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Original Research

# Diagnosis patterns among diverse populations with mild cognitive impairment and Alzheimer's disease in the USA

Olga Sánchez-Soliño *, Isabella Boroje, Emma Xiaomeng Yue, Lisa Vinikoor-Imler

*AbbVie Inc, North Chicago, IL, USA*

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ABSTRACT

*Background:* Rapid advancements in diagnostic biomarkers and criteria have created a complex and evolving environment for clinicians managing patients with cognitive complaints. Real-world data on current diagnostic processes used among diverse populations remains limited.
*Objectives:* This study aimed to investigate diagnostic patterns and use of diagnostic tests among U.S. adults with mild cognitive impairment, Alzheimer's disease, and/or dementia, stratified by gender, age, and race/ethnicity before clinical availability of blood-based biomarkers and the most recent diagnostic updates.
*Design:* Retrospective, observational cohort study.
*Setting:* The Optum® Market Clarity database from January 1, 2017, to September 30, 2021, was utilized.
*Participants:* 338,739 patients diagnosed with dementia, 81,267 with AD, and 179,419 with MCI were included in the analysis.
*Measurements:* Demographics information identified from electronic health records at the time of diagnosis was utilized. Occurrence and timing of diagnostic tests was pulled from insurance claims and electronic health records.
*Results:* Mean age at diagnosis was 69.3 years for MCI, 78.9 years for AD, and 78.6 years for dementia. Computerized tomography (CT) and magnetic resonance imaging (MRI) were used infrequently (MCI: MRI 16.6%, CT 17.5%; AD: MRI 9.0%, CT 18.4%; dementia: MRI 9.5%, CT 25.9%). Cerebrospinal fluid (CSF) biomarker tests and positron emission tomography (PET) were rarely used (MCI: PET 0.6%, CSF 1.6%; AD: PET 0.5%, CSF 0.9%; dementia: PET 0.2%, CSF 1.6%).
*Conclusions:* During the study period, diagnosis of MCI, AD, and dementia involved low use of brain imaging or CSF biomarkers, despite recommendations from guidelines. By better understanding how patients navigate their diagnostic journey in real-world settings, diagnostic practices can improve and faster support can be provided.

## 1. Introduction

When diagnosing patients presenting with cognitive decline, distinguishing between normal aging, mild cognitive impairment (MCI), Alzheimer's disease (AD), and other dementias can be difficult [1]. Neurodegenerative changes in the brain, including AD and the accumulation of amyloid, have been reported to have an onset up to 20 years before the diagnosis of dementia, and 4 years prior to MCI diagnosis [2,3].

MCI refers to a state in which the patient experiences a decline in short-term memory, with forgetfulness regarding recent events, which causes significant impairment in everyday functioning that relies on memory [4]. AD dementia is a further stage of cognitive decline and is the most common form of dementia [3,5,6]. AD has received significant attention regarding diagnostic criteria. In the last decade, the National Institute on Aging-Alzheimer's Association (NIA-AA) has developed diagnostic criteria, and a research framework [7], which allow the diagnosis of AD in living persons. The latest version of this framework recommends the use of blood biomarker-based techniques and positron emission tomography (PET) for diagnosis, and magnetic resonance imaging (MRI) for the identification of copathology [8].

With recent advances in diagnostic biomarkers and criteria [8], practitioners diagnosing and treating patients experiencing cognitive decline operate within a complex and evolving environment [1].

* Corresponding author at: AbbVie Inc, 1 N. Waukegan Road, North Chicago, 60064, IL, USA.
*E-mail addresses:* olga.sanchez@abbvie.com (O. Sánchez-Soliño), isabella.boroje@abbvie.com (I. Boroje), xiaomeng.yue@abbvie.com (E.X. Yue), lisa.vinikoorimler@abbvie.com (L. Vinikoor-Imler).

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Although there is some evidence for improving attitudes regarding the importance of a prompt diagnosis of MCI, AD, and other dementias, there is little information available detailing how recent changes have influenced diagnostic processes in real-world settings [1]. Surveys by the Alzheimer's Association reveal the impact of discrimination in dementia care, varying levels of trust from patients, and differences in concern and awareness about AD [5]. Additionally, racial disparities persist in both the health of patients and the health care provided. Knowledge gaps remain regarding the diagnosis patterns of MCI, AD, and dementia, including the extent to which biomarkers are used for diagnosis in the US, according to patient sex and race/ethnicity.

The objective of this study was to characterize diagnosis patterns among diverse patient groups in the US diagnosed with MCI, AD, and/or dementia using data extracted from electronic health records (EHRs) and insurance claims data to understand clinical diagnostic practices before clinical availability of blood-based biomarkers and the most recent NIA-AA diagnostic updates.

