

insights

& Implications

IN GERONTOLOGY

Understanding Breakthroughs in Brain Health

Top 10 Articles of 2025

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Understanding Breakthroughs in Brain Health

Introduction

Welcome to *Insights & Implications: Understanding Breakthroughs in Brain Health—Top 10 Articles of 2025*.

GSA is pleased to share this collection of articles on research and developments that shape the evolving landscape of brain health in primary care. This series provides a compilation of summaries of key articles from the past year. The article selection process aimed to identify literature presenting findings actionable for primary care providers and was guided by an expert advisory board.

The articles presented explore several issues, including current trends in disease prevalence and impact; the recent availability of blood-based biomarkers and disease-modifying therapies; strategies for early identification and management of cognitive decline; and evolving roles for primary care providers. Recent research addressing risk factors, including lifestyle,



sleep, nutrition, and oral health, is also explored. Ongoing challenges, including delays in diagnosis and gaps in care, are also addressed.

We hope this report serves as a valuable resource for clinicians, researchers, policymakers, and other stakeholders committed to advancing brain health. Thank you for your dedication to improving outcomes for individuals, families, and communities affected by cognitive impairment and dementia. You can provide feedback to kaer@geron.org.

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Article 1.

2025 Alzheimer's Disease Facts and Figures

insights

This report from the Alzheimer's Association provides an in-depth look at Alzheimer's disease (AD) in the United States, including detailed statistics at the national and state-by-state levels and a comprehensive narrative. The report begins with a discussion of brain changes that occur with AD (beginning decades before clinical symptoms emerge), risk factors for AD, and an exploration of strategies for addressing modifiable risk factors. It also provides an overview of signs and symptoms, as well as current treatment options.

Estimates from 2025 indicate that AD affects roughly 11% of people in the United States aged ≥ 65 years, which represents approximately 7.2 million people. The prevalence of AD increases steadily with age and is rising as the overall population ages. Prevalence is somewhat higher in women than men (12% of women and 10% of men), and in non-Hispanic Black and Hispanic older adults compared with White older adults.

Dementia is associated with increased health care utilization. Costs associated with health and long-term care for people living with AD and other dementias were estimated to be \$384 billion in 2025. Medicare and Medicaid cover most of these costs; roughly 25% are paid out of pocket. Additionally, roughly 12 million people act as unpaid caregivers for people with dementia, providing care valued at approximately \$413 billion. Caregivers face many stressors, including emotional, physical, and financial burdens. The report discusses the need to expand the paid workforce to provide care, including primary care providers, specialists, allied health professionals, and direct care professionals, and the need to develop more collaborative workforce models. The report concludes with a special section that presents survey results on attitudes toward early detection, diagnosis, and treatment of AD.

implications

AD is a leading cause of death and disability, and its impact is growing as the population ages. Although new treatments have the potential to slow the progression of AD when used during early stages, AD is often underdiagnosed, particularly in early stages. Care needs increase substantially as the disease progresses, and millions of unpaid caregivers provide extensive care.

There is a strong public interest in earlier diagnostic interventions, particularly with blood-based biomarker tests. Expanding access to diagnostic testing could help increase access to disease-modifying therapies and facilitate improved care planning.

Alzheimer's Association. 2025 Alzheimer's disease facts and figures. *Alzheimer's Dement.* 2025;21:e70235. <https://doi.org/10.1002/alz.70235>.



The authors suggested that the growing gap between care needs and available support was due to fragmented care coordination among formal and informal care providers.

Article 2.

Discontinuity of Social Support Among US Adults with Cognitive Impairment Before and After the Confirmed Diagnosis of Dementia: A Matched Ambidirectional Cohort Study

insights

This study assessed the impact of a diagnosis of dementia on the alignment between needs for care to manage disabilities and the support provided to address those needs. Researchers analyzed data from the Health and Retirement Study (2000–2018) of 1,261 individuals with confirmed dementia and 12,604 matched controls with cognitive impairment without a dementia diagnosis. Disability was assessed for basic activities of daily living (BADLs; dressing, walking across a room, bathing, eating, toileting, getting in and out of bed) and instrumental activities of daily living (IADLs; preparing a hot meal, shopping for groceries, making phone calls, taking medications, and managing money). Unmet social support was defined as reporting disability without receiving corresponding support.

