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Return of Research Results Across the Alzheimer's Disease Research Centers Network

--Manuscript Draft--

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Abstract:	INTRODUCTION The Consortium for Clarity in Alzheimer's Disease and Related Dementias Through Imaging (CLARiTI) Return of Results Core will develop tools and a framework for disclosing individual results at Alzheimer's Disease Research Centers (ADRCs). An understanding of current disclosure practices is necessary to generate this protocol. METHODS All 37 ADRCs received a survey between January and April 2024; 36 provided valid responses. RESULTS Most ADRCs disclose diagnosis and cognitive results to participants with impairment, and disclosure of biomarker data (e.g., amyloid and tau PET) has accelerated since 2019. Disclosure to unimpaired participants has also increased since 2019. Motivators for disclosure include to thank participants, for retention, and to inform healthcare decisions. Barriers include limited expertise and infrastructure, concerns about clinical actionability, and risks to participants. DISCUSSION The ADRC network is invested in sharing research results. While some concerns remain, CLARiTI will critically evaluate a standardized approach to sharing these results.

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Cover Letter

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May 20, 2025

Dear Drs. Welsh-Bohmer, Saykin, Biber, and La Joie,

We are pleased to resubmit our revised research article entitled "*Return of Individual Neuropsychological and Biomarker Results Across the Alzheimer's Disease Research Centers Network: Survey of Current Practices*" for consideration for the Special Issue in *Alzheimer's & Dementia* Celebrating the 40th Anniversary of the Alzheimer's Disease Research Centers (ADRC) Program and the 25th Anniversary of the National Alzheimer's Coordinating Center. We are very appreciative of the thoughtful comments from reviewers. As you will see in the attached 'Response to Reviewers' document, we have provided point-by-point responses and made edits to the paper accordingly. We are confident that the revised version is significantly improved and hope you and the reviewers feel the same.

As with the original submission, we confirm that this work is original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere. All authors have contributed substantively to the work and agree with the presented findings. Disclosures are appropriately described in the manuscript per the journal policy. This work was accomplished through the Alzheimer's Disease Research Center Consortium for Clarity in Alzheimer's Disease through Imaging (CLARiTI) project. It was supported by the NIA U01AG082350, the National Alzheimer's Coordinating Center (NIA/NIH U24AG072122), and the contributing ADRCs.

In this revised paper, we discuss the results of a cross-Center survey of current practices around returning individual research results, including cognitive results, genetic data, and biomarker results. We compare changes in disclosure practices over the past five years, using a prior survey conducted by the Advisory Group on Risk Evidence Education in Dementia (AGREED) as comparison. We also expand on the prior survey by providing detailed information regarding current frameworks for disclosure, as well as factors motivating or deterring sites from disclosing amyloid and tau imaging results. To our knowledge, this is the first paper that provides a comprehensive review of current ADRC protocols and will critically inform practices both in CLARiTI and beyond. Given the cross-Center participation in and impact of this manuscript, we are confident that the submission is well-aligned with the Special Issue and relevant for your readership.

Please address all correspondence concerning this manuscript to me at rahmanam@umich.edu.

Thank you for your consideration of this manuscript.

Sincerely,

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Assistant Professor
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Response to Reviewers

Thank you to the reviewers for taking the time to provide constructive feedback and suggestions. We are pleased that reviewers agreed on the importance of the manuscript for the field. We have addressed each comment or suggestion and provided point-by-point responses below.

Reviewer #1

- **Introduction and Discussion section: As described, the Consortium aims to develop standards and protocols for disclosure in a research setting. But will this be the only aim? The overarching goal will finally be the implementation of protocols and standards for informing/counseling (this is not taken into account by the authors, but serves as the basis for informed consent in research and clinical settings) and disclosure in clinical practice. Developing the toolkits for research purposes is the first step for piloting standards and protocols that, at a later stage, will need to be translated to memory clinics, as the decision for/against biomarker testing for checking the eligibility for DMTs and the respective biomarker test result disclosure will eventually be part of the clinical routine). I think that the manuscript lacks this contextual embedding.**
    - Thank you for this suggestion to highlight the larger potential impact of the CLARiTI Return of Results Core and Toolkit on clinical settings. While we feel strongly that protocols for returning results must differ based on the context (e.g., biomarkers used in research are often exploratory; available support and number of touch-points with participants before, during, and after disclosure is more limited in research; researchers often have less medical and contextual information about the participant), we agree that the larger goals of the CLARiTI ROR will impact clinical disclosure. Additionally, the information presented in the manuscript provides a parallel of clinical disclosure changes over the past few years. While we are somewhat restricted by word limit for the introduction, we have therefore added the following comments to the Background on pages 5 and 6:

      "The Toolkit will provide and evaluate the effectiveness of pre-test education to support participants in making informed decisions about learning their results. Additionally, training materials and templates for communicating complex biomarker information will be offered. This work has the potential to improve recruitment and retention, build trust with research participants, and leverage the ADRC network in collecting detailed post-disclosure outcomes data in a national sample. Results will also inform biomarker disclosure approaches in clinical settings, where imaging and plasma biomarkers are becoming increasingly common for the purpose of etiologic clarification and determining eligibility for DMTs."

- We have also added reference to this larger context in the Discussion (page 18, last paragraph):
  "Given the rapid development of AD biomarkers and therapeutics, several study directions remain important within the ADRC network, throughout ADRD clinical research, and in clinical settings in which biomarkers are and will be implemented."

- **How can the findings from this valuable survey inform our clinical work? What do we already know about counseling and disclosure practices outside the research setting? I am aware that the main focus of this manuscript is the research setting, but I would strongly recommend considering literature that has already been published on this issue, combining findings from research and clinical settings, and reflecting these in the Discussion section.**
  - We appreciate the suggestion to incorporate more information about how our results may inform clinical settings. We aimed to be transparent about the ways in which the Alzheimer's Disease Research Centers differ from other research settings and, to a greater extent, clinical settings. We felt that it would be beyond the scope of this paper to comment on how disclosure might happen in clinical settings given these differences. However, we have significantly revised our discussion section (starting on page 14), to address how results may parallel or even translate to the clinic, incorporating much of the suggested literature including the publications by Hendricksen et al (2023) and Perry et al. (2024). We have reformatted this section to address disclosure across the cognitive spectrum, motivations and barriers for returning results, and components of PET disclosure protocols.

- **Page 19, lines 27 - 51: Please refer to research groups that have already started to develop toolkits for counseling/disclosure in the context of AD biomarker testing and discuss the relevance of the preliminary work for your toolkit:**
  - **A publication and topics for a training module for professionals and a protocol for counseling on biomarker testing: Perry, J., Brose, J. and Radenbach, K. (2023) 'Well Advised',**
    https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdoi.org%2F10.1024%2F1662-9647%2Fa000318&data=05%7C02%7Crahmanam%40med.umich.edu%7Cdcf0d4822e4247a7cebc08dd80ce6237%7C1f41d613d3a14ead918d2a25b10de330%7C0%7C0%7C638808346103863435%7CUnknown%7CTWFpbGZsb3d8eyJFbXB0eU1hcGkiOnRydWUsIlYiOiIwLjAuMDAwMCIsIlAiOiJXaW4zMiIsIkFOIjoiTWFpbCIsIldUIjoyfQ%3D%3D%7C0%7C%7C%7C&sdat

a=TDRRZ5vsV%2BgLNU%2FnVr7JnjFWN3%2BbiCoFD9e6udvmNB0%3D&reserved=0. Hogrefe AG . doi: 10.1024/1662-9647/A000318.

- **Fruijtier AD, van der Schaar J, van Maurik IS, Zwan MD, Scheltens P, Bouwman F, Pijnenburg YAL, van Berckel BNM, Ebenau J, van der Flier WM, Smets EMA, Visser LNC. Identifying best practices for disclosure of amyloid imaging results: A randomized controlled trial. Alzheimers Dement. 2023 Jan;19(1):285-295. doi: 10.1002/alz.12630. Epub 2022 Apr 2. PMID: 35366050; PMCID: PMC10084251.**

- Thank you for drawing our attention to these papers. As mentioned above, we have carefully rewritten our discussion section to contextualize trends in our results within the larger literature. We have therefore incorporated the Perry et al. (2023) article into the discussion of training needs on page 17, and referenced the Fruijtier et al. (2023) article in the discussion of established guidelines or protocols for biomarker disclosure on page 18.

Reviewer #3: The CLARiTI RoR team surveyed the ADRC network to determine current practices related to return of research results and compared these findings to a similar survey from 2019. Generally, this paper presents interesting findings that are of a high degree of importance and relevance to the field.

- **The manuscript could be improved with minor revisions, including consideration of statistical comparison between the 2019 survey results and the present survey beyond just reporting descriptive statistics.**
  - Thank you for this suggestion. In response, we conducted chi-square comparisons of the proportion of sites who disclosed each research result in 2019 versus 2024. These results revealed no statistically significant differences; however, we believe that the patterns of changes are meaningful in the context of scientific developments in the field, and therefore have retained the descriptions from the original manuscripts in addition to the new statistical comparisons (starting in the Results section on page 8). We have added the following explanation to the first Results paragraph on p.8:

    "We also utilized chi-squared analyses to compare the proportion of sites currently returning each type of health information back to participants in 2019 versus 2024. While these analyses did not reveal statistically significant changes in disclosure patterns over the past five years, we comment on meaningful trends observed in the data in each section below."

