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Perspectives on Using Pharmacogenomics to Guide Tobacco Cessation: Survey Results From an American Indian Community

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ABSTRACT

Pharmacogenomics research has predominantly focused on populations of European ancestry, limiting the application to diverse populations such as American Indian and Alaska Native (AIAN) communities. Our community-centric study aims to understand perspectives on utilizing pharmacogenomics to guide tobacco cessation in an AIAN community using a survey with qualitative and quantitative components. We assessed participant ($n = 273$) tobacco usage and cessation history, pharmacogenomics knowledge, and perceptions of utilizing pharmacogenomics in the context of tobacco cessation. We found that the majority of participants (92%) were aware of the risks associated with tobacco usage and believed it to be a problem within their community (76%). Our results showed that 29% of participants had some level of knowledge regarding pharmacogenomics and only 6% had previously participated in pharmacogenomics research, demonstrating the need for further education and awareness. Community involvement was a priority for participants, with 64% preferring Tribal inclusion in all research stages and 63% favoring partnerships with local health centers. We also found support for future research, with 68% viewing pharmacogenomics as a beneficial tool. Concerns were raised regarding the handling of genetic material and result dissemination, emphasizing the importance of ethical research practices, transparent communication, and community partnership. Our findings serve as a foundation for shaping future research efforts and developing a framework for implementing tobacco cessation interventions. Our community-centered approach addresses the specific needs of this AIAN community and offers insights applicable to research practices within other underserved and marginalized populations, particularly those with a historical distrust of research.

JEL Classification: DEI

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Senior authors Katrina G. Claw and Erica L. Woodahl contributed equally to this work.

Summary

- What is the current knowledge on the topic?
  - Nicotine is primarily metabolized by cytochrome P450 2A6 (CYP2A6). Interindividual variability in the CYP2A6 enzyme leads to changes in enzymatic activity, and consequently, differences in use of tobacco and nicotine products and success of cessation across individuals. Most research regarding CYP2A6 variability has been conducted in people of European ancestry, potentially limiting application to the broader population.
- What question did this study address?
  - Our study addresses the question of whether research in the pharmacogenomics of tobacco and nicotine cessation is of interest to an American Indian community in Montana and what are the community's concerns and barriers toward this research. We assessed participant tobacco and nicotine usage and cessation history, pharmacogenomics knowledge, and perceptions of utilizing pharmacogenomics in the context of cessation.
- What does this study add to our knowledge?
  - Most participants viewed pharmacogenomics as a beneficial tool in tobacco and nicotine cessation and were supportive of research, however, they emphasized the importance of community engagement and building trustworthy partnerships. A priority for participants was ensuring the involvement of Tribal leadership in all aspects of the research.
- How might this change clinical pharmacology or translational science?
  - The perspectives we learned will be useful in guiding future pharmacogenomic implementation efforts in American Indian communities using a collaborative and community-centered approach. Our research will assist in addressing the inequities in access to pharmacogenomic research through inclusion of underserved and underrepresented populations.

1 | Introduction

Pharmacogenomics has the potential to tailor medication therapies based on an individual's genetic makeup, thereby optimizing treatment efficacy and minimizing adverse effects. The clinical utility of pharmacogenomics includes, but is not limited to, oncology, cardiology, psychiatry, pain, and infectious disease [1, 2]. By tailoring treatment based on individual variability, pharmacogenomics promises more effective and individualized healthcare. Integrating pharmacogenomics into tobacco cessation strategies presents an opportunity to better understand how genetics influence tobacco use behaviors and its effect on the chance of successful cessation [3–8]. Widespread use of pharmacogenomics-guided treatment, however, faces challenges due to our limited knowledge about genomic variation across diverse populations. Current research disproportionately includes populations of European ancestry and those living in large urban areas, leaving many other ancestry groups and rural populations underrepresented [9–13]. This lack of diversity can lead to biased or incomplete understandings of how genetic factors influence drug response and disease susceptibility in different populations.

American Indian and Alaska Native (AIAN) populations are notably underrepresented in pharmacogenomics research. The extent of pharmacogenomic variation among AIAN people remains largely unknown, with limited data suggesting potential variability among AIAN populations [14–16]. Concerns expressed by AIAN communities related to genetic research are due to past experiences that cultivated historical distrust, often rooted in researchers' failure to engage with AIAN communities ethically and inclusively [17–21]. AIAN communities advocate for community-based participatory research (CBPR) approaches to enhance research practices, emphasizing mutual respect and shared decision-making, as well as ensuring community needs and priorities are addressed [16, 22–25]. The emphasis on building trusting relationships and ethical engagement underscores the significance of incorporating community perspectives and values into research practices.