## 2. Methods

### 2.1. Data source

A retrospective observational cohort study using longitudinal patient-level data from Optum's Market Clarity Data (Market Clarity) was conducted. Market Clarity links medical and pharmacy claims with EHRs, including diagnosis codes and prescription information, for more than 63 million individuals from healthcare provider organizations with more than 700 hospitals and 7000 clinics across the US and captures point-of-care diagnostic data, including patient-level and clinical results from both inpatient and ambulatory settings. All 50 states in the US and all types of payors are represented in the database, including Medicare, Medicaid, commercial insurers, and self-pay/uninsured. All pertinent data available on patients within the cohort are provided back to 2007, and new patients are added to the cohort at each data refresh. The data include patient demographics, inpatient and outpatient visits, comprehensive laboratory data, medications prescribed and administered, and procedures.

The Optum data have been de-identified pursuant to the Health Insurance Portability and Accountability Act (HIPAA) and Optum, using the expert determination method, has documented the methods and results of the analysis that justify such determination as set forth in 45 C. F.R. 164.514 and the "Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the HIPAA Privacy Rule".

### 2.2. Study population

The study population included patients diagnosed with MCI, AD, and/or dementia. Cases were identified using the International Classification of Diseases, Ninth and Tenth Revisions (ICD-9-CM, ICD-10-M) diagnosis codes for MCI, AD, and dementia, and were utilized as follows: MCI - ICD-9: 331.83, ICD-10: G31.84; AD - ICD-9: 331.0, ICD-10: G30.0; Dementia - ICD-9: 290, 294.1, 294.2, 331.1, 331.82, ICD-10: F01, F02, F03, G31.0, G31.83.

The study period was from January 1, 2017, to March 31, 2022. Patients included in the study population were required to have at least one diagnosis code for MCI, AD, and/or dementia in their EHR or have at least two diagnosis codes separated by at least 30 days in insurance claims data during the study period. The date of first qualifying disease diagnosis was defined as the date of diagnosis. Patients had at least 12 months of continuous enrollment before the date of diagnosis (less than 45-day gap in coverage was allowed) and at least 1 day of continuous healthcare plan enrollment after the index date. Patients were also required to be at least 18 years of age prior to or including the date of diagnosis. Patients with both AD and dementia diagnoses were categorized based on the first of these two diagnoses; however, if an AD diagnosis was followed by a diagnosis of a specific type of dementia (e.g., Lewy body or frontotemporal dementia) then these patients were included in the dementia group.

### 2.3. Study variables

Information on age at the date of diagnosis, sex, and pre- and post-enrollment years were captured using the insurance claims and EHRs. The variables of race and ethnicity were taken from EHRs and combined to create the following categories: Hispanic (all races), Non-Hispanic Caucasian, Non-Hispanic African American, Non-Hispanic Asian, and Non-Hispanic Other/Unknown. These categories are referred to as Hispanic, Non-Hispanic Caucasian, African American, Asian and Other/Unknown in this study. The insurance claims and EHRs were also utilized to identify procedure codes for various brain imaging and biomarker diagnostic tests, including PET scans, MRI, computerized tomography (CT), and cerebrospinal fluid (CSF) tests. Further diagnoses were noted among patients with dementia or AD for whom their diagnosis switched after receiving their initial diagnosis.

### 2.4. Statistical analysis

The patient characteristics at baseline for each cohort were summarized using descriptive statistics. Continuous variables were expressed as the mean and standard deviation (SD), median, and range values, while categorical variables were expressed using frequencies and percentages.

Analyses were conducted utilizing data in the 12 months before and after the date of diagnosis. Study variables were stratified by sex, race/ethnicity, sex and race/ethnicity combined, and age.

Descriptive statistics were calculated using the SAS Studio 3.82 (SAS Institute Inc., Cary, NC, USA).

## 3. Results

### 3.1. Patient baseline demographics

A total of 179,419 newly diagnosed MCI cases, 81,267 AD cases, and 338,739 dementia cases were identified during the study period and met the inclusion criteria (Table 1). The majority of patients in the MCI, AD, and dementia cohorts were female (56.6%, 63.1%, and 60.3%, respectively; Table 1). The mean age at diagnosis in years was 69.3 $\pm$ 15.0 for MCI, 78.9 $\pm$ 8.8 for AD and 78.6 $\pm$ 9.6 for dementia (Table 1). Most identified in the database diagnosed with MCI, AD, and dementia were Non-Hispanic Caucasian (Table 1).

Patients were categorized based on their first diagnosis of AD or dementia recorded in the database. However, among the 81,267 patients with a first recorded diagnosis of AD, 34,745 later had a diagnosis code for dementia. Similarly, among the 338,739 patients with a first recorded diagnosis of dementia, 50,254 were later recorded as having a diagnosis code for AD.

