International consensus on quality indicators for comprehensive assessment of dementia in young adults using a modified e-Delphi approach

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RESEARCH ARTICLE

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# International consensus on quality indicators for comprehensive assessment of dementia in young adults using a modified e-Delphi approach

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**Objective:** To develop guidance for clinicians about essential elements that can support clinical decision-making in the diagnostic workup of young onset dementia.

**Methods/design:** Three iterations of a modified e-Delphi consensus survey comprising 23 international expert clinicians specialising in diagnosis of young onset dementia.

**Outcome measures:** A priori consensus was pre-defined as 80% of experts ranking statements in the upper threshold on a seven-point Likert scale that ranged from "not important at all" to "absolutely essential" to diagnosis.

**Results:** 80% consensus was reached on 48 statements that were rated as "absolutely essential" or "very important" to a comprehensive assessment of dementia in a younger adult. In order to inform a subsequent audit of clinical records in which compliance with these statements was assessed, the statements were divided into a Minimum Standard, (consisting of the 15 statements voted by all experts as being "absolutely essential" or "very important") and a Gold Standard where 48 statements were voted by 80% of the experts as being "absolutely essential" or "very important". The experts' response rate across the three rounds was 91.3%.

**Conclusion:** A Minimum Standard and Gold Standard have been created for the diagnostic workup of young onset dementia. The standards provide a clinically useful tool for decision-making, particularly for generalists and those with less experience in the field. The standards will be used to inform a UK case note audit of recently diagnosed patients with young onset dementia.

KEYWORDS
Delphi study, diagnosis, expert consensus, quality indicators, standards, young onset dementia

Transparency declaration - the lead authors, Mary O'Malley and Janet Carter, (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

# 1 | INTRODUCTION

## 1.1 | Young onset dementia and diagnosis

Young onset dementia (YOD) refers to dementia diagnosed in those aged 65 years and under. The differential diagnosis of YOD encompasses complex presentations of the common primary neurodegenerative diseases as well as autoimmune, inflammatory, late onset metabolic and hereditary/familial causes.[1] While Alzheimer's disease (AD) makes up the majority of cases in younger adults, it represents a significantly smaller percentage than in late onset disease (LOAD)[2,3] and presentations are generally non-amnestic in nature.[4] Because of the complexity of presentation and often atypical nature of presenting symptoms, YOD is poorly recognised and often misdiagnosed[5,6] and advice to support clinicians with identification and assessment of key symptoms in the diagnostic workup is lacking. In particular, clinicians with less familiarity of dementia in younger adults can be unaware of red flag symptoms and essential investigations that can help identify the complex subtypes of dementia which are more common in younger people. Furthermore, routine assessments tailored to older patients are often insufficient to identify the significant overlap between psychiatric disorders and neurodegenerative disease in this age group and this can lead to delay in specialist referral, clinical under-investigation, misdiagnosis, and delays in obtaining a definitive diagnosis reference (7–9).

Given these concerns, a UK-based study, called The Angela Project, aimed to develop guidance on best practice in diagnosis. An in-depth scoping review of the literature highlighted 29 papers identifying red flags in the clinical approach to diagnostic assessment of YOD and concluded that a clinically rigorous and systematic approach is necessary inorder to avoid misdiagnosis or under diagnosis for younger people with dementia.[7] To further a systematic approach to diagnosis in YOD, the present paper reports the findings from an international Delphi study with secondary care clinical experts, that identified key elements that support clinical decision-making. The Delphi method was adopted as it is an appropriate method for exploring clinical decision-making by consensus.

Our objectives were to explore the (a) key indicators essential for high quality assessment and diagnosis of YOD, and to (b) identify representative opinion from clinicians in a range of disciplines typically involved in diagnosis of YOD.

**Key points**

- Delay to diagnosis, misdiagnosis as a psychiatric condition and under-investigation of young onset dementia is common because of a lack of expertise.
- Routine assessments tailored to older patients are insufficient to identify the complex presentations usually seen in young people with dementia
- A Minimum and Gold Standard set of indicators for high quality assessment of young onset dementia have been derived using a Delphi consensus study with international experts.
- The standards provide a tool to aid clinical decision-making for those with less experience in the field.

# 2 | METHOD

## 2.1 | Delphi method

The Delphi process[10,11] is an expert consensus method that can be used to develop best practice guidelines using practice-based evidence. This process comprises a series of structured surveys and is used to collate opinions on a set of matters in order to gain a consensus of opinions.[11] In diseases where clinical evidence is lacking it is a method deemed suitable for the development of guidelines on diagnosis and management and is often used in healthcare decision-making.[12] The goal is to translate professional experience into informed judgement and to support effective decision-making with an emphasis on stability of group opinions rather than individual opinions. The Delphi approach allows anonymised individuals to freely express their opinions, reconsider them in the light of collective opinions from the whole group and, with each round, gain consensus.[13]

The Delphi process used here to determine consensus about key elements in the assessment and diagnosis of YOD involved four steps: (a) formation of the expert panels, (b) survey development informed by a literature search, (c) data collection and analysis, and (d) guidelines development. This paper will focus primarily on the first three steps, although please see O'Malley et al, (2019) for the in-depth literature review that was conducted to inform this study.[7]

*Ethics*: The Angela Project was approved by the Health Research Authority in England and by the South Central Berkshire Research Ethics Committee (REC ref.: 17/SC/0296).

