Evaluation of Self-Mediated Alternatives for Risk Testing Education and Return of Results

AGREED Meeting

April 7, 2026

eSMARTER

ALZHEIMER'S PREVENTION INITIATIVE

Hello, I’m Claire Erickson

- Staff Scientist at the Banner Alzheimer’s Institute
- Neuroscience and public affairs training
- Expertise in return of Alzheimer’s-related test results



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Background

- Availability of amyloid modifying therapies will increase the need for disclosure of Alzheimer's related genetic and biomarker test results.
- A shortage of genetic counselors and dementia specialists already exists
- 21st Century Cures Act requires the immediate return of most medical test results

<u>Need for scalable methods to responsibly communicate results</u>

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eSMARTER Study Design

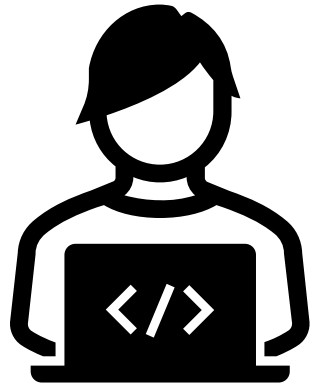
- The Evaluation of Self-Mediated Alternatives for Risk Testing Education and Return of Results (eSMARTER) (#NCT06459583)
- Decentralized, randomized, non-inferiority trial to evaluate scalable digital return of *APOE* and plasma pTau-217 results
- Participants randomized to receive results via telehealth care provider or by eHealth platform (participant-led).



Clinician-Mediated Disclosure

VS.

Digital Self-Mediated Disclosure



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eHealth Modalities

- The eHealth digital platforms covered the same information included in clinician-led disclosure.
- Content was user tested with volunteers matching the eSMARTER age inclusion criteria.
- Readability testing was completed and modifications made to achieve a readability score of 8th grade or lower when possible.
- To better understand differences in user preferences, participants in the eHealth arm had the choice of:
  - Web-based platform
  - SMS-based platform

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Eligibility Criteria

Inclusion Criteria:

- Aged 60-80
- Have internet access
- Fluency in English

No explicit inclusion or exclusion criteria for cognitive status.

Exclusion Criteria:

- Lack of psychological readiness to receive AD genetic and biomarker information
  - ≥10 on PHQ-9 AND/OR responding yes on any of the suicidal ideation questions
- Presence of current major psychiatric illness
- Communication difficulties (e.g., uncorrected or uncompensated hearing and/or vision impairment).

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eSMARTER Study Design

Visit Structure:

Visit 1: Screening	Visit 2: Randomization	Visit 3: Baseline	Visit 4: APOE Disclosure	Visits 5, 6 & 7: Post APOE Disclosure	Visit 8: Optional BBBM disclosure	Visit 9 & 10: Post optional BBBM disclosure

- Screening, Enrollment, & Baseline Data Collection
- *APOE* Disclosure via telehealth appointment or eHealth platform
- Post-*APOE* Disclosure follow-up at ≤7 days, 6 weeks, and 6 months
- Optional pTau-217 Disclosure (after 6 months post-*APOE* disclosure)
  - Remote at-home phlebotomy for blood collection
- Post-pTau-217 Disclosure follow-up at ≤7 days and 4 weeks

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eSMARTER Study Design

- **Primary Outcomes**: Changes in anxiety, AD-related knowledge, and disease-specific distress
    - Primary analysis: Non-inferiority tests to examine if self-mediated disclosure provides equivalent or improved outcomes compared to usual care.
- **Secondary Outcomes**: Satisfaction with disclosure services and digital tools, eHealth system usability, recall of results, Psychological Wellbeing Scale, impact of result disclosure, sharing result with others & health behavior changes, stigma
- Additional analyses will examine result comprehension, individual impact of learning AD genetic and biomarker information, and participant experiences using the eHealth platforms.

