Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Informed Consent in the U.S. Indigenous Peoples Context: A Systematic Literature Review

Tasha Gross
University of Washington Seattle Campus: University of Washington
Clarita Lefthand-Begay (clarita@uw.edu)
University of Washington Seattle Campus: University of Washington https://orcid.org/0000-0001-5882-8108

Research article

Keywords: Informed Consent, Literature Review, Tribes, Native American, Indigenous Peoples, Research Ethics, AI/AN, Human Subjects Research

Posted Date: February 13th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-227951/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Abstract

BACKGROUND: Tribal communities in the United States (U.S.) have a long history of subjection to unethical and exploitive medical and research practices. Today, many Tribal nations are establishing procedures in order to protect themselves from further harm and to advance culturally informed research practices. These procedures are also meant to ensure that their communities benefit from research conducted within their communities. Informed consent is a key element in protecting human subjects, but it may not be sufficient in the tribal context, as its conception is rooted in Western understandings of protection. Specifically, the informed consent emphasizes the individual, rather than the community as a whole, which is just as important in the context of conducting research with Native communities.

METHODS: We conduct a systematic literature review to answer two related questions: How is informed consent being *conceived* of by U.S. tribes? And how is informed consent being *required* by U.S. tribes? Our inclusion criteria include articles focusing on informed consent within the U.S. tribal context, written in English in 2010-2020. Articles that did not fit our inclusion criteria were excluded. Two reviewers independently reviewed and coded 30 peer-reviewed articles by using content analysis and, in an iterative process, agreed on emerging codes and themes.

RESULTS: A number of themes arise in the selected literature, including the conception of informed consent as a process, its operation at various levels (individual, collective, and government-to-government), possible alternatives to informed consent, and the need for specificity about ownership of samples and data, benefits and/or risks, and the methods and procedures that researchers use in the course of study.

CONCLUSIONS: Our key results point to a need for clear and transparent information for prospective research participants and for consent forms and processes to include the collective, as well as the individual. This will better align with the cultural values and political standing of sovereign tribes in the U.S.

Background

There is a long history in the United States (U.S.) of unethical research conducted on tribal communities, in fields from anthropology to genomics and biomedicine. The standards that should protect subjects from unethical research and medical practices, stemming from the Nuremberg Code, the Belmont Report, and the Common Rule, all fixate on the protection of the rights of the individual. However, these standards may not always be sufficient to protect Indigenous individuals and communities in the U.S. To help us understand these insufficiencies, however, let's first review the origins of informed consent. We will then discuss issues of unethical research carried among Native American communities.

Origins of Informed Consent

Informed consent, as a standard, can be traced to the Nuremberg Code which was drafted in reaction to the medical experimentation done under the Nazi regime in the 1940s. It stipulates that informed consent is achieved “when a competent individual agrees to participate in a study or procedure after having expressed clear understanding of all the material facts related to the activity in question” [1]. The Code requires that human subjects of research provide voluntary consent to the details and potential risks of participation, and that they be given the ability to withdraw from research at any time [2]. In the U.S., attention was drawn to issues of informed consent following the exposure of the Tuskegee Syphilis Study in the 1970s. During this study, “hundreds of men and their families lost their lives to a treatable disease” as a result of the withholding of both information and treatment. In response, Congress created the National Research Act (1974), which in turn created the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. In 1979, this commission published the Belmont Report, which asserted the “minimum ethical principles” required for research with human subjects [1]. One of these was the concept of informed consent, which was expanded upon by the Common Rule in 1991.

Published by the U.S. Department of Health and Human Services in 1991, the Common Rule further defined elements of the informed consent. According to the Common Rule, an informed consent must include the purpose of the proposed research, its duration and the procedures involved, a description of potential risks and benefits, and contact information for those who can respond to questions about the research and the rights of the participant in it [1]. A statement of confidentiality should also be provided, as is information about how research and data will be documented and how a participant’s information will be identified. Researchers are also to notify participants of any findings that may influence willingness to continue participation [2]. Significantly, in the fields of biomedical and genomic research in particular, the Common Rule was meant to protect individual living human subjects, and not necessarily their specimens [2]. This is an important distinction for many Native American communities, because it represents a worldview in which specimens are seen as completely separated from their providers, and therefore, the use of specimens cannot cause risk or harm to research participants. This worldview does not take into account the understanding of many Native Americans that blood and other tissues taken from the body *are* still part of the person who provided them. Given such an understanding, the way in which specimens are used, handled, stored, etc. is indeed capable of harming the individual.

Another case influenced the way in which informed consent is applied in the U.S., and how institutions ensure that their researchers comply with ethical standards. In the case of one California university, researchers did not inform their human subjects that they risked becoming sterile by participating in their study. When the participants did, indeed, become sterile, and made the common connection back to this study, they successfully won “hundreds of millions of dollars in compensation” [3]. After this incident, universities and research agencies began to use Institutional Review Boards (IRBs) to protect not only human subjects from harm but also researchers and universities from collective action claims.

Unethical Research among Native American Communities

Native American communities have often been subject to harmful and unethical research practices, even after the creation of the Nuremberg Code, the Belmont Report, and the Common Rule. Indeed, Indigenous peoples have been extensively studied by researchers from a wide variety of fields, often without having the opportunity to provide input or receive any benefits from the research [4]. “Unethical behavior, lack of clear communication, disrespect of cultural and spiritual beliefs, and a failure to address the interests and priorities” of these communities have resulted in a general mistrust of research and fatigue resulting from many years of being studied, without seeing any direct benefits, instead seeing genetic material, traditional knowledge, and other intellectual property co-opted for the benefit and enrichment of others [5].

One cannot discuss the more recent history of research abuses inflicted on Native Americans, without first addressing the 500 plus-year history of oppression and colonization and the intergenerational trauma that still affects Native American individuals and communities today. Exposure (deliberate, at times) to European diseases “brought numerous tribes to the brink of extinction,” while other policies were followed in an attempt to either remove, assimilate, or actively commit genocide against Indigenous peoples in the U.S. [6]. These federal policies, which resulted in the loss of tribal lands and sovereignty, along with centuries of economic, political, social, and cultural injustices, also created disparities in well-being and health among American Indian and Alaska Native people, such as higher incidences of heart disease, cancer, obesity, and diabetes in tribal communities [4, 7]. It is in this context that we must understand the research and medical abuses of Native American individuals and communities.

