ISSN: 2754-4737

Journal of Neurology Research Reviews & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

The Alzheimer's Tiered Progression Matrix (Pro-Ma): A Functional Framework for Clinical Staging and Care Planning in Alzheimer's Disease

Lauren Patrice Brown

Independent Researcher, USA

ABSTRACT

Alzheimer's disease is often staged using vague descriptors such as mild, moderate, and severe. These terms lack functional clarity and do not reflect the observable needs of individuals, or the support required by care teams. This paper introduces the Alzheimer's Tiered Progression Matrix (Pro-Ma), a structured framework based on functional progression and observed behavioral stability. The Matrix includes three clinically relevant progressive phases Neuroamnestic, Neuroadverse, and Neuroabsentia and three dynamic functional tiers within each phase: Emerging, Sustained, and Transitional. The Pro-Ma enhances interdisciplinary communication, care planning, and person-centered support by grounding staging in real-world observation and supplementing with biomarker-informed insight. This framework is designed for broad application across clinical, residential, and community care environments.

***Corresponding author**

Lauren Patrice Brown, Independent Researcher, USA.

Received: November 19, 2025; **Accepted:** November 24, 2025; **Published:** December 03, 2025

Keywords: Alzheimer's Disease, Dementia Staging, Functional Decline, Care Planning, Pro-Ma, Interdisciplinary Care

Introduction

What if the words we used to describe Alzheimer's were as specific as the care we want to give?

For decades, clinicians and families alike have relied on general labels like mild, moderate, and severe to describe Alzheimer's disease. These words may feel familiar, but they fail to guide care or reflect what's really happening in the person's brain - or in their life. Two people labeled "moderate" may have vastly different needs, behaviors, and support systems. These stages are too broad to be actionable and too vague to foster understanding.

The result? Miscommunication, delayed intervention, and a widespread misperception that Alzheimer's is a straight line toward disappearance. "These terms lack standardization, fail to align with cerebrospinal fluid (CSF) and neuroimaging markers, and hinder both clinical care planning and outcome measurement" [1].

Alzheimer's is often described as "The Long Goodbye." But living with Alzheimer's is far more than a farewell; it is a series of shifts: biological, cognitive, emotional, and functional. Those shifts should be clinical in terminology, in both description (qualitative) and analysis (quantitative).

This paper introduces the Alzheimer's Tiered Progression Matrix, or "Pro-Ma" - a new framework for staging Alzheimer's disease that blends scientific insight with practical clarity. The Pro-Ma offers accessible, interdisciplinary language to reflect more specifically how people experience and express Alzheimer's throughout its stages.

The Pro-Ma is grounded in existing literature on Alzheimer's biomarkers, cognitive decline patterns, and functional changes. It draws from both established neuroscience and everyday care scenarios. Each tier is defined by observable behaviors, changes in independence, and patterns of engagement, not just test scores or lab results. The goal is clarity; the purpose is dignity.

The Pro-Ma introduces three overarching progressive phases of disease progression: Neuroamnestic, Neuroadverse, and Neuroabsentia. These terms are clear and clinically accurate. Within each phase, there are three functional-level tiers - Emerging, Sustained, and Transitional - specifically tracking how stable or shifting a person's condition is.

The Pro-Ma model was designed to support researchers and clinicians, frontline staff and case managers, caregivers and support teams - anyone involved in understanding or responding to the lived experience of Alzheimer's. The model does not replace medical staging systems but augments the gap between biological diagnosis and daily care. Pro-Ma provides a way to describe what the person is doing, what they are responding to, and how we can meet them where they are.

When we can describe it better, we can support it better …
When we name what remains, we protect what matters.

Methods

Literature Review and Framework Foundation

The Alzheimer's Tiered Progression Matrix (Pro-Ma) was developed through a comprehensive review of peer-reviewed literature published between 2005 and 2025. Full-text access was obtained primarily through institutional databases, including Scopus. Earlier sources were included to acknowledge their foundational contributions to biomarker discovery and disease staging, such as the identification of Aβ42 decline as a hallmark of early Alzheimer's pathology [1].

The review emphasized functional changes over time, observational descriptors, and cross-disciplinary applicability. Priority was given to studies that described progressive cognitive-behavioral decline, changes in caregiver burden, and the limitations of existing staging systems [2-5]. More recent studies from 2023-2025 were incorporated to reflect current biomarker classifications, fluid-based testing advances, and early-detection paradigms [6-9].