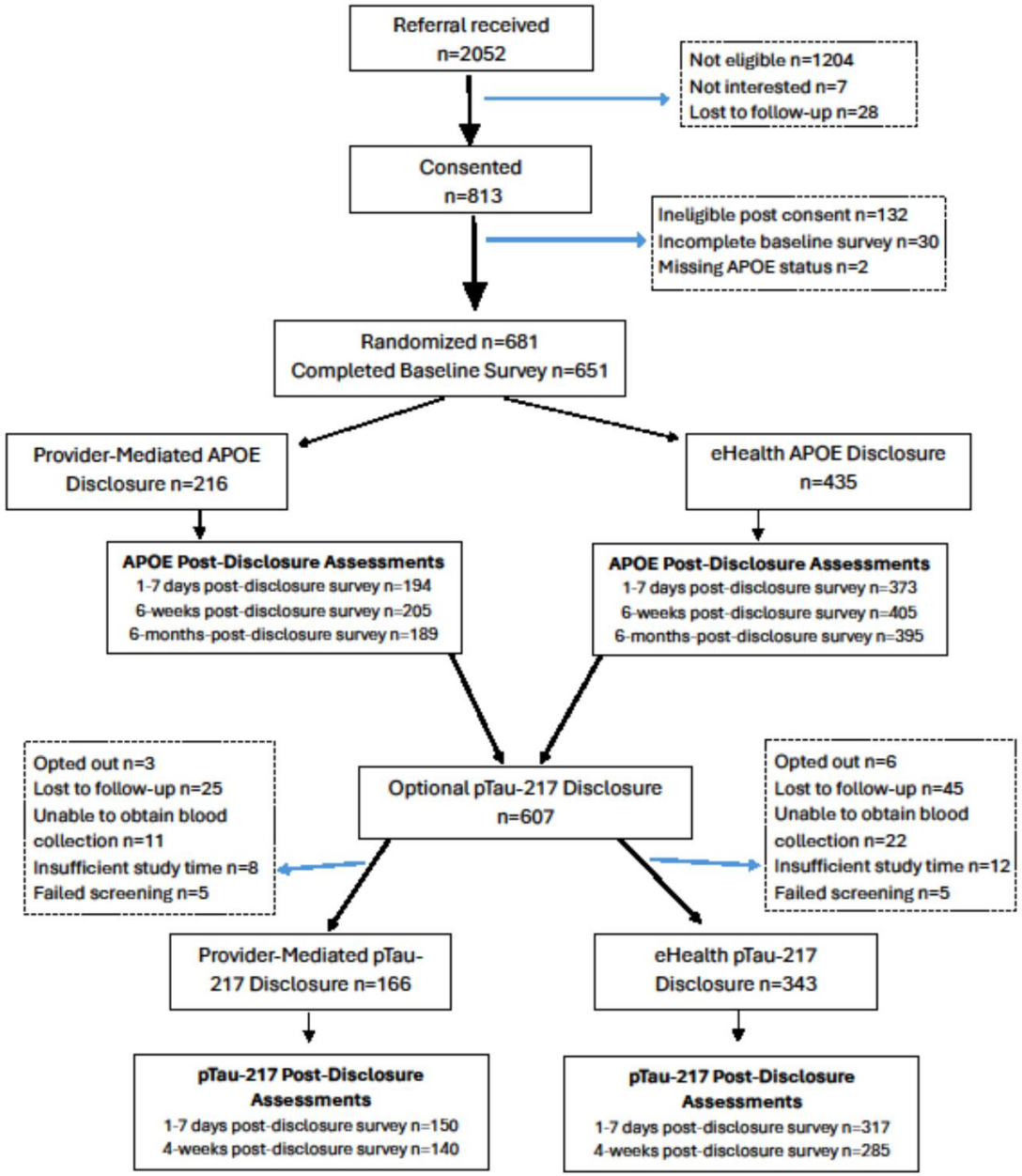
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Study Completion

