment, most MCI patients are not followed up by a memory service or cognitive service and so the very population that might benefit most from these new disease modifying drugs will not be able to access appropriate services. Clinicians will need clinical guidelines to ensure that there are appropriate referrals at each stage of the pathway. Otherwise we could see services facing high demand due to the large unmet need, and no guidelines to enable them to prioritise those with highest clinical priority. The biomarker diagnostics (amyloid PET and CSF via lumbar puncture) needed to determine if a patient has abnormal amyloid are not routinely commissioned within NHS services. This lack of capacity will need to be urgently addressed should new treatments become available. Progress with plasma biomarkers means that shortly these will be clinically validated and can offer a scalable, low-cost solution to determining those with abnormal amyloid levels. This highlights what is likely to be a rapidly evolving clinical pathway within MCI and mild Alzheimer's disease. For all these reasons clinical guidelines are urgently needed for MCI. If NICE believes there is insufficient evidence to change the guidelines, a clear steer on what evidence is needed must be provided as soon as possible.	

RICE - The Research Institute for the Care of Older People	No	No, I do not agree with this proposal. Mild cognitive impairment (MCI) is a significant and growing concern. As new, potentially disease modifying, agents start to emerge for the treatment of Alzheimer's disease it is becoming increasingly important that services are supported to enable timely, accurate diagnosis (https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(23)00274-0/fulltext?rss=yes). MCI is a heterogeneous grouping, and this increases the importance of guidance on diagnosis including on- psychometrics, biomarker use (There is growing evidence around the use of biomarkers in people with MCI to identify people at higher risk of developing dementia e.g (Blennow K, Shaw LM, Stomrud E, Mattsson N, Toledo JB, Buck K, et al. Predicting clinical decline and conversion to Alzheimer's disease or dementia using novel Elecsys Aβ(1-42), pTau and tTau CSF immunoassays. Sci Rep. 2019;9(1):19024.) and access to advanced imaging techniques and clinicians trained in lumbar puncture etc. Establishing the underlying pathology early will enable access to treatment, support, planning, and potential to be involved in active research trials. Ultimately it is vital that guidance moves away from focusing on disease stages (MCI / dementia…) and instead focuses on the underlying pathology. Separate guidance on each underlying condition would seem a logical step and align this guideline with the approach taken with other neurodegenerative diseases such as Parkinson's disease.	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
Roche Products	Yes	The word dementia is a general term that covers a range of conditions that over time can affect brain function, such as memory and behaviour. Alzheimer's Disease is the most common of these conditions. Whilst there is no need to update now, there will be a need to review and update guidelines during or immediately after license of new medicines coming for Alzheimer's Disease (AD) which is composed within dementia. Once the MHRA and NICE have approved AD drugs, clinicians will have to follow their	Thank you for providing your comments and your support. We are tracking a number of ongoing studies and will assess these as soon as possible. NICE is also aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development:

		guidance so it is important these can be at par with new innovative treatments. An update would be vital in encouraging and supporting the NHS to accurately confirm a diagnosis of AD whilst also empowering primary care to begin the early detection of AD as symptoms emerge. Treating dementia earlier can have the biggest outcome in treatment outcomes. Within the updates, consideration should be made to investing in the AD pathway across research, diagnosis and care, including supporting and expanding specialist Brain Health Clinics to help overcome inequalities; whilst also ensuring access and uptake of diagnostics for AD.	**Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
Dementia UK	No	We need a strong patient pathway for MCI, not only for patients but also for research, early diagnosis and treatment. Particularly as new disease modifying treatments are imminent, we need guidance on the identification of MCI. It's important to make progress in better classifying and stratifying MCI subtypes and standardisation is necessary for this to happen. The UK needs to be ready for when the new treatments come online. In partnership with the Neurology Academy, Dementia United supported the development of FREE Quality Improvement (QI) courses for HSCP working with people affected by MCI. Now in its third successful year, the MCI Quality Improvement projects across UK & Ireland stories are shared as a way of furthering learning and encouraging others to improve services and support around MCI in the future.	
The Royal College of Ophthalmologists	No	In summary: No, the guideline should be updated. There have been some advances in our knowledge since the previous guideline was written in 2018. There have also been some sociopolitical changes that mean early diagnosis is even more important than before. There is no mention of	Thank you for your comments. We appreciate the need for guidance on MCI but unfortunately we could not find evidence that would be sufficient to expand the scope for the NICE dementia guideline. We will be tracking a number of ongoing studies and will assess these as