Development of Phase and Tier Structure

"Clinicians often struggle to determine the presence or stage of dementia in the absence of structured, functionally aligned criteria".

The Matrix divides progression into three primary progressive phases, aligned with observed functional shifts:

- **Neuroamnestic Phase:** Defined by memory impairment and early navigation difficulties, typically coinciding with hippocampal atrophy and changes in CSF p-tau231 and Aβ42 [6,7].
- **Neuroadverse Phase:** Characterized by behavioral volatility, emotional lability, and executive function decline, often correlated with elevations in p-tau217, NfL, and GFAP [7-9].
- **Neuroabsentia Phase:** Reflects global cognitive loss with retained sensory/emotional responses. Often seen in advanced synaptic degeneration and late-stage biomarker elevation [10-13].

Each Phase Includes Three Functional Tiers: Emerging, Sustained, and Transitional designed to capture real-time shifts in daily functioning and symptom stability.

Definition and Differentiation of Functional Tiers

Emerging Tier

Captures the first signs of change, such as subtle memory lapses or mood variability. Biomarker changes (e.g., p-tau231) are often present before symptoms surface [3].

Sustained Tier

Represents a new baseline. Symptoms stabilize, routines may be maintained with support, and care needs are predictable [4].

Transitional Tier

Indicates an active decline or major change in function. Interventions may require adjustment as previous strategies become ineffective [7,11].

Table 1: Descriptive Characteristics of Functional Tiers within the Pro-Ma Model, Including Behavioral Markers and Care Planning Priorities.

Alzheimer's Tiered Progression Matrix ("ProMa")

Phase	Emerging	Sustained	Transitional
Neuroamnestic	Biomarkers positive (A+), insight intact, subtle forgetfulness begins	Memory loss evident, requires routines and reminders, functional compensation	Loss of insight, begins to withdraw socially, routines no longer sufficient
Neuroadverse	Emotional swings emerge, early executive dysfunction, safety concerns arise	Needs daily supervision, mood variability, disorientation, verbal cueing required	Language and functional decline accelerate, full-time supervision needed
Neuroabsentia	Nonverbal but emotionally responsive, smiles, reacts to touch and music	Reflexive responses, eyes follow sound or light, full support required	Minimal response, nearing end-of-life care, limited awareness of surroundings

Tier definitions were informed by tools like the FAST, CDR, and MBIC, along with findings from long-term care literature and frontline dementia care practice [4,8,9].

Terminology Development and Usability

Terminology was shaped through informal feedback from healthcare professionals, neurologists, and dementia trainers. Phrasing was refined to balance scientific accuracy with accessibility across disciplines. Terms like "severe" or "late-stage" were replaced with more descriptive, observational terms to reduce ambiguity.

Grounding in Real-World Application

The Pro-Ma is a conceptual model built to reflect lived experiences of Alzheimer's. It is not yet validated empirically but aligns with functional progression patterns reported in longitudinal research. It was designed to be useful in care planning, team communication, and interdisciplinary assessments.

Results

Overview of the Pro-Ma Framework

The Alzheimer's Tiered Progression Matrix (Pro-Ma) offers a two-dimensional model for staging Alzheimer's disease, pairing three **progressive phases: Neuroamnestic, Neuroadverse** and **Neuroabsentia**, with three **functional tiers** in each phase: **Emerging, Sustained** and **Transitional**.

These functional tiers reflect how stable or rapidly changing the person's abilities are, creating a clear, structured vocabulary - usable across roles and care settings.

A summary of phase-tier alignment is provided in Figure 1 (Appendix B).

The Alzheimer's Tiered Progression Matrix (Pro-Ma™)

This matrix illustrates the intersection of clinical phases and functional tiers in Alzheimer's disease progression. It is designed to support staging decisions based on observed changes in function and symptom stability.

	Emerging Describes the earliest observable changes. Early progression is often revealed through changing support needs.	**Sustained** Reflects a relatively stable period. Symptoms and care needs are consistent over time.	**Transitional** Indicates active change. Prior routines or supports are no longer effective.
Neuroamnestic	Memory self-awareness, early cueing; normal ADLs	Observable memory loss; IADL difficulty; routines still work	Task sequencing fails; insight fades; safety concerns rise
Neuroadverse	Mood changes, early disinhibition; cueing starts to fail	Behavior stabilized; ADL assistance required; safety risks	Delusions, volatility; risk behaviors escalate
Neuroabsentia	Nonverbal expression, reflexive responses (music, touch)	Fully dependent; nonverbal; sensory recognition preserved	Minimal response; sleep/wake fragments; comfort-focused care

Figure 1: Schematic Overview of the Alzheimer's Tiered Progression Matrix (Pro-Ma) Model, Illustrating the Progression from Neuroamnestic to Neuroadverse to Neuroabsentia phases.