One example of these unethical practices and abuses occurred from the1900s to the 1930s, when trachoma (an infectious eye disease) became a serious health risk to many Americans. Treatments already included bloodletting, rupturing of granules, and a variety of eyewashes. However, to treat trachoma in Native American men, women, and children (and sometimes to prevent infection of non-symptomatic individuals), Indian Health Services (IHS) doctors practiced a radical operation known as a “tarsectomy,” which involves the removal of the upper and lower eyelids [6]. In a 1924 clinic meant to demonstrate and teach the operation, patients experienced negative reactions, and many IHS doctors proved unable to perform the procedure satisfactorily. Despite these problems, doctors proceeded with their Southwestern Trachoma Campaign, operating on 4,285 individuals within the first year [8]. When the campaign among adults proved ineffective, the emphasis was shifted to the treatment of children at boarding schools. Still many people, including government physicians, remained reluctant to use this radical operation with both adults and children [8]. Finally, in 1928 the Meriam Report condemned the campaign as ineffective and heavily criticized the use of these operations, which were untested, unjustified, and were ultimately shown to produce negative effects. Criticism, and the resulting adverse publicity, effectively ended the Southwestern Trachoma Campaign and its widespread use of tarsectomy [8]..

Another example took place in the 1950s when the U.S. Air Force’s Arctic Aeromedical Laboratory conducted a study among Alaska Native men, women, and children that involved the ingestion of radioactive iodine (I-131) at levels that exceed current recommended dosage, and would be barred from use with children, and pregnant and potentially pregnant women today. These groups were not excluded

from involvement in the study, and language barriers among other factors presented difficulties in obtaining consent. “It is speculated,” Schanache Hodge writes, “that the villagers believed they were trading their participation for much needed medical treatment in their rural villages,” implying a certain amount of coercion (however unintentional) and power imbalance [8]. Also during the Cold War, a plan called “Project Chariot,” pushed by the U.S. government, sought to create a new seaport near Point Hope, Alaska, using nuclear explosives. While this plan was not implemented, researchers from the U.S. Geological Survey *did* conduct environmental experiments in the area of Point Hope (a predominantly Inupiat village). Radioactive elements, mixed fusion products, and radioactive soil from test sites were released into the environment in order to observe their spread. The Alaska Native residents of the area were not told of the studies being done: In fact, the experiments were not exposed until 1992 [9]. In both cases, there was a clear power imbalance, caused either by the withholding of information or the implication that participation in research was a necessary trade-off for medical treatment.

A similar implication was present in the sterilization of Native American women and girls, which was perhaps one of the most traumatizing incidents in this recent history. Between 1973-1976, 3,406 Native Americans women and children between the ages of 15 and 44 were sterilized by IHS doctors (or “contract” doctors) without their knowledge or consent. Consent forms were not in compliance with IHS standards and were often illegally obtained. It is also reported that “verbal consent” was used, and that there was a significant element of coercion: Women seeking medical care were led to believe that they would lose access to services, custody of their children, and Bureau of Indian Affairs benefits if they did not consent to the procedure” [6].

The harms inflicted by researchers upon Native people consists not only of harms to individuals, but of harms to whole communities. In 1979, the predominantly Inupiat community of Barrow, Alaska, participated in a study that was meant to “assess the role of alcohol in traumatic deaths,” in order to create beneficial interventions. The researchers from the University of Pennsylvania held a press conference to present their results, without first consulting the community, resulting in misrepresentation and stigmatization of Barrow and its residents in the mainstream press. The New York Times, for example, ran an article that quoted the researchers saying that the Native community was “practically committing suicide,” characterizing them as “a society which is alcoholic, and therefore facing extinction” [9]. When the Inupiat community criticized the researchers for not obtaining consent according to accepted “lower-48” standards and spoke about the community harm done to them, the researchers argued that there was a difference between releasing data about an identifiable individual and releasing data about a whole community [6, 9]. This is a major tension in the discussion of informed consent in a tribal context: As Champagne writes, “The basis of protection of human subjects was individual human rights” [3]. The type of protections, if any, provided to communities as a whole is an essential concern for many tribes.

Even more recently, the Havasupai case has been a large influence on the discussion of informed consent in the U.S. tribal context (and has actually become the subject of a play). In this case, researchers from Arizona State University (ASU) approached the Havasupai tribe about participation in genetic research

which, they were told, would focus on diabetes. However, the consent forms used were broad to the point of being vague about how the samples provided by Havasupai participants would be used. The language used to describe the research done in informed consent documents was “behavioral/medical problems,” while participants were told that their samples would only be used for studies of diabetes [10]. Instead of restricting research to diabetes, ASU researchers used the samples provided to perform studies on schizophrenia, alcoholism, inbreeding, and migration. Had participants been sufficiently informed, it is unlikely they would have consented to providing their samples for this research. Moreover, the ASU researchers failed to honor the confidentiality of participants, by sharing samples and codebooks with researchers outside of the university [11]. This not only demonstrates a lack of respect, but ignorance (or lack of care for) cultural norms, and lack of concern for cultural and community harms. In 2010, the case was settled out of court with payment, the return of blood samples, and other assistance to be provided by the university to the tribe. However, because the case was settled outside of court, it is unclear what kind of legal precedent may have been set. Since 2010, many scholars have discussed what the case means for informed consent, and what is required of consent for it to be considered “informed” [12].

The long history of research abuses in Native communities is not limited to biomedical and genomic research. Indeed, the publication of traditional and culturally sensitive knowledge, which may be encountered by anthropologists, oral historians, linguists, and other researchers in the social sciences and humanities, can inflict great cultural harm on the community as a whole. Palosaari relates, for just one example, the publication of Hopi religious materials by H.R. Voth. In the early twentieth century, Voth gained access to private Hopi ceremonies, in hopes of studying “the beliefs he was trying to supplant” as a missionary. His publication of photographs and written descriptions made public knowledge that the Hopi considered private and privileged [13]. In the absence of explicit physical harm to individuals some researchers may not always understand the cultural and collective harm induced by such actions. This is a gulf in understanding that must be bridged, if informed consent is to effectively protect Indigenous individuals and communities. Once again, this highlights the need for informed consent to include the protection of the community as a whole in the tribal context.

Even with this long history of abuse and mistrust, today, many Tribal nations and communities are designing ways in which to participate in research, while also protecting themselves from the kinds of unethical behavior they have been subjected to in the past. Our objective with this review is to answer two questions: How is informed consent being *conceived* of by U.S. tribes? And how is informed consent being *required* by U.S. tribes?

Methods

Search Strategy

We conducted a systematic literature review by searching the following electronic databases: JSTOR, PubMed, and Web of Science. To focus our search on informed consent and its application in the tribal context, we used the following search terms in different combinations: Informed consent, Institutional

Review Board, IRB, community based review, tribal, tribes, Indigenous, United States, AI/AN, AIAN, American Indian, and Native American. Further limitations were implemented by restricting the searches to articles published 2010-2020. In addition, after collecting our first wave of papers, we identified articles through screening references in previously identified literature in order to collect articles which fit our criteria, but may not have been included in the results of our searches.

Data Selection

Our inclusion criteria restricted selected articles to those published between 2010-2020, those written in English only, and those related to informed consent and Indigenous peoples in the U.S. We included both qualitative and quantitative peer-reviewed articles and excluded grey literature. We also excluded articles not written in English, articles reporting on studies where informed consent was briefly discussed as a part of the research process, any duplicates, and articles that focused on international indigenous communities.

