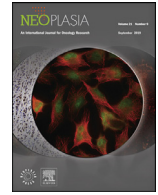


Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Neoplasia

journal homepage: www.elsevier.com/locate/neo

Indigenous peoples and inclusion in clinical and genomic research: Understanding the history and navigating contemporary engagement

Angela Waanders^{a,b}, Alex Brown^c, Nadine R. Caron^d, Alexa Plisiewicz^{b,e}, Sean T. McHugh^{b,e}, Think Q. Nguyen^{b,e}, Kaitlin Lehmann^{b,e}, Jeffrey Stevens^f, Phillip J. Storm^{b,e}, Adam Resnick^{b,e}, Tom Belle Davidson^g, Sabine Mueller^{h,i,j,k}, Cassie Kline^{l,*}

^a Department of Hematology, Oncology, and Stem Cell Transplant, Ann & Robert H Lurie Children's Hospital of Chicago, Chicago, IL, USA

^b Center for Data-Driven Discovery in Biomedicine, Division of Neurosurgery, Children's Hospital of Philadelphia, Philadelphia, PA, USA

^c Australian National University and Telethon Kids Institute, Adelaide, SA, Australia

^d University of Northern British Columbia, Prince George, BC, Canada.

^e Division of Neurosurgery, Children's Hospital of Philadelphia, Philadelphia, PA 19104, USA

^f Division of Pediatric Hematology/Oncology, University of Washington School of Medicine, Seattle Children's Hospital, Seattle Children's Research Institute, Seattle, WA, USA

^g Division of Hematology-Oncology, Cancer and Blood Disease Institute and Department of Pediatrics, Children's Hospital Los Angeles, Los Angeles, California, USA

^h Department of Neurology, University of California San Francisco, San Francisco, CA, USA

ⁱ Department of Neurological Surgery, University of California San Francisco, San Francisco, CA, USA

^j Department of Pediatrics, University of California San Francisco, San Francisco, CA, USA

^k University Children's Hospital Zurich, Zurich, Switzerland

^l Department of Pediatrics, Division of Oncology, Children's Hospital of Philadelphia, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

ARTICLE INFO

Keywords:

Diversity

Equity

Inclusion

Indigenous people

Clinical research

Pediatric neuro-oncology

ABSTRACT

Despite significant improvements in pediatric cancer survival outcomes, there remain glaring disparities in under-represented racial and ethnic groups that warrant mitigation by the scientific and clinical community. To address and work towards eliminating such disparities, the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and Children's Brain Tumor Network (CBTN) established a Diversity, Equity, and Inclusion (DEI) working group in 2020. The DEI working group is dedicated to improving access to care for all pediatric patients with central nervous system (CNS) tumors, broadening diversity within the research community, and providing sustainable data-driven solutions. To this end, the DEI working group aims to coordinate regular educational sessions centered on critical DEI topics in pediatric research and clinical care of pediatric patients, with a focus on pediatric neuro-oncology. In April 2022, the group led a moderated panel of experts on Indigenous Peoples' rights and participation in clinical research activities. The following paper serves to provide the scientific community a perspective on how to prioritize the inclusion of Indigenous Peoples in research with cultural sensitivity and with the intent of improving not only representation, but patient outcomes regardless of patient race, ethnicity, or socioeconomic background.

Background for PNOC/CBTN DEI working group and moderated panel

The Diversity, Equity, and Inclusion (DEI) working group is comprised of members across the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and Children's Brain Tumor Network (CBTN). PNOC is an international consortium with member institutions throughout the United States, Europe, Asia and Australia, all dedicated to bringing new therapies to children and young adults with central nervous system

(CNS) tumors. CBTN is an international, multi-institutional clinical and genomic repository aimed to drive innovative discoveries and accelerate open science to improve the health of children and young adults diagnosed with a CNS tumor. Through their respective roles as clinical trial and large-scale data sharing networks, each organization recognizes the essential nature of diverse patient and community participation in clinical research, data collection and open sharing. Unfortunately, historic and contemporary data demonstrate that underrepresented groups are more likely to die from cancer and less likely to enroll in clinical re-

Abbreviations: Children's Brain Tumor Network, CBTN; Pacific Pediatric Neuro-Oncology Consortium, PNOC.

* Corresponding author at: Children's Hospital of Philadelphia, Division of Oncology, 3500 Civic Center Boulevard, Room 3615, Philadelphia, PA 19104, USA.

E-mail address: klinec@chop.edu (C. Kline).

<https://doi.org/10.1016/j.neo.2023.100879>

Received 1 September 2022; Received in revised form 13 January 2023; Accepted 19 January 2023

1476-5586/© 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

search [1–5]. In addition, there is a dearth of underrepresented populations from the professional fields involved in clinical research leading to a gap in representation throughout medical and research systems [6–9].

In 2020, PNOC and CBTN added the Diversity, Equity, and Inclusion (DEI) working group to their existing portfolio of disease-specific working groups. To better understand inequities in clinical outcomes and develop mechanisms to address them, the mission of the DEI working group is to “*Work together to end inequalities in pediatric neuro-oncology by improving access to care for our patients, broadening diversity within our community, and providing sustainable data-driven solutions.*” They are fulfilling this mission by (1) collecting, analyzing, and broadly sharing data driven findings to report on what is currently known about inequities and inequalities among their patient population and the physicians and researchers that make up their teams; (2) expanding diversity within their team and, as a result, throughout the field of pediatric neuro-oncology; and (3) providing resources/education to PNOC and CBTN communities, keeping others up to date on impacting literature, current events, and presentations or talks in this field.