Data collection completed Nov-07-2025

<u>Ultimately:</u>

- N=651 received their APOE result
- N=509 received their pTau-217 result



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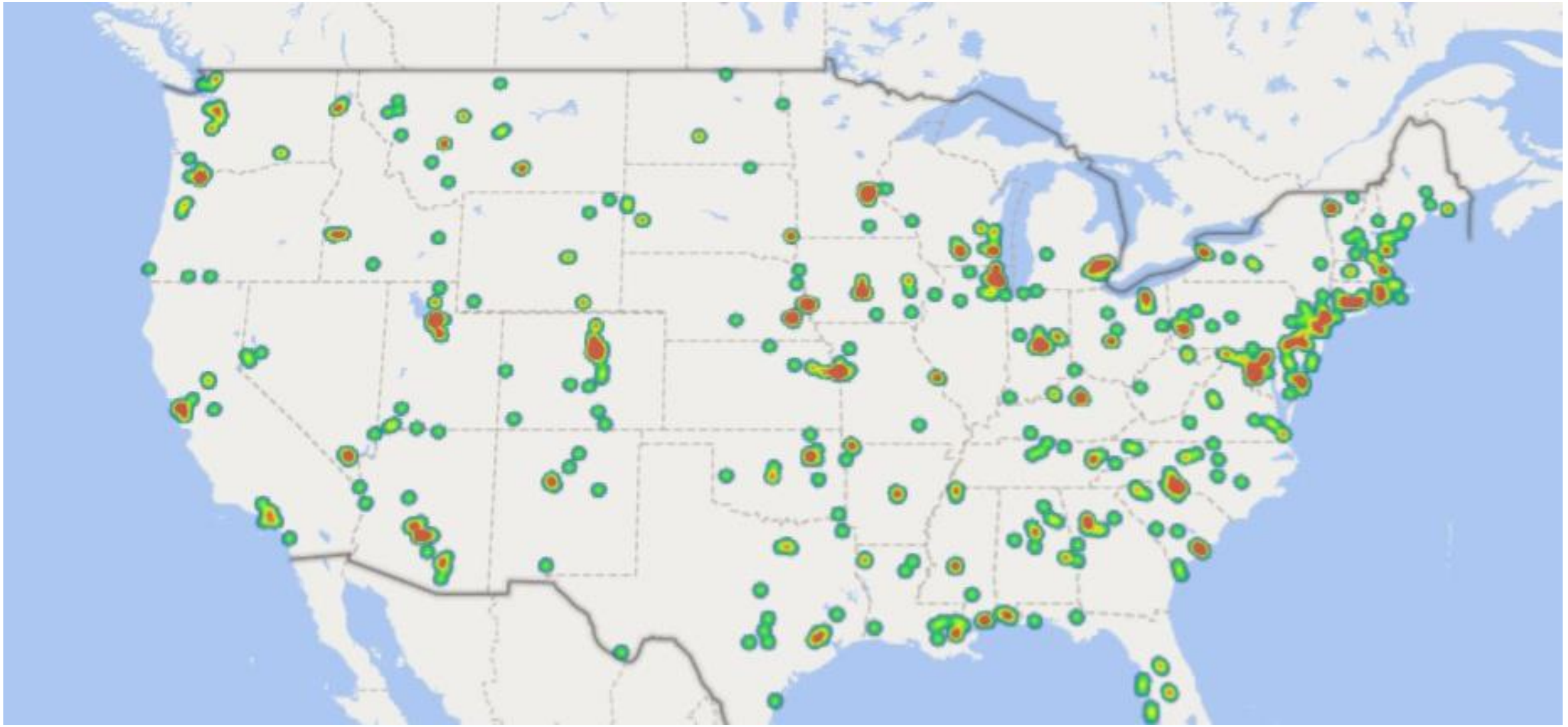
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Demographics of Enrolled Participants

Sex	
Male	225
Female	456
Average Age	67.97
Age 60 - 65	235
Age 66 - 70	238
Age 71 - 75	161
Age 76 - 80	47
Total	681
Telephone - MoCA (Range 0 - 22)	
Mean, Standard Deviation	19.0, 2.0
APOE Carrier Status	
APOE4 Homozygote	65
APOE4 Heterozygote	392
APOE4 Non-Carrier	224