Our first stage of screening was performed by one reviewer by systematically reviewing each title and abstracts of the selected articles. For quality control, a second reviewer screened at least 15% of the titles and abstracts. Both reviewers then discussed each article to determine whether to include or exclude it based solely on whether they met our inclusion criteria.

For our second stage of review, both authors reviewed and extracted data that addressed the objective of this study. This step included a review of the full text contained in each article that met our inclusion criteria. In an iterative process, both reviewers discussed all codes and any discrepancies until a consensus was reached. For each article, the authors' names, date of publication, study design, and name of database searched, were documented in a spreadsheet and word document, in order to ensure against duplicates, and to organize notes and codes effectively.

Qualitative data synthesis was conducted by both reviewers. This step consisted of reviewing our codes and synthesizing the quotes under each code in the body of this manuscript. This was done iteratively by discussing the narratives presented in the selected literature, the themes that presented themselves, and what elements seemed most widely-discussed and relevant.

Results

Identified Literature and Overarching Themes

Our study selection process is outlined in Figure 1. First, our electronic database search of JSTOR, PubMed, and Web of Science resulted in the selection of 43 articles, then an additional 28 articles were found through a manual search of the reference lists of these 43 articles. We then removed any duplicated records, leaving 71 articles. Employing our inclusion and exclusion criteria, we screened each article, which led to the exclusion of 23 articles and yielded 48 articles. We then excluded an additional 17

articles after applying a full text review of the remaining articles and ensuring each of them were relevant to our objectives and met our criteria. In the end, we identified 30 articles that are the basis of this review.

There were several overarching trends. First, of the 30 articles we reviewed, 25 were grounded in the perspective of genomic and/or biomedical research. Second, two authors discuss informed consent from the context of the social sciences or humanities, which, although less present in the literature than the genomic/biomedical context, is an equally important area in which informed consent can be discussed [3, 13]. Third, of interest are three articles that discuss informed consent at the government-to-government level, as represented by the consultation process in the U.S., and Free, Prior, and Informed Consent (FPIC) as an international standard [14, 15, 16] . In these articles, the focus is not only on biomedical/genomic research, but on actions taken by the federal government that impact the environmental and cultural well-being of tribal nations. However, the most clearly visible theme across all articles was the long shadow cast by the Havasupai case: Of the 30 selected articles, at least 13 mention the case; an additional four include a longer discussion of it; and seven others were written specifically in response to it.

Informed Consent in the U.S. Tribal Perspective

Our first objective of this review was to understand how tribal nations and their citizens in the U.S. consider informed consent. Three main themes emerge under the umbrella of this question: (1) informed consent is a process, rather than simply a document to be signed, requiring time, attention, and efforts toward cultural competence and awareness;; (2) informed consent operates at various levels, including the individual level, the collective level, and the government-to-government level as represented by the consultation process between U.S. tribal governments and the U.S. federal government; and (3) U.S. tribal nations express concern that informed consent insufficiently protects U.S. tribes from unethical research.

Informed Consent as a Process

Some authors argue that informed consent has become a formality, concentrating on providing legal protections for researchers and their institutions, rather than a process focused on informing and protecting participants [17, 18, 19]. . This may be a concern for informed consent across the board, not only in the U.S. tribal context. For instance, Smith-Morris writes that an informed consent form, no matter how specific and detailed, “can be completed in the absence of any rapport between professional and patient,” giving the relationship *legal* meaning, without providing participants with true understanding of what they are consenting to [20]. This situation can be improved, the author writes, “first, through the moral engagement of both providers and patients,” preventing the process from becoming a task to check off a list, and second, through oversight committees, community involvement or review, and other ways in which the informed consent process can be expanded, and made more meaningful [20]. Garrison, Hudson *et al.* and Winters all highlight the importance of seeking informed consent early in the research process, while Hiratsuka *et al.* report the necessity of allowing for mental processing time, so that participants can be truly informed [21, 5, 2]. Hiratsuka *et al.* also report that “clear language, free of legal jargon” in informed consent documents is necessary [21]. Williams and Harding *et al.* also note that language

barriers, as well as the complexity of modern research, can present significant obstacles in the process [22, 23].

Even if consent documents *can* be easily comprehended, and enough time given for individuals to obtain any further advice or information they need, there is still an issue with the limitations of what participants can choose to do with that information. Garrison, Rao, and Smith-Morris bring up the “all-or-nothing” approach to informed consent, where little-to-no room is left for participants to negotiate consent, and where participants are left with the choice of either consenting to everything or being excluded from the research completely [10, 20, 18]. This binary choice may leave tribal communities in particular in a difficult position: Harding *et al.* write about the “inherent coercion” present in this black-or-white approach, where tribes are already more vulnerable “because they are in the position of seeking data and research funds while struggling against simply ‘being studied’” [22]. Other authors and studies present a possible solution in the form of lists of options, allowing for participants to opt-in or -out of specific studies, procedures, etc. [24, 17, 21, 5, 25, 32]. However, Rao also points out the potential downfall of providing too many options, and the way in which information overload, like information scarcity, can present a barrier to true informed consent [18].

Informed Consent at Three Levels

Many authors speak to informed consent at the individual and collective levels, and fewer to informed consent at the government-to-government level. Whitener, Garrison, Hudson *et al.*, and Tsosie *et al.* all argue that, within the tribal context, because individual data can be used to make generalizations about the whole community, individual consent is not entirely sufficient [5, 27, 9]. Drabiak, Harding *et al.*, Sahota, James *et al.*, Champagne, Villegas, and particularly Smith-Morris also discuss the importance of seeking collective consent and of working with the appropriate tribal authorities in order to do so [3, 17, 22, 4, 20, 19, 28]. This process, as Sterling writes, “can be difficult, time-consuming, and fraught with challenges,” but is still important, and it is necessary for researchers to take the time to establish a trusting relationship with the community and its leaders [1]. Harding *et al.*, Pensabene, and Claw, among others, indicate several appropriate authorities (tribal councils and governing bodies, tribal IRBs, etc.) as bodies that have the authority to give collective consent, while also noting that each community will be different and that researchers must put in the time and work to “identify [the] appropriate avenues, protocols, and experts” to address their proposals to [29, 22, 11].

