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RESEARCH ARTICLE

Estimating prevalence of early symptomatic Alzheimer's disease in the United States

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Abstract

INTRODUCTION: Understanding the prevalence of treatment-eligible Alzheimer's disease (AD) is crucial for policy planning.

METHODS: We used a comprehensive literature review and population cascade approach to estimate the number of amyloid-positive, clinically diagnosed patients with mild cognitive impairment (MCI) or mild dementia due to AD in the United States.

RESULTS: An estimated 666,646 individuals were identified as having MCI due to AD (range: 351,926–1,227,776) and 620,850 individuals as having mild dementia due to AD (range: 445,082–820,339). In a US population of 76 million individuals aged 60 or older in 2021, the estimates of MCI and mild dementia due to AD increased with age.

CONCLUSIONS: As earlier diagnosis of AD and new disease-modifying treatments become available, accurate population estimates are required to reduce uncertainty in the number of clinically diagnosed patients eligible for amyloid-targeting therapies.

KEYWORDS
Alzheimer's disease, dementia, mild cognitive impairment, population cascade, population estimates

1 | BACKGROUND

In the United States, Alzheimer's disease (AD) is often underdiagnosed, and many individuals with AD may not know they have the condition.[1] Barriers to timely AD diagnosis include disparities in access to health-care resources and lack of awareness of the signs and symptoms of AD.[2,3] Uncertainty regarding the true prevalence of AD, especially its early stages, makes it difficult to assess health-care needs, conduct public health planning, and estimate how many patients may be eligible for treatment targeting early AD stages. As knowledge of early AD stages and availability and access to improved diagnostic testing increases, the number of patients eligible for AD treatment is expected to increase.[4] Given the increasing prevalence, mortality, and health-care costs of AD,[5] it is vital to better understand the population with AD, particularly its early stages.

An accurate estimate of the treatment-eligible patient population size in the United States will enable the medical community to better plan for new AD treatments as they become available.[6–9] Early diagnosis of AD is based on clinical presentation of symptoms that fit the pattern of memory dysfunction and loss of functional independence in one or more cognitive domains. Laboratory testing, including the use of imaging biomarkers, may help rule out reversible or treatable non-AD diagnoses that may account for cognitive changes,[10] and advances in diagnostic testing based on AD pathology are likely to improve the accuracy of AD diagnosis rates.

Early stages of AD are accompanied by changes in the brain due to accumulation of amyloid, which may be detected by positron emission tomography (PET), although use of PET is infrequent today.[11] A cerebrospinal fluid (CSF) test (lumbar puncture) may also be used to detect the presence of amyloid, but the test's invasive nature deters many patients.[12] Further, access to CSF testing can be limited due to insurance coverage and geographical restrictions. However, the use of blood-based markers to detect pathological features of AD is revolutionizing the disease diagnosis and determination of prognosis.[13]

In this study, we conducted a comprehensive literature review to estimate the numbers of patients with mild cognitive impairment (MCI) or mild dementia due to AD in the United States. In particular, we used a population cascade approach (i.e., a stepwise calculation based on multiple, independent parameters) to estimate the size of the amyloid-targeting therapy-eligible population with MCI or mild dementia due to AD in multiple age groups, evaluate uncertainty associated with different estimates reported in the literature, and identify gaps where future data collection could provide important precision.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors identified publications describing incidence, prevalence, population size, and/or morbidity in early symptomatic Alzheimer's disease (AD; mild cognitive impairment [MCI] and mild dementia) in the United States. A stepwise calculation, also known as a population cascade approach, was performed to estimate the population size of individuals aged ≥ 60 years with clinical presentation of MCI or mild dementia with amyloid positivity and diagnosed by their doctor.
2. **Interpretation**: The population cascade yielded base case population estimates similar to those reported elsewhere. This analysis provided updated estimates for early-stage AD by age category, and evaluated a range of estimates in the populations due to uncertainty in underlying parameters and alternative sources of clinical and biomarker prevalence.
3. **Future directions**: More rigorous population and epidemiology studies are needed to fill data gaps and reduce uncertainty related to the prevalence of MCI and mild dementia due to AD, especially for individuals aged < 65 years. Future work should also examine these prevalence estimates in specific demographic subpopulations.

