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RESEARCH ARTICLE

Feasibility of virtual Alzheimer's biomarker disclosure: Findings from an observational cohort

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Abstract

Introduction: Increased availability of Alzheimer's disease (AD) biomarker tests provides older adults with opportunities to seek out and learn results. We evaluated the feasibility of virtually returning AD biomarker results.

Methods: Trained study clinicians disclosed amyloid positron emission tomography (PET) results and provided dementia risk-reduction counseling via televideo to cognitively unimpaired participants already enrolled in AD research ($n = 99$; mean age ± SD: 72.0 ± 4.8; 67% women; 95% White; 28% amyloid elevated).

Results: Our study demonstrated acceptable levels of retention (93%), compliance (98%), adherence (98%), clinician competence (97%), education comprehension (quiz scores 14/15), and virtual visit functionality (rating 9.4/10). Depression, anxiety, and suicidality remained low and did not differ by amyloid result.

Discussion: Virtual return of amyloid PET results to cognitively unimpaired research participants is feasible and does not result in increased psychological symptoms. Technological barriers for some participants highlight the need for flexibility. These findings support the use of televideo in AD biomarker disclosure, although our study sample and design have important limitations for generalizability.

KEYWORDS
alzheimer's, amyloid, biomarker disclosure, feasibility, telehealth

1 | INTRODUCTION

As biomarkers of Alzheimer's disease (AD) become more widely available, more people may learn their biomarker results prior to or at the start of symptom onset through participation in clinical drug trials and observational cohort studies, and in clinical settings. Although research participants express a desire to learn their biomarker results,[1] questions around the quantifiability of dementia risk and clinical utility remain, stunting the broader adoption of disclosing AD biomarker results. It is encouraging that prior studies disclosing amyloid positron emission tomography (PET) scan results to cognitively unimpaired older adults have demonstrated that returning such information can be done both clearly and safely.[2,3] Participants express an understanding of their results, and do not report depressive or anxious symptoms after learning results. Most of these studies have been conducted as a part of clinical drug trials (e.g., A4) in which biomarker testing and disclosure is completed as part of eligibility screening for the trial.[4] Existing disclosure studies have important limitations to consider. Samples included are not representative of the broader older adult population in the United States and have been predominantly

non-Hispanic, White, and college educated. In addition, inclusion criteria have excluded people with clinical levels of depression, anxiety, and a history of suicidality. Furthermore, trained clinicians have led the disclosures. With this in mind, it remains important to assess the generalizability of prior results outside of a clinical trial setting to determine if similar outcomes are observed in the absence of a treatment trial, and to consider methods to increase translatability into future clinical practice.

One avenue of health care innovation has focused on the use of telehealth to improve accessibility and manage time constraints. Use of telehealth may expand opportunities for patients undergoing biomarker tests in either observational or clinical trial settings to receive results. Previously, telehealth practices have been used in the return of apolipoprotein E (*APOE*) genetic test results[5,6] and in teleneuropsychology assessment for cognitive impairment.[7–9] In *APOE* disclosure, return of results via telephone did not result in differences in measures of participant anxiety, depression, test-related distress, or recall of result versus in-person disclosure.[6] In assessment for cognitive impairment, neuropsychological assessments administered virtually via televideo software can distinguish between cognitively impaired and unimpaired participants,[9] and it is a valid and reliable alternative to in-person testing.[7] Virtual approaches have been successful in these situations, suggesting that telehealth could be used in the return of AD biomarkers, such as amyloid PET. However, the tolerability and feasibility of virtual AD biomarker disclosure has not yet been assessed.

The Wisconsin Registry for Alzheimer's Prevention[10] (WRAP), a longitudinal observational research cohort enriched for family history of dementia, disclosed amyloid beta (Aβ) PET results to cognitively unimpaired older adult participants and assessed the feasibility as well as the impact of disclosure on psychological well-being, health behaviors, and long-term planning. Each of the visits for this disclosure study were conducted using the telephone or Health Insurance Portability and Accountability Act (HIPAA)–compliant televideo software (note the disclosure visit was always conducted via televideo). Here, we present findings on the feasibility of disclosing amyloid PET results virtually through measures of participation, retention, compliance, adherence, competence, safety, education comprehension, and functionality of virtual visits. These results may inform biomarker disclosure practices with cognitively unimpaired adults in research studies as well as provide considerations for future implementation of AD biomarker disclosure into wider clinical practice.

RESEARCH IN CONTEXT

1. **Systematic Review**: The authors reviewed the literature using traditional (e.g., PubMed and Google Scholar) sources. Although there have not been published studies of virtual amyloid positron emission tomography (PET) disclosure, there is a growing body of work around disclosing Alzheimer's disease (AD) biomarkers, including examples of returning apolipoprotein E (*APOE*) genotype over the phone.
2. **Interpretation**: We demonstrate that virtual return of amyloid PET results to cognitively unimpaired older adults familiar with Alzheimer's research is feasible and may present a new avenue to disclose participant results, although our study has important sample and design limitations. Eligible participants were interested in and enrolled in and completed the study, never expressing worrying post-disclosure psychological symptoms. Including well-trained clinicians to lead disclosure, comprehensive psychological screening, pre-disclosure education, and post-disclosure risk-reduction counseling may have been key elements supporting the study's success. These warrant further exploration.
3. **Future Directions**: Although AD biomarkers are currently cost-prohibitive, imperfect predictors of dementia, and are mostly being disclosed in a research setting, their relevance to clinical settings is increasing.

2 | METHODS

2.1 | Sample

Participants were recruited from WRAP, a longitudinal observational research cohort of largely cognitively unimpaired adults who enrolled in late midlife. The cohort is enriched for parental family history of Alzheimer's disease clinical syndrome.[10] A subset of the cohort had completed an amyloid Pittsburgh compound-B (PiB) PET scan[11,12] within 18 months of study enrollment as a part of the parent WRAP study, were 65 years of age or older, had no active Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnoses (including active major mood disorders, psychotic disorders, alcohol/substance use disorder within the past year; history of bipolar I or schizophrenia spectrum disorders), and did not have a consensus conference diagnosis of mild cognitive impairment (MCI) or dementia from the parent study.[13,14] Participants who met these inclusion criteria were mailed recruitment letters and contacted via telephone by study staff to assess interest in study participation. Approval to conduct this human-subjects research was obtained by the University of Wisconsin-Madison Institutional Review Board. All participants provided informed consent to participate in the study. Study participation was voluntary and participants could decide not to learn their results and withdraw at any time (including prior to disclosure visit).

