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	DIAGNOSTIC CHALLENGES AND CARE PATHWAYS IN YOUNG-ONSET DEMENTIA – A NARRATIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.1(49).2026.4845
RECEIVED	14 December 2025
ACCEPTED	15 February 2026
PUBLISHED	23 February 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

DIAGNOSTIC CHALLENGES AND CARE PATHWAYS IN YOUNG-ONSET DEMENTIA – A NARRATIVE REVIEW

Natalia Surosz *(Corresponding Author, Email: natalia.surosz@gmail.com)*
MD, Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0005-1939-151X

Andrzej Myrny
MD, University Clinical Center of the Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-5592-259X

Kamil Turlej
MD, University Clinical Center of the Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-2919-284X

Dmytro Kowalczuk
MD, Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0004-1433-5052

Wiktoria Kasianik
MD, Mazovian Rehabilitation Center STOCER Ltd. Saint Anna Trauma Surgery Hospital, Warsaw, Poland
ORCID ID: 0009-0004-1540-5227

Darya Lazitskaya
MD, Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0007-8680-8826

Mykola Sobchynskyi
MD, Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-1804-1114

Valeryia Milasheuskaya
MD, Wroclaw Medical University, Wroclaw, Poland
ORCID ID: 0009-0006-4126-2375

Iga Kiełbaszewska
MD, Independent Public Healthcare Centre in Hajnówka, Hajnówka, Poland
ORCID ID: 0009-0004-9892-4769

Katsiaryna Miraniuk
Student, Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-1406-9756

Dawid Wiczkowski
MD, Independent Public Specialist Western Hospital named after St. John Paul II, Grodzisk Mazowiecki, Poland
ORCID ID: 0009-0004-7050-9598

ABSTRACT

Young-onset dementia (YOD), defined as the onset of dementia symptoms before the age of 65, is a clinically and diagnostically complex condition that significantly impacts patients and families during peak social and economic stages of life. Compared to late-onset dementia, YOD more frequently presents with atypical features such as personality changes, executive dysfunction, psychiatric symptoms, or language impairments, often leading to delayed diagnosis and misclassification as primary psychiatric disorders. This narrative review provides a comprehensive overview of current evidence on the etiology, clinical presentation, diagnostic workup, and management of YOD. Alzheimer's disease and frontotemporal dementia are the most common neurodegenerative causes, though a broad differential including autoimmune, infectious, metabolic, and hereditary disorders must be considered. Improving clinician awareness and access to age-appropriate diagnostic services is critical to reducing diagnostic delays and improving quality of life for individuals affected by YOD.

Aim of study: The aim of this study is to provide a comprehensive and updated overview of YOD, focusing on its diverse etiologies, clinical presentations, diagnostic challenges, and current management strategies. By synthesizing evidence from recent literature, the study seeks to offer practical guidance for clinicians in improving the timely recognition, differential diagnosis, and multidisciplinary care of individuals affected by YOD.

KEYWORDS

Young-Onset Dementia, Alzheimer's Disease, Frontotemporal Dementia, Neuroimaging, Neurodegeneration, Cognitive Impairment

CITATION

Natalia Surosz, Andrzej Myrny, Kamil Turlej, Dmytro Kowalczuk, Wiktoria Kasianik, Darya Lazitskaya, Mykola Sobchynskyi, Valeryia Milasheuskaya, Iga Kiełbaszewska, Katsiaryna Miraniuk, Dawid Wiczkowski. (2026) Diagnostic Challenges and Care Pathways in Young-Onset Dementia – a Narrative Review. *International Journal of Innovative Technologies in Social Science*. 1(49). doi: 10.31435/ijitss.1(49).2026.4845

1. Introduction

Young-onset dementia (YOD), defined as dementia with symptom onset before the age of 65 years, represents a significant and growing public health challenge. Recent global estimates suggest that approximately 3.9 million individuals aged 30 to 64 are living with YOD, with an age-standardized prevalence of 119 per 100,000 population (Vieira, 2013). Moreover, between 1990 and 2021, the global prevalence and incidence of YOD increased by over 200%, highlighting its rising clinical and epidemiological significance (He et al., 2025).

Unlike late-onset dementia (LOD), YOD frequently presents with atypical features, including early behavioural and psychiatric symptoms, language disturbances, and executive dysfunction, which often contribute to delays in recognition and diagnosis (Kelley et al., 2008). Misdiagnosis as a primary psychiatric disorder is common and may delay specialist referral by several years (Van Vliet et al., 2013). On average, the time from symptom onset to formal diagnosis in YOD is reported to exceed three years (Mendez, 2006).

The differential diagnosis of YOD is broad, encompassing early-onset variants of adult neurodegenerative diseases such as Alzheimer's disease (AD) - which accounts for approximately 48% of YOD cases, as well as frontotemporal dementia (FTD), dementia with Lewy bodies, and less common causes such as prion diseases (Rossor et al., 2010). In younger individuals, especially those under 35, late-onset presentations of childhood neurodegenerative disorders such as mitochondrial disorders, leukodystrophies, and lysosomal storage diseases should also be considered (Koene et al., 2012). Crucially, several reversible conditions including inflammatory, infectious, metabolic, toxic, and endocrine causes, may mimic neurodegenerative YOD and warrant prompt and thorough evaluation (Kelley et al., 2009).

Given the significant functional and psychosocial consequences of YOD, timely diagnosis is essential for initiating appropriate management, guiding genetic counselling, and supporting patient and caregiver well-being. This review aims to provide an updated and practical framework for the clinical approach to YOD.

2. Materials and Methods

A search of the PubMed database was conducted using relevant keywords to find available studies published up to April 30, 2025. Only articles written in English were included. Data were extracted and synthesized from original studies, reviews, and clinical guidelines relevant to the diagnosis and treatment of YOD.