- **…a more thorough discussion of ways to move the high number of sites that reported interest in returning results but are not yet doing so to actually be equipped to do so.**
    - Our revised Discussion (starting on page 14) reviews and addresses the logistical and ethical concerns limiting return of amyloid PET and other results across the ADRCs. We have made an effort to more clearly define action items for the Centers and 'disclosure science' researchers in general to make return of results more feasible. This section on barriers begins on page 15 and extends to page 18.

- **APOE should be italicized**
    - We have italicized all use of this acronym throughout the manuscript, including in Table 1.

- **APOE abbreviation is defined on both page 5 and page 7**
    - We have removed the second definition of *APOE* from page 7.

- **Unnecessary blank page on pages 8, 20**
    - These blank pages have been removed.

- **The term "cognitively unimpaired" is preferred over "normal cognition" throughout paper.**
    - We have replaced "normal cognition" with 'cognitively unimpaired" throughout the manuscript, including in Table 1.

- **Table 3, information not useful/actionable row, sites not returning amyloid, should be 10%, not 1%.**
    - We apologize for this error. We have checked all numbers in this table and updated the field to which the reviewer referred (Information not Useful/Actionable = 3/17 [18%]).

- **Page 10 - "8 disclose only under specific conditions" - what are those specific conditions?**
    - We have reviewed the open-ended responses associated with this item about frequency of disclosing amyloid or tau results. Sites reported making decisions about disclosure based on participant diagnosis (i.e., whether participants are asymptomatic versus cognitively impaired) or participant enrollment in a clinical trial that requires testing as part of eligibility screening. We have added a comment about this to the manuscript for clarity:

"A review of qualitative answers suggests that these conditions relate to the cognitive status of participants (e.g., only disclosing to symptomatic participants) or whether the participant is enrolled in a clinical trial through which PET was acquired for eligibility screening."

- **"Of the sites currently returning tau, none do so routinely." - why not?**
    - We have also added context for the reason that sites are not routinely disclosing tau in this section (see below). Additionally, we have added a more detailed discussion about the reasons for and barriers to disclosing tau in the Discussion section on page, starting at the top of page 16.

      "Instead, tau is largely disclosed as part of standalone studies developing procedures for communicating these results to participants."

- **In general, there are too many results listed in the discussion section, it feels very redundant with the results section when reading. I would suggest trimming the reporting of percentages in the discussion section and instead using more general terms, e.g., "nearly half of respondents" instead of "Seventeen sites (47%)"**

    - Thank you for this suggestion. We have carefully revised the Discussion section to remove some of the redundant detail and explore larger patterns and themes in results as they relate to biomarker testing and disclosure. We have drawn in significant additional literature encompassing clinical and research applications of disclosure, including existing protocols or guidelines for returning individual results and work summarizing post-disclosure outcomes. We feel that the findings are now much better contextualized and greatly appreciate this feedback.

Revised Manuscript (marked version)

Return of Research Results Across the Alzheimer's Disease Research Centers Network

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RUNNING HEAD: ADRC Return of Research Results

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Abstract

INTRODUCTION: The Consortium for Clarity in Alzheimer's Disease and Related Dementias Through Imaging (CLARiTI) Return of Results Core aims to develop tools and a framework for disclosing individual results at Alzheimer's Disease Research Centers (ADRCs). An understanding of current disclosure practices is necessary to generate this protocol.

METHODS: All 37 ADRCs received a survey between January and April 2024; 36 provided valid responses.

RESULTS: Most ADRCs disclose diagnosis and cognitive results to participants with impairment, and disclosure of biomarker data (e.g., amyloid and tau PET) has accelerated since 2019. Though less common, disclosure to unimpaired participants has increased since 2019. Motivators for disclosure include to thank participants, for recruitment/retention, and to help inform healthcare decisions. Barriers include limited expertise and infrastructure, concerns about clinical actionability, and risks to participants.

DISCUSSION: The ADRC network is invested in sharing research results. While some concerns remain, CLARiTI will critically evaluate a standardized approach to sharing these results.

1. Background

Alzheimer's disease and related dementias (ADRDs) pose significant personal and societal challenges ~~as the size of the~~with the aging of the U.S. ~~aging~~ population ~~increases~~[1]. To meet ~~these~~ this challenge~~s~~, the National Institute on Aging (NIA) began funding Alzheimer's Disease Research Centers (ADRCs) in 1984, with 37 centers currently established ~~nationally~~. ADRCs provide ADRD resources and education to local communities, train new investigators in the field, facilitate representative and inclusive recruitment into studies, and catalyze cutting-edge research around center-specific themes. Each center maintains a highly characterized longitudinal cohort of ~~older~~ adults across the cognitive spectrum~~, ranging from clinically normal to dementia~~and with etiologies including ~~. Although~~ Alzheimer's disease~~, is the most common clinical etiology across centers, other etiologies are included such as~~ Lewy body disease~~s~~, vascular injury, frontotemporal lobar degeneration, ~~etc~~ and others (https://naccdata.org/requesting-data/data-summary/uds). Annual assessments include ~~standardized~~ demographic and health information, cognitive testing, neurological examination, and optional neuroimaging, blood draw, and other research procedures. These publicly accessible data are pooled across sites through the National Alzheimer's Coordinating Center (NACC)~~ and shared broadly with the scientific community~~[2].

The coordination of the ADRC network has played a part in earlier and more accurate identification and treatment of individuals at risk for ~~the~~ cognitive decline. Advancements in biomarker testing[3-5] and the approval of disease-modifying treatments[6-7] (DMTs; e.g., anti-amyloid monoclonal antibodies) have shaped ~~the~~ research being conducted within the network. The availability of ~~disease-modifying treatments~~DMTs underscores the importance of biomarker testing for cognitively impaired participants and may suggest future relevance for unimpaired

participants. The benefits of AD biomarker testing also extend beyond eligibility for ~~disease-modifying therapies~~DMTs to include etiologic and prognostic clarification that may inform clinical, social, and financial decisions[8]. The ADRC Consortium for Clarity in ADRD Research Through Imaging (CLARiTI) aims to leverage the ADRC network to capture heterogeneous ADRD profiles in a diverse sample through standardized imaging and plasma collection at each center[10].

Driven by greater understanding of the meaning of biomarkers for disease risk and shifts in research attitudes toward bidirectional communication between studies and participants[10], ADRD research studies have increasingly sought to return neuropsychological and biomarker results to participants[11]. The most recent NIA ADRC request for applications requires sites to "assure appropriate disclosure of biomarker and other results." ~~To meet this call, there~~Therefore, we must ~~is a need to~~ understand how results can be effectively, ethically, and pragmatically relayed back to participants ~~and their families~~. To date, most research on returning results has focused on apolipoprotein-E (*APOE*) genetic information[12-14] and amyloid positron emission tomography (PET)[15]. ~~Results from these~~These studies demonstrate that such information is generally well-understood and~~,~~ ~~well-tolerated, and~~ does not cause sustained or significant ~~,~~ ~~clinically relevant~~ distress in participants across the cognitive spectrum[16-17]. However, these studies have important limitations. They include relatively homogenous samples of participants with high educational attainment, considerable resources, and low psychiatric burden, which limits the generalizability of results. The protocols for returning results are also time- and resource-intensive, thus limiting scalability. While several frameworks have been developed[18-20], no universal protocol exists. The CLARiTI Return of Results (RoR) Core, made up of interdisciplinary experts in disclosure from four ADRCs, aims to produce a flexible, community-

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informed 'Toolkit' for returning individual research results at centers nationwide. ~~This work has the potential to improve recruitment and retention, build trust with research participants, and leverage the ADRC network in collecting detailed post-disclosure outcomes data in a national sample.~~The Toolkit will provide and evaluate the effectiveness of pre-test education to support participants in making informed decisions about learning their results. Additionally, training materials and templates for communicating complex biomarker information will be offered. This work has the potential to improve recruitment and retention, build trust with research participants, and leverage the ADRC network in collecting detailed post-disclosure outcomes data in a national sample. Results will also inform biomarker disclosure approaches in clinical settings, where imaging and plasma biomarkers are becoming increasingly common for the purpose of etiologic clarification and determining eligibility for DMTs.

A scalable, ethical CLARiTI RoR framework must be informed by the current disclosure practices of ADRCs and by their capacity, interest, and needs. In 2019, researchers from the Advisory Group on Risk Evidence Education in Dementia (AGREED)[21-22] surveyed the ADRCs about disclosure practices, motivations, ~~reasons for returning (or not returning) results,~~ and perceived barriers and facilitators. Given the accelerated developments in biomarker testing and expansion of the ADRC network, an updated survey on current practices was warranted. Here, we report findings from a 2024 survey of the 37 established and exploratory centers.

2. Methods

The RoR Core developed the current questionnaire based on the Roberts et al. 2019 survey[21]. Roberts et al. aimed to assess what information was shared with participants, how this information was communicated and by whom, and why sites elected to return – or not return – research results. Given the rapidly changing landscape of biomarkers since 2019, including the approval of multiple anti-amyloid therapies, the RoR Core created additional items to explore nuanced aspects of training for and execution of returning research results. More specifically, domains covered the types of results returned (e.g., cognitive test results, research diagnosis, amyloid PET, tau PET, FDG-PET, structural neuroimaging, ~~*apolipoprotein E [APOE]*~~ or other genetic results), by whom, to whom, and under what conditions (e.g., visit modality and length). We gathered additional details regarding factors motivating or facilitating the return of research results, as compared to barriers or perceived risks.