Commercial tobacco and nicotine product use is a significant public health concern in Tribal communities [26–29]; however, identifying the most effective cessation method for individuals remains a challenge [30]. The application of pharmacogenomics into tobacco cessation efforts (e.g., nicotine replacement therapy or pharmaceutical intervention) offers an opportunity to integrate genomic information into our understanding of tobacco use behavior and cessation success. Nicotine is primarily metabolized by the drug-metabolizing enzyme cytochrome P450 2A6 (CYP2A6). Genetic variation in *CYP2A6* leads to interindividual variability in the enzymatic activity of CYP2A6 and subsequently influences the usage of commercial tobacco products and the success of cessation interventions [3–8, 31]. Pharmacogenomics can aid in developing more personalized treatment plans that could improve the chances of successful cessation. By identifying relevant genetic variation and predicting CYP2A6 activity among AIAN patients, pharmacogenomics-guided cessation strategies can also provide benefits to Tribal communities.

Integrating pharmacogenomics into tobacco cessation relies on community support, highlighting the importance of addressing historical concerns within AIAN communities and alignment with CBPR principles. We established a community–academic research partnership between the Confederated Salish and Kootenai Tribes (CSKT) and the University of Montana (UM) to increase the participation of AIAN people in pharmacogenomics research [22, 32]. The CSKT community, residing on the Flathead Reservation in northwestern Montana, is comprised of the Salish, Pend d'Oreille, and Kootenai Tribes [33]. A recent community health assessment reports there are approximately 8,000 enrolled CSKT members, with approximately 5,200 members residing within the Flathead Reservation [26]. Our partnership—particularly with the CSKT Tribal Council, CSKT Tribal Health Department, and the community advisory board for the project—addresses health challenges with an awareness of the unique needs and concerns of the CSKT community. Our ongoing collaboration strives for practical, culturally sensitive healthcare interventions developed with and for the CSKT community.

Our study aims to understand perceptions of utilizing pharmacogenomics to guide tobacco and nicotine product cessation in the CSKT community through the dissemination and analysis of a survey that was developed with a commitment to community-centered research in mind. The survey assesses the community's interests in intervention, recognizes concerns with genetic research, and identifies cultural considerations. Through our partnership between CSKT and UM, as well as collaboration with researchers from the University of Colorado, we engaged the community as partners and advisors in pharmacogenomics research. Ultimately, we aim to utilize results from the survey to inform future implementation efforts using genetics to tailor tobacco cessation methods in the CSKT community, potentially expanding genetics research to an underserved and marginalized population.

2 | Methods

2.1 | Study Setting and Recruitment

We distributed a survey with the help of CSKT partners to understand the perspectives of CSKT members and descendants on the utilization of pharmacogenomics to guide tobacco and nicotine product cessation. Flyers with information about the survey and a QR code were posted in locations across the Flathead Reservation, including Salish Kootenai College (SKC), CSKT Tribal Health Clinics, and CSKT governmental buildings; members of the study group also gave presentations about the survey at SKC. Information about the survey was also shared via email, on our website, and through social media. Due to these various survey distribution methods, it was not possible to determine how many individuals we reached with the survey; thus, we were unable to estimate a response rate. Data were collected from July 2022 to November 2023. Informed consent from participants was obtained through one-on-one interactions at in-person events and through online consent prior to the start of the electronic survey. In-person events served as an opportunity to foster our relationship with the CSKT community, building trust and offering transparency. All CSKT members (regardless of their use of commercial tobacco or nicotine products) were invited to participate in the survey. The study was approved by the UM, SKC, and University of Colorado Institutional Review Boards.

2.2 | Study Design and Analysis

The survey was developed collaboratively between members of the research group and was modeled after a prior research project [24]. Members of the CSKT community advisory board completed a pilot test of the survey and provided input for revisions and cultural appropriateness. The survey included four key sections: participant demographics, perceptions on tobacco use in the CSKT community, personal tobacco and nicotine product use and cessation efforts (only current and former tobacco and nicotine product users were instructed to complete this section), and the use of pharmacogenomics as a tool to guide cessation efforts. The survey included either 40 questions (for current and former tobacco and nicotine product users) or 27 questions (for those that have never used these products); questions were formatted as Likert scale, multiselect, yes/no, and open ended. Participants ≥ 18 years old and a self-identified CSKT member or descendant were eligible for the study. Results from participants who answered 'yes' to using nicotine-only products were combined with those who answered 'yes' to using commercial tobacco; there were no questions specific to either group. The survey took 15–20 min to complete and was offered in a print and an online format via Qualtrics (Provo, UT, USA). Surveys completed in print were manually entered into Qualtrics by members of the study team. Participants received a $15 gift card upon completion of the survey.