3. Results

3.1 Clinical presentation of Young-Onset Dementia

Young-onset dementia (YOD), defined as the onset of persistent cognitive decline before the age of 65, is a diagnostically and clinically challenging condition due to its broad differential and often atypical presentation. Unlike late-onset dementia (LOD), where memory loss is typically the dominant early symptom, YOD frequently presents with behavioral changes, language disturbance, psychiatric symptoms, or executive dysfunction. These atypical features often lead to initial misdiagnosis as primary psychiatric disorders, resulting in a significant delay in the recognition and treatment of the underlying neurodegenerative or systemic condition (Van Vliet et al., 2013).

Alzheimer's disease (AD) remains the most common cause of YOD, accounting for approximately 30–40% of cases (Rossor et al., 2010). Unlike typical late-onset AD, early-onset forms often exhibit atypical phenotypes. Patients may present with prominent visuospatial deficits (getting lost in familiar places, difficulty drawing or navigating), aphasia (word-finding difficulties, circumlocutions), acalculia, or features of posterior cortical atrophy such as visual agnosia and optic ataxia. In many cases, psychiatric symptoms such as anxiety, irritability, and depression precede overt cognitive decline. Behavioral disturbances including social withdrawal and reduced initiative are also frequently observed in early-onset presentations (He et al., 2025)(Van Vliet et al., 2013).

Frontotemporal dementia (FTD) is the second leading cause of YOD, particularly in patients under 60 years. Behavioral variant FTD often presents with insidious changes in social conduct, loss of empathy, compulsive behaviors, changes in eating habits (hyperorality, sweet preference), and emotional blunting. Language variants of FTD include semantic variant primary progressive aphasia, characterized by fluent but empty speech with impaired word comprehension, and non-fluent/agrammatic variant, marked by effortful, halting speech and grammatical errors. Patients may also show poor insight, lack of concern, or socially inappropriate behavior, often mistaken for psychiatric illness (Van Vliet et al., 2013)(Rossor et al., 2010).

Dementia with Lewy bodies (DLB), although less common in the younger population, may present with fluctuating cognition, recurrent visual hallucinations, REM sleep behavior disorder, and parkinsonism. Additional symptoms may include falls, syncope, severe sensitivity to antipsychotics, and prominent visuospatial dysfunction. Cognitive fluctuations can be dramatic, with lucid intervals alternating with confusion over hours or days (Rossor et al., 2010).

Huntington's disease (HD), a genetic condition caused by CAG trinucleotide expansion in the *HTT* gene, usually begins in the third to fifth decade of life. Initial symptoms often include personality changes, irritability, depression, and difficulty with concentration, followed by progressive motor symptoms such as chorea, dystonia, bradykinesia, and dysarthria. Later stages involve global cognitive impairment, dysphagia, and severe functional dependence (Kelley et al., 2008).

Reversible causes of YOD are essential to identify, as early treatment can alter disease progression. Multiple sclerosis (MS) may present with cognitive decline, memory complaints, inattention, and mood changes, particularly in progressive forms. Neurological symptoms such as diplopia, sensory changes, or limb weakness may provide diagnostic clues. Neurosarcoidosis may manifest with hypothalamic-pituitary dysfunction (polydipsia, amenorrhea), cranial neuropathies, myelopathy, or seizures (Loi et al., 2023).

Infectious causes such as neurosyphilis, HIV-associated neurocognitive disorders, Whipple's disease, and progressive multifocal leukoencephalopathy (PML) should be considered, particularly in immunocompromised individuals. Symptoms may include confusion, ataxia, tremor, myoclonus, hallucinations, and mood lability. HIV-associated cognitive disorder may also involve gait instability, limb apraxia, or bladder dysfunction (Rossor et al., 2010).

Toxic and metabolic encephalopathies may present with confusion, psychosis, tremor, ataxia, polyneuropathy, and myoclonic jerks. Common culprits include alcohol, benzodiazepines, heavy metals (lead, arsenic, mercury), and exposure to industrial solvents. Endocrinopathies such as hypothyroidism, adrenal insufficiency, and hyperparathyroidism may cause fatigue, slowed thinking, irritability, and attentional deficits. Vitamin deficiencies - particularly B1 (thiamine), B12, and folate—can also contribute to subacute cognitive decline, gait disturbances, and paresthesias (Mendez, 2006).

Psychiatric illnesses, especially major depressive disorder, bipolar disorder, and late-onset schizophrenia, can mimic dementia through symptoms such as impaired concentration, apathy, and slowed cognition. Unlike true dementia, these conditions often show fluctuating severity and may improve with psychiatric treatment. However, differentiation from true cognitive decline requires detailed neuropsychological testing, collateral history, and longitudinal follow-up (Van Vliet et al., 2013).

In conclusion, the clinical spectrum of YOD is broad and complex, encompassing both irreversible neurodegenerative diseases and potentially treatable conditions. Presenting symptoms often extend beyond memory loss to include prominent behavioral, psychiatric, motor, or language disturbances. A meticulous, multidisciplinary approach is essential for accurate diagnosis, guiding management, and providing prognostic information to patients and their families.

3.2. Diagnosis

3.2.1. Diagnostic Challenges in YOD

Young-onset dementia (YOD) presents with a wide and often atypical range of clinical features, which significantly contributes to diagnostic delays. The diagnosis of YOD is frequently delayed in comparison to late-onset dementia (LOD) (Papageorgiou et al., 2009). On average, there is a lag of 2 to 3 years between symptom onset and formal diagnosis of YOD. This delay is partly attributable to patients and their families often not considering dementia as a potential cause of symptoms at a younger age, resulting in postponed medical consultation. Moreover, clinicians - typically more experienced with LOD - may be less inclined to suspect dementia in younger patients. The broader differential diagnosis associated with YOD further complicates identification. Misdiagnoses are also common due to the frequent presence of prominent psychiatric features and involvement of non-memory cognitive domains (Mendez, 2006). Early changes in personality, behaviour, and executive functioning are frequently attributed to primary psychiatric conditions such as depression or anxiety. Timely and accurate diagnosis of YOD is essential, as it can significantly influence both prognosis and management strategies.

