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Sleeping Position, Deep Sleep, and Dementia Prevention: Clinical and Mechanistic Perspectives

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Editorial

Vulnerability Across Scales: From Molecular Pathways to Health System Failures

Modern medicine is increasingly defined not by isolated disease entities but by the interaction of biological systems, human behavior, and structural forces. The five papers in this issue, though diverse in subject matter, collectively illustrate a unifying principle: health outcomes emerge from multilevel vulnerability—spanning molecular mechanisms, individual physiology, occupational stress, and system-wide disruptions.

At the molecular and neurobiological level, the evolving understanding of frontotemporal lobar degeneration (FTLD) reflects a broader paradigm shift in clinical neuroscience. FTLD is no longer adequately conceptualized as a single disease or even a set of syndromes; rather, it represents a network-based neurodegenerative spectrum driven by heterogeneous proteinopathies and genetic mechanisms . The recognition of clinicopathological dissociation—where similar clinical phenotypes arise from distinct molecular substrates—underscores the limitations of traditional diagnostic frameworks and reinforces the necessity of biomarker-guided precision medicine. This shift has implications far beyond FTLD, signaling a transition toward integrated, multidimensional disease classification across neurology.

In contrast to these molecular advances, the report on sudden death among young anaesthesiologists highlights a neglected dimension of healthcare: the fragility of the workforce itself. Evidence from China and emerging observations from Libya suggests a multifactorial risk profile, in which cardiovascular instability is precipitated by chronic occupational stress, sleep deprivation, and metabolic risk factors, with a possible contribution from post-infectious cardiac pathology . These findings expose systemic deficiencies—excessive workloads, inadequate regulation, and insufficient occupational health surveillance—that transform professional environments into sources of morbidity and mortality. The absence of robust reporting systems further obscures the true scale of the problem, limiting both recognition and intervention.

The growing recognition of sleep as a biological determinant of neurodegeneration provides a critical bridge between molecular and behavioral domains. The reviewed evidence positions slow-wave sleep as a central mechanism facilitating glymphatic clearance of neurotoxic proteins, including beta-amyloid and tau, thereby linking sleep architecture directly to Alzheimer's disease pathophysiology . While emerging data on sleep position remain preliminary, the broader implication is clear: sleep is not merely restorative but actively neuroprotective, representing a modifiable target for disease prevention. This reframing elevates sleep from a secondary consideration to a core component of clinical strategy.

At the population level, the narrative review on diabetes in the context of natural and man-made disastersdemonstrates how external shocks disrupt the continuity of chronic disease management. Disasters compromise healthcare infrastructure, medication access, and socioeconomic stability, leading to deterioration in glycemic control and increased complications . The proposed multilevel causal pathway, linking environmental disruption to biological outcomes through system and behavioral intermediary linking environmental disruption to biological outcomes through system and behavioral intermediaries, offers a compelling framework for understanding how acute events translate into long-term health consequences . Notably, the findings highlight a persistent gap in global health planning: the systematic neglect of non-communicable diseases in disaster preparedness strategies.

Finally, the exploration of adiposity and survival introduces a provocative perspective on metabolic health. The hypothesis that lower body fat may be associated with reduced biological aging and improved survival challenges prevailing

assumptions and invites reconsideration of established risk models. Although interpretation is limited by potential confounding and disease-specific contexts, the work contributes to an ongoing reassessment of the relationship between body composition, inflammation, and vascular pathology.

Taken together, these studies converge on a central insight: disease cannot be understood—or effectively managed—without accounting for the interplay between biological processes and the environments in which they operate. Molecular pathology, behavioral factors, occupational stress, and system-level disruptions are not independent domains but components of a single, interconnected framework.

The implications are substantial. Clinically, there is a need to integrate biomarker-driven diagnostics with lifestyle and behavioral interventions, including sleep optimization. At the level of healthcare systems, the protection of the workforce must be recognized as a priority, requiring enforceable limits on workload and structured occupational health programs. From a public health perspective, resilience must extend beyond acute care to include continuity of chronic disease management under conditions of instability.

In this context, the future of medicine lies not in further fragmentation into subspecialties, but in reintegrating knowledge across scales, from molecular pathways to societal structures, into cohesive, adaptive models of care.

Warm regards,
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Frontotemporal Lobar Degeneration: Clinical Syndromes, Molecular Pathogenesis, Neuroimaging, and Diagnostic Frameworks

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Abstract

Background:Frontotemporal lobar degeneration (FTLD) represents a heterogeneous group of neurodegenerative disorders characterized by progressive dysfunction in behavior, executive function, and language associated with selective degeneration of frontal and temporal networks. Increasing recognition of molecular heterogeneity and clinicopathological dissociation has reshaped contemporary understanding of FTLD.

Objective: To provide a comprehensive, high-level synthesis of FTLD integrating clinical phenotypes, molecular mechanisms, genetic architecture, and neuroimaging correlates, with emphasis on advances from 2020 to 2026.

Methods: A structured narrative review was conducted, emphasizing recent literature alongside foundational studies. Evidence was synthesized across clinical, genetic, neuropathological, and neuroimaging domains to construct an integrated disease framework.

Results: FTLD encompasses multiple clinical syndromes, including behavioural variant frontotemporal dementia (bvFTD) and primary progressive aphasia (PPA) variants, underpinned by distinct proteinopathies (tau, TDP-43, FUS). enetic discoveries, particularly involving MAPT, GRN, and C9orf72 have clarified disease mechanisms but also highlighted phenotypic variability. Neuroimaging and biomarker advances have improved diagnostic precision, although substantial clinicopathological discordance persists.

Conclusions: FTLD is best conceptualized as a network-based neurodegenerative spectrum driven by molecularly distinct but clinically overlapping processes. Future diagnostic and therapeutic strategies will depend on biomarker integration and molecular stratification.

Key words:
Frontotemporal Lobar Degeneration,
Clinical Syndromes, Molecular Pathogenesis,
Neuroimaging, and Diagnostic Frameworks

Overview: Nosology, Conceptual Framework, and Evolving Classification of FTLD

Frontotemporal lobar degeneration (FTLD) constitutes a major category of neurodegenerative disease defined by progressive degeneration of frontal and anterior temporal cortices, leading to impairments in behaviour, executive function, and language (Bang et al., 2015; Knopman et al., 2021). The distinction between frontotemporal dementia (FTD) as a clinical syndrome and FTLD as a pathological construct remains central, reflecting the divergence between phenotype and underlying molecular substrate (Kirshner, 2022).

Contemporary models emphasize FTLD as a network-based neurodegenerative disorder, wherein selective vulnerability of large-scale neural networks, particularly the salience network, semantic network, and language networks, drives clinical expression (Seeley et al., 2008; Zhou et al., 2012). This network degeneration paradigm explains the relative preservation of other cognitive domains in early disease stages and the progressive convergence of syndromes over time.

A critical evolution in FTLD research has been the recognition of clinicopathological dissociation, whereby identical clinical syndromes may arise from different molecular pathologies, and conversely, identical proteinopathies may produce divergent phenotypes depending on their anatomical distribution (Irwin et al., 2015; Negro et al., 2026). This has shifted the field from a purely syndromic classification toward a multidimensional framework integrating clinical, molecular, and imaging data.

Recent consensus frameworks further stratify FTLD into proteinopathy-based categories, primarily FTLD-tau, FTLD-TDP, and FTLD-FUS, each associated with distinct genetic and pathological signatures (Mackenzie et al., 2010; Neumann et al., 2006). Importantly, these molecular classifications do not map directly onto clinical syndromes, reinforcing the complexity of diagnosis and management.

Table 1: Clinical and pathological classification of FTLD syndromes

Clinical Syndrome	Core Features	Predominant Regions	Common Pathology
bvFTD	Behavioural disinhibition, apathy, executive dysfunction	Frontal (orbitofrontal, anterior cingulate, insula)	FTLD-TDP, FTLD-tau
nfvPPA	Agrammatism, apraxia of speech	Left frontal operculum, insula	FTLD-tau
svPPA (Semantic dementia)	Loss of semantic knowledge	Anterior temporal lobes	FTLD-TDP
lvPPA	Word-finding pauses, repetition deficits	Temporoparietal junction	Alzheimer pathology
FTLD-ALS	Behavioural + motor neurone disease	Frontal cortex, motor system	FTLD-TDP (C9orf72)

Source: Adapted from Gorno-Tempini et al. (2011); Rascovsky et al. (2011); Mackenzie et al. (2010)

Etiology: Molecular Mechanisms and Proteinopathies in FTLD

FTLD pathogenesis is fundamentally driven by abnormal protein aggregation and impaired proteostasis, leading to synaptic dysfunction, neuronal loss, and network-level degeneration (Bang et al., 2015; Rohrer & Warren, 2011). Unlike Alzheimer disease, which is dominated by amyloid-β and tau pathology, FTLD encompasses multiple distinct proteinopathies with overlapping but non-identical mechanisms.

1 Major Proteinopathies

FTLD-TDP

TDP-43 proteinopathy represents the most common pathological substrate in FTLD, accounting for approximately 50% of cases (Mackenzie et al., 2010). TDP-43 is a nuclear RNA-binding protein that regulates RNA splicing, transport, and stability. Pathological processes include:

- Cytoplasmic aggregation
- Nuclear depletion
- Post-translational modifications (phosphorylation, ubiquitination)

These changes result in both loss of normal nuclear function and toxic cytoplasmic gain-of-function, disrupting RNA metabolism and neuronal homeostasis (Ling et al., 2013; Neumann et al., 2006).

Recent studies have further classified FTLD-TDP into subtypes (A–E), each associated with specific clinical phenotypes and genetic mutations, particularly GRN and C9orf72 (Mackenzie et al., 2011; Irwin et al., 2015).

FTLD-Tau
Tauopathies in FTLD involve abnormal aggregation of hyperphosphorylated tau protein, leading to microtubule destabilization and impaired axonal transport (Spillantini & Goedert, 2013). Distinct tau isoforms (3R vs 4R) underlie different pathological entities, including Pick disease, corticobasal degeneration, and progressive supranuclear palsy (Lee et al., 2001).

Tau pathology is particularly associated with nonfluent PPA and Parkinsonian syndromes, reflecting involvement of frontal and motor networks (Grossman, 2010).

FTLD-FUS
FUS proteinopathies represent a smaller subset of FTLD but are notable for their early onset and severe behavioural phenotype (Urwin et al., 2010). FUS plays a role in RNA processing, and its aggregation further reinforces the central role of RNA dysregulation in FTLD.

Table 2. Major molecular proteinopathies in FTLD

Proteinopathy	Protein	Key Mechanism	Associated Syndromes
FTLD-TDP	TDP-43	RNA dysregulation, cytoplasmic aggregation	bvFTD, svPPA, FTLD-ALS
FTLD-tau	Tau	Microtubule dysfunction, aggregation	nfvPPA, PSP, CBD
FTLD-FUS	FUS	RNA processing impairment	Early-onset bvFTD

Source: Mackenzie et al. (2010); Neumann et al. (2006); Urwin et al. (2010)

2 Pathobiological Cascades

Emerging evidence suggests that FTLD pathogenesis involves interconnected molecular cascades, including:

- Impaired autophagy and proteasomal degradation
- Mitochondrial dysfunction
- Neuroinflammation
- Synaptic failure

TDP-43 aggregation, in particular, has been shown to propagate in a prion-like manner, facilitating trans-synaptic spread of pathology (Porta et al., 2018). Similarly, tau pathology demonstrates network-based propagation consistent with disease progression patterns observed clinically.

3 Network-Based Degeneration

Selective vulnerability of specific neural networks is a defining feature of FTLD. The salience network, anchored in the anterior insula and anterior cingulate cortex, is particularly affected in bvFTD, whereas language networks involving the left perisylvian and temporal regions are targeted in PPA variants (Seeley et al., 2008; Zhou et al., 2012).

Importantly, recent clinicopathological studies emphasize that anatomical distribution of pathology may be more predictive of clinical phenotype than molecular subtype, highlighting the importance of network-level analysis (Negro et al., 2026).

Genetic Distribution and Variation: Molecular Genetics and Genotype–Phenotype Relationships

Genetic factors play a critical role in FTLD, with approximately 30–50% of cases demonstrating familial aggregation and up to 40% exhibiting autosomal dominant inheritance (Rohrer et al., 2009; Goldman et al., 2005). Advances in molecular genetics have identified key pathogenic mutations that converge on common neurodegenerative pathways.

1 Major Genes

MAPT
MAPT mutations result in altered tau splicing and aggregation, leading to FTLD-tau pathology (Hutton et al., 1998). These mutations are associated with early-onset disease and often present with bvFTD or Parkinsonism.