		visuospatial/perceptual /attentional changes in people with MCI as markers of early disease. Nor is there any exploration of potential digital screening apps in the existing guideline. Given the changes in technology and AI the guideline should be re-examined before the end of this decade. Specifically, • As it becomes more difficult to access timely care in the NHS, cost neutral and simple tests to accurately assess or predict cognitive decline or cognitive impairment or cognitive function should be available. The literature since 2017 shows advances in understanding visuospatial / perceptual differences in MCI versus normal controls and the potential of examining the VS system in the early detection of cognitive decline. See numerous articles in Frontiers of Aging Neuroscience. • Government policy to increase retirement age was introduced in 2020, two years after the last guideline. Detecting and managing MCI early in working adults is important, particularly given the impact diagnosis has on disability support in work, access to benefits before retirement age and the potential to slow the decline to give people with MCI more productive working years. • There are many studies that have found a positive correlation between eye movements and MCI. Eye tracking digital technology should be explored as a convenient non-invasive intervention for screening. Eye tracking software is now commonplace and is materially different from the technological capabilities in 2018. The current standard screening tool, the MMSE has been shown to be limited in its sensitivity to detecting early cognitive impairment. Eye tracking may enhance the accuracy of the screening tool. See Frontiers of Aging Neuroscience	soon as possible. Given the feedback from stakeholders about the value of a NICE guideline on MCI we are also routing MCI through the new NICE Prioritisation board that is being set up for further consideration. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**

2. Are you aware of any health inequality issues in this area?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Dementia UK	Yes	For many, cognitive impairment, whether leading to a diagnosis of dementia or not, can mean fear and confusion, not only for the person, but also for the people caring for them and their wider family and friends. Families have to navigate a complex and disjointed health and social care system; trying to support someone with cognitive impairment can be exhausting and overwhelming. It is easy for family carers to become isolated as they put their own lives on hold. ONS figures show that 59% of unpaid carers are women, and therefore there is a risk that unmitigated care burden may exacerbate gender health inequality. The Joseph Rowntree foundation has equally found that 44% of working-age adults who are caring for 35 hours or more a week are in poverty. There is also therefore a risk of exacerbating health inequalities within socio-economic groupings, if specialist support to this cohort is not provided. We are aware that NG97 contains guidance on supporting carers and families, however Dementia UK, through our dementia specialist Admiral Nurses, regularly see first hand the importance of specialist nursing support for this cohort. We would therefore recommend that in addition to consideration of MCI within NG97, the guidelines approach to support for carers is reviewed and updated. Dementia UK would be pleased to help with this and can provide research and	Thank you for raising these inequalities.

		evaluation on the impact of specialist nursing on carer wellbeing outcomes. In addition, there are structural and cultural inequalities in diagnosis, symptom presentation and care amongst different populations when it comes to dementia and associated conditions. A 2018 study found that black men developing dementia were less likely to be diagnosed than white men developing dementia. Previous research has also found that, symptoms of mental illness can be less frequent, less severe or different in BME older people consulting GPs. Symptoms have also been shown to be different in older people originating from the Indian sub-continent.	
Roche Diagnostics Limited	Yes	Some useful summaries of health inequalities in dementia diagnosis include: https://www.alzheimers.org.uk/about-us/policy-and-influencing/increasing-access-dementia-diagnosis And, chapter 3: Dementia health inequalities and wider socio-economic costs from https://www.futurehealth-research.com/site/wp-content/uploads/2022/05/220505_Levelling-Up-Dementia-Diagnosis-Web-.pdf	Thank you for highlighting this information. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.
Dementia Industry Group	Yes	The number of people with dementia is predicted to rise to over 1.1 million by 2030 1 The leading cause of death in England and Wales in 2022 was dementia, accounting for almost 66,000 (11.4% of all deaths)2. Dementia is a significant public health issue in the UK and is projected to be the costliest health condition by 20301. In 2021 the estimated cost of dementia in the UK was £25 billion and is expected to almost double to £47 billion by 20501 Mild cognitive impairment faces many of the stigma issues associated with dementia particularly for communities which are already health marginalised.	Thank you for raising these issues.

		Access to diagnostic tests such as amyloid PET and CSF sampling via lumbar puncture, which can determine if a patient has MCI due to Alzheimer's disease are not routinely commissioned within the NHS. Access is restricted predominantly to research settings, which results in limited and unequal access for patients seeking to understand symptoms. Only 2.2% of patients were referred for specialist investigation in 2021.3	
Cicely Saunders Institute of Palliative Care, Policy & Rehabilitation, King's College London	Yes	The quality of palliative and end-of-life care is variable for people with dementia. Many will experience unnecessary hospitalisations as they approach the end of life, with increased visits among specific patient groups, geographical locations and residential settings. An integrated palliative care approach has potential to improve outcomes, not only towards the end of life but also earlier in the illness trajectory. However, dementia is not often recognised as a life-limiting condition and there are known barriers to accessing palliative care services among people with dementia. Supporting evidence of inequalities is presented below. Further information can also be found in our recent policy briefing, 'A right to be heard: Better palliative and end-of-life care for people affected by dementia' (May 2023): https://www.kcl.ac.uk/nmpc/assets/a-right-to-be-heard-policy-brief.pdf • There are disparities in access to high-quality care for people with dementia, including by socioeconomic position, ethnicity, age, and clinical factors such as dementia subtype and presence of multiple long-term conditions. This reinforces the need for individualised, needs-based care tailored to the social, cultural and clinical needs of the individual and their primary caregivers: – Current and bereaved caregivers describe pushing for support in the absence of routine follow-up care or specialist clinical ownership, where using the emergency	Thank you for raising these inequalities. Thank you for providing references. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

