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Real-world diagnostic, referral, and treatment patterns in early Alzheimer's disease among community-based practices in the United States

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Abstract

Background: Over 90% of individuals with mild cognitive impairment (MCI) may not receive a timely diagnosis. Understanding community-based practice patterns, where most individuals are seen, is critical to improving patient care.
Objective: To understand how patients with MCI and mild dementia due to Alzheimer's disease (AD) are diagnosed and managed in community-based settings, including the use of clinical and cognitive assessments, referrals to dementia-related specialties, and receipt of treatment.
Methods: This observational study recruited community-based primary care physicians (PCPs) (N = 177) and neurologists (N = 147) in August-September 2023, through a verified physician panel with broad geographic representation across the US. Physicians abstracted medical chart data from patients diagnosed with MCI or mild AD within the previous two years. Data collected included use of neurocognitive assessments, biomarker and structural imagine tests, referrals, and treatments. Descriptive statistics were used.
Results: Medical records for 817 MCI and 467 mild AD patients were abstracted. The mean age was 70.2 years, 56.4% were female, and 67.2% were White. Symptoms were commonly reported by a family member (67.2%). Nearly 1 in 6 patients did not receive any neurocognitive assessments (16.1%), and nearly 1 in 4 did not receive a structural imaging or AD-specific biomarker test (23.7%). AD-specific biomarker tests were more common among patients aged ≥65 (87.1% versus 75.3%; $p < 0.05$). Less than 1 in 4 patients were referred for cognitive/behavioral concerns.
Conclusions: As the diagnostic and treatment landscape changes, education on symptom recognition, and physician training on new technologies may facilitate timely diagnoses and improve patient outcomes.

Keywords

Alzheimer's disease, biomarker, MCI detection, mild cognitive impairment, neurocognitive assessment

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Introduction

The prevalence of Alzheimer's disease (AD) in the United States is projected to double by 2050 due to an aging population, placing a substantial burden on caregivers and the healthcare system.[1,2] The AD continuum can be divided into preclinical AD, mild cognitive impairment (MCI) due to AD, which is the first symptomatic stage of the disease, and mild, moderate, and severe AD dementia.[1,3] Approximately 5.7 million Americans are estimated to have MCI due to AD.[4] Among them, about 15% develop AD dementia within two years, and approximately one-third do so within five years.[5,6]

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MCI due to AD and mild dementia due to AD (i.e., "mild AD"), collectively referred to as early AD, have been highlighted as focal points for early intervention.[3] Disentangling AD symptoms from the normal aging process can be challenging, particularly in the early stages of the disease, and the lack of a uniform, objective diagnostic approach can further complicate timely detection.[7] As a result, the condition often remains underrecognized until it progresses to later stages.[7,8]

In light of new therapies, which work by slowing disease progression in the early stages of disease, a timely diagnosis, particularly during the earlier stages of disease, represents a critical window when intervention can be initiated.[9] Likewise, a delayed diagnosis may mean the inability to initiate classes of treatments such as amyloid-beta therapies, intended to slow progression of the disease. Despite the importance of early identification, studies show that only 8% of patients with MCI receives a diagnosis, and less than 18% of individuals in the US is familiar with MCI, indicating a need for increased awareness.[10,11] Furthermore, disparities within the diagnostic process have been observed. Individuals who are Black or Hispanic are more likely to have a missed or delayed diagnosis, and are more likely to receive a diagnosis at a more advanced stage.[12]

Some of the barriers to a timely diagnosis posited by physicians include limited time during patient visits for a thorough cognitive assessment, high costs of new screening and specialized imaging tests, and limited access to these tests.[13,14] Such obstacles may disproportionately affect primary care physicians (PCPs), who are often the first clinicians to evaluate and identify dementia symptoms.[15,16] While these challenges may impact the accurate and timely diagnosis of early AD, they are not unique to the diagnostic process, and may persist throughout the care continuum. Referrals to specialists can help provide comprehensive and individualized care to patients. Collaboration across specialties is important to improve quality of care and outcomes for patients.[17] Referrals to community support services were cited as the most valuable navigation offering for patients with AD by approximately 68% of health care workers (i.e., medical and non-medical professionals).[1] Yet, less than 30% of healthcare physicians felt they were very knowledgeable in directing patients and caregivers to the appropriate health care resources.[1] Earlier linkage to care services may help patients and caregivers better navigate the course of disease from the initial stages of symptoms through care management and treatment.

While knowledge of the assessment and management of early AD is limited, the rapidly changing landscape of novel therapies which target early AD has compounded the need for a broader understanding of how early AD is diagnosed, especially in the community-based setting where most patients are seen. Investigating the use of clinical and cognitive assessments, referrals, and use of treatments across physician specialties can be used to understand gaps in quality of care and inform changes towards a timely AD diagnosis and treatment. Our study sought to understand the patient journey and highlight potential unmet needs for patients with MCI due to AD and mild AD in community-based primary care and neurology settings in the US.

Methods

Study design and participants

This retrospective study recruited 324 PCPs (N = 177) and neurologists (N = 147) through a verified physician panel in the US with broad national representation to abstract patient charts. Community-based PCPs or neurologists (i.e., their primary practice setting is not academic or a teaching hospital), practicing in the US for ≥3 years were eligible. Physicians were also required to have treated ≥15 early AD patients in the past 12 months, including ≥2 patients with MCI due to AD, and ≥1 patient with mild AD. Each participating physician extracted data from patient charts (i.e., medical records) using a uniform electronic case report form (eCRF). The target study population comprised patients aged 50–89 years old with a new diagnosis of MCI due to AD or mild AD within the previous 2 years, and who had a clinic visit within the past 12 months. Data were collected in August and September 2023. Our study did not involve interactions with or interventions on human subjects and all data were de-identified per US federal regulations (45 CFR 46, 102(f))20), thus it was exempt from institutional review board review, consent requirements, and registration.

