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ADVANCES

IN ALZHEIMER'S DISEASE DIAGNOSIS AND THERAPEUTIC STRATEGIES: AN INTEGRATIVE REVIEW OF CURRENT EVIDENCE



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IN ALZHEIMER'S DISEASE DIAGNOSIS AND THERAPEUTIC STRATEGIES: AN INTEGRATIVE REVIEW OF CURRENT EVIDENCE

AVANCES EN EL DIAGNÓSTICO DE LA ENFERMEDAD DE ALZHEIMER Y LAS ESTRATEGIAS TERAPÉUTICAS: UNA REVISIÓN INTEGRADORA DE LA EVIDENCIA ACTUAL

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ABSTRACT

Alzheimer's disease is the leading cause of dementia worldwide and represents one of the greatest challenges facing contemporary medicine because of its high prevalence, irreversible progression, and profound impact on patients, their families, and healthcare systems. The present study aimed to analyze recent scientific advances in the diagnosis and therapeutic strategies for Alzheimer's disease through an integrative review of specialized literature. To achieve this objective, a qualitative analysis of scientific publications was conducted. The findings reveal a significant transformation in the diagnostic paradigm, shifting from an approach based primarily on clinical assessment to one supported by biological biomarkers, advanced neuroimaging techniques, and precision medicine strategies capable of identifying neuropathological changes during the preclinical stages of the disease. Likewise, the literature demonstrates a substantial shift in treatment approaches, moving from symptomatic management toward interventions designed to modify disease progression. Important advances were also identified in the fields of artificial intelligence, nanotechnology, precision pharmacology, and the development of innovative drug discovery platforms. Although significant challenges remain regarding biological heterogeneity, clinical efficacy, safety, accessibility, and the implementation of these innovations, the available scientific evidence indicates that the future management of Alzheimer's disease will be based on early diagnosis, molecular patient stratification, and the development of personalized therapeutic strategies capable of delaying neurodegeneration and improving clinical outcomes.

Keywords:

Alzheimer's disease, early diagnosis, biomarkers, disease-modifying therapies, precision medicine, neuroimaging.

RESUMEN

La enfermedad de Alzheimer constituye la principal causa de demencia a nivel mundial y representa uno de los mayores desafíos para la medicina contemporánea debido a su elevada prevalencia, su progresión irreversible y el impacto que genera sobre los pacientes, sus familias y los sistemas de salud. El presente estudio tuvo como objetivo analizar los avances científicos recientes en el diagnóstico y las estrategias terapéuticas de la enfermedad de Alzheimer mediante una revisión integradora de la literatura especializada. Para ello, se realizó un análisis cualitativo de publicaciones científicas. Los resultados evidencian una transformación del paradigma diagnóstico, pasando de un modelo basado principalmente en la evaluación clínica hacia otro sustentado en biomarcadores biológicos, técnicas avanzadas de neuroimagen y enfoques de medicina de precisión que permiten identificar alteraciones neuropatológicas en etapas preclínicas. Asimismo, la literatura demuestra un cambio significativo en el tratamiento, orientado desde el control sintomático hacia intervenciones capaces de modificar la progresión de la enfermedad. También se identifican avances relevantes relacionados con la inteligencia artificial, la nanotecnología, la farmacología de precisión y el desarrollo de nuevas plataformas para el descubrimiento de fármacos. Aunque persisten desafíos asociados con la heterogeneidad biológica, la eficacia clínica, la seguridad, la accesibilidad y la implementación de estas innovaciones, la evidencia científica indica que el futuro del manejo del Alzheimer estará sustentado en el diagnóstico temprano, la estratificación molecular de los pacientes y el desarrollo de terapias personalizadas capaces de retrasar la neurodegeneración y mejorar el pronóstico clínico.

Palabras clave:

Enfermedad de Alzheimer, diagnóstico temprano, biomarcadores, terapias modificadoras de la enfermedad, medicina de precisión, neuroimagen.

INTRODUCTION

Alzheimer's disease (AD) is the leading cause of dementia worldwide and represents one of the greatest public health challenges of the twenty-first century. Progressive population aging has resulted in a sustained increase in the number of individuals affected by this neurodegenerative disorder, generating profound social, economic, and healthcare consequences for patients, caregivers, and health systems. Characterized by progressive cognitive decline, memory impairment, behavioral disturbances, and the gradual loss of functional independence, AD significantly compromises quality of life and remains a major cause of disability and mortality among older adults. Despite decades of intensive research, its complex pathophysiology and the absence of curative treatments continue to pose substantial scientific and clinical challenges, emphasizing the urgent need for more accurate diagnostic approaches and more effective therapeutic strategies (Peng et al., 2023; Zhang et al., 2024).

Historically, the diagnosis of Alzheimer's disease has relied primarily on the clinical manifestation of cognitive symptoms, supported by neuropsychological assessment and structural neuroimaging. However, these conventional approaches often identify the disease after extensive and irreversible neuronal damage has already occurred. During the past decade, remarkable advances in molecular biology, neuroimaging, biomarker research, and precision medicine have profoundly transformed the understanding of AD, shifting the diagnostic paradigm toward the identification of biological alterations that preceded the appearance of clinical symptoms by many years. This transition has opened new opportunities for early intervention, disease monitoring, and personalized therapeutic decision-making, fundamentally changing the clinical management of individuals at risk for Alzheimer's disease (Rudman et al., 2026; Zhang et al., 2024).