To directly address the third goal, and towards the overall mission of the DEI working group, they organize recurring panel discussion on DEI topics. The first moderated panel titled, “Indigenous Peoples and Inclusion in Clinical and Genomic Research: Understanding the History and Navigating Contemporary Engagement,” took place on April 18, 2022 via videoconference. The panel brought together experts on Indigenous Peoples’ rights, tribal engagement, and complexities of inclusion of Indigenous Peoples in clinical and genomic research from the United States, Canada, and Australia. Panelists shared historic events that contribute to Indigenous Peoples’ hesitancy to participate in clinical and genomic research, discussed concerns regarding data sharing and inequities in data utilization, individual versus tribal sovereignty, and protections of Indigenous rights in research.

Session panelists

Chief Mutáwi Mutáhash (many hearts) Lynn Malerba

Mohegan tribe chief, chairwoman of the tribal self-governance advisory committee of the federal Indian Health Service (IHS)

Dr. Malerba is the first female Chief in the Mohegan Tribe’s modern history. Prior to her role as Chief of the Mohegan Tribe, she served as Chairwoman of the Tribal Council and Executive Director of Health and Human Services. She has a Doctor of Nursing Practice from Yale University and a Masters’ Degree in Public Administration and has been awarded honorary Doctoral degrees from Eastern Connecticut State University and the University of St. Joseph. She currently chairs the Tribal Self-Governance Advisory Committee of the Indian Health Service, is the Secretary for the United South and Eastern Tribes board and is a member of the Justice Department’s Tribal Nations Leadership Council and National Institute of Health (NIH) and Treasury Tribal Advisory Committees.

Dr. Nadine Caron

Co-lead investigator, Silent genomes project

Dr. Caron is a member of the Sagamok Anishnawbek First Nation. She is a surgical oncologist and the sole Indigenous physician within BC Cancer, the only Indigenous academic faculty member at the University of British Columbia’s (UBC) School of Medicine, a Professor at UBC Northern Medical Program and Department of Surgery, and Senior Scientist at Canada’s Michael Smith Genome Sciences Center. Dr. Caron is a founding co-Director of the UBC Center for Excellence in Indigenous Health and Consultant in development of British Columbia’s first-ever Indigenous Cancer Strategy. She leads the development of the Northern Biobank Initiative, a First Nations-governed and controlled biobank, and is co-Lead investigator on the Silent Genomes project.

Professor Alex Brown

Professor of Indigenous Genomics, Telethon Kids Institute, Australian National University

Dr. Brown is an internationally recognized Aboriginal clinician and researcher who has spent his career focused on Aboriginal health. Much of his work has been at the interface of geographical isolation, cultural context, socioeconomic disadvantage, and health disparities. His trans-disciplinary research focuses on the burden and contributors to health inequality in Indigenous Australians, with a primary focus on cardiovascular disease, diabetes and cancer. His career has spanned the Menzies School of Health Research, Baker IDI Heart and Diabetes Institute, and the South Australian Health and Medical Research Institute (SAHMRI).

This session was moderated by Dr. Cassie Kline, PNOC co-Project Leader and co-Leader of the PNOC/CBTN DEI working group. Dr. Cassie Kline is a tribal member of the Pueblo of Isleta, the current Director of Clinical Research for Neuro-Oncology in the Division of Oncology at the Children’s Hospital of Philadelphia (CHOP), co-Leader of the CHOP Cancer Center Diversity Committee, and an Assistant Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania. Dr. Kline specializes in the care of children, adolescents, and young adults with CNS tumors.

Introduction

The past four decades have seen significant improvements in pediatric cancer survival, with five-year survival in children and teens reaching approximately 85% [10]. However, cancer remains the top cause of death by disease in children [11] due to several factors, including but not limited to, cancer subtypes with incredibly low survival and treatment disparities such as barriers in access to clinical trials. Race and ethnicity have been specifically associated with disparities in survival of CNS tumors [1,3–5]. Non-white children from lower socioeconomic particularly demonstrate lower overall survival compared to white children [12]. To develop disparity mitigation strategies, it is important to understand the reasons behind those disparities, directly connect with underrepresented communities, and advance interventions in ways that best meet needs with the mindset of a continual learner applying cultural humility [13–17].

As defined by the United Nations Special Rapporteur to the Sub-Commission on Prevention of Discrimination and Protection of Minorities, Jose R. Martinez Cobo,

“Indigenous communities, peoples and nations are those which having a historical continuity with pre-invasion and pre-colonial societies that developed on their territories, consider themselves distinct from other sectors of societies now prevailing in those territories, or parts of them. They form at present non-dominant sectors of society and are determined to preserve, develop, and transmit to future generations their ancestral territories, and their ethnic identity, as the basis of their continued existence as peoples, in accordance with their own cultural patterns, social institutions and legal systems.” [18]

Indigenous Peoples’ life expectancies can be as much as 20 years lower than that of non-Indigenous people worldwide [19]. In the United States, Indigenous childhood and adolescent cancer survival is worse than non-Hispanic white children and adolescents and the disparities are greatest for cancers amenable to medical intervention [20]. Further, disparities exist for American Indian/Alaskan Native children [21] in pediatric clinical trials and relevant genomic research participation. This hampers subsequent research in outcomes and therapy development that most effectively reach Indigenous Peoples. It is estimated that, between 2015 and 2018, Indigenous Peoples contribute as few as 0.02% of samples used in genome-wide association studies [22]. If the fundamental issues associated with these inequalities are not addressed, both at

the genomic and clinical trial stages, disparities may continue to grow even as pediatric oncology therapies advance.

To address the above concerning statistics, PNOG and CBTN aim to better understand Indigenous Peoples' perspective on participation in clinical research. The group also endeavors to participate in initiatives aimed at inclusion of Indigenous Peoples in research decisions and program development and to inspire members of their organizations to adopt strategies to reach and benefit Indigenous populations. The subsequent sections of this document draw from the experience and expertise of the panel experts on Indigenous rights, summarizing important concepts communicated from these experts.