### 3.2. Mean age at diagnosis stratified by race/ethnicity and sex

Further analysis stratified the mean age at diagnosis by race/ethnicity and sex (Fig. 1). The mean age at MCI, AD, or dementia diagnosis was similar overall according to sex, although very slightly higher for females among all race/ethnicity groups (Fig. 1). A trend was observed for the mean age at diagnosis when stratified by race/ethnicity; African American patients were generally the youngest group to receive MCI, AD, and dementia diagnoses (MCI: 63.6 years for males and 66.3 years for females; AD: 75.1 years for males and 77.7 years for females; dementia: 73.7 years for males and 76.4 years for males). On average, Non-Hispanic Caucasian patients received MCI, AD, and dementia diagnoses at a slightly later age than the other groups (MCI: 69.8 years for males, and 70.5 years for females; AD: 78.6 years for males and

**Table 1**
Baseline demographics of patients with newly diagnosed MCI, AD, and dementia identified between January 1, 2017, through March 31, 2022 in the Market Clarity database.

| Characteristic | MCI | AD | Dementia |
|---|---|---|---|
| Number of patients | 179,419 | 81,267 | 338,739 |
| Age, years | | | |
| Mean ± SD | 69.3 ± 15.0 | 78.9 ± 8.8 | 78.6 ± 9.6 |
| Median (min–max) | 73 (18–89) | 82 (18–89) | 82 (18–89) |
| Age Group, years, n (%) | | | |
| 18–44 | 13,613 (7.6%) | 436 (0.5%) | 2898 (0.9%) |
| 45–54 | 13,363 (7.5%) | 1,090 (1.3%) | 5,451 (1.6%) |
| 55–64 | 28,108 (15.7%) | 4,357 (5.4%) | 21,590 (6.4%) |
| 65–74 | 45,186 (25.2%) | 14,027 (17.3%) | 59,110 (17.5%) |
| 75–84 | 51,129 (28.5%) | 30,932 (38.1%) | 116,614 (34.4%) |
| 85+ | 28,020 (15.6%) | 30,425 (37.4%) | 133,076 (39.3%) |
| Sex, n (%) | | | |
| Male | 77,888 (43.4%) | 29,966 (36.9%) | 134,550 (39.7%) |
| Female | 101,531 (56.6%) | 51,301 (63.1%) | 204,189 (60.3%) |
| Race/Ethnicity, n (%) | | | |
| Hispanic | 6,083 (3.4%) | 2,810 (3.5%) | 11,073 (3.3%) |
| Non-Hispanic Caucasian | 119,076 (66.4%) | 52,193 (64.2%) | 217,062 (64.1%) |
| African American | 15,270 (8.5%) | 6,099 (7.5%) | 35,685 (10.5%) |
| Asian | 1,887 (1.1%) | 1,164 (1.4%) | 4,181 (1.2%) |
| Other/Unknown | 37,103 (20.7%) | 19,001 (23.4%) | 70,738 (20.9%) |
| Year of Index, n (%) | | | |
| 2017 | 41,867 (23.3%) | 21,747 (26.8%) | 88,987 (26.3%) |
| 2018 | 42,794 (23.9%) | 19,253 (23.7%) | 78,367 (23.1%) |
| 2019 | 43,260 (24.1%) | 18,169 (22.4%) | 75,836 (22.4%) |
| 2020 | 32,886 (18.3%) | 14,227 (17.5%) | 61,927 (18.3%) |
| 2021 | 18,612 (10.4%) | 7,871 (9.7%) | 33,622 (9.9%) |
| Pre-enrolment (years, mean ± SD) | 7.2 ± 3.7 | 7.3 ± 3.7 | 7.3 ± 3.7 |
| Post-enrolment (years, mean ± SD) | 2.0 ± 1.3 | 1.7 ± 1.3 | 1.6 ± 1.2 |

Abbreviations: AD, Alzheimer's disease; MCI, mild cognitive impairment; SD, standard deviation.

79.7 years for females; dementia: 78.2 years for males and 79.8 years for females; Fig. 1).

### 3.3. Use of brain imaging and CSF biomarkers

Brain imaging and CSF biomarker use among patients diagnosed with MCI, AD, and dementia is shown in Fig. 2. CSF biomarker use was low, with <2% of patients diagnosed with MCI, AD, or dementia each receiving these tests. MRI and CT scans were more frequent, with 16.6% of patients diagnosed with MCI receiving an MRI, and 17.5% receiving a CT scan, 9.0% and 18.4% of patients diagnosed with AD receiving an MRI or CT scan, and 9.5% and 25.9% of patients diagnosed with dementia receiving an MRI or CT scan. The proportion of patients receiving scans was similar between males and females. The proportion of patients diagnosed with MCI, AD and dementia receiving scans and biomarker tests was similar according to age group, and sex and race/ethnicity combined (Tables 2–4). Among sex and race/ethnicity groups, the highest proportion with CT scans was among African American males before diagnosis for MCI (14.9%), AD (10.6%), and dementia (15.0%; Tables 2–4). MRI scans were used most often on or after diagnosis. The highest proportion of use was among Asian females for MCI (14.8%) and among Asian males for AD (8.9%) and dementia (8.3%; Tables 2–4).

## 4. Discussion

This retrospective study investigated age at diagnosis and diagnostic tests utilized among patients diagnosed with MCI, AD, and/or dementia, stratified by age, sex, and race/ethnicity in a US clinical practice setting. The mean patient age at MCI diagnosis was lower than that of the AD and dementia cohorts. When stratified by race/ethnicity, the mean age at diagnosis was lowest among African American patients, and highest for Non-Hispanic Caucasian patients diagnosed with MCI, AD, or dementia.