		department as the path of least resistance. Those with socioeconomic privilege have the means to overcome barriers to access support, highlighting how a system that requires people to push for support is inherently skewed and may predispose some towards ED attendance [1]. – Carers of people with dementia with more years of education and higher health literacy know more about dementia [2]. This has been observed to influence access to care at the point of need [1]. – A systematic review found high-strength evidence that people with dementia who are of minoritised ethnicity are more likely to attend the emergency department towards the end of life [3]. An England-wide study of 74,486 decedents found increased emergency department attendance by people with South Asian ethnicity (IRR= 1.07, CI 95% 1.02–1.13) [4]. People of South Asian ethnicity are more likely to receive substandard end-of-life care [5], and are less likely to access dementia care [6]. – A systematic review found high-strength evidence that older age is associated with a reduced likelihood of attending the emergency department towards the end of life [3], and an England-wide study of 74,487 decedents with dementia found fewer attendances associated with older age (IRR=0.99, CI 95% 0.99-0.99) [4]. Furthermore, an England-wide study of 388,899 decedents with dementia found that older people are more likely to die at home (PR=1.11, CI 95% 1.10 to 1.13) [7]. – In a study of 19,221 people with dementia, over three quarters (76.8%) of people with dementia experienced at least one unplanned hospital admission after diagnosis. Higher rates and longer length of stay for unplanned hospital admissions	

		are observed among people with dementia who live with a dementia diagnosis for a shorter time [8]. – People with increased number of long term conditions are more likely to attend the emergency department towards the end of life [3]. Specifically, a study of 74,487 decedents with dementia found increased emergency department attendances in the last year of life associated with chronic respiratory (IRR=1.33, CI 95% 1.28–1.38), cardiovascular (IRR=1.17, CI 95% 1.14–1.20) and cerebrovascular diseases (IRR=1.14, CI 95% 1.11–1.18) as underlying causes of death [4]. • There is geographical variation in the quality of end-of-life care for people with dementia. This suggests a need for a minimum national standard of equitably accessible post-diagnostic care across the illness trajectory: – In an England-wide study of 388,899 decedents with dementia, dying at home was more likely for those living in more affluent areas (PR 1.29, CI 95% 1.26-1.31) and those living in areas with greater numbers of care home beds (PR=1.82, CI 95% 1.79-1.85) [7]. – An England-wide study of 74,487 decedents with dementia identified fewer emergency department visits associated with higher socioeconomic position (based on area-level deprivation) (IRR=0.92, 0.90–0.94), living in a rural area (IRR=0.94, 0.96–0.93) and living in a local authority area with more nursing home beds (but not residential home beds; IRR=0.87, 0.80–0.95 vs. IRR=1.02 CI 95% 0.90–1.14, respectively) [4]. – In a study of 8,880 decedents with dementia, multiple hospital admissions in the	

		last 90 days of life were associated with area-level deprivation (most vs least affluent quintile OR 0.58, 95% CI 0.37–0.90) [9]. • The quality of end-of-life care varies between people living in care homes and those who live in their own home. Greater investment in care homes and enhanced models of community care are needed to ensure equitable access to timely and responsive clinical expertise: – A systemic review found high-strength evidence that residing in residential care facilities was associated with reduced likelihood of attending the emergency department towards the end of life [3]. Care home residence was also associated with reduced emergency department attendances in the last year of life (IRR=0.81, CI 95% 0.75-0.87) in a study of 4,867 decedents with dementia [10]. – Using data from 365 primary care practices in West London, a study among decedents with dementia showed that those who had palliative care identified needs by their general practitioner were less likely to have multiple hospitalisations in the last three months of life, particularly those who lived in care homes [11]. – A study of 8,880 people with dementia from a London mental health provider found that living in a care home was associated with fewer hospitalisations in the last 90 days (OR=0.63, 95% CI 0.53-0.76) and three days of life (OR=0.80, 95% CI 0.65-0.97) [9]. – A study of formal and informal care costs in the last three months of life among 146 decedents found that care home residents with dementia had lower total costs (£23,801.3, 95% CI 20,172.0-28,083.6) compared to those living at home (£34,331.4,	

		95% CI 27,824.7-42,359.5), even considering the cost of the care home [12]. • A palliative care approach is associated with improved quality of end-of-life care among people with dementia, though barriers to access persist. It is suggested that greater prioritisation of dementia as a life-limiting condition may help to improve provision and access to an integrated palliative care approach: – A systematic review identified moderate-strength evidence that receiving community palliative care was negatively associated with emergency department attendance among people with dementia approaching the end of life [3]. – Of all decedents with dementia registered with 365 primary care practices, only one third (33.6%) had palliative care needs identified. However, this group was found to have had a lower risk of multiple hospitalisations in the last three months of life [11]. – Continuous, integrated care provided by a multidisciplinary team is needed to help achieve good palliative care for people with dementia [13]. As identified in a review of equality in hospice care by Hospice UK, exemplar initiatives involved dementia expertise and integrated primary and community care [14]. – Systematic and scoping reviews have identified multiple barriers to palliative care access among people with advanced dementia, including staff knowledge, education and attitude, poor integration and communication between services and policy influences [15, 16].	

