International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	ALZHEIMER'S DISEASE - ETIOPATHOGENESIS, CLINICAL PRESENTATION, AND CURRENT DIAGNOSTIC METHODS - A LITERATURE REVIEW
DOI	https://doi.org/10.31435/ijitss.3(51).2026.5857
RECEIVED	12 June 2026
ACCEPTED	26 August 2026
PUBLISHED	10 September 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

ALZHEIMER'S DISEASE - ETIOPATHOGENESIS, CLINICAL PRESENTATION, AND CURRENT DIAGNOSTIC METHODS - A LITERATURE REVIEW

Mateusz Cieciora *(Corresponding Author, Email: mateuszcieciora83@gmail.com)*
University of Technology and Humanities in Radom, Chrobrego 27, 26-600 Radom, Poland
ORCID ID: 0009-0008-0711-9377

Małgorzata Kawiorska
University of Technology and Humanities in Radom, Chrobrego 27, 26-600 Radom, Poland
ORCID ID: 0009-0000-3184-7659

Julia Surowiec
University of Technology and Humanities in Radom, Chrobrego 27, 26-600 Radom, Poland
ORCID ID: 0009-0009-3356-8261

Aleksandra Cieciora
University of Technology and Humanities in Radom, Chrobrego 27, 26-600 Radom, Poland
ORCID ID: 0009-0009-7999-4047

Katarzyna Zegadło
Wojskowy Instytut Medyczny, Warsaw, Mazovia, Poland
ORCID ID: 0009-0000-8489-2058

Katarzyna Kuc
Dr. Tytus Chałubiński Radom Specialist Hospital, ul. Lekarska 4, 26-610 Radom, Poland
ORCID ID: 0009-0002-9585-4377

Maciej Dobrucki
Dr. Tytus Chałubiński Radom Specialist Hospital, ul. Lekarska 4, 26-610 Radom, Poland
ORCID ID: 0009-0002-0124-1853

Krzysztof Brzezicki
Szpital Wojewódzki im. dr. Ludwika Rydygiera w Suwałkach, Suwałki, Poland
ORCID ID: 0009-0005-4315-0644

Patryk Jakubiak
Dr. Tytus Chałubiński Radom Specialist Hospital, ul. Lekarska 4, 26-610 Radom, Poland
ORCID ID: 0009-0006-9138-7213

Wiktoria Bełcikowska-Skowron
Dr. Tytus Chałubiński Radom Specialist Hospital, ul. Lekarska 4, 26-610 Radom, Poland
ORCID ID: 0009-0001-1789-1845

ABSTRACT

Introduction: Alzheimer's disease (AD) is the most common cause of dementia, accounting for 60–80% of cases, and its prevalence is increasing as the population ages. It is estimated that approximately 50 million people worldwide currently live with dementia, and this number could triple by 2050. AD is a chronic, progressive, and incurable disease leading to significant disability and high healthcare costs. Neuropathologically, it is characterized by the presence of β-amyloid plaques and tau neurofibrillary tangles.

Aim of the study: The aim of this study was to present the current state of knowledge regarding Alzheimer's disease, with particular emphasis on etiopathogenesis, risk factors, clinical symptoms, diagnostic methods, and modern biomarkers.

Material and methods: This is a review study based on an analysis of the current scientific literature on AD. The literature available in the PubMed and Google Scholar databases was analyzed using keywords.

Results and conclusions: A review of the literature indicates that AD is a disease with a complex pathogenesis involving β-amyloid accumulation, tau protein hyperphosphorylation, autophagy dysfunction, and genetic factors such as the APOE ε4 allele. Early symptoms mainly include memory and cognitive impairments. Biomarkers, including Aβ42/40, p-tau, NfL, and GFAP, as well as neuroimaging techniques such as MRI and PET, are of key importance in diagnosis. Early detection of the disease in the preclinical phase offers the possibility of implementing measures to slow its progression. Despite the lack of effective causal treatment, the development of biomarkers and diagnostic methods offers hope for improved early diagnosis and more effective monitoring of the disease's progression.