People who were diagnosed with dementia were more likely to have disability and to receive support than those without. However, the authors noted that disability increased after diagnosis, without an increase in support, resulting in a widening gap. There were differences in racial and gender subgroups regarding how often specific needs were unmet (e.g., using the phone, toileting, eating), and there was a universal rise in unmet IADL needs across all subgroups.

implications

The authors suggested that the growing gap between care needs and available support was due to fragmented care coordination among formal and informal care providers. Other factors influencing the gap could include instability in informal care arrangements over time, inadequate economic resources, insufficient or complex insurance coverage, delayed access to team-based support, and a lack of awareness of available services.

The authors called for formalizing dementia care planning activities in the care pathway following dementia diagnosis, ongoing monitoring of care needs and available support, and increased referrals to appropriate services. In primary care, a dementia diagnosis should prompt an increased focus on coordinating care, identifying unmet needs, and referrals to supports such as social work, physical therapy, or occupational therapy. Regular assessments of BADLs and IADLs and reviews of whether supports are addressing needs can be incorporated into the workflows for follow-up visits.

Zhang H, Underwood BR, London S, et al. Discontinuity of social support among US adults with cognitive impairment before and after the confirmed diagnosis of dementia: a matched ambidirectional cohort study. *BMC Med.* 2025;23(1):428. doi: 10.1186/s12916-025-04264-y.

Article 3.

The Shifting Treatment Landscape for Alzheimer's Disease in Primary Care

insights

This article provides a review of evolving approaches for diagnosing and managing Alzheimer's disease (AD) in primary care. A diagnostic evaluation for AD combines clinical assessment with tests that detect pathologic changes associated with AD, including amyloid-beta and phosphorylated tau. Historically, positron emission tomography (PET) imaging and cerebrospinal fluid tests have been used to assess the presence of these biomarkers. More recently, blood-based biomarker tests have become available, providing an option for primary care providers (PCPs).

A comprehensive treatment plan should be developed for individuals diagnosed with AD. In addition to guiding the use of nonpharmacologic and possibly pharmacologic interventions, key roles for PCPs include monitoring disease progression, coordinating with specialists, providing patient and caregiver education and support, and facilitating advance care planning.

Nonpharmacologic approaches can include physical activity, healthy dietary interventions, social engagement, music- and art-based therapies, sleep hygiene, and behavioral strategies to improve quality of life and help manage symptoms. For many years, pharmacologic treatment options were limited to acetylcholinesterase inhibitors and NMDA antagonists, which could help manage symptoms but did not impact disease progression. The recent availability of disease-modifying pharmacologic options for AD has offered the potential to alter disease trajectories for the first time. Amyloid-targeting therapies have been shown to reduce amyloid plaque burden, thereby slowing cognitive and functional decline in early AD. Biomarker testing should be conducted to confirm amyloid pathology before initiation of anti-amyloid therapy.

Amyloid-related imaging abnormalities (ARIA) are a potential adverse event associated with anti-amyloid therapy. ARIA is usually mild, temporary, and asymptomatic, and it has the potential to produce clinical manifestations or be life-threatening. Regular



monitoring is required to assess the development of ARIA and guide adjustment or discontinuation of treatment if required. In addition, genetic testing for ApoE ϵ 4 can assess risk for ARIA and help guide treatment decisions.

implications

The availability of disease-modifying therapies has prompted a shift toward emphasizing early identification and interventions for AD, underscoring the role that primary care can play in the diagnosis of AD. PCPs are often the first clinicians to identify cognitive decline. They play a critical role in early detection, often identifying symptoms during routine visits, such as Medicare Annual Wellness Visits, and incorporating emerging diagnostic tools, including blood-based biomarkers. Individuals who are diagnosed with AD should be managed with a comprehensive treatment plan, including necessary referrals where appropriate.

Davis L, Obisesan T. The shifting treatment landscape for Alzheimer's disease in primary care. *J Fam Pract.* Oct 2025 (Suppl):S37-S42. doi:10.12788/fp.0640.

Article 4.