Pensabene, Palosaari, and Smith-Morris all frame collective and individual consent within the discussion of cultural awareness and competence, noting the importance of cultural competence in understanding how consent is conceived of and in designing culturally sensitive studies [20, 13, 11]. This cultural competence and sensitivity is framed by these scholars and others as the solution to the less-than-acceptable state of informed consent in the tribal context. An informed consent process that is culturally competent and takes into account Native worldviews and beliefs, they argue, would solve many of the problems presented by the "mainstream" informed consent process. Meanwhile, other scholars argue that informed consent has, on the whole, failed to protect Native peoples, and that tribal individuals and

communities may be better served by looking into alternate strategies, such as property law [18]. This will be discussed further below: For the moment, however, it is interesting to note how many authors reference the importance of cultural competence. Hiratsuka *et al.* report on the necessity for researchers to be educated about the cultural context they are entering [21], and Shaw *et al.*, Sahota, Chadwick, Tullier *et al.*, and Claw all also address the importance of cultural awareness, if not complete competence [17, 29, 30, 31]. For example, Palosaari and Smith-Morris both note that the use of long written documents in the informed consent process, in a cultural context where this is not appropriate, can create mistrust towards researchers [20, 13]. Another example includes the lack of understanding ASU researchers had of Havasupai culture and values, made evident by their decision to use Havasupai samples for research on topics that are considered culturally inappropriate by this community. One more way in which basic cultural awareness might be demonstrated by researchers, is by acknowledging the communal values of many Native communities, and showing concern not only for individual risks and benefits, but the ways in which the entire community might benefit, or be harmed, by research.

There is not always agreement by researchers about whether consent is necessary beyond individual consent. For instance, Abadie & Heaney, while acknowledging that genomics research *does* affect both individuals and their communities, argue that "collective consent cannot overcome individual consent" [32]. It is important to note that this argument comes from the context of a report on the perspectives of Native individuals living in urban centers (as opposed to Native individuals living in a reservation, under tribal jurisdiction). Also of interest is that Abadie & Heaney mentioned that they originally approached a tribal government to conduct this study, but when their proposal was rejected, they decided to target urban individuals for participation instead [32]. Their argument might be seen in contrast to Champagne, who argues that "if a tribal citizen wants to provide knowledge to a researcher, and the provision of such information is considered inappropriate by the tribal IRB, then the researcher should honor the legal powers of tribal government" [3]. The findings from Abadie & Heaney are also a contrast to those from Hiratsuka *et al.* and Williams, both of whom report an emphasis on collective consent and privacy from their tribal study participants [21, 23, 32].

Respect for tribal sovereignty is also significant in the research context: Champagne and Harding *et al.* all note the ways in which researchers have attempted to avoid tribal oversight, while recognition of tribal sovereignty makes it "possible for Indigenous nations to perform IRB reviews and oversee research that is conducted within their communities and traditional territories" [3, 22]. Claw also speaks to this, arguing that researchers should extend recognition of sovereignty to all Indigenous nations, regardless of their legal status [29]. Recognition of sovereignty is also, of course, integral to consent at the government-to-government level. Miller, Winters, Mengden, and Garrison, Barton *et al.* all write about the consultation process between the U.S. federal government and tribal governments, most noting frustration with this process and its lack of meaning, especially since it requires federal agencies only to *listen* to tribal concerns and not actually obtain their *consent* [14, 15, 16, 2]. Miller, however, sees the process as a building block towards applying FPIC in the U.S. [15].

Informed Consent Insufficiently Protects U.S. Tribes from Unethical Research

Lastly, some scholars have expressed their dissatisfaction with the informed consent process at multiple levels. Though only a few were identified in our review, we present those examples here. Rao argues that alternative notions of informed consent should be considered [18]. In particular, Rao discusses property law (setting individual participants as the legal owners of their samples, by conceiving of tissue and genetic materials as property) as a possible solution to the perceived inadequacies of informed consent. Building on this, Pensabene and Winters argue that culturally informed or culturally competent informed consent is in fact the better defense [2, 11]. *We will elaborate on this more in our discussion.* For now, we will consider what factors compose a culturally competent informed consent process.

Requirements of Informed Consent by Tribal Nations

In our second objective we aimed to understand the requirements of informed consent by U.S. Tribes. Much of the literature is critical of "broad consent" thought sufficient by many researchers and discusses a number of areas in which greater specificity is needed for consent to be considered truly informed in the tribal context. Garrison defines broad consent in contrast to specific or tiered consent, as providing "for the most flexibility [for researchers] with future uses of samples" [10]. One example might be the consent language used by ASU researchers in their working with the Havasupai tribe: On consent forms, they defined their research as "behavioral/medical problems" [10]. This is a very broad statement, and it left the door open for them to use Havasupai samples for a wide variety of studies, and not just the diabetes studies they had initially aimed to focus on. These areas of specificity include: (1) the ownership of samples and data provided by tribal members, (2) the benefits and/or risks that tribal nations and individuals can expect from research, and (3) the methods and procedures that researchers will use in the course of research (including those used to gather data/specimens, to handle, secure, return and/or dispose of specimens, to handle requests to withdraw from research participation, etc.).

Ownership of Samples and Data

In the wake of the Havasupai case, many scholars ask whether the kind of "broad consent" obtained by ASU researchers at the time was sufficient. Sterling, Pensabene, Palosaari, Rao, and Garrison, Hudson *et al.* are among those who argue that greater specificity is needed in the consent process in order for it to be considered truly informed [24, 1, 5, 13, 18, 11]. Garrison, however, reports that researchers may be leaning in the opposite direction: tending toward broader consent forms in order to cover all possible bases, rather than addressing community concerns [10]. Mello & Wolf present another solution for biomedical research, by suggesting that individuals providing specimens should be considered "donors" rather than "subjects" [12]. Donors, they write, lose their rights and control over their organs and tissues, and since the individuals involved "are not involved in a serious way as the subjects of such research" (according to their perspective), they argue that this is an acceptable way of addressing the ethical issues of informed consent [12]. However, this strategy, like broad consent, may be seen as a way of avoiding engagement with community concerns and providing legal protection for researchers and institutions.

Harding *et al.*, Garrison, Sahota, Palosaari, Villegas, Winters, Chadwick, Copeland *et al.*, and Smith-Morris all discuss ownership as an area in which increased specificity is needed, and many argue that tribal

ownership of samples and data must be specifically recognized [17, 22, 10, 20, 7, 13, 2, 28]. Additionally, Winters and Garrison, Hudson *et al.* put forth the idea of Indigenous-governed repositories for specimens and data, as a way of addressing this issue of ownership, sovereignty, and security [5, 2]. Without clear ownership, it appears that decision-making power is left to researchers and institutions, instead of sovereign tribal nations leading the charge about what will happen to their data and/or samples.

Risk and Benefits

Harding *et al.*, Tauali'i *et al.*, Palosaari, Winters, Chadwick, Copeland *et al.*, and Smith-Morris all address specificity in how results will be reported and how benefits will be both communicated and made accessible to tribal communities and individuals [22, 20, 7, 13, 25, 2].