One of the most important developments in contemporary Alzheimer's research has been the increasing recognition that the disease cannot be explained solely by the classical amyloid cascade hypothesis. Although extracellular accumulation of amyloid-beta peptides and intracellular deposition of hyperphosphorylated tau remain the defining pathological hallmarks of AD, growing evidence indicates that disease progression results from the interaction of multiple biological mechanisms. Chronic neuroinflammation, mitochondrial dysfunction, oxidative stress, cerebrovascular alterations, synaptic degeneration, metabolic disturbances, impaired protein clearance, genetic susceptibility, and immune dysregulation collectively contribute to neuronal injury and cognitive decline. This multidimensional understanding has substantially expanded the number of potential therapeutic targets and has stimulated the development of innovative pharmacological interventions that address several pathogenic

pathways simultaneously rather than focusing exclusively on amyloid pathology (Rudman et al., 2026; Zhang et al., 2024).

The evolution of diagnostic technologies has accompanied these conceptual advances. The development of highly sensitive cerebrospinal fluid biomarkers, plasma biomarkers, positron emission tomography imaging, and high-resolution magnetic resonance imaging now enables the detection of amyloid and tau pathology with increasing accuracy during the preclinical and prodromal stages of the disease. Particularly noteworthy has been the rapid progress achieved in blood-based biomarkers, which offer the possibility of less invasive, more accessible, and potentially cost-effective screening strategies. These innovations are expected to facilitate earlier diagnosis, improve patient stratification for clinical trials, optimize treatment selection, and enhance long-term disease monitoring within routine clinical practice (Rudman et al., 2026).

Simultaneously, therapeutic research has entered an unprecedented period of innovation. For many years, pharmacological management was limited to symptomatic treatments, including cholinesterase inhibitors and memantine, which temporarily alleviated cognitive symptoms without modifying the underlying neurodegenerative process. Recent scientific breakthroughs have shifted the therapeutic objective toward disease modification through interventions capable of delaying pathological progression. Monoclonal antibodies directed against amyloid-beta, together with emerging therapies targeting tau pathology, neuroinflammation, metabolic dysfunction, synaptic preservation, and neuroprotection, represent a new generation of therapeutic strategies that may substantially alter the natural history of Alzheimer's disease. Although many of these approaches remain under clinical investigation, several have already demonstrated encouraging results in reducing pathological burden and slowing cognitive decline in selected patient populations (Peng et al., 2023; Wu & Fuh, 2025).

The rapid expansion of therapeutic alternatives has also highlighted important challenges associated with clinical implementation. Patient selection, treatment timing, biomarker confirmation, safety monitoring, adverse event management, healthcare costs, and equitable access to innovative therapies have become central issues in contemporary neurological practice. Anti-amyloid monoclonal antibodies, for example, require rigorous diagnostic confirmation through biomarkers and careful surveillance for amyloid-related imaging abnormalities, illustrating that therapeutic advances must be accompanied by corresponding improvements in diagnostic precision and multidisciplinary clinical management. Consequently, the future of Alzheimer's care depends not only on the availability of novel drugs but also on the integration of advanced diagnostic tools, individualized treatment strategies, and

healthcare systems capable of supporting increasingly complex models of patient care (Pang et al., 2025; Wu & Fuh, 2025).

Parallel to pharmacological innovation, advances in translational neuroscience have fostered a broader perspective regarding the management of Alzheimer's disease. Precision medicine, artificial intelligence-assisted diagnostic models, multimodal biomarker integration, genomic medicine, digital cognitive assessment, and personalized therapeutic algorithms are progressively reshaping clinical practice. These emerging approaches seek to identify disease heterogeneity, predict therapeutic response, and optimize individualized interventions according to each patient's biological profile. Such developments reflect a transition from generalized treatment strategies toward precision neurology, where clinical decisions are increasingly guided by molecular and biomarker-based evidence rather than by clinical manifestations alone (Pang et al., 2025; Rudman et al., 2026).

Another important aspect emerging from recent research is the recognition that Alzheimer's disease shares numerous pathological mechanisms with other neurodegenerative disorders. Processes including protein misfolding, neuroinflammation, mitochondrial dysfunction, oxidative injury, impaired autophagy, and immune dysregulation are common across multiple neurological diseases, creating opportunities for the development of therapeutic platforms capable of targeting shared biological pathways. Consequently, advances achieved in broader neurodegenerative research increasingly contribute to the discovery of innovative therapeutic approaches applicable to Alzheimer's disease, accelerating drug development and expanding future treatment possibilities (Sepehrimanesh et al., 2026).