The change in diagnoses between AD and dementia observed for some patients highlights the difficulty to diagnose accurately. The low usage of biomarkers and observed changes in dementia diagnosis can be interpreted as evidence of underlying structural diagnostic uncertainty, rather than simply the underuse of tests. This view was supported by recent studies showing that most dementia coding in community and primary care settings relies on non-specific diagnoses, with frequent code switching and diagnostic signal decline over time [9,10]. The limited sensitivity of general practitioner judgment and only moderate validity from newer diagnostic instruments further emphasize the need to understand these findings as a systems-level challenge in dementia care [11,12]. Overall, these patterns signal that ongoing diagnostic ambiguity, non-specific coding, and fluctuating diagnoses are rooted in structural issues rather than simple lapses in testing or documentation.

### 4.1. Use of brain imaging and CSF biomarkers for MCI, AD, and dementia diagnosis

This study assessed the proportion of individuals diagnosed with MCI, AD, and dementia with specific diagnostic tests, PET, MRI, CT, and CSF biomarkers, performed in the 12 months before or after diagnosis. The findings showed that despite recommendations provided in the AD Neuroimaging initiative, including standardized methods for many diagnostic tests [6], and the 2018 NIA-AA guidelines [7], brain imaging and biomarker use were low; however, MRI and CT scans were used more frequently than PET scans and CSF biomarkers. The proportion of individuals receiving scans was similar between males and females, and between different race/ethnicity groups.

The promising role of PET molecular imaging in diagnosing AD and MCI, as well as understanding the underlying pathology, has previously been highlighted [13]. In vivo imaging of dementia-related pathology with PET radioligands has multiple advantages, such as allowing for early detection by spotting initial molecular changes and improving differential diagnosis between AD and other neurodegenerative diseases [13]. These methods may also relate cognition to neurodegenerative processes and could act as markers for treatment effectiveness and potential therapeutic approaches [13]. Post-amyloid PET changes in patient diagnosis and treatment have previously been evaluated in an unselected memory cohort study, which included patients with MCI, AD, and dementia [14]. In this study, 24% of patients experienced changes in treatment post-PET, mainly involving additional investigations and therapy, while diagnostic confidence also increased post-PET [14]. Despite these potential advantages, the use of PET scans was not frequently observed in the present study.

### 4.2. Updated diagnostic guidelines and future directions for the diagnosis of MCI, AD, and dementia

The updated 2024 NIA-AA guidelines, published to guide research on AD, defined AD as a biological process measured by biomarker changes in the brain rather than clinical symptoms, beginning with AD neuropathologic change (ADNPC) while individuals are asymptomatic, progressing through increasing disease-related brain changes, and eventually leading to the development of clinical symptoms [8]. The

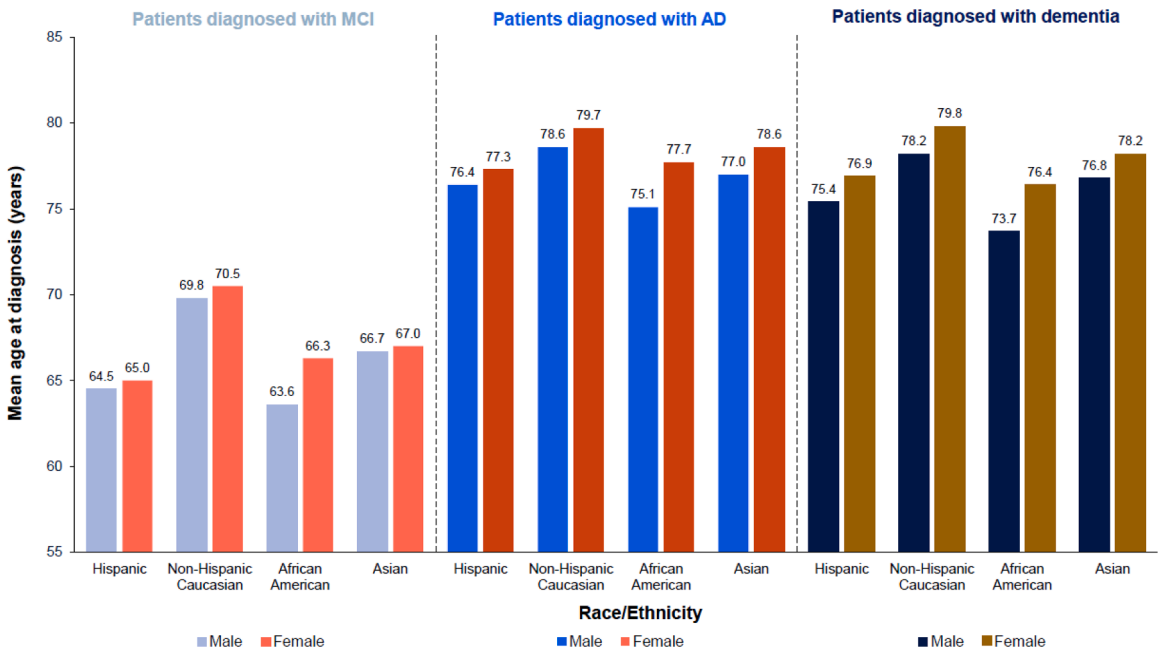


**Fig. 1.** Mean age at diagnosis among individuals diagnosed with MCI, AD, and dementia stratified by race/ethnicity and sex between January 1, 2017, through March 31, 2022, in the Market Clarity database.
Abbreviations: AD, Alzheimer's disease; MCI, mild cognitive impairment.