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The survey was coded in REDCap[23] and disseminated by NACC to each of the 37 ADRCs between January and March 2024. Sites were asked to identify one individual to complete the survey based on familiarity with local practices around disclosure; each site therefore provided only one questionnaire. Of the 37 sites invited to participate, all provided responses; however, a review of the responses determined that one site provided invalid data. Descriptive statistics were generated in R Version 4.4.2 and graphics generated by R Studio. The 36 sites represented the geographic distribution of the ADRCs nationally.

3. Results

Given the different implications of returning research results to participants with and without cognitive impairment, sites were asked to endorse which results were routinely shared with participants diagnosed with mild cognitive impairment or dementia, versus those ~~with normal cognition~~who are cognitively unimpaired (with or without subjective cognitive concerns). Responses are summarized in Table 1. We also utilized chi-squared analyses to compare the proportion of sites currently returning each type of health information back to participants in 2019 versus 2024. While these analyses did not reveal statistically significant changes in disclosure patterns over the past five years, we comment on meaningful trends observed in the data in each section below.

3.1. Return of Research Results to Participants with Cognitive Impairment

Consistent with the 2019 survey, most sites disclose neuropsychological test results gathered through annual participant evaluations (75%) as well as research diagnoses rendered through standard consensus review of the cognitive evaluation (75%). Proportions are relatively consistent with responses in 2019. Fifty-eight percent of sites currently share structural MRI results, representing an increase since 2019 (40%). Almost half (47%) are sharing amyloid PET results with impaired participants, similar to 43% of sites in 2019. In contrast, disclosure of amyloid measured through other modalities, or of other biomarkers was relatively rare, occurring in less than one quarter of centers. While tau imaging (17%), CSF biomarker results (22%), and *APOE* results (14%) are among those results shared by relatively few sites, the number reporting disclosure of these results doubled from 2019, suggesting significant growth in this area. FDG-

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PET and other genetic test results are completed and returned by a small proportion of sites (17% and 6%, respectively) and less frequently than in 2019.

3.2. Return of Research Results to Cognitively ~~Normal~~ Unimpaired Participants

Return of cognitive test results and participant research diagnoses to cognitively ~~normal~~ unimpaired participants occurs at most sites (69% each), and at a similar number of sites as in 2019. In contrast, amyloid PET (44%) and structural MRI (61%) are disclosed at more sites as compared to 2019 (27% amyloid PET and 33% structural MRI in 2019). Though still shared by only a few sites, there was an increase in the number of centers returning tau PET (11%), CSF biomarker (14%), and *APOE* results (14%) compared to 2019. As with cognitively impaired participants, fewer sites disclose FDG-PET (11%) and other genetic results (6%) to cognitively unimpaired participants compared to 2019.

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3.3. Amyloid and Tau Imaging Disclosure Across the ADRC Network

The primary focus of the CLARiTI RoR Core is to develop a structured protocol for returning amyloid and tau PET imaging results to participants. Additionally, ADRCs are now required to complete amyloid and tau PET with a subset of participants annually and have a plan to return these results. For these reasons, the focus of the survey and the responses reported refer to ADRC responses regarding amyloid and tau disclosure.

3.3.1. *Interest in Returning Amyloid and Tau Results.* Of the 36 centers that responded to the survey, 19 (53%) currently return amyloid PET imaging to participants; an additional

15 (42%) are interested in doing so in the future. Of the 19 sites who return amyloid, 11 do so 'routinely' (i.e., to most participants scanned), and 8 disclose only under specific conditions. A review of qualitative answers suggests that these conditions relate to the cognitive status of participants (e.g., only disclosing to symptomatic participants) or whether the participant is enrolled in a clinical trial through which PET was acquired for eligibility screening. The proportion of sites disclosing tau PET is much lower (6; 17%), though there is consistent interest in sharing these results in the future (25; 69%). Of the sites currently returning tau, none do so routinely. Instead, tau is largely disclosed as part of standalone studies developing procedures for communicating these results to participants.

3.3.2. *Modality of Amyloid and Tau Disclosure Visits.* Centers currently sharing amyloid and tau imaging results provided additional information regarding how related visits are completed at their site. Among the 19 sites disclosing amyloid PET results, the most common modalities used to communicate results to participants are in-person visits (68%), phone calls (53%), and virtual visits using HIPAA-compliant videoconferencing (e.g., Zoom for Health; 47%). Few sites (4, 21%) rely solely on written communication (e.g., mailed letter or report without contact from a study team member) to return amyloid results, and email is not used for sharing results at any site. Most sites reported that visits for returning results take approximately 30 minutes on average.

3.3.3. *Elements of Amyloid and Tau Disclosure Visits*. Sites who endorsed sharing amyloid and tau results were asked to confirm the key steps/elements of their disclosure process from a list of steps drawn from existing disclosure frameworks[19], including the practice guidelines previously published by NACC (Grill et al, 2023; https://files.alz.washington.edu/best-practices/biomarker-disclosure.pdf). This question allowed the RoR Core to understand both the perceived utility of these steps, as well as how sites are currently adhering to practice guidelines. As depicted in Table 2, 74% of ADRCs incorporate key pre- and post-disclosure steps, including education and decision aids, prior to disclosure and recommendations or clinical referrals post-disclosure. Only approximately half of sites provide a written summary of findings. Regarding messaging during the disclosure visit, there is relative consensus around the use of a qualitative label (most commonly 'elevated' or 'not elevated') as opposed to providing a quantitative value. Few centers (26%) utilize visual aids, including participants' scan images, during the communication of results. Of note, several sites commented on participants' strong desire for images and more specific information, and one site reported considering a tiered categorization of tau deposition, reflective of disease progression (e.g., none/low, subcortical, subcortical + cortical). As previously mentioned, clinical referrals and recommendations are regularly provided by most centers; however, only one site provides amyloid and tau PET with a personalized risk estimate.

All sites currently disclosing amyloid and tau imaging do so directly to participants and, with participant approval, their loved ones. Half of these disclosing sites reported

also sharing results with medical providers with participant approval. Only 4 of the 19 amyloid-disclosing sites include imaging results in the electronic health record, and none of the 6 tau-disclosing sites do so.

3.3.4. *Roles in the Return of Amyloid and Tau Results.* Sites were provided with a list of common team roles and disciplines and asked to endorse who at their site leads disclosure visits. While physicians (e.g., neurologists, geriatricians, psychiatrists) and advanced practice providers (e.g., nurse practitioners, physician assistants) most frequently lead disclosure visits, responses indicated that a more interdisciplinary team including neuropsychologists, counselors, and social workers is often included. One site also stated that advanced trainees (e.g., postdoctoral residents) within healthcare fields are also involved in the return of amyloid and tau results while under supervision.

3.3.5. *Motivations for Returning Amyloid & Tau Results to Participants:* Sites endorsed a multitude of reasons for sharing PET biomarker results with participants (Table 3). Many of the motivations revolved around participant needs: Sites felt that the return of results is important to meet participants' requests for their data (89% of sites returning amyloid, 100% of sites returning tau), to thank participants for their contributions to research (89% of sites returning amyloid, 67% of sites returning tau), and to support retention more broadly (89% of sites returning amyloid, 67% of sites returning tau). Most sites returning amyloid (79%) also agreed that amyloid results in particular could inform the participant's healthcare and medical decision-making,

though this was listed as a relevant motivator only among half of tau-returning sites. Some sites additionally reported having ongoing studies focused on the science of returning results (58% of sites returning amyloid, 33% of sites returning tau). No other reasons were volunteered by sites in the open-ended portion of the survey.

3.3.6. *Barriers to or Reasons for Not Returning Amyloid and Tau Results to Participants.* We also evaluated current barriers to returning PET results among sites who endorsed not returning amyloid (n=17 sites) or tau (n=30 sites). Barriers to returning amyloid and tau PET results fall into three themes: logistical barriers, concerns about biomarker validity, and participant concerns. Among the logistical or practical challenges facing sites are financial constraints (12% of sites not returning amyloid, 10% of sites not returning tau), time burden on staff (21% of sites not returning amyloid, 20% of sites not returning tau), personnel shortage (16% of sites not returning amyloid, 20% of sites not returning tau), lack of expertise in returning PET biomarker results (26% of sites not returning amyloid, 17% of sites not returning tau), or disclosure process not planned for as part of the original longitudinal cohort (58% of sites not returning amyloid, 37% of sites not returning tau). Sites also endorsed concerns about biomarker collection/analysis methods not meeting clinical regulations (16% of sites not returning amyloid, 27% of sites not returning tau) or limited clinical actionability or utility of results (16% of sites not returning amyloid, 17% of sites not returning tau). Some sites endorsed a concern about potential for unintended harms to participants with the return of individual PET scan results (35% of sites not returning amyloid, 23% of sites not returning tau) and associated legal

liability for centers themselves (11% of sites not returning amyloid, 7% of sites not returning tau). Of interest, no sites feel that a lack of interest from participants is a significant barrier to integrating return of PET results. While 6 sites endorsed 'Other' barriers, a review of associated open-ended responses suggested that these largely reiterated or combined the other barriers listed above (e.g., insufficient time and expertise to manage potential psychological distress in participants; results not clinically actionable for unimpaired participants).