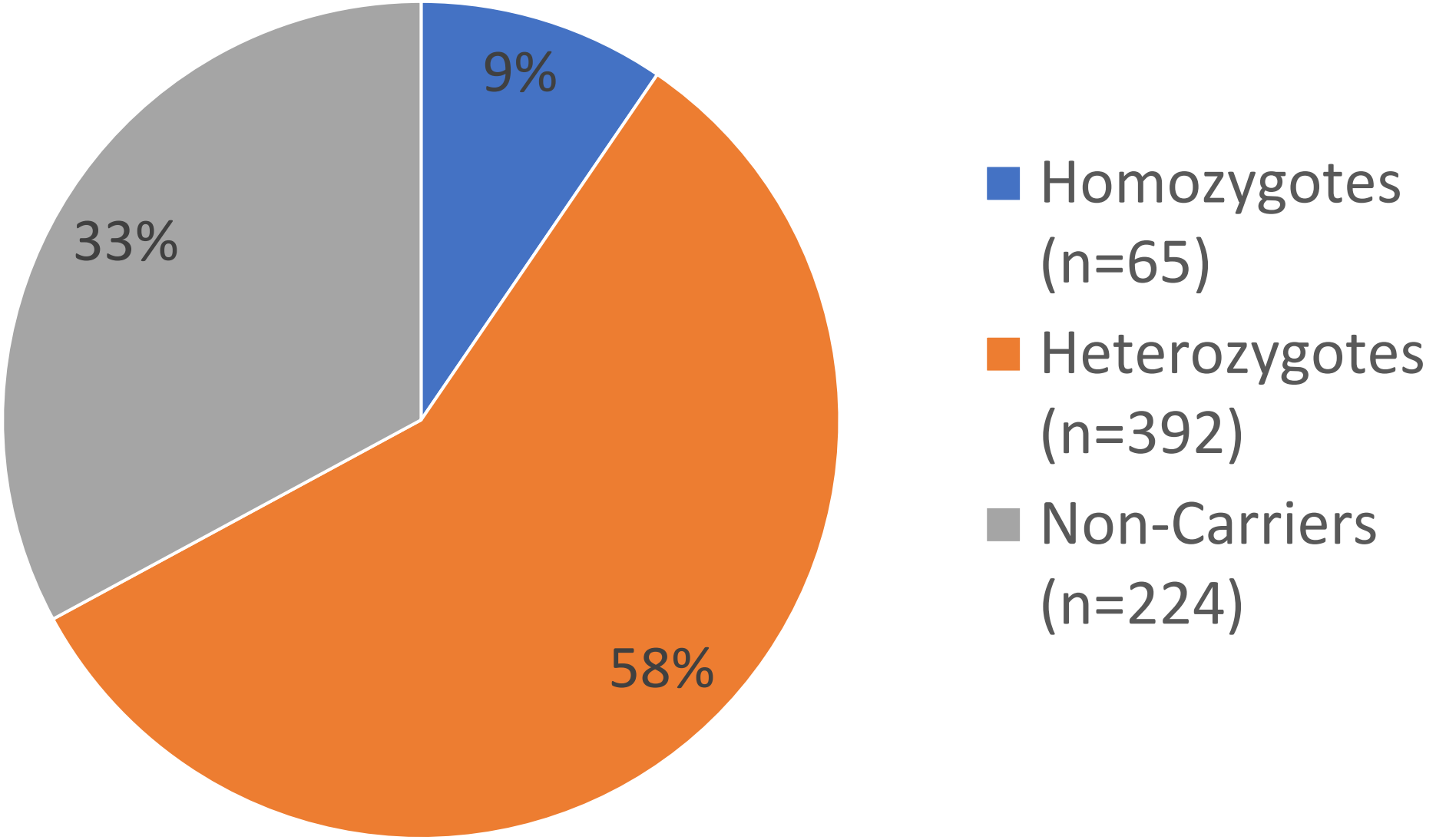
Education	
Bachelor's Degree or Higher	517
Some College	107
Trade / Vocational Training	20
Secondary level education / GED	23
Less than High School	1
Unknown	13
Race	
American Indian or Alaska Native	3
Asian	14
Black or African American	22
More than one race	22
White	610
Unknown	10
Ethnicity	
Hispanic or Latino	42
Not Hispanic or Latino	632
Unknown	7