Indigenous peoples and research participation

Indigenous people have always been researchers, using research within their own communities and the natural world to inform on how to protect their health. Despite a clear desire to perform and contribute to research, there are significant barriers to Indigenous Peoples' participation in the Western research process.

Historical cause for hesitance

An environment of mistrust developed early on between Western researchers and Indigenous communities who, as they were overtaken by colonizers, had the opinions and standards of Western culture imposed on them. Research pertaining to Indigenous Peoples was performed through a European lens, meant to benefit the colonizers, not the Indigenous people and expectations to assimilate were enforced [23–27]. The founding of the IHS in the United States within the War Department and typically as part of ceded land negotiations potentially contributed to ongoing mistrust and hesitancy to participate in future clinical research and data collection activities [28]. The initial intent of the IHS was to decrease transmission of communicable diseases between Indigenous Peoples of the US to the soldiers fighting in the Civil War, rather than to benefit Indigenous communities. These types of scenarios have undoubtedly contributed to a basis of mistrust among Indigenous patients [29].

In Australia, and likely around the world, relationships with colonial institutions have been similar. Trust issues and hesitancy around participating in research is based on strong historical context. Research has been fundamentally used as a tool of oppression and colonization, even used to justify colonizing Indigenous lands [24,26,30,31]. This research made its way into fundamental policy in Australia, including profiteering by early university institutions in the trade of Indigenous bodies and collections of skeletal remains and sacred ceremonial objects on display in museums and universities. Based on the lack of trust in processes that do not bring benefit to their communities, Indigenous people hesitate to participate in research and anticipate it to do more harm than good.

The western way

Time is a commodity that is commonly in short supply in Western medicine, but time is imperative when rebuilding individuals and community trust in healthcare and research initiatives. Further, healthcare decisions in Indigenous communities are often made according to different priorities than more individualistic Western societies. In the collective cultures of Indigenous Peoples, a community of people are involved in decision-making and decisions around participation in research activities require long-term engagement and active listening by clinical researchers.

The ideas surrounding healthcare also differ between Western and Indigenous cultures. While Western researchers focus on disease causation, Indigenous Peoples commonly aim to understand attribution. Questions center on why the disease is impacting them. Questions like: 'Why have I been diagnosed with the disease now?' and 'What have I done to develop the disease?' may arise. This additional complexity can hinder communication and the decision-making process as the two different perspectives try to understand disease through different perspectives.

Patient samples and data are regarded differently from the Indigenous to the Western perspectives as well. While protection of healthcare data in the US revolves around personal privacy, Indigenous priorities place high priority on community engagement in decision making and with potential cultural reverence of human samples like tissue. Thus, to effectively engage Indigenous people, we must leave behind common individualistic Western priorities and make the case to improve human health at the community level and in ways that will benefit all communities contributing to the research.

Access Concerns

Indigenous Peoples, as collaborative researchers and contributors, must be provided the opportunity to make an informed decision about leading or participating in research. Unfortunately, healthcare and research services are often physically or financially inaccessible or culturally inappropriate [32]. Inexperience with research participation may be a significant hindrance to Indigenous people and it is the responsibility of the researcher to share the meaning of the research and the potential to improve health in a way that is relevant to the community. Often, Indigenous communities are geographically distant from institutions performing the research and researchers and providers lack geographic and community expertise. These barriers further limit Indigenous participation. As such, research must be designed thoughtfully to include and effectively reach Indigenous people at all levels with a commitment to understand the individual Indigenous community needs, both in terms of understanding the research and benefiting from it.

The information feedback loop

Demonstration of respect to communities and building of trust relies on an iterative process that involves frontline communication, consideration, validation, and implementation. An important part of communication is returning to communities who may have taken the time to sit down with researchers, contribute to focus groups, complete surveys, and share experiences as research is being implemented. Researchers should feedback what they hear, how they will address concerns, and provide updates on research progress and community impact. Even the best listeners can fall victim to misunderstandings across cultural lines and the feedback loop ensures that research is being conducted appropriately and that tribes are validated in their concerns and shared experiences. In addition, the final product from the research must be shared, regardless of the time elapsed between the start of the project and its conclusion. This information needs to be shared with tribes on platforms that are effective for them and with materials provided in the way each individual community mandates to facilitate responsible stewardship of the research [14,33].

Indigenous perspectives on cancer research

Cancer is a relatively new disease to many Indigenous populations such as those in Australia. As cancer incidence increases with age – except for pediatric cancers – increasing life expectancies of Indigenous Peoples mean an increase in the number of cancer cases and new need for research and treatments. With increased need will come growing exposure to Western medicine. This is an opportunity for physicians and researchers to improve their interactions with Indigenous Peoples and explore partnerships and training in medicine.

The problem with generalization

"If you know one tribe in the United States, you know one tribe in the United States, we're all very different." - Chief Mutáwi Mutáhash (Many Hearts) Lynn Malerba

The wrong way to build a clinical trial, research program, or biobank is to work from a mindset of one size fits all. Researchers and academics may have previously created biobanks in different locoregional environments or with the input of a subset of tribes; however, it is false to

assume that all successes are uniformly transferable. This strategy fails because it excludes the process that builds relationships and trust and enables individual communities to share needs and understanding of research being done. Partnership, communication, and relationships are fundamental to the trust building process, ensure community buy-in for the goals of the research and increase potential inclusion and impact that the research may have on each community [34–36].