## 2.2 | Panel member selection and participants

Purposive sampling was used to select 52 experts who had a specific interest (such as through research or through their own practice) in YOD and these experts were approached to take part in a Delphi consensus study on diagnosis of YOD (UK - N = 28, Female = 4, Male = 24; International - N = 24, Female = 7, Male = 17). Criteria for experts were that they were (a) affiliated with a YOD service (b) were authors from papers found through the scoping literature review previously conducted (see O'Malley et al, 2019 review), or (c) were identified via snowball sampling techniques. We aimed to approach a similar number of UK national experts and international experts to represent diversity of practice. In response to the invitation, 23 experts agreed to participate in the Delphi study (UK (N = 15) Female = 1, Male = 14; International (N = 8), Female = 5, Male = 3). Please see Table 1 for the demographics of the Delphi experts.

**TABLE 1** Delphi panel members' specialisms

| Specialism | UK | International | Total | Experience of experts |
|---|---|---|---|---|
| Neurology | 10 | 2 | 12 | All currently clinically active |
| | | | | UK- in specialist cognitive neurology/YOD hospital-based clinics |
| | | | | International -university hospital memory services/specialist memory service |
| Psychiatry | 4 | 3 | 7 | All currently clinically active |
| | | | | UK - in YOD services/clinics in community or hospital |
| | | | | International – specialist memory clinics and active researchers |
| Neuropsychology | 0 | 3 | 3 | 2 currently clinically active -Specialist YOD care services/ communities/hospital |
| | | | | 1 active researcher |
| Gerontology | 1 | 0 | 1 | Clinically active clinician outpatient setting, leading researcher in field |
| Total | 15 | 8 | 23 | |

*Note:* International experts included those from The Netherlands, Germany, Australia, Hungary, Ireland and France.

Experts were approached by means of email and were sent a "Delphi invitation". Consent was considered implicit by completing the first round of the Delphi.

### 2.3 | Survey and rounds

The Delphi questionnaires were made available using the Bristol Online Survey (BOS) which allowed easy access for all the experts. A preliminary pilot study was conducted with a team of independent experts from a leading dementia research institution to provide initial feedback on the clinical vignette which featured in the first round on the survey.

The study was conducted in three phases spread over the period from October 2017 to May 2018.

*Delphi Round 1*: Consensus development began with four open-ended questions for experts based upon a clinical case vignette of an individual displaying possible symptoms of YOD. The vignette was developed by collating self-reports of prodromal symptoms of dementia through our public and patient involvement (PPI) forum of people affected by YOD, as well as by asking independent clinical experts in YOD. The vignette was written in such a manner as to provoke diverse and multiple opinions and/or multiple alternative pathways to further assessment (see Appendix A for the vignette and questions). Experts were encouraged to provide comments and insights into how they interpreted the clinical history and symptoms, weighed them in the balance, and made decisions about how they might proceed to further assessment. Following data collection, three of the authors met on two occasions for Round 1 workshops to read, group similar items, collapse and define the key themes that emerged from the open-ended responses.

Analysis of the key themes included selecting the most representative statement reported by the experts, using exact wording with only minor edits if necessary.

*Delphi Round 2*: Experts were asked to rate the statements generated in Round 1 via the Bristol Online Survey (www.onlinesurveys.ac.uk) on a Likert scale of 1-7, ranging from "not important at all", to "absolutely essential" (see Table 2).

*Delphi Round 3*: The statements that had overall mean scores below 6 (indicating they were moderately important or not important) and/or did not reach consensus in Round 2 were re-presented to the experts in Round 3. Experts were asked to re-read and reconsider their scoring if they wished. To provide additional decision-making support to the experts, given the variety of clinical specialisms, we provided the mean and standard deviation (SD) of the whole expert group per statement, as well the mean and SD per specialism (e.g. neurologists) dependent on the discipline of the statement/where appropriate.

## 3 | DATA ANALYSIS

### 3.1 | Round 1

Round 1 identified 138 individual items about the case vignette which were grouped across 11 key areas of assessment and investigation from the qualitative reports. (See Table 3 for an example of grouped free text quotes about mood). The items were further collapsed and grouped into universal descriptions to create a final list of 72 statements for rating.