4. Discussion

Around three-quarters of sites provide cognitive testing and research diagnosis, over half provide structural MRI results, and almost half provide amyloid PET results. Less than a quarter return additional result types. There has been notable growth since 2019 in disclosure of structural MRI, amyloid and tau PET, CSF biomarkers, and *APOE* genotype. Return of cognitive testing/research diagnosis is similar to 2019, while return of FDG-PET and non-*APOE* results has decreased.

Given our focus on amyloid and tau PET results, we additionally evaluated components of and motivations for/deterrents to returning amyloid and tau PET. More sites return amyloid PET to cognitively healthy participants compared to 2019, which aligns with literature demonstrating that unimpaired participants desire and leverage their results to drive risk reduction and advanced planning[24-25]. Return of results protocols must be adapted to clinical stage. For instance, disclosure of amyloid PET to cognitively unimpaired participants should emphasize adaptive health behaviors and clinical monitoring (as opposed to DMTs or other treatments). We expected

an increase in the proportion of sites returning amyloid PET to cognitively impaired participants, as this procedure is now commonly used in clinical and research[26] settings for etiologic clarification and treatment planning[27] in the context of FDA-approved DMTs[28]. Though sites already disclosing amyloid to cognitively impaired participants cited the clinical utility of amyloid PET as a major motivator for doing so, the overall proportion of sites returning these results did not significantly increase.

Given the more recent development of tau PET tracers and associated visual rating systems[29-31], as well as limited clinical actionability of tau PET results, it is less surprising that few sites currently disclose tau PET. However, studies have illuminated the potential utility of tau measures to enhance clinical prognostication[32] and as endpoints for clinical trials[33]. We therefore expect greater future demand for tau disclosure methods as validity, interpretability, and potential actionability of these markers increase. Indeed, most ADRCs expressed interest in disclosing tau PET in the future. The CLARiTI Return of Results Toolkit, launched in April 2025, already contains a protocol and resources supporting the disclosure of amyloid PET results. Integration of tau into the Toolkit is a critical and time-sensitive goal set for Fall 2025.

In addition to citing potential clinical benefit to participants, ADRCs recognized and were motivated by participants' desire for their individual results[10] and saw disclosure as a potential strategy for enhancing recruitment and retention in ADRD research. While we are unaware of any published literature directly linking return of participant-level results to enhanced research engagement, a variety of studies support this association. Participants[34-35] and study partners[36] suggest that personal benefit gained from ADRD research, including learning individual or family health results, can facilitate enrollment and retention in studies. In contrast, a lack of disclosure of results serves as a barrier[37].

Among sites that do not currently return amyloid or tau PET results, interest in future disclosure is near ubiquitous, highlighting the need to better understand and address implementation barriers. The most common barrier was purely logistical: disclosure was not a planned part of most ADRC longitudinal cohorts. This finding underlines that PET disclosure would require not only standalone protocols and resources for communication of this information, but rather adaptation of existing workflows and documents to ensure return of results is feasible, sustainable, and effective across the diverse contexts in which ADRCs operate. CLARiTI is not the only impetus for disclosure; many large, national multi-site studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI)[18], the Longitudinal Early-Onset Alzheimer's Disease Study (LEADS)[38], and the US POINTER Study[39] have already launched return of results programs. Indeed, the latest funding announcement for the ADRCs requires some element of disclosure to individual participants. The RoR Core will continue to partner closely with sites and leverage expertise from other studies to develop guidance around these changes.

Additional logistical barriers include lack of expertise in disclosing results and additional time burdens for staff. Data from the survey themselves demonstrate the feasibility and efficiency of returning results, with most sites indicating that sessions are completed within 30 minutes using virtual or in-person modalities. This finding reflects a growing consensus that remote return of results is a viable option[40,41]. Indeed, utilizing technology to conduct remote visits can increase site capacity and return-of-results feasibility. Though 'face-to-face' in-person and video may be linked to lower participant distress[42], participants may be given the choice of modality for receiving their results[18,40,41] to balance the needs of sites (lower time and effort burden) and participants (lower time and travel burden, enhanced capacity to involve of out-of-

area support persons). Survey results also suggest that ADRCs effectively employ a multidisciplinary disclosure team, including physicians and advanced practice providers (e.g., nurse practitioners, physician assistants), but also neuropsychologists, counselors, social workers, and advanced trainees. This may assuage concerns about both expertise and time demands for any single team member. There are no established qualifications or competencies required to communicate biomarker results; however, various studies have commented on key practices and styles that may result in better post-disclosure outcomes[42]. The CLARiTI RoR Core must meet concerns regarding lack of expertise with a variety of multimodal learning opportunities for clinicians of diverse training backgrounds. The first of these trainings was accomplished in April 2025 with a national webinar through the National Alzheimer's Coordinating Center (https://clariti.naccdata.org/for-researchers/for-adrcs#webinars). Additional in-person and asynchronous educational offerings will be developed in coming months, and will reference published or publicly available training around biomarker testing for clinicians and researchers[43].

Additional barriers to disclosure implementation include concerns about unintended harms to participants. There is growing evidence to alleviate this concern; studies of post-disclosure outcomes demonstrate that participants across the cognitive spectrum rarely experience new or exacerbated psychiatric symptoms[44,45], and do not regret learning results[46]. Nonetheless, participants may experience transient test-specific distress, worry, and experiences of stigma after learning of biomarker positivity[44,47]. These 'risks' must be discussed pre-testing and monitored post-disclosure. Furthermore, protocols should incorporate the presence of a support person[42,48] and approach the discussion of results with clarity, compassion, and validation[42], as these factors are associated with lower post-disclosure distress. The CLARiTI

RoR Toolkit will incorporate suggested language and considerations for working with both participants and their loved ones as part of the disclosure session. Additionally, the RoR Core will provide validated pre- and post-disclosure screening measures to track changes in mood, as well as recommendations for how and when they should be applied.

Another concern for researchers is the potential for participants to experience medicolegal discrimination should research results be shared with medical or insurance providers, employers, or other entities[49]. Half of the sites reported sharing results with medical providers with participant approval, and very few include PET results in the electronic health record directly. Site-specific context regarding electronic health record entry is important in that some ADRCs are stand-alone centers, whereas others are embedded within a clinic wherein adding a result to an electronic health record is part of the standard of care. Risks and benefits of sharing results with medical providers/electronic health records should be carefully discussed prior to testing, ideally. Parameters around data-sharing must be clearly defined to avoid accidental breach of confidentiality.

Overall, sites already sharing amyloid PET generally align with published guidelines for ADRD biomarker disclosure that recommend (1) determining appropriateness of returning results; (2) providing pretest education and seeking consent; (3) returning results to the individual and their support person; and (4) following up to promote recipient(s) well-being[19,20,50-52]. Most ADRCs that disclose amyloid or tau provide pre-disclosure education and post-disclosure resources (e.g., clinical referrals, lifestyle recommendations). When disclosing, most sites provide a qualitative label (most commonly ‘elevated’ or ‘not elevated’) as opposed to a quantitative value or graphic. While consistent with the FDA-approved visual read process for amyloid PET, several sites reported participants’ desire for quantitative and graphical

information, as reported elsewhere[53]. Future work is needed to evaluate the effectiveness and utility of standardized quantitative values (e.g., centiloids) and graphical risk representations. Fewer sites provide a written report to participants, despite literature suggesting that written reports may be helpful for improved participant experience and recollection of results[54,55].

This study had several limitations. First, while results from the ADRCs may generalize to other research and even clinical settings, Centers have strict parameters and workflows that do not exist in other contexts. Relative risks and benefits of testing for and disclosing biomarker information differ greatly based on these settings, as does capacity for pre-test counseling and post-disclosure follow up. Second, while this survey represents an updated review of return of results practices at ADRCs, it does not capture the nuances of disclosure at each site. For instance, we did not assess the exact language used to communicate results to participants (e.g., how dementia risk is communicated based on the qualitative result) or the timeline and nature of follow-up. As indicated in one recent scoping review[50], more information is needed to inform comprehensive and standardized guidelines for returning amyloid PET and other biomarkers. The CLARiTI Return of Results Core will contribute to these guidelines by leveraging the national ADRC network to conduct iterative program development and evaluation of disclosure.