GRN
GRN mutations cause progranulin haploinsufficiency, leading to TDP-43 pathology and increased neuroinflammation (Baker et al., 2006; Cruts et al., 2006). Clinically, GRN mutations are associated with asymmetric cortical atrophy and language-dominant presentations.

C9orf72
Hexanucleotide repeat expansions in C9orf72 represent the most common genetic cause of FTLD and are strongly linked to the FTLD-ALS spectrum (DeJesus-Hernandez et al., 2011; Renton et al., 2011). These expansions produce toxic RNA foci and dipeptide repeat proteins, contributing to neurodegeneration.

2 Additional Genetic Contributors
Emerging genes include:
- TBK1 (autophagy regulation)
- VCP (protein degradation pathways)
- CHMP2B (endosomal trafficking)
- FUS (RNA metabolism)

These genes highlight the central role of proteostasis and RNA regulation in FTLD pathogenesis (van der Zee et al., 2011).

3 Genotype–Phenotype Complexity
Although certain genotype–phenotype correlations exist, substantial variability remains. For example, C9orf72 mutations may present with bvFTD, ALS, or mixed phenotypes, while GRN mutations often produce asymmetric cortical degeneration (Rohrer et al., 2015).

This variability underscores the concept that genetic mutations influence disease biology but do not rigidly determine clinical phenotype, reinforcing the need for integrated diagnostic approaches.

Epidemiology: Global Burden and Demographic Patterns

FTLD is a leading cause of early-onset dementia, accounting for approximately 10–20% of cases in individuals under 65 years (Ratnavalli et al., 2002; Onyike & Diehl-Schmid, 2013). Prevalence estimates range from 5 to 15 per 100,000 individuals, although underdiagnosis remains a significant issue (Knopman & Roberts, 2011).

The disease typically presents between ages 45 and 65, although both earlier and later onset cases are well documented (Rabinovici & Miller, 2010). Sex distribution varies by subtype, with some evidence suggesting male predominance in bvFTD (Seelaar et al., 2011).

Prognosis: Disease Trajectory and Determinants of Outcome

FTLD is associated with progressive functional decline and reduced survival, with median survival ranging from 6 to 11 years from symptom onset (Onyike & Diehl-Schmid, 2013). Prognosis varies by subtype, with bvFTD often demonstrating more rapid progression compared to semantic dementia (Rabinovici & Miller, 2010).

The presence of motor neurone disease significantly worsens prognosis, with shorter survival observed in FTLD-ALS (Lomen-Hoerth et al., 2002). Additional prognostic factors include genetic mutations, extent of cortical involvement, and severity of executive dysfunction.

Clinical Syndromes of Frontotemporal Lobar Degeneration: Phenotypic Spectrum and Network-Based Correlates

Frontotemporal lobar degeneration is clinically expressed through a spectrum of syndromes that reflect selective degeneration of distributed neural networks rather than discrete anatomical lesions. Contemporary frameworks emphasize that these syndromes are best understood as network-driven phenotypes, with clinical manifestations emerging from disruption of large-scale functional systems, including the salience, semantic, and language networks (Seeley et al., 2008; Zhou et al., 2012).

Although categorized into behavioural and language-dominant syndromes, overlap is common, and longitudinal evolution frequently leads to convergence of phenotypes, reinforcing the concept of FTLD as a dynamic neurodegenerative continuum rather than a set of discrete disorders (Bang et al., 2015; Irwin et al., 2015).

1 Behavioural Variant Frontotemporal Dementia (bvFTD): Neurobehavioural Syndrome and Network Disintegration

Behavioural variant frontotemporal dementia represents the most prevalent clinical phenotype of FTLD and is characterized by early and progressive alterations in personality, social conduct, and executive function (Rascovsky et al., 2011; Bang et al., 2015). The syndrome reflects degeneration of frontal-insular networks that subserve emotional processing, decision-making, and social cognition.

1.1 Core Behavioural Domains

The diagnostic criteria for bvFTD emphasize six core behavioural domains, each reflecting disruption of specific neural circuits (Rascovsky et al., 2011):

1. Behavioural disinhibition
2. Apathy or inertia
3. Loss of empathy or sympathy
4. Perseverative, stereotyped, or compulsive behaviours
5. Hyperorality and dietary changes
6. Executive dysfunction with relative sparing of memory and visuospatial skills

These domains are not merely descriptive but correspond to dysfunction in distinct neuroanatomical substrates, particularly within the orbitofrontal cortex, anterior cingulate cortex, and anterior insula (Seeley et al., 2008).

Behavioural disinhibition arises from orbitofrontal dysfunction and is characterized by impulsivity, socially inappropriate behaviour, and impaired judgement. In contrast, apathy reflects medial frontal and anterior cingulate degeneration, resulting in reduced motivation and goal-directed behaviour (Rosen et al., 2005).

Loss of empathy represents a critical and often early feature, associated with degeneration of the anterior insula and limbic structures, leading to impaired emotional resonance and social awareness (Rankin et al., 2006).

1.2 Executive Dysfunction and Cognitive Profile

Executive dysfunction in bvFTD reflects impairment in frontal-subcortical circuits and manifests as deficits in planning, cognitive flexibility, response inhibition, and abstract reasoning (Perry & Hodges, 2000). Unlike Alzheimer disease, episodic memory may be relatively preserved in early stages, although subtle deficits in retrieval and organization may be present (Hornberger et al., 2008).

Importantly, traditional cognitive screening tools such as the Mini-Mental State Examination may underestimate impairment in bvFTD due to their limited sensitivity to executive dysfunction and social cognition deficits (Kipps et al., 2007).

1.3 Neuroanatomical and Network Correlates

The neuroanatomical substrate of bvFTD is centered on the salience network, which integrates emotional and cognitive information to guide behaviour (Seeley et al., 2008). Key nodes include:

- Anterior insula
- Anterior cingulate cortex
- Orbitofrontal cortex
- Ventromedial prefrontal cortex

Degeneration within this network disrupts the ability to evaluate emotional salience and regulate behaviour accordingly. Functional imaging studies demonstrate reduced connectivity within this network, correlating with behavioural severity (Zhou et al., 2012).

1.4 Pathological and Genetic Associations

bvFTD is associated with multiple underlying pathologies, most commonly FTLD-TDP and FTLD-tau (Mackenzie et al., 2010). Genetic mutations, particularly in C9orf72, MAPT, and GRN, are frequently observed and contribute to phenotypic variability (Rohrer et al., 2015).

C9orf72 expansions are often associated with prominent psychiatric features, including psychosis and behavioural dysregulation, highlighting the overlap between neurodegenerative and psychiatric disorders (Snowden et al., 2012).

1.5 Clinical Heterogeneity and Diagnostic Challenges

The heterogeneity of bvFTD poses significant diagnostic challenges, particularly in early stages when symptoms may mimic psychiatric conditions such as major depressive disorder, bipolar disorder, or personality disorders (Woolley et al., 2011). Misdiagnosis is common and contributes to delays in appropriate management.

Table 3. Core behavioural domains and neuroanatomical correlates in bvFTD

Behavioural Domain	Clinical Features	Neuroanatomical Correlates
Disinhibition	Impulsivity, socially inappropriate behaviour	Orbitofrontal cortex
Apathy	Reduced motivation, inertia	Anterior cingulate cortex
Loss of empathy	Emotional blunting, social insensitivity	Anterior insula
Compulsivity	Repetitive behaviours, rituals	Fronto-striatal circuits
Hyperorality	Dietary changes, overeating	Orbitofrontal-hypothalamic pathways
Executive dysfunction	Poor planning, cognitive rigidity	Dorsolateral prefrontal cortex

Source: Rascovsky et al. (2011); Seeley et al. (2008); Rosen et al. (2005)

2 Primary Progressive Aphasia: Language Network Degeneration and Variant-Specific Profiles

Primary progressive aphasia represents the language-dominant spectrum of FTLD and is defined by progressive impairment in language with relative preservation of other cognitive domains in early stages (Gorno-Tempini et al., 2011). The classification into three variants reflects distinct patterns of network degeneration within the language system.

2.1 Nonfluent/Agrammatic Variant (nfvPPA): Motor Speech and Syntax Network Degeneration

The nonfluent/agrammatic variant is characterized by impaired speech production and grammatical processing, reflecting degeneration of frontal language networks (Gorno-Tempini et al., 2011).

Clinical Features

- Effortful, halting speech
- Agrammatism
- Apraxia of speech
- Impaired comprehension of complex syntax

These deficits reflect disruption of neural circuits involved in motor planning and syntactic processing (Thompson et al., 2012).

Neuroanatomical Correlates

Atrophy is localized to:

- Left inferior frontal gyrus (Broca's area)
- Anterior insula
- Premotor cortex

These regions are critical for speech production and grammatical processing (Josephs et al., 2012).

Pathological Associations

nfvPPA is most commonly associated with FTLD-tau pathology, particularly corticobasal degeneration and progressive supranuclear palsy (Grossman, 2010).

2.2 Semantic Variant (svPPA / Semantic Dementia): Conceptual Knowledge Network Degeneration
Semantic dementia is characterized by progressive loss of semantic knowledge, affecting both language and conceptual understanding (Hodges & Patterson, 2007).

Clinical Features
- Severe anomia
- Impaired word comprehension
- Fluent but semantically empty speech
- Loss of object and person recognition

The impairment extends beyond language to encompass multimodal semantic memory, reflecting degeneration of conceptual knowledge systems.

Neuroanatomical Correlates
Degeneration predominantly affects:
- Anterior temporal lobes (left > right)

These regions function as a hub for semantic memory, integrating information across modalities (Patterson et al., 2007).

Right-sided involvement is associated with behavioural changes, including loss of empathy and social dysfunction, further illustrating overlap with bvFTD (Snowden et al., 2001).

Pathological Associations
Semantic dementia is strongly associated with FTLD-TDP type C pathology (Mackenzie et al., 2011).

2.3 Logopenic Variant (lvPPA): Phonological Network Disruption
The logopenic variant is characterized by impaired word retrieval and repetition, reflecting dysfunction of phonological processing networks (Gorno-Tempini et al., 2011).

Clinical Features
- Word-finding pauses
- Impaired sentence repetition
- Phonological errors
- Preserved grammar and articulation

Neuroanatomical Correlates
Atrophy involves:
- Left temporoparietal junction

This region supports phonological working memory and language integration (Rohrer et al., 2010).

Pathological Associations
Unlike other PPA variants, lvPPA is most commonly associated with Alzheimer disease pathology, highlighting the overlap between FTLD and Alzheimer spectrum disorders (Mesulam et al., 2008).

Table 4. Clinical, anatomical, and pathological features of PPA variants

Variant	Core Features	Neuroanatomical	Pathology
nfvPPA	Agrammatism, apraxia of speech	Left frontal operculum, insula	FTLD-tau
svPPA	Loss of semantic knowledge	Anterior temporal lobes	FTLD-TDP
lvPPA	Word-finding pauses, repetition deficits	Temporoparietal junction	Alzheimer pathology

Source: Gorno-Tempini et al. (2011); Mackenzie et al. (2011)

Behavioural Changes: Neuropsychiatric and Network-Level Mechanisms

Behavioural disturbances in FTLD reflect disruption of neural systems governing social cognition, reward processing, and emotional regulation. These changes are not merely secondary symptoms but represent core manifestations of network degeneration (Seeley et al., 2008).

1 Social Cognition and Theory of Mind
FTLD patients exhibit profound impairments in theory of mind and social cognition, including difficulty interpreting others' emotions and intentions (Rankin et al., 2006). These deficits are linked to degeneration of the anterior insula and medial prefrontal cortex.

2 Reward Processing and Eating Behaviour
Alterations in reward circuitry lead to hyperphagia, preference for sweet foods, and compulsive eating behaviours (Piguet et al., 2011). These changes are associated with orbitofrontal and hypothalamic dysfunction.

3 Compulsivity and Behavioural Rigidity
Repetitive behaviours and compulsions reflect dysfunction of fronto-striatal circuits and may resemble obsessive-compulsive disorder, although they are typically less anxiety-driven (Snowden et al., 2001).

4 Psychiatric Overlap and Misdiagnosis
Early FTLD frequently mimics psychiatric disorders, including depression, bipolar disorder, and schizophrenia, leading to diagnostic delays (Woolley et al., 2011). This overlap underscores the importance of integrating neurological and psychiatric evaluation.

Additional Presentations: Overlap Syndromes and Atypical Phenotypes in FTLD

Frontotemporal lobar degeneration extends beyond classical behavioural and language syndromes to include a spectrum of overlapping neurological conditions. These presentations reflect shared molecular mechanisms and network-level degeneration affecting motor, subcortical, and limbic systems (Bang et al., 2015; Irwin et al., 2015).