### 3.2 | Round 2

Of the list of 72 unique statements presented in the second round (see Appendix B), 43 of the statements reached 80% consensus after Round 2, meaning they were rated in the upper threshold with scores

**TABLE 2** The 7-point Likert scale used in the Delphi study

| | | | | | | |
|---|---|---|---|---|---|---|
| Not at all important | Low importance | Slightly important | Neutral | Moderately important | Very important | Absolutely essential |

**TABLE 3** Free text quotes from round 1 that related to mood

| Statements | Round 1 raw text quotes relating to mood |
|---|---|
| To ask about sleep | I would be concerned over the possibility and need to rule over further a depressive component to his presentation with dishevelled appearance, anhedonia and poor sleep (1023). |
| Exclude symptoms of mood disorder | poor sleep: can affect memory, could be mood related (1010). |
| Use a mood inventory such as GDS, BDI, HADS | Questionnaires to assess mood (1016). |
| | Mood screening (1011). |
| | Formal mood inventory (1003). |
| | story has elements to suggest an affective disorder, but this should not be taken at face value, especially without prior psychiatric history, and the degree of self-neglect. The ACE3 pattern is not suggestive of problems secondary to an affective disorder, for example, the low visuospatial scores, and language deficits (1013). |

of "absolutely essential" and "very important". Of these 43 statements, 15 statements were rated by all experts as being absolutely essential or very important, and a further 28 statements were rated by 80% of the experts as being "absolutely essential" or "very important". Please see Table 4 for the final list of statements that met consensus and Appendix C for statements that did not reach consensus after all rounds.

### 3.3 | Round 3

In total there were 29 statements where 80% consensus was not reached, or the statements were ranked as moderately important or less after Round 2. These were sent back to the experts for reconsideration in Round 3. In this round, experts were provided with the personal rating given for the statement in the previous round (Round 2), (a) the collective group rating of the statement and the SD (SD), (b) where applicable, the Specialist Mean Scores and Specialist SD from experts from the specific area of specialism that the statement reflects. Twenty-one of the 23 experts responded in Round 3 (response rate 91.30%), with 16 experts reconsidering and changing their scores based on overall mean scores and the mean scores of each discipline. Five experts were happy with their original Round 2 scores and did not change their scores. Round 3 resulted in the addition of five more statements reaching consensus in the upper threshold (see Table 5).

As a result, the final list of statements following the three iterative rounds consisted of 48 statements where 80% consensus was reached that they were "absolutely essential" or "very important" to diagnosis in a younger adult. (see Table 4).

At the outset of the study, consensus was agreed as achieved on an item if at least 80% of the respondents were in agreement and the composite score fell in the upper threshold, defined as scores in the "absolutely essential" or "very important" range on the 7-point Likert scale.

Earlier studies have also used the certain level of 80% agreement to identify very high levels of consensus.[14]

## 4 | RESULTS

The quality indicators identified by experts via consensus in Table 4, and particularly in free text written feedback, emphasised a general approach to the assessment, which is compassionate, collaborative and inclusive. As a philosophy of care, all experts agreed that supporting individuals and families throughout the course of their illness, offering flexible management with appropriate professionals over time and with disease progression was vital up to end of life care. However, individual autonomy was respected and recognition that a "ight touch" may be preferable to many younger people with dementia, especially early in their illness when the condition is stable, and support could be considered intrusive. Ensuring participants in the process were clear about potential outcomes, including the likelihood of receiving a diagnosis, before proceeding by employing pre-assessment counselling, was also considered important by 100% of experts.

In free text, the need to differentiate from psychiatric diagnoses was emphasised together with need to keep an open mind about the myriad of less common causes of dementia that can occur - including genetic causes, prion diseases, less common forms of degenerative disease, and the role of metabolic, endocrine and neoplastic disease. The difficulty in differentiating dementia in patients with long-standing illnesses like schizophrenia and resistant depressive / affective disorders, and individuals with prior learning difficulties where knowledge of premorbid functioning is essential, was acknowledged. Equally, that very young patients (under age 40) open a up a much wider diagnostic differential of genetic, neurometabolic and other unusual disease processes. Experts acknowledged that while a timely and accurate diagnosis was important, as patients had often experienced delays and multiple steps before reaching an expert, there were equally risks in making a premature diagnosis because of the profound impact having a diagnosis would have on the future, and the challenges and risk associated with this.