~~Our survey on return-of-results practices of ADRCs indicates that 69-75% of sites provide cognitive testing and research diagnosis results, 58-61% provide structural MRI results, 44-47% provide amyloid PET results, and <25% of sites provide additional results to research participants (11-17% FDG or tau PET, 14-22% CSF, 6-14% *APOE* or other genetic test results). Compared to a 2019 survey, structural MRI (33-40% in 2019 to 58-61% in 2024), amyloid PET (27-43% in 2019 to 44-47% in 2024), CSF biomarkers (3-10% in 2019 to 14-22% in 2024), *APOE* genotype (7% in 2019 to 14% in 2024), and tau PET (7-10% to 11-17%) are more~~

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~~frequently returned. Returns of cognitive testing/research diagnosis are similar to 2019 (70-83% in 2019 to 69-75% in 2024), while return of FDG-PET (20-27% in 2019 to 11-17% in 2024) and non-*APOE* genetic testing results (10-13% in 2019 to 6% in 2024) has decreased.~~

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~~Given our focus on amyloid and tau PET results, we additionally evaluated components of PET disclosure procedures as well as motivators for and barriers to returning amyloid and tau PET. Nineteen sites (53%) currently disclose amyloid PET results to participants, with similar rates for cognitively impaired (47%) and cognitively unimpaired (44%) participants. Although return of PET results has increased with cognitively unimpaired participants (from 27 to 47% of sites), the rate of disclosure with cognitively impaired adults remains similar (43 to 47%). This lack of increase is interesting given the demonstrated validity of this biomarker and potential increase in clinical utility of this result for individuals with cognitive impairment[24] with FDA approval of anti-amyloid therapies[25]. Given the more recent development of tau PET tracers compared with amyloid PET, the ongoing development and validation of visual rating systems, and lower clinical actionability of tau PET results, it is not surprising that fewer sites currently disclose tau PET compared to amyloid PET results (11% for unimpaired and 17% for impaired). However, as validity, interpretability, and potential actionability continue to increase, most sites expressed interest in disclosing these results. The most frequently cited motivators for returning amyloid PET results were to thank participants for their contribution, enhance retention, and by participants/family request. These motivators are consistent with the participant perspectives voiced in the Participant Bill of Rights[10]. Additional motivators were for clinical purposes (e.g., to inform participants' physicians or healthcare/medical decision-making) or as part of an ongoing disclosure-specific study. The primary motivator for returning tau PET results was a participant or family request, with other common motivators centered on thanking participants or~~

~~participant retention, and less frequently cited motivators around clinical care or disclosure studies. These findings suggest that the primary motivators for ADRC disclosure of PET results center on benefits to research participation and healthcare decision-making..~~

~~Seventeen sites (47%) do not currently disclose amyloid PET, and 30 (83%) do not currently disclose tau PET, although interest in disclosing them is high. For example, 15 (42%) expressed interest in disclosing amyloid PET and 25 (69%) in disclosing tau PET results. The most common barrier or reason for not returning amyloid or tau PET results was disclosure not being part of the original observational study or procedures (cited by 58% of non-disclosing sites). Other barriers were concerns about the potential for unintended harms to participants, lack of expertise in disclosing results, and time burdens for staff. One barrier/reason cited frequently was concerns that results do not meet clinical regulations. Fewer sites indicated concerns about legal liability, personnel shortage, or information not being useful/actionable as a reason for not disclosing PET results. Importantly, no sites selected "participants not interested" as a reason/barrier for not disclosing. Overall, these findings suggest that interest in returning amyloid or tau PET results is high in the ADRC network. Initiatives to update protocols or consent forms, train staff to disclose biomarker results, and provide standard procedures to reduce unintended harm to participants may help reduce these barriers and allow sites greater opportunity to disclose PET results.~~

~~Published frameworks to guide communication of AD biomarker results recommend a process determining the appropriateness of return of results, providing pretest education and seeking consent for testing from the individual and their support person if warranted, returning results to the individual and their support person, and following up to promote recipient well-being[19,20]. Results from our survey indicated that most ADRCs that disclose amyloid or tau provide pre-~~

~~disclosure education and post-disclosure resources (e.g., clinical referrals, recommendations or action steps). When disclosing, most sites provide a qualitative label (most commonly 'elevated' or 'not elevated') as opposed to a quantitative value or visual image. This is consistent with the FDA-approved visual read process for amyloid PET results; however, several sites reported participants' strong desire for images and more specific information, as reported elsewhere[26]. Although currently difficult to provide, future work evaluating the effectiveness and utility of providing standardized quantitative values, such as centiloid values, and visual images of results is needed, particularly once these results better inform disease stage or prognosis. Fewer sites provide a written report to participants, despite literature suggesting that written reports may be helpful for improved participant experience and recollection of results[27-28]. We did not gather more specific data on how the meaning of results is communicated to participants (e.g., how dementia risk or prognosis information is communicated based on the qualitative result) or on questions frequently asked by participants, which will be important to collect in future surveys.~~

~~While in-person visits were the most common modality for returning results, many sites also used phone calls and virtual visits. This finding reflects a growing consensus that remote return of results is a viable option[28,29]. Indeed, utilizing technology to conduct remote visits can increase site capacity and return-of-results feasibility. While the option for in-person visits should remain, participants may be given the choice of modality for receiving their results[18,28,29]. This can limit participant burden (e.g., time and travel) and allow for the involvement of out-of-area support. Most sites reported that visits for returning results took approximately 30 minutes on average. There are no published guidelines on qualifications or specific competencies recommended to communicate biomarker results to participants or patients. While survey results indicated that physicians (e.g., neurologists, geriatricians, psychiatrists) and advanced practice~~

providers (e.g., nurse practitioners, physician assistants) most frequently lead disclosure visits, a broad range of interdisciplinary clinical research team members including neuropsychologists, counselors, social workers, and advanced trainees also provide results. All sites currently disclosing amyloid and tau PET results did so directly to participants and, with participant approval, their loved ones. This is consistent with prior research suggesting the inclusion of support persons can enhance rather than hinder return of results in clinical trials by providing cognitive and emotional support to participants[30]. Half of the sites reported sharing results with medical providers with participant approval. Only 4 of the 19 amyloid-disclosing sites include PET results in the electronic health record, and none of the 6 tau-disclosing sites do so. This is consistent with literature describing potential concerns regarding discrimination based on ADRD biomarker results[31]. Site-specific context regarding electronic health record entry is important in that some ADRCs are stand-alone centers, whereas others are embedded within a clinic wherein adding a result to an electronic health record is part of the standard of care. Risks and benefits of sharing results with medical providers/electronic health records should be carefully discussed prior to testing, ideally. Parameters around data-sharing must be clearly defined to avoid accidental breach of confidentiality. Overall, the findings suggest that sites are generally consistent in following published guidelines for ADRD biomarker disclosure.

Our results should be considered within the context of their limitations. Although they reflect responses from most ADRCs, the results may not generalize to settings outside of observational research. Additionally, response biases or difficulties with recall could have impacted responses. Given CLARiTI's focus on neuroimaging, this survey gathered fewer data about other important return-of-results practices, such as disclosure of genetic risk or other potentially clinically relevant information. Importantly, these results are shaping the development of a return of

~~amyloid and tau PET results process to be disseminated as part of the CLARiTI study. Preparing sites to take on this practice will require training study personnel, exploring utilization of technology for remote visits, and integrating return of results with existing center goals and protocols. The results are being used by the CLARiTI RoR Core to meet some of these needs through the development of a toolkit and training materials that prepare sites and reduce site and participant burden (e.g., provision of templates, automated reports, educational and decision-aid tools). Given the rapid development of AD biomarkers and therapeutics, several study directions remain important in the ADRC network and beyond, such as best practices for communicating multiple biomarker results, including plasma biomarkers, culturally-informed communication of results with members of racially and ethnically diverse participants for whom less validity data exist, and developing competencies and effective training programs for ADRD biomarker testing, interpretation, and disclosure.~~

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Consent Statement

Given that human subjects were not involved in this study, individual informed consent was not required.

Acknowledgments

None.

Conflicts of Interest

SCJ has in the past three years served in an advisory capacity to Enigma Biomedical, Eli Lilly, and AlzPath. NAC has served as a consultant for NewAmsterdam Pharma in 2023 and on a 2-day advisory board for Eli Lilly in 2025. Authors ARF, HK, JMR, CME, BCD, NTA, ECM, and LRC have no conflicts to disclose.

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Legends

Table 1. Proportion of ADRCs Disclosing Individual Research Results, by Participant Diagnosis

Table 2. Elements of Amyloid and Tau PET Return of Results Sessions

Table 3. Motivations and Barriers to Returning Amyloid and Tau PET Results

Return of Research Results Across the Alzheimer's Disease Research Centers Network

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Abstract

INTRODUCTION: The Consortium for Clarity in Alzheimer's Disease and Related Dementias Through Imaging (CLARiTI) Return of Results Core aims to develop tools and a framework for disclosing individual results at Alzheimer's Disease Research Centers (ADRCs). An understanding of current disclosure practices is necessary to generate this protocol.

METHODS: All 37 ADRCs received a survey between January and April 2024; 36 provided valid responses.

RESULTS: Most ADRCs disclose diagnosis and cognitive results to participants with impairment, and disclosure of biomarker data (e.g., amyloid and tau PET) has accelerated since 2019. Though less common, disclosure to unimpaired participants has increased since 2019. Motivators for disclosure include to thank participants, for recruitment/retention, and to help inform healthcare decisions. Barriers include limited expertise and infrastructure, concerns about clinical actionability, and risks to participants.

DISCUSSION: The ADRC network is invested in sharing research results. While some concerns remain, CLARiTI will critically evaluate a standardized approach to sharing these results.

