HSD61

The Diagnostic Journey of Patients with Mild Cognitive Impairment and Alzheimer's Disease Dementia, and the Importance of Biomarker Testing for Timely Diagnosis: A Real-World Survey in Europe

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OBJECTIVE

- To describe the diagnostic journey of patients with MCI and AD dementia in Europe.
- To gain insight into the perspectives of medical specialists regarding the challenges in making a timely diagnosis for MCI in the real world and the importance of biomarkers in the future in identifying AD in MCI patients.

CONCLUSION

- In the European sample, AD patients are diagnosed late as reflected by a mean MMSE score of 22 (4 SD), which necessitates increasing the urgency of timely diagnosis. Key specialist-reported reasons for delays are time to referral and scheduling consultations, and time taken to schedule a diagnostic test and receive test results.
- The diagnostic journey of MCI and AD dementia can be accelerated with improved access to specialised diagnostic services. While biomarker testing is considered crucial in identifying AD pathology in MCI patients in the future, only a small percentage of patients currently undergo such testing today.
- Specialists believe that delays in patients seeking help due to a lack of awareness or stigma, a lack of understanding of normal ageing amongst patients and families, and a wide variation in how patients typically present are key barriers to early identification of AD pathology in MCI patients.
- Resolving barriers to presentation and delays in diagnosis will be necessary to ensure patients can benefit as early as possible from interventions that slow disease progression.

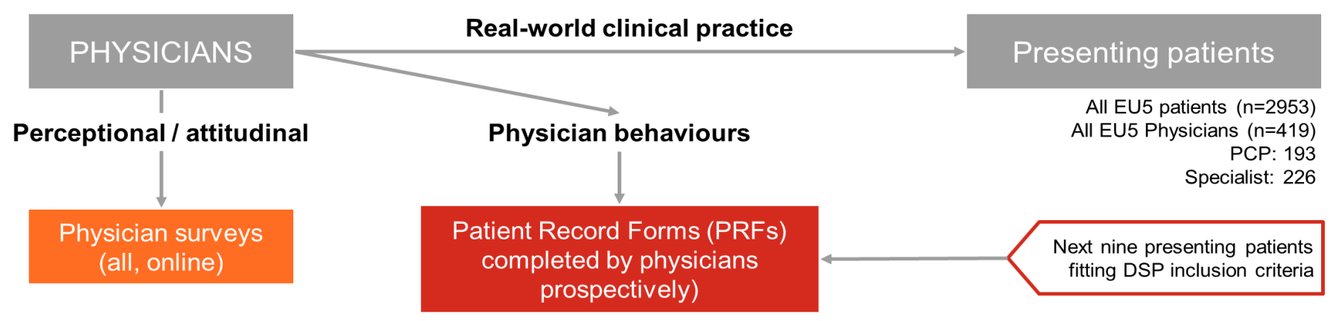
BACKGROUND Alzheimer's disease (AD) dementia is characterised by a decline in cognitive function, functional and behavioural impairment. AD progresses along a continuum from mild cognitive impairment (MCI) due to AD to dementia due to AD[1].

Whilst historically diagnosed through clinical symptoms, research has identified pathophysiological alterations linked to amyloid plaques and neurofibrillary tangles in the brain which can be used to support clinical diagnosis[2]. Such pathology can be identified through cerebrospinal fluid (CSF) and amyloid positron emission tomography (PET), yet very few patients currently receive this type of testing[3]. Recent clinical trials have shown promising results for amyloid targeting therapies (ATTs). Early identification of both MCI and AD dementia is key to optimising the effectiveness of these new treatments in slowing down disease progression[4].

STUDY DESIGN Data were drawn from the Adelphi Real World AD disease specific programme (DSP)™, a cross-sectional survey, with elements of retrospective data collection, of primary care physicians (PCPs) and specialists (neurologists/ geriatric psychiatrists/geriatricians/psychiatrists/neuropsychiatrists) conducted in France, Germany, Italy, Spain, and the United Kingdom (UK), between December 2022 – June 2023.