Enrollment Heatmap



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APOE Summary Data

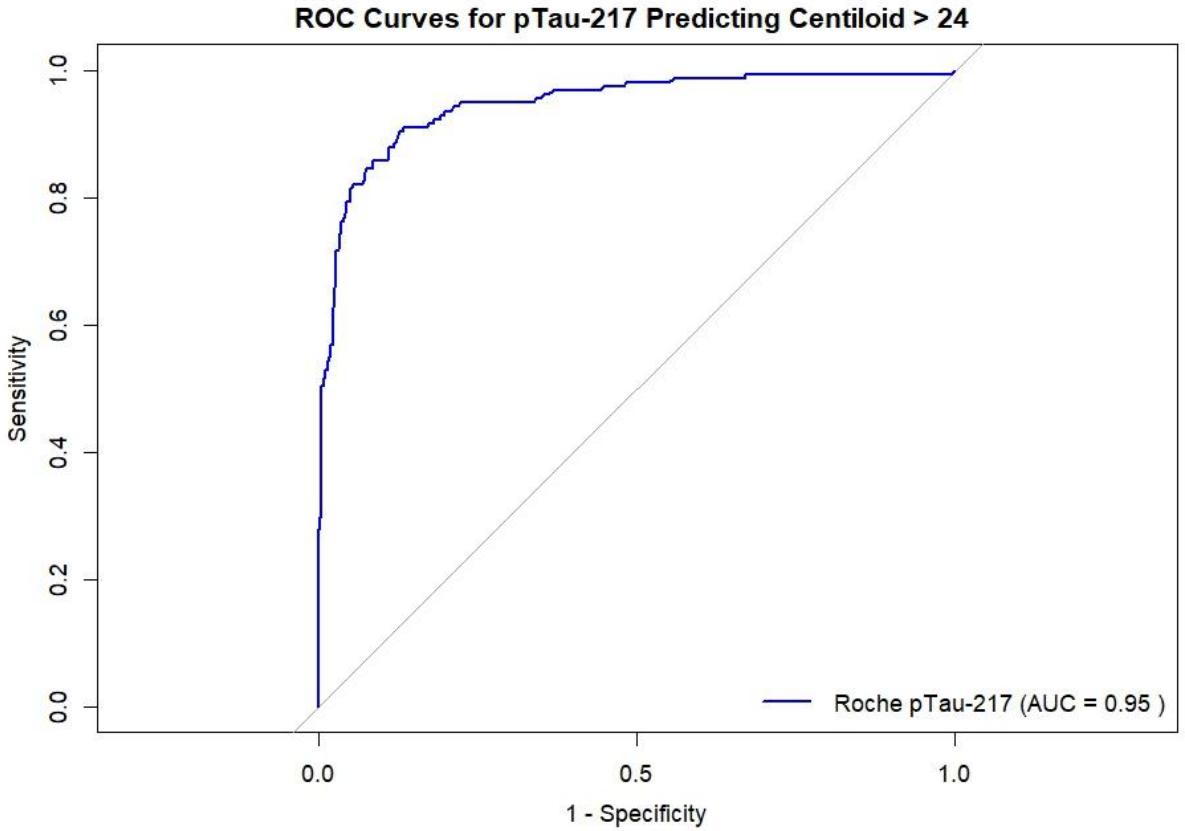


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pTau-217 Summary Data

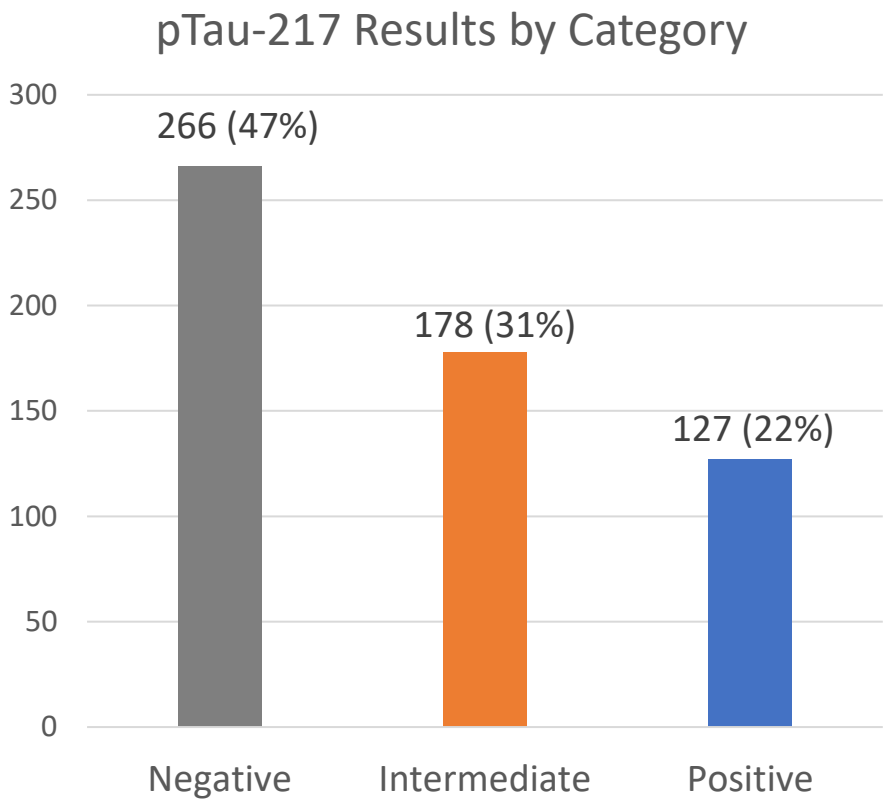
- 575 blood samples collected using remote phlebotomy (571 tested).