1. Background

Alzheimer's disease and related dementias (ADRDs) pose significant personal and societal challenges with the aging of the U.S. population[1]. To meet this challenge, the National Institute on Aging (NIA) began funding Alzheimer's Disease Research Centers (ADRCs) in 1984, with 37 centers currently established. ADRCs provide ADRD resources and education to local communities, train new investigators in the field, facilitate representative and inclusive recruitment into studies, and catalyze cutting-edge research around center-specific themes. Each center maintains a highly characterized longitudinal cohort of adults across the cognitive spectrum and with etiologies including Alzheimer's disease, Lewy body disease, vascular injury, frontotemporal lobar degeneration, and others (https://naccdata.org/requesting-data/data-summary/uds). Annual assessments include demographic and health information, cognitive testing, neurological examination, and optional neuroimaging, blood draw, and other research procedures. These publicly accessible data are pooled across sites through the National Alzheimer's Coordinating Center (NACC)[2].

The coordination of the ADRC network has played a part in earlier and more accurate identification and treatment of individuals at risk for cognitive decline. Advancements in biomarker testing[3-5] and the approval of disease-modifying treatments[6-7] (DMTs; e.g., anti-amyloid monoclonal antibodies) have shaped research being conducted within the network. The availability of DMTs underscores the importance of biomarker testing for cognitively impaired participants and may suggest future relevance for unimpaired participants. The benefits of AD biomarker testing also extend beyond eligibility for DMTs to include etiologic and prognostic clarification that may inform clinical, social, and financial decisions[8]. The ADRC Consortium for Clarity in ADRD Research Through Imaging (CLARiTI)[9] aims to leverage the ADRC network to

capture heterogeneous ADRD profiles in a diverse sample through standardized imaging and plasma collection at each center[10].

Driven by greater understanding of the meaning of biomarkers for disease risk and shifts in research attitudes toward bidirectional communication between studies and participants[10], ADRD research studies have increasingly sought to return neuropsychological and biomarker results to participants[11]. The most recent NIA ADRC request for applications requires sites to "assure appropriate disclosure of biomarker and other results." Therefore, we must understand how results can be effectively, ethically, and pragmatically relayed back to participants. To date, most research on returning results has focused on apolipoprotein-E (*APOE*) genetic information[12-14] and amyloid positron emission tomography (PET)[15]. These studies demonstrate that such information is generally well-understood and does not cause sustained or significant distress in participants across the cognitive spectrum[16-17]. However, these studies have important limitations. They include relatively homogenous samples of participants with high educational attainment, considerable resources, and low psychiatric burden, which limits the generalizability of results. The protocols for returning results are also time- and resource-intensive, thus limiting scalability. While several frameworks have been developed[18-20], no universal protocol exists. The CLARiTI Return of Results (RoR) Core, made up of interdisciplinary experts in disclosure from four ADRCs, aims to produce a flexible, community-informed 'Toolkit' for returning individual research results at centers nationwide. The Toolkit will provide and evaluate the effectiveness of pre-test education to support participants in making informed decisions about learning their results. Additionally, training materials and templates for communicating complex biomarker information will be offered. This work has the potential to improve recruitment and retention, build trust with research participants, and leverage the ADRC network in collecting detailed

post-disclosure outcomes data in a national sample. Results will also inform biomarker disclosure approaches in clinical settings, where imaging and plasma biomarkers are becoming increasingly common for the purpose of etiologic clarification and determining eligibility for DMTs.

A scalable, ethical CLARiTI RoR framework must be informed by the current disclosure practices of ADRCs and by their capacity, interest, and needs. In 2019, researchers from the Advisory Group on Risk Evidence Education in Dementia (AGREED)[21-22] surveyed the ADRCs about disclosure practices, motivations, and perceived barriers and facilitators. Given the accelerated developments in biomarker testing and expansion of the ADRC network, an updated survey on current practices was warranted. Here, we report findings from a 2024 survey of the 37 established and exploratory centers.

2. Methods

The RoR Core developed the current questionnaire based on the Roberts et al. 2019 survey[21]. Roberts et al. aimed to assess what information was shared with participants, how this information was communicated and by whom, and why sites elected to return – or not return – research results. Given the rapidly changing landscape of biomarkers since 2019, including the approval of multiple anti-amyloid therapies, the RoR Core created additional items to explore nuanced aspects of training for and execution of returning research results. More specifically, domains covered the types of results returned (e.g., cognitive test results, research diagnosis, amyloid PET, tau PET, FDG-PET, structural neuroimaging, *APOE* or other genetic results), by whom, to whom, and under what conditions (e.g., visit modality and length). We gathered additional details regarding factors motivating or facilitating the return of research results, as compared to barriers or perceived risks.

The survey was coded in REDCap[23] and disseminated by NACC to each of the 37 ADRCs between January and March 2024. Sites were asked to identify one individual to complete the survey based on familiarity with local practices around disclosure; each site therefore provided only one questionnaire. Of the 37 sites invited to participate, all provided responses; however, a review of the responses determined that one site provided invalid data. Descriptive statistics were generated in R Version 4.4.2 and graphics generated by R Studio. The 36 sites represented the geographic distribution of the ADRCs nationally.

3. Results

Given the different implications of returning research results to participants with and without cognitive impairment, sites were asked to endorse which results were routinely shared with participants diagnosed with mild cognitive impairment or dementia, versus those who are cognitively unimpaired (with or without subjective cognitive concerns). Responses are summarized in Table 1. We also utilized chi-squared analyses to compare the proportion of sites currently returning each type of health information back to participants in 2019 versus 2024. While these analyses did not reveal statistically significant changes in disclosure patterns over the past five years, we comment on meaningful trends observed in the data in each section below.

3.1. Return of Research Results to Participants with Cognitive Impairment

Consistent with the 2019 survey, most sites disclose neuropsychological test results gathered through annual participant evaluations (75%) as well as research diagnoses rendered through standard consensus review of the cognitive evaluation (75%). Proportions are relatively consistent with responses in 2019. Fifty-eight percent of sites currently share structural MRI results, representing an increase since 2019 (40%). Almost half (47%) are sharing amyloid PET results with impaired participants, similar to 43% of sites in 2019. In contrast, disclosure of amyloid measured through other modalities, or of other biomarkers was relatively rare, occurring in less than one quarter of centers. While tau imaging (17%), CSF biomarker results (22%), and *APOE* results (14%) are among those results shared by relatively few sites, the number reporting disclosure of these results doubled from 2019, suggesting significant growth in this area. FDG-

PET and other genetic test results are completed and returned by a small proportion of sites (17% and 6%, respectively) and less frequently than in 2019.

3.2. Return of Research Results to Cognitively Unimpaired Participants

Return of cognitive test results and participant research diagnoses to cognitively unimpaired participants occurs at most sites (69% each), and at a similar number of sites as in 2019. In contrast, amyloid PET (44%) and structural MRI (61%) are disclosed at more sites as compared to 2019 (27% amyloid PET and 33% structural MRI in 2019). Though still shared by only a few sites, there was an increase in the number of centers returning tau PET (11%), CSF biomarker (14%), and *APOE* results (14%) compared to 2019. As with cognitively impaired participants, fewer sites disclose FDG-PET (11%) and other genetic results (6%) to cognitively unimpaired participants compared to 2019.

3.3. Amyloid and Tau Imaging Disclosure Across the ADRC Network

The primary focus of the CLARiTI RoR Core is to develop a structured protocol for returning amyloid and tau PET imaging results to participants. Additionally, ADRCs are now required to complete amyloid and tau PET with a subset of participants annually and have a plan to return these results. For these reasons, the focus of the survey and the responses reported refer to ADRC responses regarding amyloid and tau disclosure.

3.3.1. *Interest in Returning Amyloid and Tau Results.* Of the 36 centers that responded to the survey, 19 (53%) currently return amyloid PET imaging to participants; an additional

15 (42%) are interested in doing so in the future. Of the 19 sites who return amyloid, 11 do so 'routinely' (i.e., to most participants scanned), and 8 disclose only under specific conditions. A review of qualitative answers suggests that these conditions relate to the cognitive status of participants (e.g., only disclosing to symptomatic participants) or whether the participant is enrolled in a clinical trial through which PET was acquired for eligibility screening. The proportion of sites disclosing tau PET is much lower (6; 17%), though there is consistent interest in sharing these results in the future (25; 69%). Of the sites currently returning tau, none do so routinely. Instead, tau is largely disclosed as part of standalone studies developing procedures for communicating these results to participants.

3.3.2. *Modality of Amyloid and Tau Disclosure Visits.* Centers currently sharing amyloid and tau imaging results provided additional information regarding how related visits are completed at their site. Among the 19 sites disclosing amyloid PET results, the most common modalities used to communicate results to participants are in-person visits (68%), phone calls (53%), and virtual visits using HIPAA-compliant videoconferencing (e.g., Zoom for Health; 47%). Few sites (4, 21%) rely solely on written communication (e.g., mailed letter or report without contact from a study team member) to return amyloid results, and email is not used for sharing results at any site. Most sites reported that visits for returning results take approximately 30 minutes on average.