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Eisai Limited	Yes	Eisai agrees with the two topic expert's statements in section 1.4 of the equality and health inequalities assessment and is not aware of any additional health inequality issues in this area.	Thank you for your comments.
Alzheimer's Society	No answer	----------	
London Dementia Clinical Network	No answer	----------	
NHS England	Yes	yes - language and culture play an integral role in access to health services. dementia diagnosis in the BAME population is lower than expected - https://www.alzheimers.org.uk/for-researchers/black-asian-and-minority-ethnic-communities-and-dementia-research. presumably the MCI has similar inequalities	Thank you for raising these inequalities. Thank you for also highlighting new evidence. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

		https://www.bsms.ac.uk/research/neuroscience/cds/dementia-research-conference-2023.aspx Gender and ethnic disparities in dementia research Response: The similar issue of lack of assessment tools for the BAME communities in dementia are also present with MCI patients. Although a lot of awareness work is done for the South Asian communities to come forward for dementia assessment we still see low response rates from this group of population and more needs to be done to improve the health inequalities for this population.	
Eli Lilly and Company	Yes	Lack of guidelines for MCI can lead to substantial geographical variation in the standard of care available to patients.	Thank you for raising this issue.
British Geriatrics Society	Yes	In clinical practice, people with MCI may experience significant delays in accessing assessment and appropriate support due to lack of understanding and clear guidance on symptoms and management. As illustrated in the evidence to date, early intervention including targeted cognitive activities and multi-component interventions for brain health are shown to have benefit. Whilst these are included in other guidelines, it is unlikely that people with MCI will be offered targeted intervention, advice and support without specific guidelines in place. In relation to Dementia with Lewy bodies (DLB), numerous studies have found that people have a longer and more complex route to diagnosis (Kane et al 2018, O'Brien at al 2021) which leads to caregiver distress and can result in inappropriate treatment, earlier hospitalisation and increased mortality. As MCI has been identified as one of the prodromal features, clarity on the assessment of this would support improved identification of those at risk of going on to develop DLB or indeed one of the other types of dementia.	Thank you for raising these inequalities. Thank you for also providing references. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

		Specific guidelines on MCI would support improved and earlier assessment, diagnosis and management of people who are currently at risk of further deterioration and would benefit from targeted interventions to prevent further progression. People with mild cognitive impairment are inherently as risk of inequalities as there is currently insufficient guidance on how best to manage them. In addition 'Cognitive Function and Ageing Studies' show that the prevalence of MCI is increasing over time and as such is improvements in assessment and identification is becoming increasingly important. See: https://pubmed.ncbi.nlm.nih.gov/31489532/	
Alzheimer's Research UK	Yes	- Mild cognitive impairment faces many of the stigma issues associated with dementia particularly for communities which are already health-marginalised. - Access to diagnostic tests such as amyloid PET and CSF sampling via lumbar puncture, which can determine if a patient has MCI due to Alzheimer's disease are not routinely commissioned within the NHS. Access is restricted predominantly to research settings, which results in limited and unequal access for patients seeking to understand symptoms.	Thank you for raising these issues.
RICE - The Research Institute for the Care of Older People	Yes	MCI is not widely or well understood. People with MCI face significant delays in accessing assessment and appropriate support. Early support through multi-component interventions for brain health works but hosting this in a separate guideline means that these interventions are less likely to be accessed. Time to diagnosis is a critical problem across the spectrum of neuro-degenerative diseases. Improved guidance on early diagnosis at a prodromal or MCI stage of illness will improve the timeliness of diagnosis. There is value in accurate timely diagnosis (O'Brien MMC, Hannigan O, Power C, Lawlor B, Robinson D. Family members' attitudes towards telling the patient with Alzheimer's disease their diagnosis: a 20-year repeat study. Eur Geriatr Med. 2021;12(4):881-5.) Specific guidelines would support improved and earlier assessment. It would support	Thank you for raising these inequalities. Thank you for also providing references. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

