

Results of the eSMARTER Study: A randomized non-inferiority study of provider versus digital return of *APOE* genotype results

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BACKGROUND

- APOE* genotyping has increasing testing indications due to treatment implications for anti-amyloid therapy.
- Traditional genetic counseling to all patients by genetic counselors (GC) or other providers is resource-intensive and infeasible given the limited workforce of GCs employed in Alzheimer's disease specialty departments.
- Evaluation of alternative efficient and scalable delivery models for return of *APOE* results is needed.

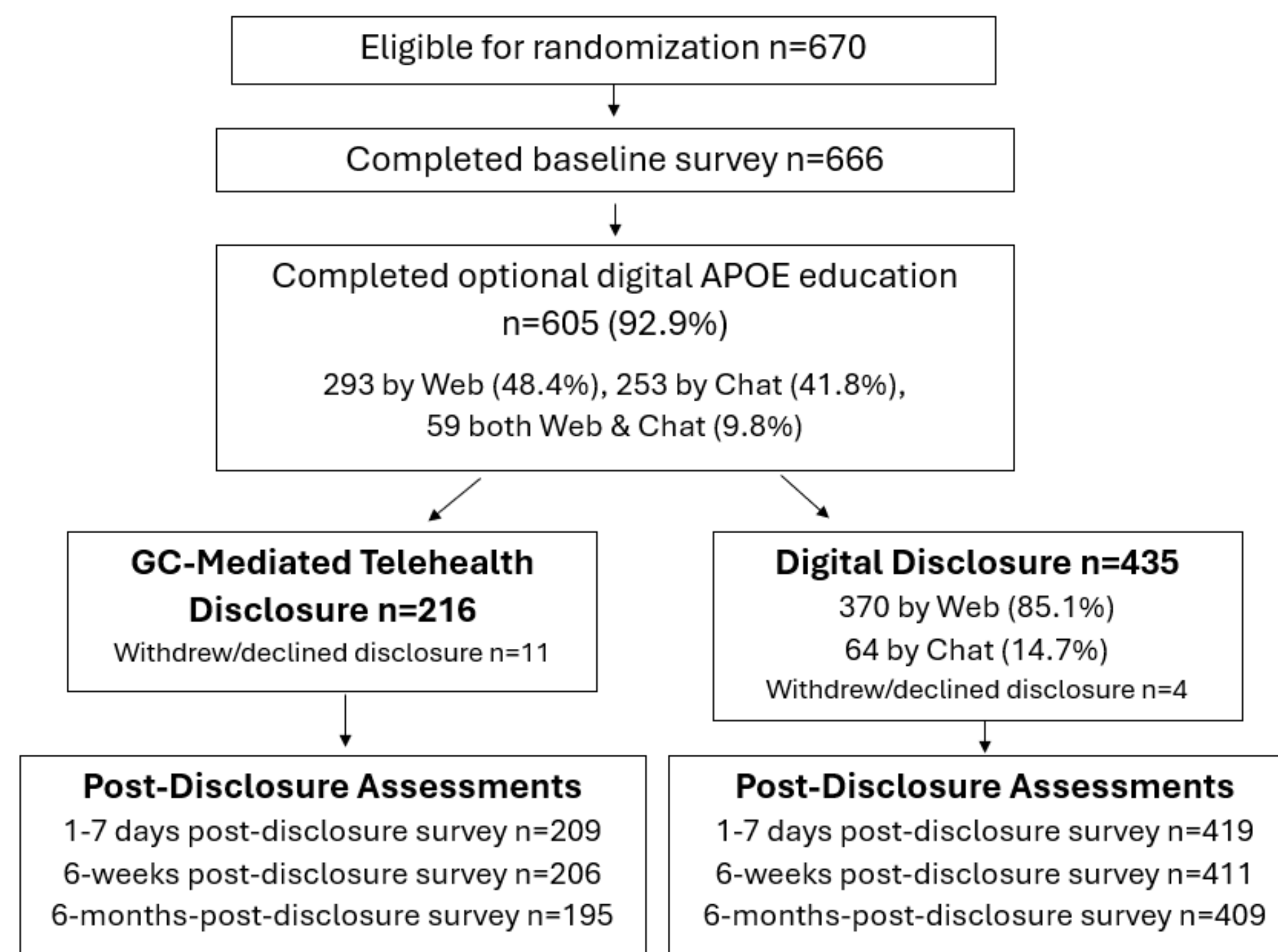
METHODS

- Study Design:** The evaluation of **Self-Mediated Alternatives for Risk Testing Education and Return of results** (eSMARTER) study is a randomized clinical trial to evaluate self-directed, scalable digital return of *APOE* genotype (primary) and pTau-217 blood biomarker (exploratory) results.* (#NCT06459583)
- Sample:** Adults age 60-80 years enrolled in the GeneMatch program, which conducts *APOE* genotyping in CLIA/CAP laboratories. Eligible participants had no prior knowledge of their *APOE* results. Psychological readiness for disclosure was assessed and used as exclusion criteria. Cognitive status was assessed using the Telephone Montreal Cognitive Assessment (T-MoCA).
- Primary non-inferiority outcomes:** Changes in anxiety, genetic knowledge, and disease-specific distress.
- Analysis:** Non-inferiority was concluded if the upper bound of the one-side 1.67% confidence interval did not cross the pre-defined non-inferiority threshold in a direction that would favor usual care (GC-mediated).

Table 1: Overview of Demographics (n=651)	Values
Average Age	67.90 yrs
Sex: Female	439 (67%)
Race: White	585 (91%)
Ethnicity: Not Hispanic	608 (94%)
Average T-MoCA score (0-22)	19.00
<i>APOE</i> Carrier Status	
e4 Homozygote	66 (10%)
e4 Heterozygote	377 (58%)
Non-Carrier	208 (32%)

