

Dementia and Alzheimer's Disease: A Panoramic Review of Recent Advances in Pathogenesis, Diagnosis, Therapy, and Public Health



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ABSTRACT

Dementia, particularly Alzheimer's disease (AD), has emerged as one of the most pressing global health challenges. With populations aging rapidly, the demand for updated knowledge on disease mechanisms, diagnostics, and therapeutic strategies has never been greater. This review synthesizes recent findings from 2024 to 2025 on dementia and AD, covering the pathophysiology, modern diagnostic techniques, emerging treatments, preventive strategies, and policy frameworks. Special attention is given to breakthroughs in biomarker research, combination therapies, nonamyloid therapeutic targets, and the implementation of the expanded Global Plan on Dementia. By consolidating evidence from the World Health Organization (WHO), the Lancet Commission, and leading academic studies, this review aims to guide clinicians, researchers, and policymakers in shaping the future of dementia care.

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INTRODUCTION

Globally, dementia affects over 57 million people, with Alzheimer's disease (AD) representing the majority of cases.¹⁻³ Projections indicate that by 2050, the prevalence may double, placing an unprecedented burden on healthcare systems, caregivers, and economies, particularly in low- and middle-income countries. The economic toll of dementia is staggering; in the United States alone, costs are expected to reach \$781 billion in 2025, with much of it stemming from long-term care and informal caregiving.⁴

In response, the WHO has expanded its Global Action Plan on Dementia through 2031, emphasizing the development of national strategies, improved diagnostics, caregiver support, and the integration of dementia-friendly policies into public health frameworks.^{3,5} Alongside these global initiatives, research advances in molecular biology, imaging, and therapeutics have created opportunities to transform both the understanding and management of dementia.

ETIOLOGY AND PATHOGENESIS

A Multifactorial Landscape

Alzheimer's disease does not arise from a single cause. Age remains the most potent risk factor, but genetic predisposition, sex differences, environmental exposures, lifestyle behaviors, and chronic diseases all play pivotal roles.^{6,7} The APOE ε4 allele is

widely recognized as a key genetic risk factor for late-onset AD. However, contemporary studies reveal that factors such as chronic inflammation, insulin resistance, and hormonal changes—particularly estrogen deficiency after menopause—also contribute substantially to disease development.^{7,8}

Infection and Systemic Health

Emerging evidence indicates that infections promote neurodegenerative processes. *Porphyromonas gingivalis*, a bacterium linked to periodontal disease, can accelerate amyloid-β deposition and tau pathology, potentially by breaching the blood-brain barrier and triggering neuroinflammation.⁶ Such findings underscore the importance of oral and systemic health as modifiable contributors to dementia risk, suggesting that preventive interventions could extend beyond conventional lifestyle modifications.

Metabolic, Vascular, and Lifestyle Factors

Metabolic disorders, ranging from insulin resistance and diabetes to hypertension and dyslipidemia, are closely associated with increased dementia risk.^{7,9} Lifestyle behaviors, including sedentary habits, limited cognitive stimulation, poor diet, and exposure to environmental pollutants, compound these risks. Importantly, these factors are modifiable, providing a clear rationale for early lifestyle interventions to delay the onset or progression of cognitive decline.¹⁰

EPIDEMIOLOGY AND PUBLIC HEALTH

Recent WHO surveillance data and the global dementia observatory show a steady rise in global dementia cases, exceeding 57 million today.^{1,2} The 2024 Lancet Commission report estimates that up to 45% of cases could be prevented or delayed through modification of 14 key risk factors, including sensory impairments, hypertension, obesity, diabetes, low education, smoking, and social isolation.¹⁰⁻¹²

Despite the evidence, many nations have yet to implement comprehensive national dementia strategies, and public awareness often remains limited. This highlights the urgent need for policies that promote early detection, caregiver support, and dementia-friendly societal infrastructures. Coordinated global efforts are essential to translate scientific advances into practical health solutions.

ADVANCES IN DIAGNOSIS AND BIOMARKERS

Biomarker Innovation and Early Detection

The integration of biomarkers with clinical assessment has revolutionized early diagnosis. Cerebrospinal fluid analysis measuring amyloid-β, total tau, and phosphorylated tau, coupled with advanced imaging techniques such as amyloid/tau PET and MRI, enables the detection of disease processes even before

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clinical symptoms manifest.^{6,7} Artificial intelligence now enhances image analysis, increasing accuracy and reproducibility. Risk stratification algorithms, combining genetic, metabolic, and lifestyle data, facilitate personalized monitoring and intervention strategies.