2.2 | Study design

The Amyloid Disclosure Study included three core study visits comprising an education session, disclosure of amyloid PET scan results, and care planning session focused on reducing modifiable risk factors

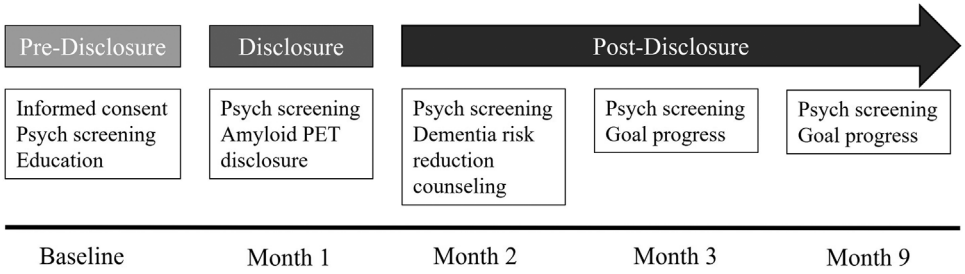


FIGURE 1 Amyloid Disclosure Study visit flow. Participation included six visits across about 9 months of study follow-up.

for dementia, as well as three follow-up phone calls to assess additional research outcomes of interest (Figure 1). All participants spoke English and all visits were conducted in English. In total, study duration was about 9 months. Study staff demonstrated how to use the televideo software. Participants without necessary technology (e.g., internet bandwidth or device), or who preferred onsite visits, were offered to complete the disclosure study visit virtually on campus using a study device to complete a televideo visit with the study clinician in a separate room, and additional study visits via telephone.

2.2.1 | Visit 1: Informed consent, baseline assessment, and education session

During the first study visit, participants met virtually with study staff to review the informed consent document. After providing informed consent, participants completed questionnaires on psychological symptoms (9-item Patient Health Questionnaire [PHQ-9],[15] 10-item Geriatric Anxiety Scale [GAS-10],[16] Columbia-Suicide Severity Rating Scale [C-SSRS][17]), concern about AD,[18] subjective memory,[19] lifespan perspective,[20] attitudes toward medical research,[21] willingness to enroll in research studies, and beliefs about and participation in healthy lifestyle behaviors[22–27] and long-term care planning.[28] Participants were then assessed on their baseline knowledge of AD and meaning of amyloid PET results utilizing a 15-question quiz with multiple choice and true/false questions (Figure 2). Next, participants were guided through a 15-minute interactive presentation providing education on AD and potential amyloid PET results. The same quiz was administered again after the education session. Participants were required to demonstrate adequate understanding (e.g., obtain a quiz score of 12/15 following teach-back) to continue in the study.

2.2.2 | Visit 2: Amyloid PET disclosure ± follow-up

Two weeks to 4 weeks after the initial informed consent and education visit, the study clinician (physician or nurse practitioner) met with participants over televideo either from their home or from a separate room at the clinical research center. The study clinician began by asking pre-disclosure questions, including if any recent stressful life events have occurred, any experiences with AD, how the participant was feeling about learning their amyloid PET result and how prepared they felt, and if they had any questions or concerns to address before learning their result. This pre-disclosure, semi-structured interview allowed clinicians to assess participant readiness and potential psychological impact from learning results. In addition, prior to results disclosure, participants completed the View and Perceptions of Amyloid Imaging questionnaire to characterize reasons for learning their amyloid PET results.[29] After confirming that participants wanted to learn their results, using standardized language, the clinician disclosed the PET scan result (either elevated or non-elevated based on visual rating[12] determined by two neuroradiologists and one neuropsychologist) to the participant. After answering questions, the clinician confirmed participant understanding of the result (e.g., what the result showed, what it meant to the participant) and responded to any additional questions/concerns. Participants were provided with a results summary sheet indicating their PET scan results. One day to 3 days after the disclosure visit, study staff called participants to check-in. At this telephone check-in, participants completed questionnaires to assess for psychological symptoms as well as results-related distress (Impact of Events Scale,[30] Impact of Neuroimaging in AD[31,32]).

2.2.3 | Visit 3: Personalized dementia risk-reduction counseling

About 1 month after disclosure, participants completed one session focused on dementia risk reduction. In addition to general education about dementia risk factors, study staff discussed individual risk factors, asked participants to rate how well they felt they were doing in areas related to brain health (diet, exercise, stress, sleep, cognitive stimulation), and reviewed participant health history and recent biometric, medical lab data available from biennial WRAP visits. Based on these responses, participants chose an area they wanted to improve on, and study clinicians used the SMART goals framework to help them set a specific goal. Study clinicians worked with participants to then standardize their goal into a measurable outcome using the goal-attainment scaling approach.[33] Participants received a goal summary sheet based on their conversation with study staff.

2.2.4 | Telephone visits

Two telephone visits were conducted 1 month and 6 months after the dementia risk-reduction counseling visit. Study coordinators collected