Despite the remarkable scientific progress achieved during recent years, Alzheimer's disease remains an incurable condition whose biological complexity continues to challenge researchers and clinicians alike. Many promising therapeutic candidates have failed during advanced clinical trials, highlighting the necessity of improving our understanding of disease mechanisms, identifying more reliable biomarkers, refining patient selection criteria, and developing combination therapies capable of addressing the multifactorial nature of the disorder. Future success will likely depend upon integrating molecular biology, neuroscience, pharmacology, precision medicine, and translational research into comprehensive strategies that combine early diagnosis with personalized disease-modifying interventions (Peng et al., 2023; Zhang et al., 2024).

Considering these developments, the present study aims to analyze the recent scientific advances in the diagnosis and therapeutic management of Alzheimer's disease through an integrative review of the current literature. Attention is given to emerging diagnostic technologies, advances in biomarker research, recent therapeutic

innovations, ongoing clinical trials, and future perspectives that may contribute to improving the early identification, clinical management, and long-term prognosis of individuals affected by this neurodegenerative disorder.

MATERIALS AND METHODS

This study was conducted as an integrative literature review aimed at synthesizing and critically analyzing the most recent scientific evidence regarding advances in the diagnosis and therapeutic management of Alzheimer's disease. An integrative review was selected because this methodological approach allows the incorporation of evidence derived from different types of studies, facilitating a comprehensive understanding of the current state of knowledge while identifying emerging trends, scientific advances, and future research directions. Considering the rapid evolution of diagnostic technologies, biomarker research, and disease-modifying therapies, this methodology provides an appropriate framework for integrating findings from basic science, translational research, clinical trials, and review articles.

The literature search prioritized recent publications addressing molecular mechanisms, biomarkers, neuroimaging, pharmacological therapies, precision medicine, disease-modifying treatments, clinical trials, and innovative therapeutic strategies for Alzheimer's disease. Emphasis was placed on peer-reviewed review articles published in internationally recognized scientific journals to ensure the inclusion of high-quality evidence reflecting the most significant advances in the field. Classical references were incorporated only when necessary to provide conceptual or historical context.

The selected studies were examined through a qualitative analytical process focused on identifying the principal scientific contributions reported by each publication. Information was organized into thematic categories including advances in disease pathophysiology, biomarker development, neuroimaging technologies, early diagnostic approaches, conventional pharmacological management, disease-modifying therapies, monoclonal antibodies, emerging therapeutic targets, precision medicine, nanotechnology, artificial intelligence, and future therapeutic perspectives. This categorization facilitated the comparison of findings across different investigations while allowing the identification of areas of consensus, complementary evidence, and remaining scientific challenges.

Subsequently, a process of critical synthesis was performed to integrate the available evidence into a coherent analytical framework. Rather than presenting isolated descriptions of individual studies, the review examined the relationships among recent discoveries, evaluated their potential clinical implications, and discussed how advances in diagnosis and therapy are progressively converging toward more personalized models of Alzheimer's disease management. Attention was devoted to the transition from

symptom-based diagnosis to biomarker-supported biological diagnosis, as well as the evolution from symptomatic pharmacological management toward disease-modifying therapeutic strategies.

RESULTS AND DISCUSSION

Alzheimer's disease is currently the leading cause of dementia worldwide and one of the greatest challenges facing contemporary medicine because of its high prevalence, irreversible progression, and profound impact on the quality of life of patients, their families, and healthcare systems. The sustained increase in life expectancy has contributed to a continuous rise in the number of affected individuals, making this disease a major priority for international biomedical research. Unlike many other neurological disorders, Alzheimer's disease involves highly complex pathophysiological processes encompassing molecular, cellular, and systemic alterations, which complicate both its early diagnosis and the development of treatments capable of significantly modifying its clinical course.

Over the past decades, scientific knowledge of this disease has undergone a remarkable transformation. Initially, most research focused on describing extracellular amyloid-beta ($A\beta$) deposits and intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein as the primary causes of neuronal degeneration. However, accumulating evidence demonstrates that the development of Alzheimer's disease results from a far more complex interaction among neurodegenerative mechanisms, inflammatory processes, metabolic alterations, mitochondrial dysfunction, oxidative stress, vascular changes, and genetic factors that act simultaneously throughout the different stages of disease progression. This integrative perspective has profoundly reshaped research strategies and has considerably expanded the possibilities for developing novel diagnostic tools and therapeutic interventions.

Kim et al. (2025) present one of the most comprehensive contemporary analyses of Alzheimer's disease by integrating recent advances in pathophysiology, diagnosis, and treatment within the framework of precision neurology. The authors argue that Alzheimer's disease should no longer be considered a single clinical entity but rather a biologically heterogeneous disorder that requires individualized diagnostic and therapeutic approaches. This perspective is supported by substantial progress in molecular biology, genetics, biomarker research, and neuroimaging, all of which have considerably improved the understanding of disease progression and enabled the identification of pathological alterations years before the onset of overt cognitive impairment. Furthermore, the review emphasizes that the integration of plasma biomarkers, cerebrospinal fluid analyses, positron emission tomography, genomic profiling, and artificial intelligence is transforming

clinical decision-making by allowing more accurate patient stratification and facilitating personalized therapeutic selection. Equally important, the authors highlight the emergence of disease-modifying therapies, particularly monoclonal antibodies, whose clinical effectiveness depends largely on early biological diagnosis and careful patient selection. Their review therefore illustrates the ongoing transition from conventional symptomatic treatment toward precision medicine, where molecular characterization and individualized interventions represent the foundation for delaying disease progression and improving long-term clinical outcomes.