Survey responses were exported to an Excel spreadsheet from Qualtrics. Demographics were summarized, and we utilized Pearson's Chi-square test of association to assess if there were significant differences in responses between age or gender. Members of the research group (M.L.W. and D.M.W.) independently analyzed the open-ended questions in a deductive manner using thematic analysis and further collaborated to combine results and assess for potential bias. Responses were grouped into common themes and representative quotes were identified. We further used themes identified from the open-ended questions to analyze all Likert scale, multiselect, and yes/no questions in an inductive manner. In response to a question raised by a CSKT community member during a presentation about the research results, we performed a post hoc analysis using Pearson's Chi-square test of association between the use of tobacco for cultural reasons and participants' desire to quit tobacco products altogether.

We also generated a word cloud from participants' written responses to the statement "Please share any questions, concerns, or comments you have regarding the use of pharmacogenomics in tobacco cessation" using Zygomatic (Amersfoort, Netherlands). The word cloud was used to identify common words expressed by participants to be further grouped with themes identified by the survey. Participants who did not provide comments ($n = 56$) were not included. Common everyday words like "a," "the," and "and" were automatically excluded and these exclusions were double-checked manually.

3 | Results

3.1 | Participant Demographics

We received 304 responses to our survey. Participants were excluded from analysis if self-identified Tribal affiliations were not CSKT ($n = 21$) and if survey completeness was less than 75% ($n = 10$). After these exclusions, a total of 273 participants were included in the final analysis (Table 1). Of the 273 participants, 222 identified as current or former users of tobacco or nicotine products and were asked additional questions regarding personal tobacco and nicotine use and cessation efforts (Table 2). Participant demographics are comparable to those of respondents in a recent CSKT community health assessment report [26]. We found no significant differences between responses based on age or gender.

TABLE 1 | Participant demographics ($n = 273$).

Characteristics	*n* (%)
Age	
18–39	153 (56.0%)
40–59	92 (33.7%)
60 and over	22 (8.1%)
Prefer not to answer	6 (2.2%)
Gender	
Man	101 (37.0%)
Woman	163 (59.7%)
Transgender or do not identify as male or female	2 (0.7%)
Prefer not to answer	7 (2.6%)
Education level	
Some high school	31 (11.4%)
High school diploma/GED	84 (30.8%)
Some college	47 (17.2%)
Associate degree	38 (13.9%)
Bachelor's degree	38 (13.9%)
Master's degree	8 (2.9%)
Doctorate	1 (0.4%)
Technical school	8 (2.9%)
Vocational school	11 (4.0%)
Prefer not to say	7 (2.6%)

TABLE 2 | Tobacco and nicotine products use and cessation efforts of current or former tobacco users ($n = 222$).

Characteristics	*n* (%)
Approximately how old were you when you started using tobacco and nicotine products?	
< 18	77 (34.7%)
18–25	87 (39.2%)
26–35	10 (4.5%)
36–40	1 (0.5%)
40–55	5 (2.3%)
> 55	2 (0.9%)
Do not know/not sure	12 (5.4%)
Prefer not to answer	28 (12.6%)
Have you attempted to quit using all tobacco and nicotine products in the past year?	
Yes	47 (21.2%)
No	162 (73.0%)
Prefer not to answer	13 (5.9%)
How soon would you like to quit using all tobacco and nicotine products?	
Within the next month	18 (8.1%)
Within the next 6 months	27 (12.2%)
Within the next 12 months	15 (6.8%)
Someday but not the next 12 months	47 (21.2%)
Not interested in quitting	62 (27.9%)
Prefer not to answer	53 (23.9%)

3.2 | Community Insight on Tobacco Use and Awareness

We gained insights from participants regarding their awareness and opinions on tobacco and nicotine products. Our survey results revealed an overwhelming majority (92%) of participants had a high level of awareness concerning the health risks associated with tobacco products (Figure 1A). We also found that 76% of participants expressed that tobacco usage is a problem in the CSKT community (Figure 1B). One participant's comment demonstrated the community's focus on finding ways to decrease tobacco usage: "I think it would be a great help to the Native community if there was a way to increase the cessation of tobacco, as to my knowledge a large percent of us smoke." Our study also highlighted a personal connection to the risks of tobacco usage, with 78% of participants reporting loved ones or close friends affected by tobacco consumption (Figure 1C). Some reasons expressed by participants to quit using tobacco products include: "Didn't want my daughter to think smoking was okay"; "My grandchildren"; and "My newborn baby." These quotes show the influence of friends and family on the desire to quit tobacco products. These findings highlight the widespread recognition among participants of the community-wide impact of tobacco use, emphasizing a collective sense of responsibility toward addressing this public health challenge with future generations in mind.