- Full data is reported for Germany, Italy, Spain and interim data for France and the UK.
- Specialists completed a survey detailing their attitudes and experience in the management of dementia patients. All physicians completed patient record forms for the next nine consecutively consulting patients (**Figure 1**).
- The DSP methodology has been previously published[5,6,7].
- Analyses were categorical, summarised as percentages, mean (standard deviation (SD)), or median [interquartile range (IQR)]. Sample sizes varied between variables due to missing data; missing data was not imputed.

Figure 1. Overall AD DSP study design



LIMITATIONS No patient selection verification procedures were applied to the AD DSP, and identification of the participants included was based on physician judgement/ perception rather than formal medical coding (e.g., diagnostic codes). Nevertheless, this process is typical of physicians' real-world classification of their patients.

The cross-sectional design of the DSP does not allow for causal relationships; however, the identification of associations is possible.

RESULTS Of 419 Physicians, Specialists (54%) and PCPs (46%), reported data on 2953 patients (1073 with MCI and 1880 with AD dementia; **Table 1**). Despite 74% of specialists reporting that biomarker testing will be 'important'/'extremely important' for identifying AD in MCI patients in the future, few patients diagnosed by specialists underwent AD dementia-specific biomarker testing including CSF (13%) and amyloid PET scan (5%). The patient diagnostic journey, key reasons for delay in diagnosis and tests used to aid diagnosis in MCI and AD dementia are summarised in **Figures 2 – 4**, while specialist-reported barriers for early identification of patients with MCI are summarised in **Figure 5**.

Table 1: Patient demographics and clinical characteristics

Patient demographics	2953
Mean age (SD)	76 (8)
Female n (%)	1542 (52)
Patient sample, n**	**2953**
Germany	680
Italy	686
France***	449
Spain	729
United Kingdom***	409
Physician-defined diagnosis, n (%)	**2953**
MCI - suspected AD	926 (31)
MCI - unknown AD	147 (5)
AD dementia	1880 (64)
Initial diagnosis MMSE*, n (%)	**1980**
MCI (MMSE: 27-28)	142 (7)
Mild AD (MMSE 20-26)	1356 (69)
Moderate AD (MMSE 10-19)	460 (23)
Severe AD (MMSE 0-9)	22 (1)
MMSE score at initial diagnosis	**2007+**
Mean (SD)	21.8 (4)

MCI, mild cognitive impairment; AD, Alzheimer's disease; SD, standard deviation
*The MMSE bandings in the UK differs; MCI 27-28, Mild AD 21-26, Moderate AD 10-20, Severe AD 0-9.
**The patient sample differs between countries to reflect the point of recruitment of the country at the time of the data cut.
*** Interim data
Mean country MMSE at initial diagnosis (SD) at the time of data cut: Germany: 21.3 (4), Italy: 21.5 (4), France: 22.1 (4), Spain: 22.2 (4), UK: 21.9 (4)
+27 patients had MMSE scores of 29 and 30 at initial diagnosis, they are included in the overall mean, but excluded from the classification which accounts for the base difference.

Figure 2. Reasons for time gap between first consultation and receiving an initial diagnosis