Consultation, discussion, and storytelling are important aspects of program-building. Story-sharing is a critical component to survey or focus group feedback and investigators must be open to this step as a means to understand tribal history, perspective, and needs. Each tribe has unique approaches to how the gift of biologic specimens and data are treated and shared. Some tribes believe that the biologic material ultimately needs to be returned to the person while others ask that there be a ceremony performed for tissue that is discarded [14]. Critical research must be done to ensure research activities are done according to tribal considerations.

The power of decision

The ideal concept of research success is not that Indigenous people uniformly participate in research, but that Indigenous people are given the opportunity to thoughtfully and insightfully participate in research. The same choices and opportunities for understanding that are offered to non-Indigenous Peoples, must be provided within the cultural context of Indigenous patients and the communities. An important aspect of this decision-making power, as it pertains to Indigenous Peoples, is the role that the community holds. Individual autonomy is recognized in tribal communities, but it is bound within collectivist responsibilities and obligations to the larger community [37]. It can be challenging for clinicians and mainstream institutions from an individualistic society to interact with families and communities who prioritize the broader implications of a decision on community above that of the individual person. While an individual can decide for themselves, when the research has the potential to impact the larger tribe, it is imperative for the tribe to contribute to the decision. A substantial consideration in the community decision regarding clinical research participation is the balance of risk and benefit of broad sharing of biospecimens and associated genomic data [14]. Engaging a local or tribal regulatory and/or ethics board should be considered to navigate distinctions between tribal and federal regulations [33].

Balancing risk and benefit

Due to long-lasting impact of harmful efforts shrouded under research and the community-based nature of Indigenous Peoples, tribes can be hypervigilant about risk. Conversely, research narratives, catering to the individualistic Western societal structure, are more focused on perceived or potential benefit. Even when considering benefit, it is essential that tribes define it on their own and balance those benefits against potential risks. While researchers can facilitate conversations around risk and benefit, it is not their place to define them for the communities.

An important risk that must be considered is the risk of identification or over-reaching inferences that are harmful to the community. The protection of privacy is more challenging with small tribes that share genomic information, as these small tribes run a greater risk of de-identification. These risks should be transparently discussed with tribal leaders and with protections put in place to prevent or lessen these risks. There should be an *a priori* plan for how data will be used, who has access to data, and how findings are disseminated. Several contemporary instances demonstrate situations where tribal consent was given for genomic research, but then resulted in data use beyond the scope of consent and resulting in harm to the contributing tribe [38–43]

Benefit is also a critical consideration for Indigenous Peoples when participating in research. When discussing the perceived risks and benefits of biobanking, Dr. Caron quoted one tribal Chief's comments on

genomic sharing, “*My Ferrari will never break down on Highway 16.*” Highway 16 is a highway in British Columbia with sharp curves around Talbot Lake and into the mountains of Alberta. It is commonly obstructed by landslides in the spring and avalanches in the winter and always traversed by wildlife. Highway 16 is not conducive to speed and a Ferrari is the last car you would want on such a dangerous highway. The Chief's point was that he will never own a Ferrari and thus, will never have to consider the risks or benefits of driving one on Highway 16. Similarly, if there is never the opportunity to participate in research and biobanking, tribal members will never be faced with the risks or potential benefits of these options. In response to this statement, Dr. Cron subsequently spent a whole weekend with tribal leaders educating on the sharing of information, lack of biobanks in Northern British Columbia, and potential opportunities of data contribution from the local Indigenous communities. These types of efforts are imperative to most effectively engaging and respecting tribal participation in research.

Building community researchers

One of the most thorough ways to ensure that the needs of Indigenous communities are met and that research is effectively communicated is to integrate Indigenous people into the research process, allow them a seat at the table, and provide them resources to build their own tables [3]. This engenders trust and ensures tribes feel supported by a research team that has their best interests in mind. One mechanism to establish researchers within communities is to create sustainable pipeline and training programs to grow interest and potential of students and trainees. It is imperative to provide educational opportunities and support mentorship. Such engagement will facilitate a path towards continued scientific research and grow the next generation of Indigenous researchers – ideally leading to independent researchers that drive supported research within individual tribes. Efforts can start with the youngest students, even at the primary school level, exposing children to science and providing resources from which they can grow interest and enthusiasm. At the level of secondary education, mentorship and hands-on research should be offered. In an ideal setting, institutions partner with tribes to facilitate basic science and clinical research programs for tribal students, establishing resources and opportunities that may not have previously existed. This will ensure a population of researchers that are well-versed at tribal traditions as well as clinical research practices and knowledge for how to bring these priorities together.

An example of effective pipeline building can be seen through the University of British Columbia Centre for Excellence in Indigenous Health. The University of British Columbia (UBC) established the Centre for Excellence in Indigenous Health in 2014 after consultation with Aboriginal communities, the First Nations Health Authority, educational partners, government liaisons, and non-profit groups. The Centre serves as a single coordinating point for Indigenous health initiatives within UBC and is dedicated to advancing Indigenous people's health through education, research, and traditional practice. Students are a top priority of the Centre and efforts to inspire future Indigenous researchers begin even before students reach the university. The UBC provides scholarships and infrastructure to ensure students succeed academically and personally. One highlight of the UBC program is the UBC 23 24 Indigenous Cultural Safety (ICS) Program. The program prepares future healthcare professionals to provide quality and culturally based care to Indigenous communities and was developed in response to the Truth and Reconciliation Commission of Canada's 94 Calls to Action. The 23rd and 24th calls to action, specifically state:

“#23: We call upon all levels of government to:

- Increase the number of Aboriginal professionals working in the health-care field;
- Ensure the retention of Aboriginal health-care providers in Aboriginal communities; and