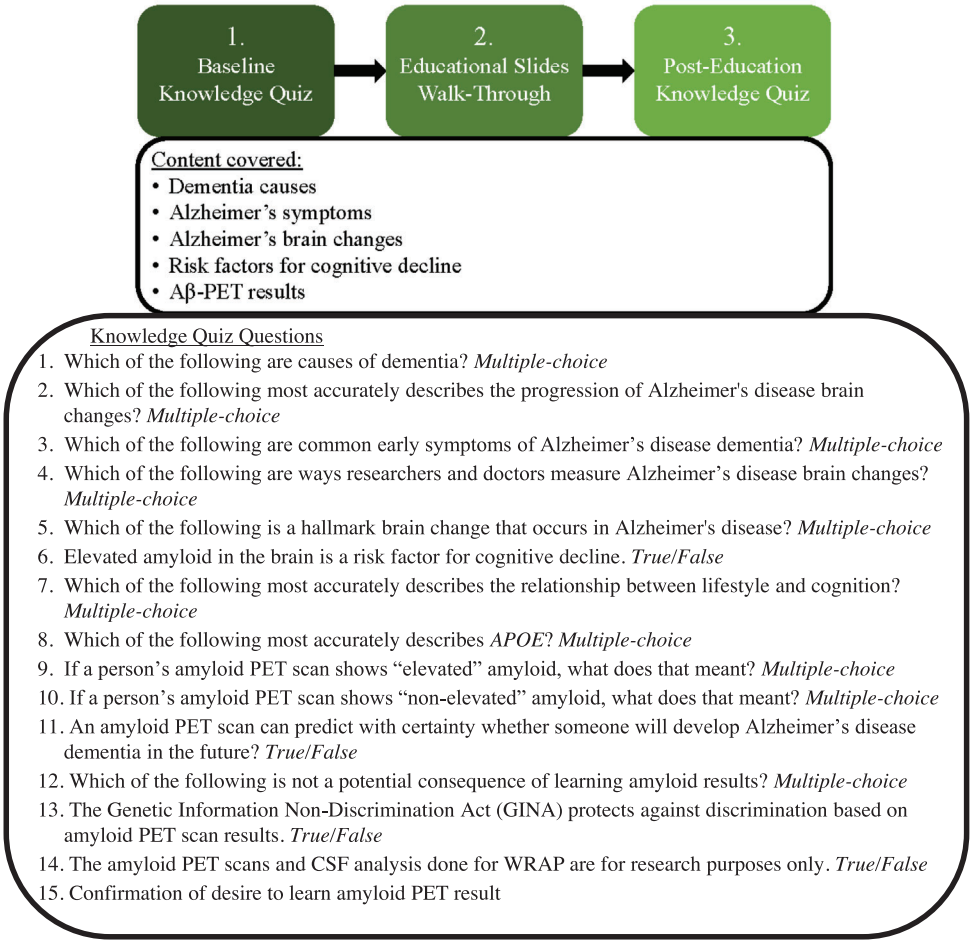


FIGURE 2 Education session visit flow.

measures of psychological symptoms, post-disclosure distress, SMART goal progress, and visit satisfaction.

2.3 | Study feasibility measures

Assessment of virtual disclosure feasibility was determined by measures of participation, retention, compliance with completing study questionnaires, adherence to meeting brain health goals, competence of intervention elements, and safety.[34,35] In addition, we assessed the effectiveness of the education session and functionality of virtual visits.

Participation was measured as the percentage of eligible WRAP participants enrolled into the study (number participants enrolled/number participants recruited).

Retention was measured as the percentage of participants who completed all visits (three televideo and three telephone visits) (number participants completed all visits/number enrolled participants).

Compliance was measured as the percentage of enrolled participants who completed all study questionnaires at each visit (number participants completed all study questionnaires/number enrolled participants).

Adherence was measured as progress on SMART goal set at the dementia risk-reduction counseling visit. At the telephone follow-ups, participants rated their current progress on the SMART goal on a scale of −2 (same as before goal-setting) to 2 (much more than goal). Our study goal was adherence scores ≥−1 (more than activity level before goal-setting) at each follow-up.

Competence of study clinicians was measured for the disclosure visit and the dementia risk-reduction counseling visit by the number of self-reported key elements performed (out of 24; e.g., reviewed visit purpose with participant, reviewed mood assessment scores, and confirmed participant wanted to proceed) and clinician self-report assessment of how the visit went (scores 1–5; 1: "not at all well," 3: "well," 5: "extremely well."). In addition, participants rated their satisfaction with each of the clinician-led visits (scores 1–4; 1: "not at all satisfied," 4: "very much satisfied").

Safety was measured through assessment of mood (PHQ-9[15]), anxiety (GAS-10[16]), and suicidality (C-SRRS[17]). Active suicidal ideation with intent or plan was indicated by a response of "yes" to C-SSRS item 4 or 5, respectively. Severe depression was indicated by PHQ-9 scores ≥20. Severe anxiety was indicated by GAS-10 scores ≥18. Assessments for severe depression or anxiety or active suicidal ideation were

TABLE 1 Sample characteristics.

	Overall	Amyloid elevated	Amyloid non-elevated	*p*-value
Sample size (*n*)	99	28	71	
Age	72.0 ± 4.8	71.1 ± 3.9	72.3 ± 5.1	$p = 0.23$
Sex (% female, *n*)	66.7% (66)	60.7% (17)	69.0% (49)	$p = 0.45$
Bachelor's degree (%, *n*)	69.4% (68)	71.4% (20)	67.6% (48)	$p = 0.78$
Self-identified race (%, *n*)	94.9% (94) White, 4.0% (4) Black or African American, 1.0% (1) Asian	89.3% (25) White, 10.7% (3) Black or African American, 0% Asian	97.2% (69) White, 1.4% (1) Black or African American, 1.4% (1) Asian	$p = 0.27$
Family dementia history (%, *n*)	64.6% (64)	71.4% (20)	62.0% (44)	$p = 0.37$
Baseline PHQ-9 (Range: 0–27)	1.6 ± 1.8	1.5 ± 1.7	1.6 ± 1.8	$p = 0.87$
Baseline GAS-10 (Range: 0–30)	1.9 ± 1.9	2.0 ± 1.8	1.9 ± 2.0	$p = 0.88$

evaluated pre-disclosure (Visit 1, Visit 2) and post-disclosure (1–3 days post-disclosure telephone check-in, Visit 3, 1 month follow-up telephone visit, 6-month follow-up telephone visit).

Education Comprehension was measured by the 15-item knowledge quiz.

Functionality of Virtual Visits was measured by the mean value of the virtual visit quality rating reported by the study staff (value range: 1–10, where 1 = could not use televideo software and 10 = no issues). This rating focused on the extent of technological issues encountered. In addition, we reported any issues that arose during the virtual visits.

2.4 | Statistical analysis

Descriptive statistics (percentages, means) were used to evaluate sample characteristics and feasibility metrics of participation, compliance, adherence, competence, safety, and functionality of virtual visits. Education comprehension was evaluated by comparing within-person differences on pre- and post-education quiz scores using a paired *t*-test. Because the data were not normally distributed, we also performed a Mann-Whitney *U* test. T-tests and chi-square tests were also used to compare sample characteristics between elevated and non-elevated participants. Safety was evaluated using linear mixed-effects regression models including amyloid result (elevated vs non-elevated), time (study visit), and their interaction as predictor variables and PHQ-9 total score or GAS-10 total score as outcome variables. Covariates included gender, age, and family history of dementia. Random effects were allowed to co-vary and included individual intercepts and time-related slopes.