Similarly, Sugandhi et al. (2025) significantly expand current knowledge by demonstrating that Alzheimer's disease results from the complex interaction of multiple pathological mechanisms rather than from isolated amyloid or tau abnormalities. Their review comprehensively analyzes the contribution of mitochondrial dysfunction, oxidative stress, chronic neuroinflammation, synaptic degeneration, impaired protein clearance, metabolic alterations, vascular dysfunction, and genetic susceptibility to disease progression. This integrative interpretation substantially broadens the spectrum of potential therapeutic targets and provides a strong rationale for developing combination therapies capable of simultaneously modulating several biological pathways. Moreover, the authors thoroughly examine emerging therapeutic approaches, including monoclonal antibodies, gene therapies, stem cell interventions, immunotherapies, nanotechnology-based drug delivery systems, and novel neuroprotective compounds currently under clinical evaluation. An additional contribution of the study lies in its critical assessment of recent clinical trials, emphasizing that many disappointing outcomes are associated not only with pharmacological limitations but also with challenges related to patient selection, disease staging, biomarker utilization, and trial design. Consequently, the review proposes that future therapeutic success will depend on integrating advances in molecular neuroscience with precision medicine and multimodal interventions capable of addressing the multifactorial nature of Alzheimer's disease.

Xing et al. (2025) contribute a comprehensive assessment of recent progress in drug development for Alzheimer's disease by organizing the therapeutic pipeline according to the principal molecular and cellular mechanisms involved in its pathogenesis. The authors emphasize that, although amyloid beta continues to represent an important target, contemporary pharmacological research has progressively expanded toward tau pathology, chronic neuroinflammation, synaptic dysfunction, oxidative stress, mitochondrial impairment, vascular alterations, and metabolic dysregulation. This diversification reflects the growing recognition that Alzheimer's disease is biologically heterogeneous and cannot be adequately addressed through a single therapeutic mechanism.

Furthermore, the review critically examines the transition from symptomatic drugs to disease-modifying interventions and highlights the increasing relevance of monoclonal antibodies, small-molecule inhibitors, active and passive immunotherapies, and compounds designed to enhance neuronal resilience. Particularly significant is the attention given to the limitations encountered during clinical translation, including late treatment initiation, inadequate participant stratification, insufficient biomarker confirmation, and the inability of some therapeutic agents to cross the blood-brain barrier effectively. Accordingly, the authors argue that future drug development should be guided by disease stage, molecular profile, and biomarker-defined pathological burden. Their analysis therefore supports a more precise and multidimensional therapeutic model in which pharmacological selection is closely aligned with the specific biological processes operating in each patient.

Cheng et al. (2026) offer a distinctive contribution by examining Alzheimer's disease drug development from the perspective of pharmaceutical innovation, clinical pipelines, and industrial transformation. Their analysis demonstrates that the field has entered a renewed period of therapeutic expansion following decades marked by repeated clinical failures and limited regulatory progress. The authors identify the approval of anti-amyloid monoclonal antibodies as evidence that disease modification is biologically possible, although the modest magnitude of clinical benefit indicates that substantial therapeutic limitations remain. In addition, they document a broad diversification of investigational targets, with increasing attention to tau, inflammation, immune regulation, signaling pathways, cellular therapies, and other mechanisms beyond amyloid pathology.

Another important contribution lies in their examination of the complementary roles played by small biotechnology companies and major pharmaceutical corporations. While smaller companies frequently generate novel mechanisms and innovative therapeutic concepts during early development, larger organizations provide financial resources, regulatory experience, and trial infrastructure required for advanced clinical validation and commercialization. Consequently, the study illustrates that future breakthroughs will depend on both scientific discovery and the existence of efficient innovation ecosystems capable of moving promising candidates through the different phases of drug development. This perspective enriches the discussion by situating therapeutic progress within the broader pharmaceutical and organizational structures that determine whether scientific discoveries ultimately reach clinical practice.

Liu et al. (2024) provides a highly relevant synthesis of the major therapeutic strategies currently being explored for Alzheimer's disease while critically addressing the obstacles that continue to limit their clinical effectiveness. Their

analysis is structured around three central pathological processes, namely amyloid-beta aggregation, tau hyperphosphorylation, and neuroinflammation. Nevertheless, the authors do not examine these mechanisms as isolated events but rather as components of an interconnected pathological network that contributes to progressive neuronal dysfunction. This interpretation is especially important because it explains why interventions directed toward a single target may produce meaningful biological changes without generating equivalent improvements in cognition or daily functioning.