- pTau-217 testing completed using the Roche cobas e801 platform.

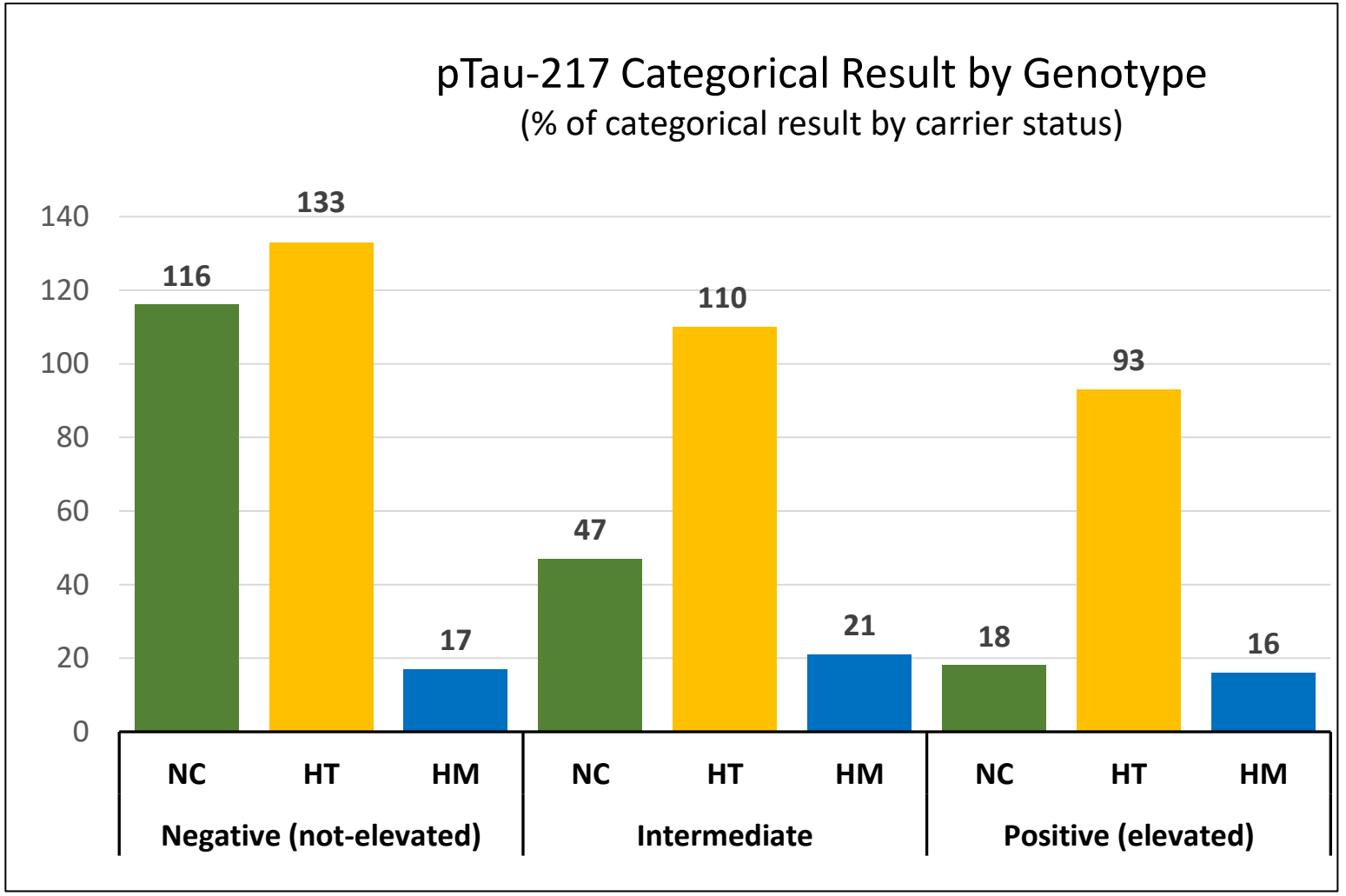
Developing pTau-217 Thresholds	
Data: 616 WRAP participants **Amyloid PET positivity**: >24 CLs	**PPV**:85% **NPV**: 98% **Discriminative accuracy for amyloid positivity**: 95%