3 | RESULTS

3.1 | Sample characteristics

The final sample of participants who received their amyloid PET results included 99 participants (mean age ± SD = 72.0 ± 4.8; Table 1). The sample was predominantly female (66.7%), college-educated (69.4%), White (94.9%), and with a family history of dementia (64.6%). There were no significant demographic differences between participants with amyloid elevated and non-elevated results.

3.2 | Study feasibility

A summary of the study feasibility results is provided in Table 2.

Participation: Of the 156 participants contacted, 105 chose to enroll (67% participation rate). Twenty-seven participants did not respond to recruitment efforts. Seven participants were ineligible for the study due to either cognitive diagnosis (e.g., three had received a diagnosis of MCI or dementia) or scan date (e.g., four had PET scans completed outside of the 18-month window). Seventeen participants were not interested in completing the study either due to ongoing stress related to the coronavirus disease 2019 (COVID-19) pandemic ($n = 4$), health issues ($n = 3$), only interested in clinical trials ($n = 1$), uninterested in learning amyloid result ($n = 3$), or no reason given ($n = 6$).

Retention: Seven participants withdrew from the study (6.7%); three were withdrawn at the informed consent and education visit (Visit 1) due to not meeting eligibility criteria; and three withdrew at the disclosure visit (Visit 2) prior to learning amyloid PET results based on clinician reported hesitance to learn results following pre-disclosure questions. One participant withdrew after the disclosure visit and 1 to 3 day telephone check-in were completed, and a second participant withdrew after the dementia risk-reduction counseling visit (Visit 3) due to non–study-related health issues (93.3% retention; Retention = (Total enrolled-Withdrew)/Total enrolled).

Compliance: One hundred three of 105 participants fully completed the questionnaires at the informed consent and education visit (98.1% compliance), 98 of 102 participants fully completed the disclosure visit questionnaires (96.1% compliance), 94 of 99 participants fully completed post-disclosure telephone follow-up questionnaires (94.9% compliance), 97 of 98 participants fully completed the dementia risk-reduction counseling visit questionnaires (99.0% compliance), 98 of 98 participants fully completed the post-care planning telephone

TABLE 2 Summary of study feasibility measures.

Feasibility Measure	Analysis	Result
Participation	Percentage of eligible Wisconsin Registry for Alzheimer's Prevention (WRAP) participants enrolled into the study (number participants enrolled/number participants recruited)	**66.9% participation** (105 enrolled/157 contacted)
Retention	Percentage of participants who completed all visits (number participants completed all visits/number enrolled participants).	**93.3% retention** [(105 enrolled-7 withdrew)/105 enrolled]
Compliance	Percentage of enrolled participants who completed all study questionnaires at each visit (number participants completed all study questionnaires/number enrolled participants).	Informed consent/education visit: **98.1% compliance** Disclosure visit: **96.1% compliance** Post-disclosure follow-up: **94.9% compliance** Dementia risk-reduction counseling visit: **99.0% compliance** Post-care planning telephone follow-up: **100% compliance** 6-month follow-up: **99.0% compliance**
Adherence	Progress on SMART goal set at the dementia risk-reduction counseling visit rated on a scale of −2 (same as before goal setting) to 2 (much more than goal).	1-month post risk-reduction counseling visit: **91% adherence** 6-months post risk-reduction counseling visit: **86% adherence**
Clinician competence	Number of self-reported key elements performed at disclosure and risk-reduction counseling visits (out of 24; e.g., reviewed visit purpose with participant, reviewed mood assessment scores, and confirmed participant wanted to proceed) and clinician self-report assessment of how the visit went (scores 1–5; 1: "not at all well," 3: "well," 5: "extremely well."). Furthermore, participants rated their satisfaction with each of the clinician-led visits (scores 1–4; 1: "not at all satisfied," 4: "very much satisfied").	Disclosure visit: >**97% clinician competence** • Average clinician visit rating: 3.9 of 5 • Average participant visit rating: 3.9 of 4 Risk-reduction counseling visit: >**96% clinician competence** • Average clinician visit rating: 4.3 of 5 • Average participant visit rating of 3.3 of 4
·**Safety**	Active suicidal ideation with intent or plan was indicated by a response of "yes" to Columbia Suicide Severity Rating Scale (C-SSRS) item 4 or 5, respectively. Severe depression was indicated by PHQ-9 scores ≥20. Severe anxiety was indicated by GAS-10 scores ≥18. Depression, anxiety, and suicidality were collected pre- and post-disclosure. Linear mixed-effects modeling using depression (PHQ-9) and anxiety (GAS-10) symptoms as outcomes. • Predictors: Amyloid result (elevated vs non-elevated), study visit (i.e., time), and their interaction • Covariates: Gender, age, and family history of dementia • Random effects: Individual intercepts and time-related slopes.	**No participants who learned their results ever expressed severe depression or anxiety, or suicidality after results**. • Patient Health Questionnaire-9 (PHQ-9) and Geriatric Anxiety Scale-10 item version (GAS-10) scores did not statistically significantly change after disclosure nor did they vary by amyloid result, study visit (i.e., time), or the interaction of amyloid result by study visit.
Education comprehension	Within-person differences on pre- and post-education quiz scores using paired *t*-tests. Because the data were not normally distributed, we also performed a Mann-Whitney *U* test.	**Post-education quiz scores were on average 2 points higher than baseline scores** ($T = 12.8$, $df = 140.54$, $p < 0.0001$; $U = 940$, $p < 0.0001$)
Functionality of virtual visits	Mean value of the virtual visit quality rating reported by the study staff (value range: 1–10, where 1 = could not use televideo software and 10 = no issues)	**On average, the virtual visit quality, with regard to technological function, was rated as 9.4 of 10** • Common issues: • Electronic remote consent software dysfunction • Issues and interruptions with televideo connection • Resorting to using a phone to call the participant • Participant difficulty accessing necessary technology • Participant difficulty navigating technology

follow-up questionnaires (100% compliance), and 97 of 98 participants fully completed the 6-month telephone follow-up questionnaires (99.0% compliance).