Time to Diagnosis in Dementia: A Systematic Review with Meta-Analysis

This systematic review and meta-analysis determined that the average time to diagnosis (TTD) for dementia after symptom onset (as rated by patients or caregivers) is 3.5 years. Young-onset dementia and frontotemporal dementia were associated with longer TTD than those of people who were older and those with AD. Access to specialty memory clinics was associated with shorter TTD for patients with AD or alcohol-related dementia. A total of 13 studies, including 30,257 participants from multiple countries, were identified for the meta-analysis. Importantly, definitions of TTD differed across studies, creating challenges for interpretation.



implications

It is reasonable to expect some delay in TTD for several reasons. For example, some people delay seeking help from the health care system, particularly if symptoms are subtle or are mistaken for normal aging. Even after entering the health care system, steps to conduct a thorough diagnostic evaluation, including the need for potential specialist referral and associated scheduling challenges, can be lengthy. However, even when accounting for these factors, the current TTD appears suboptimal.

Improving TTD can improve clinical outcomes by connecting people with interventions that can prevent or delay progression, as well as supports that improve quality of life and overall health and well-being. Furthermore, cognition can impact how people self-manage other chronic conditions that are common in this population. Thus, recognizing that a person has impaired cognition can prompt the implementation of additional supports to help people self-manage all of their health conditions.

Strategies to improve TTD include promoting awareness of the benefits associated with identifying symptoms early, improving referral pathways, and expanding availability and access to diagnostic services. Embedding cognitive assessments into primary care workflows can help detect cognitive impairments and may reduce TTD for dementia.

Kusoro O, Roche M, Del-Pino-Casado R, et al. Time to diagnosis in dementia: a systematic review with meta-analysis. *Int J Geriatr Psychiatry*. 2025;40(7):e70129. doi: 10.1002/gps.70129.

Article 5.

Implementing Early Detection of Cognitive Impairment in Primary Care to Improve Care for Older Adults

insights

This article describes how primary care providers (PCPs) can aid in the detection of mild cognitive impairment (MCI) and Alzheimer's disease and related dementias (ADRD). Approximately 20% of older adults in the United States have MCI, and another roughly 14% have ADRD. While early detection can improve patient outcomes, underdiagnosis and delayed diagnosis are common. For example, only approximately 8% to 11% of MCI cases are detected early. Underdiagnosis and delayed diagnosis are more common in Black and Hispanic populations.

Early detection is beneficial for patients with MCI and ADRD because reversible causes (e.g., medications, vitamin deficiencies) can be identified, leading to better care planning and potential eligibility for disease-modifying therapies. Furthermore, undetected MCI or ADRD in patients with chronic conditions can lead to decreased capacity for self-management resulting in poor medication adherence and increased risk for hospitalization. Diagnosing MCI or ADRD can facilitate care planning to support an individual's care needs.

As one of the most consistent points of contact with the health care system for older adults, PCPs can play an integral role in conducting initial screenings and diagnosis, coordinating referrals, and educating patients about brain health. Although specialists (e.g., geriatricians, neurologists) traditionally have played key roles in diagnosing ADRD, there are not enough specialists to meet the growing needs of an aging population. The increasing availability of digital screening tools and blood-based biomarkers increases the feasibility of diagnostic roles for PCPs.

implications

PCPs can potentially play central roles in diagnosing MCI and ADRD. However, barriers such as time constraints, limited training, stigma, and lack of reimbursement can hinder implementation. Advances in screening tools and the implementation of blood-based biomarkers are making early detection more feasible for PCPs.

The authors suggest several approaches for PCPs to implement early detection into their practices, including incorporating screenings into Medicare Annual Wellness Visits and utilizing other members of the care team to conduct assessments. They also emphasize the importance of normalizing discussions about brain health to help reduce stigma. New diagnostic approaches can help address barriers, including limited time for patient assessment in the primary care environment.

Attention to cognitive issues can improve outcomes in several other ways. For example, because up to 45% of ADRD cases are attributable to modifiable risk factors, PCPs can improve outcomes by educating patients about strategies for reducing risk or slowing the progression of cognitive decline. These strategies include lifestyle interventions, such as physical activity, healthy dietary choices, cognitive and social engagement, and management of cardiovascular risk from conditions such as hypertension, diabetes, obesity, and dyslipidemia.

Fowler NR, Partrick KA, Taylor J, et al. Implementing early detection of cognitive impairment in primary care to improve care for older adults. *J Intern Med.* 2025;298(1):31-45. doi: 10.1111/joim.20098.

Primary care teams can improve outcomes by educating patients about strategies for reducing risk or slowing the progression of cognitive decline.