Obtaining a collateral history was considered to be an essential component of history taking mentioned by 100% of experts, in particular, noting any discrepancy between patient self-report and that of a

**TABLE 4** Minimum and Gold Standard statements

| Group | Statements rated by experts | Mean | SD | total sum of respondents rating 6 or 7 |
|---|---|---|---|---|
| Pre-assessment and communication | Multiple professionals are required over time to allow flexible assessment with support to end of life | 6.17 | 1.07 | 21 |
| Pre-assessment and communication | Diagnosis of YOD is a clinical judgement and has a profound impact on the future, so it important to convey this to patient and their family and remain open to the need to review and potentially modify opinion | 6.70 | 0.47 | 23 |
| Pre-assessment and communication | Establishing rapport to enable open reporting of symptoms | 6.74 | 0.45 | 23 |
| Pre-assessment and communication | The assessment should start with counselling to ascertain What patient and supporters require | 6.00 | 0.90 | 19 |
| Pre-assessment and communication | Ensuring the patient has capacity | 6.09 | 0.90 | 19 |
| History taking: importance of the following information when taking a history | To ask an informant (eg, wife/husband) for a collateral history | 6.91 | 0.29 | 23 |
| History taking: importance of the following information when taking a history | To understand the symptom type and the mode of onset | 6.83 | 0.39 | 23 |
| History taking: importance of the following information when taking a history | More information about loss of sympathy/empathy towards others, disinhibited behaviour, change in food preferences and changes in personality | 6.74 | 0.45 | 23 |
| History taking: importance of the following information when taking a history | To enquire about changes in physical health | 6.52 | 0.51 | 23 |
| History taking: importance of the following information when taking a history | If there have been any changes in activities of daily living | 6.87 | 0.34 | 23 |
| History taking: importance of the following information when taking a history | To ask about changes in behaviour | 6.91 | 0.29 | 23 |
| History taking: importance of the following information when taking a history | To consider previous medical conditions | 6.52 | 0.67 | 21 |
| History taking: importance of the following information when taking a history | To take a drug history | 6.70 | 0.63 | 21 |
| History taking: importance of the following information when taking a history | To ask about sleep | 6.39 | 0.72 | 20 |
| History taking: importance of the following information when taking a history | To take an alcohol history | 6.74 | 0.54 | 22 |
| Family history | To ask if a first degree relative has had young onset dementia | 6.83 | 0.39 | 23 |
| Family history | To obtain a three-generation history of young onset dementia from the patient | 6.17 | 0.89 | 20 |
| Medical history | To have a full medical history (including cardiovascular history) | 6.70 | 0.47 | 23 |
| Physical examination | A Physical Examination | 6.17 | 1.11 | 20 |
| Risk assessment | To evaluate risks, for example driving or in the work place | 6.61 | 1.08 | 22 |
| Psychiatric assessment | A thorough psychiatric history should be conducted. | 6.52 | 0.67 | 21 |

(Continues)

**TABLE 4** (Continued)

| Group | Statements rated by experts | Mean | SD | total sum of respondents rating 6 or 7 |
|---|---|---|---|---|
| Past psychiatric history | Ask about past psychiatric symptoms | 6.52 | 0.67 | 21 |
| Psychiatric assessment | Include mental state examination | 6.22 | 1.02 | 19 |
| Psychiatric assessment | Exclude Symptoms of mood disorder | 6.70 | 0.56 | 22 |
| Psychiatric assessment | Exclude psychotic symptoms | 6.39 | 0.58 | 22 |
| Psychiatric assessment | Establish if there is a known history of learning disability | 5.91 | 1.41 | 19 |
| Neurological assessment | A thorough neurological assessment should be conducted | 6.83 | 0.39 | 23 |
| Neurological examination: key components should include | Eye movements | 6.52 | 0.67 | 21 |
| Neurological examination: key components should | Cerebellar signs | 6.48 | 0.67 | 21 |
| Neurological examination: key components should include | Tongue or limb fasciculation | 6.43 | 0.73 | 20 |
| Neurological examination: | Frontal signs | 6.17 | 1.19 | 20 |
| Neurological examination: | Extrapyramidal features | 6.52 | 0.73 | 22 |
| Neurological examination: examine for | Motor skills | 6.57 | 0.59 | 22 |
| Neurological examination examine for | Praxis | 6.65 | 0.49 | 23 |
| Neurological examination examine for | Parkinsonism | 6.65 | 0.49 | 23 |
| Neuroimaging | A thorough neuroimaging investigation should be included | 6.87 | 0.34 | 23 |
| Neuroimaging investigation should include | Baseline structural neuroimaging | 6.74 | 0.54 | 22 |
| Neuroimaging | MRI should be the initial imaging investigation | 6.48 | 0.95 | 20 |
| Neuroimaging | MRI head to agreed dementia protocol | 6.22 | 0.83 | 19 |
| Dementia protocol should include | T1 | 6.30 | 1.15 | 19 |
| Dementia protocol should include | T2 | 6.13 | 1.01 | 19 |
| Neuroimaging | FLAIR | 6.17 | 0.98 | 20 |
| Neuroimaging include | Assessment of MTL atrophy on MRI | 5.87 | 1.29 | 18 |
| Neuropsychological assessment | An ACE -III is useful to understand the cognitive profile | 5.83 | 0.64 | 18 |
| Neuropsychological assessment | Patterns of cognitive deficits provide clues to disease aetiology on the ACE-III | 5.91 | 0.72 | 18 |
| Neuropsychological assessment | Detailed neuropsychology testing should be considered if there is under-performance on screening measures | 6.13 | 0.95 | 18 |
| Neuropsychological assessment | The profile of results is important on the ACE-III, that is, the pattern of what looks impaired and what is less affected, rather than the score itself | 6.26 | 0.92 | 20 |
| Support to end of life | Support is required from diagnosis to end of life care | 6.70 | 0.47 | 23 |