		timely diagnosis and appropriate management. Specific advice on treatment / post diagnostic support would help with access to funding.	
Roche Products	Yes	There are health inequalities in all disease areas but dementia is even more impacted. Dementia affects around 1 million people with over 210000 people newly diagnosed with the condition annually. We know that modifiable risk factors contribute to up to 40% of dementia cases. More than 10 identifiable risk factors have been identified, including diet, exercise, cardiovascular disease and education. Taking these modifying risk factors into account will help us better estimate the diagnosis rate, which is important, because receiving a diagnosis is a ticket to receiving onward care support through the UK healthcare system. The UK government's target for the dementia diagnosis rate is only 66%. To estimate the diagnosis rate, we need to be able to estimate the number of people living with dementia in any given area. Currently, the UK government's estimates only use two factors: age and gender. This basic calculation allows an estimate of how many people live with dementia in each region of the UK, but using this approach does not give an accurate view of disease prevalence. Modifiable risk factors are not included and the specificity of the population is not taken into account. By including those modifiable risk factors, we can better identify underdiagnosed populations. This data is readily available at a population level so it can be used to give a more accurate estimation of the diagnosis rate, regionally and locally. Taking the risk factors into account could help achieve fairer distribution of resources: in addition to age and gender, we could add history of stroke, level of education, diabetes, high blood pressure, currently smoking, high alcohol intake, isolation and more. This is already informing clinical trial recruitment. Taking a population approach can also help identify areas of unmet need, where particular risk factors might be associated with dementia. This could inform NHS and social care resource planning, even without additional resources as existing resources can be directed differently to tackle inequalities. Most importantly it could impact the understanding of the diagnosis rate. These models can lead to a clearer understanding of where people living with dementia need most care and support.	Thank you for raising these inequalities.

Dementia UK	Yes	Yes. There is a lack of cultural inclusivity across dementia and MCI services. Language and lack of access to necessary translation services acts as a barrier when attempting to access health and care services. Dementia United have a programme of work to actively include marginalised communities Active inclusion of marginalised communities - Dementia United (dementia-united.org.uk)	Thank you for raising these inequalities.
The Royal College of Ophthalmologists	Yes	Widespread variation in the rates of MCI diagnosis across the UK memory services. (Dunne, et al 2021) Subclinical cognitive impairment is unknown, but has important implications for prevention, planning and policy, particularly retirement, WCA and PIP benefits, and ability to access digital services including ID gateway, banking, NHS and wider social activities. Richardson et al 2019 concludes prevalence of MIC is stable with a decline in severe impairment, but an increase in milder forms of impairment accompanying physical illnesses.	Thank you for raising these inequalities. Thank you for also providing references. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

3. Are you aware of any ongoing trials in MCI?

Stakeholder	Overall response	Comments	NICE response
Dementia UK	No answer	N/A	
Roche Diagnostics Limited	Yes	We would like to draw NICE's attention to the following pilot in South London and Maudsley NHS Foundation Trust: FEASIBILITY AND ACCEPTABILITY OF A UK BASED REMOTE BRAIN HEALTH CLINIC FOR PATIENTS WITH MILD COGNITIVE IMPAIRMENT	Thank you for highlighting this pilot.

		(MCI) Research Summary: Research summary This project aims to understand feasibility, acceptability and real-world evidence of a novel UK based remote brain health clinic for patients with mild cognitive impairment (MCI). A timely and accurate diagnosis of dementia is a priority in the UK and MCI is indicative of future risk of cognitive decline. An accurate etiological diagnosis of MCI (MCI-subtyping - distinguishing those who are likely to go on to develop dementia and those who are not) is vital for treatment planning. Whilst the assessment of molecular biological markers (biomarkers) for etiological diagnosis of MCI and Alzheimer's disease is increasingly recommended and employed internationally, the uptake is low in UK memory clinics. The Brain Health Clinic has been specifically designed as a state-of-the art diagnostic centre for those with MCI. Procedures will include a range of clinical and biomarker assessments, with molecular biomarkers based on lumbar puncture and cerebrospinal fluid (CSF) analysis. Additionally, the clinic will employ remote neuropsychiatric assessments using digital and telephonic methods. This allows for regular contact and assessment of participants, whilst adhering to changes in clinical practice and national guidance due to the COVID-19 pandemic. The research team's overarching objectives are to firstly establish the acceptability and feasibility of the remote brain health clinic and its novel clinical and biomarker assessment programme. Then secondly establish the impact of care under the Brain Health Clinic on: i) care management decisions (e.g. follow up and treatment planning); ii) time to etiological diagnosis of MCI (MCI-subtyping); and iii) time to diagnosis of dementia and severity of dementia at time of diagnosis. Link: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/pilot-of-a-uk-remote-brain-health-clinic-for-patients-with-mci-v1/	