Types of Research Methods and Procedures

Harding *et al.*, Palosaari, and Chadwick, Tullier *et al.* also discuss specificity in the area of methodology and what procedures will be used by researchers to obtain specimens and/or data [22, 30, 13]. Moreover, Hiratsuka reports that information not only about the research and its procedures, but also about the researchers themselves, along with their experience and interests, is necessary [21].The storage, security, and treatment of specimens and/or data is much-discussed, including who will have access to biospecimens and data, how and whether tribes and individuals will be contacted and will have to re-consent for secondary use of their biospecimens, etc. Drabiak, Mello & Wolf, Caplan & Moreno, Pensabene, and Winters look to the Havasupai case as an example where ambiguity and lack of specificity led to misunderstanding and misjudgements [12, 33, 19, 2, 11]. Sahota reports a concern among Native individuals about specimen misuse and continued specimen use without re-consenting participants [17]. Tauali'i *et al.* report similar concerns among some Native Hawaiians [25]. Addressing these concerns, Sterling, Winters, and Claw argue that researchers should obtain new informed consent for secondary uses of data and biospecimens [29, 1, 2]. Participants in the study from Hiratsuka *et al.* suggest that informed consent documents should specify how specimens will be stored and re-used, whether they will be shared with other researchers and institutions, and even include options for a "destroy-by" date, etc. [21]. Whitener, Harding *et al.*, James *et al.*, Angal *et al.*, Palosaari, and Chadwick, Copeland *et al.* also discuss issues of confidentiality, storage, and consent and re-consent [22, 4, 7, 13, 9, 26]. Finally, Garrison (2013) and Garrison, Hudson *et al.* (2019) raise the issue of historical collections of specimens, or specimens collected at a time when informed consent standards were very different, and argue that, because these samples cannot be used according to modern ethical standards, they should be returned to the communities that provided them [10, 5].

There is also a requirement for clear and specific communication about the rights of participants to withdraw their consent at any point during research. Drabiak and Winters point to instances where requests to withdraw from participation in research were denied, or where researchers had few protocols to support this [19, 2]. For example, Chadwick, Copeland *et al.* report that the absence of protocols for participant withdrawal from research was a significant issue for their potential tribal partners [7]. Palosaari provides a perspective on this issue from outside of biomedical/genomic research. Speaking

specifically about linguistic research, Palosaari argues that researchers must consider and plan for how requests to withdraw from research will be handled, and clearly communicate those protocols to participants [13].

Discussion

It is impossible to discuss almost any aspect of informed consent in the tribal context without first touching on the Havasupai case. Based simply on the number of articles that reference it, it is evident that the case has played a large part in shaping the way in which informed consent is discussed, is being conceived of and required by tribes in the U.S. Indeed, some of the conceptions and requirements of informed consent in the tribal context might be traced back to the inadequacies of the consent obtained by ASU researchers in their genomic research with the Havasupai tribe. Perhaps it is partially due to the influence of the Havasupai case that so much of the literature reviewed comes from the perspective of biomedical and genomic science though, this may also be a result of the types of databases our study targeted (specifically Web of Science and PubMed). The inadequacy of the "broad consent" obtained by the ASU researchers in this case, in addition to the insufficiency of the information Havasupai participants were given and on which they were expected to make a decision as to whether to give or withhold their consent to participate, seems to be a significant influence behind requirements of increased specificity in the informed consent process.

Conception of Informed Consent

Based on the scope of this study, there appears to be three main themes in the conception of informed consent in the tribal context: the conception of informed consent as a process, its operation at various levels, and its viability as a defense against unethical research (as opposed to other suggested solutions, such as property law).

Notable is the conception of informed consent as a process and ongoing dialogue, requiring time, attention, a trusting relationship, and cultural awareness, if not cultural competence. This is in contrast to the "mainstream" paradigm of informed consent, which is framed more as a one-time transaction, and potentially less genuine**.** Rao seems particularly critical of informed consent as it is currently applied, referring to the "venerable doctrine" as "a charade, a collective fiction which thinly masks the uncomfortable fact that the subjects of human research are not actually afforded full information regarding the types of research that may be contemplated, nor do they provide meaningful consent" [18]. Rao, it might be remembered, concludes that the language of property rights may provide more substantial protections. Yet, most of the other authors (Sahota, Drabiak, Smith-Morris, and others) seem to be seeking not an alternative to informed consent, but an update of it, or as Sahota describes it, a "paradigm shift": a version of informed consent that is more critical, interactive, negotiable, and sensitive to cultural norms [17].

The idea of including lists of options as a way to combat broad, all-or-nothing consent, in favor of specific and negotiable consent, is put forth by many authors. Angal *et al.* provide an example of its use

in their study, when their collaboration with the Oglala Sioux Tribe Research Review Board led to the creation of consent forms that did, indeed, present the participant with options, allowing them to either accept or decline involvement in specific study components [26]. The study from Hiratsuka *et al.* suggests that options are desirable not only for procedures and specimen uses, but also for disposal or destruction [21]. This may provide even more flexibility in allowing tribal peoples to participate in research, by addressing concerns about the unending use and re-use of specimens. In this way, researchers are not forcing individuals to choose between giving up their agency or compromising on their beliefs and giving up any possible benefits that participation in research could provide. However, there is also the concern, as voiced by Rao, that providing so many options might, instead of creating understanding and providing more choices and room for negotiation, result in information overload, making it difficult for individuals to take advantage of any of the options being presented [18]. Balancing the provision of specific information and a variety of options, and the need for an easily-comprehended, jargon-free informed consent process may be challenging, but both needs are highlighted in the literature. Harding *et al.* in particular note the increasingly complex nature of modern research (specifically genomic and biomedical research), which may be so complicated that "even a fully competent non-specialist might not understand the disclosed information enough to make a truly informed decision" [22]. Extra time and attention dedicated to explanation, and ensuring that participants are truly informed, is needed. The authors add that trained tribal staff and projects that help build "skills, understanding, data, or equipment" within a tribe may also be helpful in achieving adequate informed consent in the long-term [22]. This recalls the idea of a paradigm shift in informed consent, away from the long, complex, legalistic forms to be filled out and signed, and towards the dedication of time, care, and long-term relationship-building to the process. Although the idea of informed consent forms with a list of options seems to be popular, one must wonder which of these conceptions it really fits into.

The conception of informed consent on different levels (individual, collective, and government-to-government) is a large part of how informed consent is being thought and written about in the tribal context. Perhaps this is because of the tension between the worldview that created informed consent as we know it, with its hyperfixation on individual rights, and a worldview that recognizes individuals within the context of a community, and how easily risk can be transferred from an individual to their community. This tension is representative of a fundamental cultural difference, as many authors point out, and perhaps, therefore, begs for a more culturally aware approach. Garrison, Hudson *et al.* and Tsosie *et al.* all note the particular risk in genetic and biomedical research, where data gleaned from one individual can be used to make inferences about the entire community, and possibly subjecting it, as a whole, to harm and stigmatization [5, 27]. Because of this, Tsosie *et al.* ask: If risk to the community is not communicated to individual participants, then is that participant giving truly informed consent [27]?