An important finding from our survey was that 63% of participants use tobacco for traditional purposes, highlighting a unique cultural consideration for AIAN populations (Figure 2). A CSKT community member raised an interesting question during a presentation of the research results: "were individuals who used tobacco for cultural reasons less likely to want to quit?" We found no statistical significance between those who use traditional tobacco and a desire to quit tobacco products altogether. Therefore, it is important to consider people's traditional tobacco use, but not to assume that this is always a barrier to cessation. This information can also be used to potentially recognize each individual's unique treatment goals as some participants had varying opinions on their cultural tobacco versus commercial tobacco use.

3.3 | Participants' Desire for More Information About Pharmacogenomics

Our results revealed that although some participants had experience with pharmacogenomics, an opportunity for further

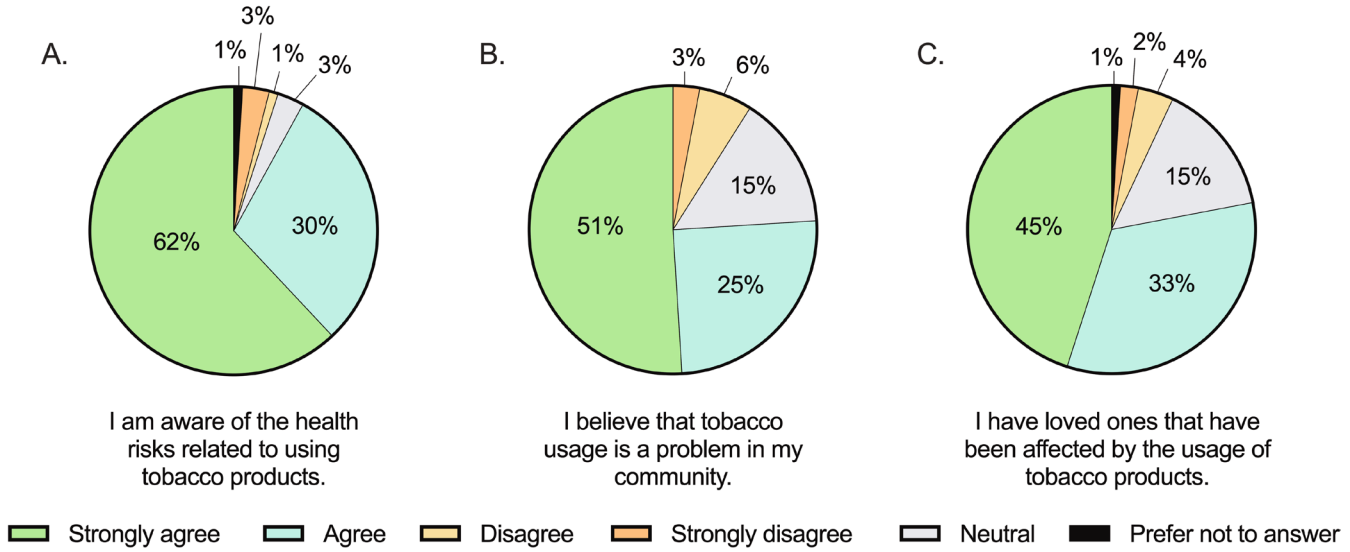

FIGURE 1 | Participant responses regarding tobacco usage and awareness. Percentage of participants that answered "strongly agree" (green), "agree" (teal), "strongly disagree" (orange), "disagree" (yellow), "neutral" (gray), or "prefer not to answer" (black) to the following questions regarding: (A) awareness of health risks due to tobacco use; (B) tobacco use as a problem for the CSKT community; and (C) whether their loved ones have been affected by tobacco use.

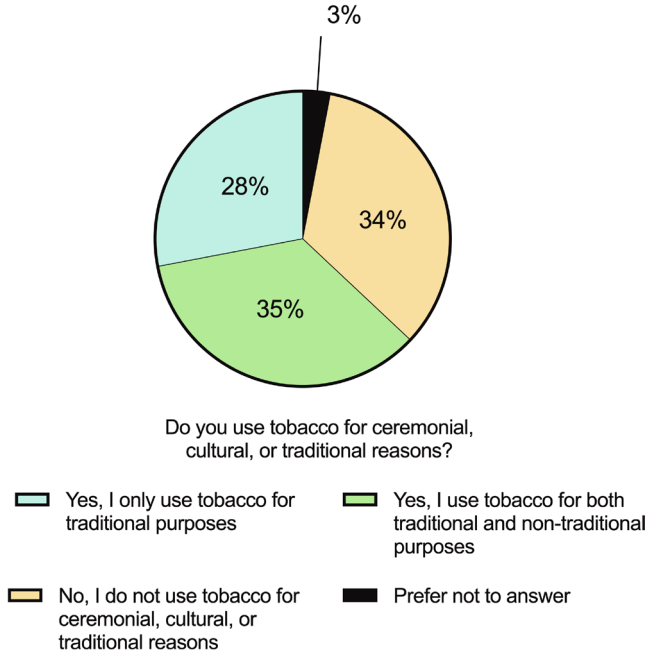

FIGURE 2 | Prevalence of traditional tobacco use among participants. Percentage of participants that answered "yes" (green or teal) or "no" (yellow) to using tobacco for traditional purposes ("prefer not to answer" in gray).