*Note:* The following table includes the 48 statements that have been highlighted by 80% of the experts as being "absolutely essential" or "very important" to making a comprehensive assessment of dementia in a younger adult. The right column indicates the number of experts that rated each statement as 'absolutely essential' or 'very important' and the statements have been grouped according to aspects of the clinical assessment. Statements highlighted in green, indicate statements that were rated by all experts (ie, 100% consensus) as being absolutely essential or very important and is our Minimum Standard for diagnosis. Mean results scores of 6 reflect statements being "very important", while the top score of 7 reflects the statement being "absolutely essential". ACE-III refers to the Addenbrooke's Cognitive Examination-III.

**TABLE 5** Statements that made the final list for the Gold Standard following reconsideration during Round 3 of the Delphi

| Group | Statements rated by experts | Round 2 mean | Round 2 SD | Number of respondents | Round 3 mean | Round 3 SD | Number of respondents |
|---|---|---|---|---|---|---|---|
| Psychiatric assessment | Include mental state examination | 6.13 | 1.10 | 17 | 6.22 | 1.02 | 19 |
| Neuroimaging | MRI head to agreed dementia protocol | 5.91 | 1.35 | 17 | 6.22 | 0.83 | 19 |
| Neuropsychological assessment | An ACE-III is useful to understand the cognitive profile | 5.70 | 0.76 | 16 | 5.83 | 0.64 | 18 |
| Neuropsychological assessment | Patterns of cognitive deficits provide clues to disease aetiology on the ACE-III | 5.83 | 0.89 | 16 | 5.91 | 0.72 | 18 |
| Neuropsychological assessment | Detailed neuropsychology testing should be considered if there is underperformance on screening measures | 5.91 | 0.95 | 16 | 6.13 | 0.95 | 18 |

knowledgeable informant. Enquiry regarding precise type of symptom onset, chronology and progression, and the current symptom profile, should be ascertained in addition to determining which key areas have *not* changed; for example, physical health/ neurological status. Further information about social and family factors was considered essential - these factors included any stresses and current level of family resource/support/children and their concerns and views, relevant financial and legal matters, and any difficulties at work and how difficulties were impacting on day-to-day activities. Weight was given to changes in non-cognitive symptoms, particularly appearance, behaviour and personality, with salience particularly in direct enquiry about international consensus criteria for behavioural variant Frontotemporal dementia (FTD).

The experts emphasised ascertaining information to aid discrimination between a possible cognitive disorder and a functional or dual diagnosis - such as symptoms of depression and the role of any aetiological factor such as alcohol or illicit drug use. Caution advised against taking a history of such conditions at face value as explanation of current presentation, especially in the absence of any previous psychiatric history.

Identifying "red flags" to differentiate from mood disorders and other psychiatric conditions was reflected in consensus on taking a thorough psychiatric history and mental state examination to enquire about symptoms of mood/sleep and abnormal beliefs or perceptions. Experts reached consensus about the value of self- or observer-rated scales of mood or behaviour, but did not agree on which tool was most appropriate. It may be that whilst experts recognised the importance of a mood inventory, they may not have had the "discipline specific" expertise to call judgement on which specific tool is most suitable.

Consensus was reached on the value of obtaining further background information about biography and family history of dementia. This included other neurological conditions if known (including subtype and any genetic mutations) in first degree relatives, and by taking a three-generation family history.

Taking a full medical history, particularly with regard to medication and cardiovascular risk factors, and performing a focused physical and neurological examination reached 100% consensus. Dementia blood screens, autoimmune disorder screens and other baseline investigations such as chest X-ray and ECG to exclude physical causes did not. Many experts made it clear in free text that there is an expectation that such investigations would already have been performed by GPs before referral, supporting the view that it is important to check for reversible or rare physical causes in a young person.

Neurological examination was regarded as absolutely essential, and the preferred approach advocated exclusion of abnormal eye movements, cerebellar signs, extrapyramidal features, motor skills, frontal release signs and tongue and limb fasciculation. Examination for praxis and parkinsonism was considered to be the minimum standard required.

The clinical experts considered that the Addenbrookes Cognitive Examination-III (ACE-III) was a useful tool and the cognitive profile and pattern of deficits were more important than objective scores in helping understand aetiology. Detailed neuropsychology should be considered if there is underperformance on cognitive measures or in cases of clinical uncertainty with normal imaging. Normal cognitive scores in younger people in the presence of impaired activities of daily living did not prompt experts to identify functional assessments with an Occupational Therapist as a valuable complementary tool, reaching only 70% consensus (16 of the 23 experts rated this as "absolutely essential" or "very important"), although it was not considered unimportant.