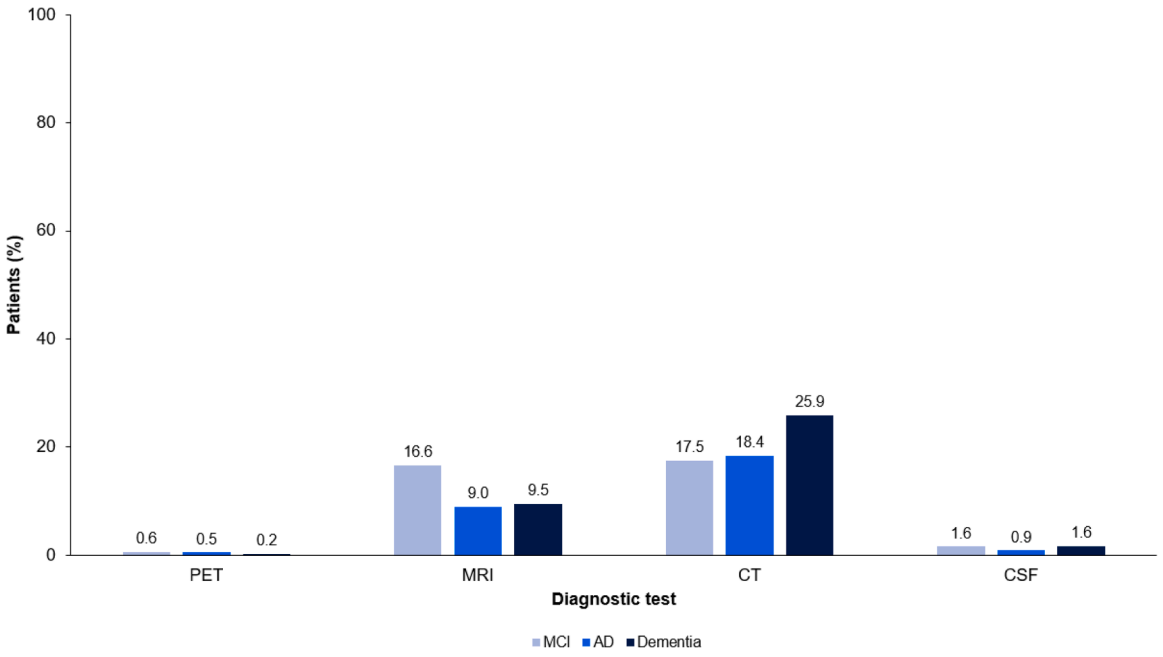


**Fig. 2.** Proportion of individuals diagnosed with MCI, AD, and dementia with specific imaging or biomarker diagnostic tests performed in the 12 months before or after diagnosis identified between January 1, 2017, through March 31, 2022, in the Market Clarity database.
Abbreviations: AD, Alzheimer's disease; CSF, cerebrospinal fluid; CT, computerized tomography; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; PET, positron emission tomography.

revised criteria provide general principles for diagnosing and staging AD. AD biomarkers are intended for evaluating symptomatic individuals and are not currently used for assessing AD-related brain changes in asymptomatic individuals for clinical care, though integrated plasma biomarkers are utilized in AD diagnosis and staging [8].

Plasma biomarkers were not available for the diagnosis of AD in the usual clinical practice in the study period of the present study, though little use of CSF biomarkers for diagnoses of MCI, AD, or dementia was observed. The updated NIA-AA guidelines include the use of future fully validated blood-based biomarkers [8]. Greater use of these biomarkers may result in improving diagnosis methods, and potential earlier diagnosis of MCI, AD and differential diagnosis with other types of dementia irrespective of sex or race/ethnicity.