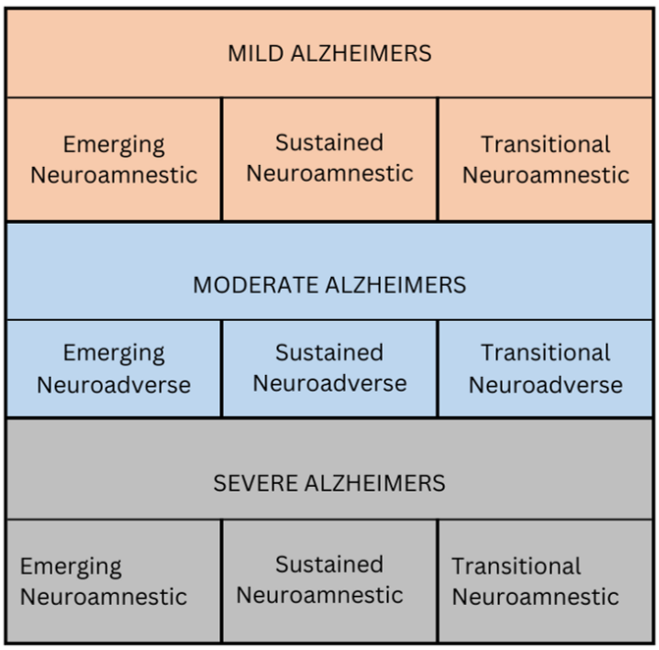

Figure 2: Comparison Chart between Traditional Staging Language (Mild, Moderate, Severe) and The Functional Tiers of the Alzheimer's Pro-Ma Model (Emerging, Sustained, Transitional).

Clinical Utility and Application

The Pro-Ma provides clarity where existing stage labels fall short. By recognizing where a person is in their condition and how fast they are changing, clinicians and caregivers can anticipate needs to avoid crisis-driven care decisions. This model aligns with observed biomarker trajectories but centers on function, giving every team member - from physicians to aides - a common language to act on.

In addition, such clarity is paramount in the evaluation of medical treatments. This matrix gives more specificity to observed change.

Phase 1: Neuroamnestic Phase

Where it begins; memory changes with insight intact

Emerging Tier
The person begins to notice forgetfulness, missing words, misplacing items, or rereading paragraphs. This is often internalized and dismissed as "normal aging." Biomarkers like Aβ42 and p-tau231 may already be abnormal in CSF or plasma, even when clinical assessments remain normal [3,6].

Sustained Tier
Memory issues are now noticeable to others. The person may rely on notes, struggle with IADLs like managing bills, or forget social commitments. Insight is typically preserved, and emotional reactions, such as frustration, withdrawal, or increased anxiety, may rise" [4,8].

Transitional Tier
New disorientation emerges, getting lost while driving, mismanaging medications, or failing to track conversations. This is often the point of formal diagnosis. Clinical markers may show p-tau217 elevation, and hippocampal atrophy becomes more pronounced [7,9].

Phase 2: Neuroadverse Phase
Middle phase: behavioral, executive, and emotional dysregulation

Emerging Tier
Emotional regulation begins to unravel. The person may become suspicious, irritable, or apathetic. They may initiate tasks but fail to complete them. Executive function declines while mobility and verbal fluency remain relatively intact [8,9].

Sustained Tier
A new behavioral baseline emerges: consistent wandering, repetitive questioning, resistance to help. Cortical thinning is observable on MRI, and NfL levels continue to rise [6,11]. ADLs require increasing support; in this stage, caregivers often begin to report exhaustion.

Transitional Tier
Rapid shifts in mood, activity, and alertness occur. Sundowning, paranoia, hallucinations, or delusions may begin. Risk behaviors escalate, and safety concerns (e.g., wandering, fire risk) become critical. Functional interventions may lose effectiveness [11,12].