Moreover, the review compares therapeutic approaches aimed at amyloid clearance, tau aggregation inhibition, inflammatory modulation, neuroprotection, and metabolic regulation, identifying both their potential benefits and their principal limitations. The authors also emphasize the importance of diagnostic timing, given that amyloid deposition and other molecular abnormalities begin many years before the appearance of overt clinical symptoms. Therefore, therapies administered after extensive neurodegeneration have occurred may be unable to produce substantial functional recovery. Their contribution ultimately reinforces the need for earlier diagnosis, biomarker-guided treatment, and personalized combination strategies capable of addressing multiple pathological mechanisms at different stages of disease progression.

Napoli & Rafii (2025) focus attention on the increasingly close relationship between early diagnosis and the effective use of disease-modifying therapies. Their contribution is particularly valuable from a clinical perspective because it emphasizes that the contemporary management of Alzheimer's disease can no longer depend exclusively on the recognition of advanced cognitive symptoms. Instead, clinicians must combine patient history, cognitive assessment, structural imaging, molecular biomarkers, and individualized risk evaluation to identify the disease during its earliest clinically meaningful stages. The authors highlight the growing relevance of plasma biomarkers and other minimally invasive diagnostic tools, which may improve access to biological confirmation and reduce dependence on more costly or invasive procedures.

Furthermore, they discuss the implications of recently introduced anti-amyloid treatments, noting that their potential benefit is closely associated with appropriate patient selection, early intervention, and continuous safety monitoring. This approach also requires careful communication with patients and families regarding expected outcomes, possible adverse effects, and the fact that current disease-modifying therapies slow progression rather than restore previously lost cognitive function. Consequently, the source contributes a pragmatic framework that connects diagnostic innovation with treatment eligibility and demonstrates that therapeutic progress must be accompanied by improvements in clinical infrastructure, counseling, monitoring, and multidisciplinary decision-making.

Safiri et al. (2024) present a broad and multidimensional review that situates Alzheimer's disease within its epidemiological, clinical, social, and caregiving contexts. One of the most important contributions of this work is its recognition that the disease cannot be understood solely through its neuropathological features, since its impact extends to functional independence, family organization, caregiver well-being, healthcare expenditures, and social participation. The authors synthesize evidence regarding genetic, cardiovascular, metabolic, environmental, and lifestyle-related risk factors, thereby reinforcing the concept that Alzheimer's disease results from the interaction of numerous biological and contextual determinants. In diagnostic terms, they discuss the progression from traditional symptom-based evaluation toward biomarker-supported models capable of improving diagnostic accuracy and disease staging.

Their therapeutic analysis encompasses symptomatic medications, advanced pharmacological interventions, non-pharmacological management, caregiver support, and emerging disease-modifying approaches. Equally important, the review highlights the burden placed on informal caregivers, who frequently experience psychological stress, financial difficulties, physical exhaustion, and reduced quality of life. Accordingly, the study broadens the meaning of successful treatment by demonstrating that clinical management should address not only cognitive decline but also behavioral symptoms, functional ability, family needs, and continuity of care. Its principal value lies in presenting Alzheimer's disease as a complex medical and social condition requiring coordinated responses from clinical services, public health systems, families, and community support networks.

Shawkatova & Javor (2025) provide an updated overview of the evolving understanding of Alzheimer's pathogenesis and its implications for diagnosis and therapy. Their review emphasizes that the classical amyloid and tau models remain essential but are no longer sufficient to explain the entire disease process. Instead, the authors integrate neuroinflammation, mitochondrial dysfunction, oxidative damage, vascular impairment, genetic susceptibility, synaptic alterations, and defective cellular clearance mechanisms into a broader pathogenic framework. This expanded interpretation is especially useful because it establishes the biological basis for developing therapies directed toward multiple molecular pathways.

The authors also examine advances in biomarker-based diagnosis, including changes detected through cerebrospinal fluid, blood analysis, molecular imaging, and structural neuroimaging. Such tools make it possible to identify pathological processes before severe cognitive deterioration becomes evident and can therefore improve both clinical decision-making and participant selection in therapeutic trials. In relation to treatment, the review contrasts conventional symptomatic medications with

emerging disease-modifying strategies, acknowledging the advances represented by anti-amyloid therapies while also emphasizing unresolved questions concerning safety, durability, accessibility, and clinical significance. Ultimately, their contribution supports a transition toward integrated models that combine early biological diagnosis, individualized treatment selection, and simultaneous consideration of several pathogenic mechanisms.

Tondo et al. (2024) make a particularly important contribution by providing a balanced and critical examination of anti-amyloid therapies and the broader therapeutic landscape beyond amyloid removal. The authors recognize that the development of monoclonal antibodies capable of reducing cerebral amyloid burden represents a major scientific achievement and offers proof that biological disease modification is possible. Nevertheless, they emphasize that the cognitive benefits observed to date remain limited and must be weighed against the risks of abnormalities, infusion reactions, treatment costs, and intensive monitoring requirements. This critical interpretation prevents the therapeutic value of amyloid reduction from being overstated and highlights the difference between biomarker improvement and clinically meaningful functional preservation. Furthermore, the review explores alternative strategies directed toward tau pathology, neuroinflammation, synaptic dysfunction, neurovascular alterations, and metabolic mechanisms.