community engagement and education remains. We found that 11% of participants had previously provided a DNA sample for a research study (Figure 3A) and 6% had participated in pharmacogenomics research (Figure 3B). We found it encouraging that 29% of participants either "strongly agree" or "agree" that they are knowledgeable in pharmacogenomics; however, there is still work to be done to more effectively engage the community. It is crucial not to overlook perspectives of individuals without knowledge of pharmacogenomics and expand educational efforts alongside research endeavors, empowering community members to make informed decisions regarding research participation. The majority of participants (55%) agreed that they would participate in a pharmacogenomics research study if they had more knowledge and information (Figure 5A). One participant's comment was encouraging that community members see a community-centric model of pharmacogenomics research as a useful tool to improve health, "I think [this approach] would be a better method for Native Americans to understand pharmacogenetics and epigenetics to motivate the healing process." Several other participants expressed a desire for more information about pharmacogenomics: "More awareness in the community about what [pharmacogenomics] is. Our community has a huge tobacco issue."; "How does [pharmacogenomics] work? And why hasn't it been used in more studies?"; and "I would like to know more about [pharmacogenomics]."

3.4 | Importance of Community Involvement in Pharmacogenomics Research

Our survey assessed the community's opinions on research methods in order to inform future research and implementation of pharmacogenomics. Our results demonstrated that the majority (64%) of participants agree that pharmacogenomics research should include the Tribal community in all aspects of the research process (e.g., planning and design, data collection, analysis, and distribution of results). Likewise, most participants (63%) would prefer that pharmacogenomics research be conducted in partnership with their local Tribal Health center or clinic. These preferences for Tribal partnerships underscore the importance of conducting studies within familiar and trusted community settings, aligning with principles of CBPR to promote culturally sensitive research practices.

The community's desire for support was also exemplified in a word cloud highlighting the most commonly used word in describing

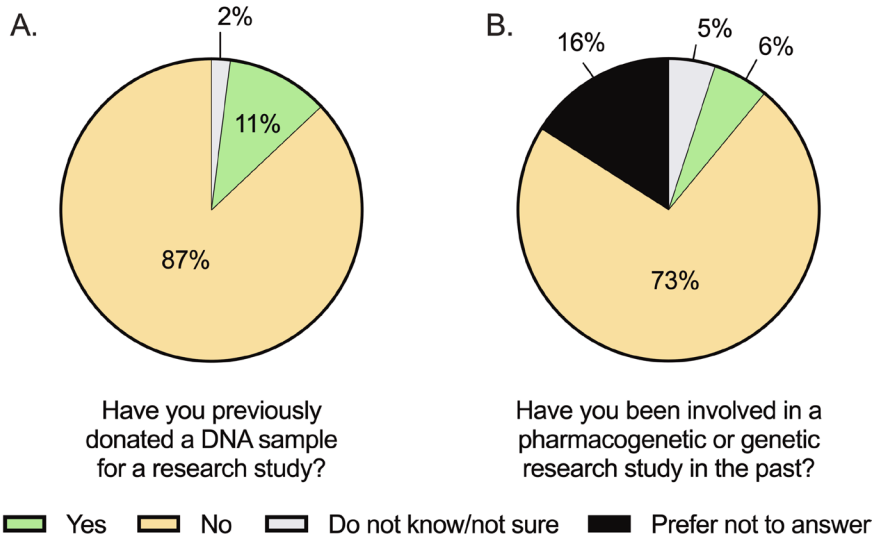

FIGURE 3 | Prior participation in pharmacogenomics research. Percentage of participants that answered "yes" (green), "no" (yellow), "do not know/not sure" (black), or "prefer not to answer" (gray) to whether they have (A) previously donated a DNA sample for a research study or (B) been involved in a genetics study in the past.

