

From Signal to Scale: Advancing Alzheimer's Research with Digital Health Technologies

P2-06

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Signals of disease progression are obscured by technical measurement limitations, participant burden, and operational complexity. Adopting sensitive, frequent, and scalable digital endpoints as co-primary tools can transform AD research from episodic experiments into a continuous, learning-driven process that accelerates the development of effective treatments.

INTRODUCTION- Why this matters

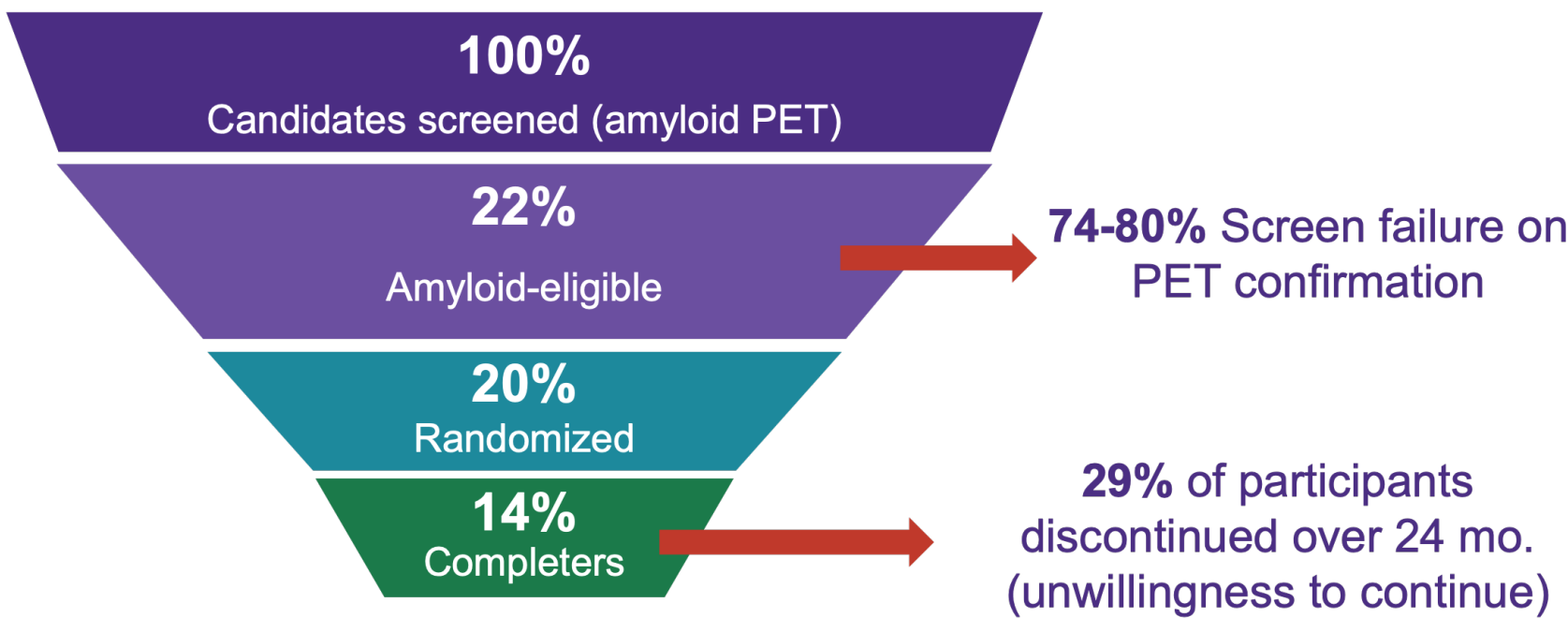
A Disease That Starts Decades Before Diagnosis
In Alzheimer's, genetic and molecular changes cause amyloid buildup, tau issues, and synaptic problems 15-20 years before symptoms. Trials are most likely to succeed in early stages, but these populations show weak, slow, and variable signals on traditional clinical outcome assessments. The current measures, meant to identify short-term changes over brief periods, are not suited for this challenge.

Digital Technologies Enable a New Kind of Measurement
Digital health technologies enable continuous measurement of activity, motor behavior, sleep, language, and cognitive performance that episodic clinic visits cannot. Wearables, smartphones, and passive sensing provide higher temporal resolution, lower floor effects, and the ability to detect subtle, long-term changes.

THE CHALLENGE- Detecting change

Amyloid-PET screening accounts for 74-80% of screen failures (Huoh et al., 2025), and long trial durations drive high attrition, with 29% discontinuing in A4, mostly due to unwillingness rather than medical need (Raman et al., 2025). Compounding this, rater- and site-level endpoint variability erodes statistical power, while payers increasingly demand real-world evidence of effectiveness that biomarker and short-term outcomes alone can't provide.