KEYWORDS

Alzheimer's Disease, Neurodegeneration, Beta-Amyloid, Tau Protein, Neuroimaging, Cerebrospinal Fluid

CITATION

Cieciora, M., Kawiorska, M., Surowiec, J., Cieciora, A., Zegadło, K., Kuc, K., Dobrucki, M., Brzezicki, K., Jakubiak, P., & Bełcikowska-Skowron, W. (2026). Alzheimer's disease - etiopathogenesis, clinical presentation, and current diagnostic methods - a literature review. *International Journal of Innovative Technologies in Social Science*, 3(51). https://doi.org/10.31435/ijitss.3(51).2026.5857

Introduction

The aging of populations is leading to a steady increase in the number of people affected by dementia. The most common cause is Alzheimer's disease, which accounts for approximately 60–80% of all cases. This condition is chronic and poses a significant challenge to public health worldwide, as it is one of the most serious diseases affecting brain function [1].

The first description of this condition dates back to 1906 and was presented by the German physician Alois Alzheimer [2]. While analyzing postmortem brain tissue from a patient named Auguste Deter, who had exhibited memory impairments and personality changes prior to her death, the researcher identified the presence of amyloid deposits and extensive neuronal degeneration. He described the observed changes as a severe disease of the cerebral cortex [2,3]. It is estimated that there are currently about 50 million people living with dementia worldwide, and projections indicate that this number could triple by 2050. This phenomenon is associated with increased disability, a greater burden on healthcare systems, and rising costs of treatment and care [4].

In highly developed countries, early-stage Alzheimer's disease affects approximately 10% of people over the age of 65. In the very elderly (85 years and older), this percentage increases significantly—symptoms of the disease may occur in as many as one-third of the population [2]. Currently available treatments are purely symptomatic and do not lead to a cure. Due to the long asymptomatic (prodromal) period, early prevention becomes particularly important, as it can slow the progression of the disease. In this context, epidemiological studies play a key role in identifying risk factors and protective factors influencing cognitive function [4]. Global data indicate that in 2020, the total costs of treatment and care for people with Alzheimer's disease amounted to approximately $305 billion. It is projected that by 2050, these expenses could exceed $1 trillion [5].

Etiopathogenesis

The molecular mechanisms underlying Alzheimer's disease have been the subject of intensive research for many years. Recent reports indicate that in the course of neurodegenerative diseases, not only does pathological protein aggregation occur, but also disturbances in the functioning of neural networks, abnormalities in cellular energy metabolism, changes in cytoskeletal structure, and disruptions in the homeostasis of proteins and metal ions. These processes are accompanied by a decline in cognitive functions, such as memory, language skills, and thinking [6]. The best-characterized molecular markers of Alzheimer's disease are considered to be the deposition of extracellular amyloid plaques, composed of β-amyloid (Aβ), as well as the formation of intracellular neurofibrillary tangles (NFTs), formed by hyperphosphorylated tau protein present in brain neurons [7].

Amyloidosis is classified based on the location of amyloid fiber deposition. There are two forms: localized, confined to a specific tissue, and systemic, affecting multiple organs. Amyloid plaques are composed of amyloid proteins, with the β-amyloid (Aβ) peptide playing a key role in the pathogenesis of Alzheimer's disease; it is considered one of the main factors responsible for the development of this condition [8].

In addition to the accumulation of β-amyloid plaques, neurofibrillary tangles (NFTs), composed of abnormally aggregated forms of the tau protein, are a key feature of the pathological picture of Alzheimer's disease. This protein is associated with microtubules and plays a key role in maintaining their stability and integrity within neurons. It also plays an important role in the proper functioning of nerve cells, including the transport of nutrients within the neuron [9]. In the course of Alzheimer's disease, tau undergoes abnormal post-translational modifications, such as hyperphosphorylation, which leads to a disruption of its physiological function. Modified tau molecules tend to self-aggregate, forming insoluble structures in the form of paired helices (PHF) and straight filaments (SF). These pathological aggregates constitute the main component of neurofibrillary tangles present in the brains of patients [9,10].