Study procedures

Physicians were asked to abstract between 3–5 patient charts, including 2–4 charts from patients with MCI due to AD, and 1–3 charts from patients with mild AD. Data collected included patient demographic and clinical characteristics, information about the diagnostic process, referral information, use of treatments, and the frequency of follow-up visits. The eCRF included branching and skip logic to reduce survey burden. All questions were closed-ended, except those requiring a continuous numeric response (i.e., patient age at diagnosis and number of referrals).

Statistical analyses

Descriptive statistics were generated for all patient characteristics and outcomes. Outcomes of interest included the use of neurocognitive assessments, AD-specific biomarker tests, structural imaging tests, apolipoprotein E4 (*APOE* ϵ4) genetic testing, referrals to dementia care specialties, including memory care clinics, and AD treatments. AD-specific biomarker tests were defined as the receipt of

any of the following: tau positron emission topography (PET) scan, cerebrospinal fluid (CSF) tests, blood test for AD pathology, or amyloid PET scan. Structural imaging tests were defined as the receipt of any of the following: fluorodeoxyglucose PET (FDG-PET) scan, magnetic resonance imaging (MRI), functional MRI (fMRI), computerized tomography (CT) scan, or diffusor tension imaging (DTI).

Continuous variables were summarized using means with standard deviations (SD) and medians with interquartile ranges, and categorical variables were summarized using frequency counts and percentages. T-tests were used to compare the means for continuous variables, and chi-square or Fisher's exact tests were used to compare categorical variables. Descriptive statistics for the main results were stratified by patient diagnosis (i.e., MCI due to AD or mild AD). Several subgroup analyses were assessed to identify areas of unmet need and better understand the potential variability of care across these key demographics: patient age at diagnosis, patient sex, patient race, and patient's geographic location of residence.

All data were analyzed using SAS Enterprise Guide (version 7.1) and R statistical software (version 4.2.1).

Results

Patient demographics

Overall, 1284 patient charts were abstracted, representing 817 and 467 patients, who were newly diagnosed with MCI due to AD and mild AD, respectively. Patient demographics by diagnosis are shown in Table 1. The mean age at diagnosis was 70.2 years, and 43.1% of patients were female. Approximately 67.2% were identified as White, and 31.4% were identified as other races (i.e., 17.0% Black, 10.0% Asian, 2.2% American Indian or Alaska Native, 0.8% Native Hawaiian or Other Pacific Islander, 1.4% Other, and 1.9% Unknown). The majority of patients lived in a private residence with a family member or caregiver (76.4%), in a suburban or urban area (80.9%), and had Medicare insurance coverage (74.4%). The demographic and clinical characteristics of patients with MCI due to AD and those with mild AD were broadly similar, although patients with MCI due to AD were slightly younger than patients with mild AD (69.8 years versus 71.1 years; $p < 0.001$).

Initial presentation of symptoms, use of neurocognitive assessments, AD-specific biomarker tests and structural imaging tests

In 67.2% of patients, the initial symptom that triggered the diagnostic process was memory concerns stated by family members or caregivers, and patient self-reported symptoms for 54.1% of them (Figure 1). Memory complaints from a family member or caregiver were more common among patients with mild AD (71.9% versus 64.5%; $p < 0.01$), while self-reported memory concerns were more common among patients with MCI due to AD (56.8% versus 49.5%; $p < 0.05$).

The Mini-Mental State Examination (MMSE) was the most commonly used standard neurocognitive assessment (48.1%), followed by the Clock Drawing Test (24.1%), and the Montreal Cognitive Assessment (MoCA) (20.3%); 16.1% of patients did not receive any standard neurocognitive assessments, and only 10.8% of patients received the Mini-Cog (Figure 2). No significant differences in the use of specific neurocognitive assessments across conditions were detected. When stratified by race, patients of other races were less likely to receive a neurocognitive assessment (80.1% versus 85.5%; $p < 0.05$) (Supplemental Table 1). Use of the MoCA was more common in rural settings (28.2% versus 19.9%; $p < 0.01$), while use of the Alzheimer's Disease Assessment Scale – Cognitive (ADAS-Cog) was more common in urban or suburban settings (19.2% versus 11.6%; $p < 0.01$) (Supplemental Table 2).

Nearly a quarter of patients did not receive a structural imaging test (24.1%). Among those who did, MRI was the most frequently used structural imaging test for both conditions (63.4% for MCI and 63.6% for mild AD), followed by CT scans (18.7% for MCI and 17.3% for mild AD). AD-specific biomarker tests were used less frequently, with 84.6% of patients not receiving an AD-specific biomarker test. While amyloid PET scans were the most commonly used test, they were used in less than 10% of patients (8.1% for MCI due to AD and 8.6% for mild AD). However, among those who received an amyloid PET scan, 84.0% had an abnormal result. Likewise, few patients (6.6%) received a blood test for AD pathology and/or neurodegeneration (e.g., $A\beta_{42/40}$ ratio or PrecivityAD®), and only 3.3% of patients received a CSF test for AD pathology and/or neurodegeneration. Taken together, nearly a quarter of patients (23.1%) did not receive either a structural imaging tests or an AD-specific biomarker test (24.6% for MCI due to AD and 20.6% for mild AD) (Figure 3). No significant differences in the use of structural imaging and AD-specific biomarker tests across conditions were observed.