Adherence: At the telephone visit 1 month after the Dementia Risk-Reduction Counseling visit, 91% of participants indicated they had made progress on their goal above their baseline activity. At the final telephone visit 6 months after the dementia risk-reduction counseling visit, 86% of participants reported making progress on their goal.

Competence: Clinicians leading the disclosure visit on average met 23.5 of 24 essential visit components (>97%) and reported that the visit went "very well" (average score on clinician self-report quality: 3.9/5, median: 4). Participants reported an average satisfaction rating of 3.9 of 4 for the disclosure visit (median: 4, "very much satisfied"). Clinicians leading the dementia risk-reduction counseling visit on average met 23.6 of 24 essential visit components (> 96%) and reported that the visit went "very well" (average score on clinician self-report quality: 4.3/5, median: 4). Participants reported an average satisfaction rating of 3.3 of 4 for care planning visit (median: 4, "very much satisfied").

Safety: Only two participants expressed suicidality (related to ongoing mental health disorder) or had a history of suicide attempt, and they were withdrawn at the first visit prior to the disclosure visit. No participants who learned their results ever expressed severe depression or anxiety or suicidality after results. At the follow-up 1 to 3 days post-disclosure, PHQ-9 scores were on average 1.2 ± 1.6 of 27 (range: 0–7) and GAS-10 scores were 1.3 ± 1.6 of 30 (range: 0–7). Across the 6 months of follow-up after disclosure, PHQ-9 and GAS-10 scores remained low for both individuals with amyloid elevated and non-elevated results (Figure 3). The amyloid result by study visit interaction was not a significant predictor of PHQ-9 ($p = 0.66$) or GAS-10 scores ($p = 0.87$) (Figure 3). Gender (β: 0.92, $p = 0.001$), age (β: 0.40, $p = 0.003$), and family history (β: 0.57, $p = 0.03$) all significantly predicted PHQ-9 scores. There were no significant predictors of GAS-10 scores.

Education Comprehension: Post-education quiz scores were on average 2 points higher than baseline scores (T = 9.48, df = 197.65, $p < 0.0001$; U = 940, $p < 0.0001$) (Figure 4).

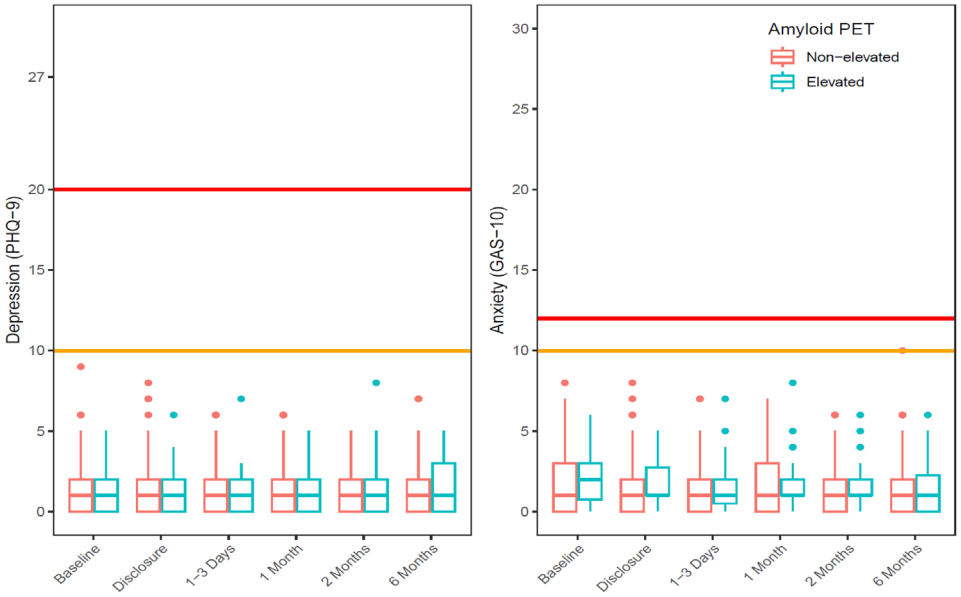
Functionality of Virtual Visits: Study staff rated the quality of 508 virtual visits across the study. On average, the virtual visit quality, with regard to technological function, was rated as 9.4 of 10, indicating high-quality. The education visit average was 8.95, disclosure visit average was 9.43, post-disclosure telephone check-in visit was 9.85, counseling visit average was 8.78, 1-month telephone visit average was 9.43, and 6-month telephone visit average was 9.97. The most common issues reported during the virtual visits included electronic remote consent software dysfunction, issues and interruptions with televideo connection, resorting to using a phone to call the participant, participant difficulty accessing necessary technology, and participant difficulty navigating technology (Table 3). These issues occurred at maximum 12% of the time and were more prevalent at the first visit than at later visits. Thirty-six of 102 participants (35%) came onsite for the disclosure televideo visit and completed remaining visits via telephone due to technological inaccessibility ($n = 19$, 53%) or personal preference ($n = 13$, 36%) [$n = 4$ (11%) were completed at beginning of study before at-home virtual disclosure visit was offered]. Sixty-six of 102 participants (65%) completed visits from home via televideo software.

TABLE 3 Summary of challenges encountered during virtual visits.

Virtual visit issue	Frequency of issue at each visit
E-consent software dysfunction	Consent/education: 12 Rest of visits n/a
Audio interruption (incl. lagging, spotty connection, or dropped call)	Consent/education: 9 Amyloid PET disclosure: 5 Post-disclosure telephone follow-up: 2 Dementia risk-reduction counseling: 8 Post-counseling telephone follow-up: 4 6-month telephone follow-up: 0
Video dysfunction (incl. lagging, spotty connection, difficulty sharing screen)	Consent/education: 11 Amyloid PET disclosure: 6 Dementia risk-reduction counseling: 9 Telephone visits: n/a
Had to use phone because of issues experienced	Consent/education: 6 Amyloid PET disclosure: 3 Dementia risk-reduction counseling: 9 Telephone visits: n/a
Participant difficulty accessing necessary technology (computer, WiFi, phone)	Consent/education: 6 Amyloid PET disclosure: 1 Post-disclosure telephone follow-up: 0 Dementia risk-reduction counseling: 2 Post-counseling telephone follow-up: 0 6-month telephone follow-up: 0
Participant difficulty navigating computer	Consent/education: 4 Amyloid PET disclosure: 0 Dementia risk-reduction counseling: 1 Telephone visits: n/a