Dementia Industry Group	yes	As of January 25, 2022, there were 143 agents in 172 clinical trials for Alzheimer's Disease. The pipeline included 31 agents in 47 trials in Phase 3, 82 agents in 94 trials in Phase 2, and 30 agents in 31 trials in Phase 1.4 Disease-modifying therapies represent 83.2% of the total number of agents in trials; symptomatic cognitive enhancing treatments represent 9.8% of agents in trials; and drugs for the treatment of neuropsychiatric symptoms comprise 6.9%.4. MCI due to Alzheimer's Disease and mild Alzheimer's dementia comprise the most common population included in current clinical trials accounting for 36% of Phase 3 trials and 52% of Phase 2 trials.2 Six of the trials in Phase 3 are prevention trials enrolling cognitively normal participants known to be at risk for AD (preclinical AD); one trial enrolling both preclinical participants and participants with MCI to mild AD dementia (DIAN-TU trial); 17 trials enrolling early AD defined as prodromal AD and mild AD dementia; 11 trials including participants with mild to moderate AD dementia; and 12 trials of participants with mild-to-severe AD dementia.4 In the USA there are ≈10 million individuals in the United States with mild cognitive impairment (MCI), half of whom (5 million) have MCI due to AD. The total number of persons in the United States with symptomatic forms of AD—MCI due to AD and AD dementia—is 11.2 million.4 At the DIG World Dementia Council Satellite "The future of Dementia Diagnosis in the UK" on 31st of March 2023 , the question was posed on where are the current gaps in the health system to achieving the ideal pathway for the diagnosis of early Alzheimer's disease. The contributors agreed that the lack of a dedicated UK dementia strategy and no clinical consensus for MCI diagnosis are two key obstacles to achieving the ideal state. The contributors to this satellite were representatives from Alzheimer's Society, Aneurin Bevan University Health Board, Alzheimer's Research UK, Biogen, Brain Sciences Scotland, Cosgate, DHSC, Eisai, Health and Global Policy Institute, Lilly, Mednet Group, Medical Research Council , MSD, NHSE, NIHR, OLS, RCGP, Roche Diagnostics, UCL, UK DRI, University of Newcastle, University of Oxford and World Dementia Council. Clinicians will need clinical guidelines to ensure that there are appropriate referrals at each stage of the pathway. Otherwise, we could see services facing high demand due	Thank you for highlighting this ongoing research. Please see surveillance report for details of the ongoing studies we will be tracking.

		to the large unmet need, and no guidelines to enable them to prioritise those with highest clinical priority. Given the high proportion of Disease modifying agents in the development pipeline and the number of agents in late phase (phase 3) development it is highly likely that therapies that benefit people in the earlier phases of Alzheimer's disease, and MCI due to Alzheimer's disease, could be available in the UK imminently. The DIG believes that the current scope of NICE GL* would exclude people who would benefit from timely detection of Alzheimer's disease and who could benefit from interventions at an earlier stage of disease progression, due to the scope requiring either the suspicion of or confirmed diagnosis of dementia, this scope may exclude a significant proportion of people who have MCI with Alzheimer's disease pathology but not yet displaying more obvious symptoms of Dementia. *The NICE guideline on dementia (NICE guideline NG97) currently excludes mild cognitive impairment in the scope. However, the scope does include people with mild cognitive impairment if they are suspected of or have a confirmed diagnosis of dementia. The guideline itself did not have any specific review questions around mild cognitive impairment. If yes, please could you add references or links. 1. The Economic Burden of Dementia in the UK. Luengo-Fernandez, R. & Landeiro, F. (in preparation). 2. Weiner MW, Aisen PS, Beckett LA, et al. Editorial: How will aducanumab approval impact AD research? J Prev Alzheimers Dis. 2021; 8: 391- 392. 3. National Audit of Dementia Memory Assessment Services Spotlight Audit 2021 - https://www.hqip.org.uk/wp-content/uploads/2022/08/Ref-317-NAD-Memory-Assessment-Services-Spotlight-Audit-2021_FINAL.pdf 4. Alzheimer's disease drug development pipeline: 2022 Jeffrey Cummings, Garam Lee, Pouyan Nahed, Mina Esmail Zadeh Nojoo Kambar, Kate Zhong, Jorge Fonseca, Kazem Taghva 5. (Mild Cognitive Impairment: the Manchester consensus | Age and Ageing | Oxford Academic (oup.com))	

Cicely Saunders Institute of Palliative Care, Policy & Rehabilitation, King's College London	No answer	N/A	
Eisai Limited	yes	Whilst we acknowledge there are many trials ongoing in MCI at various stages of development, Eisai has two ongoing studies involving participants with MCI treated with lecanemab. 1) BAN2401-G000-201 (Study 201) open-label extension study (NCT01767311). Core study publication: Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Abeta protofibril antibody. Alzheimers Res Ther. 2021 Apr 17;13(1):80. doi: 10.1186/s13195-021-00813-8. Erratum In: Alzheimers Res Ther. 2022 May 21;14(1):70. 2) BAN2401-G000-301 (Study 301, Clarity AD) open-label extension study (NCT03887455). Core study publication: van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023 Jan 5;388(1):9-21. doi: 10.1056/NEJMoa2212948.	Thank you for highlighting this ongoing research. Please see surveillance report for details of the ongoing studies we will be tracking. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
Alzheimer's Society	Yes	Clinical trials for both donanemab and lecanemab both included patients with MMSE scores above the NICE recommended maximum for Alzheimer's disease suggesting these people would have an MMSE score from 26-30 – which would categorise them as having mild cognitive impairment. A Study to Confirm Safety and Efficacy of Lecanemab in Participants With Early Alzheimer's Disease - Full Text View - ClinicalTrials.gov A Study of Donanemab (LY3002813) in Participants With Early Alzheimer's Disease	Thank you for highlighting this ongoing research. Please see surveillance report for details of the ongoing studies we will be tracking. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222**