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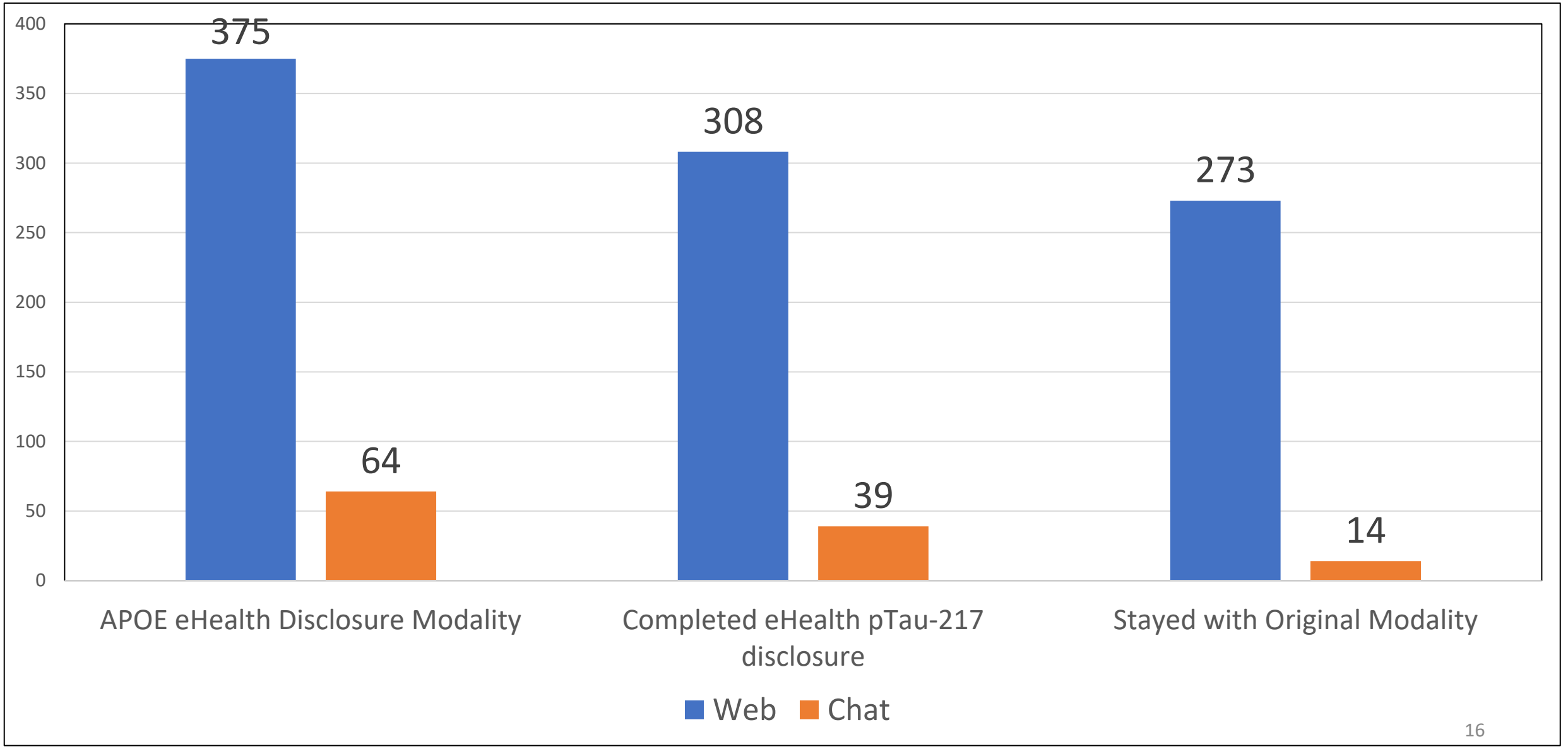
pTau-217 Summary Data