The Compounding Attrition Funnel



~1 in 7 individuals initially identified as potential participants ultimately complete enrollment and participate in a clinical trial

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EVIDENCE- Digital health readiness

The case for digital endpoints is now supported by evidence showing that digital and blood-based tools outperform standard assessments in detecting early change, scalability, and participant adherence in modern AD trials.

	Domain / Construct	Feasibility	Analytical validity	Clinical validity	Regulatory readiness	Trial adoption	Readiness
Active	Remote cognition <i>Active cognitive testing</i>	●●●	●●●	●●●	●●	●●●	High
	Speech / language <i>Acoustic & linguistic</i>	●●●	●●	●●	●	●●	Moderate
	Graphomotor / drawing <i>Drawing & fine motor</i>	●●●	●●	●●	●	●	Emerging
Wearable / physiological	Gait & mobility <i>Sensor-based motor</i>	●●●	●●●	●●	●●	●●	High
	Sleep / circadian <i>Rest activity rhythm</i>	●●	●●	●●	●	●	Moderate
Passive / behavioral	Life-space / GPS mobility <i>GPS & life-space</i>	●●●	●●	●	●	●	Emerging
	Multi-modal phenotyping <i>Sensor fusion</i>	●●	●●	●	●	●	High

Across modalities, digital measures vary in maturity along five trial-readiness dimensions. Remote cognition and gait lead; passive and multimodal phenotyping show strong feasibility but emerging clinical/regulatory validity.

The Remote Cognitive Landscape

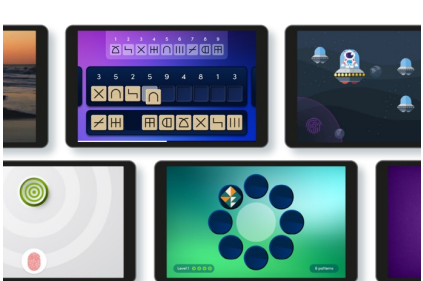
A 2025 review of 1,904 reports identified 23 validated remote cognitive tools for preclinical AD. In one study (Papp et al., 2025), participants repeated a memory task at home; adults with AD pathology but no symptoms showed less daily improvement, revealing a deficit that standard tests missed.

altoida



- The NeuroMarker Platform assesses cognition and activities of daily living
- An augmented reality-derived digital score distinguished healthy controls from amyloid-positive individuals, including the preclinical group
- Demonstrated feasibility of at-home AR-based assessment for early AD

Cumulus



- The NeuLogiq Platform combines a wireless EEG headset with cognitive tasks and mood, speech, and sleep assessments
- Achieved 77% adherence across 69 requested sessions
- Showed that people with mild AD can and will self-administer EEG and cognitive tests at home for a year