AD-specific biomarker tests appeared to be used more frequently used among patients aged <65 years old at the time of diagnosis compared to patients ≥65 years old (24.7% versus 12.9%; $p < 0.001$) (Supplemental Table 3). However, patients <65 years old received fewer structural imaging tests than patients ≥65 years old (70.2% versus 77.4%; $p < 0.05$). AD-specific biomarker (16.7% versus 10.6%; $p < 0.05$) and structural imaging tests (78.1% versus 70.4%; $p < 0.05$) were more commonly used when the patient's residence was located in an urban/suburban setting compared to rural locations.

Only 18.3% of patients received an *APOE* ϵ4 genetic test; among them, 52.8% were identified as carriers. Physicians reported cost or insurance concerns as the

Table 1. Patient demographics and clinical characteristics Among patients with MCI due to AD and mild AD.

	Overall N = 1284	MCI due to AD N = 817	Mild AD N = 467	p[a]
Patient demographics				
Mean age at diagnosis (SD)	70.2 (7.9)	69.8 (7.9)	71.1 (7.9)	<0.01 *
Sex				
Male	724 (56.4)	471 (57.6)	253 (54.2)	0.25
Female	554 (43.1)	342 (41.9)	212 (45.4)	0.24
Unknown	6 (0.5)	4 (0.5)	2 (0.4)	1.00
Living arrangement, n (%)				
Private residence (with family or caregiver)	981 (76.4)	622 (76.1)	359 (76.9)	0.82
Private residence (alone)	225 (17.5)	151 (18.5)	74 (15.8)	0.26
Institution	48 (3.7)	25 (3.1)	23 (4.9)	0.12
Unknown	28 (2.2)	17 (2.1)	11 (2.4)	0.90
Other	2 (0.2)	2 (0.2)	0 (0.0)	0.54
Educational attainment, n (%)				
High school diploma or equivalent	347 (27.0)	214 (26.2)	133 (28.5)	0.41
Bachelor's degree	301 (23.4)	209 (25.6)	92 (19.7)	<0.05 *
Some college or associate's degree	239 (18.6)	152 (18.6)	87 (18.6)	1.00
Advanced degree (master's, professional, or doctoral degree)	104 (8.1)	74 (9.1)	30 (6.4)	0.12
Less than a high school diploma	125 (9.8)	70 (8.5)	55 (11.8)	0.08
Unknown	168 (13.1)	98 (12.0)	70 (15.0)	0.15
Geographic location of clinic where diagnosis was made, n (%)				
Suburban/Urban	1098 (85.5)	706 (86.4)	392 (84.0)	0.26
Rural	163 (12.7)	96 (11.8)	67 (14.3)	0.21
Unknown	23 (1.8)	15 (1.8)	8 (1.7)	1.00
Patient race, n (%)[b]				
White	863 (67.2)	554 (67.8)	309 (66.2)	0.59
Black or African American	218 (17.0)	133 (16.3)	85 (18.2)	0.42
Asian	129 (10.0)	90 (11.0)	39 (8.4)	0.15
American Indian or Alaska Native	28 (2.2)	15 (1.8)	13 (2.8)	0.36
Native Hawaiian or Other Pacific Islander	10 (0.8)	4 (0.5)	6 (1.3)	0.18
Other	18 (1.4)	13 (1.6)	5 (1.1)	0.61
Unknown[c]	25 (1.9)	14 (1.7)	11 (2.4)	0.55
Ethnicity, n (%)				
Not Hispanic/Latino	1071 (83.4)	686 (84.0)	385 (82.4)	0.53
Hispanic/Latino	115 (9.0)	68 (8.3)	47 (10.1)	0.34
Unknown	98 (7.6)	63 (7.7)	35 (7.5)	0.98
Insurance type, n (%)				
Medicare	955 (74.4)	590 (72.2)	365 (78.2)	<0.05 *
Private health insurance	292 (22.7)	199 (24.4)	93 (19.9)	0.08
Medicaid	107 (8.3)	63 (7.7)	44 (9.4)	0.34
Other	4 (0.3)	4 (0.5)	0 (0.0)	0.30
Unknown[c]	25 (1.9)	17 (2.1)	8 (1.7)	0.80
Patient was not insured[c]	17 (1.3)	13 (1.6)	4 (0.9)	0.32

AD: Alzheimer's disease; IQR: inter-quartile range; MCI: mild cognitive impairment; SD: standard deviation.
[a]T-tests were used to compare means for continuous variables and chi-square or Fisher's exact tests were used to compare categorical variables. Significance was defined as a p-value of <0.05, denoted with an asterisk (*).
[b]A total of 7 patients indicated two races. Percentages shown allows for summary of all selections.
[c]This response option was exclusive.

main reason for not performing *APOE* ϵ4 testing (55.2%), followed by uncertainty of the clinical utility (46.2%). The median time between an initial visit and receipt of a diagnosis was 4.0 months for both conditions, corresponding to an average of approximately 2.7 physician visits (Table 2). Patients of other races had a slightly longer time to diagnosis compared to patients of White race (median: 4.0 versus 3.0 months; $p < 0.01$). Patients <65 years had more visits between the initial visit and receipt of diagnosis compared to patients ≥65 years (median: 3.0 versus 2.0 visits; $p < 0.001$).