Phase 3: Neuroabsentia Phase
Late phase: global decline - but presence remains

Emerging Tier
The person is largely non-verbal but may still hum to music, smile at a familiar scent, or grasp a hand responsively. Synaptic markers such as neurogranin and SNAP-25 are often elevated [10].

Sustained Tier
A person in this tier has become fully dependent on assistance for all ADLs. Mobility is limited, but they may still respond to rhythm, tone of voice, or facial expressions. Sleep cycles begin to fragment. Sensory responses remain important cues for care [3,10].

Transitional Tier
Reflexes fade. Eye contact diminishes. Verbal sounds become rare or absent. This is often considered the pre-terminal stage, where palliative care and comfort-based measures become the focus [13].

Table 2: Biomarker Alignment across the Three Functional Phases of the Pro-Ma Model, Outlining CSF, Blood Plasma, and Imaging Data.

Tier	Functional Snapshot	Typical Biomarkers	Care Planning Focus
Emerging	Self-recognized errors; full independence	Aβ42↓, p-tau231↑	Confirm diagnosis, initiate education
Sustained	Observable lapses in IADLs; routines begin to falter	p-tau217↑, hippocampal atrophy, NfL mild↑	Routine support, reduce cognitive burden
Transitional	Disorientation; memory disruption; safety concerns	p-tau217↑↑, NfL↑, structural decline on MRI	Safety-first care, formal care team activation

Neuroadverse Phase Overview Table

Tier	Functional Snapshot	Typical Biomarkers	Care Planning Focus
Emerging	Disinhibition, poor judgment, irritability	NfL↑, GFAP↑, frontal lobe atrophy	Adjust expectations, monitor for safety risks
Sustained	Routine-driven behavior, cue dependence	p-tau217↑, frontal atrophy, executive decline	Create structure, train caregivers in redirection
Transitional	Hallucinations, paranoia, crisis risk	Braak IV–V, neocortical tau spread, high NfL	Safety-first planning, prepare for possible transfer

Neuroabsentia Phase Overview Table

Tier	Functional Snapshot	Typical Biomarkers	Care Planning Focus
Emerging	Minimal verbal ability, reflexive responses to emotion/music	Synaptic decline, widespread tau, neurogranin↑	Sensory engagement, presence-based care
Sustained	Fully dependent; nonverbal; responds to tone/ touch	NfL↑, EEG slowing, reflexive arousal	Total care routines, comfort-based interaction
Transitional	Reflexes fade, minimal responsiveness, approaching death	EEG flat/low complexity, biomarkers plateau	End-of-life planning, comfort, dignity

Discussion
The Alzheimer's Tiered Progression Matrix (Pro-Ma) offers a functional reframing of Alzheimer's staging - one that reflects how individuals live with the disease, not just how it appears on scans. Traditional terms like mild, moderate, and severe fall short because they don't account for variability, overlap, or lived meaning of symptoms. The Pro-Ma addresses this gap by aligning functional changes with recognizable clinical patterns across three phases and three dynamic functional tiers.

Bridging Biology and Behavior

Recent advances in biomarker science have dramatically improved our ability to detect Alzheimer's early, often years before functional changes become observable [3,6]. However, clinical teams and caregivers still need a language to describe what's happening once symptoms appear. The Pro-Ma provides that bridge. While biomarkers anchor the phases, they do not dominate the framework. Observable behaviors, caregiver concerns, and support needs accompany functional tier placement, ensuring that real-time function drives care decisions.

Enhancing Interdisciplinary Communication

By offering a dual-axis system, the Pro-Ma creates a shared vocabulary across disciplines. Whether in a team huddle, an electronic medical record, or a care plan meeting, a designation like Neuroadverse - Transitional conveys more than a test score; it tells the team that behavioral symptoms are escalating and that safety plans may need revision. This level of precision can prevent misinterpretations, reduce duplication of assessments, and create clearer paths for intervention.

Promoting Person-Centered Planning

The Pro-Ma encourages dynamic care, not static labels. It indicates the person's decline in one area, while stabilizing in another. Functional tiers allow for flexible planning, honoring retained abilities, anticipating transitions, and building continuity across environments. This is especially important for caregivers navigating decisions about home care, hospitalization, or residential transitions.