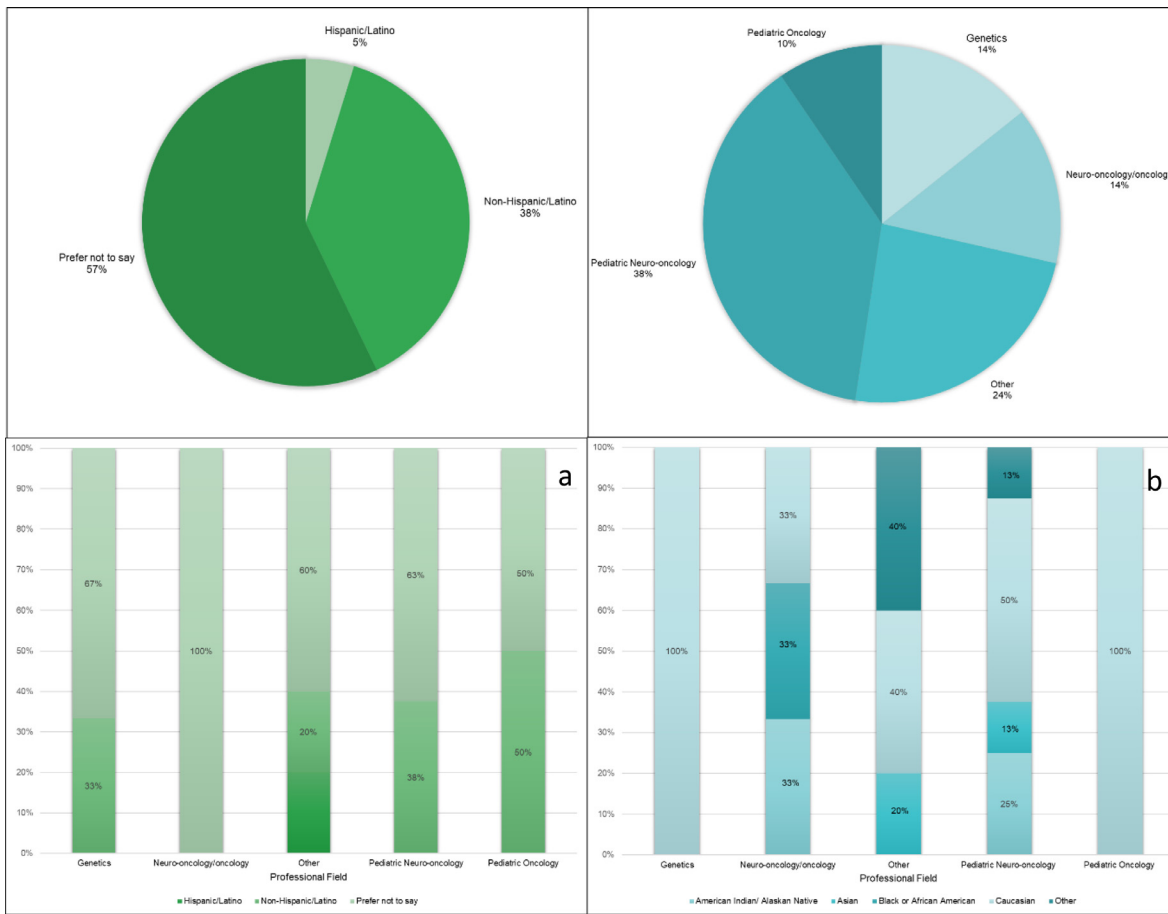


Fig. 1. Proportions of self-reported race, ethnicity, and professional field of panel attendees. Majority of respondents preferred not to identify ethnicity (57%) and a minority identified as Hispanic/Latino (5%; 1a). Majority of respondents were in the field of pediatric neuro-oncology (38%) followed by other (24%) and neuro-oncology/oncology (14%; 1b). Historically under-represented groups in medical and research fields similarly made up a minority of respondents with a substantial proportion of respondents preferring not to report on ethnicity across professional fields (1c) and with Caucasian respondents making up the majority across professional fields (1d).

- Provide cultural competency training for all health-care professionals.

#24: We call upon medical and nursing schools in Canada to require all students to take a course dealing with Aboriginal health issues, including the history and legacy of residential schools, the United Nations Declaration on the Rights of Indigenous Peoples, Treaties and Aboriginal rights, and Indigenous teachings and practices. This will require skill-based training in intercultural competency, conflict resolution, human rights, and anti-racism.”

UBC 23 24 ICS provides a curriculum based on Indigenous perspectives of history, the legacy of colonialism in Canada, Indigenous Peoples’ health and Canada’s healthcare system and utilizes combined training from both Indigenous and non-Indigenous people to forge allyship and promote inclusion. Although such efforts may not be able to be mirrored within all organizations, facilitating connections between Indigenous students and healthcare at any level will solidify interest and build systems that are transparent to all. Potential opportunities for Indigenous students to be directly mentored by Indigenous researchers will only further students’ success, but undoubtedly requires commitment throughout an institution.

“I think we can ask the question, rather than what’s wrong with Indigenous people, what our Indigenous people offer the world. And that beginning point is a start of a much deeper, much more nuanced, much more connected, much more spiritual conversation about how important Indigenous people and their knowledge is as we consider how we live and survive on this planet.

If we can do that, we’ve got a really good starting point for reconstructing a better way forward for all of us.” - Professor Alex Brown

Conclusions

There are undeniable historic and contemporary hardships faced by Indigenous Peoples regarding access to medical treatments, research opportunities, clinical trial participation, and careers. The goal of the PNOC/CBTN DEI working group is to bring such inequities to our pediatric neuro-oncology community and beyond and start to develop and collaborate towards solutions. A key step towards this is education, as was the major goal of moderated panel discussions on DEI topics. Our panel had 69 live attendees and provided opportunity for later review of the recording. In a post-discussion survey of the live panel, 100% (n=21) reported that they 1) enjoyed the panel, 2) would attend future discussions, and 3) learned something, further supporting our work and motivating the occurrence of future panel discussions. Unfortunately, even in our motivated attendees, there remain under-representation with only 5% of respondents identified as being of American Indian/Alaskan Native heritage and 5% as Hispanic/Latino (Fig. 1). It is imperative that more research is conducted to remove the barrier that lies between Indigenous individuals and all under-represented groups and accessibility to clinical research opportunities, as patients and investigators. For this to happen in Indigenous communities and arguably all communities, opportunities must be accessible and adaptive to fit specific community needs.