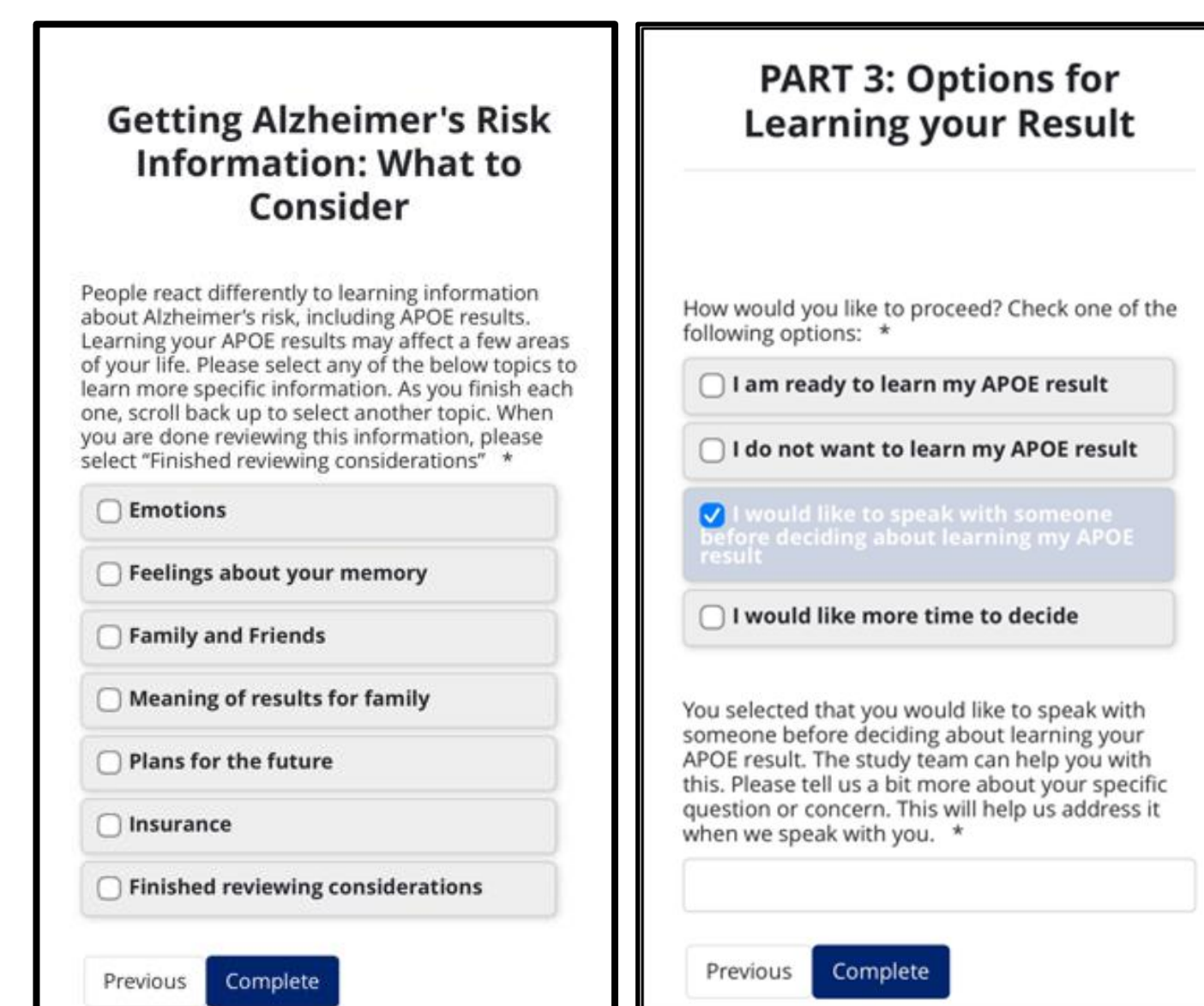
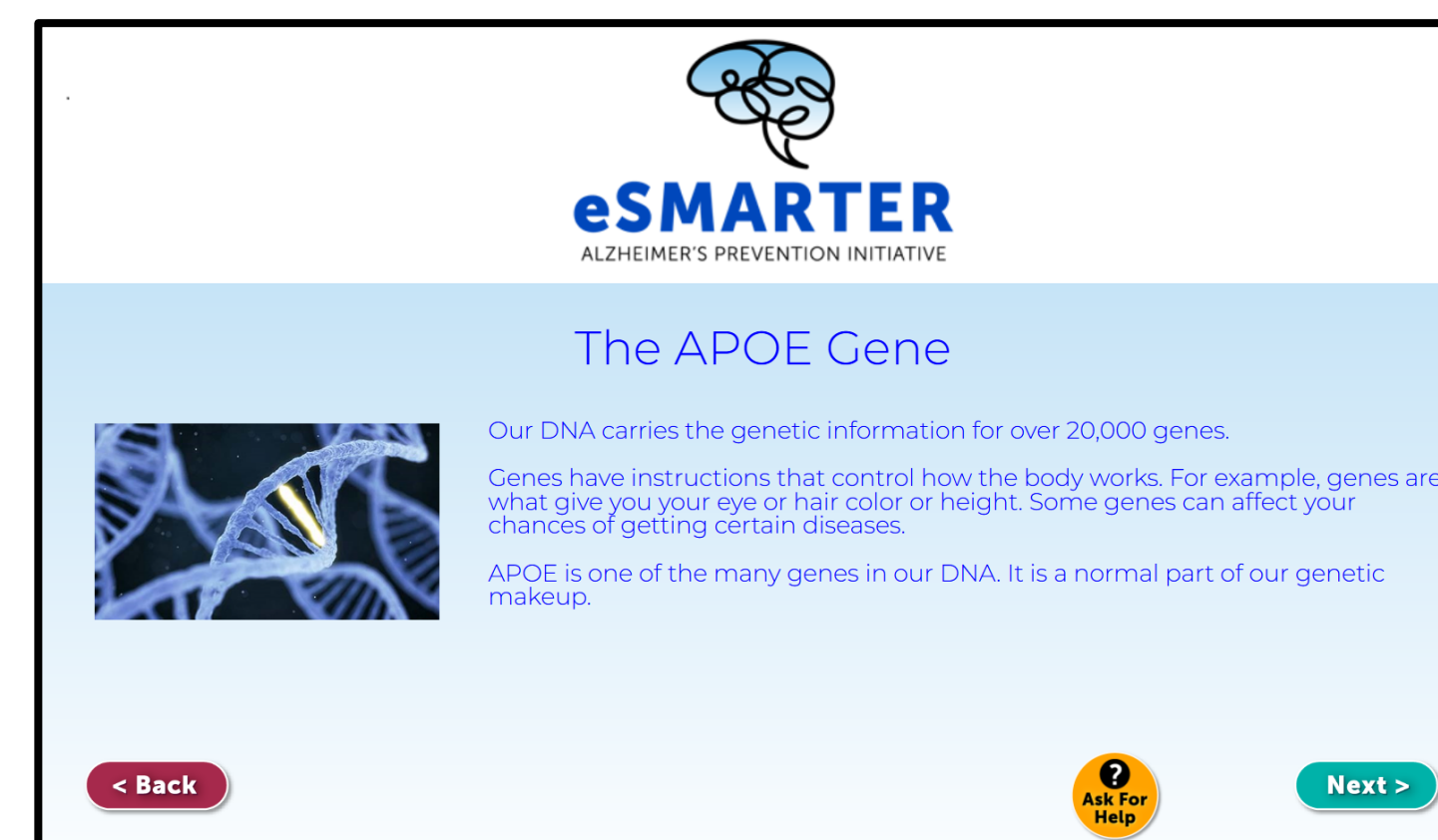
*Please visit the following AAIC posters for more eSMARTER content:
Monday-0529: Erickson, C., et al. & Wednesday-0374: Langbaum, J., et al.