Genetic factors also play a significant role in the development of Alzheimer's disease, including the apolipoprotein E (APOE) gene, located on chromosome 19. There are three most common alleles of this gene: ε2, ε3, and ε4. Among these, the APOE ε4 allele is considered the most important genetic risk factor for late-onset Alzheimer's disease, which is also its most common form. The presence of a single copy of this allele increases the likelihood of developing the disease, while having two copies is associated with a significant increase in risk. The ε4 allele promotes increased β-amyloid aggregation and limits its removal from the brain, leading to the accumulation of amyloid plaques. Additionally, carriers of this allele are more likely to exhibit heightened inflammatory processes in the nervous system and greater neuronal damage compared to individuals who do not possess this gene variant [10].

Impaired Autophagy

Autophagy is a vital cellular mechanism involving the degradation of unnecessary proteins and damaged organelles by transporting them to lysosomes. This process plays a key role in maintaining the cell's metabolic balance and structural renewal [8]. In Alzheimer's disease, autophagy is disrupted, resulting in a reduced ability of cells to eliminate toxic aggregates of β-amyloid (Aβ) and amyloid precursor protein (APP). When this mechanism malfunctions, APP may undergo transformations leading to increased Aβ production, which promotes disease progression [8]. Studies indicate that the activation of autophagy, including via the SIRT5 protein, contributes to the reduction of inflammation and has a neuroprotective effect. In contrast, inhibition of this process negates its beneficial protective effects [11].

Early symptoms

Most often, the disease begins with memory impairment, manifested by difficulty remembering new information and a tendency to forget things. Patients may ask the same questions repeatedly, misplace objects, or fail to recall important events. As the disease progresses, language disorders emerge, including problems with word retrieval and selection, grammatical and syntactic errors, and disruptions in the coherence of speech. Additionally, there are difficulties in understanding speech, errors in writing, and general communication disorders that may prevent effective communication with others. Even in the early stages, executive function impairment may occur, manifesting as problems with logical thinking, performing complex tasks, decision-making, and financial management, as well as a decline in social and professional competencies [12].

Initially, there may be subtle impairments in executive function, manifested by an increase in the time required to perform daily activities and a higher frequency of errors. As these deficits worsen, difficulties arise

with mental arithmetic, memorizing, and recalling new information. Impaired visuospatial function includes disorientation in one's surroundings (regarding time, place, and people), loss of awareness of one's own identity (e.g., name, age, occupation), getting lost even in familiar places, as well as problems recognizing faces and everyday objects. Social cognitive impairments manifest as personality changes and the emergence of socially inappropriate behaviors [13].

In the frontal variant of Alzheimer's disease, symptoms associated with damage to the frontal lobes appear relatively early, such as behavioral disturbances, including apathy and a lack of control over one's own reactions. Psychiatric symptoms, such as delusions, may also occur. Executive functions deteriorate significantly, followed by symptoms associated with damage to the temporal-parietal regions, such as severe memory impairment, reduced mathematical ability, and difficulties with spatial orientation. Marked cognitive deficits are also observed in individuals with trisomy 21, who exhibit characteristic physical features and intellectual disability [14].

Diagnosis

The diagnosis of Alzheimer's disease is based primarily on a thorough medical history and the results of a physical examination, supplemented by a detailed analysis of the ABC symptoms. Imaging methods, such as magnetic resonance imaging (MRI) and other structural techniques, as well as functional brain imaging, including positron emission tomography (PET) and single-photon emission computed tomography (SPECT), are also of significant importance. Diagnosis is supplemented by the measurement of biomarkers in blood and cerebrospinal fluid, as well as other ancillary tests, which increase the accuracy of the diagnosis and enable the differentiation of disease subtypes [15,16].

The first step in evaluating patients with suspected Alzheimer's disease is typically a clinical assessment and cognitive testing. This involves taking a detailed medical history, conducting a physical examination, and using standardized cognitive assessment tools. The most commonly used screening tests include the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) [10]. The MMSE, which has a maximum score of 30 points, assesses, among other things, orientation, attention, memory, language skills, and visuospatial functions. In people with Alzheimer's disease, a more rapid decline in scores is observed compared to healthy individuals. Episodic memory tests, such as the FCSRT, CERAD-WL, and RAVLT, also have high diagnostic value, as they demonstrate high sensitivity and specificity in predicting the progression of mild cognitive impairment (MCI) to full-blown Alzheimer's disease [17].