Patient referral and treatment patterns

Approximately 22.8% of patients were referred to another physician for cognitive or behavioral concerns, and 70.3%

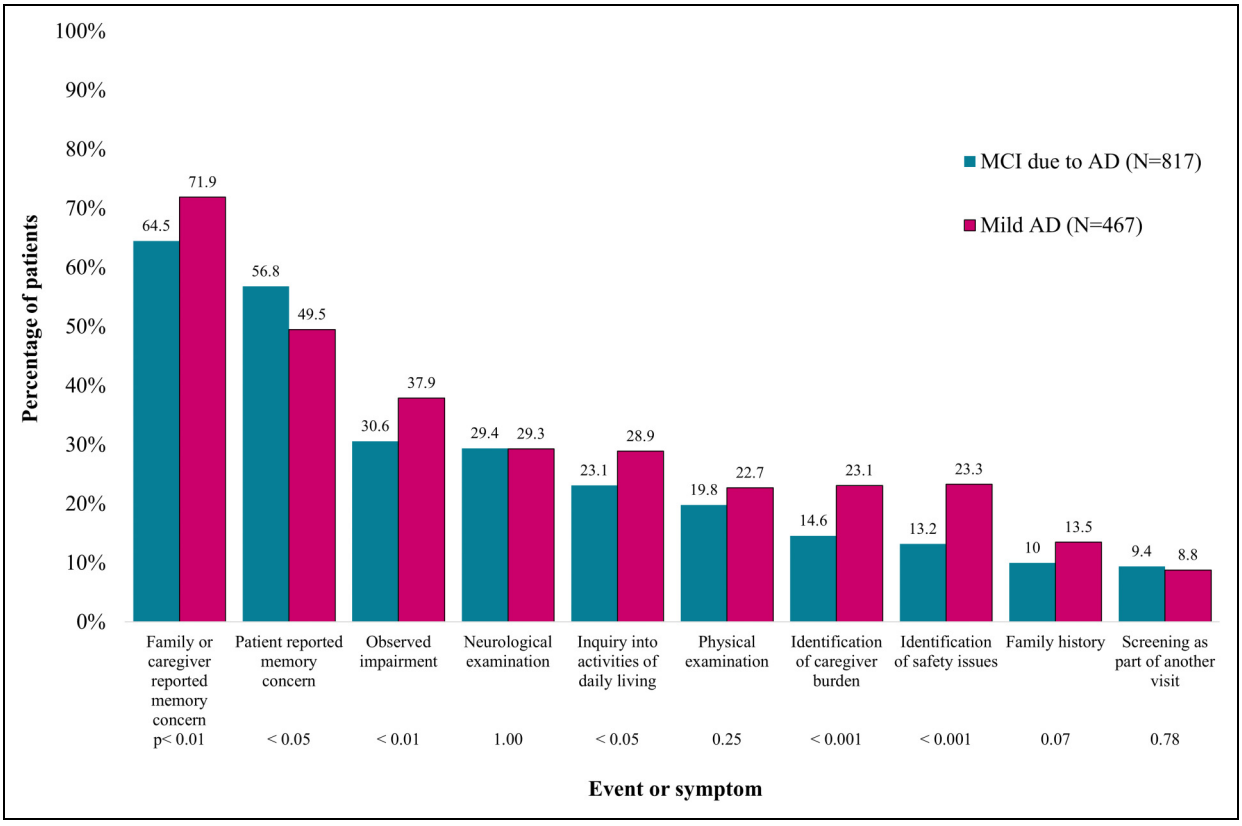

Figure 1. Initial event or symptom that triggered diagnostic process by diagnosis. AD, Alzheimer's disease; MCI, mild cognitive impairment.

were seen within three months (Table 2). Memory decline was the top reason for a referral for patients with MCI due to AD and mild AD (61.8% versus 58.3%; $p = 0.63$) (Figure 4). PCPs referred more patients to other physicians than neurologists (31.3% versus 13.2%; $p < 0.001$). Among patients who received a referral, more patients with mild AD were referred to a neurologist (61.7% versus 58.4%; $p = 0.66$), while more patients with MCI due to AD were referred to a neuropsychologist (38.2% versus 33.0%; $p = 0.44$). Other referral targets, such as memory clinics, geriatricians, social workers, and other settings, were infrequently selected (Supplemental Figures 1a and 1b).

Approximately 75.6% of patients with MCI due to AD and 89.5% of patients with mild AD were prescribed AD medications (Table 2). Donepezil was the most frequently prescribed medication, particularly among patients with mild AD (66.6% versus 59.0%; $p < 0.001$). Monoclonal antibody agents targeting amyloid-beta were infrequently prescribed, with only 5.9% of patients with MCI due to AD and 5.4% of patients with mild AD receiving a monoclonal antibody agent targeting amyloid-beta (i.e., either aducanumab or lecanemab; $p = 0.79$). Monoclonal antibody agents targeting amyloid-beta were prescribed more frequently among patients <65 years (15.6% versus 3.0%; $p < 0.001$). Patients in rural areas were less likely to be prescribed monoclonal antibody agents targeting amyloid-beta than patients in urban/suburban areas (6.5% versus 2.3%; $p < 0.05$) (Supplemental Table 2).