2 | METHODS

2.1 | Cascade calculation

We used a stepwise calculation to estimate the number of amyloid-targeting therapy-eligible individuals aged ≥ 60 years with MCI and mild dementia due to AD, which represents a patient population comparable to those evaluated in many clinical trials for early-stage AD[7] (estimates were generally not available for people < age 60). The cascade began with the total US population distributed over 5-year increments starting at age 60 to 64 years, and multiple prevalence values were subsequently applied to estimate the populations of interest. Each estimate's lower and upper 95% confidence intervals (CIs) were used to calculate the overall lower and upper estimates of the prevalence rates. Our stepwise cascade calculation begins with estimates of the undiagnosed prevalence, but excludes individuals with undiagnosed AD by restricting the estimate of amyloid-targeting therapy-eligible individuals to patients who see a doctor and those estimated to have amyloid positivity identified by PET imaging.

2.2 | Literature review

We conducted a targeted literature review to identify scientific and gray literature publications from 2017 onward pertaining to incidence, prevalence, or population size, and/or morbidity in early symptomatic AD (MCI and mild dementia) in the United States. Initial and follow-up searches were performed in April 2022 and December 2022, respectively. The PubMed MEDLINE and Ovid Embase database searches were limited to 5 years to yield the most recent population estimates.

2.3 | Identification strategy and article screening

Two independent reviewers screened article titles and abstracts for potential inclusion, with any discrepancies resolved by team discussion. During abstract screening, we identified systematic literature reviews (SLRs) conducted in MCI or AD and reviewed the studies included in those SLRs to ensure that all relevant studies had been identified. The complete search strategies for PubMed MEDLINE and Ovid Embase are reported in, respectively, Tables S1 and S2 in supporting information. All articles retrieved were screened for inputs relevant to the population cascade. Data obtained from SLRs and meta-analyses with US-specific results were preferred, followed by nationally representative US data analyses and non-US analyses.

2.4 | Data extraction

Data from selected articles were extracted by two independent reviewers (with any discrepancies resolved or adjudicated), including details of study design, inclusion and exclusion criteria, and population characteristics. Study inclusion and exclusion criteria and included study characteristics are included in, respectively, Tables S3 and S4 in supporting information. Input values (with lower and upper 95% CI values) used in the cascade calculations are provided in Table S5 in supporting information.