Many authors, including Smith-Morris and Tsosie *et al.*[1] speak to the over-valuing of individual consent in research and the necessity of obtaining consent at both the individual *and* the collective level [20, 27]. Most come from the perspective, again, of biomedical and genomic research. Palosaari provides a helpful perspective from the social sciences/humanities: fields in which traditional, and culturally

sensitive, knowledge may come up. It befits the researcher, in this context, to be aware and sensitive to the fact that individuals who hold certain knowledge or information may not have the authority to consent to sharing it [13]. Where knowledge (language and sacred sites, for example) is regarded as a community resource rather than an individual's competence, collective consent and cultural competence become incredibly important [13]. There is the question, then, of who *is* authorized to give collective consent on the behalf of the community. Pensabene notes that the entity authorized to do so will vary, depending on the tribe and their elected form of governance, but tribal councils and other governing bodies, as well as community-guided or tribal IRBs, are referenced by a number of authors [11]. Similarly, as a way to address both the individual and collective concerns related to the research being conducted, Harding *et al.* indicate that additional IRB approval from other organizations, like the IHS, may be required by tribes before giving their collective consent [22].

How tribes without federal or state recognition or Native peoples living outside of reservations can protect themselves is a question of great interest, since, as Champagne writes, the recognition of tribal sovereignty makes tribal IRB review and other means of tribal oversight of research possible [3]. Since off-reservation Native communities and intertribal organizations do not have the legal status of tribal governments, researchers are not obliged to seek any kind of collective consent or to go through the tribal IRB process. This means that Native Americans living outside of reservations are protected only by whatever state and federal human subjects protocols are applicable [3]. If these regulations do not address tribal needs and concerns, non-recognized tribes and other Native communities are left vulnerable. Despite Claw's argument that researchers should extend recognition of sovereignty to all tribal groups, regardless of their legal status, they are not *required* to, and therefore, are unlikely to regard such advice [29]. The study from Abadie & Heaney is interesting in this context, not only because they themselves exhibit the behavior of approaching off-reservation and urban Native individuals after having their research proposal rejected by a tribal government, but also because their results and arguments are a contrast to those presented by most other scholars reviewed here [32]. The authors ask, as genomic research and biobanking become more routine in medical care, will Native Americans not living on reservations "be aware of their tribe['s] position regarding genomic research and, if so, would they cho[o]se to follow it or would they instead trust their medical providers and participate in the collection of genetic material?" [32]. They report that their participants see the decision of whether or not to take part in research as an individual, not a tribal decision (or, as a matter of individual consent rather than collective, tribal consent) [32]. The authors *do* acknowledge the controversy of the issue, stating that "other studies involving Native Americans living on reservations might lead to very different results" [32]. Indeed, the emphasis placed on community consent and privacy by Alaska Native participants in Hiratsuka *et al.*'s study, and Native participants from the Southwest in Williams *et al.*'s study seem to indicate that this difference *is* present [21, 23].

At the government-to-government level, the informed consent process is approximated by the process of consultation. Significantly, however, the process *does not actually require that consent from tribal governments be obtained*, only that federal agencies hear tribal concerns about proposed projects [16]. Several authors reference the idea that consultation is simultaneously "too much" and "too little,"

meaning that it requires a great deal of time and resources from tribal governments, with no guarantee that the tribe's position will be respected. As Miller writes, many tribal governments "do not have sufficient numbers of employees, government officials, and/or the funding to effectively study, plan, travel, and fully engage in all of these requested consultations" [15]. Meanwhile, the federal government does not provide any real mechanisms for tribes to oppose proposals, and, similarly to the "mainstream" conception of informed consent at the individual and collective levels, the process becomes just "another procedural step before a federal agency can commence their action" [16].

Frustration with informed consent at all these levels leads to the question of whether, even with adaptations, it is really the best way for U.S. tribes to protect themselves from unethical research. Rao, arguing for the use of property law, writes that, as autonomous individuals, participants should "not only possess the power to contribute their biological materials, but also the right to help control the course of research, and to share in the resulting benefits or profits" [18]. Using the language of body property may be uncomfortable for many, Rao acknowledges, because it can bring to mind the idea of slavery and of human beings as property. However, he writes, this type of language "might enable research subjects to regain power and a measure of self-sovereignty," if informed consent has proved inadequate in this regard [16]. Winters, meanwhile, frames culturally competent informed consent as the better option to protect participants in biomedical research [2]. Like Winters, Pensabene maintains that "informed consent remains a stronger alternative to protect Native American test subjects" [11]. Property rights, the author writes, "fail to protect the genetic information contained in the genetic material," and property interests can be silenced when an individual agrees to transfer this material to another person or institution [11]. Informed consent, unlike property law, recognizes the self-determination and autonomy (and, at other levels, collective or tribal sovereignty) of participants when they, with all the information required for them to make a truly informed decision, consent to provide their genetic material to researchers [11]. This debate also reminds one of the tension between providing consent forms with long lists of options and engaging in a culturally appropriate informed consent process, which may take more time and effort, but perhaps avoid the risk of information overload. Here, too, we might ask what kind of paradigm each solution fits into: Would the use of property law make an already complicated and legalistic transaction even more so? And does a more culturally competent approach to informed consent contribute to a more critical process, based in dialogue and the building of relationships?

Requirements of Informed Consent

The overarching theme within the discussion of what is actually being asked of informed consent is the inadequacy of the "broad consent" that has been obtained by many researchers, including the ASU researchers involved in the Havasupai case. Mello & Wolf, as well as Rao, ask: If broad consent is insufficient, then what *actually* constitutes informed consent, especially in the genomic and biomedical context [12, 18]? Because the Havasupai case was settled outside of court, it may leave a moral and ethical indication of what informed consent should involve, but not a legal precedent. Of particular interest here is Pensabene's discussion of the Common Rule, and how the district court involved in the Havasupai case chose to focus on the broad consent that *was* given, instead of how *informed* that

consent actually was [11]. If they *had* considered the Common Rule, and accordingly judged the consent given based on whether the information provided to participants was sufficient, instead of whether consent (regardless of how informed it was) was given or not, Pensabene indicates that the result may have been quite different [11]. The Common Rule's requirement of specifics as to the risks and benefits of research, the procedures involved, confidentiality, informing participants of results and changes that may affect their willingness to continue involvement, etc. seems to indicate the inadequacy of "broad consent," even according to "mainstream" standards. As we discuss the areas in which increased specificity is being asked for by U.S. tribes, it might be worth noting how many of these requirements are indeed expansions to the way informed consent is perceived according to the Common Rule and other standards, and how many of these requirements overlap.