Benefits of DCAs include automatic scoring, which provides faster results, and ease of integration with electronic health records.

Article 6.

Acceptable Standards for Clinic-Based Digital Cognitive Assessments: Recommendations from the Global CEO Initiative on Alzheimer's Disease

This article describes standards for clinic-based digital cognitive assessments (DCAs) for the early detection and diagnosis of mild cognitive impairment (MCI) and dementia developed by the Global CEO Initiative on Alzheimer's disease (AD). The article describes how to evaluate the performance of DCAs in three clinical situations: initial detection, diagnostic support, and characterization of cognitive profiles for helping to identify etiology (e.g., AD).

Key variables for screening assessments include the sensitivity and specificity of a test (i.e., how often these tests will produce false negatives and false positives). DCAs do not replace biomarker testing. When DCAs are used as part of the diagnostic evaluation, they should be used in combination with clinical history taking, functional assessments, and labs and/or imaging studies, rather than as stand-alone tests. They are used to help determine underlying etiologies and to identify cognitive patterns, particularly in complex or unclear cases.

The authors note that the workgroup intends to address additional issues in the future, including implementation issues for DCAs and the use of remote (unsupervised) DCAs, which have the potential to improve accessibility but pose several challenges.

implications

The article presents DCAs as an option for use by primary care providers to reduce barriers to the assessment of MCI and dementia and thus to improve early detection. It also discusses how DCAs fit with overall approaches to cognitive evaluation and presents important caveats.

Benefits of DCAs include automatic scoring, which provides faster results, and ease of integration with electronic health records. These benefits can reduce the staff time spent administering assessments and streamline workflows. However, existing DCAs have variable sensitivity and specificity and must be rigorously validated and compared with existing assessments. Additionally, it is essential that people who complete assessments receive their results and that any diagnoses are communicated promptly and thoughtfully.

Patient population characteristics and individual patient needs should be considered when evaluating the appropriateness of an assessment. To ensure inclusivity, adaptations should be available for different cultures, languages, education levels, and socioeconomic backgrounds, all of which can impact test accuracy. (For example, if a test is highly sensitive to the effects of education on cognitive performance, and the person being assessed has a low level of education, then the test could indicate the presence of MCI or dementia, even when it is not present.) Sensory or motor impairments should be considered, including low vision or arthritis, which may make some assessments difficult to complete. Other issues to address include digital literacy barriers, data privacy, and technology requirements.

Thompson LI, Gaster B, Hammers DB, et al; CEOi Digital Cognitive Assessment Workgroup. Acceptable standards for clinic-based digital cognitive assessments: recommendations from the Global CEO Initiative on Alzheimer's Disease. *Alzheimers Dement*. 2025;21(12):e70966. doi: 10.1002/alz.70966.

Article 7.

Structured vs Self-Guided Multidomain Lifestyle Interventions for Global Cognitive Function: The US POINTER Randomized Clinical Trial

insights

The US Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (US POINTER) was a large, randomized clinical trial that evaluated whether lifestyle interventions can help maintain or improve cognitive function. The study included 2,011 older adults aged 60 to 79 years with normal cognition at baseline who were at increased risk for cognitive decline due to sedentary activity levels, suboptimal diet, family history of memory loss, and/or cardiometabolic risk factors.

Participants were randomized to either a structured lifestyle intervention or a self-guided intervention for two years. The structured lifestyle intervention included 38 facilitated peer team meetings that provided education, goal setting, and accountability to address physical exercise, nutrition (focused on the MIND diet), cognitive and social activities, and guideline-based health coaching. The self-guided lifestyle intervention included six facilitated peer team meetings to address education, tools to support self-guided plans, and general support for healthy lifestyle behaviors.

Improvements in global cognition over two years were noted in both groups; the improvements were significantly greater in the structured intervention group than in the self-guided group. Benefits were consistent across many population subgroups.



implications

This study demonstrated that interventions that address lifestyle factors associated with future dementia can help preserve cognition, and that structured, supported programs are more effective than self-guided efforts.

These findings suggest that the structured interventions used to address lifestyle factors in the study can serve as a model for developing effective intervention strategies to preserve cognition in older adults. They are consistent with previous research showing that implementing and sustaining healthy behavior changes is challenging, and that interventions that successfully support behavior change can improve clinical outcomes.