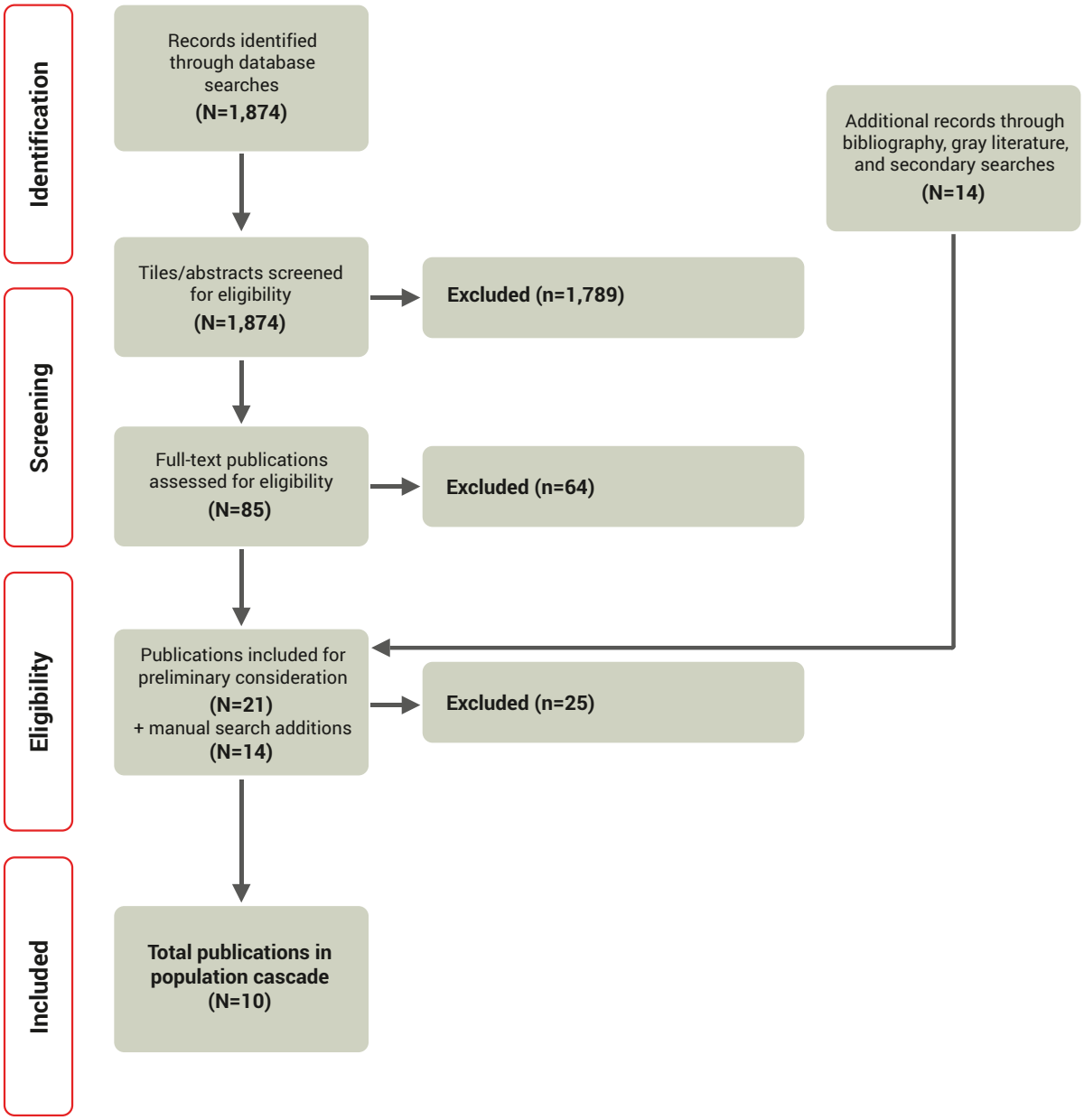

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram showing study selection process.

3 | RESULTS

3.1 | Selection of relevant literature

As shown in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram in Figure 1, the literature search performed through April 2022 identified 1609 articles, and the search performed through December 2022 identified 1874 articles. Gray literature and secondary sources contributed an additional 14 articles. After full-text article review, 10 articles were selected from which to estimate the population cascade comprising US individuals aged ≥ 60 years with MCI or mild dementia due to AD.

3.2 | Quantifying the population cascade: total US population

The population cascade began with the total US population distributed over 5-year increments starting at age 60 to 64 years.[14]

3.2.1 | MCI due to AD

We estimated the prevalence of MCI among individuals aged ≥ 60 years based on published data from a meta-analysis.[15] Of these, we estimated the proportion of individuals with MCI who see a doctor.[16]

The proportion of amyloid positivity reported for these individuals with MCI[17] was used to estimate the prevalence of MCI due to AD (i.e., patients with MCI and amyloid positivity were assumed to have MCI due to AD). Almost all publications used reflect US population data; only the studies estimating amyloid positivity in dementia and MCI due to AD included a mixed, global population.

3.2.2 | Mild dementia due to AD

The prevalence rates of general dementia were obtained from US-specific results of a meta-analysis performed by Alzheimer's Disease International (ADI).[18,19] Among individuals with general dementia, the Alzheimer's Association estimates that 60% to 80% have clinical presentation consistent with AD.[20] Therefore, our base case analysis used an AD prevalence of 70% (with 60% and 80% used for uncertainty analyses). After estimating the overall prevalence of mild dementia clinically presumed to be AD,[21] we calculated the proportion of patients with AD who see a doctor.[22] Finally, we estimated the proportion of these patients with amyloid positivity identified using PET imaging.[17]

3.3 | Scenario analyses

To evaluate the variability of the estimates, alternative scenarios were considered. In scenario 1, we used alternative prevalence values for general dementia and MCI and applied amyloid positivity prevalence values using PET amyloid testing; in scenario 2, we applied amyloid positivity values using CSF amyloid testing; and in scenario 3, we evaluated the impact of an increase in people seeking out diagnosis.

