Tribal Consultation Report and Response

Alzheimer's Disease (AD) and AD-Related Dementias (ADRD) Real-World Data Platform

National Institute on Aging

National Institutes of Health

Disclaimer

This report accurately reflects perspectives on this project as of January 5, 2024. Insights from this consultation will be valuable as NIA considers future real-world data activities.

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Executive Summary

In March 2023, the National Institute on Aging (NIA) published a Notice of Funding Opportunity for the Alzheimer's Disease (AD) and AD-Related Dementias (ADRD) Real-World Data Platform (RWDP) cooperative agreement. Before the opportunity is awarded, NIA initiated a Tribal Consultation to seek input of Tribal Nations and request their ongoing collaboration with NIA and the cooperative agreement awardee in establishing the RWDP, including considerations for data governance; data collection, usage, and storage; participation in clinical research; outlets for ongoing partnerships with American Indian / Alaskan Native (AI/AN) communities; and inclusion of non-reservation-dwelling people who self-identify as AI/AN. Input will be used to inform and shape development and planning of the Platform.

The RWDP aims to transform the way dementia research is conducted; to increase and diversify participation in clinical studies by people from groups underrepresented in research; and ultimately produce evidence for new treatments, strategies, and policies for the management and prevention of AD-ADRD and support for caregivers. The need for a transformative effort in research is critical because the number of people with dementia is expected to rise as more people enter old age. Furthermore, disparities between advantaged and disadvantaged groups regarding the prevalence and treatment of dementia continue to exist; those same disadvantaged groups also tend to be underrepresented in clinical studies.

During the Consultation on January 5, 2024, the following topics and themes emerged:

- NIA must engage in clear, ongoing communication with Tribes throughout this initiative. Communication should be frequent, should occur through formal channels when possible, and should be explained in plain language.
- NIA must recognize and account for the diversity of opinion and of governance structure across all 574 federally recognized Tribes, leveraging formal processes and NIH resources to ensure communication and clarity about individual Tribes' data governance and sovereignty policies and preferences.
- NIA must recognize that resources like the NIH THRO and NIH TAC are facilitators of communication with Tribal Nations, but they do not speak for Tribal Nations.
- The RWDP should honor and respect Tribes' sovereignty and control over their data.
- NIA must ensure data quality within the RWDP, including ensuring representativeness of all AI/AN people, especially non-reservation dwelling people who identify as AI/AN.
- NIA and the awardee should ensure the inclusion of urban-dwelling and non-reservation dwelling people who identify as AI/AN.
- Research that uses RWDP data should provide direct and meaningful benefits to Tribes and AI/AN people.
- Research that uses RWDP data should focus on prevention and early detection.
- NIA should consider potential points of collaboration between RWDP and other organizations and entities that serve Tribal Nations and AI/AN people.

NIA and the awardee will pursue ongoing engagement with Tribal Nations throughout the life of the RWDP initiative to shape policies that respect and honor each Tribes' ordinances and wishes surrounding their members and their data. NIA will also work with the awardee to ensure representation of non-reservation dwelling AI/AN people within the Platform and will

pursue dialogue and partnerships with the organizations and initiatives suggested by Tribal leaders and representatives.

Description of the Critical Event

In March 2023, NIA issued a request for applications to establish a cooperative agreement to build an Alzheimer's disease (AD) and AD-related dementias (ADRD) Real-World Data Platform (RWDP). The Platform aims to create a resource that will transform the way dementia research is conducted in order to address the growing impact of AD-ADRD in the United States population. Real-world health data throughout a person's lifespan that may provide insight into potential dementia treatments will be linked in a way that preserves privacy via a variety of data sources across 70%-90% of the U.S. population. This resource will provide both a source of data for observational, real-world studies as well as a source for clinical trial recruitment for people who choose to participate.

AD-ADRD RWDP Program Background

AD and AD-related dementias are a prominent and growing concern for an aging population, particularly for AI/AN populations. One forecast says that between the years 2014 and 2060, the number of AI/AN people aged 65 and older living with dementia in 2060 will be five times higher than the number of people in 2014.[1] There is also evidence of a disparity between AI/AN people and white people in the development of dementia. A recent study estimated that 23% of AI/AN Medicare beneficiaries 65 and older may have dementia compared with 12% of their white counterparts.[2]

While there have been advances in our understanding of dementia since the passage of the National Alzheimer's Project Act in 2011, there are obstacles in how dementia research is conducted today that hinder researchers' ability to uncover knowledge and generate and share treatments and prevention strategies for AD-ADRD.