While we recognize that our centers of operation may be geographically distant from traditional Indigenous lands, we feel that the global networks we represent and the catchment area of our footprint has the potential to be far-reaching. We hope our work will serve as a first step to recognize barriers and cultural distinctions that have limited Indigenous Peoples' involvement in our work and hope to expand partnerships for patient care, clinical research, and pipeline programs. We also hope this publication serves as a statement of our dedication to the work and facilitates outreach for groups that have been historically under-represented. To this end, our current working group initiatives include both broad efforts to expand diversity in inclusion and targeted efforts to reach and facilitate recruitment of under-represented groups like Indigenous Peoples. To expand generational knowledge on cultural barriers and distinctions, we plan to continually host educational talks, training opportunities, and events that enforce and educate participants on racial and ethnic biases along with current topics concerning diversity, equity, and inclusion. We will continue to collect and improve collection of social determinants of health (SDoH) to further enhance research findings, close gaps, and to produce future publications and solution-directed strategies as based on evidence-based data. These aforementioned initiatives are advertised and marketed with cultural sensitivity to widespread audiences to amplify awareness through a variety of channels.

With a multifaceted, longitudinal approach to the issues, our team intends to expand on the single event in the current work to enhance our understanding of cultural barriers and further develop solutions to dismantle the problems at hand. As of November 2022, our efforts have led to improving our consent practices by educating CBTN and PNOG team members on cultural sensitivity as well as amplifying inclusivity by translating our informed consent forms into more non-English languages and considering self-report data collection measures for SDoH. These discussions and efforts are first steps, but the CBTN and PNOG team plan to continue implementing culturally sound tactics to combat inequities within our research practices. We recognize historic inequities and cultural insensitivities and hope that we set the stage for our future work as we continue as growing consortia. We hope for our current work to be a statement to hold ourselves accountable and driven towards this mission while encouraging other consortia and institutions to begin similar efforts.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRedit authorship contribution statement

Angela Waanders: Conceptualization, Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Alex Brown:** Data curation. **Nadine R. Caron:** Data curation. **Alexa Plisiewicz:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing, Visualization. **Sean T. McHugh:** Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing, Visualization. **Think Q. Nguyen:** Data curation, Project administration, Writing – original draft, Writing – review & editing, Visualization. **Kaitlin Lehmann:** Conceptualization, Project administration, Data curation, Writing – original draft. **Jeffrey Stevens:** Conceptualization, Writing – review & editing. **Phillip J. Storm:** Resources. **Adam Resnick:** Resources, Supervision. **Tom Belle Davidson:** Conceptualization, Project administration, Writing – review & editing. **Sabine Mueller:** Conceptualization, Supervision, Writing – review & editing. **Cassie Kline:** Conceptualization, Formal analysis, Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing, Visualization.

Acknowledgements

The authors would like to deeply thank Drs. Malerba, Caron, and Brown for providing insight and education during the panel presentation. Additionally, we want to sincerely thank the Drs. Gracelyn Smallwood and Mark Wenitong for their support and guidance. We are also incredibly grateful to Caitlyn Barrett for her contributions to reviewing the panel recording and assisting with the initial draft of this work and Margetta Thomas, Judi Lee, and Tiffani Copeland at CureSearch for Children's Cancer for reviewing and providing edits to the content. Our gratitude also goes out to Rachael Cassells, with whom this panel may not have been possible, the full PNOG/CBTN Diversity, Equity, and Inclusion (DEI) Working Group, the leadership of PNOG and CBTN, and all DEI members for prioritizing diversity, equity and inclusion in the consortia and leading this panel. Finally, our sincere appreciation to the brave Indigenous leaders that are creating space for Indigenous Peoples to drive genomic and clinical research that meets their needs.