TRIAL CONSORT



Participants were randomized 2:1 to the self-mediated digital arm or GC-mediated telehealth arm.

DIGITAL CONTENT



Example screenshots of the digital tools (website and chat) designed for and utilized in the eSMARTER study for *APOE* education and disclosure.

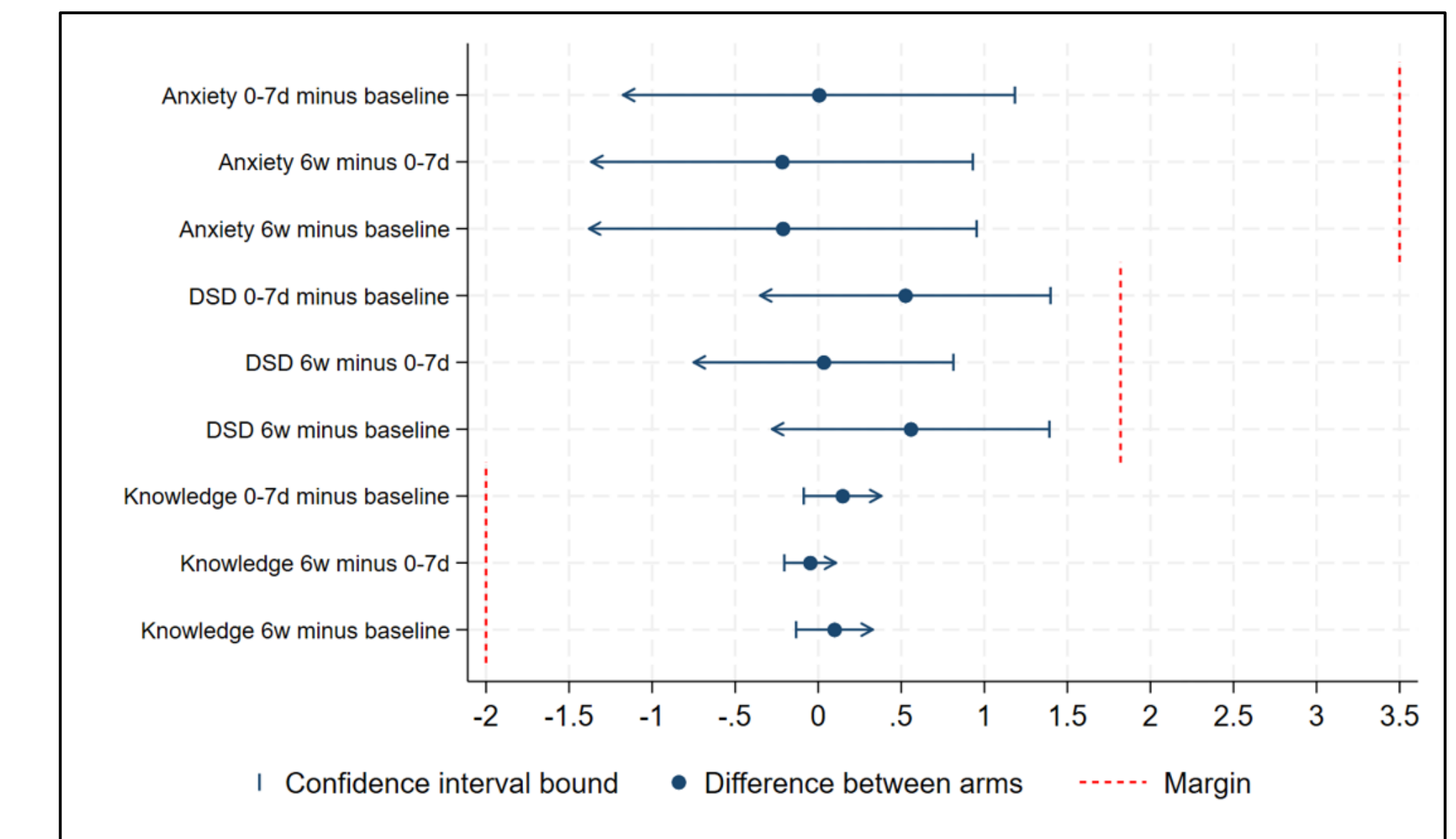
RESULTS

Table 2: Primary Outcomes - Change from Baseline

Outcome	Timepoint Values	GC-Mediated Telehealth n=216	Digital (Web/Chat) n=435	P-value
		Mean (Standard Deviation)		
Genetic Knowledge	Baseline	7.03 (1.26)	7.00 (1.28)	0.7790
	Change to 1-7 days	0.05 (1.29)	0.19 (1.30)	0.1821
	Change to 6 weeks	0.12 (1.29)	0.22 (1.27)	0.3677
Anxiety T-Score	Baseline	47.80 (6.85)	47.56 (7.01)	0.6863
	Change to 1-7 days	-0.74 (6.08)	-0.73 (6.81)	0.9930
	Change to 6 weeks	-0.95 (6.89)	-1.16 (6.35)	0.6977
Disease Specific Distress (DSD)	Baseline	4.44 (5.55)	4.46 (5.03)	0.9632
	Change to 1-7 days	-0.36 (4.13)	0.17 (5.20)	0.2011
	Change to 6 weeks	-1.56 (4.32)	-1.01 (4.82)	0.1552

Genetic knowledge assessed using a modified 8 item scale focused on *APOE*. Anxiety assessed using the PROMIS Anxiety measure. Disease specific distress assessed by 8 items from the Impact of Events Scale (IES).

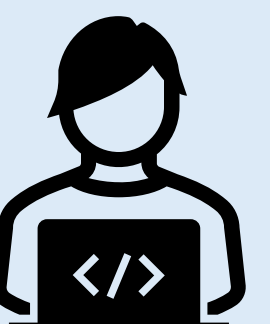
Figure 1: Non-Inferiority Analysis of Primary Outcomes



DISCUSSION



GC-Mediated Telehealth Disclosure vs. Self-Mediated Digital Disclosure



These findings support digital platforms as scalable, non-inferior modalities to return *APOE* genotype results.

- Non-inferiority was met for short-term (1-7 days) primary outcomes including knowledge, anxiety and disease-specific distress.
- Non-inferiority was also met for these outcomes at 6 weeks.
- Next steps include analyses of secondary outcomes, outcomes by genotype and per-protocol, as-treated and moderator analyses.

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