Discussion

The need to identify AD in earlier stages and address disparities in the diagnostic process is increasingly important in light of emerging therapies that are likely more effective when used in earlier stage disease. Thus, a delayed diagnosis may mean a missed opportunity for patients to potentially benefit from newer classes of therapies that may have helped to reduce disease progression.[9] Notable findings from our study emphasize the low use of diagnostic tools when diagnosing early AD, with nearly 1 in 5 patients not receiving a neurocognitive assessment, and 1 in 4 patients not receiving a structural imaging test. Additionally, 84.6% of patients did not receive an AD-specific biomarker test, which are more sensitive to AD pathology, and nearly 1 in 4 patients did not receive either a structural imaging or AD-specific biomarker test. Our findings suggest potential opportunities to promote consistent use of diagnostic tools and technologies, such

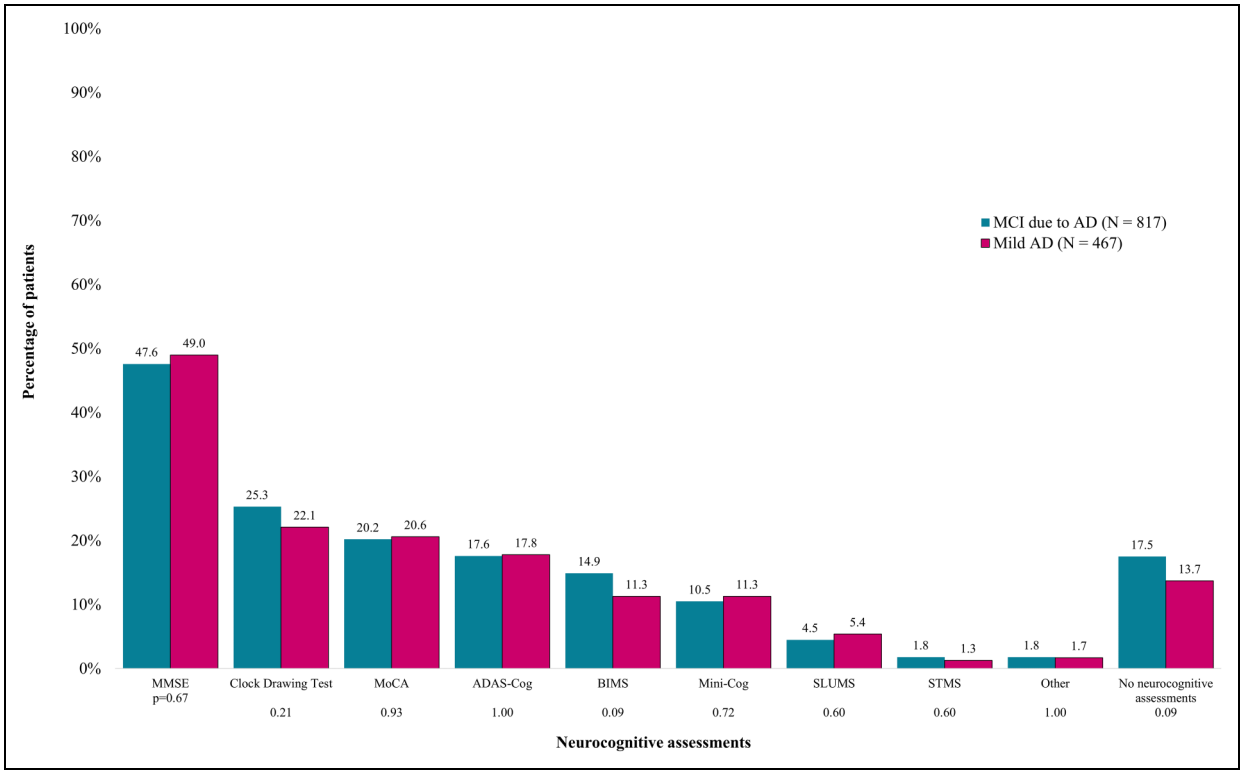

Figure 2. Neurocognitive assessments used during the diagnostic process by diagnosis. AD: Alzheimer's disease; ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale; BIMS: Brief Interview for Mental Status; MCI: mild cognitive impairment; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; SLUMS: Saint Louis University Mental Status Exam; STMS: Short Test of Mental Status.

as neurocognitive assessments, structural imaging, and even blood-based biomarkers through education and improved access. Patient education as a means to advocate for care, and efforts to improve access to diagnostic technologies - especially as new technologies become available, may help close the gaps documented in our study, as well as the supporting literature.

Clinical practice guidelines recommend the use of validated neurocognitive assessments for the standardized measurement of various cognitive domains and to help differentiate cognitive impairments due to early AD from the normal ageing process.[18,19] While no singular cognitive assessment has been identified as the best assessment to identify MCI/dementia, studies suggest that brief objective measures (such as the Mini-Cog) may be more sensitive to mild AD, and are faster and easier to administer, making them ideal for care settings where time constraints may otherwise limit the diagnostic process.[19,20] Yet, our study found that the Mini-Cog was used in less than 11% of patients, while options such as the MMSE and MoCA recommended as a comprehensive neuropsychological screening tools, were used in less than 50% and 21% of patients, respectively. Furthermore, approximately 16% of patients with early AD did not receive a neurocognitive assessment during the diagnostic process. In addition, despite known increases in the risk of developing AD among racial minority groups, our study observed that patients of White race were more likely to receive neurocognitive assessments than patients of other races.[12]