**Table 2**
Brain imaging and biomarker use among patients diagnosed with MCI, stratified by age group, and sex and race/ethnicity combined identified between January 1, 2017, through March 31, 2022, in the Market Clarity database.

| Characteristic | PET | | MRI | | CT | | CSF | |
|---|---|---|---|---|---|---|---|---|
| | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis |
| Age Group, n (%) | | | | | | | | |
| 18–44 | 63 (0.5%) | 61 (0.5%) | 1,308 (9.6%) | 1,517 (11.1%) | 1,318 (9.7%) | 1,008 (7.4%) | 87 (0.6%) | 87 (0.6%) |
| 45–54 | 22 (0.2%) | 37 (0.3%) | 1,396 (10.5%) | 1,607 (12.0%) | 1,413 (10.6%) | 1,096 (8.2%) | 135 (1.0%) | 132 (1.0%) |
| 55–64 | 44 (0.2%) | 120 (0.4%) | 2,837 (10.1%) | 3,580 (12.7%) | 3,094 (11.0%) | 2,677 (9.5%) | 293 (1.0%) | 311 (1.1%) |
| 65–74 | 85 (0.2%) | 327 (0.7%) | 3,950 (8.7%) | 5,175 (11.5%) | 4,336 (9.6%) | 4,193 (9.3%) | 398 (0.9%) | 411 (0.9%) |
| 75–84 | 72 (0.1%) | 254 (0.5%) | 3,552 (7.0%) | 4,934 (9.7%) | 5,114 (10.0%) | 5,368 (10.5%) | 397 (0.8%) | 433 (0.9%) |
| 85+ | 21 (0.1%) | 50 (0.2%) | 1,276 (4.6%) | 1,512 (5.4%) | 3,582 (12.8%) | 3,886 (13.9%) | 219 (0.8%) | 199 (0.7%) |
| Sex and Race/Ethnicity, n (%) | | | | | | | | |
| Hispanic Male | <5 | 9 (0.4%) | 233 (9.6%) | 273 (11.3%) | 304 (12.6%) | 290 (12.0%) | 27 (1.1%) | 22 (0.9%) |
| Non-Hispanic Caucasian Male | 110 (0.2%) | 278 (0.5%) | 4,900 (9.3%) | 5,897 (11.2%) | 6,673 (12.7%) | 6,418 (12.2%) | 690 (1.3%) | 654 (1.3%) |
| African American Male | 8 (0.1%) | 12 (0.2%) | 491 (8.2%) | 624 (10.5%) | 888 (14.9%) | 817 (13.7%) | 60 (1.0%) | 63 (1.1%) |
| Asian Male | <5 | 9 (1.1%) | 79 (9.7%) | 115 (14.2%) | 86 (10.6%) | 89 (11.0%) | 5 (0.6%) | 6 (0.7%) |
| Hispanic Female | 9 (0.3%) | 7 (0.2%) | 319 (8.7%) | 390 (10.7%) | 351 (9.6%) | 316 (8.6%) | 43 (1.2%) | 27 (0.7%) |
| Non-Hispanic Caucasian Female | 81 (0.1%) | 247 (0.4%) | 5,979 (9.0%) | 7,416 (11.1%) | 8,033 (12.1%) | 7,586 (11.4%) | 541 (0.8%) | 585 (0.9%) |
| African American Female | 10 (0.1%) | 22 (0.2%) | 751 (8.1%) | 1,043 (11.2%) | 1,067 (11.5%) | 1,059 (11.4%) | 70 (0.8%) | 81 (0.9%) |
| Asian Female | <5 | 11 (1.0%) | 89 (8.3%) | 159 (14.8%) | 63 (5.9%) | 104 (9.7%) | 7 (0.7%) | 7 (0.7%) |

Abbreviations: CSF, cerebrospinal fluid; CT, computerized tomography; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; PET, positron emission tomography.
Optum requires reported sample sizes to be n≥5.

**Table 3**
Brain imaging and biomarker use among patients diagnosed with AD, stratified by age group, and sex and race/ethnicity identified between January 1, 2017, through March 31, 2022, in the Market Clarity database.