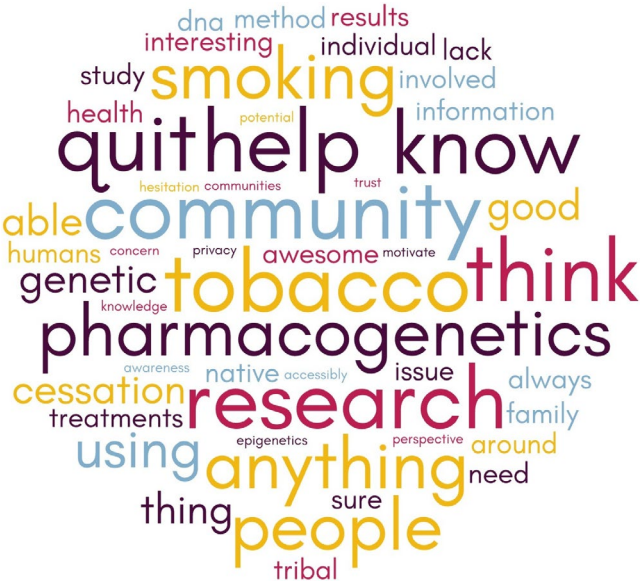

FIGURE 4 | Word cloud visualization of participant views on pharmacogenomics for tobacco cessation. The word cloud illustrates the most frequently occurring words from short answer responses, with words with the highest frequency corresponding to the largest words in the word cloud. Colors were randomly assigned for higher readability.

participant's views on using pharmacogenomics for tobacco cessation (Figure 4). The word cloud revealed that participants most often used words such as "community," "help," "know," "people," "research," and "quit," suggesting that the community is seeking support in various forms, whether it is through access to resources, knowledge about pharmacogenomics, or assistance with quitting tobacco use. The prominence of words like "community" and "people" underscores the importance of collective action and shared responsibility in addressing tobacco cessation within the CSKT community. Additionally, the frequent use of words like "help" and "know" indicates a desire for guidance and understanding, highlighting the need for education and outreach initiatives tailored to the community's specific needs and concerns.

3.5 | Community Perspectives on Pharmacogenomics Research

The CSKT community expressed support and interest in furthering research in pharmacogenomics for tobacco cessation and participants saw the research as beneficial for the community. The majority of participants (68%) said they believe using pharmacogenomics to guide tobacco cessation would be a good resource for their community (Figure 5B). Likewise, support was shown through short answer responses such as: "I believe that using [pharmacogenomics] research to guide tobacco cessation efforts would be a good resource for my community"; "I'm grateful it's being done, anything to help Indigenous people live healthy, full lives is so good in my eyes"; and "I think this would be very beneficial to our Tribal community". The majority of participants (53%) indicated they would be willing to donate a sample of DNA for a future study (Figure 5C). This level of interest in the CSKT community is promising to further research efforts and to implement pharmacogenomics as a clinical tool.

3.6 | Concerns With Handling Biospecimens and Results Dissemination

Although the support many participants expressed toward pharmacogenomics research is promising, there is still a large proportion of participants (29%) with concerns regarding pharmacogenomics (Figure 5D). One common theme was concerns in the handling of biospecimens and genetic material. Some participant quotes are as follows: "The story of Henrietta [Lacks] always plays in my mind, when considering using genetic materials for anything in non-white communities" and "The DNA results [are] what I would worry about. Privacy I'm sure would be a cause for hesitation." Both of these quotes show the community's concern for data and sample stewardship. Participants also expressed the need to disseminate research results to the community with one participant saying, "My only concern is how we can put out [pharmacogenomics] information to the general public more accessibly." This quote emphasizes why