		(TRAILBLAZER-ALZ 2) - Full Text View - ClinicalTrials.gov There are currently 497 active trials into mild cognitive impairment listed on clincialtrials.gov.	**Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
London Dementia Clinical Network	No answer	----------	
NHS England	Yes	https://www.bsms.ac.uk/research/neuroscience/cds/dementia-research-conference-2023.aspx Developing digital tools to support people diagnosed with dementia or mild cognitive impairment Rebecca Atkinson, Research Fellow, BSMS Response: In Birmingham we are planning to launch a pilot along with Neurologists and we are keen to develop MCI pathway as well to see how this work can be taken forward. The following is the current protocol and project detail we will be using which highlights the need for the MCI and Early AD diagnosis. We are in the process of getting some funding sorted for this work: The identification of a highly reliable 'Alzheimer's Disease (AD) Blood Test', able to rapidly and inexpensively confirm AD remains a key goal of AD research. This project aims to identify such a blood test. Importantly such a blood test could also inform development of therapies targeting entirely novel and unexploited disease pathways in AD, such as glial-cell activation. Promising blood biomarkers are emerging but there is no guarantee that current candidates will respond to disease modification or identify prodromal AD-the pre-symptomatic stage at which an interventional agent is most likely to be able to halt AD progression.	Thank you for highlighting this ongoing research. Please see surveillance report for details of the ongoing studies we will be tracking.

		Hypotheses: That novel blood glial cell markers will provide objective indication of AD disease state and will correlate with disease severity and clinical phenotype. Objectives 1. To compare candidate glial-cell biomarkers in early AD and Mild Cognitive Impairment (MCI) to Healthy and Disease Controls (HC & DC). 2. To compare conventional (Aβ and Tau) AD and glial cell biomarkers to novel glial-cell blood markers across AD early disease stages. Primary Outcome measure 1. The primary outcome measure will be the demonstration of raised peripheral novel glial-cell blood markers in Early and MCI-AD individuals compared to HC & DC. Key Secondary outcome measures 1. Correlation of peripheral novel glial blood markers with CSF Aβ and tau (AD markers) and with AD disease severity as measured by Addenbrooke's Cognitive Examination-III (ACE-III) and Mini-Mental State Examination (MMSE). 2. Identification of altered (higher) blood levels of novel glial-cell markers in Early and MCI-AD compared to controls. Apart from the above protocol there has been recent publications from the British Psycholgocal Society focuing the issue on MCI which I am attaching for you to consider looking at and see the progress that is being made on the further understanding of this issue. So there are number of scientific developments and also more understanding being developed around further broadening this unexplored area.	
Eli Lilly and Company	Yes	There are many ongoing clinical trials in MCI listed on ClinicalTrials.gov. Lilly's ongoing clinical trials including patients with MCI due to Alzheimer's Disease are: A Study of LY3002813 in Participants With Early Symptomatic Alzheimer's Disease (TRAILBLAZER-ALZ) NCT03367403 A Study of Donanemab (LY3002813) in Participants With Early Alzheimer's Disease	Thank you for highlighting these studies. Please see surveillance report for details of the ongoing studies we will be tracking.

		(TRAILBLAZER-ALZ 2) NCT04437511 A Study of Donanemab (LY3002813) Compared With Aducanumab in Participants With Early Symptomatic Alzheimer's Disease (TRAILBLAZER-ALZ 4) NCT05108922 A Study of Different Donanemab (LY3002813) Dosing Regimens in Adults With Early Alzheimer's Disease (TRAILBLAZER-ALZ 6) NCT05738486	NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
British Geriatrics Society	No	No	
Alzheimer's Research UK	Yes	There are over 100 interventional studies listed on clinicaltrials.gov which include Mild Cognitive Impairment, they can be viewed here: Search Results | Beta ClinicalTrials.gov Cumming et al undertook a pipeline review from 2023, which searched ClinicalTrials.gov for all current Phase 1, 2 and 3 clinical trials for AD and mild cognitive impairment (MCI) attributed to AD." Alzheimer's disease drug development pipeline: 2023 - Cummings - 2023 - Alzheimer's & Dementia: Translational Research & Clinical Interventions - Wiley Online Library	Thank you for highlighting this ongoing research. Please see surveillance report for details of the ongoing studies we will be tracking.
RICE - The Research Institute for the Care of Older People	Yes	There are numerous ongoing studies involving people with MCI stage cognitive issues. A number of these are drug trials - indeed at present there 31 agents in phase 3 trials for AD of which 21 are disease modifying treatments (Cummings J, Lee G, Nahed P, Kambar M, Zhong K, Fonseca J, et al. Alzheimer's disease drug development pipeline: 2022. Alzheimers Dement (N Y). 2022;8(1):e12295.). A number relate to non-drug interventions... Examples include: Maintain study (dementia/MCI) https://sites.exeter.ac.uk/maintainstudy/	Thank you for highlighting these studies. Please see surveillance report for details of the ongoing studies we will be tracking. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**