Scenario 1 used a more recently published analysis[23] based on prevalence data not included in the meta-analyses. Specifically, that analysis estimated the prevalence of both general dementia and MCI in a nationally representative analysis of the Harmonized Cognitive Assessment Protocol (HCAP), a recent sampling of individuals in the Health and Retirement Study (HRS) population.[23] Because prevalence estimates in the HCAP were limited to individuals aged ≥ 65 years, we used general dementia prevalence estimate from another study for the cohort aged 60 to 64 years,[24] and the MCI prevalence from an additional study.[15]

Scenario 2 used amyloid positivity prevalence rates from a pooled study of 85 cohorts, which found that CSF-based estimates were up to 10% higher than PET-based estimates in people without dementia (i.e., MCI), but similar in patients with dementia.[17] The base case used the smaller PET scan–based estimate.

Scenario 3 assumed the percentage of people that would seek out diagnoses would increase by 10% with the introduction of a new therapy based on expert opinion in a recently published analysis.[25]

Uncertainty analyses evaluated the effect of using all lower 95% CI values or all upper 95% CI values to calculate the population of interest. All studies reported 95% CI values, except those that reported the ADI 2015 prevalence estimates of general dementia[18,19] (for which inputs were not changed from the base case) with the assumption that 70% of people with dementia have AD (for which 60% and 80% were used as the 95% CI values).

3.4 | Base case estimates

The population estimates were calculated in a stepwise fashion over 5-year age groups (Table 1). Among the entire US population aged ≥ 60 years in 2021 (76,930,000 individuals), a total of 1.67% (1,287,496 individuals) were estimated to have amyloid-positive mild dementia or MCI due to AD and to be diagnosed by a doctor, including 0.81% (620,850 individuals) with mild dementia due to AD and 0.87% (666,646 individuals) with MCI due to AD. The number of individuals with MCI or mild dementia due to AD increased with age, from 103,947 individuals aged 60 to 64 years to 264,915 individuals aged ≥ 90 years.

3.5 | Analysis of variability

Figures 2 and 3 show the variability associated with using the lower and upper 95% CI estimates in the mild dementia and MCI population cascade calculations, respectively. For patients with MCI, the lower and upper 95% CI estimates were 351,926 and 1,227,776, respectively (differences of −314,720 [−47.2%] or +561,130 [84.2%] individuals, respectively). For patients with mild dementia due to AD, the lower and upper 95% CI estimates were 445,082 and 820,339, respectively (differences of −175,768 [−28.3%] or +199,489 [+32.1%] individuals, respectively).

3.6 | Scenario results

Estimates of the total number of individuals with MCI or mild dementia due to AD for the base case and scenarios are shown in Table 2. When the prevalence values identified by Manly et al.[23] were used, the population of interest increased by 19.9%, from 1,287,496 to 1,543,128 individuals. When CSF was used instead of PET to estimate amyloid positivity prevalence, the population of interest increased by 6.4%. In both scenarios, the increase was primarily driven by increased prevalence values in the MCI subgroup.

The impact of using lower and upper 95% CI values was larger than the impact of using different input sources. The base case total population of interest was 1,287,496 individuals, with a lower estimate of 797,008 (a decrease of 490,488 individuals [38.1%]) and an upper estimate of 2,048,115 (an increase of 760,619 individuals [59.1%]).

The impact of assuming the proportion of individuals who would seek diagnosis increased by 10% led to a similar increase in the estimated prevalence. The total population of interest in this scenario was 1,416,245 individuals (range 876,709 to 2,252,926), an increase of 128,748 (10.0%) above the base case.

TABLE 1 Population cascade estimates.