1 FTLD with Motor Neurone Disease (FTLD-ALS Spectrum)
The overlap between FTLD and amyotrophic lateral sclerosis (ALS) represents one of the most significant clinicopathological intersections in neurodegenerative disease. Approximately 10–15% of patients with FTLD develop motor neurone disease, while up to 50% of ALS patients demonstrate cognitive or behavioural impairment consistent with FTLD (Lomen-Hoerth et al., 2002; Phukan et al., 2007).

This overlap is strongly associated with TDP-43 pathology, particularly in the context of C9orf72 hexanucleotide repeat expansions, which represent the most common genetic cause of the FTLD-ALS spectrum (DeJesus-Hernandez et al., 2011; Renton et al., 2011).

Clinically, FTLD-ALS may present with:
- Behavioural changes preceding motor symptoms
- Concurrent cognitive and motor dysfunction
- Progressive weakness, fasciculations, and bulbar symptoms

The presence of ALS significantly worsens prognosis and accelerates disease progression (Olney et al., 2005).

2 Parkinsonian Syndromes Associated with FTLD
FTLD frequently overlaps with atypical Parkinsonian disorders, particularly:
- Progressive supranuclear palsy (PSP)
- Corticobasal syndrome (CBS)

These syndromes are typically associated with FTLD-tau pathology and may present with motor symptoms preceding or following cognitive impairment (Dickson et al., 2011).

Progressive Supranuclear Palsy (PSP)
Characterized by:
- Vertical gaze palsy
- Axial rigidity
- Postural instability
- Executive dysfunction

PSP reflects degeneration of subcortical and brainstem structures, including the midbrain and basal ganglia (Höglinger et al., 2017).

Corticobasal Syndrome (CBS)
Features include:
- Asymmetric rigidity and dystonia
- Limb apraxia
- Alien limb phenomenon
- Cortical sensory deficits

CBS is associated with widespread cortical and subcortical degeneration and demonstrates significant clinicopathological heterogeneity (Armstrong et al., 2013).

3 Right Temporal Variant FTLD
Right temporal lobe degeneration produces a distinct clinical phenotype characterized by:
- Loss of empathy
- Emotional blunting
- Prosopagnosia
- Behavioural rigidity

This variant highlights the role of the right anterior temporal lobe in social and emotional processing and often overlaps clinically with bvFTD (Snowden et al., 2001; Chan et al., 2009).

4 Mixed and Atypical Pathologies
Recent neuropathological studies emphasize the frequent coexistence of multiple proteinopathies within the same patient, including combinations of FTLD-TDP, tau, amyloid-β, and α-synuclein (Negro et al., 2026; Robinson et al., 2018).

These mixed pathologies contribute to:
- Atypical clinical presentations
- Diagnostic uncertainty
- Variability in disease progression

Importantly, such findings reinforce that clinical phenotype alone is insufficient to determine underlying pathology, underscoring the need for biomarker-based approaches.

Physical Examination: Neurological and Behavioural Assessment

Physical examination in FTLD extends beyond standard neurological assessment to include detailed evaluation of behaviour, executive function, and social cognition. Findings vary depending on the clinical subtype and disease stage.

1 General Neurological Findings
Early in the disease course, neurological examination may be relatively normal, particularly in bvFTD. However, as disease progresses, findings may include:
- Frontal release signs (grasp reflex, palmomental reflex)
- Primitive reflexes
- Motor abnormalities

These signs reflect frontal lobe dysfunction and disinhibition of primitive motor pathways (Perry & Hodges, 2000).

2 Motor System Examination
Motor findings are particularly relevant in overlap syndromes:
- Upper and lower motor neurone signs (FTLD-ALS)
- Rigidity and bradykinesia (PSP, CBS)
- Apraxia and dystonia (CBS)

Bulbar dysfunction, including dysarthria and dysphagia, may occur in advanced stages or in association with ALS (Phukan et al., 2007).

3 Behavioural and Cognitive Bedside Assessment
Bedside evaluation should include:
- Assessment of social appropriateness
- Emotional responsiveness
- Insight and judgement
- Language function

Loss of insight (anosognosia) is a hallmark feature of bvFTD and contributes significantly to caregiver burden (Hornberger et al., 2012).

Differential Diagnosis: Analytical Framework and Diagnostic Pitfalls

Differentiating FTLD from other neurodegenerative and psychiatric disorders remains a major clinical challenge due to overlapping symptoms and heterogeneous presentations.

1 Alzheimer Disease
Alzheimer disease is the most common differential diagnosis, particularly in early stages. Key distinguishing features include:
- Prominent episodic memory impairment in Alzheimer disease
- Early behavioural or language dysfunction in FTLD

However, overlap occurs, particularly in logopenic PPA, which is often associated with Alzheimer pathology (Mesulam et al., 2008).

2 Psychiatric Disorders
FTLD is frequently misdiagnosed as a primary psychiatric disorder, especially in younger patients. Common misdiagnoses include:
- Major depressive disorder
- Bipolar disorder
- Schizophrenia

Features suggesting FTLD rather than psychiatric illness include:
- Progressive course
- Loss of empathy
- Executive dysfunction
- Neurological signs

(Woolley et al., 2011)

3 Lewy Body Dementia and Parkinsonian Disorders
Differentiation from Lewy body dementia and Parkinson disease dementia is based on:
- Presence of hallucinations and REM sleep behaviour disorder (Lewy body dementia)
- Parkinsonian features preceding cognitive decline

(McKeith et al., 2017)

4 Vascular Dementia
Vascular dementia may mimic FTLD, particularly in cases with frontal-subcortical involvement. Neuroimaging is critical for differentiation (O'Brien & Thomas, 2015).

Table 5. Differential diagnosis of FTLD

Disorder	Key Features	Distinguishing Points
Alzheimer disease	Memory impairment	Early episodic memory loss
Psychiatric disorders	Mood/behavioural changes	Non-progressive, preserved cognition
Lewy body dementia	Hallucinations, Parkinsonism	Fluctuating cognition
Vascular dementia	Stepwise decline	Imaging evidence of vascular lesions

Source: Woolley et al. (2011); McKeith et al. (2017); Mesulam et al. (2008)

Laboratory and EEG Studies

Laboratory investigations in FTLD primarily serve to exclude reversible causes of cognitive impairment rather than to confirm diagnosis.

1 Laboratory Testing
Routine evaluation includes:
- Thyroid function tests
- Vitamin B12 levels
- Metabolic panel

Emerging biomarkers include:
- Neurofilament light chain (NfL)
- Progranulin levels

Elevated NfL levels have been associated with disease severity and progression in FTLD (Meeter et al., 2016).

2 EEG Findings
Electroencephalography is typically normal or shows nonspecific slowing in FTLD, contrasting with Alzheimer disease, where more pronounced abnormalities may be observed (Bonanni et al., 2008).

Language and Neuropsychological Testing: Domain-Specific Assessment

Neuropsychological evaluation is central to the diagnosis and characterization of FTLD, particularly in distinguishing between subtypes and differentiating from other dementias.

1 **Executive Function Assessment**
Tests include:
- Wisconsin Card Sorting Test
- Stroop Test
- Trail Making Test

These assessments reveal deficits in cognitive flexibility, inhibition, and planning, reflecting frontal lobe dysfunction (Perry & Hodges, 2000).

2 Language Assessment
Language testing is critical in PPA and includes:
- Naming tests (e.g., Boston Naming Test)
- Repetition tasks
- Comprehension assessments

Each PPA variant demonstrates a distinct profile, aiding in classification (Gorno-Tempini et al., 2011).

3 Social Cognition Testing
Assessment of social cognition includes:
- Theory of mind tasks
- Emotion recognition tests

These are particularly relevant in bvFTD and may detect deficits not captured by traditional cognitive tests (Rankin et al., 2006).

Table 6. Neuropsychological profiles across FTLD subtypes

Domain	bvFTD	nfvPPA	svPPA	lvPPA
Executive function	Severely impaired	Mild	Mild	Moderate
Language fluency	Reduced	Nonfluent	Fluent	Logopenic
Semantic knowledge	Mild	Preserved	Severely impaired	Mild
Memory	Partially preserved	Preserved	Preserved early	Impaired

Source: Gorno-Tempini et al. (2011); Perry & Hodges (2000)

Management: Evidence-Based Strategies and Multidimensional Care in FTLD

Management of frontotemporal lobar degeneration (FTLD) remains primarily symptomatic, reflecting the current absence of approved disease-modifying therapies. However, advances in understanding the neurobiology of FTLD have led to more targeted approaches addressing behavioural dysregulation, caregiver burden, and functional decline. Importantly, management must be multidisciplinary, incorporating pharmacologic, behavioural, and supportive interventions tailored to the dominant clinical phenotype and disease stage (Boxer & Boeve, 2007; Finger, 2016).

A key principle in FTLD management is that behavioural symptoms, not cognitive deficits, are often the primary drivers of disability and caregiver distress, particularly in behavioural variant FTD. Therefore, treatment strategies prioritize modulation of neuropsychiatric symptoms and environmental adaptation rather than cognitive enhancement (Bang et al., 2015; Olney et al., 2017).

1 Pharmacologic Management
Pharmacologic therapy in FTLD is largely extrapolated from neuropsychiatric and dementia literature, with limited randomized controlled trial evidence. Importantly, medication responses are variable, and inappropriate pharmacologic choices, particularly cholinergic agents, may exacerbate symptoms.

Core pharmacologic approaches include:
- Selective serotonin reuptake inhibitors (SSRIs)
  - Reduce disinhibition, compulsivity, irritability
  - May improve eating behaviours and emotional regulation
  - Common agents: sertraline, citalopram, fluoxetine
- Trazodone
  - Beneficial for agitation, irritability, and sleep disturbance
  - Evidence suggests improvement in behavioural symptoms
- Atypical antipsychotics (use with caution)
  - Indicated for severe agitation, aggression, or psychosis
  - Increased risk of cerebrovascular events and mortality
  - Agents: quetiapine, risperidone
- Stimulants (selected cases)
  - May improve apathy and executive dysfunction
  - Limited evidence; requires careful monitoring

- Avoidance of cholinesterase inhibitors and memantine
  - Generally ineffective in FTLD
  - May worsen behavioural symptoms in some patients

(Huey et al., 2006; Boxer & Boeve, 2007; Finger, 2016)

2 Non-Pharmacologic and Behavioural Interventions

Non-pharmacologic strategies represent the cornerstone of FTLD management, particularly given the limited efficacy of pharmacologic treatments. These interventions target environmental modification, behavioural reinforcement, and caregiver support.

Key interventions include:

- Structured daily routines
  - Reduce behavioural variability and anxiety
  - Enhance predictability and functional independence
- Behavioural modification strategies
  - Reinforcement of appropriate behaviours
  - Minimization of triggers for disinhibition or agitation
- Speech and language therapy (PPA variants)
  - Focus on compensatory communication strategies
  - Use of augmentative communication tools
- Occupational therapy
  - Adaptation of activities of daily living
  - Environmental safety modifications
- Caregiver education and support programs
  - Essential for reducing caregiver burden
  - Improve disease understanding and coping strategies

(O'Connor et al., 2016; Bang et al., 2015)

3 Management of Specific Clinical Domains

Given the heterogeneity of FTLD, symptom-targeted management is essential.

Behavioural symptoms

- SSRIs and trazodone as first-line agents
- Environmental modification to reduce triggers

Apathy

- Structured engagement strategies
- Consider stimulant therapy in selected patients

Language impairment (PPA)

- Speech therapy and communication aids
- Early intervention to preserve function

Motor symptoms (overlap syndromes)

- Parkinsonian features → limited response to dopaminergic therapy
- ALS features → multidisciplinary motor neurone disease care

4 Emergency and Acute Clinical Considerations in FTLD

Although FTLD is typically a chronic neurodegenerative condition, patients may present with acute or crisis situations that require urgent evaluation and intervention. These scenarios are often behavioural rather than neurological emergencies but carry significant risk to the patient and others.

Acute presentations frequently arise from severe disinhibition, aggression, impulsivity, or impaired judgement, reflecting frontal lobe dysfunction. Additionally, overlap with motor neurone disease may lead to acute respiratory or bulbar complications in advanced stages (Olney et al., 2005; Phukan et al., 2007).