Table 3: Example of SMART Goal Adaptations for Clinical and Caregiver Team Alignment across Functional Stages

✅ Sample SMART Goals by Pro-Ma Stage

Phase	Tier	SMART Goal Example
Neuroamnestic	**Emerging**	"By end of month, caregiver will implement 3 personalized memory cues (e.g., whiteboard reminders, phone alarms, labeled drawers) to support medication adherence."
	Sustained	"Client will receive daily verbal prompts to initiate hygiene tasks with 75% compliance by end of week, documented by staff checklist."
	Transitional	"Care plan will be updated within 5 days to include 24/7 supervision due to two disorientation incidents this week."
Neuroadverse	**Emerging**	"Team will track mood changes using behavior chart over 10 days to identify triggers for agitation and adjust daily schedule accordingly."
	Sustained	"Resident will receive structured sensory box 2× daily to reduce pacing during afternoon shift, evaluated over 7 days."
	Transitional	"Emergency safety protocol will be implemented within 24 hours following verbal aggression during care, including de-escalation plan and staff rotation."
Neuroabsentia	**Emerging**	"Within 3 days, staff will introduce daily playlist of familiar music and document any reflexive response (e.g., smile, vocalization, movement)."
	Sustained	"Resident will be repositioned and comfort-checked every 2 hours to reduce pressure risks and maintain sensory contact."
	Transitional	"Family will be notified to schedule final visits within next 72 hours; comfort care team will initiate vigil plan."

Implications for Research and Policy

The Pro-Ma has the potential to improve how clinical trials define inclusion criteria, how long-term care facilities assess acuity, and how insurance systems classify levels of care. It provides a functional staging option that complements biomarker and diagnostic models without requiring specialized testing. Researchers could use Pro-Ma functional tiers to stratify participants by daily function rather than MMSE score alone, improving real-world applicability of trial findings.

Limitations and Future Directions

While informed by clinical literature, the Pro-Ma has not yet been validated through longitudinal or empirical testing. Future studies should assess inter-rater reliability, tier transition timing, and usability in diverse care settings. Incorporating caregiver feedback, environmental context, and population-specific adaptations (e.g., language, cultural norms) will also be critical for equitable implementation.

Conclusion

The Alzheimer's Tiered Progression Matrix (Pro-Ma) represents a paradigm shift in how we stage, communicate, and support the progression of Alzheimer's disease. By integrating functional observation with biomarker-informed insight, the Pro-Ma reframes disease progression as a dynamic, lived process, not a linear descent.

Rather than relying on vague and subjective descriptors, the Matrix offers precise language rooted in behavior, daily function, and real-world care experience. Its dual-axis format empowers clinicians, researchers, caregivers, and policy leaders to speak the same language a language that translates across disciplines, roles, and environments.

Adopting the Pro-Ma can lead to more informed decision-making, improved patient outcomes, and a more cohesive approach to dementia care.

And When We Name What Remains, We Protect What Matters.

Systematic Review

This framework was developed through a targeted review of peer-reviewed literature from 2005 to 2025, with priority given to studies that described progressive cognitive-behavioral decline, biomarker evolution, and functional outcomes across the Alzheimer's trajectory [1-13]. Sources were identified using structured keyword searches and selected based on their contributions to biomarker staging systems (e.g., AT[N]), functional assessment models (e.g., FAST, CDR), and care planning frameworks.

Interpretation

While current literature often centers on biomarker thresholds and diagnostic tools, this paper introduces a framework grounded in observable function. It complements biological models by offering a user-friendly, clinically relevant method to document and respond to symptom progression across diverse care settings.

Future Directions

Ongoing development should include cross-setting validation of the Matrix, scenario-based training for staff, and integration into care planning systems and clinical trials. Future adaptations may explore culture-specific language, caregiver burden alignment, and tier-based predictive modeling.

Ethics and Inclusion

The Alzheimer's Tiered Progression Matrix was created to uphold the dignity of individuals living with Alzheimer's disease by moving away from vague, stigmatizing labels and toward observable, respectful, and actionable language. No human subjects were involved, and no personal health information was collected in the development of this conceptual model.

Language was reviewed for cross-disciplinary and cross-cultural applicability. Informal feedback from clinicians, care coordinators, and dementia trainers helped shape language into a format that could be used in both professional and family settings. All terminology used in the scientific version of the Pro-Ma avoids metaphors or symbolic descriptors to maintain clarity and clinical neutrality.

Table 4: DSM vs Pro-Ma – Functional Comparison Table

This table provides offers a side-by-side comparison of how Alzheimer's staging is approached under DSM-5-TR vs. the Pro-Ma framework. Where DSM categories are static and vague, Pro-Ma tiers are functional, observable, and precise.