Cascade value, *n*	Source	60–64 years	65–69 years	70–74 years	75–79 years	80–84 years	85–89 years	90+ years	Total
Population aged 60+ years	US Census 2021[14]	21,094,000	18,162,000	14,878,000	10,172,000	6,632,000	3,367,708	2,624,292	**76,930,000**
Population with general dementia	ADI 2015[18,19] weighted by sex information from US Census 2021	241,255	352,602	518,094	669,932	823,346	744,220	1,328,805	**4,678,254**
Population with clinical dementia due to AD	Assumption of 70%[20]	168,879	246,821	362,666	468,952	576,342	520,954	930,163	**3,274,778**
Population with clinical dementia (mild) due to AD	Yuan et al. 2021[21]	85,115	124,398	182,784	236,352	290,476	262,561	468,802	**1,650,488**
People with clinical dementia (mild) due to AD who see a doctor	Chen et al. 2019[22] weighted by sex information from US Census 2021	37,660	55,167	81,440	105,013	130,555	108,900	220,069	**738,803**
Population with clinical dementia (mild) due to AD and amyloid positivity (PET) that see a doctor	Jansen et al. 2022[17]	33,141	48,050	70,160	89,419	109,731	90,332	180,016	**620,850**
Population with MCI	Petersen et al. 2018[15]	1,413,298	1,525,608	1,502,678	1,505,456	1,671,264	1,266,258	986,734	**9,871,296**
Population with MCI that see a doctor	Qian et al. 2021[16]	169,596	183,073	180,321	180,655	200,552	151,951	118,408	**1,184,556**
Population with MCI and amyloid positivity (PET) that see a doctor	Jansen et al. 2022[17]	70,806	85,953	94,128	103,605	125,144	102,111	84,899	**666,646**
Total (mild dementia and MCI due to AD)	**N/A**	**103,947**	**134,003**	**164,288**	**193,024**	**234,875**	**192,443**	**264,915**	**1,287,496**

Abbreviations: AD, Alzheimer's disease; ADI, Alzheimer's Disease International; MCI, mild cognitive impairment; N/A, not applicable; PET, positron emission tomography.

4 | DISCUSSION

4.1 | Overall interpretation

This study provides an updated estimate of the prevalence of clinical diagnosis of MCI and mild dementia due to AD among US older adults aged ≥ 60 years who may be eligible for amyloid-targeting therapies.[18,26,27] Although studies of AD prevalence, incidence, and mortality face challenges related to variations in diagnosis and disease stage classifications, epidemiologic data suggest that the medical community will face significant and increasing numbers of patients presenting with potential AD risk factors in the near future. Therefore, there will be a need to identify patients most likely to benefit from treatment early in the disease process.[28] However, due to too few dementia specialists and access barriers to imaging and other resources, the capacity of the US health-care system is insufficient to meet the projected demand of treatment-eligible patients with early AD.[8]

4.2 | Summary of main results

We estimated that ≥ 620,000 individuals had mild dementia due to AD (range: 445,082–820,339), and ≥ 666,000 individuals had MCI due to AD (range: 351,926–1,227,776) clinically diagnosed by a health-care provider. The population with MCI or mild dementia due to AD increased with age.

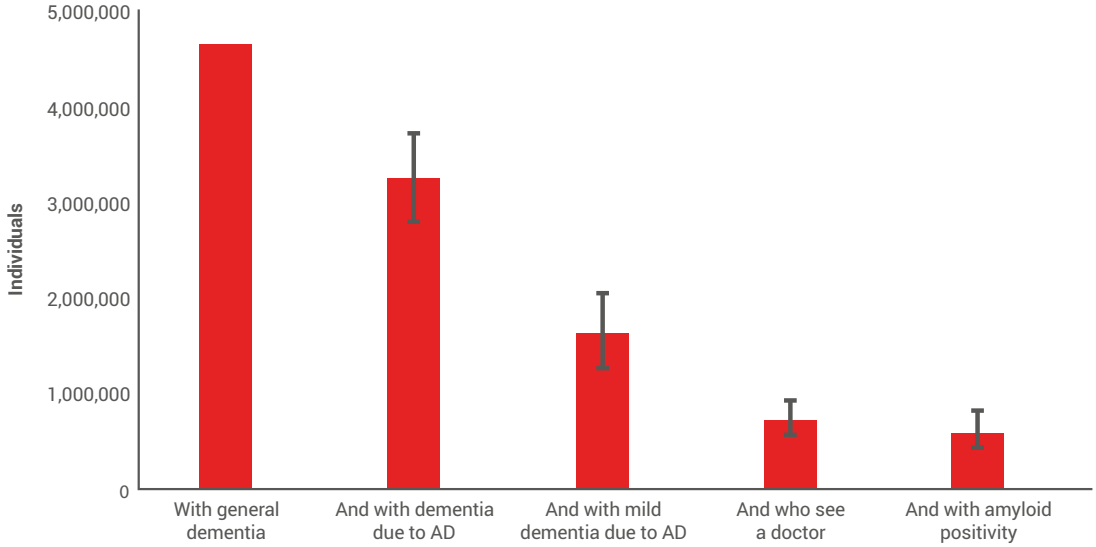

FIGURE 2 Population cascade estimates and uncertainty for patients with mild dementia due to AD. AD, Alzheimer's disease.

