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Current diagnostic pathways for Alzheimer's Disease - A comparison of six countries

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Introduction

- Alzheimer's disease (AD) is characterized by β-amyloid deposition (amyloid pathology) and tau pathology in the brain, with clinical symptoms including cognitive complaints or impairment.[1]
- Across geographies, diagnostic pathways for people presenting with cognitive complaints or impairment are heterogenous, and may consist of a combination of:
  - Clinical assessments (e.g., patient/family medical history-taking and/or cognitive assessments); and
  - Routine laboratory tests (e.g., blood and/or urine tests) to rule out other causes of symptoms.[2,3]
- Confirmatory diagnostic tests for amyloid pathology such as cerebrospinal fluid (CSF) biomarker analysis and/or imaging (amyloid-positron emission tomography [PET] or magnetic resonance imaging [MRI]) can be used.[2,3]
- Understanding the complexity and heterogeneity of the current diagnostic pathways is important to inform study design for the validation and implementation of a blood-based biomarker (BBBM) test for amyloid pathology,* particularly given the imminent availability of disease-modifying therapies (DMTs) for AD.[4]

Objective

- **To quantify and compare the current diagnostic pathways for patients presenting with cognitive complaints or impairment in six countries.***

*Results for "Roadmap to implementation of a fully automated blood-based biomarker test to facilitate diagnosis and treatment in early Alzheimer's disease" are presented in poster P-69080, at this congress.

Methods

- Data were collected using a quantitative survey (n=1,694 healthcare professionals [HCPs], including primary care physicians [PCPs], nurses, and specialists [geriatricians, neurologists, and psychiatrists]), conducted in the following countries from October–December 2021:

- By completing patient record forms (PRFs) alongside the survey, HCPs provided data for 6,744 patients, including patient demographics, presenting symptoms, and diagnostic tests and procedures conducted and/or ordered.
- The inclusion criteria for HCPs were: familiarity with aspects of AD and diagnostic biomarker tools; see ≥3 (PCPs/nurses) or ≥5 (specialists) people with subjective/objective cognitive impairment and be involved in these individuals' diagnosis; ≥75% (PCPs/nurses) or ≥60% (specialists) time spent in clinical practice; board certified (USA only); ability to refer to patient records (excluding Spain).
- Descriptive analyses were conducted for all patients and further stratified by country and HCP speciality (PCPs vs. specialists).

Conclusions

- **Overall, patient presentation and referral was similar across geographies, but there was heterogeneity in the diagnostic tests used between countries and specialties.**
- **This study is relevant to populate diagnostic pathways, fill data gaps, inform study design for the implementation of a BBBM test, and advance patient care in AD by supporting future evidence generation, especially once DMTs are available.**

Results

Patient presentation

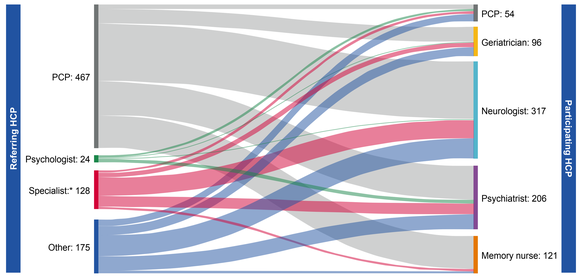
- Across all countries examined, the most common symptoms that initiated HCP interaction included memory issues (89.9%), physical/behavioral problems (87.1%), issues with cognitive skills (72.2%), and language problems (71.4%).
- Predominantly, patients or their families initiated the interaction with a HCP (mean of 57.9% across all countries; **Table 1**, ranging from 49.4% in the UK to 62.4% in Spain).

Table 1. Proportion of patients with symptoms of cognitive complaint or impairment, according to the person who initiated the interaction with a HCP (all countries).

Initiation of interaction with HCP for cognitive complaint or impairment	Number of patients (%)
Patient/family	3,906 (57.9)
Physician who carried out survey	1,998 (29.6)
Referral from another physician	794 (11.8)
Missing/unknown	46 (0.7)

Referral pathways

Figure 1. Flow of patients from the referring HCP to the participating HCP, by speciality (all countries).



*Neurologists, psychiatrists, and geriatricians.
Left side: specialty referring to the HCP participating in the study; Right side: specialty of the participating HCP referred to.

- The referral pathways were similar across all countries examined.
- Patients were most often referred from their PCP to a participating neurologist (**Figure 1**).
- This was followed by specialists referring the patient to a participating neurologist (**Figure 1**).

Diagnostic tests and procedures conducted

- Of the patients with data on diagnostic tests by country and speciality (n=6,525), 96.0% underwent clinical tests and 95.5% underwent cognitive tests (**Table 2**).
- Overall, mini-mental state examination (MMSE) was the most frequently used cognitive test, and approximately half of patients received routine blood-tests (**Table 2**).
- In China, cognitive tests, especially MMSE, were more commonly used by specialists (81.9%) than PCPs (41.6%), whilst in the UK, blood tests were more commonly used by PCPs (62.5%) than specialists (46.2%).