- **Disconnected Real-World Data**. Information generated from things like electronic health records, lab results, medical claims and billing, medical images, mobile devices and wearables, and other data from real-world sources would help build a health profile across people's lifespans. Longitudinal profiles like these are critical, as AD and many AD-related dementias typically begin in the brain many years before symptoms appear. Linking these data sources together will help researchers generate evidence, identify patterns, evaluate potential treatments and interventions, and share those treatments and interventions with those who need it. But these data are disconnected and are spread across a number of different providers, organizations, and other sources that, at this point, make conducting wide-ranging research of this scope practically impossible.
- **Unrepresentative Studies**. Many of the studies and clinical trials examining dementia fail to recruit and retain participants that reflect the individuals and communities disproportionately affected by the disease. Participants in research tend to be

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[1] Alzheimer's Association and Centers for Disease Control and Prevention. Healthy Brain Initiative: Road Map for Indian Country. https://www.cdc.gov/aging/healthybrain/pdf/executive-summary-road-map-for-indian-country508.pdf

[2] Moon HE, Kaholokula JK, MacLehose RF, Rote SM. Prevalence of dementia in American Indians and Alaska Natives compared to White, Black, and Hispanic Medicare Beneficiaries: Findings from the National Health and Aging Trends Study. J Racial Ethn Health Disparities. 2023;10(4):1527-1532. doi:10.1007/s40615-022-01338-y

overrepresented by those who have more financial resources, live in or near urban areas, and identify as white.

- **Slow Rate of Innovation**. The lack of access for real-world data means that most studies today rely on a single source of data. This limits the kinds of AD-ADRD-related questions that can be explored and the types of answers that can be generated. This slows down efforts to bring new treatments, support, and prevention strategies to people with AD-ADRD and their caregivers.

The AD-ADRD Real-World Data Platform aims to address these shortcomings by connecting and harmonizing real-world data in a secure and privacy-preserving environment as a resource for AD-ADRD researchers and for people affected by AD-ADRD. The Platform's objectives are to:

1. Improve applicability and generalizability of findings through larger datasets that include more diverse populations;
2. Capture more complete information about individuals and populations by linking together a variety of data sources;
3. Increase the speed at which scientific questions can be answered and results shared with the community;
4. Enable more inclusive clinical trial recruitment and research participation;
5. Improve researchers' ability to answer questions that cannot be feasibly or readily answered via clinical trial

Description of AD-ADRD RWDP

The Real-World Data Platform will include data from a number of different types of data sources. These sources could include electronic health records from clinics, hospitals, pharmacies, or other points-of-care; data from insurance claims; consumer spending; data about the environments and neighborhoods we live in; or sensor data from things like smartphones and medical devices. Together, data representing 70%-90% of the total U.S. population – and 80% of the U.S. population with AD-ADRD – will be included in the Platform.

These data sources can be linked together in a way that preserves peoples' privacy. Authorized users who access the Platform to analyze real-world data will not see identifying information about individuals, and access to the Platform and rules surrounding data usage and governance will be overseen by NIA, the cooperative agreement awardee, appropriate Institutional Review Boards, and other external experts and people with lived experience with AD-ADRD.

The Platform will open a number of different opportunities to enhance research, develop new treatments and interventions, and refine existing treatments and interventions. These opportunities may include identifying risk factors and protective factors that play a role in the onset of dementia; developing more accurate screening tools for AD-ADRD; exploring whether medications that are currently used for other purposes are also effective for dementia treatment; and developing new treatments and methods that could improve the quality of life for people with AD-ADRD and their caregivers.

The Platform will also increase access to clinical trial participation for groups who are typically underrepresented in clinical research. The cooperative agreement awardee must provide a plan to facilitate more inclusive and diverse recruitment into clinical trials, that incorporates innovative methods to remove as many barriers to clinical research participation as possible. This plan

could include "virtual" data collection through smartphones or wearables, or "in-person" where a person usually receives their normal health care without requiring several long trips to a dedicated research center.

The cooperative agreement awardee must also partner with groups that are underrepresented in clinical research to incorporate their insights about the Platform, help develop its core ethical framework, establish policies about data privacy and governance, and help in the development and refinement of ways to make clinical trial participation accessible to a wider and more diverse set of people.

The Platform will be built as part of a cooperative agreement between NIA and the awardee. As a cooperative agreement, NIA will have substantial programmatic involvement, including providing oversight of the Platform and facilitating Platform activities. As part of its oversight and facilitation role, NIA will seek out partnerships and meaningful engagement with groups and communities that are underrepresented in clinical research in shaping the Platform, including developing policies about data privacy, research participation consent, data governance, how to communicate the results of research findings, and other aspects of the RWDP. It is in this spirit that NIA initiated a Tribal Consultation to begin an ongoing conversation with Tribal Nations to help shape the RWDP.