Clinical guidelines also recommend biomarker and imaging tests as part of a multi-tiered approach for patients with suspected MCI.[21] More than half of the patients in our study (63.5%) received an MRI, which has historically been used to rule-out structural processes, such as past stroke, normal pressure hydrocephalus or brain tumors, as etiology treatable of cognitive decline.[22] Although MRI is increasingly being used in research settings to identify characteristic patterns of cerebral alteration, its use in clinical practice for identifying early AD is still limited.[22] Several new tests that are specific for neurodegenerative processes, such as amyloid PET and tau PET scans, may offer improved diagnostic confidence for detecting early AD. In particular, amyloid PET has shown improved sensitivity over tau PET in the early phases of an AD diagnosis, as amyloid is the first biomarker to become abnormal during the AD course.[23] Our study found less than 10% of patients diagnosed with early AD received an amyloid PET or tau PET scan. While prior debates on the utility of amyloid PET scans may have been influenced by a lack of available treatments that alter the disease course, the introduction of

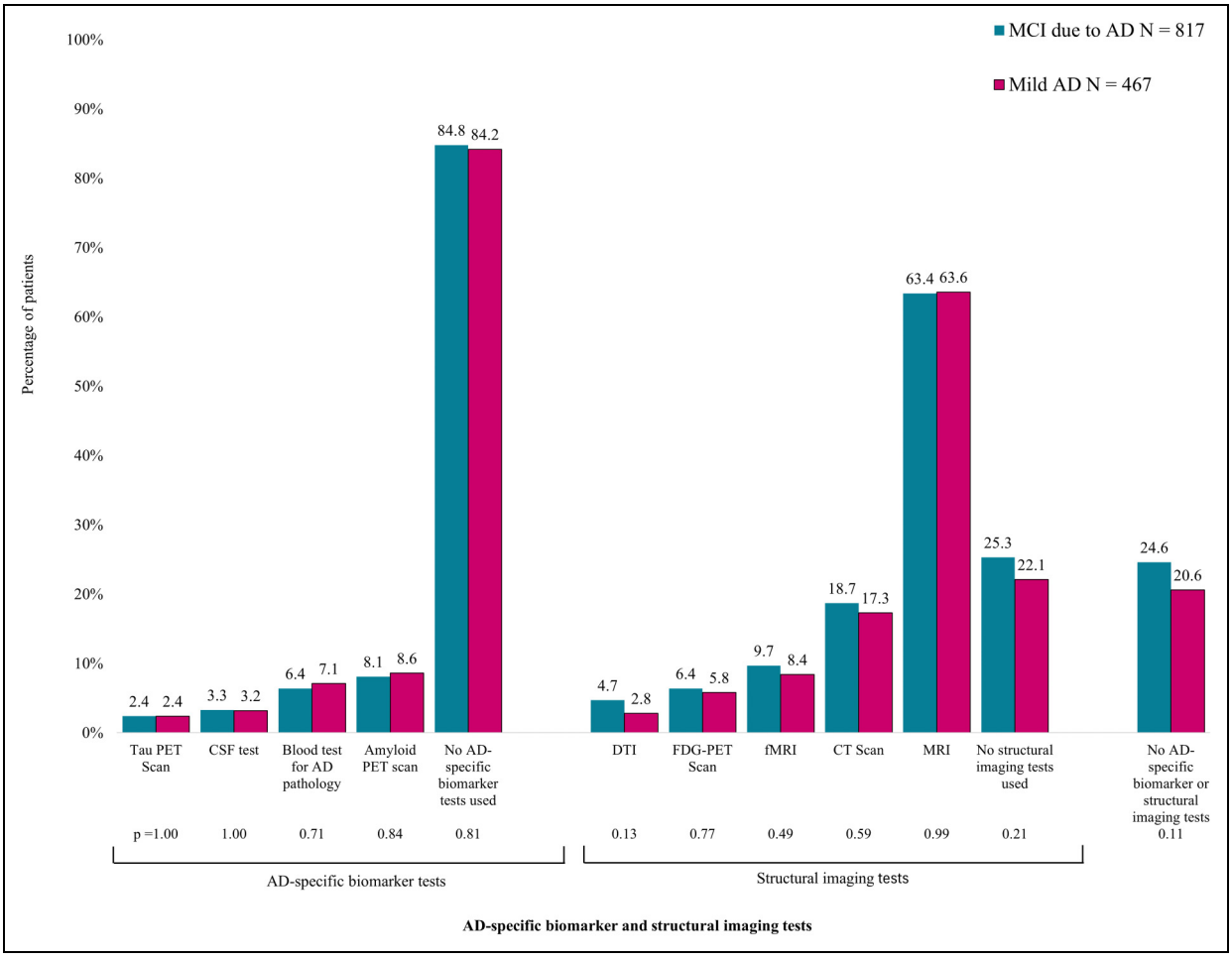

Figure 3. Biomarkers and imaging tests used during the diagnostic process by diagnosis. CSF: cerebrospinal fluid; CT: computerized tomography; DTI: diffusion tensor imaging; FDG-PET: fluorodeoxyglucose-positron emission tomography; MRI: magnetic resonance imaging. [1] Among patients who received an amyloid PET scan, 53 (80.3%) of patients with MCI due to AD, and 36 (90%) patients with mild AD had an abnormal result.

new monoclonal antibody agents that target amyloid-beta has resulted in shifting views, as evidenced by the recent decision by the Centers for Medicare and Medicaid Services to expand access to coverage for amyloid PET scans in October 2023.[24]