Common emergency scenarios include:

- Severe behavioural dyscontrol
  - Aggression, violence, or socially dangerous behaviour
  - Immediate need for environmental control and pharmacologic sedation
- Psychiatric crises
  - Acute psychosis or severe agitation (especially in C9orf72-related disease)
  - May require short-term antipsychotic use
- Wandering and safety risks
  - Impaired judgement leading to hazardous situations
  - Requires supervision and environmental safeguards
- Nutritional complications
  - Hyperphagia or unsafe eating behaviours
  - Risk of aspiration or metabolic complications
- Bulbar or respiratory compromise (FTLD-ALS)
  - Dysphagia, aspiration pneumonia
  - Respiratory insufficiency requiring urgent support

Acute management principles:

- Ensure patient and caregiver safety first
- Use low-dose, short-term pharmacologic interventions when necessary
- Avoid over-sedation and polypharmacy
- Address underlying triggers (infection, environmental stressors)
- Consider hospitalization in severe cases

Future Directions: Toward Molecularly Targeted and Biomarker-Driven Therapies

The future of FTLD research is increasingly focused on precision medicine approaches, driven by advances in molecular biology, genetics, and biomarker development. A major paradigm shift is underway, from syndrome-based diagnosis to mechanism-based classification and treatment (Rohrer et al., 2020; Meeter et al., 2017).

Emerging therapeutic strategies aim to target the underlying molecular drivers of disease, including protein aggregation, RNA dysregulation, and neuroinflammation. These approaches are particularly promising in genetically defined forms of FTLD, where disease mechanisms are more clearly delineated.

Key future directions include:

1. Gene-targeted therapies

- Antisense oligonucleotides (ASOs) targeting C9orf72 repeat expansions
- Progranulin replacement strategies in GRN mutation carriers
- MAPT-targeted approaches for tauopathies

2. Protein-targeted therapies

- Tau aggregation inhibitors and anti-tau antibodies
- TDP-43 modulation strategies (currently experimental)

3. Biomarker development

- Fluid biomarkers (neurofilament light chain, progranulin levels)
- Imaging biomarkers (tau PET, advanced MRI techniques)
- Blood-based diagnostics for early detection

4. Network-based interventions

- Neuromodulation approaches targeting affected networks
- Non-invasive brain stimulation techniques

5. Clinical trial innovation

- Stratification based on genetic and molecular profiles
- Adaptive trial designs
- Earlier intervention in pre-symptomatic individuals

6. Digital and AI-based diagnostics

- Machine learning models for early detection
- Speech and behavioural analysis tools
- Wearable technologies for monitoring disease progression

Conclusion

Frontotemporal lobar degeneration (FTLD) represents one of the most complex and heterogeneous groups of neurodegenerative disorders, characterized by a striking dissociation between clinical phenotype, molecular pathology, and genetic architecture. The contemporary understanding of FTLD has evolved substantially from a purely syndromic framework toward an integrated, multidimensional model incorporating network degeneration, proteinopathy, and genetic drivers. This paradigm shift has clarified that clinical syndromes such as behavioural variant frontotemporal dementia and primary progressive aphasia are not discrete diseases but rather expressions of selective vulnerability within large-scale neural systems (Bang et al., 2015; Seeley et al., 2008).

A major challenge in FTLD remains the clinicopathological heterogeneity, whereby identical clinical presentations may arise from distinct molecular substrates, including TDP-43, tau, and FUS proteinopathies. This heterogeneity complicates diagnostic accuracy and limits the effectiveness of symptom-based classification systems. Increasing evidence suggests that anatomical distribution and network involvement may be more predictive of phenotype than molecular subtype, reinforcing the need for multimodal diagnostic approaches integrating imaging, genetics, and fluid biomarkers (Irwin et al., 2015; Negro et al., 2026).

Advances in neuroimaging have enabled more precise characterization of disease-specific atrophy patterns and network dysfunction, while molecular and genetic discoveries, particularly involving C9orf72, MAPT, and GRN, have provided critical insights into disease mechanisms. Nevertheless, despite these advances, therapeutic options remain limited, and current management strategies are largely symptomatic, focusing on behavioural control, supportive care, and caregiver interventions (Finger, 2016; Bartoshyk et al., 2025).

The future of FTLD research lies in the transition toward precision medicine, with an emphasis on early detection, molecular stratification, and targeted therapies. Emerging approaches, including antisense oligonucleotides, progranulin replacement, and tau-directed therapies, offer promising avenues for disease modification, particularly in genetically defined subgroups (Rohrer et al., 2020; Tartaglia et al., 2023). In parallel, advances in biomarker development and artificial intelligence-driven diagnostics are expected to enhance early diagnosis and improve clinical trial design (Dattola et al., 2025).

In summary, FTLD should be conceptualized as a biologically diverse, network-based neurodegenerative spectrum, requiring integrative diagnostic frameworks and individualized therapeutic strategies. Continued progress will depend on bridging the gap between molecular mechanisms and clinical expression, ultimately enabling disease-modifying interventions and improved patient outcomes

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Briefing: Sudden Death Among Young Anaesthesiologists, Evidence from China and Emerging Findings from Libya

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Sudden deaths are always a critical topic that attracts the public, physicians, and health professionals' attention. However, recently Anaesthesiologists in Libya have experienced increased sudden deaths, which are increasing dramatically for unknown reasons, and there is no clinical report about this exceptional phenomenon.

Libyan anaesthesiologists in particular have become a concerning topic on social media, social issues, and contemporary health problems.

According to media reports, 'The Libya Observer' suggests, according to Tariq Shuhaima, Deputy Head of the General Syndicate of Doctors in July 2025, that 14 Libyan doctors died of sudden cardiac arrest within just one month, the majority of whom were Anaesthesiologists (Tables 2, 3).

Sudden death among young physicians, particularly anaesthesiologists, has emerged as a concerning occupational health issue. It is typically defined as an unexpected natural death occurring within a short time frame, often without prior symptoms, unforeseen, and unexplained. In both China and, more recently, Libya, reports suggest an increased incidence among young anaesthesiology professionals (1, 2).

In China, analyses of national databases, media reports, and official records show a clear rise in physicians' workloads in recent years. Deaths related to overwork have become an increasing concern, posing challenges for both medical education and hospital management. In 2017, 34 physician deaths were reported, with the highest risk observed among male anaesthesiologists aged 30–45 working in first-tier cities between 2013 and 2014.

Female physicians may face additional pressures beyond clinical duties, including household responsibilities and caregiving for children and elderly relatives. When combined with heavy workloads, this may increase fatigue and vulnerability to overwork-related harm.

Despite this, deaths among male physicians were fifteen times higher than among females (Table 1, 3). This may reflect greater financial, social, and familial pressures in men, particularly those aged 34–48, alongside poorer health behaviours such as smoking, excessive alcohol intake, and high consumption of carbonated drinks (1,2).

Overwork death was the highest among anaesthesiologists, which was also consistent with the study of Zhang HF et al. Physicians in this group might undergo more work stress.

Data from a United States database indicated that causes of death were identified in 94.6% of anaesthesiologists, with heart disease, cancer, and other circulatory system disorders being the most common(3).

It has been argued by Huang J, Lee J. 2017, that young anaesthesiologists' mortality from drug-related causes, the availability of substances in the anaesthesia field, the ease of access, addiction, and abuse, all remain taboo and a cultural stigma, hard to discuss, and might be the potential contributors to those deaths (3).

Chinese medical staff still face the risk of harm at work. These heavy physical and psychological burdens potentially contribute to the increasing overwork death of physicians in China (2). The imbalance has forced many medical staff to work overtime, and numerous cit-

Established evidence on both continents (China and Libya):

Table 1: summarises evidence from China

Evidence from China	Early studies in China show that sudden death disproportionately affects anaesthesiologists, mainly young men around 35–40 years old.
Cardiovascular Events (Primary Cause)	Most deaths are cardiac, especially fatal arrhythmias and sudden arrest, often linked to undiagnosed heart conditions.
Occupational Overload and Burnout	Long hours, night shifts, and heavy workloads contribute significantly, with fatigue and sleep loss raising cardiovascular risk.
Psychosocial Stressors	Patient expectations, workplace violence, medico-legal risks, and publication pressure all add significant stress.
Systemic Healthcare Factors	Overcrowded hospitals and staff shortages increase workload. Young anaesthesiologists face heavy frontline duties early in their careers.
Lifestyle and Health Neglect	Poor health habits include irregular meals, smoking, and lack of exercise.

Table 2: presents emerging Libyan observations

Emerging Evidence from Libya	Recent multicentre data (2022) show a similar pattern of sudden deaths among anaesthesiologists in Libya.
Multifactorial Risk Profile	High rates of obesity (70%), smoking, and hypertension. Marked stress from economic hardship, isolation, and family conflict.
Cardiovascular Abnormalities	About 30% had unexplained cardiac abnormalities despite normal tests. Chest pain was a common symptom.
Post-COVID-19 Associations	Some had prior COVID-19 infection or vaccination, possibly linked to myocarditis or arrhythmias. This is an emerging hypothesis needing further study.
Occupational Stress and Burnout	Similar to China, prolonged working hours and high-responsibility roles were central contributors.

Table 3: Comparative Analysis (China vs Libya)

Cause	China	Libya
Primary mechanism	Cardiac arrhythmia	Cardiac anomalies (often unexplained)
Workload	Extremely high	High
Psychosocial stress	High (violence, academic pressure)	High (economic + social stress)
Lifestyle risk	Present	Strongly evident
COVID-related factors	Not prominent (earlier data)	Emerging association

Across both settings, sudden death appears multifactorial, with a crucial conduit involving cardiovascular instability triggered by:

- Chronic occupational stress
- Sleep deprivation and insomnia
- Metabolic and lifestyle risk factors

The Libyan data introduce a potential post-COVID cardiac element, expanding the etiological framework beyond traditional occupational and cardiovascular explanations. Thus, the inferences would emphasize a need for a routine cardiovascular screening for anaesthesiologists, setting up regulations, legislation, and limitations on working hours and night shifts, providing support for mental health and physical burnout prevention, and doing more research on post-viral cardiac risks (e.g., COVID-19).

After all, sudden death among young anaesthesiologists represents an occupational hazard driven by the interaction of cardiovascular vulnerability and systemic work-related stressors. While Chinese data established the phenomenon, emerging Libyan evidence reinforces its global relevance and introduces new potential mechanisms, particularly post-infectious cardiac effects.

A survey conducted by Zhang and colleagues claimed that anaesthesiologists in China suffer from work overload and that sudden death is on the rise. He stated that in the period between 2013 and 2014, more than 10 anaesthesiologists had cardiac arrest, which was the contributing factor to sudden death due to cardiopulmonary arrest (2). However, the pathophysiological relationship is lacking and unclear. He argued that any work week longer than 70 hours equates to an increased incidence of sudden death. Additionally, the post-mortem autopsy is not available, which raises other plausible explanations for the sudden deaths (2).

This multicentre case-control study of 88 Libyan anaesthesiologists in 2025 found that sudden death risk is linked to combined occupational, metabolic, and psychosocial factors. The cohort (mean age 39) showed high rates of overweight (36%) and obesity (35%), alongside significant smoking exposure and varied employment duration. Key stressors included financial hardship, family conflict, and isolation. Clinically, chest pain, hypertension, and strong family disease history were prominent risk indicators. Laboratory results showed higher triglycerides in males and higher HDL and D-dimer in females. Although most cardiac tests were normal, 29.5% had unexplained anomalies, frequently associated with prior COVID-19 infection and mixed vaccination status (4). Current Libyan data remain limited and largely observational.

This briefing is meant to look at this new phenomenon encountered among the young Libyan anaesthesiologists versus their Chinese colleagues. One of the main troubles in Libya for overworking is the low income of medical professionals, generally speaking, which contributes to the workloads for some doctors in the private sector and working more shifts without a break or rest, which would lead to chronic fatigue, anxiety, frustration, violence, and exhaustion. However, there are limitations to this, as there is no actual reporting or database to pull from, and it's difficult to determine the actual causation of the sudden death among young, fit, and well Libyan anaesthesiologists. Additionally, there isn't any actual reporting about each deceased anaesthesiologist's work hours. This briefing is meant to shed light and bring to attention the self-alert, self-awareness, and self-protection of anaesthesiologists' mental well-being and functionality within safe, healthy work limits (1).

Physician burnout is a global problem and mostly affects anaesthesiologists, and their loss is just the tip of the iceberg of the medical communities (2).

Finally, working under tremendous pressure, long shift hours would intensify burnout, especially if the environment is not helping or encouraging, which would contribute to the whole situation for young Libyan anaesthesiologists. As the literature has shown, overwork death among Chinese physicians is already established, and the government has promulgated a series of laws and regulations to improve working conditions and improve the hierarchy of the medical system (3).

Young anaesthesiologists normally grow into independent specialists in the operative care, engaging in long multiple-night shifts (3).