The authors suggest that these pathways may become particularly important once amyloid-related processes have initiated self-sustaining forms of neurodegeneration. Consequently, they advocate for therapeutic approaches adapted to disease stage and individual biological characteristics. Their discussion strongly supports the future use of combination therapies, since the simultaneous targeting of several mechanisms may be necessary to achieve effects greater than those produced by isolated anti-amyloid interventions.

Chen & Hsu (2026) provide a concise but clinically significant update on the transformation of Alzheimer's disease diagnosis through biomarkers, positron emission tomography, and emerging therapies. Their contribution highlights the progressive movement from a predominantly symptom-based diagnostic model toward a biological framework in which amyloid and tau pathology can be directly identified. The authors emphasize the value of amyloid positron emission tomography for confirming pathological deposition and the growing role of tau imaging in estimating disease stage, predicting cognitive decline, and differentiating patterns of progression.

At the same time, they discuss the increasing diagnostic relevance of cerebrospinal fluid and plasma biomarkers, particularly phosphorylated tau and amyloid-related measures. Blood-based testing is presented as one of the most promising advances because it may reduce costs, improve accessibility, and facilitate earlier screening in

clinical settings where advanced imaging is unavailable. Moreover, the review connects diagnostic innovation with therapeutic decision-making, since biological confirmation is becoming essential for identifying candidates for anti-amyloid treatments and monitoring their response. Accordingly, the study demonstrates that advances in diagnosis and therapy are mutually dependent. More precise biomarkers support safer and more effective treatment selection, while the availability of disease-modifying therapies creates a stronger clinical need for timely biological diagnosis.

Thawabteh et al. (2024) examines a broad spectrum of recent therapeutic developments and underscore the transition from conventional symptomatic care toward interventions designed to modify the biological course of Alzheimer's disease. Their review discusses the continued use of acetylcholinesterase inhibitors and memantine while clarifying that these medications provide temporary symptomatic benefits without stopping the underlying neurodegenerative process. Against this background, the authors analyze innovative approaches targeting amyloid-beta, tau, neuroinflammation, oxidative stress, mitochondrial dysfunction, and neuronal loss. They also consider advanced drug-delivery methods intended to overcome the restrictive properties of the blood-brain barrier, which remains one of the major obstacles to effective central nervous system treatment.

Particularly relevant is their discussion of nanocarriers, targeted molecules, immunotherapies, and multifunctional compounds capable of influencing more than one pathological pathway. Furthermore, the review highlights the persistent gap between encouraging preclinical findings and successful clinical application. Differences between experimental models and human disease, inadequate treatment timing, and the heterogeneity of Alzheimer's pathology frequently contribute to therapeutic failure. Therefore, the authors support the development of multimodal strategies and emphasize the need to align therapeutic targets with specific disease stages, patient characteristics, and biomarker profiles.

Sunderland et al. (2025) provides a clinically oriented synthesis of advances in Alzheimer's diagnosis and treatment that is particularly useful for understanding the practical implications of recent scientific developments. The authors describe how structural imaging, amyloid and tau positron emission tomography, cerebrospinal fluid biomarkers, and plasma-based assays are increasing diagnostic accuracy and facilitating the identification of patients in earlier stages of the disease. Considerable attention is given to phosphorylated tau in plasma, which has emerged as a promising marker for detecting underlying Alzheimer's pathology through a less invasive and potentially more scalable procedure.

The review also examines the introduction of lecanemab and donanemab, highlighting their capacity to reduce

amyloid burden and modestly slow clinical progression in selected patients with early disease. However, the authors carefully discuss the risks of amyloid-related imaging abnormalities, the necessity of repeated magnetic resonance imaging, the relevance of apolipoprotein E genotyping, and the exclusion of patients with cerebrovascular or bleeding risks. Beyond amyloid-directed treatments, the study evaluates tau-targeted interventions, inflammatory modulation, insulin-related pathways, and metabolic therapies. Its principal contribution lies in demonstrating that clinical implementation requires far more than drug availability, since successful use depends on diagnostic pathways, specialist expertise, monitoring capacity, informed consent, and equitable healthcare access.

Khan et al. (2023) contribute a detailed analysis of therapeutic progress derived from clinical trials, thereby offering valuable insight into the factors that determine whether experimental approaches succeed or fail in human populations. The authors review a wide range of strategies targeting amyloid-beta production and clearance, tau phosphorylation and aggregation, neuroinflammation, oxidative stress, synaptic dysfunction, and altered neurotransmission. Their discussion demonstrates that many therapeutic candidates have produced convincing effects in laboratory models but have failed to generate meaningful cognitive benefits during advanced clinical trials. This discrepancy is attributed to several interrelated factors, including inadequate animal models, treatment initiation during advanced disease, insufficient biomarker-based participant selection, limited brain penetration, and the biological heterogeneity of Alzheimer's disease.