Only 17% of experts valued CT brain scans as important baseline investigations, the remainder agreeing that MRI should be the first investigation. A defined dementia protocol including as T1, T2, and T2 FLAIR images but not Diffusion Weighted Imaging (DWI) or

Susceptibility Weighted Imaging (SWI) reached 80% consensus in our upper threshold (i.e. "absolutely essential"; or "very important" to diagnosis).

Consensus about the value of access to quantitative volumetric analysis of medial temporal atrophy as a valuable biomarker in this age group was not reached, although assessment of medial temporal lobe atrophy by visual analysis was not.

In the event of normal baseline imaging, the experts were asked to rate which further investigations would be considered helpful. Cerebrospinal fluid (CSF) analysis for Tau and Amyloid biomarkers was rated by 15 experts as "absolutely essential" or "very important" with none rating it as of low importance although it did not reach consensus. Comparatively, Amyloid PET was rated as "absolutely essential" or "very important" by nine experts and four rated it as of "low importance" or "not at all important". There was general agreement that HMPAO SPECT was of limited value especially if FDG-PET was available.

## 5 | DISCUSSION

Using data from a three-stage modified Delphi study, consensus was reached on 48 essential components of a high-quality diagnostic workup for YOD as determined by clinical experts. Our results are consistent with previous literature reviews which identified the need for a systematic approach to clinical history taking, examination and investigation in YOD.[7,15]

In line with our results, other studies have stressed the need for rigorous enquiry and physical examination to assess key features of YOD including the potentially wide range of physical presentations of secondary dementias or dementia "plus" syndromes[16]; the increased likelihood of familial and genetically inherited conditions as a cause of young onset dementia[17]; and the salience of direct enquiry about international consensus criteria for behavioural variant Frontotemporal dementia (FTD)[18] where discrimination of FTD from Alzheimer's disease using conventional cognitive testing maybe unhelpful. In line with best practice in imaging,[15,16] a defined MRI dementia protocol including as T1, T2, and T2 FLAIR images was supported as was use of visual inspection of medial temporal lobe regional atrophy to discriminate Alzheimer's disease.

Consensus regarding the importance of mental state examination and the value of self- or observer-rated scales of mood or behaviour is designed to mitigate the high rates of psychiatric misdiagnosis of YOD, particularly as depression, identified in the literature.[19]

Despite the potential advent of disease modifying treatments and the value in identifying prodromal dementia and high-risk populations, most likely to be those with YOD, no consensus was reached about the role of molecular biomarkers for diagnosis.

### 5.1 | Strengths and limitations of the study

In order to ensure that opinions were not biased, the researchers adopted a rigorous approach maintaining anonymity throughout to allow frank discussion. Written feedback about decision-making was encouraged to limit bias and avoid preconceptions. However the lack of representation of allied health professionals, such as occupational therapists and speech and language therapists, in the expert panel is likely to have influenced outcomes, although medically trained professionals are more likely to be directly involved in the final diagnostic decision. This is relevant to the Delphi results as working in a multidisciplinary environment with access to other key professionals was considered an important criterion by the participants.

As with all Delphi studies, the views expressed represent those of experts in specific disciplines and do not necessarily reflect the views of all experts in that field. In our study, the range of experts who agreed to participate may indicate bias in the selection process with those who have strong views being more likely to participate. As the sample was varied in terms of expertise in secondary care, care was taken to ensure that statements of importance by certain professional groups were not overlooked due to a lower number of experts from their discipline by providing experts with the "discipline" average score as well as the overall average when reviewing scores in Round 3. Thus, a statement not making the final list may have been due to lack of representation from a professional group in the expert panel, rather than it not being important to the diagnostic workup.

Whilst there is possibility of bias around particular concepts of assessment, we selected experts from diverse institutions who are highly qualified in the field, and conducted the survey in a rigorous manner by maintaining the anonymity of all participants to limit potential bias. The free text feedback was used to ensure that the structure and content of the survey did not impose preconceptions and experts were able to comment freely. Feeding back the scores of specialists from other disciplines on the statements facilitated re-consideration of opinions, and suggests that final values were true reflections of expert views.

Other Delphi studies provide evidence that panels of similarly trained experts, especially where there is limited evidence and small numbers of experts in a field, can be used to develop reliable criteria to inform judgement and support clinical decision-making. The response rate of 91.3% across the three rounds is considerably higher than guidance suggests is necessary for a reliable Delphi study, where a response rate of 70% or higher is necessary. Although there is recognition that the sample size for constructing a Delphi panel is not a statistically-bound decision, reliable outcomes have been obtained from Delphi panels consisting of a relatively small number of Delphi experts. Recent analysis using bootstrapping methodology demonstrated that the response characteristics of a small expert panel in a well-defined knowledge area are stable in light of augmented sampling.[13]

Although steps have been taken to conduct the study in a rigorous manner, the template outlined is provided for guidance only and not as a definitive tool. It is hoped that it may help improve standards and provide a clinically useful tool, particularly for those with less experience in the field.