The mechanism of sudden deaths among Libyan anaesthesiologists remains unclear and is an emerging and concerning issue.

The whole situation is disturbing and mandates the attention of the higher Libyan authorities and the policy makers to look into why this has happened in the first place, and they should employ and invest some efforts to reduce such a tragic mortality loss.

They should guarantee the legitimate rights and interests of doctors, and the system should establish a reasonable working hour. Also, those who lost their life should be investigated further to find the root cause of the problem. Moreover, doctors should look after their health, get enough sleep, exercise, and lead a healthy lifestyle by example for their patients and communities. However, doctors' loss and reduced quality of work will worsen if appropriate measures are not taken into account.

This briefing aims to help gain an understanding of the scale of the problem and find ways of preventing such tragic losses from occurring, hopefully in the future. It also calls for systemic reforms, including reduced working hours, better health monitoring, and institutional support, to protect physicians' well-being and reduce preventable mortality within the medical workforce, to improve productivity and satisfaction.

To conclude, the cases of the Libyan anaesthesiologists who died suddenly are an alarming and unprecedented problem.

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Impact of natural and man-made disasters on people living with diabetes mellitus: a narrative review

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Abstract

Objective: Assess the direct impact of natural and man-made disasters on people living with diabetes (PLWD), emphasizing disrupted medical care access and adverse health outcomes.

Design:
Narrative review

Participants: People living with diabetes exposed to natural or man-made disasters.

Results: Natural and man-made disasters substantially disrupt medical systems, key services, and socioeconomic stability. As a result, PLWD are disproportionately affected because of reliance on continuous care, medications, and stable living conditions. Disruptions within healthcare infrastructure, medication access, and food security contribute to worsening glycaemic control, increased complications, and higher emergency healthcare utilization. Furthermore, socioeconomic inequalities and health disparities worsen these outcomes.

Conclusion: This evidence shows that people living with diabetes are highly vulnerable to the impacts of natural or manmade disasters. Therefore, strengthening disaster preparedness, enhancing the durability of the healthcare system, and implementing targeted interventions are vital to mitigate adverse health outcomes.

Key words:
Natural and man made disasters, people living with diabetes, access to medical care, adverse health outcomes

Introduction

The rising frequency and severity of natural disasters and the global increase in diabetes have made people living with diabetes more vulnerable (1)(2). Natural disasters result from the interplay of hazard exposure, population vulnerability, and limited adaptive capacity (3). In recent decades, climate-related events such as hurricanes, floods, bushfires, earthquakes, and heatwaves have intensified, disproportionately impacting low-income countries and Small Island Developing States, particularly in the Caribbean (4).

Many small islands cause very little climate pollution but face big climate risks. The same situation can be applied in some developing countries with low and very low income. This is because they are isolated, have weak buildings, depend on tourism, and rely on food and medicine from other places (4)(5). Their problems get worse because many people there have diabetes (1). This makes people with diabetes more at risk when disasters happen.

This review examines how natural and man-made disasters affect people with diabetes in areas at risk. It focuses on problems with getting healthcare, social factors, health effects, and what we can learn from disasters around the world. It points out what keeps people from getting care, what makes health problems worse, and offers ideas to help prepare for and respond to disasters.

Methods

This review examines how disaster responses address diabetes care, synthesizes evidence from peer-reviewed studies, global health reports, and policy documents, and cites key sources, including the World Health Organization (WHO), International Diabetes Federation (IDF), United Nations agencies, World Meteorological Organization (WMO) and national disaster frameworks. I selected literature on diabetes care during disasters, health system resilience, medication access, and clinical outcomes among Patient Living with Diabetes. I included case studies of major disasters and conflicts to provide contextual and comparative insights.

Results

1. Impact of Disasters on Health Systems and Infrastructure

Natural disasters cause extensive economic and structural damage worldwide, amounting to hundreds of billions of US dollars annually (5). In the Caribbean and other low-income countries, this devastation acutely undermines fragile healthcare systems (5). Hospitals, supply chains, and staff are frequently damaged or overwhelmed, threatening healthcare delivery.

These vulnerabilities result in critical disruptions to healthcare: the destruction of clinics, loss of refrigeration for insulin storage, interruption of laboratory services, and breakdown of electronic medical records. Such systemic failures reduce the ability to maintain continuity of care for chronic diseases such as diabetes (6)(7). Furthermore, disasters such as pandemics compound these challenges by adding pressure to already weakened systems (8).

2. Barriers to Healthcare Access

During disasters, essential lifelines, including electricity, water supply, transportation, and communication often severely disrupted (9). These failures directly impair diabetes management by limiting access to insulin, oral medications, monitoring devices, and healthcare professionals (10).

Medication shortages are usual due to interrupted supply chains and damaged distribution infrastructure (11). Patients frequently lose access to their prescriptions and medical documentation, further complicating continuity of care (11). Healthcare facilities may also experience staffing shortages, reducing capacity to deliver acute anchronic care services (11).

Historical disasters, including Hurricane Katrina (12) and the Great East Japan Earthquake (13), demonstrate prolonged healthcare system disruption lasting weeks to months, with significant impacts on chronic disease management.

3. Health Disparities and Vulnerability

Disasters exacerbate existing health and social inequities. Individuals with lower socioeconomic status, limited healthcare access, or pre-existing comorbidities experience disproportionately worse outcomes (14).

Ethnic minorities and marginalized populations are often the most affected due to structural inequalities in housing, healthcare access, and insurance coverage (14). In disaster settings, these groups frequently experience delayed access to emergency care, medication shortages, and reduced post-disaster recovery support (14).

The cumulative effect of poverty, limited resources, and high disease burden intensifies vulnerability among PLWD in low-resource settings (14).

4. Clinical and Metabolic Outcomes in Patients Living with Diabetes mellitus

Imagine facing a natural or man-made disaster as someone living with diabetes, in such times, controlling blood sugar becomes much harder: studies show that disasters lead to spikes in HbA1c, blood pressure, and cholesterol, causing dangerous swings in glucose levels (10)(13)(15).

Several mechanisms contribute to poor metabolic outcomes:

- Disruption of medication regimens, particularly insulin
- Irregular access to food and water
- Psychological stress and trauma
- Reduced physical activity or increased exertion without adequate nutrition

These factors increase the risk of both acute and chronic complications. Emergency department utilization rises due to diabetic ketoacidosis (DKA), hyperosmolar hyperglycaemic state (HHS), hypoglycemia, infections, and cardiovascular complications.

5. Lessons from Major Disasters

5.1 Hurricane Katrina (United States) (16)

Hurricane Katrina exposed major weaknesses in the management of chronic diseases during disasters (16). Key challenges included insulin shortages, loss of medical records, and inadequate preparedness in shelters. Diabetes was often underestimated in emergency planning, leading to insufficient supplies and delayed treatment.

Post-disaster consequences included poor glycaemic control, increased complications, and elevated morbidity and mortality (17). Coordination among healthcare providers, pharmaceutical companies, and humanitarian organizations improved results but was initially fragmented (16).

Key lessons include the need for:

- Strong disaster preparedness planning
- Reliable medication supply chains
- Patient education on emergency self-management
- Integration of chronic disease management into disaster response systems

5.2 Puerto Rico (Hurricane Maria) (18)

A study of diabetic patients before, during, and after Hurricane Maria showed significant deterioration in outcomes (18). Mortality increased dramatically, while glycaemic control and lipid levels remained poorly managed (18). Healthcare costs also rose post-disaster.

The findings show the long-term impact of infrastructure collapse on chronic disease outcomes and highlight the significance of continuous care systems and emergency preparedness frameworks aligned with American Diabetes Association (10) and Centre of Disease Control guidelines (19).

5.3 Japan (Great East Japan Earthquake) (13)

The 2011 earthquake exposed vulnerabilities in healthcare infrastructure, especially electricity, water, transport, and communication. Hospitals faced prolonged outages disrupting records, lab testing, and nutrition.

In response, Japan developed structured disaster preparedness frameworks (13), including the “Manual for Disaster Diabetes Care” and specialized response systems such as Diabetes Medical Assistance Teams (DiaMAT). These systems improved coordination, training, and deployment of diabetes-focused emergency care teams.

5.4 Australia (Bushfires, Floods, Heatwaves) (20)(21)(22)

Australia has shown uneven levels of disaster preparedness and response. This led to the creation of a diabetes-focused disaster guide (booklet-emergency-guide-services-councils-not-for-profit.pdf). In 2015, an Expert Reference Group developed resources to support people with diabetes, communities, and relevant authorities in managing diabetes during emergencies. They stressed individual emergency care plans, tools to help self-management after disasters, and widespread community education, given the large number of people affected.

Following this, the guide was first released in 2015 and later revised in 2021 and 2025 to incorporate updated evidence and best practices. Its overall goal is to reduce illness and death among people with diabetes during disasters while also reducing pressure on healthcare services. These strategies are interconnected and should be incorporated into routine health and disaster management systems. Doing so would support a sustainable approach to minimizing indirect morbidity and mortality among people with NCDs in disaster settings.

A study conducted by Ryan et al (2016), in Queensland, Australia, involved interviews and a focus group with disaster service providers (22). It showed a clear link between disaster impacts on health infrastructure and worsening health outcomes for people with NCDs. Participants identified a range of mitigation measures across all phases of the disaster cycle, including expanding telemedicine, improving coordination with medical suppliers, strengthening infrastructure and urban planning, ensuring power to evacuation centres, prioritizing the evacuation of high-risk individuals, and strengthening data collection and inter-agency information sharing (22).

These findings show that disaster service providers are key to improving health system resilience and reducing NCD-related risks. Embedding these approaches into routine planning, policy, and monitoring systems can strengthen disaster preparedness and response, support global disaster risk reduction efforts, and better safeguard at-risk populations throughout all disaster phases (22).

In 2018, Ryan et al conducted a study in Queensland, Australia, applied a multi-stage Delphi approach involving individuals with NCDs, disaster responders, coordinators, and government officials to identify and prioritize risk reduction strategies (23). A total of 31 strategies were identified across 12 areas of public health infrastructure.

Among the top priorities identified were assuring consistent access to safe water, followed by improvements in communication, sanitation, workforce capacity, and the availability of medical supplies. Key recommendations included equipping water treatment facilities with backup power, establishing dedicated primary healthcare hubs after disasters, and simplifying processes for accessing medications. For emergency planners, Australia's disaster experiences point out the importance of multi-level preparedness strategies, including individual emergency plans, community education, and national coordination (23).

Key lessons include guaranteeing continuous access to insulin, medications, monitoring equipment, food, water, and power supply. Emergency services must be prepared to detect and manage hypo- and hyperglycaemic emergencies.

5.5 Pakistani experience (24)

Diabetes care in humanitarian crises in Pakistan, especially following the 2005 Kashmir earthquake and the 2022 floods, has been significantly compromised by challenging terrain and a fragile medical system. A review of 197 sources published between 2000 and 2022, including peer-reviewed studies and reports from humanitarian organizations, highlights a lack of preparedness to manage chronic conditions such as diabetes in both emergency and routine contexts. Major gaps identified include disruptions within healthcare delivery and insufficient availability of critical medications, such as insulin. Furthermore, international response efforts have predominantly prioritized acute and infectious diseases, mental health, and high-risk groups, frequently overlooking diabetes care. The study stresses the need for national disaster preparedness plans to clearly incorporate non-communicable disease management, particularly diabetes, to remedy these ongoing deficiencies.

5.6. Syria and Iraq experiences (25)

This review demonstrates that political and military conflicts in Iraq (post-2003) and Syria (post-2011) have profoundly disrupted diabetes care by undermining medical systems, damaging infrastructure, and perpetuating instability. Mass displacement and refugee influxes have additionally strained already limited resources in both origin and host settings (25). Diabetes management, particularly for type 1 diabetes, has been largely overlooked, with severe insulin shortages and restricted availability to essential medications in both camp and non-camp environments. The privileging of communicable diseases over chronic conditions has created substantial gaps in care. The findings stress the urgent need to incorporate diabetes management into disaster preparedness and health system planning (25).

5.7. Pacific Region experiences (26)

A disaster is a significant disruptive event that results in injury, loss of life, or property damage and necessitates additional resources. As the global prevalence of diabetes continues to rise alongside the increasing occurrence of both natural and human-made disasters, people living with diabetes are particularly vulnerable, especially in regions such as the Pacific, where disasters are frequent. Addressing these risks requires coordinated preparedness and response efforts involving individuals, healthcare systems, governments, and multiple sectors (26).