Recognizing Disease Heterogeneity

Dementia is often heterogeneous, with mixed pathologies complicating diagnosis. AD may coexist with vascular changes, Lewy bodies, or frontotemporal degeneration, while early-onset cases frequently involve distinct genetic or infectious factors.^{8,12} Accurate subtyping is essential to guide therapy and predict disease trajectory, emphasizing the importance of multidisciplinary evaluation.

THERAPEUTIC STRATEGIES AND CLINICAL BREAKTHROUGHS

Symptomatic Treatments

Traditional treatments, such as cholinesterase inhibitors and memantine, continue to offer modest but meaningful improvements in cognition, function, and behavioral symptoms, particularly in mild-to-moderate AD.⁶

Disease-modifying Therapies

Monoclonal antibodies targeting amyloid- β , including lecanemab and donanemab, have been approved for early stage AD and have demonstrated moderate slowing of cognitive decline.⁹ Administration is intravenous, and careful monitoring is required due to potential side effects such as amyloid-related imaging abnormalities. These therapies highlight the shift toward precision medicine in dementia care.

Beyond Amyloid: Emerging Targets

Research from MIT and Harvard has identified alternative pathways involved in neurodegeneration, including DNA repair, RNA modification, and neuroinflammatory mechanisms.⁶⁻⁸ Combination therapies addressing multiple pathogenic mechanisms are being explored. Tau-targeted drugs, autophagy modulators, and kinase inhibitors are undergoing preclinical and early clinical trials, representing next-generation treatment approaches.

Drug Repurposing and Technology-enhanced Interventions

Repurposing existing drugs and integrating digital therapeutics, such as AI-guided cognitive training and tele-rehabilitation, are emerging as adjunctive strategies. Early

evidence suggests these approaches may enhance cognitive resilience and extend functional independence in patients with early or mild dementia.^{6,7}

NONPHARMACOLOGICAL AND MULTIMODAL INTERVENTIONS

Nondrug interventions remain central to comprehensive dementia care. Cognitive stimulation, physical activity, diet optimization, sleep hygiene, social engagement, and sensory support (hearing and vision correction) improve quality of life and reduce caregiver burden.¹⁰⁻¹² Structured programs that integrate caregiver education, social support, and behavioral management enhance patient outcomes and help sustain long-term care at home or in community settings.

PREVENTION, RISK FACTOR MODIFICATION, AND MULTIDOMAIN TRIALS

Prevention strategies focus on managing cumulative risk factors. Evidence supports multifactorial interventions targeting education, vascular and metabolic health, head injury prevention, and sensory rehabilitation.^{10,11} Randomized multidomain trials confirm that combining lifestyle, cognitive, and pharmacologic interventions can delay dementia onset and slow progression, particularly when applied early.

SOCIOECONOMIC AND GLOBAL POLICY CONSIDERATIONS

Dementia imposes a substantial economic burden, with costs exceeding \$780 billion in the US alone, primarily due to informal caregiving, hospitalization, and productivity losses.^{1,4} Globally, policymakers are advocating for dementia-friendly legislation, national registries, trained workforces, and integrated social and healthcare systems.^{3,5,13} Investment in preventive strategies and public health infrastructure is both ethically and economically essential.

FUTURE DIRECTIONS AND RESEARCH GAPS

While recent advances, from anti-amyloid therapies to multiomic research, have been promising, critical gaps remain. These include equitable access to diagnostics and therapeutics, personalized multimodal interventions, strengthened interdisciplinary

collaborations, and better support for caregivers.⁶⁻⁸ Future research must also explore scalable interventions suitable for diverse healthcare contexts and low-resource settings.

CONCLUSION

The period 2024–2025 marks a transformative phase in dementia and AD research. Progress in molecular biology, diagnostics, therapeutic innovations, and public health frameworks is reshaping how dementia is understood and managed. By integrating evidence-based clinical strategies, holistic nonpharmacological care, and robust policy initiatives, the global community can begin to mitigate the burden of dementia. Sustained investment, interdisciplinary collaboration, and strategic implementation are essential to translate scientific discoveries into meaningful improvements in patient outcomes and societal well-being.

SOURCE OF SUPPORT

None.

CONFLICT OF INTEREST

None.

ETHICAL CLEARANCE

Not applicable.

PATIENT CONSENT

Not applicable.

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