3.3.3. *Elements of Amyloid and Tau Disclosure Visits*. Sites who endorsed sharing amyloid and tau results were asked to confirm the key steps/elements of their disclosure process from a list of steps drawn from existing disclosure frameworks[19], including the practice guidelines previously published by NACC (Grill et al, 2023; https://files.alz.washington.edu/best-practices/biomarker-disclosure.pdf). This question allowed the RoR Core to understand both the perceived utility of these steps, as well as how sites are currently adhering to practice guidelines. As depicted in Table 2, 74% of ADRCs incorporate key pre- and post-disclosure steps, including education and decision aids, prior to disclosure and recommendations or clinical referrals post-disclosure. Only approximately half of sites provide a written summary of findings. Regarding messaging during the disclosure visit, there is relative consensus around the use of a qualitative label (most commonly 'elevated' or 'not elevated') as opposed to providing a quantitative value. Few centers (26%) utilize visual aids, including participants' scan images, during the communication of results. Of note, several sites commented on participants' strong desire for images and more specific information, and one site reported considering a tiered categorization of tau deposition, reflective of disease progression (e.g., none/low, subcortical, subcortical + cortical). As previously mentioned, clinical referrals and recommendations are regularly provided by most centers; however, only one site provides amyloid and tau PET with a personalized risk estimate.

All sites currently disclosing amyloid and tau imaging do so directly to participants and, with participant approval, their loved ones. Half of these disclosing sites reported

also sharing results with medical providers with participant approval. Only 4 of the 19 amyloid-disclosing sites include imaging results in the electronic health record, and none of the 6 tau-disclosing sites do so.

3.3.4. *Roles in the Return of Amyloid and Tau Results.* Sites were provided with a list of common team roles and disciplines and asked to endorse who at their site leads disclosure visits. While physicians (e.g., neurologists, geriatricians, psychiatrists) and advanced practice providers (e.g., nurse practitioners, physician assistants) most frequently lead disclosure visits, responses indicated that a more interdisciplinary team including neuropsychologists, counselors, and social workers is often included. One site also stated that advanced trainees (e.g., postdoctoral residents) within healthcare fields are also involved in the return of amyloid and tau results while under supervision.

3.3.5. *Motivations for Returning Amyloid & Tau Results to Participants:* Sites endorsed a multitude of reasons for sharing PET biomarker results with participants (Table 3). Many of the motivations revolved around participant needs: Sites felt that the return of results is important to meet participants' requests for their data (89% of sites returning amyloid, 100% of sites returning tau), to thank participants for their contributions to research (89% of sites returning amyloid, 67% of sites returning tau), and to support retention more broadly (89% of sites returning amyloid, 67% of sites returning tau). Most sites returning amyloid (79%) also agreed that amyloid results in particular could inform the participant's healthcare and medical decision-making,

though this was listed as a relevant motivator only among half of tau-returning sites. Some sites additionally reported having ongoing studies focused on the science of returning results (58% of sites returning amyloid, 33% of sites returning tau). No other reasons were volunteered by sites in the open-ended portion of the survey.

3.3.6. *Barriers to or Reasons for Not Returning Amyloid and Tau Results to Participants.* We also evaluated current barriers to returning PET results among sites who endorsed not returning amyloid (n=17 sites) or tau (n=30 sites). Barriers to returning amyloid and tau PET results fall into three themes: logistical barriers, concerns about biomarker validity, and participant concerns. Among the logistical or practical challenges facing sites are financial constraints (12% of sites not returning amyloid, 10% of sites not returning tau), time burden on staff (21% of sites not returning amyloid, 20% of sites not returning tau), personnel shortage (16% of sites not returning amyloid, 20% of sites not returning tau), lack of expertise in returning PET biomarker results (26% of sites not returning amyloid, 17% of sites not returning tau), or disclosure process not planned for as part of the original longitudinal cohort (58% of sites not returning amyloid, 37% of sites not returning tau). Sites also endorsed concerns about biomarker collection/analysis methods not meeting clinical regulations (16% of sites not returning amyloid, 27% of sites not returning tau) or limited clinical actionability or utility of results (16% of sites not returning amyloid, 17% of sites not returning tau). Some sites endorsed a concern about potential for unintended harms to participants with the return of individual PET scan results (35% of sites not returning amyloid, 23% of sites not returning tau) and associated legal

liability for centers themselves (11% of sites not returning amyloid, 7% of sites not returning tau). Of interest, no sites feel that a lack of interest from participants is a significant barrier to integrating return of PET results. While 6 sites endorsed 'Other' barriers, a review of associated open-ended responses suggested that these largely reiterated or combined the other barriers listed above (e.g., insufficient time and expertise to manage potential psychological distress in participants; results not clinically actionable for unimpaired participants).

4. Discussion

Around three-quarters of sites provide cognitive testing and research diagnosis, over half provide structural MRI results, and almost half provide amyloid PET results. Less than a quarter return additional result types. There has been notable growth since 2019 in disclosure of structural MRI, amyloid and tau PET, CSF biomarkers, and *APOE* genotype. Return of cognitive testing/research diagnosis is similar to 2019, while return of FDG-PET and non-*APOE* results has decreased.

Given our focus on amyloid and tau PET results, we additionally evaluated components of and motivations for/deterrents to returning amyloid and tau PET. More sites return amyloid PET to cognitively healthy participants compared to 2019, which aligns with literature demonstrating that unimpaired participants desire and leverage their results to drive risk reduction and advanced planning[24-25]. Return of results protocols must be adapted to clinical stage. For instance, disclosure of amyloid PET to cognitively unimpaired participants should emphasize adaptive health behaviors and clinical monitoring (as opposed to DMTs or other treatments). We expected

an increase in the proportion of sites returning amyloid PET to cognitively impaired participants, as this procedure is now commonly used in clinical and research[26] settings for etiologic clarification and treatment planning[27] in the context of FDA-approved DMTs[28]. Though sites already disclosing amyloid to cognitively impaired participants cited the clinical utility of amyloid PET as a major motivator for doing so, the overall proportion of sites returning these results did not significantly increase.

Given the more recent development of tau PET tracers and associated visual rating systems[29-31], as well as limited clinical actionability of tau PET results, it is less surprising that few sites currently disclose tau PET. However, studies have illuminated the potential utility of tau measures to enhance clinical prognostication[32] and as endpoints for clinical trials[33]. We therefore expect greater future demand for tau disclosure methods as validity, interpretability, and potential actionability of these markers increase. Indeed, most ADRCs expressed interest in disclosing tau PET in the future. The CLARiTI Return of Results Toolkit, launched in April 2025, already contains a protocol and resources supporting the disclosure of amyloid PET results. Integration of tau into the Toolkit is a critical and time-sensitive goal set for Fall 2025.

In addition to citing potential clinical benefit to participants, ADRCs recognized and were motivated by participants' desire for their individual results[10] and saw disclosure as a potential strategy for enhancing recruitment and retention in ADRD research. While we are unaware of any published literature directly linking return of participant-level results to enhanced research engagement, a variety of studies support this association. Participants[34-35] and study partners[36] suggest that personal benefit gained from ADRD research, including learning individual or family health results, can facilitate enrollment and retention in studies. In contrast, a lack of disclosure of results serves as a barrier[37].

Among sites that do not currently return amyloid or tau PET results, interest in future disclosure is near ubiquitous, highlighting the need to better understand and address implementation barriers. The most common barrier was purely logistical: disclosure was not a planned part of most ADRC longitudinal cohorts. This finding underlines that PET disclosure would require not only standalone protocols and resources for communication of this information, but rather adaptation of existing workflows and documents to ensure return of results is feasible, sustainable, and effective across the diverse contexts in which ADRCs operate. CLARiTI is not the only impetus for disclosure; many large, national multi-site studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI)[18], the Longitudinal Early-Onset Alzheimer's Disease Study (LEADS)[38], and the US POINTER Study[39] have already launched return of results programs. Indeed, the latest funding announcement for the ADRCs requires some element of disclosure to individual participants. The RoR Core will continue to partner closely with sites and leverage expertise from other studies to develop guidance around these changes.

Additional logistical barriers include lack of expertise in disclosing results and additional time burdens for staff. Data from the survey themselves demonstrate the feasibility and efficiency of returning results, with most sites indicating that sessions are completed within 30 minutes using virtual or in-person modalities. This finding reflects a growing consensus that remote return of results is a viable option[40,41]. Indeed, utilizing technology to conduct remote visits can increase site capacity and return-of-results feasibility. Though 'face-to-face' in-person and video may be linked to lower participant distress[42], participants may be given the choice of modality for receiving their results[18,40,41] to balance the needs of sites (lower time and effort burden) and participants (lower time and travel burden, enhanced capacity to involve of out-of-

area support persons). Survey results also suggest that ADRCs effectively employ a multidisciplinary disclosure team, including physicians and advanced practice providers (e.g., nurse practitioners, physician assistants), but also neuropsychologists, counselors, social workers, and advanced trainees. This may assuage concerns about both expertise and time demands for any single team member. There are no established qualifications or competencies required to communicate biomarker results; however, various studies have commented on key practices and styles that may result in better post-disclosure outcomes[42]. The CLARiTI RoR Core must meet concerns regarding lack of expertise with a variety of multimodal learning opportunities for clinicians of diverse training backgrounds. The first of these trainings was accomplished in April 2025 with a national webinar through the National Alzheimer's Coordinating Center (https://clariti.naccdata.org/for-researchers/for-adrcs#webinars). Additional in-person and asynchronous educational offerings will be developed in coming months, and will reference published or publicly available training around biomarker testing for clinicians and researchers[43].