3.2.2. Clinical Assesment

The clinical assessment of YOD requires a thorough, multidisciplinary approach due to the condition's broad differential diagnosis and frequently atypical presentation.

History-taking is foundational and should include detailed symptom chronology, behavioral changes, occupational and functional decline, and family history of neurological or psychiatric disorders. Particular attention should be paid to risk factors such as head trauma, substance use, and autoimmune or infectious exposures. A collateral history from a reliable informant is crucial, as individuals with YOD often have poor insight into their deficits (Van Vliet et al., 2013).

Neurological examination may reveal motor signs such as rigidity, ataxia, or weakness, which can point toward specific etiologies like frontotemporal dementia, Huntington's disease, or demyelinating conditions. Neuropsychiatric evaluation is also essential, as mood and behavioral symptoms often predominate in early stages (Warren et al., 2013).

Cognitive screening tools - such as the Montreal Cognitive Assessment (MoCA) or Mini-Mental State Examination (MMSE) in detecting early or non-amnestic impairments typical of YOD (Hsieh et al., 2013). Formal neuropsychological testing provides a detailed cognitive profile, distinguishing between neurodegenerative, psychiatric, and functional causes of impairment.

3.2.3. Neuroimaging in YOD

Neuroimaging plays a pivotal role in the diagnostic evaluation of young-onset dementia (YOD), aiding in the differentiation between neurodegenerative, inflammatory, vascular, and potentially reversible causes. Given the heterogeneous presentation of YOD, imaging not only supports diagnosis but also helps to refine differential considerations, detect atypical patterns of atrophy, and exclude structural lesions such as tumors, hydrocephalus, or demyelinating processes.

Magnetic resonance imaging (MRI) is the primary structural imaging modality and should be performed early in the diagnostic process. A dedicated dementia protocol includes high-resolution T1-weighted images for assessment of cortical and subcortical atrophy, T2-weighted and FLAIR sequences for evaluating white matter changes, and diffusion-weighted imaging (DWI) for detecting acute infarcts or prion disease (Harper et al., 2014). In AD, particularly early-onset variants, MRI may reveal bilateral hippocampal atrophy and posterior parietal involvement, while the logopenic variant may show asymmetric left temporoparietal atrophy. In FTD imaging typically demonstrates focal atrophy in the frontal and/or anterior temporal lobes, which may be asymmetric and correlate with clinical subtypes (Whitwell & Jack, 2007).

Radiological visual rating scales, such as the medial temporal lobe atrophy (MTA) score, the posterior atrophy (PA) scale, and the frontal lobe atrophy scale, provide semi-quantitative assessments that enhance diagnostic accuracy, especially in centers lacking advanced volumetric software. However, the interpretation of these scales requires adequate radiological expertise and should be considered within the clinical context (Harper et al., 2014)(Ferreira et al., 2020).

Functional neuroimaging can further increase diagnostic precision, particularly when MRI findings are equivocal or non-specific. Fluorodeoxyglucose positron emission tomography (FDG-PET) is highly sensitive in detecting regional cerebral hypometabolism, which typically precedes structural atrophy. In AD, FDG-PET often reveals hypometabolism in the temporoparietal cortex and posterior cingulate, whereas in FTD, hypometabolism is observed in the frontal and anterior temporal lobes (Whitwell & Jack, 2007). Single-photon emission computed tomography (SPECT), although less specific than PET, may be used in resource-limited settings to assess cerebral perfusion deficits suggestive of neurodegenerative pathology.

Emerging molecular imaging techniques offer new avenues for early and specific diagnosis. Amyloid PET imaging, using radiotracers such as florbetapir or Pittsburgh compound B, allows for in vivo detection of β-amyloid plaques, a hallmark of AD. A positive amyloid scan supports an AD diagnosis in the appropriate clinical context, while a negative scan effectively excludes it. However, amyloid burden does not necessarily correlate with symptom severity, as amyloid deposition may precede clinical manifestation by years (Johnson et al., 2013). Tau PET imaging, though still largely confined to research settings, offers potential for diagnosing AD and other tauopathies by visualizing regional tau deposition, which more closely correlates with clinical phenotype and disease stage (Villemagne et al., 2015). Tau PET may also assist in distinguishing AD from non-tau neurodegenerative conditions such as TDP-43-related FTD or α-synucleinopathies.

Neuroimaging also plays a crucial role in identifying non-neurodegenerative causes of YOD. White matter hyperintensities on FLAIR sequences may suggest vascular pathology, demyelinating disease, or toxic-metabolic etiologies. In cases of suspected multiple sclerosis, MRI may show periventricular, juxtacortical, or infratentorial lesions fulfilling dissemination in space and time.

Neuroimaging is an essential component of the diagnostic workup in YOD. Structural MRI remains the cornerstone, but functional and molecular imaging increasingly contribute to diagnostic accuracy, particularly in complex or atypical cases.

3.2.4. Genetic Testing in YOD

Genetic testing plays an increasingly important role in the evaluation of young-onset dementia (YOD), particularly in patients with early symptom onset (<60 years), a positive family history, or clinical features suggestive of hereditary neurodegenerative syndromes. While most dementia cases are sporadic, up to 15% of YOD is attributable to autosomal dominant mutations, and identifying a genetic etiology can offer diagnostic certainty, guide family counseling, and inform eligibility for targeted therapies or research trials (Goldman et al., 2011)(Rohrer et al., 2009).

In early-onset Alzheimer's disease (EOAD), pathogenic variants in three genes - *APP* (amyloid precursor protein), *PSEN1* (presenilin 1), and *PSEN2* (presenilin 2) - are well-established causes of autosomal dominant AD. Mutations in *PSEN1* are the most common and often associated with early onset (before age 50), rapid progression, and atypical features such as seizures or myoclonus (Ryman et al., 2014). *APP* mutations may result in cerebral amyloid angiopathy and hemorrhage, while *PSEN2* mutations are rare and show more variable penetrance.