The recent approvals of blood-based biomarkers offer an additional promising, more accessible option for assessing AD pathology, with studies supporting equivalency to the more invasive CSF testing.[25] One study found that 72% of caregivers favored blood-based biomarker tests for an AD diagnosis, with a significant increase in favorability when such tests were linked to improved prospects of treatment.[26] While the observed utilization of these tests in our study was low, the timing of our study coincided with their early introduction and the ongoing development of cost and reimbursement policies. Therefore, it is possible that this use could be perceived as high given the timing of data collection. Blood-based biomarker tests may also be more feasible to conduct at the point of care and do not require specialized on-site facilities, allowing for expanded access, and reducing overall time to diagnosis. These benefits can have a heightened impact in resource constrained environments, allowing for a quick, cost-effective tool that may reduce cost burden on patients and health plans, and help to minimize disparities in care through their expanded accessibility.[27] Nearly a quarter of patients in rural areas in our study did not receive any biomarker or imaging tests, suggesting a critical need for expanded access. Findings from our study and supporting literature suggest that while biomarker and imaging tests could offer earlier and more reliable detection, access to these tests is still limited by cost considerations and physician understanding of their clinical utility, heightening the need for new reimbursement options and additional clinical training. Further, as new technologies become available, efforts focused on expanding access are critical, as to not widen the gap in existing disparities. Proper implementation efforts of easier to use, and more feasible technologies, should help to close such gaps.

Table 2. Diagnostic, referral, and treatment patterns stratified by diagnosis.

	Overall N = 1284	MCI due to AD N = 817	Mild AD N = 467	p[a]
Diagnostic and Referral Process				
Time between initial visit and diagnosis, mean (SD)				
Number of visits between initial visit and diagnosis[b]	2.7 (1.6)	2.6 (1.7)	2.7 (1.4)	0.65
Number of months between initial visit and diagnosis[b]	4.9 (4.5)	4.9 (4.7)	4.9 (4.2)	0.78
Patient was referred to another provider for cognitive/behavioral concerns, n (%)	293 (22.8)	178 (21.8)	115 (24.6)	0.27
Months between initial date of referral and date the patient saw the referral, n (%)				
≤ 1 month	72 (24.6)	43 (24.2)	29 (25.2)	0.56
2–3 months	134 (45.7)	85 (47.8)	49 (42.6)	1.00
>3 months	84 (28.6)	48 (27.0)	36 (31.3)	0.25
Patient received APOE ϵ4 test				
No	920 (71.7)	586 (71.7)	334 (71.5)	0.99
Yes	235 (18.3)	147 (18.0)	88 (18.8)	0.76
Physician not familiar with *APOE4* testing	80 (6.2)	51 (6.2)	29 (6.2)	1.00
Unknown	49 (3.8)	33 (4.0)	16 (3.4)	0.69
Among patients not tested for APOE ϵ4: Reasons for not testing[c]				
Cost or insurance concerns	508 (55.2)	321 (54.8)	187 (56.0)	0.77
Unsure of clinical utility or will not alter treatment options	425 (46.2)	266 (45.4)	159 (47.6)	0.56
Does not provide clinical insight specific to mild AD/MCI	179 (19.5)	112 (19.1)	67 (20.1)	0.79
Test accuracy or reliability concerns	150 (16.3)	97 (16.6)	53 (15.9)	0.86
Not familiar with test or not trained in its use or interpretation	107 (11.6)	66 (11.3)	41 (12.3)	0.72
Concerns about ordering process (e.g., unsure how to order)	69 (7.5)	46 (7.8)	23 (6.9)	0.69
Treatment Patterns				
Patient did not receive any treatment for early AD[d]	248 (19.3)	199 (24.4)	49 (10.5)	<0.001*
Donepezil (Aricept)	793 (61.8)	482 (59.0)	311 (66.6)	<0.01*
Monoclonal antibody agents that target amyloid-beta[e]	73 (5.7)	48 (5.9)	25 (5.4)	0.79

AD: Alzheimer's disease; IQR: inter-quartile range; MCI: mild cognitive impairment; SD: standard deviation.
[a]T-tests were used to compare means for continuous variables and chi-square or Fisher's exact tests were used to compare categorical variables. A significant difference of <0.05 was denoted with an asterisk (*).
[b]The median number of visits for each sample was 2.0 months. The median number of months between the initial visit and diagnosis was 4.0 months for MCI due to AD versus 3.0 months for mild AD.
[c]Assessed only among patients who were not tested for *APOE* ϵ4; A total of N = 586 patients with MCI due to AD and N = 334 patients with mild AD did not receive an *APOE* ϵ4 test.
[d]Treatments included: donepezil, memantine, memantine and donepezil, rivastigmine patch, rivastigmine oral, galantamine, aducanumab, and lecanemab.
[e]Monoclonal antibody agents targeting amyloid-beta was defined as the receipt of aducanumab or lecanemab.

Throughout the diagnostic and treatment process, patient access to an interdisciplinary care team to help navigate their disease course is key, from the diagnostic process through treatment and management to support their complex needs and provide educational opportunities. In our study, only 6.5% of all patients were referred to a memory clinic, and only 3.4% were referred to a social worker or other community support. These trends may highlight a potential need to expand interdisciplinary care options for patients with early AD, which have been shown to help patients and caregivers understand the diagnostic process, provide specialized knowledge and expertise, and improve care outcomes.[28] As physicians often have limited time, care linkage to other resources and the incorporation of individuals such as care navigators may allow for a more comprehensive, and potentially earlier diagnosis. Only three-quarters of patients treated by PCPs were referred to a neurologist in our study, highlighting the importance of closing gaps in the knowledge, skills, and resources of PCPs who manage patients with early AD and facilitate the implementation of biomarker testing in primary care settings.