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		PrAISED2 study https://www.nottingham.ac.uk/research/groups/healthofolderpeople/projects/praised/ Dental health e.g. https://www.bristol.ac.uk/dental/research/mysmile/ Drug trials Ongoing Aducanumab, Lecanemab, Donanemab trials. Phase 1 studies e.g. https://www.clinicaltrialsarena.com/news/first-subjects-ibcs-trial-ibc-ab002/	
Roche Products	yes	https://classic.clinicaltrials.gov/ct2/show/NCT04639050 https://classic.clinicaltrials.gov/ct2/show/NCT04023994 https://classic.clinicaltrials.gov/ct2/show/NCT03828747	Thank you for highlighting these studies. Please see surveillance report for details of the ongoing studies we will be tracking. NICE is aware of the new therapies for mild cognitive impairment and mild dementia and currently has 2 technology appraisals in development: **Donanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease ID6222** **Lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]**
Dementia UK	Yes	https://pubmed.ncbi.nlm.nih.gov/31526625/ [pubmed.ncbi.nlm.nih.gov] https://www.alzheimer-europe.org/our-work/current-work/aboard [alzheimer-europe.org] The LINUS project is looking at over 55's with hypertension. An IPad based test is done and a risk of MCI produced. Ross Dunne has a memory clinic where options for lumbar puncture looking for bio markers may already be taking place.	Thank you for highlighting this research. Please see surveillance report for details of the ongoing studies we will be tracking.

The Royal College of Ophthalmologists	Yes	There are 221 current trials registered as researching MCI. Some studies particularly lookin visual involvement in MCI, including: • Modulation of Visual-Spatial learning in patients with MCI • EVASION: Effect of VisuAI Stimulation on attention • Vision-based Speed of Processing Cognitive Training and MCI **References:** • Dunne RA, Aarsland D, O'Brien JT, *et al*. Mild Cognitive Impairment: the Manchester consensus *Age and Ageing*, Volume 50, Issue 1, January 2021, Pages 72–80. https://doi.org/10.1093/ageing/afaa228 • Richardson C, Stephan BCM, Louise Robinson L et al. Two-decade change in prevalence of cognitive impairment in the UK. *Eur J Epidemiol*. 2019 Nov;34(11):1085-1092. Doi: 10.1007/s10654-019-00554-x.	Thank you for highlighting these studies. Please see surveillance report for details of the ongoing studies we will be tracking.

4. Additional Comments

Stakeholder	Overall response	Comments	NICE response
RCGP SIG Group in Learning Disability		Needs revision to include -Clinicians should be aware that patients with LD are likely to suffer dementia at earlier ages especially if the LD is associated with Down Syndrome -Clinicians should be aware that patients with LD may not present with "textbook symptoms" of dementia but with behaviour problems - Patients with LD meeting the criteria of AD should be considered for medication to prevent deterioration	Thank you for highlighting these issues.

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		- The early diagnosis often considers the progressive changes of behaviour and these can be detected using questionnaires and these should be a recognised part of the AHC for patients over the age of 35 years (I wouldn't fight about the age) - Secondary dementia is likely to me more common in patients with LD and AHS have a purpose in preventing this by vascular prevention, PA and hypothyroid disease, loss of mental activity with increasing age - End of life care and advanced directives have particular importance in the care of patients with LD and dementia - Special attention is required for patients with LD from ethnic minorities and socio-economically deprived areas	
Dementia United		Dementia united confirms that they disagree with the proposal not to update. Link to project booklet here	Thank you for providing this link.
Specsavers		I note that the above guidelines are being reviewed to see if they need to be updated. The guidelines do not currently include reference to the importance of treating age related hearing loss to mitigate and / or prevent dementia. The research in this area is constantly evolving and the attached article in Lancet Public Health in April is the most definitive to date in asserting that correcting age-related hearing loss will prevent dementia in some patients. (Treatment with hearing aids reduces dementia risk to the same level as patients without hearing loss.) Incidence of age related hearing loss (sensorineural loss / Presbycusis) increases at roughly 1% per year of age so with > 50% of over 50s likely to suffer a age-related hearing loss, the potential for hearing tests and dispensing of hearing aids, where indicated, to be a major mitigation of risk of dementia.	Thank you for highlighting this issue and providing a reference. Please see surveillance report for details of how the evidence was assessed and included in the surveillance review.

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