Disasters can profoundly disrupt diabetes management by restricting access to essential needs, including shelter, electricity, communication, nutritious food, clean water, medications, healthcare services, and medical records. Such disruptions heighten the risk of poor glycemic control, infections, acute and chronic complications, cardiovascular events, and mortality. High-risk groups include children, older adults, individuals with type 1 diabetes, pregnant women, and those with pre-existing complications or frailty (26).

Even short-term disasters may lead to long-term health consequences, including deterioration in cardiometabolic health and elevated cardiovascular risk. Therefore, proactive planning and collaboration among key stakeholders, such as healthcare providers, emergency responders, transportation systems, media, and policymakers, are critical to minimizing adverse outcomes and ensuring continuity of care (26).

Pacific island nations face direct and harsh threats from climate change. Higher temperatures, altered rainfall, rising sea levels, and intensified extreme weather are already affecting key sectors, putting communities, ecosystems, and infrastructure at risk (42).

Despite the availability of scientific climate data, translating this information into practical planning and decision-making can be challenging, leading to underuse or misapplication. This can contribute to ineffective policies, missed opportunities for adaptation, and poorly informed actions (43).

The South Pacific confronts an existential threat from climate change, as rising sea levels, intensifying storms, and environmental degradation undermine livelihoods, economies, and the long-term habitability of islands such as Tuvalu, Kiribati, and Fiji. To tackle this crisis, immediate regional and global action is necessary (43).

5.8 Global Conflict Settings

Conflicts such as the Ukraine war and Ethiopia's Tigray conflict lay bare the deep suffering war inflicts on people with diabetes. As medical systems collapse almost overnight, lives are endangered by sudden insulin shortages, interrupted dialysis, and heartbreaking increases in preventable deaths (27) (28)(29)(30).

In reaction to these challenges, humanitarian organizations such as the International Diabetes Federation (IDF), NGOs, and pharmaceutical companies intervened to restore partial access to insulin and key medications. Nevertheless, long-term obstacles continue due to ongoing displacement, infrastructure destruction, and insecurity.

6. System-Level Challenges in Disaster Response

Common systemic issues across disasters include (31):
- Communication failures
- Lack of backup electronic medical record systems
- Food and water shortages
- Medication and insulin stock depletion
- Limited shelter preparedness
- Insufficient training among healthcare staff

Utilities such as electricity and water are critical for maintaining diabetes care infrastructure. Their disruption affects laboratory services, insulin storage, and hospital nutrition systems.

7. Clinical Management Challenges in Disasters (32)

Acute Metabolic Emergencies
Disasters increase the incidence of (33):
- Hypoglycaemia
- Hyperglycaemia
- Diabetic ketoacidosis (DKA)
- Hyperosmolar hyperglycaemic state (HHS)

Management priorities include preventing dehydration, maintaining insulin therapy, and ensuring access to glucose monitoring. Mild hyperglycaemia may be tolerated temporarily, while severe cases require emergency treatment.

Medication Considerations (34)
- Insulin remains essential, especially in type 1 diabetes
- GLP-1 receptor agonists and DPP-4 inhibitors are r elatively safe in emergencies
- Sulfonylureas increase hypoglycaemia risk and require dose adjustment
- Metformin may be contraindicated in dehydration or acute illness
- SGLT2 inhibitors carry dehydration and infection risks in disaster settings

8. Complications and Comorbidities

Disasters also increase the risk of (33):
- Cardiovascular disease (acute coronary syndrome, heart failure, stress cardiomyopathy)
- Hypertension (“disaster hypertension”)
- Cerebrovascular disease (stroke)
- Acute kidney injury (including crush syndrome)
- Deep vein thrombosis due to immobility
- Infections due to poor hygiene and overcrowding

Psychological stress further worsens glycaemic control and increases cardiovascular risk.

9. Mental Health Impacts (35)

Disasters are associated with high rates of:
- Post-traumatic stress disorder (PTSD)
- Depression
- Anxiety disorders
- Substance use disorders

Patients Living with Diabetes are particularly vulnerable due to stress related to medication access, food insecurity, and fear of disease complications (35). Mental health disturbances directly worsen glycaemic control and reduce self-management capacity (35).

10. Disaster Preparedness and Response Strategies (36)

Effective diabetes disaster preparedness includes:
- Individual emergency kits with insulin, medications, glucose monitoring tools, and food supplies
- Medication stockpiling for at least 1–2 weeks
- Emergency medical identification and documentation
- Backup communication systems
- Patient education on sick-day rules
- Training of healthcare workers in disaster diabetes management

Healthcare systems should ensure:
- Continuity of insulin supply chains
- Backup power and water systems
- Mobile diabetes response teams e.g., Diabetes Mobile Action Teams (DiaMAT)
- Integrated chronic disease management in disaster planning
- Multidisciplinary collaboration among physicians, nurses, pharmacists, dietitians, and technicians

Discussion

People living with diabetes in many disaster-prone regions encounter compounded vulnerabilities due to high baseline disease prevalence, fragile medical systems, and socioeconomic inequalities (36). Disasters worsen these challenges by disrupting access to healthcare, medication supply, and metabolic stability.

To reduce the heightened risks facing people with diabetes during disasters, immediate investment in structured preparedness systems is imperative (36). Policymakers, healthcare providers, and stakeholders need to urgently address health disparities, strengthen infrastructure robustness, and fully integrate chronic disease care into disaster planning to reduce preventable morbidity and mortality.

11.1. Theoretical Framework

This study uses an integrated approach that explicitly connects the Social Ecological Model (SEM)(37) and the Stress Process Model. SEM examines how individuals communicate with their environment at multiple levels: individual, interpersonal, organizational, community, and policy. The Stress Process Model explores how stressors, resources, and coping mechanisms impact health outcomes. By uniting these models, the study clarifies how multiple levels, from health system disruptions and social determinants (such as income or housing) to individual biological and behavioural responses, shape diabetes outcomes for people living with diabetes (PLWD) during and after disasters (37).

The Social Ecological Model (SEM) claims that health outcomes are determined by active interactions throughout multiple levels of influence. These include individual, interpersonal, organizational, community, and policy domains (37). During natural or man-made disasters, each level contributes to interruptions in diabetes management. At the individual level, a patient with Diabetes mellitus may have diminished capacity for self-management. Causes include stress, displacement, or loss of medical supplies (38). At the interpersonal level, reduced caregiver and family support may limit adherence to medication and dietary regimens (38). At the organizational level, damage to health services infrastructure, pharmacy closures, and interruptions in routine clinical services constrain entry to essential diabetes care (38). At the community level, food insecurity, unsafe water, and transportation barriers hinder disease management (38). At the policy level, variability in disaster preparedness planning, emergency response coordination, and the durability of the healthcare system determines the continuity of chronic disease services (38). Collectively, these structural disruptions compromise the continuity of diabetes care and self-management.

The Stress Process Model (39) explains that exposure to major life stressors affects health via three key mechanisms: psychological, behavioural, and physiological pathways (40). In natural or man-made disasters, primary stressors are direct exposures, life-threatening events, displacement, and injury (41), while secondary stressors include loss of income, medication shortages, and healthcare disruptions. Psychologically, stress increases anxiety, depression, and trauma-related symptoms (42). Physiologically, neuroendocrine activation, particularly increased cortisol levels, leads to hyperglycemia and metabolic imbalance (39). Behaviourally, stress may reduce therapy adherence, disturb dietary intake, decrease activity, and disrupt sleep (39). Collectively, these mechanisms worsen glycaemic control and increase the risk of acute diabetes complications (39).

The combination of the Social Ecological Model and the Stress Process Model delivers a comprehensive explanatory framework in which disaster-related structural disruptions at multiple system levels interact with individual stress responses to produce adverse diabetes outcomes (39). Specifically, natural and man-made disasters disrupt medical service systems and community resources, which, in turn, generate cascading stressors that affect psychological well-being and physiological regulation (39). The severity of these effects is not uniform and is modified by contextual and individual-level protective factors, including socioeconomic status, health literacy, baseline disease control, access to insurance, and the presence of disaster preparedness plans (39).

Accordingly, this study (39) conceptualizes diabetes outcomes during disasters as the product of a multilevel causal pathway: environmental shocks disrupt health care systems and social supports, which in turn activate stress-mediated biological and behavioural responses. These responses ultimately worsen glycemic control, increase acute complications (e.g., diabetic ketoacidosis and hypoglycemia), raise hospitalization rates, and increase mortality risk. This system informs both the selection of study variables and the examination of system-level and individual-level determinants of diabetes outcomes in disaster-affected populations.

Conclusion

Natural and man-made disasters pose a major threat to diabetes management globally, particularly in vulnerable regions. Disruptions in medical care systems, medication supply chains, and necessary services significantly worsen clinical outcomes for patients living with diabetes.

Strengthening health system infrastructure, ensuring medication continuity, enhancing disaster preparedness, and confronting social determinants of health are critical strategies to reduce adverse outcomes. Integrated, multidisciplinary, and system-wide approaches are essential to boost resilience plus safeguard patients living with diabetes during future disasters.

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Sleeping Position, Deep Sleep, and Dementia Prevention: Clinical and Mechanistic Perspectives

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Abstract

Sleep has emerged as a central, modifiable determinant of neurodegenerative disease risk, particularly Alzheimer's disease (AD). Increasing evidence demonstrates that slow-wave sleep (SWS) plays a critical role in facilitating glymphatic clearance of neurotoxic proteins, including beta-amyloid and tau, which are central to AD pathophysiology. Disruption of sleep architecture, especially reduction in deep sleep, has been associated with increased amyloid burden, impaired cognitive function, and accelerated neurodegeneration. In parallel, emerging experimental and observational data suggest that sleeping position may influence glymphatic transport, with lateral positioning potentially enhancing cerebrospinal fluid (CSF) dynamics and waste clearance. However, human evidence remains limited and causality is not established. This review provides a clinically oriented synthesis of current evidence (2020–2026), integrating epidemiological, mechanistic, and translational perspectives on sleep, sleep position, and dementia prevention. While optimization of deep sleep represents a robust and evidence-based preventive strategy, sleep posture remains an evolving and promising adjunctive factor. Future research should focus on integrating sleep architecture modulation and positional interventions into comprehensive dementia prevention frameworks.

Key words: sleeping positiion, deep sleep, dementia

Introduction

Dementia represents a major global public health challenge, with prevalence projected to exceed 150 million cases by 2050, driven largely by population aging and increased longevity (Livingston et al., 2020). Alzheimer's disease (AD), the most common subtype, is characterized by progressive accumulation of extracellular beta-amyloid plaques and intracellular tau neurofibrillary tangles, leading to synaptic dysfunction and neuronal loss. While genetic factors contribute to disease risk, a substantial proportion of dementia cases are attributable to modifiable lifestyle and environmental factors, among which sleep has gained increasing prominence (Livingston et al., 2020; Scheltens et al., 2021).

Sleep disturbances are highly prevalent in older adults and have traditionally been considered a consequence of neurodegeneration. However, accumulating longitudinal evidence suggests that sleep disruption may precede clinical cognitive decline by years or even decades, supporting a potential causal role in disease development (Ju et al., 2020; Pase et al., 2023). This paradigm shift has positioned sleep as both a biomarker and a therapeutic target in dementia prevention strategies.

The discovery of the glymphatic system, a brain-wide perivascular clearance pathway, has provided a compelling mechanistic link between sleep and neurodegeneration. This system facilitates the removal of metabolic waste products, including beta-amyloid and tau, and is highly active during sleep, particularly during slow-wave sleep (Benveniste et al., 2021; Nedergaard & Goldman, 2020). Impairment of this clearance mechanism has been implicated in the accumulation of neurotoxic proteins and the progression of Alzheimer's pathology.

More recently, attention has expanded beyond sleep duration and quality to include sleep architecture and body posture during sleep. Experimental studies suggest that sleeping position may influence glymphatic efficiency, with the lateral position potentially optimizing cerebrospinal fluid flow and interstitial exchange (Lee et al., 2015; Hablitz et al., 2020). Although these findings are primarily derived from animal models, they raise important translational questions regarding the role of sleep posture in human neurodegenerative disease.

This review aims to provide a comprehensive and clinically oriented synthesis of current evidence linking deep sleep, sleep position, and dementia risk, integrating epidemiological data, mechanistic insights, and emerging clinical implications. Particular emphasis is placed on recent literature (2020–2026) and on translating mechanistic findings into practical preventive strategies.