In frontotemporal dementia (FTD), monogenic causes are more prevalent than in AD. Mutations in *MAPT* (microtubule-associated protein tau), *GRN* (progranulin), and expansions in *C9orf72* (chromosome 9 open reading frame 72) are the most frequent. *MAPT* mutations lead to tauopathies with behavioral and motor symptoms, *GRN* mutations are associated with TDP-43 pathology and asymmetrical cortical atrophy, while *C9orf72* repeat expansions are the most common genetic cause of both FTD and amyotrophic lateral sclerosis (ALS), often with early psychosis or parkinsonism (Gass et al., 2006)(DeJesus-Hernandez et al., 2011).

Other genetic causes of YOD include Huntington's disease, caused by CAG trinucleotide expansions in the *HTT* gene; CADASIL, due to *NOTCH3* mutations; and rare inherited prion diseases. Additionally, risk-modifying alleles such as *APOE ε4* increase susceptibility to AD, particularly in homozygous carriers, although *APOE* is not a deterministic gene and is not routinely recommended for diagnostic use in isolation (Liu et al., 2013).

Modern genetic testing utilizes next-generation sequencing (NGS) platforms, which allow for simultaneous analysis of multiple genes. Clinical options include:

- Targeted gene panels focused on known dementia-associated genes
- Whole exome sequencing (WES) for broader analysis of coding regions

- Whole genome sequencing (WGS) for evaluation of both coding and non-coding variants

These technologies can identify pathogenic variants, likely pathogenic variants, or variants of uncertain significance (VUS), each of which has different clinical implications. Importantly, NGS may miss repeat expansions (e.g., *C9orf72*) and structural variants, which require specific testing methods such as repeat-primed PCR or MLPA (multiplex ligation-dependent probe amplification) (Sims et al., 2020).

In summary, genetic testing is a critical tool in, particularly in familial or atypical cases. Advances in sequencing technologies continue to expand our understanding of genetic contributions, though interpretation requires clinical expertise and careful counseling to ensure ethical and meaningful application.

3.2.5. Lumbar Puncture in the Assessment of YOD

Lumbar puncture (LP), or cerebrospinal fluid (CSF) analysis, is a valuable diagnostic tool in the evaluation of young-onset dementia (YOD), particularly when the etiology remains unclear after initial clinical and imaging assessments. Its role spans the identification of neurodegenerative biomarkers, detection of infectious or inflammatory causes, and exclusion of rapidly progressive conditions such as prion disease (Duits et al., 2016).

In patients with suspected **Alzheimer's disease (AD),** CSF analysis enables in vivo assessment of amyloid and tau pathology. The typical AD biomarker profile includes reduced levels of amyloid-β1–42 (Aβ42) and elevated total tau (t-tau) and phosphorylated tau (p-tau), reflecting amyloid plaque deposition and neuronal injury, respectively. This profile can support an AD diagnosis in cases with atypical presentations or where imaging findings are inconclusive (Blennow & Zetterberg, 2018). In younger patients, these markers are particularly useful in differentiating early-onset AD from FTD, psychiatric disorders, or functional cognitive symptoms (McGrowder et al., 2021).

CSF analysis is also critical in identifying **inflammatory** or **infectious** etiologies. Elevated white cell count, increased protein, or oligoclonal bands may point toward conditions such as autoimmune encephalitis, neurosarcoidosis, multiple sclerosis, or CNS infections. Detection of specific antibodies (anti-NMDA receptor, LGI1) or pathogens (HIV, Treponema pallidum, JC virus) is essential for initiating targeted immunotherapy or antimicrobial treatment (Graus et al., 2016).

Despite its diagnostic utility, LP is underused in dementia evaluation, particularly in non-specialist settings. LP is generally safe when performed by trained clinicians, with post-lumbar puncture headache being the most common complication. Pre-procedure imaging is recommended in patients with signs of raised intracranial pressure or space-occupying lesions (Engelborghs et al., 2017).

3.3. Management in Young-Onset Dementia

3.3.1. Medical management

The medical management of young-onset dementia (YOD) presents distinct challenges due to its heterogeneous etiology, variable clinical presentations, and the significant personal, occupational, and social impact on patients and their families. Treatment strategies must therefore be highly individualized, taking into account the specific diagnosis, comorbidities, functional capacity, and psychosocial context. While no curative therapies currently exist for the majority of neurodegenerative dementias, a combination of symptomatic pharmacological treatment, management of neuropsychiatric features, and appropriate non-pharmacologic support is essential for optimizing patient outcomes and quality of life.

Pharmacologic treatment in YOD largely mirrors that used in late-onset dementia (LOD), although evidence in younger populations is often extrapolated from studies involving older adults. In AD, cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) are the mainstay of symptomatic therapy and have shown modest benefits in cognition, global function, and behavior (Birks, 2006). Memantine, an NMDA receptor antagonist, may be added in moderate to severe stages to improve daily functioning and reduce agitation (Reisberg et al., 2003). Though younger patients may show more prominent behavioral symptoms, response rates to these agents are comparable to those in LOD.

In FTD, cholinesterase inhibitors and memantine have not demonstrated efficacy and may even exacerbate symptoms such as disinhibition or agitation (Reisberg et al., 2003). Instead, pharmacological management in FTD is symptom-driven. Selective serotonin reuptake inhibitors (SSRIs), such as sertraline and citalopram, may be beneficial in managing compulsivity, apathy, and irritability. In some cases, low-dose atypical antipsychotics may be considered for severe agitation or psychosis, but their use requires caution due to the risk of extrapyramidal side effects and increased mortality in dementia patients (Huey et al., 2006).

For patients with Lewy body dementia (LBD), cholinesterase inhibitors are often effective for improving attention and visual hallucinations. However, extreme caution is necessary with antipsychotics due to profound

neuroleptic sensitivity. When pharmacologic intervention for psychosis is unavoidable, quetiapine or clozapine are preferred agents due to their relatively lower risk of worsening motor and cognitive symptoms (McKeith et al., 2017).