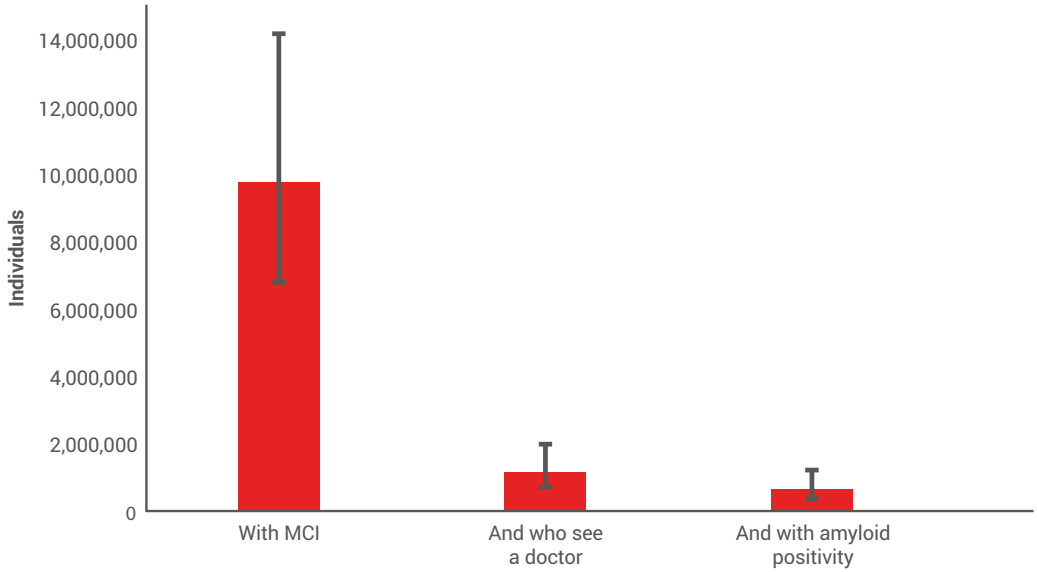

FIGURE 3 Population cascade estimates and uncertainty for patients with MCI due to AD. AD, Alzheimer's disease; MCI, mild cognitive impairment.

Because of challenges associated with diagnosis and access to specialists (including PET and CSF facilities), only a portion of the value of recent AD treatment advances may be realized.[29] Our population estimate may have direct relevance for short-term resource planning, as an estimate of the number of individuals who may want to engage their providers in a discussion about whether treatment is appropriate for them. The estimated number of individuals with mild dementia due to AD and MCI due to AD who see a doctor without confirmed amyloid positivity can be interpreted as the population that may be eligible for PET or CSF testing, if available. In the longer term, an even more precise estimate of the size of the amyloid-targeting therapy-eligible population could be possible with improved patient and provider awareness of treatment options; improved access to PET, CSF, pathology services, and less invasive tests; and more conclusive data to elucidate benefit of amyloid removal among patients with complicated medical histories. However, better data collection and more research is needed. When we evaluated alternative scenarios using alternative data sources, the population estimates increased by 6.4% and 19.9%, respectively. The increases in both scenarios are primarily driven by increased estimates in the MCI subgroup.

4.3 | Comparison of the results with other estimates

Several studies have attempted to estimate a population cascade for AD in recent years. The criteria used in the present study have

TABLE 2 Population cascade estimates under alternative scenarios.