References

- [1] U.N. Chukwueke, S. Hervey-Jumper, A. Porter, Disparities and inequities among patients with central nervous system tumor, *Hematol. Oncol. Clin. North Am.* 36 (1) (2022) e1–e8, doi:10.1016/j.hoc.2021.10.002.
- [2] U.N. Chukwueke, E. Vera, A. Acquaye, S.L. Hervey-Jumper, Y. Odia, L.J. Klesse, E. Dunbar, A. Sharma, E. Fonkem, A.A. Thomas, T.E. Werbowetski-Ogilvie, S. Camelo-Piragua, N.T.N. Gatson, M.I. de la Fuente, T.S. Armstrong, A.B. Porter, S. Jackson, SNO 2020 diversity survey: defining demographics, racial biases, career success metrics and a path forward for the field of neuro-oncology, *Neuro-oncol.* 23 (11) (2021) 1845–1858, doi:10.1093/neuonc/noab172.
- [3] S.J. Reihl, N. Patil, R.A. Morshed, M. Mehari, A. Aabedi, U.N. Chukwueke, A.B. Porter, V. Fontil, G. Cioffi, K. Waite, C. Kruchko, Q. Ostrom, J. Barnholtz-Sloan, S.L. Hervey-Jumper, A population study of clinical trial accrual for women and minorities in neuro-oncology following the NIH Revitalization Act, *Neuro-oncol.* 24 (8) (2022) 1341–1349, doi:10.1093/neuonc/noac011.
- [4] B. Taha, G. Winston, U. Tosi, B. Hartley, C. Hoffman, N. Dahmane, C.E. Mason, J.P. Greenfield, Missing diversity in brain tumor trials, *Neuro-Oncol. Adv.* 2 (Issue 1) (2020), doi:10.1093/oaajnl/vdaa059.
- [5] P.Y. Wen, M. Weller, E.Q. Lee, B.M. Alexander, J.S. Barnholtz-Sloan, F.P. Barthel, T.T. Batchelor, R.S. Bindra, S.M. Chang, E.A. Chiocca, T.F. Cloughesy, J.F. DeGroot, E. Galanis, M.R. Gilbert, M.E. Hegi, C. Horbinski, R.Y. Huang, A.B. Lassman, E., ... Le Rhun, M.J. van den Bent, Glioblastoma in adults: a Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions, *Neuro-oncol.* 22 (8) (2020) 1073–1113, doi:10.1093/neuonc/noaa106.
- [6] E. Lett, H. Moses Murdock, W.U. Orji, J. Aysola, R. Sebro, Trends in racial/ethnic representation among us medical students, *JAMA Network Open* 2 (Issue 9) (2019) e1910490, doi:10.1001/jamanetworkopen.2019.10490.
- [7] E. Lett, W.U. Orji, R. Sebro, Declining racial and ethnic representation in clinical academic medicine: a longitudinal study of 16 US medical specialties, *PLoS One* 13 (11) (2018) e0207274, doi:10.1371/journal.pone.0207274.
- [8] Rodriguez, & Campbell. (n.d.). Where are the rest of us? Improving representation of minority faculty in academic medicine. *South. Med. J.* https://www.researchgate.net/profile/Jose-Rodriguez-273/publication/269716899/Where_Are_the_Rest_of_Us_Improving_Representation_of_Minority_Faculty_in_Academic_Medicine/links/571fb7ce08aefa64889a8250/Where-Are-the-Rest-of-Us-Improving-Representation-of-Minority-Faculty-in-Academic-Medicine.pdf
- [9] E. Salsberg, C. Richwine, S. Westergaard, M.P. Martinez, T. Oyeyemi, A. Vichare, C.P. Chen, Estimation and comparison of current and future racial/ethnic representation in the US health care workforce, *JAMA Network Open* 4 (3) (2021) e213789–e213789, doi:10.1001/jamanetworkopen.2021.3789.
- [10] N. Howlader, A.M. Noone, M. Krapcho, D. Miller, A. Brest, M. Yu, J. Ruhl, Z. Tatalovich, A. Mariotto, D.R. Lewis, Others, SEER Cancer Statistics Review, 1975–2018, National Cancer Institute, Bethesda, MD, 2021.
- [11] *Underlying cause of death 1999–2020*. (n.d.). Retrieved August 8, 2022, from <https://wonder.cdc.gov/wonder/help/ucd.html>
- [12] A. Beltrami, A. Hilliard, A.L. Green, Demographic and socioeconomic disparities in pediatric cancer in the United States: current knowledge, deepening understanding, and expanding intervention, *Cancer Epidemiol.* 76 (2022) 102082, doi:10.1016/j.canep.2021.102082.
- [13] K.G. Claw, M.Z. Anderson, R.L. Begay, K.S. Tsosie, K. Fox, N.A. Garrison, Summer internship for Indigenous peoples in Genomics (SING) Consortium, A framework for enhancing ethical genomic research with Indigenous communities, *Nat. Commun.* 9 (1) (2018) 2957, doi:10.1038/s41467-018-05188-3.
- [14] K.L. Henare, K.E. Parker, H. Wihongi, C. Blenkiron, R. Jansen, P. Reid, M.P. Findlay, B. Lawrence, M. Hudson, C.G. Print, Mapping a route to Indigenous engagement in cancer genomic research, *Lancet Oncol.* 20 (6) (2019) e327–e335, doi:10.1016/S1470-2045(19)30307-9.
- [15] J.P. Kronenfeld, K.D. Graves, F.J. Penedo, B. Yanez, Overcoming disparities in cancer: a need for meaningful reform for hispanic and latino cancer survivors, *Oncologist* 26 (6) (2021) 443–452, doi:10.1002/onco.13729.