In Huntington's disease (HD), treatment is aimed at managing both motor and psychiatric symptoms. Tetrabenazine or deutetrabenazine can be used to reduce chorea, while antidepressants and antipsychotics may address mood disturbances and irritability. Cognitive enhancers have not demonstrated consistent benefit in HD, and care is largely supportive (Armstrong & Miyasaki, 2012).

Importantly, a subset of YOD cases are reversible or partially treatable. Inflammatory causes such as multiple sclerosis, neurosarcoidosis, or autoimmune encephalitis may respond to corticosteroids, immunosuppressants, or IVIG/plasmapheresis, depending on the underlying pathology. Infectious causes including HIV-associated dementia, neurosyphilis, or Whipple's disease require targeted antimicrobial therapy. Metabolic deficiencies (vitamin B12, thiamine) and endocrine abnormalities (hypothyroidism, Addison's disease) must be identified and corrected to prevent irreversible damage (Kelley et al., 2008).

Medical management of YOD requires tailored, diagnosis-specific approaches that balance symptomatic relief with safety, psychosocial support, and preservation of function. Early identification of reversible causes, appropriate pharmacologic use, and coordinated multidisciplinary care are central to improving outcomes in this unique population.

3.3.2 Non-Pharmacological Interventions

Non-pharmacological interventions represent a cornerstone of care in young-onset dementia (YOD), not only because pharmacologic treatments are often limited in efficacy, but also due to the distinct psychosocial, vocational, and familial challenges that this population faces. YOD often affects individuals in their most economically and socially active years, and management must extend beyond symptom control to include functional support, role adaptation, and quality-of-life preservation. Tailored multidisciplinary interventions are critical for addressing the cognitive, behavioral, emotional, and practical dimensions of the disease.

Cognitive interventions aim to preserve or enhance functional abilities through structured stimulation, strategy training, and environmental adaptation. Cognitive stimulation therapy (CST) has demonstrated modest benefits in global cognition and quality of life, particularly in the earlier stages of dementia. While most studies focus on late-onset Alzheimer's disease, preliminary evidence supports the use of similar approaches in younger populations, especially when adapted for individual needs and learning preferences (Spector et al., 2003). Cognitive rehabilitation, which involves goal-oriented support for specific daily tasks (e.g. managing schedules, navigating environments), may offer functional benefits and reinforce autonomy in motivated patients with insight (Clare et al., 2010).

Occupational therapy plays a vital role in maximizing independence in activities of daily living (ADLs) and instrumental ADLs. Tailored environmental modifications, routines, and assistive technologies can help compensate for executive dysfunction and memory loss (Bennett et al., 2011). Speech-language therapy is essential in syndromes with early language involvement such as primary progressive aphasia and may also assist with communication strategies, swallowing safety, and social engagement.

Physical activity and exercise programs have been shown to improve mood, sleep quality, and physical function while potentially slowing cognitive decline. Structured aerobic and resistance training, even when initiated after diagnosis, may reduce apathy and agitation while enhancing mobility and fall prevention (Forbes et al., 2013). In YOD, exercise also serves a social purpose, combating isolation and providing a sense of routine and self-efficacy.

Psychosocial support is integral and should begin at diagnosis. Younger individuals with dementia frequently experience distress due to role loss, altered identity, stigma, and changes in relationships. Access to counseling, support groups, and peer networks can foster coping skills, normalize emotional responses, and reduce caregiver strain (Ducharme et al., 2014). Partners and children of individuals with YOD often require specific support, given the likelihood of being in the workforce or school, and the lack of age-appropriate caregiving resources.

Vocational rehabilitation and employment counseling are important in the early stages of YOD. Some individuals may wish to continue working, with adjustments to workload, schedule, or role. Occupational health professionals and employers can facilitate supportive transitions, though in many cases, progressive decline necessitates planning for work cessation and long-term financial stability (Roach & Keady, 2008).

Advanced care planning, including discussion of legal, financial, and end-of-life decisions, is often more difficult in younger individuals but remains essential. Early engagement in these conversations, before

substantial cognitive decline, ensures that the person's preferences are documented and honored. (Van Vliet et al., 2011).

A multidisciplinary team approach is vital to delivering non-pharmacological care, ideally including neurologists, psychiatrists, psychologists, nurses, social workers, occupational and physical therapists, and speech-language pathologists. Regular team reviews ensure that care plans are dynamic, person-centered, and responsive to evolving needs.

Non-pharmacological interventions are fundamental to the holistic management of young-onset dementia. While pharmacologic treatments may address core cognitive symptoms or behavioral disturbances, it is often the supportive, rehabilitative, and adaptive strategies that sustain autonomy, preserve dignity, and improve quality of life for individuals with YOD and their families.

4. Discussion and Conclusions

Young-onset dementia (YOD) remains a diagnostically and therapeutically complex group of disorders with substantial clinical, psychosocial, and economic implications. Unlike late-onset dementia, YOD often presents with atypical cognitive, behavioral, or psychiatric features, which contributes significantly to diagnostic delays. This diagnostic uncertainty is further compounded by the broad differential diagnosis, which spans neurodegenerative, autoimmune, metabolic, infectious, genetic, and psychiatric etiologies.

Our review highlights that while Alzheimer's disease remains the leading cause of YOD, atypical phenotypes - such as posterior cortical atrophy or logopenic aphasia - are more prevalent in this population. Frontotemporal dementia, particularly with behavioral or language-dominant presentations, represents the second most common cause and carries a high genetic burden. Other less common but important causes, such as Huntington's disease, prion disorders, must also be considered, particularly when neuropsychiatric or motor features predominate.