Guidelines in themselves may not ensure change in supportive behaviours.[10] Therefore, our next steps are to use these standards to

explore current practice in the UK through a clinical case note audit of diagnosis of YOD using a digital platform. The goal is to identify compliance with the quality indicators in mental health settings across the UK to assess current clinical practice and to identify potential barriers and facilitators to high quality assessment.

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## CONFLICT OF INTEREST

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

## AUTHOR CONTRIBUTIONS

Janet Carter, Jan Oyebode and Jacqueline Parkes initiated, planned and co-ordinated the study for this paper. Mary O'Malley and Janet Carter conducted the research, drafted and proof-read the paper, and Jacqueline Parkes, Jan Oyebode, Jenny LaFontaine and Vasileios Stamou contributed to drafting, proof-reading and worked on the final draft of the paper.

## DATA AVAILABILITY STATEMENT

We the authors agree to sharing data from this work, upon reasonable request

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## APPENDIX: Round 1, patient vignette and open-ended questions

| |
|---|
| Please read the vignette below: |
| *Mr Smith, a 60-year old, right handed retired accountant is referred to your clinic by his GP (Primary care physician US). He attends alone. His wife is concerned about his memory but she is at work and unable to attend. Mr Smith is a little dishevelled, and somewhat over familiar in manner. Mr Smith, does not feel he has any particular problems, says his wife is always nagging him and he sometimes worries she may be having an affair. He agrees that he sometimes forgets what he wants to say mid-sentence, has occasionally misplaced his keys and has lost interest in reading which he previously enjoyed. His golf buddies joke with him that he has poor head for numbers and they help him keep track of the scores. He has no significant past medical history, takes no regular medication and lives at home with his wife. His mother died in her 60s in a care home, with dementia. On further enquiry, Mr S reports that for the past 6 months, he has been sleeping poorly and admits that he worries about his son who is going through a difficult divorce. He still drives and manages the family accounts. Basic cognitive testing with the ACE-III demonstrates a total score of 77/100 with the following subset scores: Attention 16/18, memory 19/26, verbal fluency 10/14, VS 10/16, language 22/26.* |
| With regards to this vignette, and making a diagnosis, please answer the following questions: |
| Which are the key elements in the history that raise concern, if any? Could you outline them and explain why they are of note? |
| What further information would you require in order to refine your thinking? |
| What other tests might you undertake at this stage? |
| Please feel free to note any concerns or additional information you regard as important when diagnosing YOD: |

## APPENDIX: Statements formulated for Round 2

| Group and group statements | Specific statements |
|---|---|
| Pre-assessment counselling | Start with pre-assessment counselling to ascertain what patient and supporters require |
| Baseline Assessments - Please rate how important you personally deem the following baseline assessments to be in making a diagnosis of Young Onset Dementia | A basic/route dementia blood screen |
| | A chest x-ray |
| | An ECG |
| | A Physical Examination |
| | A screen for autoimmune disorders (eg, ANA, ANCA, paraneoplastic) |
| Please rate the importance of obtaining the following information when taking a clinical history in a younger person with possible cognitive impairment: | To ask an informant (eg, wife/husband) for a collateral history |
| | To understand the symptom type and the mode of onset |
| | More information about loss of sympathy/empathy towards others, disinhibited behaviour, change in food preferences and changes in personality |
| | To enquire if there are any swallowing difficulties |
| | To enquire about changes in physical health |
| | To ask about sleep |
| | To have a full medical history (including cardiovascular history) |
| | To understand the patients occupational history |
| | To consider previous medical conditions |
| | To assess for previous head injuries |
| | To take a drug history |
| | To take an alcohol history |
| | To ask about stressful life events |
| | If there have been any changes in activities of daily living |