4 | DISCUSSION

Overall, the Amyloid Disclosure Study demonstrated that virtual return of amyloid PET results to cognitively unimpaired older adult research participants is feasible and may present a new avenue to disclose results to participants. Eligible participants were interested in the study, enrolled, and remained in the study. Virtual data collection was successful and streamlined the data entry process. Study clinicians and staff competently led the disclosure and dementia risk-reduction counseling visits. Both study clinicians/staff and participants reported that these visits went well. Participants unsurprisingly entered the study with a lot of AD knowledge (average baseline quiz score: 12/15). This is likely due to participants already being enrolled in ongoing



	Depression (PHQ-9)			Anxiety (GAS-10)		
Predictors	Estimates	CI	p	Estimates	CI	p
(Intercept)	0.51	-0.12 – 1.14	0.111	1.01	0.30 – 1.71	0.005
Gender	0.92	0.39 – 1.45	0.001	0.51	-0.12 – 1.14	0.111
Age, centered	0.40	0.14 – 0.65	0.003	0.16	-0.15 – 0.46	0.309
Family History of Dementia	0.57	0.04 – 1.09	0.034	0.53	-0.09 – 1.15	0.095
Study Visit	-0.03	-0.08 – 0.03	0.303	-0.03	-0.09 – 0.02	0.256
Amyloid Result	-0.00	-0.77 – 0.76	0.991	0.15	-0.62 – 0.93	0.702
Study Visit x Amyloid Result	0.02	-0.08 – 0.13	0.660	-0.01	-0.11 – 0.09	0.869

FIGURE 3 (Top) Box plots of 9-item Patient Health Questionnaire and 10-item Geriatric Anxiety Scale scores at baseline, disclosure visit, 1-month post-disclosure, 2 months post-disclosure, and 6 months post-disclosure for participants with an elevated and non-elevated amyloid positron emission tomography (PET) result. Thresholds for moderate depression (PHQ-9: 10) and anxiety (GAS-10: 10) are designated by the yellow line. Thresholds for severe depression (PHQ-9: 20) and anxiety (GAS-10: 12) are designated as the red line. (Bottom) Statistical output for linear mixed-effects regression models for 9-item Patient Health Questionnaire and 10-item Geriatric Anxiety Scale (Study Visit represents time; Amyloid Result = elevated or non-elevated).

AD research. However, post-education quiz scores were on average 2 points higher than baseline, suggesting that participants still benefitted from the education session. Most participants elected at-home virtual disclosure visits rather than coming to the research center for an onsite, virtual disclosure visit. Participants who lacked access to necessary technology and were unable to complete visits at home or preferred to come onsite for disclosure highlighted the need for multiple modalities to be offered. Learning AD biomarker information is highly personal, and, therefore, it will be important to maintain patient-centric practices and offer flexibility in how people learn results (e.g., at home or in clinic).

Most importantly, virtual disclosure was safe. No participants exceeded clinically significant thresholds for severe depression, severe anxiety, or suicidality measures at any visit. Scores remained low throughout the study and there were no significant increases in psychological symptom scores across the study. There were also no differences in measures between those who learned elevated or non-elevated results at any of the visits. These results match prior work demonstrating the safety of returning AD risk information to individuals without active psychological disorders.[3,20,32,36–39] Three participants passed pre-disclosure psychological screeners but were identified as "high risk" during the clinician semi-structured pre-disclosure interview. Following further discussion with the clinician, these participants elected to opt out of learning their results. These experiences demonstrate the potential benefit of having a semi-structured interview in addition to psychological screening questionnaires and trained clinicians leading disclosure visits.

The COVID-19 pandemic accelerated adoption of virtual methods in clinical and research settings, including its use in this study.[40] With regard to the virtual nature of the study, visits went well with minimal disruptions due to technological issues. Sixty-five percent of participants completed visits from home using televideo software, and 35%

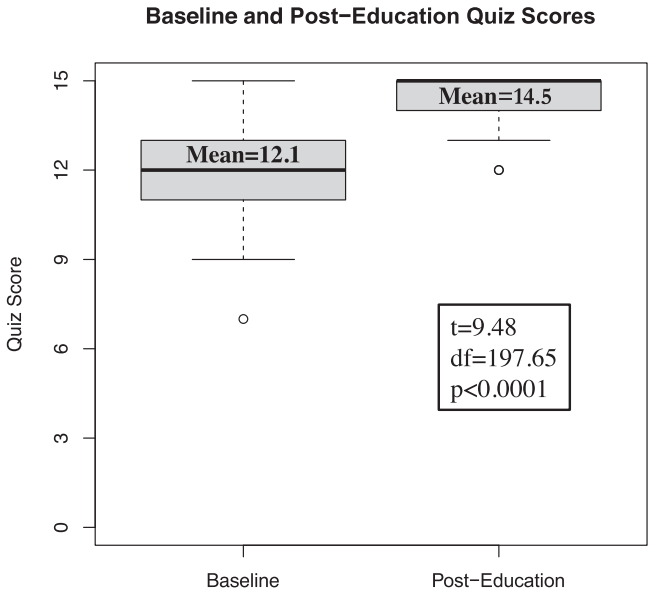


FIGURE 4 Box plots of pre- and post-education quiz scores.

of participants completed the amyloid PET disclosure visit via televideo at the research center and other visits via telephone due to personal preference or lack of access to device or adequate internet bandwidth. Study coordinators reported that the virtual components of each visit went well. Unsurprisingly, the telephone follow-up visits were ranked higher than the visits that incorporated televideo. This is likely due to challenges related to sustaining a solid connection throughout the visits that required video and screen sharing. The most common issues reported included disruptions with the audio and video. It is encouraging that there were minimal reports of participant difficulty in navigating the technology used for the visits. On the whole, our findings suggest that the virtual return of AD biomarker information can be feasible. Virtual disclosure may increase access for participants to receive biomarker results in future studies or in a clinical setting. Although virtual visits can reduce participant burden for travel, and even increase a participant's comfort as they are able to learn potentially sensitive results from the comfort of their homes,[40] exclusively offering virtual visits may exacerbate health disparities and not match personal preference. The technology necessary for telehealth visits is expensive, can be challenging to learn to use, and is not available in all communities, especially in rural areas. In addition, some people may prefer to learn their results in-person. For these reasons, individuals should be able to choose how they learn their results, virtually or in-person.