Steps Taken to Initiate a Consultation

NIA met with representatives from the NIH Tribal Health Research Office (THRO) and NIH Tribal Advisory Committee (TAC) in a series of meetings in February 2023 and March 2023, and again in June 2023, to provide background information on the Platform and discuss how to appropriately and meaningfully engage Tribal leadership and communities.

NIA convened a two-hour virtual Tribal Consultation and Urban Confer on the AD-ADRD Real-World Data Platform on January 5, 2024, from 2:00 to 4:00 p.m. EST. A Dear Tribal Leader Letter announcing the Tribal Consultation was sent to Tribal leaders along with a Framing Letter with information about the Platform.

Topics suggested for consideration at the Tribal Consultation included the following:

- How should AI/AN data be collected, stored, and shared responsibly for Alzheimer's disease and related dementias research?
- How should NIA approach communication, outreach, engagement, and long-term inclusion and sustainable involvement in clinical research and trials?
- How would AI/AN communities want to be involved in data governance and access?
- How can the Real-World Data Platform team build and sustain meaningful partnerships with representatives of AI/AN communities?
- How should NIA approach data stewardship and governance for rural, urban, or non-reservation dwelling individuals who self-identify as AI/AN?

Perspectives and Recommendations Provided During the Consultation Process and NIA Response

Several themes and topics emerged during discussion with Tribal leaders and representatives during consultation. Those topics and NIA responses are summarized below.

Ongoing Communication

Tribal leaders and representatives emphasized the need for ongoing communication with Tribes given the broad and ongoing scope of the RWDP and the depth, breadth, and complexity of information that needs to be conveyed to Tribal and AI/AN communities. Multiple consultations will be needed to keep Tribes informed and to gain their input throughout the life of this initiative. Explaining concepts in plain-language is also critical, as Tribal leaders and elders, by nature of their position, have many responsibilities and may or may not have the technical background necessary to read through and understand jargon related to a database of this size and scope. Attendees also requested that materials for presentations be sent out in advance to help give Tribal representatives more time to absorb information.

NIA Response

The RWDP will be a living and evolving initiative. NIA understands that ongoing communication and consultation between Tribes, NIA, and the cooperative agreement awardee is critical to ensure the Platform and its data policies honor Tribal sovereignty. NIA will also ensure that supplemental materials for future consultations and other communications be sent out well in-advance and will take care to use clear language and avoid jargon when explaining Platform concepts.

Recognize and Account for Diversity across Tribes

Perspectives regarding the RWDP and data governance and privacy between all Tribes across the country are diverse. Tribes have varying organizational structures and capacities to examine RWDP-related questions – for example, Tribes may or may not have their own Institutional Review Boards and may partner with other Tribes and entities to use their Institutional Review Boards. Tribal representatives suggested leveraging NIH resources, such as the NIH TAC and the NIH THRO, to initiate formal processes and coordinate communication between NIA and Tribal Nations regarding RWDP data governance, development of consent procedures for research recruitment, data privacy, and other considerations. They also suggested receiving input from Institutional Review Boards that serve AI/AN populations, such as those from Tribes or from the Indian Health Service (IHS). Attendees emphasized using these formal processes as much as possible to help streamline and facilitate engagement with all Tribes. They also suggested ongoing communication with consortia and regulatory bodies representing many Tribes, such as the Northwest Portland Indian Health Board, as a way to streamline communication when possible.

NIA Response

NIA recognizes that each Tribe will have different perspectives to consider and governance structures and processes to respect. NIA intends to honor that diversity for all Tribes. NIA is in ongoing discussions with NIH TAC and NIH THRO about the Platform and how best to open and maintain communication with Tribes and intends to do so throughout the life of the Platform. NIA and the cooperative agreement awardee together will engage in formal processes for Tribal Nation outreach. NIA welcomes any feedback from leaders of all Tribes about the best ways to establish ongoing points-of-contact within their communities in an efficient but meaningful way, especially with those Tribes that may operate independently of any regulatory consortia. NIA and the awardee will honor and respect individual Tribes' laws, regulations, and opinions about RWDP data governance.

Recognize Only Tribal Nations Speak for Tribal Nations

Attendees encouraged NIA's engagement with NIH and other federal government resources to enable communication with Tribal Nations, but reminded NIA that those entities – NIH TAC, NIH THRO, IHS, and others – do not speak for Tribes.