Biomarkers in Diagnostics

A biomarker is defined as a measurable indicator of an organism's biological state, most often in the form of a molecule, that reflects changes occurring under both physiological and pathological conditions [18]. An optimal biomarker should exhibit high reproducibility of results, be simple to measure, as non-invasive as possible, cost-effective, and characterized by high diagnostic precision, enabling the differentiation of similar disease states [19]. The use of biomarkers enables the detection of Alzheimer's disease even before the onset of clinical symptoms, which facilitates earlier initiation of therapy and increases its effectiveness. Some researchers emphasize that diagnosis should take into account both the presence of abnormal biomarkers and clinical manifestations, treating biomarker changes alone as a state of increased risk. On the other hand, asymptomatic diagnostics are used in many fields of medicine to initiate treatment as early as possible. Although not every person with abnormal biomarker results will develop a fully symptomatic disease, this should not be a basis for limiting access to therapy, even if it entails potential psychological, social, or economic consequences [20].

Biomarkers associated with Alzheimer's disease can be divided into several groups, the most important of which include markers present in cerebrospinal fluid (CSF) and biomarkers measured in blood [10,20].

Cerebrospinal fluid is the substance surrounding the brain and spinal cord [20]. A key feature of this fluid is its direct contact with the brain's extracellular space, which allows for the exchange of various molecules between neural tissue and the fluid. For this reason, the first biomarkers of Alzheimer's disease were identified in this biological material. However, collecting cerebrospinal fluid requires a lumbar puncture, which is an invasive procedure and is typically performed only in specialized centers. An alternative is blood biomarkers, which are significantly less invasive, easier to obtain, and applicable on a broader scale, including

in non-specialized settings or in areas with limited access to advanced diagnostics. At the same time, their use may involve certain costs [21].

The β-amyloid (Aβ) peptide, which is the main component of amyloid plaques, exists in several variants, of which the C-terminal forms—Aβ40 and Aβ42—are of key importance [22]. Aβ42 is most commonly used in diagnostics. Its concentration is inversely proportional to the number of amyloid plaques in the brain—the lower the Aβ42 level, the greater the accumulation of Aβ deposits. Additionally, the Aβ42-to-Aβ40 ratio is used as an indicator of disease progression risk and has good diagnostic value [10].

Hyperphosphorylated forms of tau protein, such as p-tau181, p-tau217, and p-tau231, also constitute an important group of biomarkers that can be measured in both cerebrospinal fluid and plasma. They enable the differentiation of Alzheimer's disease from other types of dementia and from normal health [23]. Particularly high diagnostic value is attributed to p-tau181 in plasma, whose levels are markedly elevated in individuals with mutations in the PSEN1 or APP genes [24]. Among the listed markers, p-tau217 is considered more specific to Alzheimer's disease than p-tau181. It is more effective in distinguishing patients from healthy individuals, and its elevation is observed even at a stage preceding changes detectable in tau-PET scans. Furthermore, it better predicts cognitive decline and enables monitoring of disease progression, although its levels may vary by gender. The use of models combining p-tau181 and p-tau217 with additional factors allows for more accurate prediction of dementia development [18]. The p-tau231 marker appears very early in the course of Alzheimer's disease, but its diagnostic value is lower compared to p-tau217. Among the newer, promising biomarkers is MTBR-tau243, which shows a strong correlation with tau-PET imaging results and may be useful in assessing disease progression and treatment efficacy. Additionally, the N-terminal fragment of tau protein (NT1), measured in plasma, may serve as a predictor of cognitive decline in the elderly [25].

Plasma levels of β-amyloid (Aβ), like those in cerebrospinal fluid, are being studied as potential biomarkers for Alzheimer's disease. In blood, a reduction in the Aβ42/Aβ40 ratio of approximately 10–15% is observed; however, this decrease is significantly smaller than in CSF, where it is approximately 50%. For this reason, their diagnostic value still requires further confirmation. Elevated levels of phosphorylated tau (p-tau) are also found in the plasma of patients with Alzheimer's disease. Phosphorylation at threonine 231 is indicated as an early marker of changes, whereas in later stages of the disease, phosphorylation increases at other sites on the protein, including T217, T218, and T205.