One of these areas where increased specificity is being required is the ownership of data and samples given by tribal participants for the purposes of research. It has already been noted that Caplan & Moreno's proposed solution to the complexities that present themselves here, of considering research participants "donors" who give up their rights to their specimens and not "subjects" who have a stake in what happens to their bodily tissues and genetic material, might be seen as a way of avoiding tribal concerns altogether [33]. This attitude may already be part of the mainstream: As Garrison explains, consent forms that don't specifically address ownership almost automatically "[make] samples the property of the research institution, leaving participants with little control over research uses" [10]. This approach, which "emphasizes the split of the biological material from the person as soon as it is removed and therefore gives the person no rights in the now separate material", is antithetical to the worldview of many Indigenous peoples [2]. Of particular interest here is Sahota's study of Native American perspectives on specimen disposition. Specifically, the author's exploration of Native American perceptions of who is considered to be the owner of specimens once they are taken. It is reported that 50% of the participants believed the provider of the specimen to be the owner, and 44% believed the researcher to be [17]. Participants also had a variety of views about how informed consent affects ownership, some viewing the informed consent form as a transfer of property rights, and others viewing it as a written agreement on the limitations of how a specimen may be used [17]. This variety of perspectives may indicate that, regardless of the actual position taken, consent documents need to specifically state what expectations there are with regard to ownership. Without making those expectations explicit, neither researchers nor Indigenous participants (or their tribal representatives) can negotiate for the kind of ownership that is needed, and confusion and misunderstanding may cause a multitude of problems.

Palosaari , once again providing a perspective from outside the context of biomedical science, draws a close relationship between informed consent and intellectual property rights [13]. The author argues that researchers, in order to ensure that the consent process has indeed been *informed*, must "inform participants of their rights regarding data" [13]. Palosaari cites the Navajo Nation Code, which "explicitly claims ownership over cultural intellectual property," as an example of the way in which tribes are already giving attention to the issues that might arise if ownership is not addressed in the consent process [13]. Palosaari also looks at the professional and ethical standards that are already expected of researchers from the social science and humanities fields. Oral historians, for example, have a set of professional

standards that expressly give ownership and copyright of interviews to the interviewee, unless they transfer those rights to another individual or institution [13]. However, in many fields, existing protocols are insufficient for ethical research involving Indigenous communities.

In biomedicine and genomics as well, it may not be sufficient for researchers to only inform individuals and tribal communities of what ownership and rights they have to the data and samples they provide. It may be a responsibility of researchers that they assert tribal communities as the owners, or at least shared-owners, of data and specimens collected. This is part of respecting tribal sovereignty and of being culturally aware enough to recognize that tribal individuals and communities are the only ones who can make decisions about what happens to their data and their specimens. For example, Harding *et al.* describe a model material data-sharing agreement (MDSA) for the use of researchers and tribes. The MDSA is meant to assure that the materials and data collected by researchers "are and remain tribal property" and to assert that they "are not to be shared with third parties without the written permission of tribal authorities" [22]. Such an agreement between researchers and those authorized to give collective consent for their community, by making clear statements about ownership and by deliberately affirming the property rights of the tribe, may go a long way in avoiding misunderstandings. Chadwick, Copeland *et al.* report that many tribal IRBs and health boards in Oklahoma (where the authors conducted their research) already proactively and specifically address ownership, by including it in their contracts with researchers [7]. Again, by directly asserting and affirming the rights to and ownership of data and specimens by tribes, these documents can disrupt the common assumption that researchers and institutions become the owners of data and specimens once a tribal community or individual has consented to participate in research.

The methods by which researchers plan to procure samples and/or data (drawing blood samples, distributing questionnaires, conducting interviews or focus groups, etc.) is also mentioned by a few authors, including Palosaari and Harding *et al.* [22, 13]. This may seem like the most obvious area in which researchers should be specific: How can anyone consent to involvement in a study without being aware of the procedures they are being asked to undergo? Perhaps this *is* self-evident, because it is less-often a subject of discussion in the articles selected. Palosaari writes that researchers "should inform participants of the purposes of the research, provide the expected duration of participation, and describe the procedures" [13]). The American Anthropological Association, for example, notes that the lack of transparency about research goals and methodology impacts whether consent is fully informed [13]. Harding *et al.*, in their MDSA model, include a section on the types of material and data that will be collected by researchers. This can include data of many kinds, including sampling results, demographic attributes, organic material, transcriptions of interviews and focus group discussions, questionnaires, etc. [22]. The provision of this information, perhaps especially the expected duration of the study, is incredibly important.

The risks and benefits participants can expect as part of their participation in research, and how these will be communicated to participants, is another area in which increased specificity is being requested. Part of addressing this issue may be in dismantling the false binary often presented of either agreeing to any

and all components of research, or opting out and being excluded from research, and from its possible benefits. As previously mentioned, consent forms that provide lists of options, or a consent process that includes and welcomes negotiation, may go some way in ensuring that participants can receive the benefits of research, without being coerced into procedures they might otherwise be reluctant to consent to. Another part of this is simply communicating to potential participants what the risks, and benefits, of participation might be. This is already required by the Common Rule, but as we have already seen, these standards might not be sufficient in the U.S. tribal context. The Common Rule, once again, concentrates in the potential risks and benefits to the individual. Indeed, Chadwick, Copeland, *et al.* (2019), writing about the reasons that their tribal partners withheld their consent to participate in genomic research, report that the proposed consent form "stated that if a genetic abnormality were to be discovered, individuals would not be notified of the results, nor would any genetic education or counseling be provided." [7]. Some tribal IRBs objected to this, on the basis that participants in research should be notified of abnormalities and that researchers should share potentially beneficial information, if discovered [7]. Although potential risks and benefits to the individual are important, the Common Rule does not address possible cultural harms, or the risks and benefits that research might present to the community as a whole. Harding *et al.* (2012), for example, include in their MDSA model a section about the "risks and benefits of research to the tribal community," in which the risks *and benefits* expected from research should be summarized, covering risks and benefits for both individuals and for the community [22]. Likewise, researchers should consider benefits not just to the individual, but to the community as a whole.

Finally, there is the necessity of reporting results back to the tribal community, and ensuring that the benefits of the research and knowledge gained are made accessible. As Winters argues, the informed consent process should include processes for reporting findings to the participants [2]. In practice, this is not always done: Palosaari notes, for example, that linguists have a professional obligation to make their research available to the public, but do not have a standard that addresses the dissemination of research to the participants themselves, or consideration of research benefits to participants [13]. Yet, this is an elementary part of ensuring that participants see the benefits of research, and one that researchers must consider and plan for since the "mainstream" methods of publishing research (in academic journals, conferences, etc.) may not be accessible for many Native communities and individuals. This is, in some ways, related to the ownership of data and specimens already discussed, in that both involve giving the results of the research (and the decision of what to do with those results) back to the community, whether that is done by returning specimens, specifying tribal ownership of data, or simply by ensuring that results are published and shared with the community in an accessible way.