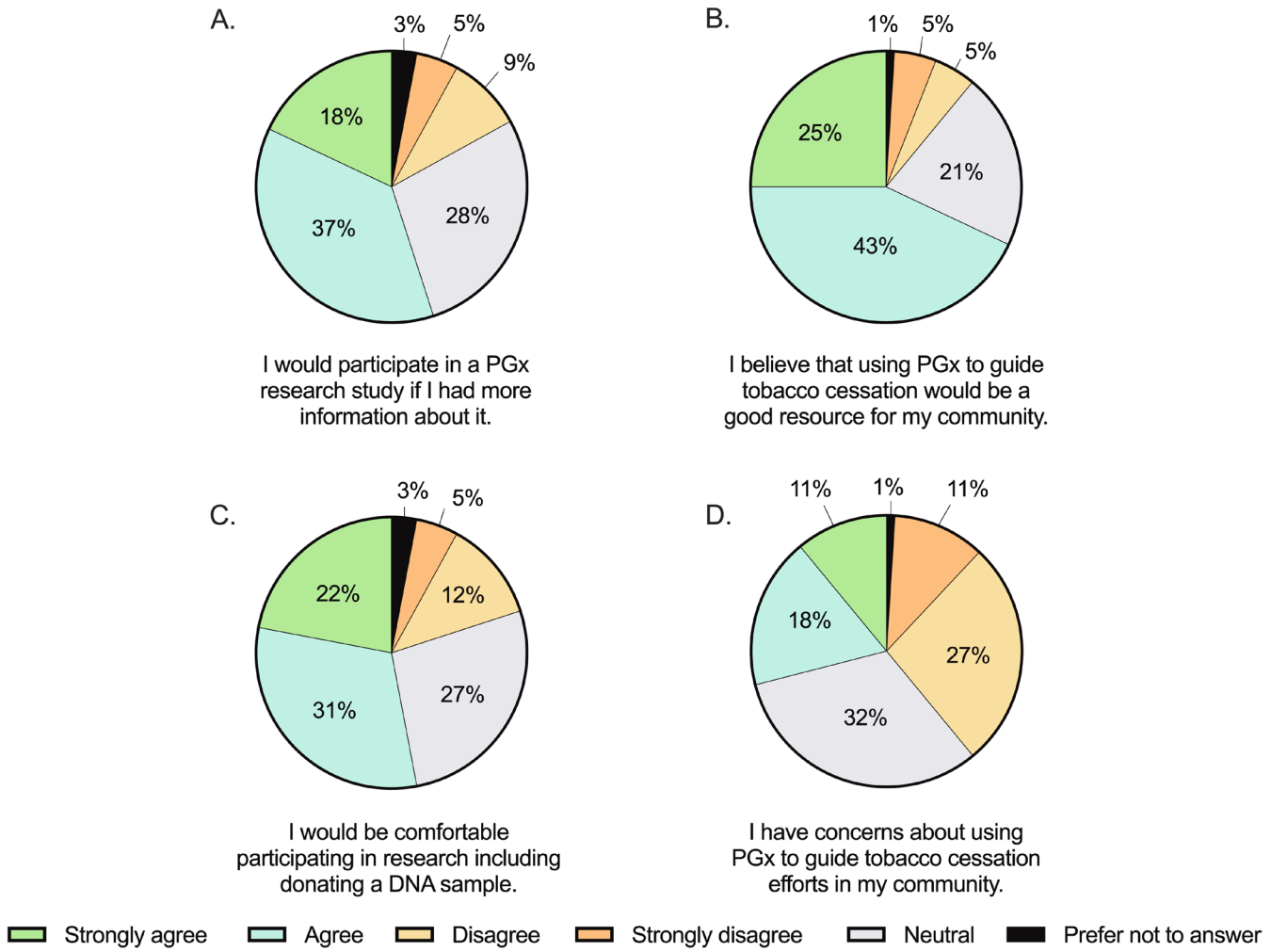

FIGURE 5 | Views of using pharmacogenomics as a tool to guide tobacco cessation efforts. Percentage of participants that answered "strongly agree" (green), "agree" (teal), "strongly disagree" (orange), "disagree" (yellow), "neutral" (gray), or "prefer not to answer" (black) to the following questions regarding: (A) whether they would participate in a pharmacogenomic study with more information; (B) whether pharmacogenomics is a good resource for the CSKT community; (C) whether there is comfortability donating a DNA sample for pharmacogenomic research; and (D) concerns regarding pharmacogenomic research are present in the community.

dissemination of research results is crucial to increasing awareness and developing a trusting and collaborative relationship. We are committed to prioritizing research dissemination, including publishing in the Tribal newspaper [34], creating informative videos and brochures, presenting at community events, and remaining accessible for questions.

4 | Discussion

Our study highlights the attitudes, perspectives, and concerns regarding the utilization of pharmacogenomics to guide tobacco and nicotine cessation within AIAN communities. Through a comprehensive survey, we unveiled optimism among CSKT members about the potential benefits of pharmacogenomics initiatives for tobacco cessation. Despite historical issues and mistrust in genetic research, our findings suggest a willingness among CSKT community members to engage in transparent dialogue and participate in future pharmacogenomics research. Concerns regarding data stewardship, dissemination of results, and the need for further education highlight that work is still needed. Researchers should address community concerns by prioritizing communication and transparency, engaging community leaders in decision-making processes, respecting Tribal sovereignty, ensuring that research benefits the community, and respecting community ownership of data and biospecimens. Inclusive research practices are essential in building trust and ensuring that pharmacogenomics research respects the autonomy and dignity of AIAN communities, leading to equitable health outcomes.

We found that the majority of CSKT participants exhibited high awareness of tobacco-related health risks and expressed concern about usage prevalence in their community. A significant number of participants had personal connections to tobacco use, with some sharing stories of loved ones affected by tobacco use and how their loved ones' usage inspired their cessation efforts. The majority of participants agreed that tobacco use is a problem in their community, highlighting that this research is a priority for the community. The CSKT community has prioritized tobacco cessation through a number of initiatives, including educational programs for community members on tobacco

cessation, cessation treatment programs through the CSKT Tribal Health Department, and expanding research efforts. This highlights the critical need for alignment between community health priorities and research endeavors, emphasizing how research should directly address and support the needs of the community.