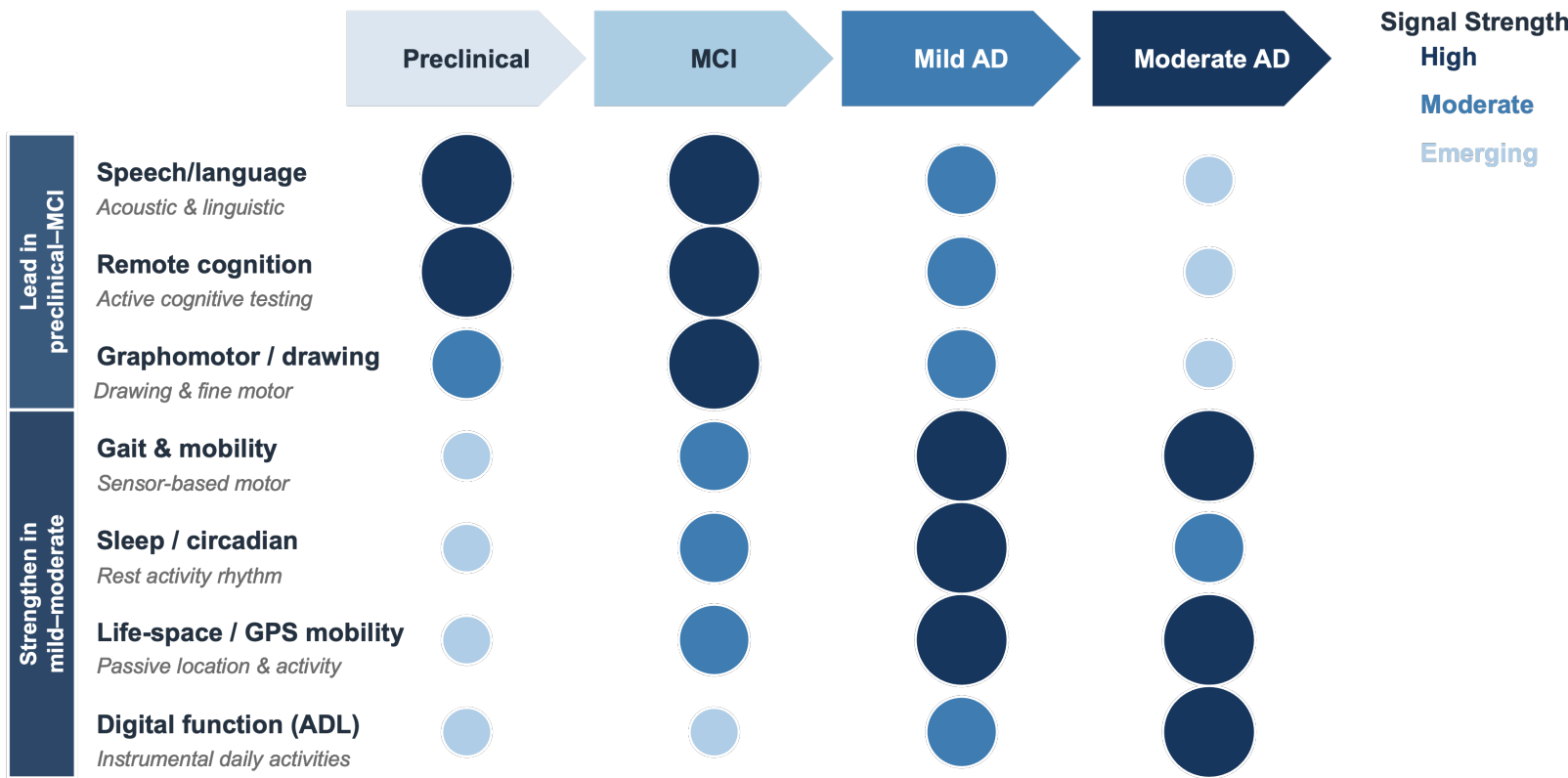
Papp et al. (2025). Detecting early cognitive deficits in preclinical Alzheimer's disease using a remote digital multi-day learning paradigm. *npj Digital Medicine*, 8, 24.
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PATH FORWARD- From episodic to continuous

Digital measures across the AD continuum

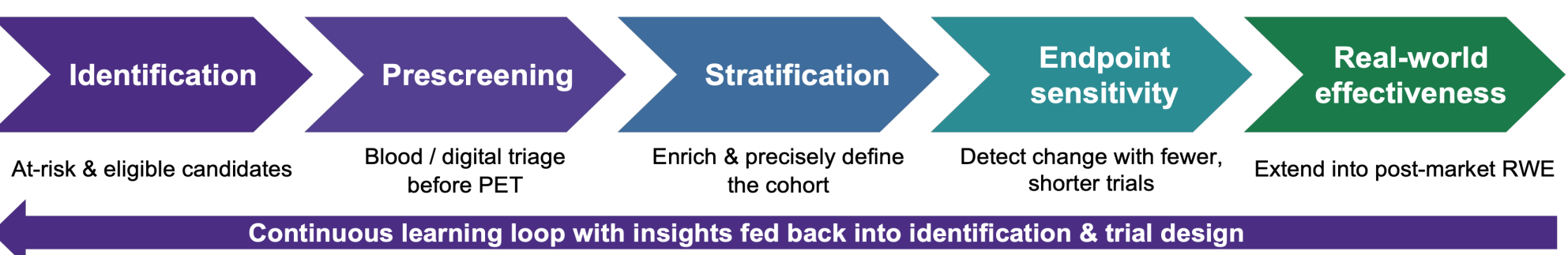
- No single digital measure is optimal across the entire disease course because sensitivity varies by stage.
- Speech and remote cognitive measures are most effective in preclinical and MCI stages, where subtle changes first emerge.
- Wearable, passive-monitoring, and digital functional measures become more useful in mild-to-moderate AD, as motor, behavioral, and functional declines become more detectable.



Matching each stage to its most sensitive measures ensures a strong signal across the continuum, and the infrastructure in Ph 2 carries into Ph 3, creating a continuous evidence base while improving recruitment, easing burden, and boosting retention.

THE MODEL- signal to scale

Conceptual model for embedding digital measures across the development lifecycle, in which digital endpoints carry candidates from identification through real-world effectiveness, with a continuous learning loop feeding insights back into trial design.



The Moment for Action Is Now

The tools are ready, the evidence is mounting, and the path is clear. By systematically adopting digital endpoints, the field can ensure that the next generation of promising compounds succeeds or fails on their mechanisms alone.