Light neurofilament (NfL), released as a result of neuronal damage, serves as a marker of neurodegeneration and cognitive decline. In people with Alzheimer's disease, its blood levels can be more than 2.5 times higher than in healthy individuals. GFAP, a protein present in astrocytes, shows increased concentrations as Alzheimer's disease progresses. Importantly, elevated levels can be observed as early as the preclinical phase, making it a potentially useful early biomarker for AD [10].

Neuroimaging

Neuroimaging is increasingly being incorporated as a tool to support the diagnostic criteria for Alzheimer's disease, as it enhances diagnostic certainty [26]. The most common imaging finding is cortical atrophy resulting from neuronal loss. This process is typically symmetrical and primarily affects the temporal and parietal lobes. In the case of late-onset Alzheimer's disease, as well as in individuals with the APOE ε4 polymorphism, hippocampal atrophy is particularly evident, with relative sparing of central areas [27]. It is worth noting that significant asymmetry in hippocampal atrophy does not rule out a diagnosis of the disease; however, such a pattern more often suggests other conditions, such as frontotemporal dementia [26].

Modern imaging techniques allow for the assessment of subtle microstructural changes. Magnetic resonance imaging (MRI) plays an important role in differentiating the causes of cognitive disorders, monitoring disease progression, and evaluating treatment efficacy [10]. Positron emission tomography (PET) is increasingly used for diagnosis; this involves administering a radiotracer into the bloodstream that selectively binds to specific molecular structures in the brain. This substance emits positrons, and their detection allows for the acquisition of three-dimensional images showing the distribution of the tracer. In Alzheimer's disease, PET allows for the detection of both β-amyloid plaques and tau-related pathologies [28].

Conclusions

A review of the available literature confirms that Alzheimer's disease is a multifactorial and progressive neurodegenerative disorder whose pathogenesis involves β-amyloid deposition, tau protein hyperphosphorylation, neuroinflammatory processes, and disturbances in cellular mechanisms such as autophagy. Genetic factors also play a significant role in the development of the disease, particularly the presence of the APOE ε4 allele, which increases the risk of developing the disease and contributes to the progression of neurodegenerative changes.

The analyzed data indicate that the initial clinical symptoms center on memory deficits and a gradual decline in cognitive function, including executive, language, and attention functions, as well as visuospatial orientation. Given the long asymptomatic period, early diagnosis of pathological changes becomes a priority. It allows for the faster implementation of therapeutic strategies aimed at slowing the progression of the disease and improving the standard of patient care.

Modern diagnosis of Alzheimer's disease increasingly relies on biomarkers and advanced neuroimaging techniques. Markers such as the Aβ42/40 ratio, phosphorylated tau proteins (particularly p-tau181 and p-tau217), as well as NfL and GFAP, play a significant diagnostic and prognostic role. At the same time, imaging methods, including magnetic resonance imaging (MRI) and positron emission tomography (PET), allow for the precise identification of structural and molecular changes typical of this disease, which significantly improves the quality of diagnosis and monitoring of disease progression.

Despite significant progress in understanding the etiology and pathogenesis of Alzheimer's disease, as well as in its diagnosis, there is still no effective causal treatment. However, the rapid development of blood biomarkers and modern imaging methods offers hope for improved early diagnosis, more effective monitoring of disease progression, and the implementation of therapies at the earliest possible stage of the disease. Given the growing epidemiological and socioeconomic significance of Alzheimer's disease, further research into its mechanisms of development, methods of early detection, and effective prevention strategies remains essential.