Risk factors to receiving a diagnosis

- Patients were less likely to receive a diagnosis of AD from a PCP than a specialist (hazard ratio=1.1).
- Compared with the USA, patients in China and Germany were less likely to receive a diagnosis of AD; patients in the UK, France, and Spain were more likely to receive a diagnosis of AD.
- Presenting symptoms, age, and interaction type had no significant influence on the risk of receiving a diagnosis.

Table 2. Diagnostic tests conducted and/or ordered at any appointment.

	Tests conducted	All n (%)	China n (%)	France n (%)	Germany n (%)	Spain n (%)	UK n (%)	USA n (%)
	ALL	6,525 (100.0)	1,185 (100.0)	858 (100.0)	849 (100.0)	1,012 (100.0)	919 (100.0)	1,702 (100.0)
Cognitive tests	Any cognitive tests	6,229 (95.5)	1,076 (90.8)	827 (96.4)	800 (94.2)	982 (97.0)	893 (97.2)	1,651 (97.0)
	Standard psychological/ psychiatric evaluation	4,477 (68.6)	593 (50.0)	667 (77.7)	669 (78.8)	865 (85.5)	511 (55.6)	1,172 (68.9)
	MMSE	5,141 (78.8)	901 (76.0)	766 (89.3)	626 (73.7)	897 (88.6)	638 (69.4)	1,313 (77.1)
	Mini-Cog	2,577 (39.5)	508 (42.9)	198 (23.1)	266 (31.3)	487 (48.1)	328 (35.7)	790 (46.4)
	ADAS-Cog	1,570 (24.1)	395 (33.3)	127 (14.8)	132 (15.5)	505 (49.9)	132 (14.4)	279 (16.4)
	GPCOG	1,211 (18.6)	115 (9.7)	98 (11.4)	128 (15.1)	377 (37.3)	239 (26.0)	254 (14.9)
	CANTAB mobile device test	672 (10.3)	62 (5.2)	79 (9.2)	89 (10.5)	262 (25.9)	37 (4.0)	143 (8.4)
	Cognigram, Cognivue, Cognision or ANAM device tests	784 (12.0)	69 (5.8)	98 (11.4)	103 (12.1)	277 (27.4)	67 (7.3)	170 (10.0)
	BEHAVE-AD	1,161 (17.8)	202 (17.0)	97 (11.3)	97 (11.4)	394 (38.9)	104 (11.3)	267 (15.7)
	Other cognitive tests	626 (9.6)	38 (3.2)	107 (12.5)	149 (17.6)	66 (6.5)	130 (14.1)	136 (8.0)
Clinical tests	Any clinical tests	6,261 (96.0)	1,169 (98.6)	829 (96.6)	810 (95.4)	961 (95.0)	894 (97.3)	1,598 (93.9)
	Clinical examination/discussion of symptoms	5,672 (86.9)	998 (84.2)	772 (90.0)	751 (88.5)	875 (86.5)	831 (90.4)	1,445 (84.9)
	Current medications taken	5,483 (84.0)	968 (81.7)	723 (84.3)	692 (81.5)	881 (87.1)	799 (86.9)	1,420 (83.4)
	Family history	5,337 (81.8)	968 (81.7)	735 (85.7)	700 (82.4)	867 (85.7)	702 (76.4)	1,365 (80.2)
	MRI	3,837 (58.8)	804 (67.8)	642 (74.8)	549 (64.7)	562 (55.5)	350 (38.1)	930 (54.6)
	CT scan	2,446 (37.5)	435 (36.7)	243 (28.3)	241 (28.4)	600 (59.3)	357 (38.8)	570 (33.5)
	CSF biomarker testing	866 (13.3)	52 (4.4)	136 (15.9)	159 (18.7)	249 (24.6)	87 (9.5)	183 (10.8)
	PET amyloid confirmation	970 (14.9)	72 (6.1)	147 (17.1)	136 (16.0)	262 (25.9)	98 (10.7)	255 (15.0)
Blood test	Any blood tests	3,329 (51.0)	377 (31.8)	429 (50.0)	464 (54.7)	689 (68.1)	485 (52.8)	885 (52.0)
	APOE-e4 or any other relevant genetic mutations	1,312 (20.1)	159 (13.4)	144 (16.8)	165 (19.4)	358 (35.4)	110 (12.0)	376 (22.1)
	Blood tests to rule out other causes*	2,687 (41.2)	271 (22.9)	367 (42.8)	376 (44.3)	552 (54.5)	434 (47.2)	687 (40.4)
	Other blood tests	199 (3.0)	16 (1.4)	26 (3.0)	26 (3.1)	34 (3.4)	31 (3.4)	66 (3.9)
	Other	282 (4.3)	1 (0.1)	52 (6.1)	38 (4.5)	40 (4.0)	59 (6.4)	92 (5.4)
	None of these	486 (7.4)	14 (1.2)	68 (7.9)	63 (7.4)	103 (10.2)	94 (10.2)	144 (8.5)

*These include tests to rule out treatable causes of cognitive decline.
ADAS-Cog, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ANAM, Automated Neuropsychological Assessment Metrics; APOE-e4, e4 allele of Apolipoprotein E gene; BEHAVE-AD, Behavioural Pathology in Alzheimer's Disease Rating Scale; CANTAB, Cambridge Neuropsychological Test Automated Battery; CT, computed tomography; GPCOG, General Practitioner Assessment of Cognition.

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