Physicians reported the median time from initial presentation to receipt of a diagnosis as 4 months, or 3 visits, and noted that patients and caregivers most often initiated the diagnostic process. Shifting the detection and diagnosis of AD from moderate and severe stages of dementia to earlier disease periods has many documented benefits for patients, their caregivers, and society, including better disease management, preserving patient autonomy, and the implementation of more coordinated treatment plans.[3,13,29,30] Earlier AD treatment also has a long-term economic impact. One assessment reported a 17% decrease in net economic benefit, defined using a combination of healthcare costs and quality-adjusted life years, for every year that symptomatic treatment was delayed in patients with AD.[31] The integration of collaborative approaches such as linkage to care navigator may help facilitate sociocultural awareness

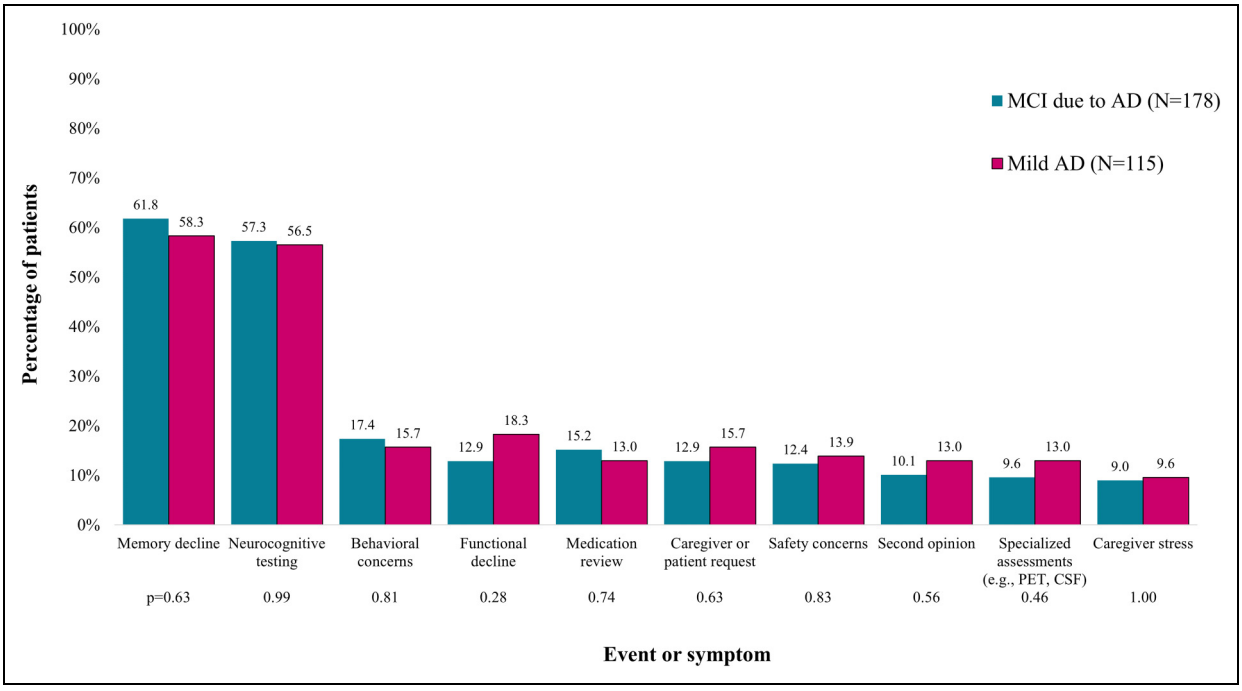

Figure 4. Reasons for referral to another provider stratified by diagnosis. AD: Alzheimer's disease; CSF: cerebrospinal fluid; MCI: mild cognitive impairment; PET: positron emission tomography.

of patient barriers to care, including providing educational opportunities so that patients and caregivers may more readily recognize AD dementia symptoms, and can engage in care. Likewise, such community-based resources can be used to identify and mitigate disparities in care. It is critical that as more novel therapies become available, physicians must be able to increase their capacity to identify patients with AD early in their disease, and that gaps in care related to sociodemographic factors are closed.

Strengths and limitations

As our study was a retrospective chart review study, the data presented relied on the accuracy of reporting by the physician who conducted the chart abstractions. Responses were also limited to response options available in the survey; therefore, it is possible physicians used other diagnostic tools that were not specifically addressed in the survey. Data not documented in the patient's medical chart was not considered. Given that the survey was voluntary and was a convenience sample, a risk of selection bias among participating versus non-participating physicians regarding the information they provided applies. Our study required physicians to have treated at least three early AD patients in the prior year, and therefore the results may not reflect practice patterns of all PCPs or neurologists who treat fewer patients with these conditions. However, our study provides insights into a broadly geographic national sample of community-based physicians who care for early AD patients and provides objective data on current practices and the patients they care for.

Conclusions

Nearly a fifth of patients with early AD did not receive a standard neurocognitive assessment and approximately one quarter of patients did not receive any AD-specific biomarker or structural imaging tests, despite clinical recommendations. Programs that shorten the time to diagnosis, promote appropriate referral consults and use of AD-specific biomarker and imaging tests may help reduce the time to detection and treatment of early AD. As the diagnostic and treatment landscape changes, there is a need for clinical pathways to guide the diagnostic and treatment of patients with early AD. Access to care and educational programs for patients, caregivers, and physicians may reduce the overall burden of AD.

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Statements and declarations

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Data availability

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

Supplemental material

Supplemental material for this article is available online.

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