Phase	Tier	DSM Equivalent	Pro-Ma Functional Description
Neuroamnestic	**Emerging**	Mild NCD (not clearly defined)	Self-recognized memory issues; full independence
	Sustained	Mild/Major NCD (ambiguous)	Observable lapses in IADLs; external compensation begins
	Transitional	Major NCD (point of diagnosis)	New disorientation; formal diagnosis likely
Neuroadverse	**Emerging**	Major NCD + behavioral disturbance	Executive & mood changes; judgment impaired
	Sustained	Major NCD + functional dependence	Behavioral patterns stabilize; daily structure needed
	Transitional	Major NCD, high acuity	Escalating behavior, hallucinations, safety risk
Neuroabsentia	**Emerging**	Major NCD (nonverbal)	Nonverbal, responds to music and touch
	Sustained	Major NCD (total dependence)	Fully dependent; responds to rhythm, tone, presence
	Transitional	Major NCD (end-stage/severe)	Reflexes fade; active dying process

Conflict of Interest Statement

The author is the founder of The Alzheimer's Experience; a dementia consulting and advocacy platform focused on improving care systems through training and community education. This work was developed independently and without funding from commercial, pharmaceutical, or institutional sponsors. The author declares no financial conflicts of interest.

Artificial Intelligence (AI) Authoring Tools

Artificial Intelligence (AI) was used in the preparation of this manuscript for organizational support, citation integration, language refinement, and formatting assistance. Specifically, OpenAI's ChatGPT-4 was used as a collaborative drafting tool under the direction and intellectual authorship of Lauren P Brown.

All content; ideas, framework design, and final decisions were made by the human author. The author retains full responsibility for the accuracy, integrity, and originality of the work, including any sections where AI-assisted language was used. No data analysis or image generation was conducted using AI tools. The AI was not used for literature selection or interpretation beyond formatting support.

Funding: This research received no external funding.

References

1. De Paula VJR, Radanovic M, Diniz BS, Forlenza OV (2005) Alzheimer's disease. Subcell Biochem 38: 1-34.
2. Blennow K, Zetterberg H (2009) Biomarkers for Alzheimer's disease: current status and prospects for the future. J Intern Med 266: 140-153.
3. Jack CR Jr, Bennett DA, Blennow K, Maria C Carrillo, Billy Dunn, et al. (2018) NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimers Dement 14: 535-562.
4. Wattmo C, Londos E, Minthon L (2016) Predictors of long-term cognitive outcome in Alzheimer's disease patients: A real-world 15-year longitudinal study. Alzheimers Res Ther 8: 17.
5. Holsinger T, Deveau J, Boustani M, Williams JW Jr (2007) Does this patient have dementia? JAMA 297: 2391-2404.
6. Shi J, Ou Q, Chen X (2024) Blood-based biomarkers of Alzheimer's disease: A guideline for clinical use. Medicine Plus 1: 100057.
7. Krishnamurthy HK, Jayaraman V (2025) An overview of

the genes and biomarkers in Alzheimer's disease. Ageing Res Rev 104: 102599.

8. Li H, Zhang X (2025) Blood biomarkers for clinical applications in Alzheimer's disease: A narrative review. Medicine Plus 2: 100043.
9. Cheng Q, Fan Y, Zhang P (2024) Biomarkers of synaptic degeneration in Alzheimer's disease. Ageing Res Rev 84: 102642.
10. Afrin MR, Upadhyaya PG (2025) Advanced biomarkers: Beyond amyloid and tau Emerging non-traditional biomarkers for Alzheimer's diagnosis and progression. Ageing Res Rev 105: 102736.
11. Palmqvist S, Tideman P, Mattsson Carlgren N (2024) The earliest accumulation of beta-amyloid occurs within the default-mode network and concurrently affects brain connectivity. Sci Transl Med 16: eabn2927.
12. Pascoal TA, Aguzzoli CS, Lussier FZ (2024) Insights into the use of biomarkers in clinical trials in Alzheimer's disease. EBioMedicine 108: 105322.
13. Schöll M, Verberk IMW, Marta Del Campo, Constance Delaby, Joseph Therriault, et al. (2024) Challenges in the practical implementation of blood biomarkers for Alzheimer's disease. Lancet Healthy Longev 5: 100630.