| Characteristic | PET | | MRI | | CT | | CSF | |
|---|---|---|---|---|---|---|---|---|
| | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis |
| Age Group, n (%) | | | | | | | | |
| 18–44 | <5 | <5 | 29 (6.7%) | 25 (5.7%) | 39 (8.9%) | 31 (7.1%) | <5 | 10 (2.3%) |
| 45–54 | <5 | 11 (1.0%) | 65 (6.0%) | 92 (8.4%) | 74 (6.8%) | 118 (10.8%) | 12 (1.1%) | 14 (1.3%) |
| 55–64 | 21 (0.5%) | 39 (0.9%) | 288 (6.6%) | 331 (7.6%) | 367 (8.4%) | 449 (10.3%) | 26 (0.6%) | 42 (1.0%) |
| 65–74 | 34 (0.2%) | 109 (0.8%) | 835 (6.0%) | 1,039 (7.4%) | 1,003 (7.2%) | 1,497 (10.7%) | 65 (0.5%) | 81 (0.6%) |
| 75–84 | 43 (0.1%) | 125 (0.4%) | 1,414 (4.6%) | 1,790 (5.8%) | 2,287 (7.4%) | 3,872 (12.5%) | 128 (0.4%) | 175 (0.6%) |
| 85+ | 12 (0.0%) | 35 (0.1%) | 684 (2.3%) | 982 (3.2%) | 2,708 (8.9%) | 4,621 (15.2%) | 100 (0.3%) | 154 (0.5%) |
| Sex and Race/Ethnicity, n (%) | | | | | | | | |
| Hispanic Male | <5 | <5 | 31 (3.3%) | 60 (6.4%) | 85 (9.0%) | 150 (15.9%) | <5 | 7 (0.7%) |
| Non-Hispanic Caucasian Male | 29 (0.2%) | 88 (0.5%) | 1,014 (5.1%) | 1,280 (6.5%) | 1,944 (9.9%) | 3,219 (16.3%) | 141 (0.7%) | 193 (1.0%) |
| African American Male | <5 | 7 (0.4%) | 93 (4.7%) | 133 (6.7%) | 208 (10.6%) | 298 (15.1%) | 8 (0.4%) | 14 (0.7%) |
| Asian Male | <5 | <5 | 17 (3.9%) | 39 (8.9%) | 30 (6.8%) | 73 (16.6%) | <5 | <5 |
| Hispanic Female | <5 | 11 (0.6%) | 72 (3.9%) | 108 (5.8%) | 138 (7.4%) | 236 (12.6%) | 5 (0.3%) | 11 (0.6%) |
| Non-Hispanic Caucasian Female | 41 (0.1%) | 127 (0.4%) | 1,526 (4.7%) | 1,827 (5.6%) | 3,164 (9.8%) | 5,045 (15.6%) | 135 (0.4%) | 191 (0.6%) |
| African American Female | <5 | 7 (0.2%) | 162 (3.9%) | 248 (6.0%) | 359 (8.7%) | 550 (13.3%) | 12 (0.3%) | 18 (0.4%) |
| Asian Female | <5 | <5 | 22 (3.0%) | 39 (5.4%) | 35 (4.8%) | 84 (11.6%) | <5 | 6 (0.8%) |

Abbreviations: AD, Alzheimer's disease; CSF, cerebrospinal fluid; CT, computerized tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.
Optum requires reported sample sizes to be n≥5.

### *4.3. Study limitations*

The nature of this study is descriptive, and as such, no attempt has been made to identify etiologies or risk factors that may account for the differences found according to age, sex, or race/ethnicity. Without considering information on factors such as disease severity, duration, or comorbidities, explanations on the difference in age cannot be disentangled. Several factors, including burden of vascular and metabolic risk

**Table 4**
Brain imaging and biomarker use among patients diagnosed with dementia, stratified by age group, and sex and race/ethnicity identified between January 1, 2017, through March 31, 2022, in the Market Clarity database.

| Characteristic | PET | | MRI | | CT | | CSF | |
|---|---|---|---|---|---|---|---|---|
| | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis | Before Diagnosis | On or After Diagnosis |
| Age Group, n (%) | | | | | | | | |
| 18–44 | <5 | 10 (0.4%) | 163 (5.6%) | 205 (7.1%) | 315 (10.9%) | 325 (11.2%) | 23 (0.8%) | 29 (1.0%) |
| 45–54 | 5 (0.1%) | 17 (0.3%) | 366 (6.7%) | 500 (9.2%) | 708 (13.0%) | 793 (14.6%) | 75 (1.4%) | 69 (1.3%) |
| 55–64 | 14 (0.1%) | 101 (0.5%) | 1,471 (6.8%) | 2,053 (9.5%) | 3,083 (14.3%) | 3,715 (17.2%) | 238 (1.1%) | 331 (1.5%) |
| 65–74 | 32 (0.1%) | 204 (0.4%) | 3,334 (5.6%) | 5,033 (8.5%) | 7,498 (12.7%) | 10,702 (18.1%) | 512 (0.9%) | 780 (1.3%) |
| 75–84 | 36 (0.0%) | 195 (0.2%) | 5,001 (4.3%) | 7,777 (6.7%) | 13,179 (11.3%) | 21,290 (18.3%) | 872 (0.8%) | 1,291 (1.1%) |
| 85+ | 15 (0.0%) | 63 (0.1%) | 3,336 (2.5%) | 5,350 (4.0%) | 16,634 (12.5%) | 26,898 (20.2%) | 699 (0.5%) | 1,008 (0.8%) |
| Sex and Race/Ethnicity, n (%) | | | | | | | | |
| Hispanic Male | <5 | 7 (0.2%) | 210 (4.7%) | 336 (7.5%) | 629 (14.0%) | 974 (21.6%) | 39 (0.9%) | 62 (1.4%) |
| Non-Hispanic Caucasian Male | 29 (0.0%) | 198 (0.2%) | 4,338 (5.0%) | 6,558 (7.6%) | 12,726 (14.7%) | 19,443 (22.4%) | 995 (1.2%) | 1,399 (1.6%) |
| African American Male | <5 | 16 (0.1%) | 691 (5.0%) | 1,031 (7.5%) | 2,072 (15.0%) | 2,995 (21.7%) | 165 (1.2%) | 186 (1.4%) |
| Asian Male | <5 | 3 (0.2%) | 80 (4.8%) | 139 (8.3%) | 167 (10.0%) | 345 (20.6%) | 19 (1.1%) | 27 (1.6%) |
| Hispanic Female | <5 | 15 (0.2%) | 286 (4.4%) | 450 (6.9%) | 755 (11.5%) | 1,165 (17.8%) | 34 (0.5%) | 65 (1.0%) |
| Non-Hispanic Caucasian Female | 40 (0.0%) | 203 (0.2%) | 5,700 (4.4%) | 8,731 (6.7%) | 18,576 (14.3%) | 28,272 (21.7%) | 859 (0.7%) | 1,257 (1.0%) |
| African American Female | 8 (0.0%) | 16 (0.1%) | 1,077 (4.9%) | 1,479 (6.8%) | 3,023 (13.8%) | 4,390 (20.1%) | 143 (0.7%) | 197 (0.9%) |
| Asian Female | <5 | 9 (0.4%) | 88 (3.5%) | 178 (7.1%) | 251 (10.0%) | 455 (18.2%) | 12 (0.5%) | 22 (0.9%) |