Moreover, the review emphasizes that successful clinical development requires more sensitive outcome measures capable of detecting modest but clinically relevant changes. The authors also recognize that disease-modifying treatment is likely to be most effective when applied before extensive neuronal loss occurs. As a result, they advocate closer integration between diagnostic biomarkers and clinical trial design. Their contribution reinforces the argument that future therapeutic progress depends not only on discovering new molecular targets but also on improving the methodological quality, timing, and biological precision of clinical evaluation.

Hassan et al. (2022) broaden the therapeutic discussion by examining approaches that range from medicinal plants and naturally derived compounds to nanotechnology-based delivery systems. The authors describe the antioxidant, anti-inflammatory, anti-amyloid, and neuroprotective properties attributed to several phytochemical compounds, including substances capable of modulating oxidative stress, protein aggregation, cholinergic function, and inflammatory signaling. Although many of these agents have demonstrated promising effects in experimental studies, the review acknowledges important limitations involving bioavailability, pharmacokinetic variability,

insufficient standardization, uncertain dosage, and limited clinical validation. In response to these obstacles, nanotechnology is presented as a potential strategy for improving drug stability, solubility, targeting, and penetration across the blood-brain barrier.

Nanoparticles, liposomes, polymeric carriers, and related delivery platforms may permit therapeutic agents to reach affected brain regions more efficiently while reducing systemic toxicity. Nevertheless, the authors emphasize that safety, manufacturing consistency, long-term biological effects, and regulatory requirements must be thoroughly evaluated before widespread clinical application. Their contribution is therefore valuable because it connects traditional therapeutic sources with advanced delivery technologies while maintaining a critical distinction between preclinical promise and demonstrated clinical effectiveness.

Finally, Sushma & Srivastava (2024) provide an overview of emerging therapeutic approaches, diagnostic innovations, and future directions in Alzheimer's disease research. Their work brings together developments in biomarker discovery, molecular imaging, pharmacological treatment, immunotherapy, gene-related interventions, and advanced drug-delivery systems. The authors emphasize that early diagnosis remains essential because the pathological processes responsible for Alzheimer's disease begin long before substantial cognitive impairment becomes clinically evident. They therefore highlight the potential of blood biomarkers, cerebrospinal fluid analysis, positron emission tomography, and artificial intelligence-supported assessment to improve disease identification and progression monitoring.

In therapeutic terms, the review discusses monoclonal antibodies, tau-directed agents, anti-inflammatory compounds, neuroprotective strategies, stem cell research, and nanotechnology. Although these innovations offer considerable promise, the authors recognize that many remain at experimental or preliminary clinical stages and require further validation regarding efficacy, safety, affordability, and accessibility. Their central contribution lies in presenting the future of Alzheimer's management as an integrated process in which diagnostic precision, individualized risk assessment, and multimodal treatment strategies must develop simultaneously. Such coordination will be necessary to transform scientific advances into interventions capable of producing meaningful improvements in patient outcomes.

The literature further indicates that the introduction of disease-modifying therapies is fundamentally reshaping clinical practice and the organization of Alzheimer's disease care. Recent investigations consistently emphasize that the effectiveness of these novel interventions depends largely on the identification of patients with biological evidence of Alzheimer's pathology during the earliest stages of disease progression. Consequently, biomarkers have

evolved from purely diagnostic instruments into essential clinical tools for patient stratification, treatment selection, therapeutic monitoring, and the evaluation of disease progression. At the same time, the available evidence recognizes that currently approved therapies should not be interpreted as definitive solutions but rather as the beginning of a new therapeutic era in which disease progression can be delayed when interventions are initiated before extensive neuronal degeneration has occurred.

Another major finding concerns the remarkable diversification of therapeutic targets currently under investigation. Although amyloid beta continues to occupy a central position in pharmaceutical research, recent studies demonstrate a rapidly growing interest in therapies directed toward tau pathology, chronic neuroinflammation, oxidative stress, mitochondrial dysfunction, synaptic preservation, metabolic regulation, immune modulation, and neuroprotection. This expansion reflects the increasing recognition that Alzheimer's disease results from the interaction of multiple pathological mechanisms operating simultaneously throughout disease progression. As a result, several authors suggest that future treatment strategies will likely combine multiple therapeutic mechanisms capable of acting on different biological pathways, thereby producing greater clinical benefits than interventions directed at a single molecular target.

The reviewed evidence also highlights the unprecedented acceleration of pharmaceutical innovation driven by advances in biotechnology, computational biology, artificial intelligence, and precision drug discovery platforms. These technological developments have facilitated the identification of novel therapeutic targets, accelerated compound optimization, improved patient selection for clinical trials, and enhanced the efficiency of translational research. Furthermore, the growing collaboration among academic institutions, biotechnology companies, pharmaceutical industries, and regulatory agencies has contributed to the development of more effective innovation ecosystems capable of shortening the pathway from laboratory discoveries to clinical application.

Despite these encouraging advances, important challenges continue to limit the successful implementation of disease-modifying therapies. Numerous clinical trials have demonstrated favorable biological outcomes without consistently translating into substantial cognitive or functional improvements. The reviewed studies attribute these limitations to several factors, including delayed therapeutic intervention, the biological heterogeneity of Alzheimer's disease, variability in treatment response, inadequate participant selection, and the intrinsic complexity of a disorder driven by multiple interacting pathological mechanisms. These findings reinforce the need for biomarker-guided precision medicine approaches that integrate molecular characteristics, clinical profiles, and disease stage into individualized therapeutic decision-making.