Additional barriers to disclosure implementation include concerns about unintended harms to participants. There is growing evidence to alleviate this concern; studies of post-disclosure outcomes demonstrate that participants across the cognitive spectrum rarely experience new or exacerbated psychiatric symptoms[44,45], and do not regret learning results[46]. Nonetheless, participants may experience transient test-specific distress, worry, and experiences of stigma after learning of biomarker positivity[44,47]. These 'risks' must be discussed pre-testing and monitored post-disclosure. Furthermore, protocols should incorporate the presence of a support person[42,48] and approach the discussion of results with clarity, compassion, and validation[42], as these factors are associated with lower post-disclosure distress. The CLARiTI

RoR Toolkit will incorporate suggested language and considerations for working with both participants and their loved ones as part of the disclosure session. Additionally, the RoR Core will provide validated pre- and post-disclosure screening measures to track changes in mood, as well as recommendations for how and when they should be applied.

Another concern for researchers is the potential for participants to experience medicolegal discrimination should research results be shared with medical or insurance providers, employers, or other entities[49]. Half of the sites reported sharing results with medical providers with participant approval, and very few include PET results in the electronic health record directly. Site-specific context regarding electronic health record entry is important in that some ADRCs are stand-alone centers, whereas others are embedded within a clinic wherein adding a result to an electronic health record is part of the standard of care. Risks and benefits of sharing results with medical providers/electronic health records should be carefully discussed prior to testing, ideally. Parameters around data-sharing must be clearly defined to avoid accidental breach of confidentiality.

Overall, sites already sharing amyloid PET generally align with published guidelines for ADRD biomarker disclosure that recommend (1) determining appropriateness of returning results; (2) providing pretest education and seeking consent; (3) returning results to the individual and their support person; and (4) following up to promote recipient(s) well-being[19,20,50-52]. Most ADRCs that disclose amyloid or tau provide pre-disclosure education and post-disclosure resources (e.g., clinical referrals, lifestyle recommendations). When disclosing, most sites provide a qualitative label (most commonly ‘elevated’ or ‘not elevated’) as opposed to a quantitative value or graphic. While consistent with the FDA-approved visual read process for amyloid PET, several sites reported participants’ desire for quantitative and graphical

information, as reported elsewhere[53]. Future work is needed to evaluate the effectiveness and utility of standardized quantitative values (e.g., centiloids) and graphical risk representations. Fewer sites provide a written report to participants, despite literature suggesting that written reports may be helpful for improved participant experience and recollection of results[54,55].

This study had several limitations. First, while results from the ADRCs may generalize to other research and even clinical settings, Centers have strict parameters and workflows that do not exist in other contexts. Relative risks and benefits of testing for and disclosing biomarker information differ greatly based on these settings, as does capacity for pre-test counseling and post-disclosure follow up. Second, while this survey represents an updated review of return of results practices at ADRCs, it does not capture the nuances of disclosure at each site. For instance, we did not assess the exact language used to communicate results to participants (e.g., how dementia risk is communicated based on the qualitative result) or the timeline and nature of follow-up. As indicated in one recent scoping review[50], more information is needed to inform comprehensive and standardized guidelines for returning amyloid PET and other biomarkers. The CLARiTI Return of Results Core will contribute to these guidelines by leveraging the national ADRC network to conduct iterative program development and evaluation of disclosure.

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Consent Statement

Given that human subjects were not involved in this study, individual informed consent was not required.

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None.

Conflicts of Interest

SCJ has in the past three years served in an advisory capacity to Enigma Biomedical, Eli Lilly, and AlzPath. NAC has served as a consultant for NewAmsterdam Pharma in 2023 and on a 2-day advisory board for Eli Lilly in 2025. Authors ARF, HK, JMR, CME, BCD, NTA, ECM, and LRC have no conflicts to disclose.

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Keywords: Biomarkers, Positron Emission Tomography, Return of Results, Disclosure, Risk Communication

Legends

Table 1. Proportion of ADRCs Disclosing Individual Research Results, by Participant Diagnosis

Table 2. Elements of Amyloid and Tau PET Return of Results Sessions

Table 3. Motivations and Barriers to Returning Amyloid and Tau PET Results

Table 2. Elements of Amyloid and Tau PET Return of Results Sessions

Disclosure Element	**Amyloid Disclosing Sites (*n*=19) # (%)**	**Tau Disclosing Sites (*n*=6) # (%)**
Pre-disclosure Education	14 (74%)	3 (50.0%)
Summary Report	10 (53%)	3 (50.0%)
Visual Aids/Scan Images	5 (26%)	2 (33%)
Recommendations/Action Steps	17 (90%)	5 (83%)
Clinical Referral	13 (68%)	3 (50%)

Note. PET = Positron Emission Tomography

Table 1. Proportion of ADRCs Disclosing Individual Research Results by Participant Diagnosis, 2019 vs. 2024

	Participant Diagnostic Group					
	Participants with Mild Cognitive Impairment or Dementia			**Participants Who Are Cognitively Unimpaired or have Subjective Memory Concerns**		
Type of information	**Roberts Survey 2019 (*n*=30)**	**CLARiTI Survey 2024 (*n*=36)**	***p***	**Roberts Survey 2019 (*n*=30)**	**CLARiTI Survey 2024 (*n*=36)**	***p***
Consensus research diagnosis	25 (83%)	27 (75%)	.52	23 (77%)	25 (69%)	.31
Neuropsychological test results	22 (73%)	27 (75%)	.87	21 (70%)	25 (69%)	.50
Amyloid PET results	13 (43%)	17 (47%)	.99	8 (27%)	16 (44%)	.51
MRI results	12 (40%)	21 (58%)	.45	10 (33%)	22 (61%)	.24
FDG PET results	8 (27%)	6 (17%)	.40	6 (20%)	4 (11%)	.32
Genetic test results, not APOE*	4 (13%)	2 (6%)	.41	3 (10%)	2 (6%)	.41
Tau PET results	3 (10%)	6 (17%)	.73	2 (7%)	4 (11%)	.99
CSF biomarker results	3 (10%)	8 (22%)	.36	1 (3%)	5 (14%)	.40
APOE genetic test results	2 (7%)	5 (14%)	.47	2 (7%)	5 (14%)	.70
Plasma biomarker results	N/A	9 (25%)	N/A	N/A	9 (25%)	N/A
Clinical Blood Labs	N/A	22 (61%)	N/A	N/A	23 (64%)	N/A

Note: * Indicated in present survey as "Other"; CLARiTI = Alzheimer's Disease Research Centers Consortium for Clarity in Alzheimer's Disease through Imaging; PET = positron emission tomography; MRI = magnetic resonance imaging; FDG-PET = fludeoxyglucose-positron emission tomography; APOE = apolipoprotein-E; CSF = cerebrospinal fluid; N/A = not applicable; these data elements were not part of the 2019 survey.

Table 3. Motivations and Barriers to Returning Amyloid and Tau PET Results

Motivation/Reason to Return PET Results	Amyloid-Returning Sites (*n* = 19) # (%)	Tau-Returning Sites (*n*=6) # (%)
Participant or Family Requested Results	17 (89%)	6 (100%)
Participant's Physician Requested Results	10 (53%)	2 (33%)
Inform Participant's Healthcare or Medical Decision-Making	15 (79%)	3 (50%)
Thanking Participants for Their Contribution to Research	17 (89%)	4 (67%)
Retention of Participants in Research	17 (89%)	4 (67%)
Ongoing Disclosure-Specific Study	11 (58%)	2 (33%)
Barrier/Reason Not to Return PET Results	**Sites Not Returning Amyloid (*n* = 17 sites) # (%)**	**Sites Not Returning Tau (*n* = 30) # (%)**
Information not Useful/Actionable	3 (18%)	5 (17%)
Financial Burdens	2 (12%)	3 (10%)
Time Burdens for Staff	4 (24%)	6 (20%)
Personnel Shortage	3 (18%)	6 (20%)
Participants Not Interested	0 (0%)	0 (0%)
Lack of Expertise in Disclosing Results	5 (29%)	5 (17%)
Not Part of Original Study (or in Consent)	11 (65%)	11 (37%)
Results Do Not Meet Clinical Regulations	3 (18%)	8 (27%)
Potential for Unintended Harms to Participants	6 (35%)	7 (23%)
Concerns About Legal Liability	2 (12%)	2 (7%)
Other	6 (35%)	4 (13%)

Note: PET = positron emission tomography

Highlights

- Individual research result disclosure has increased significantly since 2019.
- Results are shared more frequently with cognitively unimpaired participants.
- Disclosure requires interdisciplinary teams including physicians and psychologists.
- Disclosure motivations include enhancing retention and supporting clinical care.
- Barriers include limited resources/expertise, and potential participant risks.

Research in Context

Systematic Review: The Consortium for Clarity in Alzheimer's Disease Through Imaging (CLARiTI) Return of Results Core surveyed all 37 participating Alzheimer's Disease Research Centers (ADRCs) regarding practices around returning individual research results (e.g., cognitive data, biomarkers) to participants. Specific details regarding the disclosure of amyloid and tau positron emission tomography results were also requested.

Interpretation: Our findings demonstrate growing interest in and implementation of individual results disclosure in the ADRC network. Centers are highly motivated by participants' desire for their results and by the associated positive impact disclosure may have on trust-building, recruitment, and retention.

Future Directions: Specific practices commonly used across sites will inform the CLARiTI Return of Results framework being developed as part of a toolkit for sites. Barriers to returning results must also be addressed through a combination of capacity-building, training and resources to limit logistical challenges, and policy change to reduce risks to participants.

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