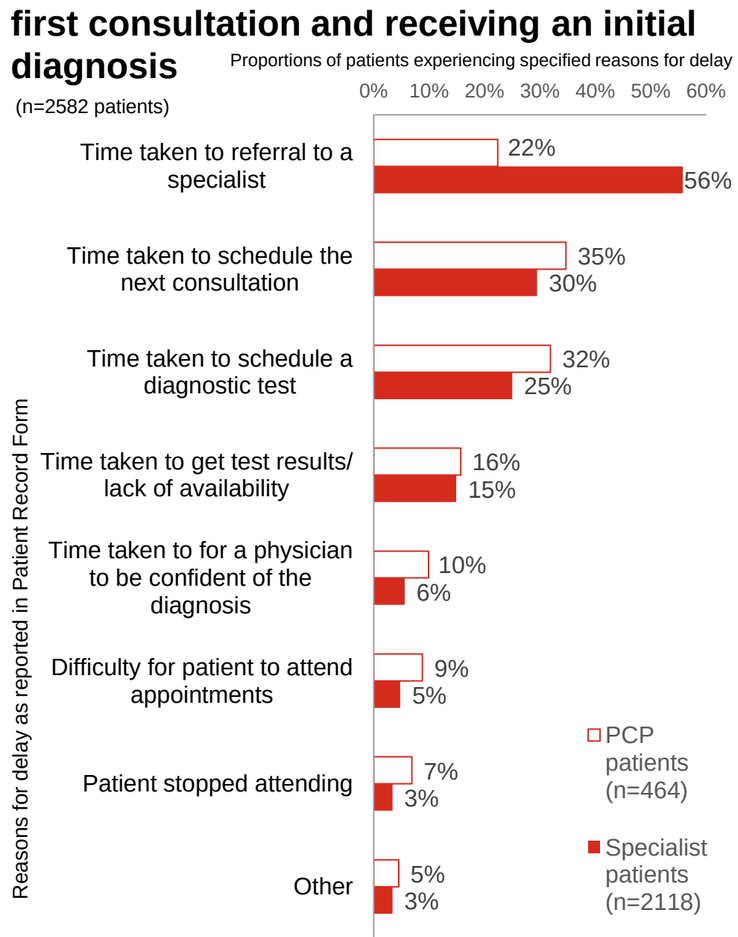
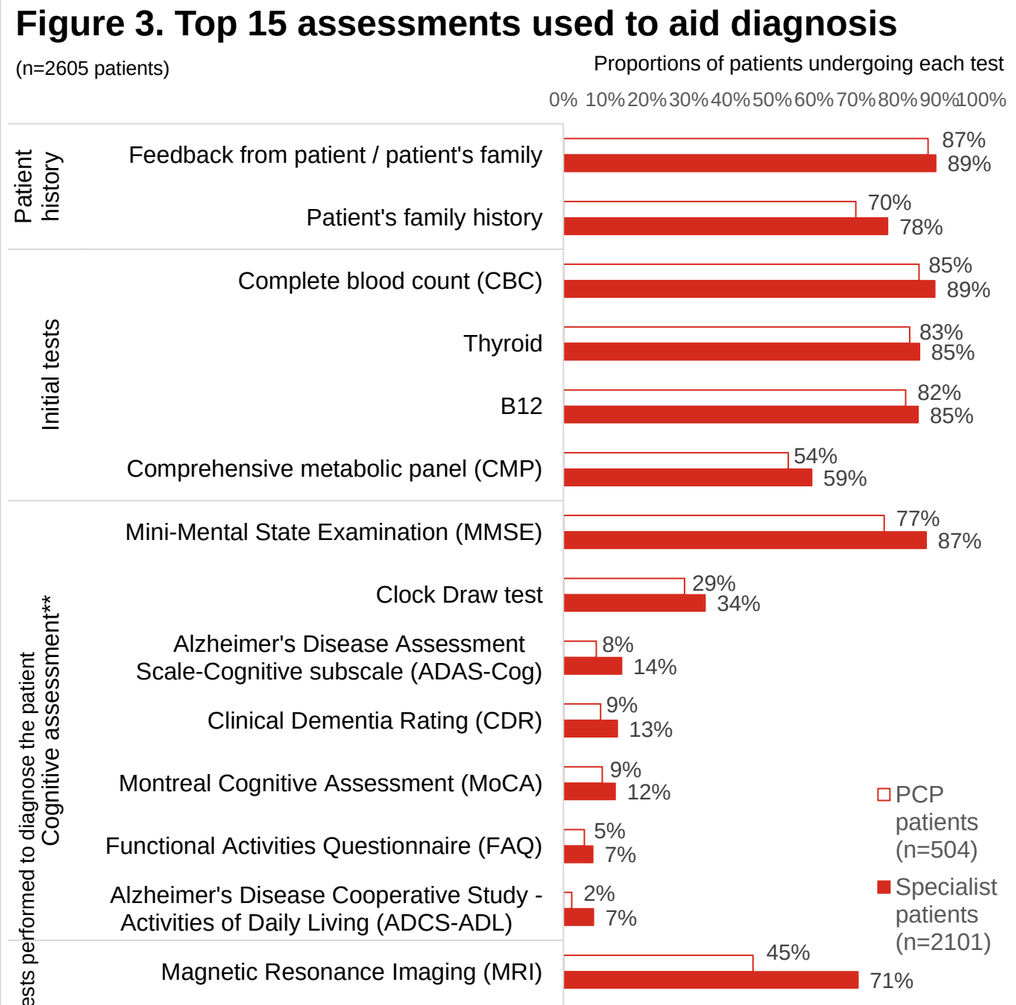
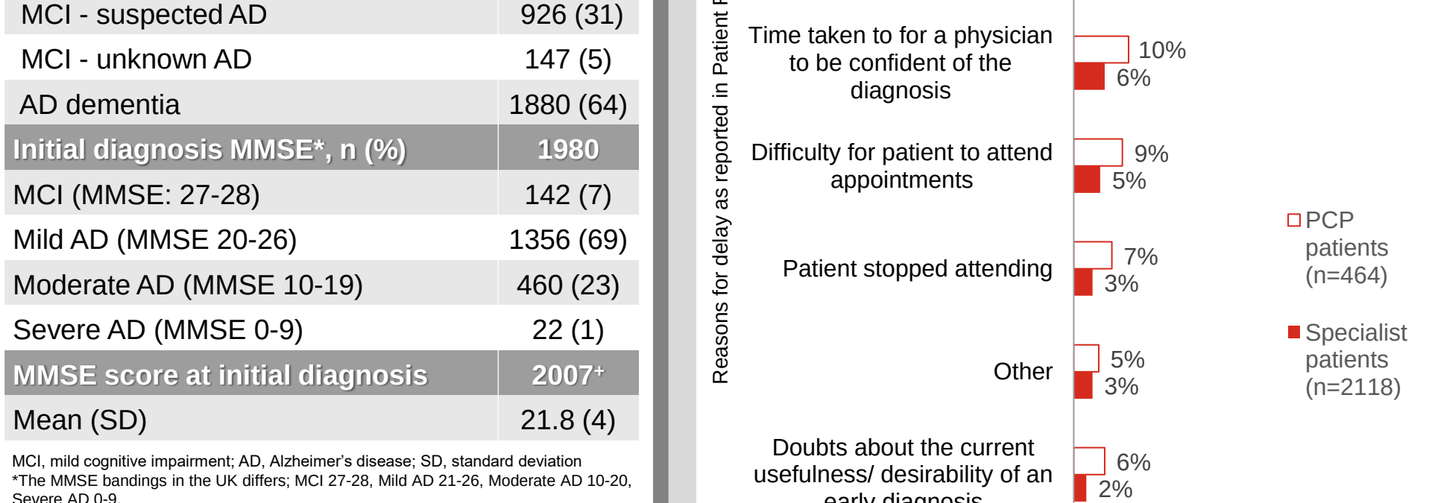


Figure 3. Top 15 assessments used to aid diagnosis



*Blood biomarkers include tests measuring protein pathology and levels of hormones which can indicate the onset of dementia
**Cognitive assessments are tools developed to assess the patient's level of cognitive function

Figure 4. Patient diagnostic journey



*'Other' includes alternative carers such as nurses and physician assistants; ** Immediately diagnosed are those who indicated the patient was diagnosed at first consultation or a duration of zero between first consultation and diagnosis and are not included in the median weeks.
Note: The median MMSE scores between countries show minimal variation. The bases change across the patient journey as not all patients have the full consultation history. MMSE at diagnosis is for all patients where we have data (which includes those diagnosed immediately and those at a subsequent consultation). PCP = Primary Care Physician

Figure 5. Specialist-perceived barriers to early identification of patients with MCI

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