Author's contribution:

Conceptualization: Mateusz Cieciora, Patryk Jakubiak

Methodology: Mateusz Cieciora, Małgorzata Kawiorska, Patryk Jakubiak, Julia Surowiec, Wiktoria Bełcikowska-Skowron, Aleksandra Cieciora, Krzysztof Brzezicki, Katarzyna Zegadło, Katarzyna Kuc, Maciej Dobrucki

Software: Mateusz Cieciora, Katarzyna Kuc, Krzysztof Brzezicki

Check: Mateusz Cieciora, Aleksandra Cieciora

Formal analysis: Mateusz Cieciora, Aleksandra Cieciora, Małgorzata Kawiorska, Katarzyna Zegadło

Investigation: Wiktoria Bełcikowska-Skowron, Katarzyna Kuc, Julia Surowiec, Maciej Dobrucki

Resources: Maciej Dobrucki, Katarzyna Kuc, Aleksandra Cieciora, Julia Surowiec

Data curation: Patryk Jakubiak, Maciej Dobrucki, Krzysztof Brzezicki

Writing – original draft preparation: Mateusz Cieciora, Maciej Dobrucki, Katarzyna Zegadło, Katarzyna Kuc, Małgorzata Kawiorska, Julia Surowiec

Writing-review and editing: Mateusz Cieciora, Julia Surowiec, Aleksandra Cieciora, Krzysztof Brzezicki, Małgorzata Kawiorska, WIktoria Bełcikowska-Skowron

Visualization: Patryk Jakubiak, Julia Surowiec, Małgorzata Kawiorska

Supervision: Krzysztof Brzezicki, Julia Surowiec, Patryk Jakubiak

Project administration: Mateusz Cieciora, Maciej Dobrucki

All authors have read and agreed with the published version of the manuscript.

Funding Statement: No funding was sought or obtained in relation to this review article.

Acknowledgments: The authors wish to emphasize that they do not express gratitude to any individuals or institutions

Conflict of Interest Statement: The authors declare no conflicts of interest.