Sleep and Dementia: Epidemiological Evidence

1 Sleep Duration and Dementia Risk

A substantial body of epidemiological evidence supports a U-shaped relationship between sleep duration and dementia risk, with both short and long sleep associated with adverse cognitive outcomes. Large prospective cohort studies have demonstrated that individuals sleeping less than 6 hours per night have an increased risk of developing dementia, independent of other risk factors such as cardiovascular disease and depression (Sabia et al., 2021). Conversely, long sleep duration (>9 hours) has also been associated with increased dementia risk, although this relationship may reflect underlying pathology or preclinical disease rather than a direct causal effect (Leng et al., 2020).

Importantly, recent meta-analyses incorporating data from multiple longitudinal cohorts have confirmed that sleep duration is not merely a correlate but a predictor of cognitive decline, with risk increasing progressively as sleep deviates from the optimal range of approximately 7–8 hours per night (Zhang et al., 2025; Pase et al., 2023). These findings highlight the importance of maintaining adequate sleep duration as part of dementia prevention strategies.

2 Sleep Quality and Fragmentation

Beyond duration, sleep quality and continuity are critical determinants of cognitive health. Sleep fragmentation, characterized by frequent awakenings and reduced sleep efficiency, has been strongly associated with impaired cognitive performance and increased risk of Alzheimer's disease (Lim et al., 2020). Actigraphy-based studies have demonstrated that individuals with highly fragmented sleep exhibit greater beta-amyloid deposition on positron emission tomography (PET) imaging, suggesting a direct link between disrupted sleep and pathological protein accumulation (Ju et al., 2020).

Mechanistically, sleep fragmentation reduces the amount of time spent in slow-wave sleep, thereby impairing glymphatic clearance and promoting neuroinflammation (Winer et al., 2021). Furthermore, disrupted sleep has been associated with alterations in synaptic homeostasis, leading to impaired memory consolidation and increased neuronal vulnerability.

3 Sleep Disorders and Dementia Risk

Sleep disorders, particularly obstructive sleep apnea (OSA), represent a major modifiable risk factor for dementia. OSA is characterized by recurrent episodes of upper airway obstruction during sleep, resulting in intermittent hypoxia, sleep fragmentation, and sympathetic activation. These physiological disturbances contribute to vascular dysfunction, oxidative stress, and impaired glymphatic clearance, all of which are implicated in neurodegeneration (Bubu et al., 2020; Leng et al., 2023).

Longitudinal studies have demonstrated that untreated OSA is associated with increased risk of mild cognitive impairment and Alzheimer's disease, while treatment with continuous positive airway pressure (CPAP) may slow cognitive decline (Osorio et al., 2021). These findings underscore the importance of early identification and management of sleep disorders in dementia prevention.

Circadian rhythm disturbances also play a significant role, particularly in older adults. Disruption of circadian timing has been associated with increased amyloid deposition and neuroinflammation, further contributing to cognitive decline (Musiek & Holtzman, 2022).

The Glymphatic System and Neurodegeneration

The glymphatic system is a brain-wide perivascular network that facilitates the exchange of cerebrospinal fluid (CSF) and interstitial fluid (ISF), enabling the clearance of metabolic waste products from the central nervous system. First described in detail over the past decade, this system has become central to understanding how sleep influences neurodegenerative disease processes (Nedergaard & Goldman, 2020; Benveniste et al., 2021). The glymphatic pathway relies on the movement of CSF along periarterial spaces into the brain parenchyma, followed by exchange with interstitial fluid and subsequent clearance along perivenous routes. This convective flow is distinct from purely diffusive processes and allows efficient removal of large molecular solutes, including beta-amyloid and tau proteins, which are central to Alzheimer's disease pathology (Iliff et al., 2012; Rasmussen et al., 2022).

A critical component of glymphatic function is the role of astrocytic aquaporin-4 (AQP4) water channels, which are densely localized at the endfeet of astrocytes surrounding cerebral vasculature. Proper polarization of AQP4 channels is essential for maintaining directional fluid flow. Disruption of AQP4 localization, which has been observed in aging and Alzheimer's disease, leads to impaired glymphatic transport and accumulation of neurotoxic proteins (Zeppenfeld et al., 2020; Mestre et al., 2020). Age-related loss of AQP4 polarization may therefore represent a key mechanistic link between aging, sleep dysfunction, and neurodegeneration.

Importantly, glymphatic activity is highly state-dependent, with significantly increased function during sleep compared to wakefulness. Experimental studies have demonstrated that sleep is associated with expansion of interstitial space, facilitating greater convective exchange and enhanced clearance of solutes (Xie et al., 2013; Hablitz et al., 2020). Recent human imaging studies using MRI and tracer-based techniques have confirmed that glymphatic transport is enhanced during sleep and is reduced in individuals with sleep disorders and neurodegenerative conditions (Taoka et al., 2023; Han et al., 2024). These findings provide direct translational evidence supporting the role of sleep in maintaining brain homeostasis.
Furthermore, vascular pulsatility, respiration, and arterial compliance play important roles in driving glymphatic flow. Cardiovascular risk factors such as hypertension and atherosclerosis may impair these driving forces, thereby reducing clearance efficiency and increasing susceptibility to neurodegeneration (Kiviniemi et al., 2021). This highlights the interplay between vascular health, sleep physiology, and glymphatic function.

Key Mechanistic Components of the Glymphatic System

- Periarterial CSF influx into brain parenchyma
- AQP4-mediated fluid exchange at astrocytic endfeet
- Perivenous clearance pathways
- Dependence on sleep state and slow-wave activity
- Modulation by vascular pulsatility and respiration

Table 1. Glymphatic System Dysfunction and Dementia Pathogenesis

Component	Dysfunction	Consequence	Clinical Implication
AQP4 polarization	Loss with aging	Reduced fluid transport	Increased amyloid accumulation
CSF–ISF exchange	Impaired during wakefulness	Toxic protein retention	Higher AD risk
Vascular pulsatility	Reduced in vascular disease	Slower clearance	Link with vascular dementia
Sleep disruption	Reduced glymphatic activity	Accumulation of tau/amyloid	Target for intervention

Deep Sleep (Slow-Wave Sleep) and Neuroprotection

1 Neurophysiology of Slow-Wave Sleep

Slow-wave sleep (SWS), also referred to as stage N3 non-rapid eye movement (NREM) sleep, is characterized by high-amplitude, low-frequency delta oscillations (0.5–4 Hz) on electroencephalography (EEG). This stage represents the deepest phase of sleep and is associated with reduced neuronal firing, decreased metabolic demand, and synchronized cortical activity (Steriade et al., 2020). From a neurophysiological perspective, SWS provides a unique environment in which restorative processes can occur, including synaptic downscaling and metabolic clearance.

Importantly, aging is associated with a progressive decline in slow-wave sleep, both in duration and intensity. This reduction is thought to contribute to increased vulnerability to neurodegenerative disease, as the loss of deep sleep impairs the brain's ability to clear toxic metabolites (Mander et al., 2020; Winer et al., 2021).

2 Deep Sleep and Glymphatic Activation

Slow-wave sleep is the primary driver of glymphatic activity. During this stage, reduced neuronal activity leads to decreased interstitial resistance, allowing cerebrospinal fluid to flow more freely through brain tissue. Experimental studies have shown that glymphatic clearance is significantly enhanced during SWS, with increased removal of beta-amyloid and other metabolites (Xie et al., 2013; Hablitz et al., 2020).

Recent human studies have demonstrated that greater slow-wave activity is associated with lower levels of amyloid deposition, as measured by PET imaging (Winer et al., 2021). Additionally, sleep deprivation studies have shown rapid increases in beta-amyloid levels following even a single night of disrupted sleep, highlighting the sensitivity of glymphatic function to sleep quality (Shokri-Kojori et al., 2018; Ju et al., 2020).

3 Synaptic Homeostasis and Memory Consolidation

Beyond its role in metabolic clearance, slow-wave sleep is critical for synaptic homeostasis. The synaptic homeostasis hypothesis proposes that sleep serves to downscale synaptic strength accumulated during wakefulness, thereby preventing neuronal overexcitation and preserving network efficiency (Tononi & Cirelli, 2020). This process is essential for memory consolidation and cognitive function.

Disruption of slow-wave sleep impairs these processes, leading to deficits in learning, memory, and executive function. In older adults, reduced slow-wave sleep has been associated with hippocampal atrophy and impaired memory performance, further linking sleep architecture to neurodegeneration (Mander et al., 2020).

4 Clinical Evidence Linking Reduced Deep Sleep to Dementia

Clinical studies consistently demonstrate that reduced slow-wave sleep is associated with increased risk of cognitive decline and Alzheimer's disease. Longitudinal studies have shown that individuals with lower slow-wave activity are more likely to develop amyloid pathology and exhibit faster cognitive decline (Winer et al., 2021; Pase et al., 2023).

Moreover, interventions aimed at enhancing slow-wave sleep—such as acoustic stimulation, physical activity, and sleep hygiene interventions, have shown promise in improving cognitive outcomes and reducing amyloid burden, although long-term data remain limited (Papalambros et al., 2019; Ong et al., 2021).

Key Neuroprotective Functions of Deep Sleep

- Enhancement of glymphatic clearance of amyloid and tau
- Reduction of neuroinflammation and oxidative stress
- Synaptic downscaling and network stabilization
- Memory consolidation and cognitive resilience

Table 2. Deep Sleep and Dementia Prevention: Mechanistic Pathways

Mechanism	Physiological Process	Evidence	Clinical Relevance
Glymphatic activation and clearance	Increased CSF flow	Strong (animal + human)	Reduces amyloid burden
Synaptic homeostasis	Downscaling synapses	Strong	Improves cognition
Anti-inflammatory effects	Reduced cytokines	Moderate	Neuroprotection
Oxidative stress reduction	Metabolic recovery	Moderate	Slows degeneration

Sleeping Position and Brain Physiology

1 Conceptual Framework: Why Position May Matter

While sleep architecture has been firmly established as a determinant of glymphatic function, the role of body posture during sleep has emerged more recently as a potentially important modifier of cerebrospinal fluid (CSF) dynamics and brain waste clearance. Theoretical and experimental models suggest that gravitational forces, vascular geometry, and intracranial pressure gradients may influence the efficiency of glymphatic transport, raising the possibility that sleep position could have measurable effects on neurodegenerative risk (Lee et al., 2015; Hablitz et al., 2020).

The glymphatic system depends on convective flow along perivascular spaces, which is influenced by arterial pulsatility, venous outflow, and intracranial compliance. Changes in body posture can alter these parameters by modifying venous drainage patterns, intracranial pressure, and cerebrovascular resistance (Kiviniemi et al., 2021). In this context, sleep position represents a biomechanical variable that may interact with physiological processes governing brain clearance.

2 Experimental Evidence: Lateral vs Supine Position

The most influential experimental study examining sleep position and glymphatic function demonstrated that the lateral (side) position was associated with significantly greater glymphatic transport compared with supine or prone positions in animal models (Lee et al., 2015). Using dynamic contrast imaging, investigators showed that tracer clearance from the brain was most efficient in the lateral decubitus position, suggesting that this posture may optimize CSF–interstitial fluid exchange.

Subsequent experimental work has supported these findings, indicating that lateral positioning may reduce resistance to CSF inflow and enhance venous outflow, thereby facilitating more efficient clearance of metabolic waste (Hablitz et al., 2020; Mestre et al., 2020). These effects are thought to be mediated by improved alignment of vascular structures and reduced compression of venous pathways.

However, it is important to emphasize that these findings are largely derived from animal models, and translation to human physiology remains an area of active investigation. Differences in brain size, posture, and cardiovascular dynamics may influence the applicability of these results to clinical populations.

3 Supine Position: Potential Adverse Effects

The supine (back) position has been associated with several physiological changes that may negatively impact brain clearance mechanisms. One of the most clinically relevant factors is the increased risk of upper airway obstruction and obstructive sleep apnea (OSA) in the supine position. Supine sleep promotes posterior displacement of the tongue and soft tissues, increasing airway collapsibility and leading to intermittent hypoxia and sleep fragmentation (Bubu et al., 2020).

In addition to respiratory effects, the supine position may alter intracranial hemodynamics. Studies suggest that supine posture can increase intracranial venous pressure and reduce venous outflow efficiency, potentially impairing glymphatic clearance (Kiviniemi et al., 2021). Elevated venous pressure may reduce the pressure gradient required for CSF–interstitial fluid exchange, thereby limiting convective flow.

Observational studies have reported that individuals with neurodegenerative diseases, including Alzheimer's and Parkinson's disease, tend to spend more time in the supine position during sleep. However, whether this represents a causal factor or a consequence of disease-related motor or behavioural changes remains unclear (Bliwise, 2020).

4 Prone Position: Limited Evidence

The prone (face-down) position has been less extensively studied in the context of glymphatic function. While prone positioning may improve oxygenation in certain clinical settings, such as acute respiratory distress syndrome, its effects on brain clearance mechanisms are poorly understood.