NIA Response
NIA confirms that IHS, NIH THRO, NIH TAC, and other offices will be consulted to facilitate communication with Tribal Nations. NIA recognizes that those organizations do not represent the viewpoint of Tribes and do not speak for them.

Respect Data Sovereignty

There are different approaches among the 574 federally-recognized Tribes to manage consent to participate in research studies. In many communities, there is a complex interaction between community- and individual-level consent to participate in research, and not all communities approach the consent process in the same way. It is important for NIA and the cooperative agreement awardee to respect these different approaches.

Attendees also noted that a healthcare clinic on one Tribe's land may serve members of multiple different Tribes. Obtaining permission and going through a particular clinic's or Tribe's review processes does not necessarily mean that *all* appropriate Tribal processes have been observed. NIA and the awardee must engage all appropriate parties in decisions about data collection.

Attendees asked how NIA and the RWDP team can support the capacity of Tribes to control their data that is being collected in this project. They emphasized that respecting Tribes' ownership and control of their physical and electronic data is critical for building meaningful relationships with Tribal Nations.

NIA Response
NIA and the awardee will engage in ongoing communication with Tribes and AI/AN communities to establish, maintain, and evolve protocols for the appropriate handling of data associated with AI/AN people. NIA will respect individual and community policies and ordinances and will not report or use any data on Tribes or Tribal members without consulting and getting Tribal and/or individual permission and will respect all requests to discontinue use of all or portions of an individual's or community's data. NIA will follow all appropriate ordinances with respect to the Common Rule. NIA and the cooperative agreement awardee will adhere to strict privacy standards to ensure the Platform is secure according to federal guidelines, preserves individual privacy, respects community and Tribal privacy policy, and includes policies that will respect people's decisions on whether they want to be contacted to participate in clinical research.

Ensure Data Integrity and Quality

Comments from Tribal leaders and representatives encouraged including electronic health record and claims data beyond that which exists via IHS and its facilities into the Platform to make sure that as many potential health care touchpoints for AI/AN people as possible were included in the Platform. Data from an IHS health site on a given Tribe's land may not be singularly representative of all health data for that Tribe.

Comments also urged clarity on how clinical diagnosis codes are used to conduct analyses, particularly regarding diagnoses of memory loss, traumatic brain injury, and cognitive decline.

Attendees said that those conditions are likely underdiagnosed and identified a need for more complete data about those conditions in Tribal health settings. Discussion also focused on the lack of current data regarding dementia risks, such as family history, and efforts to conduct early screening.

A question was also posed regarding how NIA plans to correct any misclassification of AI/AN people for data in the Platform.

> *NIA Response*
> NIA and the cooperative agreement awardee will have continuing conversations with Tribal Nations and groups representing AI/AN people about which data should be included in the Platform in order to improve representativeness and create robust longitudinal health data profiles, no matter where they receive their care. NIA and the cooperative agreement awardee will engage AI/AN experts and communities to address misclassification of AI/AN people whose data are included in the Platform.
>
> One of the key features of the Platform will be linking multiple sources of data across time to build longitudinal health profiles. These profiles can help researchers better identify people at-risk for dementia. This includes people who may not have a formal clinical diagnosis in their electronic health record or who may not have formal documentation of other dementia risk factors such as memory loss or family history. These data sources will include insurance claims, electronic health records, and laboratory results, but will also include consumer data, publicly available environmental and Census data, among others.
>
> NIA welcomes further input regarding best approaches to addressing misclassification issues.

Ensure Involvement of Urban Programs and Non-Reservation-Dwelling AI/AN People

Attendees urged NIA to include urban clinics and other entities that serve non-reservation-dwelling AI/AN people. With many Tribes, most of their members are served within Urban Indian Health Programs rather than in health facilities on a reservation.

> *NIA Response*
> NIA acknowledges this and will work with the cooperative agreement awardee, the NIH THRO, and any other parties who can help ensure representation of urban-dwelling AI/AN people into the Platform and give as many people as possible the choice to be included in research studies using RWDP data.

Ensure Tribes and AI/AN People Receive Meaningful Benefits

Recognizing that the number of people with AD-ADRD will rise as more people in Tribal and AI/AN populations live longer, representatives emphasized that actionable and meaningful benefits must be directly realized for Tribes and AI/AN people, especially for people who are most in need. Opportunities for performing research, participating in research, and having an active voice in the conduct of research must be available to Tribes and not be limited to universities or other entities that have benefited most from such efforts in the past. Attendees also said that Tribes should be appropriately represented in terms of their overall risk for AD-ADRD within both the Platform and in studies using Platform data. Attendees also asked if

clinical trials using Platform data would be focusing recruitment in geographically local areas or if they would be nationwide in scope. In other contexts, some Tribes have assisted members who were struggling to get access to treatment, putting them in contact with local institutes conducting clinical trials for cancer. The hope is that Tribes would be able to do the same for its members with AD-ADRD and investigators using RWDP data.