The Amyloid Disclosure Study has important limitations to consider. First, we amended our protocol throughout data collection. This was done to be responsive to evolving COVID-19 safety protocols and to reduce participant burden. Second, because we are using a convenience sample drawn from a longitudinal, observational AD research study, and all participants elected to participate in a study about disclosure, and because our study sample is predominantly White, college educated, and has a family history of dementia, the generalizability of results is constrained. Third, participants were screened and excluded for current depression and history of suicidality. It will be important to explore the impact of AD biomarker results disclosure in more representative samples and made up of individuals not intimately familiar with AD research. This will be particularly imperative for the continuation of using effective education materials and assessments. Fourth, the process described includes ample time with participants to ensure their safety and understanding and is likely not scalable in its entirety for clinical practice. Elements of the disclosure process implemented in the Amyloid Disclosure Study likely contributed to its success. These include having a well-trained clinician lead disclosure, psychological screening, an education session, and importantly the risk-reduction counseling visit, which may have given participants actionable steps after disclosure. It is also important to acknowledge that this study is not a randomized controlled trial and there was no option to learn results in-person. Despite these limitations, this study provides important preliminary information regarding the feasibility of virtual AD biomarker disclosure.

5 | CONCLUSION

Although our study has important limitations regarding the structuring, resources required, and sample used, findings from the Amyloid Disclosure Study support that conducting AD biomarker disclosure remotely is feasible. AD biomarkers are currently cost-prohibitive, imperfect predictors of dementia, and are mostly being disclosed in a research setting; however, their relevance to clinical settings is increasing as advancements improve clinical validity and utility and reduce testing costs,[41] and as disease-modifying treatments that target AD pathology become accessible. Developing best practices for disclosure, especially virtually, will be necessary to maintain patient safety, increase self-efficacy,[42] and control health care costs.[43]

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CONFLICT OF INTEREST STATEMENT

S.C.J. has in the past 2 years served on advisory boards to Roche Diagnostics, Prothena, AlzPath, Merck, and Eisai. His institution has received research funding from Cerveau Technologies. The rest of the authors have no relevant conflicts of interest to disclose. Author disclosures are available in the Supporting Information.

CONSENT STATEMENT

All study activities were approved by the University of Wisconsin-Madison Institutional Review Board. All human subjects provided written informed consent.

REFERENCES

1. Stites SD. Cognitively healthy individuals want to know their risk for Alzheimer's disease: what should we do? *J Alzheim Dis*. 2018;62(2):499-501. doi:10.3233/jad-171089
2. de Wilde A, van Buchem MM, Otten RHJ, et al. Disclosure of amyloid positron emission tomography results to individuals without dementia: a systematic review. *Alzheim Res Ther*. 2018;10. doi:10.1186/s13195-018-0398-3
3. Erickson CM, Chin NA, Johnson SC, Gleason CE, Clark LR. Disclosure of preclinical Alzheimer's disease biomarker results in research and clinical settings: why, how, and what we still need to know. *Alzheimers Dement (Amst)*. 2021;13(1):e12150. doi:10.1002/dad2.12150
4. Harkins K, Sankar P, Sperling R, et al. Development of a process to disclose amyloid imaging results to cognitively normal older adult research participants. *Alzheimers Res Ther*. 2015;7(1):26. doi:10.1186/s13195-015-0112-7
5. Largent EA, Bhardwaj T, Abera M, et al. Disclosing genetic risk of Alzheimer's disease to cognitively unimpaired older adults: findings from the study of knowledge and reactions to APOE Testing (SOKRATES II). *J Alzheimers Dis*. 2021;84(3):1015-1028. doi:10.3233/JAD-210675
6. Christensen KD, Uhlmann WR, Roberts JS, et al. A randomized controlled trial of disclosing genetic risk information for Alzheimer disease via telephone. *Genet Med*. 2018;20(1):132-141. doi:10.1038/gim.2017.103
7. Cullum CM, Hynan LS, Grosch M, Parikh M, Weiner MF. Teleneuropsychology: evidence for video teleconference-based neuropsychological assessment. *J Int Neuropsychol Soc*. 2014;20(10):1028-1033. doi:10.1017/S1355617714000873
8. Kitaigorodsky M, Loewenstein D, Curiel Cid R, Crocco E, Gorman K, González-Jiménez C. A teleneuropsychology protocol for the cognitive assessment of older adults during COVID-19. *Front Psychol*. 2021;12:651136. doi:10.3389/fpsyg.2021.651136
9. Wadsworth HE, Dhima K, Womack KB, et al. Validity of teleneuropsychological assessment in older patients with cognitive disorders. *Arch Clin Neuropsychol*. 2018;33(8):1040-1045. doi:10.1093/arclin/acx140
10. Johnson SC, Koscik RL, Jonaitis EM, et al. The wisconsin registry for Alzheimer's prevention: a review of findings and current directions. *Alzheimers Dement (Amst)*. 2017;10:130-142. doi:10.1016/j.dadm.2017.11.007
11. Racine AM, Clark LR, Berman SE, et al. Associations between performance on an abbreviated cogstate battery, other measures of cognitive function, and biomarkers in people at risk for Alzheimer's disease. *J Alzheimers Dis*. 2016;54(4):1395-1408. doi:10.3233/JAD-160528
12. Johnson SC, Christian BT, Okonkwo OC, et al. Amyloid burden and neural function in people at risk for Alzheimer's disease. *Neurobiol Aging*. 2014;35(3):576-584. doi:10.1016/j.neurobiolaging.2013.09.028
13. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):270-279. doi:10.1016/j.jalz.2011.03.008
14. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):263-269. doi:10.1016/j.jalz.2011.03.005
15. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613. doi:10.1046/j.1525-1497.2001.016009606.x
16. Mueller AE, Segal DL, Gavett B, et al. Geriatric Anxiety Scale: item response theory analysis, differential item functioning, and creation of a ten-item short form (GAS-10). *Int Psychogeriatr*. 2015;27(7):1099-1111. doi:10.1017/S1041610214000210
17. Posner K, Brown GK, Stanley B, et al. The Columbia–suicide severity rating scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. *Am J Psychiatry*. 2011;168(12):1266-1277. doi:10.1176/appi.ajp.2011.10111704
18. Roberts JS, Connell CM. Illness representations among first-degree relatives of people with Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2000;14(3):129-136, Discussion 127-128. doi:10.1097/00002093-200007000-00003
19. Gilewski MJ, Zelinski EM, Schaie KW. The Memory Functioning Questionnaire for assessment of memory complaints in adulthood and old age. *Psychol Aging*. 1990;5(4):482-490. doi:10.1037//0882-7974.5.4.482
20. Grill JD, Raman R, Ernstrom K, et al. Short-term psychological outcomes of disclosing amyloid imaging results to research participants who do not have cognitive impairment. *JAMA Neurology*. 2020;77(12):1504-1513. doi:10.1001/jamaneurol.2020.2734
21. Rubright JD, Cary MS, Karlawish JH, Kim SYH. Measuring how people view biomedical research: reliability and validity analysis of the research attitudes questionnaire. *J Empir Res Hum Res Ethics*. 2011;6(1):63-68. doi:10.1525/jer.2011.6.1.63
22. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Health Promot*. 1997;12(1):38-48. doi:10.4278/0890-1171-12.1.38
23. Johns MW. A new method for measuring daytime sleepiness: the epworth sleepiness scale. *Sleep*. 1991;14(6):540-545. doi:10.1093/sleep/14.6.540
24. Stewart AL, Mills KM, King AC, Haskell WL, Gillis D, Ritter PL. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. *Med Sci Sports Exerc*. 2001;33(7):1126-1141. doi:10.1097/00005768-200107000-00010
25. Schinka JA, McBride A, Vanderploeg RD, Tennyson K, Borenstein AR, Mortimer JA. Florida cognitive activities scale: initial development and validation. *J Int Neuropsychol Soc*. 2005;11(1):108-116. doi:10.1017/S1355617705050125
26. Morris MC, Tangney CC, Wang Y, et al. MIND diet slows cognitive decline with aging. *Alzheimers Dement*. 2015;11(9):1015-1022. doi:10.1016/j.jalz.2015.04.011
27. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-1395. doi:10.1249/01.MSS.0000078924.61453.FB
28. Sörensen S, Pinquart M. Developing a measure of older adults' preparation for future care needs. *Int J Aging Hum Dev*. 2001;53(2):137-165. doi:10.2190/1R0D-30TC-F4K1-F0DW
29. Ryan MM, Gillen DL, Grill JD. Reasons for undergoing amyloid imaging among cognitively unimpaired older adults. *Ann Clin Transl Neurol*. 2021;8(8):1646-1655. doi:10.1002/acn3.51414
30. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. *Psychosom Med*. 1979;41(3):209-218. doi:10.1097/00006842-197905000-00004
31. Chung WW, Chen CA, Cupples LA, et al. A new scale measuring psychological impact of genetic susceptibility testing for Alzheimer's disease. *Alzheimer Dis Assoc Disord*. 2009;23(1):50-56.
32. Burns JM, Johnson DK, Liebmann EP, Bothwell RJ, Morris JK, Vidoni ED. Safety of disclosing amyloid status in cognitively normal older adults. *Alzheimers Dement*. 2017;13(9):1024-1030. doi:10.1016/j.jalz.2017.01.022