From a biomechanical perspective, prone positioning may increase cervical rotation and venous compression, potentially impairing cerebral venous drainage. However, empirical data are limited, and no definitive conclusions can be drawn regarding its role in neurodegenerative risk.

5 Interaction With Respiratory and Cardiovascular Physiology

An important consideration in evaluating sleep position is its interaction with respiratory and cardiovascular physiology, both of which are critical determinants of glymphatic function. Respiratory cycles contribute to CSF movement through pressure oscillations, while arterial pulsatility drives perivascular flow (Dreha-Kulaczewski et al., 2015; Kiviniemi et al., 2021).

Sleep positions that impair respiration (e.g., supine position in OSA patients) may therefore have indirect effects on glymphatic clearance by disrupting these physiological drivers. Conversely, positions that promote stable respiration and efficient venous return may enhance clearance mechanisms.

Key Physiological Effects of Sleep Position

- Modulation of venous outflow from the brain
- Influence on intracranial pressure gradients
- Interaction with airway patency and oxygenation
- Effects on arterial pulsatility and CSF movement

Table 3. Physiological Effects of Sleep Position on Brain Function

Position	Glymphatic Flow	Venous Drainage	Respiratory Impact	Clinical Interpretation
Lateral	High (experimental)	Optimized	Reduced apnea risk	Potentially protective
Supine	Moderate–Low	Impaired	Increased apnea risk	Possible risk factor
Prone	Uncertain	Variable	Variable	Limited evidence

Human Evidence Linking Sleep Position and Dementia

1 Observational Studies

Human evidence examining the relationship between sleep position and dementia remains limited and largely observational. Studies using actigraphy and polysomnography have suggested that individuals with neurodegenerative diseases tend to spend a greater proportion of sleep time in the supine position, compared with cognitively normal controls (Bliwise, 2020). This finding has been interpreted as a potential link between sleep posture and disease risk.

However, these observations must be interpreted with caution. Neurodegenerative diseases are often associated with reduced mobility, altered motor control, and behavioral changes, which may influence sleep position independently of glymphatic function. Thus, reverse causation remains a significant concern.

2 Indirect Human Evidence

Indirect evidence supporting a role for sleep position comes from studies of obstructive sleep apnea, which is more severe in the supine position. Patients with positional OSA exhibit improved respiratory parameters when sleeping in the lateral position, suggesting that posture can significantly influence physiological processes relevant to brain health (Cartwright, 2020).

Given the strong association between OSA and dementia risk, it is plausible that sleep position may exert indirect effects on neurodegeneration through its impact on respiratory physiology and oxygenation (Leng et al., 2023).

6.3 Imaging and Biomarker Studies

Recent advances in neuroimaging have allowed for more direct assessment of glymphatic function in humans. MRI-based techniques, including diffusion tensor imaging and intrathecal contrast studies, have demonstrated altered CSF dynamics in individuals with sleep disorders and Alzheimer's disease (Taoka et al., 2023; Han et al., 2024).

However, studies specifically examining the effect of sleep position on glymphatic transport in humans are still lacking. This represents a major gap in the literature and a key area for future research.

4 Limitations of Current Evidence

The current evidence base is limited by several important factors:

- Predominance of animal studies
- Lack of longitudinal human trials
- Difficulty in accurately measuring sleep position over time
- Confounding by comorbid conditions such as OSA and mobility impairment

These limitations highlight the need for well-designed prospective studies incorporating objective measures of sleep position, glymphatic function, and cognitive outcomes.

Summary of Human Evidence

- Association between supine sleep and neurodegeneration observed
- Strong indirect link via OSA and hypoxia
- No definitive causal evidence
- Significant methodological limitations

Integrated Model: Deep Sleep and Sleep Position in Dementia Prevention

The relationship between sleep and neurodegeneration is increasingly understood as a multidimensional interaction between sleep architecture, physiological dynamics, and biomechanical factors. While deep sleep has been firmly established as a key driver of glymphatic clearance, the role of sleep position can be conceptualized as a modulatory factor that influences the efficiency of this process. Integrating these components provides a more comprehensive framework for understanding how sleep contributes to dementia prevention.

Slow-wave sleep facilitates glymphatic function through reduced neuronal activity, expansion of interstitial space, and enhanced cerebrospinal fluid exchange, creating optimal conditions for clearance of neurotoxic proteins (Xie et al., 2013; Hablitz et al., 2020). In this context, sleep position may influence the mechanical aspects of fluid transport, including venous outflow, intracranial pressure gradients, and vascular alignment (Lee et al., 2015; Kiviniemi et al., 2021). The lateral position, in particular, appears to provide a biomechanical environment that complements the physiological processes activated during deep sleep.

This integrated model suggests that maximal glymphatic efficiency occurs when both physiological and mechanical conditions are optimized. Deep sleep provides the biological activation of clearance pathways, while lateral positioning may facilitate fluid dynamics and reduce resistance to flow. Conversely, disruption of either component—such as reduced slow-wave sleep or prolonged supine positioning may impair clearance and contribute to accumulation of neurotoxic proteins.

Importantly, this model also accounts for the interaction between sleep position and respiratory physiology. For example, supine positioning increases the likelihood of obstructive sleep apnea, which in turn disrupts slow-wave sleep and reduces glymphatic activity (Bubu et al., 2020; Leng et al., 2023). Thus, sleep position may influence dementia risk both directly (via fluid dynamics) and indirectly (via sleep architecture and oxygenation).

Conceptual Model of Sleep and Brain Clearance

- Deep sleep → physiological activation of glymphatic system
- Lateral position → mechanical facilitation of CSF flow
- Respiratory stability → support of arterial/CSF pulsatility
- Combined effect → optimal clearance of amyloid and tau

Clinical Implications and Prevention Framework

1 Sleep as a Modifiable Risk Factor

From a clinical perspective, sleep represents one of the most accessible and modifiable risk factors for dementia prevention. Unlike genetic or non-modifiable factors, sleep can be measured, optimized, and treated, making it an attractive target for intervention. Strong epidemiological and mechanistic evidence supports the role of sleep optimization in reducing dementia risk, particularly through enhancement of slow-wave sleep and treatment of sleep disorders (Pase et al., 2023; Leng et al., 2023).

Clinicians should therefore consider sleep assessment as a routine component of cognitive health evaluation, particularly in older adults and individuals at increased risk of neurodegenerative disease. This includes evaluation of sleep duration, quality, fragmentation, and presence of sleep disorders such as obstructive sleep apnea.

2 Enhancing Deep Sleep

Strategies to enhance slow-wave sleep represent a key component of dementia prevention. Behavioral interventions, including regular physical activity, sleep hygiene optimization, and cognitive behavioural therapy for insomnia (CBT-I), have been shown to improve sleep quality and increase slow-wave activity (Ong et al., 2021). Pharmacological interventions remain limited, as many sedative agents do not specifically enhance slow-wave sleep and may have adverse cognitive effects.

Emerging approaches, such as acoustic stimulation synchronized with slow-wave oscillations, have shown promise in increasing slow-wave activity and improving memory performance, although further research is needed to establish long-term benefits (Papalambros et al., 2019).

3 Management of Sleep Disorders

The treatment of sleep disorders, particularly obstructive sleep apnea, is critical for preserving cognitive function. Continuous positive airway pressure (CPAP) therapy has been shown to improve sleep architecture, reduce hypoxia, and potentially slow cognitive decline in patients with OSA (Osorio et al., 2021). Early identification and treatment of OSA should therefore be prioritized in individuals at risk of dementia.

Circadian rhythm disorders should also be addressed, as disruption of circadian timing has been linked to increased amyloid deposition and neuroinflammation (Musiek & Holtzman, 2022).

4 Role of Sleep Position in Clinical Practice

While evidence supporting sleep position as a preventive strategy remains limited, current data suggest that encouraging lateral sleeping may be reasonable, particularly in individuals with sleep apnea or high dementia risk. Positional therapy, which involves the use of devices or behavioral strategies to maintain lateral sleep, has been shown to reduce apnea severity and improve sleep quality in selected patients (Cartwright, 2020).

However, it is important to emphasize that sleep position should be considered an adjunctive intervention, rather than a primary strategy, given the limited evidence for a direct causal relationship with dementia risk.

Clinical Recommendations for Dementia Prevention via Sleep

- Maintain 7–8 hours of sleep per night
- Promote slow-wave sleep through behavioural interventions
- Screen and treat obstructive sleep apnea
- Address circadian rhythm disturbances
- Encourage lateral sleeping position when feasible

Table 4. Integrated Model of Sleep, Position, and Dementia Risk

Factor	Mechanism	Effect on Brain Clearance	Clinical Impact
Slow-wave sleep	Increased interstitial space	Enhanced glymphatic flow	Strong protection
Lateral position	Improved venous drainage	Reduced resistance to CSF flow	Moderate protection
Supine position	Increased airway collapse	Reduced clearance efficiency	Potential risk
Sleep apnea	Hypoxia + fragmentation	Impaired glymphatic function	Strong risk factor

Table 5. Clinical Intervention Framework

Intervention	Evidence Level	Mechanism	Recommendation
Sleep duration optimization	Strong	Restorative sleep	Essential
Deep sleep enhancement	Strong	Glymphatic activation	Core strategy
OSA treatment (CPAP)	Strong	Reduces hypoxia	High priority
Circadian regulation	Moderate	Reduces inflammation	Recommended
Lateral sleeping	Emerging	Improves fluid dynamics	Adjunct

Future Directions

Despite significant advances in understanding the relationship between sleep and neurodegeneration, several key questions remain unanswered. One of the most important priorities is the need for longitudinal human studies that directly assess the impact of sleep position on glymphatic function and cognitive outcomes. Advances in wearable technology and home-based monitoring systems may facilitate large-scale studies capable of capturing sleep posture over extended periods.

Another critical area of research involves the development of interventions specifically targeting slow-wave sleep. While current approaches such as acoustic stimulation and behavioural interventions show promise, more effective and scalable strategies are needed. Pharmacological agents that selectively enhance slow-wave sleep without adverse cognitive effects represent a particularly important area of investigation.

Emerging imaging techniques, including advanced MRI methods and tracer-based studies, offer new opportunities to directly visualize glymphatic function in humans. These tools may enable the identification of early biomarkers of impaired clearance and facilitate the evaluation of targeted interventions (Taoka et al., 2023; Han et al., 2024).

Finally, the integration of sleep optimization into multimodal dementia prevention strategies represents a promising direction. Combining sleep interventions with cardiovascular risk reduction, physical activity, and cognitive training may provide synergistic benefits and improve long-term outcomes.

Conclusion

Sleep plays a central role in maintaining brain health and preventing neurodegeneration. Among the various components of sleep, slow-wave sleep emerges as the most critical factor, providing a physiological environment that supports glymphatic clearance, synaptic homeostasis, and metabolic recovery. Robust evidence demonstrates that disruption of deep sleep is associated with increased amyloid burden, cognitive decline, and elevated risk of Alzheimer's disease.

In contrast, the role of sleeping position remains an emerging area of research. Experimental studies suggest that lateral positioning may enhance glymphatic transport and optimize cerebrospinal fluid dynamics, but human evidence remains limited and causality has not been established. Nonetheless, given its potential physiological benefits and minimal risk, encouraging lateral sleep may represent a reasonable adjunctive strategy, particularly in individuals with sleep-disordered breathing.

Overall, the integration of sleep optimization, particularly enhancement of deep sleep, with emerging insights into sleep posture offers a novel and promising framework for dementia prevention. Future research should focus on translating these mechanistic insights into clinically effective interventions that can be implemented at scale.

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The Guide to Lifestyle Medicine

This excellent book from Professor Almoutaz Alkhier Ahmed Abdulrahman is a vital resource for regional and global Arabic speaking doctors and health professionals.

One of the greatest needs globally is for accurate medical advice and information in doctor's native language, especially in high risk and complicated areas of disease management such as diabetes and cardiovascular disease patients.

Treatment involves accurate diagnosis and patient management which in itself requires a high degree of rapport between doctor and patient in areas of compliance with medication and lifestyle issues, along with ongoing monitoring of a patient's welfare. Language and guidance needs to be individualised to each patient.

The book is composed of about 500 pages, with 13 chapters, covering the principles and pillars of lifestyle medicine as well as the landmark studies in the field. A special chapter was added to guide those who are interested in undertaking postgraduate qualifications in lifestyle medicine, providing what, how and where to start. The book emphasises on the clinical skills as well as the basic knowledge in the field.

The Author, Professor AlMoutaz is a highly learned and credentialled author and physician who has passed on his knowledge in this excellent title.

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