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eHealth Modality Choice



Study Discussion

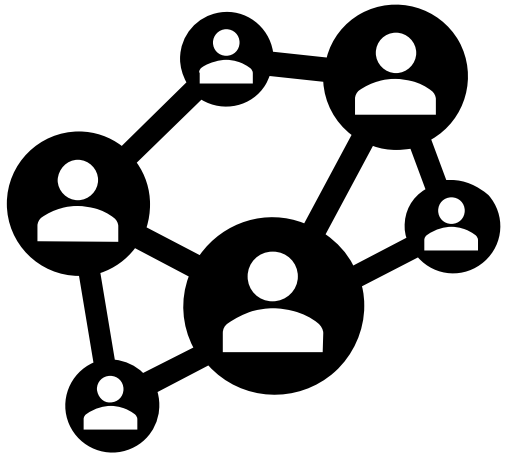
The eSMARTER study has begun addressing the need for practical and scalable methods to responsibly communicate AD genetic and biomarker results.

- Digital platforms will be made available.
  - This can support healthcare providers in returning genetic and/or biomarker results to individuals in clinical and research settings.
- All data and samples collected will be made available for public sharing.

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Study Discussion

Implementing a decentralized study generated unique challenges requiring flexibility, creative thinking, and complex problem solving.



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Study Discussion

As decentralized trials are relatively new, novel approaches have been used including:

- **Sites specializing in decentralized studies**, with PIs licensed across the country.
  - Allows for national reach for recruitment.
- **Remote genetic counselors** licensed across the country.
- **Modified remote eConsent** to adequately assess capacity.
- **Concierge services** to support sites with study activity referral and coordination.
- Customized **digital tools enabling completion of eCOAs on personal devices.**
  - Allows for independent assessment completion by participants, while still monitoring psychological safety and well-being.
- **Mobile phlebotomy** to collect blood samples.
  - Caveat: Coverage not available in some areas and shipping delays resulted in recollections.

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Next Steps

<u>Primary, non-inferiority analysis is currently underway</u>

- Results will be presented at AAIC 2026



<u>Additional analyses beginning soon</u>

- Examining result comprehension, individual impact of learning AD genetic and biomarker information, and participant experiences using the eHealth platforms



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Study Team

This study would not have been possible without the tremendous efforts of study team members!

- Jessica Langbaum (PI)
- Angela Bradbury
- Carolyn Langlois
- Brian Egleston
- Jason Karlawish
- Emily Largent
- Kristin Harkins
- Beth McCarty Wood
- Rajia Mim
- Sarah Howe
- Demetrios Ofidis
- Samantha John
- Nick Ashton
- Scott Roberts
- Marisa Denkinger
- Jessica Enos
- Hayley Salata
- Diana DeSantiago
- Scott Roberts
- Josh Grill

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Questions?



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