Scenario	First prevalence source	Amyloid positivity testing	Percentage seeing a doctor	Lower 95% CI (%)	Average (%)	Upper 95% CI (%)
				People with mild dementia due to AD who see a doctor, *n* (%)		
Base case	ADI 2015[18,19]	PET	≈ 44.4%[22]	445,082 (0.59%)	620,850 (0.81%)	820,339 (1.07%)
Scenario 1	Hendriks et al. 2021[24] Manly et al. 2022[23]	PET	≈ 44.4%[22]	325,284 (0.42%)	668,947 (0.87%)	1,113,739 (1.45%)
Scenario 2	ADI 2015[18,19]	CSF	≈ 44.4%[22]	412,319 (0.54%)	591,337 (0.77%)	814,308 (1.06%)
Scenario 3	ADI 2015[18,19]	PET	≈ 48.9%[22,25]	489,590 (0.64%)	682,935 (0.89%)	902,373 (1.17%)
				People with MCI due to AD who see a doctor, n (%)		
Base case	Petersen et al. 2018[15]	PET	12.0%[16]	351,926 (0.46%)	666,646 (0.87%)	1,227,776 (1.60%)
Scenario 1	Petersen et al. 2018[15] Manly et al. 2022[23]	PET	12.0%[16]	581,267 (0.76%)	874,181 (1.14%)	1,379,650 (1.79%)
Scenario 2	Petersen et al. 2018[15]	CSF	12.0%[16]	416,398 (0.54%)	778,942 (1.01%)	1,410,138 (1.83%)
Scenario 3	Petersen et al. 2018[15]	PET	13.2%[16,25]	387,119 (0.50%)	733,311 (0.95%)	1,350,554 (1.76%)
				Total, *n* (%)		
Base case		PET		797,008 (1.04%)	1,287,496 (1.67%)	2,048,115 (2.66%)
Scenario 1		PET		906,651 (1.18%)	1,543,128 (2.01%)	2,493,389 (3.24%)
Scenario 2		CSF		828,717 (1.08%)	1,370,279 (1.78%)	2,206,781 (2.87%)
Scenario 3		PET		876,709 (1.14%)	1,416,245 (1.84%)	2,252,926 (2.93%)

Note: Scenario 1 = alternative prevalence values for general dementia and MCI based on PET amyloid testing; Scenario 2 = prevalence values based on CSF amyloid testing; Scenario 3 = increase in people seeking out diagnosis.
Abbreviations: AD, Alzheimer's disease; ADI, Alzheimer's Disease International; CI, confidence interval; CSF, cerebrospinal fluid; MCI, mild cognitive impairment; PET, positron emission tomography.

produced base case population estimates that are lower than those reported elsewhere: for example, Gauthier et al. recently estimated 6 million individuals with dementia due to AD (including all severities) and 5 million individuals with MCI due to AD, corresponding to a total of 11 million individuals in 2022.[18]

Gillis et al. performed a literature review to obtain population estimates of MCI or mild dementia due to AD based on age and race or ethnicity.[26] In their study, among those aged ≥ 65 years in the United States, ≈ 9.2% and 3.7% of non-Hispanic Whites, 13.6% and 7.0% of non-Hispanic Blacks, 11.1% and 5.3% of Hispanics, and 9.7% and 3.9% of those of other races or ethnicities were living with MCI due to AD and mild dementia due to AD, respectively.[26] Our current analysis provided updated estimates by age but did not evaluate data for specific racial or ethnic groups. Compared to those reported by Gillis et al., our base case estimates for individuals aged ≥ 65 years with mild dementia or MCI due to AD are lower, with the differences primarily driven by the source of dementia prevalence data; the estimates used in our calculation[30] used data from meta-analyses and were smaller than those used by Gillis et al.,[26,31] which used data from a single study and may not be generalizable to the entire United States. The differences may also be attributed to the changing nature of the evidence-gathering process and variations in classifying the stages of AD.

Another recent study, by Gustavsson et al., estimated global prevalence statistics across the AD continuum (dementia due to AD, prodromal AD, and preclinical AD) categorized by age group, sex, and geographic region.[27] This study's prodromal AD population was defined similarly to how we defined MCI due to AD in the present study; the estimated populations with prodromal AD and clinical AD of any severity were 5.6 million and 2.8 million individuals, respectively.[27] Population estimates for MCI due to AD in our study were comparable but slightly lower than the prodromal AD population in the Gustavsson et al. study; however, it is difficult to compare the estimates directly because, while our study only considered mild dementia due to AD, Gustavsson et al. considered mild, moderate, and severe dementia due to AD.[27]

4.4 | Strengths and limitations

Strengths of our study include use of a comprehensive literature review; analysis of uncertainty and consideration of alternate scenarios; the consideration of only amyloid-positive, clinically diagnosed patients; and reporting of study details for the included articles. Our study has some limitations. Overall, currently available population data remain limited, especially given the small number of studies reporting AD neuropathology and disease stage estimates. Prevalence estimates for mild dementia due to AD and MCI due to AD in the population aged < 65 years were rare; hence, our estimates for the age group of 60 to 64 years may have considerable uncertainty. Some input values were applied to the entire population instead of adjusting the values for each age category.