Abbreviations: CSF, cerebrospinal fluid; CT, computerized tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.
Optum requires reported sample sizes to be n≥5.

factors, timing of advanced symptom presentation, or differential diagnostic and coding practices may be influencing this finding. In the evaluation of AD and dementia diagnoses occurring after the original diagnosis, it is possible that the second code was different due to being recorded in a more general way by a different health care provider, and not due to a change in the actual diagnosis. The analysis performed did not evaluate at what care systems the diagnosis was recorded (i.e. primary care versus specialist; academic versus community setting; independent practice versus hospital system). It was not possible to distinguish between rural communities and urban communities, which may also be a source of disparities in the use of diagnostic tools. There is an intrinsic limitation of this study in the use of a retrospective EHR and insurance claims database utilizing ICD codes. The validation of a diagnosis of MCI, AD or dementia in the population analyzed was not determined. In real-world practice, MCI codes may capture a heterogeneous mix of true MCI, subjective cognitive complaints, and non-AD cognitive syndromes, while AD and dementia codes are sometimes used interchangeably or evolve over time. However, the aim of this study wasnt to establish the true prevalence of these conditions, but rather to analyze the real-world approach to their diagnosis in a transitional period prior to the clinical availability of blood-based biomarkers and the most recent diagnostic updates. Additionally, although this study had a large sample size, the study population is not necessarily generalizable to the overall population. Furthermore, the analysis is purely descriptive and unadjusted; therefore, the findings should be viewed as initial observations for hypothesis-generation with respect to disparities and system-level factors, rather than definitive results.

### *4.4. Conclusions*

The mean age at MCI diagnosis was lower than that of AD and dementia. The mean age at diagnosis also varied by race/ethnicity, being lowest among African American patients. The change in diagnoses between AD and dementia observed for some patients highlights the difficulty to diagnose accurately. During the period observed in this analysis, the diagnosis of MCI, AD, and dementia involved low use of brain imaging or CSF biomarkers, despite recommendations from guidelines at the time. All these factors evidence the structural diagnostic uncertainty of MCI, AD and dementia in the pre-blood-based biomarkers era. This knowledge of the patient populations and diagnostic experiences in a real-world setting would allow for greater understanding and growth to improve diagnosis across diverse groups and subsequentially would lead to faster support. This could be achieved for example by using real-world evidence data to track equity in access to blood-based biomarkers and advanced imaging across different races, ethnicities, and care settings. These data could also be used to monitor how changes in coverage and guidelines affect diagnostic coding patterns over time. Thus, following up how the new diagnostic tools are accepted and applied in the real-world setting, and how their use expands across diverse populations, would demonstrate their impact into changes in the public health policies in the diagnosis and routine clinical care of MCI, AD and dementia.

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## Consent statement

The Optum data have been de-identified pursuant to the HIPAA and Optum, using the expert determination method, has documented the methods and results of the analysis that justify such determination as set forth in 45 C.F.R. 164.514 and the “Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the HIPAA Privacy Rule”.

## Data sharing

This study used third party data made available under licence that the authors do not have permission to share. Requests to access the data should be directed to Optum at https://business.optum.com/en/data-analytics/life-sciences/real-world-data/market-clarity-data.html.

## Artificial intelligence statement

The authors declare that there has been no use of Artificial Intelligence (AI) in this manuscript.

## CRediT authorship contribution statement

**Olga Sánchez-Soliño:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Isabella Boroje:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Conceptualization. **Emma Xiaomeng Yue:** Writing – review & editing, Visualization, Validation, Software, Methodology, Investigation, Formal analysis. **Lisa Vinikoor-Imler:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Formal analysis, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Olga Sánchez-Soliño reports a relationship with AbbVie Inc that includes: employment, equity or stocks, funding grants, and non-financial support. Isabella Boroje reports a relationship with AbbVie Inc that includes: employment, equity or stocks, funding grants, and non-financial support. Lisa Vinikoor-Imler reports a relationship with AbbVie Inc that includes: employment, equity or stocks, funding grants, and non-financial support. Emma Yue reports a relationship with AbbVie Inc that includes: employment, equity or stocks, funding grants, and non-financial support. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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