Primary care providers can inform their patients about the importance of maintaining healthy lifestyle behaviors for supporting cognition and share information about the value of structured supports. Ideally, they can locate programs in their communities that offer structured lifestyle support (local fitness centers, health coaches, nutritionists, etc.) and make referrals when appropriate.

Baker LD, Espeland MA, Whitmer RA, et al. Structured vs self-guided multidomain lifestyle interventions for global cognitive function: The US POINTER Randomized Clinical Trial. *JAMA*. 2025;334(8):681-691. doi: 10.1001/jama.2025.12923.

Article 8.

Multi-Dimensional Sleep Health and Dementia Risk: A Prospective Study in the UK Biobank

insights

This article describes a large prospective study investigating the impact of sleep health on the incidence of dementia in 313,258 adults aged ≥ 50 years. Participants who did not have dementia at baseline (2006–2010) were followed through 2022. Sleep health was self-reported. Researchers identified six distinct multidimensional sleep patterns of the participants:

1. Relatively healthy sleep
2. Insomnia with short sleep time and morning chronotype (i.e., a “morning person”)
3. Nonrestorative sleep with evening chronotype (i.e., a “night person”)
4. Insomnia with short sleep duration, non-restorative sleep, and evening chronotype
5. Napping with snoring, long sleep duration, and daytime sleepiness
6. Severely disturbed sleep with multiple symptoms and daytime impairment



Those with poor overall self-reported sleep health were at an increased risk for all-cause dementia and vascular dementia. Adjusting for cardiovascular risk factors had a modest attenuating impact. Compared to healthy sleep, all other sleep patterns were associated with increased overall dementia risk and vascular dementia. Sleep pattern 6 (severely disturbed sleep) had the highest risk and was the only pattern associated with increased AD risk. Individual factors (e.g., snoring as a stand-alone factor) had less impact than the multidimensional patterns.

The authors noted several possible biological mechanisms of how sleep health could impact brain health. For example, healthy sleep has been associated with clearance of waste products from the brain, resulting in reduced β -amyloid deposition.

implications

This study adds to the growing body of research that identifies sleep health as an important factor influencing brain health. Furthermore, sleep health is interconnected to many other conditions that can also impact brain health, such as diabetes and hypertension.

It is also important to recognize that poor sleep can impact cognition in the absence of dementia. Furthermore, some sleep disorders are associated with cognitive decline that may be reversible with treatment of the sleep problem. Primary care providers can educate patients about sleep hygiene, screen for sleep disorders, and treat any identified conditions to prevent both cognitive decline and the development of other conditions that also impact cognition.

Huang T, Beydoun MA, Kianersi S, et al. Multi-dimensional sleep health and dementia risk: a prospective study in the UK Biobank. *BMC Med.* 2025;23(410). doi: 10.1186/s12916-025-04251-3.

Article 9.

Association Between Supplemental Nutrition Assistance Program (SNAP) Participation and Cognitive Decline Among Older Americans: A 10-Year Longitudinal Study

insights

This retrospective cohort study evaluated the impact of SNAP participation on cognition in older adults eligible for SNAP (household income $\leq 130\%$ of the federal poverty threshold). Data were obtained from the Health and Retirement Study, a publicly available, nationally representative sample of US adults aged ≥ 50 years. A total of 5,068 participants were SNAP-eligible at baseline (2010), of whom 2,347 had at least two global cognition scores between 2010 and 2020.

Compared with eligible adults who did not participate in SNAP, those who participated had significantly slower declines in global cognition, memory, and executive function. The authors noted that participation in SNAP could delay the onset of dementia by several years. Race-based disparities were noted among SNAP participants, including slightly faster declines in global cognition among non-Hispanic Black and Hispanic SNAP participants, compared with White participants.



implications

Prior research has indicated that food security, as well as healthy dietary intake, including adequate protein and micronutrient intake, is associated with delays in cognitive decline and the onset of dementia. The current study demonstrates that a nutritional program, SNAP, that increases food security has a positive long-term impact on brain health. Thus, improving access to and enrollment in SNAP or other nutritional programs could have a protective impact in preventing or delaying cognitive decline. These findings underscore the importance of identifying individuals who are experiencing food insecurity and connecting them with available resources.