The importance of a structured, multidisciplinary assessment cannot be overstated. A thorough clinical history and collateral information are essential, particularly in cases where insight is limited. Bedside cognitive screening tools such as MoCA and ACE-III, combined with detailed neuropsychological assessment, help distinguish neurodegenerative from psychiatric or functional etiologies. Neuroimaging, particularly MRI with a dedicated dementia protocol, serves as a cornerstone of evaluation, with functional and molecular imaging enhancing diagnostic precision in select cases. Cerebrospinal fluid analysis provides critical information on Alzheimer biomarkers and potential inflammatory or infectious processes. Genetic testing, when appropriately indicated and preceded by counseling, offers diagnostic clarity in familial cases and aids in risk stratification.

Management of YOD requires more than pharmacological treatment. While cholinesterase inhibitors and memantine have utility in early-onset AD, their use in other dementias is limited and often symptom-based. Non-pharmacological strategies, including cognitive rehabilitation, structured exercise, occupational and speech therapy, and psychosocial support, are integral. Vocational, financial, and legal counseling, alongside tailored caregiver support, are crucial in maintaining function and family stability, especially given the younger age and life stage of most patients.

Despite advances, barriers to early diagnosis and access to appropriate care persist. Misdiagnosis with psychiatric disorders, lack of age-appropriate services, and underutilization of lumbar puncture or advanced imaging remain key gaps in practice. Clinician education and public awareness must improve to reduce time to diagnosis and enhance care pathways.

Young-onset dementia represents a growing and under-recognized clinical challenge. Its heterogeneous etiologies, frequent non-amnestic presentations, and high rates of misdiagnosis require clinicians to adopt a systematic, multidisciplinary approach to diagnosis and management. Early recognition, supported by targeted neuroimaging, cerebrospinal fluid biomarkers, and genetic testing, enables more accurate diagnosis, timely intervention, and improved outcomes. Beyond symptom control, comprehensive care must address the complex psychosocial needs of patients and their families. Future efforts should focus on increasing access to specialized diagnostic services, expanding genetic and biomarker testing, and developing tailored support frameworks to meet the unique needs of individuals with YOD.

REFERENCES

1. Armstrong, M. J., & Miyasaki, J. M. (2012). Evidence-based guideline: Pharmacologic treatment of chorea in Huntington disease [RETIRED]: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*, *79*(6), 597–603. https://doi.org/10.1212/WNL.0b013e318263c443
2. Bennett, S., Shand, S., & Liddle, J. (2011). Occupational therapy practice in Australia with people with dementia: A profile in need of change: OCCUPATIONAL THERAPY FOR PEOPLE WITH DEMENTIA. *Australian Occupational Therapy Journal*, *58*(3), 155–163. https://doi.org/10.1111/j.1440-1630.2011.00930.x
3. Birks, J. S. (2006). Cholinesterase inhibitors for Alzheimer's disease. *Cochrane Database of Systematic Reviews*, *2016*(3). https://doi.org/10.1002/14651858.CD005593
4. Blennow, K., & Zetterberg, H. (2018). Biomarkers for Alzheimer's disease: Current status and prospects for the future. *Journal of Internal Medicine*, *284*(6), 643–663. https://doi.org/10.1111/joim.12816
5. Clare, L., Linden, D. E. J., Woods, R. T., Whitaker, R., Evans, S. J., Parkinson, C. H., Van Paasschen, J., Nelis, S. M., Hoare, Z., Yuen, K. S. L., & Rugg, M. D. (2010). Goal-Oriented Cognitive Rehabilitation for People With Early-Stage Alzheimer Disease: A Single-Blind Randomized Controlled Trial of Clinical Efficacy. *The American Journal of Geriatric Psychiatry*, *18*(10), 928–939. https://doi.org/10.1097/JGP.0b013e3181d5792a
6. DeJesus-Hernandez, M., Mackenzie, I. R., Boeve, B. F., Boxer, A. L., Baker, M., Rutherford, N. J., Nicholson, A. M., Finch, N. A., Flynn, H., Adamson, J., Kouri, N., Wojtas, A., Sengdy, P., Hsiung, G.-Y. R., Karydas, A., Seeley, W. W., Josephs, K. A., Coppola, G., Geschwind, D. H., … Rademakers, R. (2011). Expanded GGGGCC Hexanucleotide Repeat in Noncoding Region of C9ORF72 Causes Chromosome 9p-Linked FTD and ALS. *Neuron*, *72*(2), 245–256. https://doi.org/10.1016/j.neuron.2011.09.011
7. Ducharme, F., Kergoat, M.-J., Antoine, P., Pasquier, F., & Coulombe, R. (2014). Caring for Individuals with Early-Onset Dementia and Their Family Caregivers: The Perspective of Health Care Professionals. *Advances in Alzheimer's Disease*, *03*(01), 33–43. https://doi.org/10.4236/aad.2014.31005
8. Duits, F. H., Martinez-Lage, P., Paquet, C., Engelborghs, S., Lleó, A., Hausner, L., Molinuevo, J. L., Stomrud, E., Farotti, L., Ramakers, I. H. G. B., Tsolaki, M., Skarsgård, C., Åstrand, R., Wallin, A., Vyhnalek, M., Holmber-Clausen, M., Forlenza, O. V., Ghezzi, L., Ingelsson, M., … Blennow, K. (2016). Performance and complications of lumbar puncture in memory clinics: Results of the multicenter lumbar puncture feasibility study. *Alzheimer's & Dementia*, *12*(2), 154–163. https://doi.org/10.1016/j.jalz.2015.08.003
9. Engelborghs, S., Niemantsverdriet, E., Struyfs, H., Blennow, K., Brouns, R., Comabella, M., Dujmovic, I., Van Der Flier, W., Frölich, L., Galimberti, D., Gnanapavan, S., Hemmer, B., Hoff, E., Hort, J., Iacobaeus, E., Ingelsson, M., Jan De Jong, F., Jonsson, M., Khalil, M., … Teunissen, C. E. (2017). Consensus guidelines for lumbar puncture in patients with neurological diseases. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *8*(1), 111–126. https://doi.org/10.1016/j.dadm.2017.04.007
10. Ferreira, D., Nordberg, A., & Westman, E. (2020). Biological subtypes of Alzheimer disease: A systematic review and meta-analysis. *Neurology*, *94*(10), 436–448. https://doi.org/10.1212/WNL.0000000000009058
11. Forbes, D., Thiessen, E. J., Blake, C. M., Forbes, S. C., & Forbes, S. (2013). Exercise programs for people with dementia. In The Cochrane Collaboration (Ed.), *Cochrane Database of Systematic Reviews* (p. CD006489.pub3). John Wiley & Sons, Ltd. https://doi.org/10.1002/14651858.CD006489.pub3
12. Gass, J., Cannon, A., Mackenzie, I. R., Boeve, B., Baker, M., Adamson, J., Crook, R., Melquist, S., Kuntz, K., Petersen, R., Josephs, K., Pickering-Brown, S. M., Graff-Radford, N., Uitti, R., Dickson, D., Wszolek, Z., Gonzalez, J., Beach, T. G., Bigio, E., … Rademakers, R. (2006). Mutations in progranulin are a major cause of ubiquitin-positive frontotemporal lobar degeneration. *Human Molecular Genetics*, *15*(20), 2988–3001. https://doi.org/10.1093/hmg/ddl241
13. Goldman, J. S., Hahn, S. E., Catania, J. W., Larusse-Eckert, S., Butson, M. Barber., Rumbaugh, M., Strecker, M. N., Roberts, J. S., Burke, W., Mayeux, R., & Bird, T. (2011). Genetic counseling and testing for Alzheimer disease: Joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genetics in Medicine*, *13*(6), 597–605. https://doi.org/10.1097/GIM.0b013e31821d69b8
14. Graus, F., Titulaer, M. J., Balu, R., Benseler, S., Bien, C. G., Cellucci, T., Cortese, I., Dale, R. C., Gelfand, J. M., Geschwind, M., Glaser, C. A., Honnorat, J., Höftberger, R., Iizuka, T., Irani, S. R., Lancaster, E., Leypoldt, F., Prüss, H., Rae-Grant, A., … Dalmau, J. (2016). A clinical approach to diagnosis of autoimmune encephalitis. *The Lancet Neurology*, *15*(4), 391–404. https://doi.org/10.1016/S1474-4422(15)00401-9
15. Harper, L., Barkhof, F., Scheltens, P., Schott, J. M., & Fox, N. C. (2014). An algorithmic approach to structural imaging in dementia. *Journal of Neurology, Neurosurgery & Psychiatry*, *85*(6), 692–698. https://doi.org/10.1136/jnnp-2013-306285
16. He, Q., Wang, W., Zhang, Y., Xiong, Y., Tao, C., Ma, L., You, C., Ma, J., & Jiang, Y. (2025). Global burden of young-onset dementia, from 1990 to 2021: An age-period-cohort analysis from the global burden of disease study 2021. *Translational Psychiatry*, *15*(1), 56. https://doi.org/10.1038/s41398-025-03275-w