Recognizing the role of cultural tobacco use is vital in addressing tobacco cessation among Tribal populations. Our study found that the majority of participants acknowledged using tobacco for ceremonial, traditional, or cultural reasons. It is important to recognize key differences between cultural and commercial tobacco usage, such as variations in formulation and contents of the tobacco, means of inhalation, and frequency of use. Individuals may think about the use of cultural tobacco and commercial tobacco differently, and therefore, the goals of care for CSKT patients may need to consider continued use for traditional purposes. Understanding this prior to the implementation of pharmacogenomics in tobacco cessation is critical to providing personalized care.

While we were encouraged that a relatively high number of participants expressed prior knowledge of pharmacogenomics research, more outreach is needed, with many describing the need for further education alongside research and implementation efforts. As research leads to clinical implementation, providing adequate education is necessary to empower individuals to make informed decisions about their healthcare. Importantly, a significant portion expressed a preference for community involvement in all stages of pharmacogenomics research, emphasizing the role of education in fostering community participation and trust. Furthermore, the majority indicated a preference for conducting research in partnership with the CSKT Tribal Health Department and CSKT Tribal leadership, aligning with the CBPR principles of our CSKT-UM partnership. Our findings underscore the significance of community engagement and education in shaping research agendas and promoting equitable health outcomes [13, 16, 22, 23, 25].

The CSKT community described important considerations regarding how the research is conducted. Several participants explicitly expressed concerns regarding the handling of biospecimens belonging to community members and the accessibility of research results to the community. These concerns are grounded in a history of misuse of specimens, lack of confidentiality and transparency, and stigmatizing interpretations specifically for AIAN populations [16, 22, 25]. Yet, barriers to participation in pharmacogenomics research may result in limited benefits for AIAN people in genetics-guided treatment, potentially perpetuating health disparities. Researchers must prioritize understanding community needs and priorities through active engagement within the community. Our research has also shown the importance of ensuring accessibility to pharmacogenomics research and implementation, as well as addressing concerns around the handling of data and biospecimens. Our approach includes utilizing CBPR methods and building upon our longstanding relationships with the CSKT community, particularly with the CSKT Tribal Council, CSKT Tribal Health Department, and the community advisory board for the partnership. Maintaining open channels of communication and addressing community concerns will remain central to our research efforts and moving toward interventional strategies to incorporate pharmacogenomics into tobacco cessation efforts.

As we navigate the outcomes of our research, it is important to acknowledge the limitations we encountered, which shed light on areas for improvement in our approach. The majority of participants enrolled in our study identified as women—partially explained by recruitment at a women's health and wellness event on the Flathead Reservation—which may mean the perspectives of men and other gender identities are less well characterized in our study. This is consistent with our previous research projects with the CSKT; however, higher participation of women is common [13, 14, 35]. Another consideration is that our participant population may be biased toward the inclusion of individuals who already have a more positive view of research, possibly leaving out perspectives from people who may have less favorable views toward research, and thus were less interested in participating. Additionally, some terminology used in the survey is of a higher reading level due to the nature of the topic and the inability to change terms (e.g., DNA, gene, metabolism, pharmacogenetics, and pharmacogenomics), which could hinder comprehension. In order to address this concern, however, our survey began with a definition of these technical terms. Furthermore, our research presents perspectives from only one AIAN community, and AIAN communities are not homogenous. Given the dearth of perspectives from AIAN people in research, however, our findings represent opinions and considerations from communities that are often excluded from research. Although we acknowledge these limitations, they have served as invaluable lessons, guiding us toward a deeper understanding of our research process and underscoring the need for continued community collaboration.

Our research serves as a foundational step in informing future pharmacogenomic studies with AIAN communities within the context of tobacco and nicotine cessation. Understanding the frequency of known *CYP2A6* genetic variants and the identification of rare or novel variants that influence CYP2A6-mediated nicotine metabolism in the CSKT population could inform tobacco cessation strategies specifically tailored to this community. Ultimately, our goal is to implement tobacco and nicotine cessation interventions informed by pharmacogenomics to improve patient care within the CSKT community through personalized treatment approaches. Beyond the CSKT community, our study sheds light on the importance of community-centric approaches to further research when working with underserved and marginalized populations. Through continued collaboration, transparent communication, and ethical community engagement, our research paves the way for more equitable and effective healthcare practices for AIAN populations worldwide.

Author Contributions

Wrote manuscript: M.L.W., D.M.W., S.R.K., K.G.C., and E.L.W. Designed research: L.I.M., B.N.C., K.G.C.; and E.L.W. Performed research: M.L.W., D.M.W., S.R.K., K.E.B., K.A., and J.S. Analyzed data: M.L.W., D.M.W., S.R.K., and J.S. Contributed new reagents/analytical tools: M.L.W., D.M.W., S.S.G.M., K.G.C., and E.L.W.

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Conflicts of Interest

As an Associate Editor for Clinical and Translational Science, Erica Woodahl was not involved in the review or decision process for this paper.

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