33. Bovend'Eerdt TJH, Botell RE, Wade DT. Writing SMART rehabilitation goals and achieving goal attainment scaling: a practical guide. *Clin Rehabil*. 2009;23(4):352-361. doi:10.1177/0269215508101741
34. Lancaster GA, Thabane L. Guidelines for reporting non-randomised pilot and feasibility studies. *Pilot Feasibility Stud*. 2019;5(1):114. doi:10.1186/s40814-019-0499-1
35. El-Kotob R, Giangregorio LM. Pilot and feasibility studies in exercise, physical activity, or rehabilitation research. *Pilot Feasibility Stud*. 2018;4(1):137. doi:10.1186/s40814-018-0326-0
36. de Wilde A, van Buchem MM, Otten RHJ, et al. Disclosure of amyloid positron emission tomography results to individuals without dementia: a systematic review. *Alzheimers Res Ther*. 2018;10:72. doi:10.1186/s13195-018-0398-3
37. Lim YY, Maruff P, Getter C, Snyder PJ. Disclosure of positron emission tomography amyloid imaging results: a preliminary study of safety and tolerability. *Alzheimers Dement*. 2016;12(4):454-458. doi:10.1016/j.jalz.2015.09.005
38. Grill JD, Cox CG, Harkins K, Karlawish J. Reactions to learning a "not elevated" amyloid PET result in a preclinical Alzheimer's disease trial. *Alzheimers Res Ther*. 2018;10:125. doi:10.1186/s13195-018-0452-1
39. Wake T, Tabuchi H, Funaki K, et al. The psychological impact of disclosing amyloid status to Japanese elderly: a preliminary study on asymptomatic patients with subjective cognitive decline. *Int Psychogeriatr*. 2018;30(5):635-639. doi:10.1017/S1041610217002204
40. Erickson CM, Chin NA, Coughlin DM, et al. Virtual disclosure of preclinical Alzheimer's biomarkers: preliminary experiences. *J Am Geriatr Soc*. 2021;69(7):2044-2047. doi:10.1111/jgs.17184
41. Largent EA, Wexler A, Karlawish J. The future is P-Tau—anticipating direct-to-consumer Alzheimer disease blood tests. *JAMA Neurology*. 2021;78(4):379-380. doi:10.1001/jamaneurol.2020.4835
42. Walter S, Taylor A, Tyrone J, et al. Disclosing individual results in dementia research: a proposed study participant's bill of rights. *J Alzheimers Dis*. 2022;90(3):945-952. doi:10.3233/JAD-220810
43. Erickson CM, Clark LR, Ketchum FB, Chin NA, Gleason CE, Largent EA. Implications of preclinical Alzheimer's disease biomarker disclosure for US policy and society. *Alzheimers Dement (Amst)*. 2022;14(1):e12339. doi:10.1002/dad2.12339

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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