REFERENCES

1. Stefaniak, O., Dobrzyńska, M., Drzymała-Czyż, S., & Przysławski, J. (2022). Diet in the prevention of Alzheimer's disease: Current knowledge and future research requirements. *Nutrients*, *14*(21), 4564. https://doi.org/10.3390/nu14214564
2. Twarowski, B., & Herbet, M. (2023). Inflammatory processes in Alzheimer's disease-pathomechanism, diagnosis and treatment: A review. *International Journal of Molecular Sciences*, *24*(7), 6518. https://doi.org/10.3390/ijms24076518
3. Breijyeh, Z., & Karaman, R. (2020). Comprehensive review on Alzheimer's disease: Causes and treatment. *Molecules*, *25*(24), 5789. https://doi.org/10.3390/molecules25245789
4. Zhang, X. X., Tian, Y., Wang, Z. T., Ma, Y. H., Tan, L., & Yu, J. T. (2021). The epidemiology of Alzheimer's disease modifiable risk factors and prevention. *The Journal of Prevention of Alzheimer's Disease*, *8*(3), 313–321. https://doi.org/10.14283/jpad.2021.15
5. Wong, W. (2020). Economic burden of alzheimer disease and managed care considerations. *The American Journal of Managed Care*, *26*(8 Suppl), S177–S183. https://doi.org/10.37765/ajmc.2020.88482
6. Wilson, D. M., III, Cookson, M. R., Van Den Bosch, L., Zetterberg, H., Holtzman, D. M., & Dewachter, I. (2023). Hallmarks of neurodegenerative diseases. *Cell*, *186*(4), 693–714. https://doi.org/10.1016/j.cell.2022.12.032
7. Orobets, K. S., & Karamyshev, A. L. (2023). Amyloid precursor protein and Alzheimer's disease. *International Journal of Molecular Sciences*, *24*(19), 14794. https://doi.org/10.3390/ijms241914794
8. Ma, C., Hong, F., & Yang, S. (2022). Amyloidosis in Alzheimer's disease: Pathogeny, etiology, and related therapeutic directions. *Molecules (Basel, Switzerland)*, *27*(4), 1210. https://doi.org/10.3390/molecules27041210
9. Moloney, C. M., Lowe, V. J., & Murray, M. E. (2021). Visualization of neurofibrillary tangle maturity in Alzheimer's disease: A clinicopathologic perspective for biomarker research. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *17*(9), 1554–1574. https://doi.org/10.1002/alz.12321
10. Kamatham, P. T., Shukla, R., Khatri, D. K., & Vora, L. K. (2024). Pathogenesis, diagnostics, and therapeutics for Alzheimer's disease: Breaking the memory barrier. *Ageing Research Reviews*, *101*, 102481. https://doi.org/10.1016/j.arr.2024.102481
11. Wu, S., Wei, Y., Li, J., Bai, Y., Yin, P., & Wang, S. (2021). SIRT5 represses neurotrophic pathways and Aβ production in Alzheimer's disease by targeting autophagy. *ACS Chemical Neuroscience*, *12*(23), 4428–4437. https://doi.org/10.1021/acschemneuro.1c00468
12. Jia, J., Xu, J., Liu, J., Wang, Y., Wang, Y., Cao, Y., Guo, Q., Qu, Q., Wei, C., Wei, W., Zhang, J., & Yu, E. (2021). Comprehensive management of daily living activities, behavioral and psychological symptoms, and cognitive function in patients with Alzheimer's disease: A Chinese consensus on the comprehensive management of Alzheimer's disease. *Neuroscience Bulletin*, *37*(7), 1025–1038. https://doi.org/10.1007/s12264-021-00701-z
13. Jessen, F., Amariglio, R. E., van Boxtel, M., Breteler, M., Ceccaldi, M., Chételat, G., Dubois, B., Dufouil, C., Ellis, K. A., van der Flier, W. M., Glodzik, L., van Harten, A. C., de Leon, M. J., McHugh, P., Mielke, M. M., Molinuevo, J. L., Mosconi, L., Osorio, R. S., Perrotin, A., … Subjective Cognitive Decline Initiative (SCD-I) Working Group (2014). A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *10*(6), 844–852. https://doi.org/10.1016/j.jalz.2014.01.001
14. Prasad, S., Katta, M. R., Abhishek, S., Sridhar, R., Valisekka, S. S., Hameed, M., Kaur, J., & Walia, N. (2023). Recent advances in Lewy body dementia: A comprehensive review. *Disease-a-Month: DM*, *69*(5), 101441. https://doi.org/10.1016/j.disamonth.2022.101441
15. Gordon, B. A., Blazey, T. M., Su, Y., Hari-Raj, A., Dincer, A., Flores, S., Christensen, J., McDade, E., Wang, G., Xiong, C., Cairns, N. J., Hassenstab, J., Marcus, D. S., Fagan, A. M., Jack, C. R., Jr., Hornbeck, R. C., Paumier, K. L., Ances, B. M., Berman, S. B., … Benzinger, T. L. S. (2018). Spatial patterns of neuroimaging biomarker change in individuals from families with autosomal dominant Alzheimer's disease: A longitudinal study. *The Lancet Neurology*, *17*(3), 241–250. https://doi.org/10.1016/S1474-4422(18)30028-0
16. Chen, Y., Al-Nusaif, M., Li, S., Tan, X., Yang, H., Cai, H., & Le, W. (2024). Progress on early diagnosing Alzheimer's disease. *Frontiers of Medicine*, *18*(3), 446–464. https://doi.org/10.1007/s11684-023-1047-1
17. Daou, L., El Alayli, A., Constantinos, F., Dib, G., & Barakat, M. (2023). Can neurocognitive assessment be a lower-cost substitute for biomarkers in predicting progression from mild cognitive impairment (MCI) to Alzheimer's disease (AD)? a narrative review. *Biomarkers in Neuropsychiatry*, *9*, 100069. https://doi.org/10.1016/j.bionps.2023.100069
18. Nunkoo, V. S., Jurcau, A., Les, M., Cristian, A., Militaru, M., Marge, C., Iovanovici, D. C., & Jurcau, M. C. (2025). Circulating biomarkers for the early diagnosis of Alzheimer's disease. *International Journal of Molecular Sciences*, *26*(15), 7268. https://doi.org/10.3390/ijms26157268
19. Varesi, A., Carrara, A., Pires, V. G., Floris, V., Pierella, E., Savioli, G., Prasad, S., Esposito, C., Ricevuti, G., Chirumbolo, S., & Pascale, A. (2022). Blood-based biomarkers for Alzheimer's disease diagnosis and progression: An overview. *Cells*, *11*(8), 1367. https://doi.org/10.3390/cells11081367