NIA Response

NIA is committed to maintaining meaningful dialogue with the communities from which it receives data, and to ensuring study results are communicated in a timely manner. The cooperative agreement awardee must have a plan to translate findings from studies using RWDP data into clinical practice and real-world evidence that can benefit people living with AD-ADRD and their caregivers. The cooperative agreement awardee must also have a plan for ensuring groups that have been historically excluded from clinical research have a meaningful voice in the development of the Platform and its governance. While individual studies and trials using Platform data will have different recruitment goals, NIA will work with researchers to ensure they are meeting required benchmarks for diversity within their studies and will work with Tribal Nations and Urban Indian Health Programs to help enable their peoples' participation in clinical trials.

Address Prevention

Tribal leaders and representatives emphasized that while treatment for those with dementia is important, research should also focus on identifying and addressing early risk factors and potential protective factors for dementia, especially those factors that are unique to AI/AN people. Examples mentioned in the consultation include the effects of air and water pollution, or potential protective benefits of foods associated with traditional diets of various Tribes.

NIA Response

The Platform's planned linkages of several data sources that give insights into a person's health across time – not just data from insurance claims and EHRs, but also the types of food, goods, and services they buy and the types of environments and neighborhoods they live in – will help researchers explore potential protective factors and early risk factors that could delay or prevent the onset of dementia. NIA encourages continued dialogue and exploration of opportunities for engaging AI/AN researchers and communities to help generate ideas for further research.

Potential Partnerships

Attendees suggested several different entities for NIA to reach out to for potential involvement with the RWDP. These include: the Centers for Disease Control (CDC) Building Our Largest Dementia Infrastructure (BOLD); the NIH All of Us initiative; the National Congress of American Indians (NCAI); and the National Indian Health Board (NIHB).

Tribal leaders and representatives also asked about the possibility for Tribes to develop a consortium or partner with other existing organizations for maintaining communication with NIA and the cooperative agreement awardee, or for working with Platform data.

NIA Response

NIA will seek out and work with the organizations above and all other organizations that can provide meaningful input into the RWDP initiative and apply the lessons learned

from their efforts and experience. NIA will also support the formation of working groups to help coordinate Tribes' engagement with RWDP and explore areas for collaboration.

Other Considerations

Attendees reiterated a preference to have funds for initiatives distributed through existing mechanisms rather than having funds distributed through grant awards to limit Tribes competing against each other for the same pool of resources. Attendees suggested that funds could be provided to Tribes via Title VI Administration for Community Living (ACL) funds.

NIA Response

While this consultation meeting was meant to spur discussion about ways to honor Tribal data sovereignty and gain Tribal input with the creation of the RWDP, NIA appreciates this feedback and will consider all potential mechanisms to encourage equitable and fair support in future funding opportunities.

Next Steps

NIA will emphasize ongoing engagement with Tribal Nations and the NIH TAC and THRO throughout the life of this initiative. NIA hopes that all parties will work together to brainstorm ways to create meaningful discussions with all Tribal Nations in order to understand and honor their wishes regarding their members' data in the Platform and how best to handle the consent process for Tribal members to participate in clinical research. NIA will pursue communication with Tribal Nations via all formal channels available.

NIA will also work with the cooperative agreement awardee to reach out to appropriate entities to ensure inclusion of data representing urban-dwelling and non-reservation-dwelling AI/AN people within the Platform. The IHS Office of Urban Indian Health Programs will be engaged to help accomplish this. The RWDP team will also work together with the awardee to initiate discussion with other points of potential collaboration identified by Tribal representatives in this consultation, including the BOLD initiative, All of Us, NCAI, NIHB, and others.

NIA will also review prior Tribal Consultation reports and connect with colleagues from similar efforts (e.g., NCATS, All of Us) to incorporate the lessons learned from those initiatives.

Closing

NIA and the RWDP team are grateful for Tribal Nations' insights gained through this consultation, and we look forward to ongoing collaboration with Nations and with the future awardee to ensure the Platform provides the greatest possible benefit to people with AD-ADRD and their caregivers while honoring and respecting Tribes' sovereignty over their data.