17. Hsieh, S., Schubert, S., Hoon, C., Mioshi, E., & Hodges, J. R. (2013). Validation of the Addenbrooke's Cognitive Examination III in Frontotemporal Dementia and Alzheimer's Disease. *Dementia and Geriatric Cognitive Disorders*, *36*(3–4), 242–250. https://doi.org/10.1159/000351671
18. Huey, E. D., Putnam, K. T., & Grafman, J. (2006). A systematic review of neurotransmitter deficits and treatments in frontotemporal dementia. *Neurology*, *66*(1), 17–22. https://doi.org/10.1212/01.wnl.0000191304.55196.4d
19. Johnson, K. A., Minoshima, S., Bohnen, N. I., Donohoe, K. J., Foster, N. L., Herscovitch, P., Karlawish, J. H., Rowe, C. C., Carrillo, M. C., Hartley, D. M., Hedrick, S., Pappas, V., & Thies, W. H. (2013). Appropriate Use Criteria for Amyloid PET: A Report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *Journal of Nuclear Medicine*, *54*(3), 476–490. https://doi.org/10.2967/jnumed.113.120618
20. Kelley, B. J., Boeve, B. F., & Josephs, K. A. (2008). Young-Onset Dementia: Demographic and Etiologic Characteristics of 235 Patients. *Archives of Neurology*, *65*(11), 1502. https://doi.org/10.1001/archneur.65.11.1502
21. Kelley, B. J., Boeve, B. F., & Josephs, K. A. (2009). Rapidly Progressive Young-Onset Dementia. *Cognitive and Behavioral Neurology*, *22*(1), 22–27. https://doi.org/10.1097/WNN.0b013e318192cc8d
22. Koene, S., Rodenburg, R. J., Van Der Knaap, M. S., Willemsen, M. A. A. P., Sperl, W., Laugel, V., Ostergaard, E., Tarnopolsky, M., Martin, M. A., Nesbitt, V., Fletcher, J., Edvardson, S., Procaccio, V., Slama, A., Den Van Heuvel, L. P. W. J., & Smeitink, J. A. M. (2012). Natural disease course and genotype-phenotype correlations in Complex I deficiency caused by nuclear gene defects: What we learned from 130 cases. *Journal of Inherited Metabolic Disease*, *35*(5), 737–747. https://doi.org/10.1007/s10545-012-9492-z
23. Liu, C.-C., Kanekiyo, T., Xu, H., & Bu, G. (2013). Apolipoprotein E and Alzheimer disease: Risk, mechanisms and therapy. *Nature Reviews Neurology*, *9*(2), 106–118. https://doi.org/10.1038/nrneurol.2012.263
24. Loi, S. M., Cations, M., & Velakoulis, D. (2023). Young-onset dementia diagnosis, management and care: A narrative review. *Medical Journal of Australia*, *218*(4), 182–189. https://doi.org/10.5694/mja2.51849
25. McGrowder, D. A., Miller, F., Vaz, K., Nwokocha, C., Wilson-Clarke, C., Anderson-Cross, M., Brown, J., Anderson-Jackson, L., Williams, L., Latore, L., Thompson, R., & Alexander-Lindo, R. (2021). Cerebrospinal Fluid Biomarkers of Alzheimer's Disease: Current Evidence and Future Perspectives. *Brain Sciences*, *11*(2), 215. https://doi.org/10.3390/brainsci11020215
26. McKeith, I. G., Boeve, B. F., Dickson, D. W., Halliday, G., Taylor, J.-P., Weintraub, D., Aarsland, D., Galvin, J., Attems, J., Ballard, C. G., Bayston, A., Beach, T. G., Blanc, F., Bohnen, N., Bonanni, L., Bras, J., Brundin, P., Burn, D., Chen-Plotkin, A., … Kosaka, K. (2017). Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. *Neurology*, *89*(1), 88–100. https://doi.org/10.1212/WNL.0000000000004058
27. Mendez, M. F. (2006). The Accurate Diagnosis of Early-Onset Dementia. *The International Journal of Psychiatry in Medicine*, *36*(4), 401–412. https://doi.org/10.2190/Q6J4-R143-P630-KW41
28. Papageorgiou, S. G., Kontaxis, T., Bonakis, A., Kalfakis, N., & Vassilopoulos, D. (2009). Frequency and Causes of Early-onset Dementia in a Tertiary Referral Center in Athens. *Alzheimer Disease & Associated Disorders*, *23*(4), 347–351. https://doi.org/10.1097/WAD.0b013e31819e6b28
29. Reisberg, B., Doody, R., Stöffler, A., Schmitt, F., Ferris, S., & Möbius, H. J. (2003). Memantine in Moderate-to-Severe Alzheimer's Disease. *New England Journal of Medicine*, *348*(14), 1333–1341. https://doi.org/10.1056/NEJMoa013128
30. Roach, P., & Keady, J. (2008). Younger people with dementia: Time for fair play. *British Journal of Nursing*, *17*(11), 690–690. https://doi.org/10.12968/bjon.2008.17.11.29604
31. Rohrer, J. D., Guerreiro, R., Vandrovcova, J., Uphill, J., Reiman, D., Beck, J., Isaacs, A. M., Authier, A., Ferrari, R., Fox, N. C., Mackenzie, I. R. A., Warren, J. D., De Silva, R., Holton, J., Revesz, T., Hardy, J., Mead, S., & Rossor, M. N. (2009). The heritability and genetics of frontotemporal lobar degeneration. *Neurology*, *73*(18), 1451–1456. https://doi.org/10.1212/WNL.0b013e3181bf997a
32. Rossor, M. N., Fox, N. C., Mummery, C. J., Schott, J. M., & Warren, J. D. (2010). The diagnosis of young-onset dementia. *The Lancet Neurology*, *9*(8), 793–806. https://doi.org/10.1016/S1474-4422(10)70159-9
33. Ryman, D. C., Acosta-Baena, N., Aisen, P. S., Bird, T., Danek, A., Fox, N. C., Goate, A., Frommelt, P., Ghetti, B., Langbaum, J. B. S., Lopera, F., Martins, R., Masters, C. L., Mayeux, R. P., McDade, E., Moreno, S., Reiman, E. M., Ringman, J. M., Salloway, S., … And the Dominantly Inherited Alzheimer Network. (2014). Symptom onset in autosomal dominant Alzheimer disease: A systematic review and meta-analysis. *Neurology*, *83*(3), 253–260. https://doi.org/10.1212/WNL.0000000000000596
34. Sims, R., Hill, M., & Williams, J. (2020). The multiplex model of the genetics of Alzheimer's disease. *Nature Neuroscience*, *23*(3), 311–322. https://doi.org/10.1038/s41593-020-0599-5
35. Spector, A., Thorgrimsen, L., Woods, B., Royan, L., Davies, S., Butterworth, M., & Orrell, M. (2003). Efficacy of an evidence-based cognitive stimulation therapy programme for people with dementia: Randomised controlled trial. *British Journal of Psychiatry*, *183*(3), 248–254. https://doi.org/10.1192/bjp.183.3.248