20. Jack, C. R., Jr., Andrews, S. J., Beach, T. G., Buracchio, T., Dunn, B., Graf, A., Hansson, O., Ho, C., Jagust, W., McDade, E., Molinuevo, J. L., Okonkwo, O. C., Pani, L., Rafii, M. S., Scheltens, P., Siemers, E., Snyder, H. M., Sperling, R., Teunissen, C. E., & Carrillo, M. C. (2024). Revised criteria for the diagnosis and staging of Alzheimer's disease. *Nature Medicine*, *30*(8), 2121–2124. https://doi.org/10.1038/s41591-024-02988-7
21. Lista, S., Mapstone, M., Caraci, F., et al. (2024). A critical appraisal of blood-based biomarkers for Alzheimer's disease. *Ageing Research Reviews*, *96*, 102290. https://doi.org/10.1016/j.arr.2024.102290
22. Andersen, E., Casteigne, B., Chapman, W. D., Creed, A., Foster, F., Lapins, A., Shatz, R., & Sawyer, R. P. (2021). Diagnostic biomarkers in Alzheimer's disease. *Biomarkers in Neuropsychiatry*, *5*, 100041. https://doi.org/10.1016/j.bionps.2021.100041
23. Guo, Y., Huang, Y. Y., Shen, X. N., Chen, S. D., Hu, H., Wang, Z. T., Tan, L., Yu, J. T., & Alzheimer's Disease Neuroimaging Initiative (2021). Characterization of Alzheimer's tau biomarker discordance using plasma, CSF, and PET. *Alzheimer's Research & Therapy*, *13*(1), 93. https://doi.org/10.1186/s13195-021-00834-3
24. Zetterberg, H., & Blennow, K. (2020). Blood biomarkers: Democratizing Alzheimer's diagnostics. *Neuron*, *106*(6), 881–883. https://doi.org/10.1016/j.neuron.2020.06.004
25. Horie, K., Salvadó, G., Barthélemy, N. R., Janelidze, S., Li, Y., He, Y., Saef, B., Chen, C. D., Jiang, H., Strandberg, O., Pichet Binette, A., Palmqvist, S., Sato, C., Sachdev, P., Koyama, A., Gordon, B. A., Benzinger, T. L. S., Holtzman, D. M., Morris, J. C., … Bateman, R. J. (2023). CSF MTBR-tau243 is a specific biomarker of tau tangle pathology in Alzheimer's disease. *Nature Medicine*, *29*(8), 1954–1963. https://doi.org/10.1038/s41591-023-02443-z
26. Furtner, J., & Prayer, D. (2021). Neuroimaging in dementia. Bildgebung in der Demenzdiagnostik. *Wiener Medizinische Wochenschrift (1946)*, *171*(11-12), 274–281. https://doi.org/10.1007/s10354-021-00825-x
27. Frisoni, G. B., Bocchetta, M., Chételat, G., Rabinovici, G. D., de Leon, M. J., Kaye, J., Reiman, E. M., Scheltens, P., Barkhof, F., Black, S. E., Brooks, D. J., Carrillo, M. C., Fox, N. C., Herholz, K., Nordberg, A., Jack, C. R., Jr., Jagust, W. J., Johnson, K. A., Rowe, C. C., … ISTAART's NeuroImaging Professional Interest Area (2013). Imaging markers for alzheimer disease: Which vs how. *Neurology*, *81*(5), 487–500. https://doi.org/10.1212/WNL.0b013e31829d86e8
28. Crișan, G., Moldovean-Cioroianu, N. S., Timaru, D. G., Andrieș, G., Căinap, C., & Chiș, V. (2022). Radiopharmaceuticals for PET and SPECT imaging: A literature review over the last decade. *International Journal of Molecular Sciences*, *23*(9), 5023. https://doi.org/10.3390/ijms23095023