

Advances In the Development of Scalable Platforms for Returning Alzheimer's Test Results: Design and Rationale of the eSMARTER Trial



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KEY TAKEAWAYS: Patients are increasingly learning Alzheimer’s disease (AD) genetic and biomarker results via electronic health records, without traditional genetic counseling or clinician communication. Evaluation of alternative scalable delivery models for return of AD risk information is needed to best support patient understanding and psychological well-being.

INTRODUCTION		METHODS & RESULTS										CONCLUSIONS																																																																																																																																																																																																																																																																																														
- In the United States (US), the 21st Century Cures Act mandates the immediate return of most medical tests, including AD genetic and biomarker results. - Although prior studies demonstrate that return of APOE genotype and brain amyloid neuroimaging results is generally safe & well-tolerated, these studies all used clinician-mediated disclosure. - It remains unknown whether return of results via digital platforms, such as one that could be integrated into an electronic health record (EHR), is comparable to a clinician-mediated telehealth session.	- eSMARTER was a decentralized and fully remote randomized, non-inferiority trial comparing returning <i>APOE</i> genotype results via digital platform or clinician-mediated telehealth session (NCT06459583).¹ - Participants were offered optional plasma pTau-217 disclosure 6mo after learning APOE results. - Key outcomes were changes in measures of anxiety, disease-specific distress, and AD-related knowledge following disclosure. - Participants age 60-80 were recruited from GeneMatch, a trial-independent research enrollment program.	<table><tr><th colspan="11">Schedule of Events Table</th></tr><tr><th>Assessments</th><th>Visit 1 Screening</th><th>Visit 2 Enrollment</th><th>Visit 3 T₀: Baseline</th><th>Visit 4 APOE disclosure</th><th>Visit 5 T₁: 0-7 days post APOE disclosure</th><th>Visit 6 T₁: 6-wks post APOE disclosure</th><th>Visit 7 T₁: 6-mos post APOE disclosure</th><th>Visit 8 Optional pTau-217 disclosure</th><th>Visit 9 T₂: 0-7 days post Opt. pTau- 217 disclosure</th><th>Visit 10 T₂: 4-wks post Opt. pTau-217 disclosure</th></tr><tr><td>Informed Consent & I/E Review</td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Demographics</td><td>x</td><td></td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Assessments of Psychological Readiness for Disclosure</td><td>x</td><td></td><td></td><td></td><td></td><td></td><td>x</td><td></td><td></td><td></td></tr><tr><td>Prior Knowledge of APOE Status</td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Telephone Montreal Cognitive Assessment (T-MoCA)</td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Blood Draw</td><td></td><td></td><td></td><td></td><td></td><td>x</td><td></td><td></td><td></td><td></td></tr><tr><td>Randomization</td><td></td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>APOE eHealth Pre-disclosure Education</td><td></td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>APOE Disclosure</td><td></td><td></td><td></td><td>x</td><td></td><td></td><td></td><td></td><td></td><td>x</td></tr><tr><td>Health Literacy & Comfort with Technology</td><td></td><td></td><td>x</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Knowledge of APOE</td><td></td><td></td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td></td><td></td><td></td></tr><tr><td>Disclosure Modality Preference</td><td></td><td></td><td>x</td><td></td><td>x</td><td></td><td></td><td></td><td>x</td><td></td></tr><tr><td>Satisfaction with Disclosure Services and Digital Tools</td><td></td><td></td><td></td><td></td><td>x</td><td></td><td></td><td></td><td>x</td><td></td></tr><tr><td>Psychological Wellbeing Scale: Modified Version</td><td></td><td></td><td>x</td><td></td><td></td><td></td><td>x</td><td></td><td></td><td>x</td></tr><tr><td>Impact of Result Disclosure Assessments</td><td></td><td></td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td></td><td>x</td><td>x</td></tr><tr><td>Current Psychological 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(optional)</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>x</td><td></td><td></td></tr><tr><td>Knowledge of Biomarkers & Recall of Result (pTau-217)</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>x</td><td>x</td></tr></table>										Schedule of Events Table											Assessments	Visit 1 Screening	Visit 2 Enrollment	Visit 3 T ₀ : Baseline	Visit 4 APOE disclosure	Visit 5 T ₁ : 0-7 days post APOE disclosure	Visit 6 T ₁ : 6-wks post APOE disclosure	Visit 7 T ₁ : 6-mos post APOE disclosure	Visit 8 Optional pTau-217 disclosure	Visit 9 T ₂ : 0-7 days post Opt. pTau- 217 disclosure	Visit 10 T ₂ : 4-wks post Opt. pTau-217 disclosure	Informed Consent & I/E Review	x										Demographics	x		x								Assessments of Psychological Readiness for Disclosure	x						x				Prior Knowledge of APOE Status	x										Telephone Montreal Cognitive Assessment (T-MoCA)	x										Blood Draw						x					Randomization		x									APOE eHealth Pre-disclosure Education		x									APOE Disclosure				x						x	Health Literacy & Comfort with Technology			x								Knowledge of APOE			x		x	x	x				Disclosure Modality Preference			x		x				x		Satisfaction with Disclosure Services and Digital Tools					x				x		Psychological Wellbeing Scale: Modified Version			x				x			x	Impact of Result Disclosure Assessments			x		x	x	x		x	x	Current Psychological Status			x		x	x	x		x	x	Assessments											Recall of Result – APOE					x	x	x				Cognitive Function Instrument (CFI)			x				x				Sharing Result with Others & Health Behavior Changes							x			x	Stigma					x	x	x		x	x	pTau217 eHealth Pre-disclosure Education							x				pTau217 Disclosure (optional)								x			Knowledge of Biomarkers & Recall of Result (pTau-217)									x	x	- eSMARTER results support the comparability of self-mediated digital platforms and clinician-telehealth sessions.² - Digital platforms offer a scalable approach to address the growing need for return of AD genetic and biomarker results to patients at elevated risk for AD dementia. - This represents a growing area for development of patient-centric, AI systems to return results prior to a clinician visit. - Future studies should compare return of results via digital platforms vs. EHR portal.
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- eSMARTER enrolled 681 adults from the contiguous US from October 2024-February 2025. - Data collection was completed November 2025.										¹ Erickson et al. Alzheimer's & Dementia: TRCI 2025;11(4):e70177 ² AAIC 2026 Posters Monday-0529 (Erickson) & Monday-0959 (Wood) eSMARTER was supported by funding from the National Institute on Aging under Award Numbers R01AG058468 and P30AG072980 Questions? Email Jessica.Langbaum@@bannerhealth.com																																																																																																																																																																																																																																																																																																