36. Van Vliet, D., De Vugt, M. E., Bakker, C., Koopmans, R. T. C. M., Pijnenburg, Y. A. L., Vernooij-Dassen, M. J. F. J., & Verhey, F. R. J. (2011). Caregivers' perspectives on the pre-diagnostic period in early onset dementia: A long and winding road. *International Psychogeriatrics*, *23*(9), 1393–1404. https://doi.org/10.1017/S1041610211001013
37. Van Vliet, D., De Vugt, M. E., Bakker, C., Pijnenburg, Y. A. L., Vernooij-Dassen, M. J. F. J., Koopmans, R. T. C. M., & Verhey, F. R. J. (2013). Time to diagnosis in young-onset dementia as compared with late-onset dementia. *Psychological Medicine*, *43*(2), 423–432. https://doi.org/10.1017/S0033291712001122
38. Vieira, R. T. (2013). Epidemiology of early-onset dementia: A review of the literature. *Clinical Practice & Epidemiology in Mental Health*, *9*(1), 88–95. https://doi.org/10.2174/1745017901309010088
39. Villemagne, V. L., Fodero-Tavoletti, M. T., Masters, C. L., & Rowe, C. C. (2015). Tau imaging: Early progress and future directions. *The Lancet Neurology*, *14*(1), 114–124. https://doi.org/10.1016/S1474-4422(14)70252-2
40. Warren, J. D., Rohrer, J. D., & Rossor, M. N. (2013). Frontotemporal dementia. *BMJ*, *347*(aug12 3), f4827–f4827. https://doi.org/10.1136/bmj.f4827
41. Whitwell, J. L., & Jack, C. R. (2007). Neuroimaging in Dementia. *PET Clinics*, *2*(1), 15–24. https://doi.org/10.1016/j.cpet.2007.09.002