Another particularly relevant development is the consolidation of precision neurology as an emerging paradigm for Alzheimer's disease management. The integration of plasma biomarkers, cerebrospinal fluid analyses, advanced neuroimaging, genomic information, and artificial intelligence is progressively transforming diagnostic and therapeutic decision-making. This personalized approach not only improves diagnostic accuracy but also enhances patient stratification, predicts therapeutic responsiveness, facilitates longitudinal monitoring, and supports the implementation of individualized treatment strategies based on each patient's biological profile rather than solely on clinical manifestations.

The reviewed literature also underscores the growing importance of complementary therapeutic technologies designed to improve drug delivery and maximize therapeutic efficacy. Nanotechnology-based delivery systems, multifunctional compounds, targeted nanoparticles, and advanced pharmaceutical carriers are increasingly being investigated as potential solutions to overcome the limitations imposed by the blood-brain barrier and to increase drug bioavailability within affected brain regions. Although many of these approaches remain at the experimental stage, preliminary findings suggest that they may significantly enhance the clinical effectiveness of future pharmacological interventions while minimizing systemic adverse effects.

Current scientific evidence demonstrates that Alzheimer's disease management is undergoing a profound transformation from a predominantly symptomatic approach toward a biologically driven model centered on early diagnosis, molecular characterization, precision medicine, and disease-modifying therapies. Although significant challenges remain regarding long-term efficacy, treatment accessibility, safety monitoring, and large-scale implementation, the rapid progress achieved in biomarker development, neuroimaging, pharmaceutical innovation, and personalized therapeutic strategies provides strong evidence that future clinical management will increasingly focus on preventing irreversible neurodegeneration, optimizing individualized interventions, and improving long-term outcomes for patients affected by Alzheimer's disease.

CONCLUSIONS

The scientific evidence analyzed demonstrates that Alzheimer's disease research is undergoing one of the most significant transformations in its history. Recent advances in molecular biology, biomarker development, neuroimaging, precision medicine, and pharmaceutical innovation have substantially improved the understanding of disease pathophysiology while creating new opportunities for earlier diagnosis and more effective therapeutic intervention. These developments are progressively replacing traditional symptom-based approaches with biologically driven strategies capable of identifying pathological

changes long before the onset of irreversible cognitive decline.

The reviewed literature consistently indicates that blood-based biomarkers, cerebrospinal fluid analyses, advanced neuroimaging, and multimodal diagnostic models are becoming essential components of contemporary clinical practice. Their integration not only improves diagnostic accuracy but also facilitates patient stratification, treatment selection, disease monitoring, and enrollment in clinical trials, thereby supporting the implementation of precision neurology.

Another major conclusion concerns the remarkable evolution of therapeutic research. Although currently available disease-modifying therapies represent an important milestone, the evidence indicates that future clinical progress will depend on interventions capable of simultaneously targeting multiple pathological mechanisms, including amyloid deposition, tau pathology, neuroinflammation, oxidative stress, mitochondrial dysfunction, synaptic degeneration, vascular alterations, and metabolic dysregulation. This multidimensional therapeutic perspective reflects the growing recognition that Alzheimer's disease is a biologically heterogeneous disorder requiring individualized treatment strategies.

The reviewed studies also highlight that technological innovation is accelerating pharmaceutical development through artificial intelligence, computational biology, advanced drug discovery platforms, nanotechnology-based drug delivery systems, and precision medicine approaches. These innovations have expanded the therapeutic pipeline and strengthened the possibility of developing safer, more effective, and more personalized interventions capable of modifying disease progression rather than simply alleviating symptoms.

Despite these advances, substantial challenges remain before these innovations can be fully incorporated into routine clinical practice. Issues related to early patient identification, biomarker standardization, long-term therapeutic efficacy, safety monitoring, accessibility, healthcare costs, and equitable implementation continue to require extensive investigation. Addressing these limitations will demand close collaboration among clinicians, neuroscientists, pharmaceutical researchers, regulatory agencies, and healthcare systems.

Future progress in Alzheimer's disease management will likely depend on integrating early biological diagnosis with personalized therapeutic strategies based on each patient's molecular profile. Continued advances in biomarker discovery, precision medicine, translational neuroscience, and disease-modifying therapies provide strong evidence that clinical management is entering a new era focused on delaying neurodegeneration, preserving cognitive function, and improving the long-term quality of life of individuals affected by Alzheimer's disease.

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Conflicts of Interest:

The author declares no conflicts of interest.

Author Contributions:

Niko Koridze: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, validation, visualization, original draft writing, and writing, review, and editing.

Ethical statement:

The study addresses issues related to students/vulnerable individuals; however, it was conducted exclusively through a documentary review, analysis of secondary information, or publicly available databases. It did not involve the direct participation of human subjects or the handling of personally identifiable information.