| Group and group statements | Specific statements |
|---|---|
| | To ask about changes in behaviour |
| | To obtain for a three generation history of young onset dementia from the patient |
| | To ask if a first degree relative has had young onset dementia |
| | To evaluate risks, for example driving or in the work place |
| A thorough psychiatric history should be conducted. Please rate this: | Exclude Symptoms of mood disorder |
| The psychiatric assessment should: | Use a mood inventory such as GDS, BDI, HADS |
| | Exclude psychotic symptoms |
| | Use an inventory for neuropsychiatric symptoms such as NPI |
| | Establish if there is a known history of learning disability |
| | Ask about past psychiatric symptoms |
| A thorough neurological assessment should be conducted. Please rate this: | Praxis |
| Key components of the neurological examination should include assessment of: | Eye movements |
| | Cerebellar signs |
| | Extrapyramidal features |
| | Motor Skills |
| | Parkinsonism |
| | Tongue or limb fasciculation |
| | Frontal signs |
| A thorough psychiatric assessment should be conducted. Please rate this: | A mental state examination |
| Key components of the psychiatric assessment should include: | |
| Please rate the following statements: | Ensuring the patient has capacity |
| | Diagnosis of YOD is a clinical judgement and has a profound impact on the future, so it important to convey this to patient and their family and remain open to the need to review and potentially modify opinion. |
| | Establishing rapport to enable open reporting of symptoms |
| Neuroimaging investigation should include: | Baseline structural neuroimaging |
| | CT |
| | MRI should be the initial imaging investigation |
| | volumetric analysis of MRI |
| | Assessment of MTL atrophy on MRI |
| | MRI head to agreed dementia protocol |
| Dementia Protocol should include each of the following: | 3D T1 |
| | FLAIR |
| | T2 |
| | SWI |
| | DWI |
| In the event of normal baseline imaging, it would be best to consider: | CSF analysis for routine constituents |
| | CSF analysis for biomarkers that is, TAU and AB42 markers |
| | FDG-PET if available |
| | HMPAO-SPECT if available |

(Continues)

| Group and group statements | Specific statements |
|---|---|
| | AMYLOID-PET if available |
| | Genotyping |
| | Please add any additional comments below to explain your reasoning |
| Cognitive Assessment. Please rate the following statements: | An ACE-III is useful to understand the cognitive profile |
| | Pre-morbid occupational functioning is a guide to expected performance on ACE-III |
| | Assessment of sub-optimal performance on ACE-III depends on pre-morbid level of functioning |
| | Patterns of cognitive deficits provide clues to disease aetiology on the ACE-III |
| | Detailed neuropsychology testing is **essential** if there is under performance on screening measures |
| | Detailed neuropsychology testing should be **considered** if under performance on screening measures |
| | The profile of results is important on the ACE-III, that is, the pattern of what looks impaired and what is less affected rather than the score itself |
| Functional Assessment (day to day activities): | A functional assessment with an Occupational Therapist (OT) is useful. |
| Approach to management. Please rate the following statements: | Multiple professionals are required over time to allow flexible assessment with disease progression |
| | Support is required from diagnosis to end of life care |

## APPENDIX: Statements where consensus was not reached and or rated not important after all rounds

| Statements | Round 3 mean | SD | Sum of experts rating statements as very important[6] or absolutely essential[7] | Sum of experts rating statements as not at all important[1] or low importance[2] |
|---|---|---|---|---|
| A basic/routine dementia blood screen | 5.96 | 1.27 | 16 | 0 |
| A chest x-ray | 2.57 | 1.47 | 1 | 14 |
| An ECG | 2.96 | 1.43 | 1 | 8 |
| A screen for autoimmune disorders (eg, ANA, ANCA, paraneoplastic) | 3.83 | 1.43 | 2 | 4 |
| To enquire if there are any swallowing difficulties | 5.87 | 0.99 | 16 | 0 |
| To understand the patient's occupational history | 5.91 | 0.78 | 17 | 0 |
| To assess for previous head injuries | 5.87 | 0.80 | 14 | 0 |
| To ask about stressful life events | 6.00 | 0.83 | 17 | 0 |
| Use a mood inventory such as GDS, BDI, HADS | 4.22 | 1.38 | 3 | 4 |
| Use an inventory for neuropsychiatric symptoms such as NPI | 4.13 | 1.57 | 4 | 4 |
| CT | 3.48 | 1.56 | 4 | 7 |
| Volumetric analysis of MRI | 4.87 | 1.54 | 8 | 2 |
| SWI | 5.87 | 0.90 | 16 | 0 |
| DWI | 5.83 | 0.96 | 16 | 0 |
| CSF analysis for routine constituents | 4.57 | 1.58 | 4 | 3 |
| CSF analysis for biomarkers that is, TAU and AB42 markers | 5.61 | 0.97 | 15 | 0 |
| FDG-PET if available | 5.30 | 1.04 | 9 | 0 |
| HMPAO-SPECT if available | 3.57 | 1.84 | 4 | 8 |
| AMYLOID-PET if available | 5.00 | 1.25 | 9 | 2 |
| Genotyping | 4.04 | 1.55 | 5 | 5 |
| Pre-morbid occupational functioning is a guide to expected performance on ACE-III | 5.39 | 1.21 | 13 | 1 |

| Statements | Round 3 mean | SD | Sum of experts rating statements as very important[6] or absolutely essential[7] | Sum of experts rating statements as not at all important[1] or low importance[2] |
|---|---|---|---|---|
| Assessment of sub-optimal performance on ACE-III depends on pre-morbid level of functioning | 5.65 | 0.87 | 16 | 0 |
| Detailed neuropsychology testing is essential if there is under performance on screening measures | 5.13 | 1.68 | 11 | 3 |
| A functional assessment with an Occupational Therapist (OT) is useful. | 4.91 | 1.02 | 7 | 1 |