- [16] M. Tervalon, J. Murray-García, Cultural humility versus cultural competence: a critical distinction in defining physician training outcomes in multicultural education, *J. Health Care Poor Underserved* 9 (2) (1998) 117–125, doi:10.1353/hpu.2010.0233.
- [17] K.A. Yeager, S. Bauer-Wu, Cultural humility: essential foundation for clinical researchers, *Appl. Nurs. Res.* 26 (Issue 4) (2013) 251–256, doi:10.1016/j.apnr.2013.06.008.
- [18] DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS Division for Social Policy and Development Secretariat of the Permanent Forum on Indigenous Issues. (n.d.). WORKSHOP ON DATA COLLECTION AND DISAGGREGATION FOR INDIGENOUS PEOPLES (UN Doc. E/CN.4/Sub.2/1986/7 and Add. 1-4.). United Nations.
- [19] United Nations Publications State of the World's Indigenous People, United Nations, 2016.
- [20] A. Delavar, J.M. Barnes, X. Wang, K.J. Johnson, Associations between race/ethnicity and US childhood and adolescent cancer survival by treatment amenability, *JAMA Pediatrics* 174 (5) (2020) 428–436, doi:10.1001/jamapediatrics.2019.6074.
- [21] C.A. Rees, A.M. Stewart, S. Mehta, E. Avakame, J. Jackson, J. McKay, E.N. Portillo, K.A. Michelson, C.P. Duggan, E.W. Fleegler, Reporting of participant race and ethnicity in published us pediatric clinical trials from 2011 to 2020, *JAMA Pediatrics* 176 (5) (2022) e220142, doi:10.1001/jamapediatrics.2022.0142.
- [22] M.C. Mills, C. Rahal, A scientometric review of genome-wide association studies, *Commun. Biol.* 2 (2019) 9, doi:10.1038/s42003-018-0261-x.
- [23] J. Born, Carlisle Indian Industrial School forced Native American children to assimilate, NPR (2022) <https://www.npr.org/2022/03/18/1087448526/carlisle-indian-industrial-school-forced-native-american-children-to-assimilate>.
- [24] C. MacDonald, A. Steenbeek, The impact of colonization and western assimilation on health and wellbeing of Canadian aboriginal people, *Int. J. Regional Local History* 10 (1) (2015) 32–46, doi:10.1179/2051453015Z.00000000023.
- [25] N.E. Macdonald, R. Stanwick, A. Lynk, Canada's shameful history of nutrition research on residential school children: the need for strong medical ethics in Aboriginal health research, *Paediatrics Child Health* 19 (2) (2014) 64, doi:10.1093/pch/19.2.64.
- [26] I. Mosby, Administering colonial science: nutrition research and human biomedical experimentation in aboriginal communities and residential schools, 1942–1952, *Histoire Sociale. Social History* 46 (1) (2013) 145–172, doi:10.1353/his.2013.0015.
- [27] J. Vazquez, cultural genocide” and native American children, Equal Justice Initiative, 2014 <https://eji.org/news/history-racial-injustice-cultural-genocide/>.
- [28] S.J. Kunitz, The history and politics of US health care policy for American Indians and Alaskan Natives, *Am. J. Public Health* 86 (10) (1996) 1464–1473, doi:10.2105/ajph.86.10.1464.
- [29] T. Carr, L. Arcand, R. Roberts, J. Sedgewick, A. Ali, G. Groot, The experiences of Indigenous people with cancer in Saskatchewan: a patient-oriented qualitative study using a sharing circle, *CMAJ Open* 8 (4) (2020) E852–E859, doi:10.9778/cmajo.20200012.
- [30] Robson Charmaine, Medical experimentation and indigenous intergenerational memory in the context of twentieth-century Hansen's disease treatment in Australia, *Health History* 20 (2) (2018) 54–74, doi:10.5401/healthhist.20.2.0054.
- [31] E. Clarke, Indigenous women and the risk of reproductive healthcare: forced sterilization, genocide, and contemporary population control, *J. Human Rights Soc. Work* 6 (2) (2021) 144–147, doi:10.1007/s41134-020-00139-9.
- [32] Errico Stefania, Ortiz Isabel, Behrendt Christina, Oelz Martin, Schoellmann Ilka, *Social Protection for Indigenous People*, International Labour Office, 2018.
- [33] T.N. Brockie, K. Hill, P.M. Davidson, E. Decker, L.K. Krienke, K.E. Nelson, N. Nicholson, A.M. Werk, D. Wilson, D. Around Him, Strategies for culturally safe research with Native American communities: an integrative review, *Contemp. Nurse* (2022) 1–25, doi:10.1080/10376178.2021.2015414.
- [34] M.P. Andrasik, G.B. Broder, S.E. Wallace, R. Chaturvedi, N.L. Michael, S. Bock, C. Beyrer, L. Oseso, J. Aina, J. Lucas, D.R. Wilson, J.G. Kublin, G.A. Mensah, Increasing black, indigenous and people of color participation in clinical trials through community engagement and recruitment goal establishment, *PLoS One* 16 (10) (2021) e0258858, doi:10.1371/journal.pone.0258858.
- [35] A.D. Boyd, X. Song, C.M. Furgal, A systematic literature review of cancer communication with Indigenous populations in Canada and the United States, *J. Cancer Educ.* 36 (2) (2021) 310–324, doi:10.1007/s13187-019-01630-2.
- [36] A. Diaz, I. Soerjomataram, S. Moore, L.J. Whop, F. Bray, H. Hoberg, G. Garvey, Collection and reporting of indigenous status information in cancer registries around the world, *JCO Global Oncol.* 6 (2020) 133–142, doi:10.1200/JGO.19.00119.
- [37] S. Shahid, S.C. Thompson, An overview of cancer and beliefs about the disease in Indigenous people of Australia, Canada, New Zealand and the US, *Aust. N. Z. J. Public Health* 33 (2) (2009) 109–118, doi:10.1111/j.1753-6405.2009.00355.x.
- [38] After Havasupai litigation, Native Americans wary of genetic research. (2010). *Am. J. Med. Genet. A*, 152A(7), fmix. doi:10.1002/ajmg.a.33592.
- [39] L. Arbour, D. Cook, DNA on loan: issues to consider when carrying out genetic research with aboriginal families and communities, *Community Genet.* 9 (3) (2006) 153–160, doi:10.1159/000092651.
- [40] Dalton, R. (n.d.). *Tribe blasts “exploitation” of blood samples*. Nature Publishing Group UK. <https://doi.org/10.1038/420111a>
- [41] N.A. Garrison, M. Hudson, L.L. Ballantyne, I. Garba, A. Martinez, M. Tualii, L. Arbour, N.R. Caron, S.C. Rainie, Genomic research through an indigenous lens: understanding the expectations, *Annu. Rev. Genomics Hum. Genet.* 20 (2019) 495–517, doi:10.1146/annurev-genom-083118-015434.
- [42] A. Harmon, Indian Tribe Wins Fight to Limit Research of Its DNA April 21, *The New York Times*, 2010 <https://www.nytimes.com/2010/04/22/us/22dna.html>.
- [43] *Lessons from Havasupai Tribe v. Arizona State... - UMD DRUM*. (n.d.). <https://drum.lib.umd.edu/handle/1903/25744>