Overall, the stepwise population cascade approach (a commonly used approach for estimating patient population size) is inherently limited by the fact that each set of inputs was estimated in a different population at different times. Although meta-analyses were used when available to reduce bias, more rigorous population studies are warranted, especially for the early symptomatic stages of AD (MCI and mild dementia).

Finally, our study did not account for patients < 60 years because of the limited data available. Although this age group accounts for only a small fraction of the total number of dementia and MCI cases,[24] clinical trials for lecanemab and aducanumab included patients aged 50 to 90 years.

4.5 | Existing challenges and future work

Data gaps exist regarding the prevalence of dementia and MCI due to AD, particularly for individuals < 65 years of age. As earlier diagnosis of AD becomes possible, population studies should be performed to fill these gaps. Future work should also examine whether these results can be generalized to subpopulations, including those underrepresented historically in AD clinical trials. Criteria to identify MCI due to AD and to distinguish it from other causes, including cardiovascular disease and Lewy body dementia, need to be developed; the presence of amyloid plaques are the defining characteristic of MCI due to AD. Because MCI may be under-coded in administrative claims data, future burden-of-illness studies should consider augmenting the estimates with additional data sources. Indeed, a study not generalizable to the full population (and therefore not used for our stepwise population cascade calculation or uncertainty analyses) found that 26.7% of people with MCI would be likely to engage with the medical system (see a doctor),[32] which is more than twice the value estimated by Qian et al. (the value used in our calculations),[16] and which would more than double our population estimate for MCI due to AD. In addition, as therapy becomes more available and more sought after, it is likely that the demand for screening will increase. A recent analysis estimated an increase of 10% for cognitive screening with the addition of new medication, which would result in 10% more patients seeking treatment (62,085 individuals in the mild dementia due to AD group and 66,665 individuals in the MCI due to AD group). The high uncertainty in the population estimates is evident from the size of the CIs: the error bars are nearly as large as the estimated value itself. Additionally, amyloid positivity rates are best defined in research and clinical study settings; amyloid positivity prevalence in other settings may be lower.

4.6 | Implications for policy and practice

Planning and intervention at both institutional and societal levels requires accurate assessment of the AD population and diagnosis rates. Our population cascade study sets a path for improving future population estimates as novel AD therapies evolve. Diagnostic testing for AD pathology is becoming more accessible and will improve diagnosis accuracy in the future. This study provides a reference point as the health-care environment changes, and more patients choose to present at a physician's office to undergo diagnosis. Updated incidence and prevalence data for early AD stages can help inform strategies for management of AD. This "point-in-time" estimate highlights the need to obtain more comprehensive data that could be useful in planning of public health strategies, and the small number of studies and variation in disease definitions may limit rigorous interpretation of our results. Variations in diagnosis, consensus criteria, and the interpretation of biomarkers and neuropsychiatric tests are obstacles in AD studies; innovative approaches will likely be required to accurately understand the impact of treatment on slowing disease progression.

Our study identifies key knowledge gaps and uncertainties in the evidence regarding the prevalence of early, symptomatic, treatment-eligible AD. Our findings serve as a call to action for continuous evidence generation that would enable the medical community to plan for adequate support and address the burden of AD in vulnerable populations. Reliable population data will be needed to optimize future research, track impact of changes in the health-care environment, and improve public health resource planning.

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CONFLICT OF INTEREST STATEMENT

D.S., E.K., and A.H. are employees of Eli Lilly and Company, who funded this study. R.Z. is an employee of IQVIA and has a consulting agreement with Eli Lilly and Company. P.L. and P.S. have a consulting agreement with Eli Lilly and Company and are affiliated with The Center for the Evaluation of Value and Risk in Health (CEVR), which is funded by multiple parties, including the PhRMA Foundation; Arnold Ventures; and other government, foundation, and pharmaceutical industry sources. CEVR also maintains the Cost-Effectiveness Analysis Registry and SPEC database, which are supported by several dozen organizations, including drug industry and academic and nonprofit foundation sources. Author disclosures are available in the supporting information.

CONSENT STATEMENT

This research did not involve any human subjects and, therefore, consent is not required.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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