Da L, Jin Z, Xu Q, et al. Association between Supplemental Nutrition Assistance Program (SNAP) participation and cognitive decline among older Americans: a 10-year longitudinal study. *J Am Geriatr Soc.* 2025;73(11):3464-3474. doi: 10.1111/jgs.70122.

Addressing oral health in midlife and in older adults can have a protective effect on cognitive decline.

Article 10.

The Impact of Oral Health and Dental Services on the Prevalence of Subjective Cognitive Decline Among Middle-Aged and Older US Adults: Behavioral Risk Factor Surveillance System, 2022

insights

Researchers studied a sample of 83,479 adults aged 45 years or older who had completed the cognitive decline module in the 2022 Behavioral Risk Factor Surveillance System (BRFSS) to assess relationships between oral health, use of dental services, and subjective cognitive decline (SCD).

Overall, respondents with good oral health were significantly less likely than those with poor oral health to report SCD (crude estimates of 13.6% vs 7.7%). Additionally, using dental services within the past year was associated with a lower prevalence of SCD compared with those who had not used dental services. In an age-stratified, fully adjusted model, middle-aged adults (aged 45 to 64 years) with poor oral health had a higher prevalence of SCD than those with good oral health. Having six or more teeth removed was associated with a higher prevalence of SCD than having one to five teeth removed (however, having all teeth removed was associated with a lower prevalence than having six or more teeth removed). Among adults ≥ 65 years, having some teeth removed remained associated with a higher prevalence of SCD, and SCD prevalence generally increased with the number of teeth lost. However, this trend did not impact those with all teeth removed.

implications

Addressing oral health in midlife and in older adults can have a protective effect on cognitive decline. Primary care providers can support oral health by educating people about the links between oral health and cognition and encouraging regular dental visits.

The authors proposed several mechanisms to explain the relationship between oral health and cognitive decline. Poor oral health is associated with periodontitis and oral bacteria, which can influence neurodegenerative processes. Further, tooth loss and/or reduced chewing ability can alter diet and lead to nutritional deficiencies that may impair brain health. Findings that denture use may reduce risk for dementia support some of these proposed mechanisms. For example, denture use may improve chewing ability and nutritional status.

Alshanbari MH, Cheney AM, Alhazmi HA, et al. The impact of oral health and dental services on the prevalence of subjective cognitive decline among middle-aged and older US adults: Behavioral Risk Factor Surveillance System, 2022. *Prev Chronic Dis.* 2025;22:E57. doi: 10.5888/pcd22.250083.



2025 Additional Suggested Readings

1. Charisis S, Lu S, Melgarejo JD, et al. Association of blood lipoprotein levels with incident Alzheimer disease in community-dwelling individuals: the Framingham Heart Study. *Neurology*. 2025;104(12):e213715. doi: 10.1212/WNL.00000000000213715.
2. Francis L, Seshadri S, Dillard LK, et al. Self-reported hearing aid use and risk of incident dementia. *JAMA Neurol*. 2025;82(11):1195–1197. doi: 10.1001/jamaneurol.2025.2713.
3. Mattke S, Chen J, Hanson M, et al. Estimation of the value-based price of a blood test for Alzheimer's disease pathology in primary and specialty care in the U.S. *J Prev Alzheimer's Dis*. 2025;12(7):100219. doi: 10.1016/j.tpad.2025.100219.
4. Sawyer RP, Bennett A, Blair J, et al. Circulating biomarkers of neurodegeneration and risk of cognitive impairment. *Neurology*. 2025;105(4):e213935. doi: 10.1212/WNL.00000000000213935.
5. Tideman P, Karlsson L, Strandberg O, et al. Primary care detection of Alzheimer's disease using a self-administered digital cognitive test and blood biomarkers. *Nat Med*. 2025;31(12):4131–4139. doi: 10.1038/s41591-025-03965-4.
6. Trieu C, van Harten AC, van Leeuwenstijn MSSA, et al. Longitudinal blood-based biomarkers and clinical progression in subjective cognitive decline. *JAMA Netw Open*. 2025;8(12):e2545862. doi: 10.1001/jamanetworkopen.2025.45862.
7. Zimmerman SC, Choi M, Jiang C, et al. Statin initiation and dementia incidence in a large health care system from 1997 to 2020: a target trial emulation study. *Neurology*. 2025;105(2):e213855. doi: 10.1212/WNL.00000000000213855.



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