The storage, security, and treatment of specimens and/or data is a well examined area in which greater specificity is required for informed consent. This may include who will have access to specimens and data, plans for the disposal or return of specimens and data, whether tribes and participants will be contacted when and if researchers wish to use their samples for different research directions, etc. Once again, the actions of the ASU researchers involved in the Havasupai case seem to have played a large role in bringing this issue to the forefront. The researchers' description of the study as relating to diabetes,

and the broad consent forms obtained, allowed the researchers perhaps technical (but not ethical) permission to use the samples for a variety of other secondary uses that the Havasupai, if they had been provided with the specifics, would not have agreed to [2]. According to Drabiak , a breach of confidentiality happened when the original ASU researchers allowed others, including those from other institutions, to access the Havasupai samples and the codebooks that allowed for identification of the samples [19]. These breaches are particularly egregious, because the informed consent document signed by the participants asserted that research would be carried out at ASU and that all information would be kept private: This seems to have been not simply a case of the informed consent document not being specific enough, but of researchers violating even the general protections the document *did* provide [19].

It is not surprising, then, to see calls for increased specificity on the subjects of storage, security, re-consenting for secondary research, etc. Caplan & Moreno report, as of 2010, that, according to federal regulations, samples that are de-identified and cannot be traced back to an individual are within the rights of researchers to be re-used in studies not related to the original informed consent document [33]. Indeed, if a sample is anonymized, it may not be *possible* to seek informed consent again. This bypasses the participant's right to make those decisions for themselves but also ignores the role of tribal authorities and IRBs in determining whether the proposed research poses a risk to the community. It also highlights, once again, the basis of "mainstream" informed consent on individual rights and risks, not acknowledging collective or cultural harms that may occur as a result of research. This is also relevant in fields where research may involve traditional or culturally sensitive information. Consent, Palosaari writes, cannot really be considered voluntary "without a complete understanding of who will access the data [provided by the participant] and how the data will be used" [13]. And, as in biomedical research, there are issues with contacting participants for obtaining informed consent for new research directions: As new technologies make new research possible, researchers may have difficulty obtaining new consent if they cannot contact the participant or if the research environment is difficult to get to [13]. And again, it may be difficult to re-consent individual participants if samples are completely anonymized.

A few solutions to concerns about the misuse of specimens include a "destroy by" date, the option to have a sample destroyed after the participant's death, or options for specimen re-use and storage on informed consent forms [21]. In fact, Chadwick, Copeland *et al.* report that most tribal boards in Oklahoma now require that consent forms include an expiration date, after which researchers must obtain new consent, or otherwise return or dispose of the sample provided [7]. Additionally, researchers must seek IRB re-approval for continued or secondary use. Proposal and consent forms must also state specifically the disease being studied, how samples will be used, as well as any secondary uses of specimens and how they will be stored and secured. Most of these tribal boards also require that third parties, or other researchers interested in utilizing the specimens, must seek a new research agreement and IRB approval. The expiration date, or the date after which samples will be destroyed or returned to the tribe, not only guards against unauthorized uses of the specimens, but also gives the tribe a timeframe during which their oversight will be needed, and a date by which they can expect research data to be analyzed and reported [7].

Also, significant, and closely related to the storage and possibilities for future uses of specimens and data, is the clear and specific communication of protocols affirming the right of participants to withdraw from research at any time. Once again, this seems to be complicated by the de-identifying of specimens and data, which can prevent participants from having their samples returned or destroyed if they decide to withdraw their consent and researchers from being able to contact participants to seek new informed consent for new research. Deeply concerning are reports that many researchers' protocols may not sufficiently address this: Drabiak cites Leslie E. Wolf *et al.*, relating that some research protocols clarified that researchers would remove identifiers from a sample if a subject requested to withdraw, but that they would not actually withdraw the sample [12, 19]. Others put restrictions on withdrawal and state that de-identified samples would not be withdrawn, or that samples would not be withdrawn if the researchers deemed them "necessary for the integrity of the project" [19]. Winters refers to the Havasupai case, where the participants requested to withdraw from research when they learned about the ways in which their specimens were being used and shared. This request was denied [2].

Palosaari, speaking specifically about the field of linguistics, writes about the necessity for researchers to consider how withdrawal requests may affect their methodology to plan for how these requests will be handled *before research begins* and to know how to explain their withdrawal protocols to participants [13]. This is particularly important because of the tension between individual and collective rights in this context that can create a great deal of complexity. On the one hand, a participant may be requesting to withdraw because they do not wish to reveal communally-held traditional or culturally sensitive knowledge [13]. On the other hand, if the goal of the research is language documentation for the benefit of the community, withdrawal and destruction of data may be antithetical to the goals of both the researcher and the community they are working with [13]. The same attention might be applied in biomedical and genomic science to help ensure that participants are, in fact, able to exercise their right to withdraw from research. Clashing worldviews and conceptions of ownership may be contributing to the manner in which this issue has been handled in biomedicine and genomic research in the past: If researchers are working from a paradigm in which specimens are no longer connected to their providers, and therefore the use of their specimens has no ability to harm them, then of course simply de-identifying them might seem like a sufficient response to a request to withdraw from research. However, if one is working from a paradigm in which bodily tissues, blood, and other materials are still considered part of the individual who provided them, and in which community and cultural harms are acknowledged in addition to individual risks and harms, such a response is inappropriate.

[1] In fact, the authors entitle their article "Overvaluing individual consent ignores risks to tribal participants."

Conclusion

With respect to the first research question seeking to address how informed consent is being conceived of by U.S. tribes, the literature reviewed highlighted the following themes: First, the process of informed consent itself is not sterile, and the time, attention, and efforts towards cultural competence or awareness

given to the process is very significant. Also of significance is the treatment of informed consent as a *process*, rather than as a document that needs to be signed so the task can be checked off of a list. Second, there are different levels at which informed consent operates, the most-discussed being the individual and the collective levels. It is highlighted many times over that, for U.S. tribes, individual consent is important but not sufficient. In many tribal worldviews, individuals are understood within the context of their communities and relationships with others, rather than as solitary and completely independent actors. Especially in research where the risk of harm to the individual is easily transferred to the community as a whole, the informed consent of the community, through its authorities and representatives, is required. Informed consent at the government-to-government level is exemplified by the consultation process, which shares some of the insufficiencies of the consent process at the individual and collective levels. In particular, it is insufficient because of its treatment as an item to check off a list, and because, although consultation is mandated, actually obtaining consent is not. Third, some scholars have seen the language of property law as a preferable alternative to informed consent, as a way to protect the rights of tribal individuals. Most articles reviewed, however, seemed to support informed consent over the language of property law as the best defense for Native American communities, granted with significant adaptations appropriate for the tribal context.

When discussing what tribal communities and governments are asking of informed consent, it may be helpful to highlight the Haudenosaunee concept of “seven generations,” as described by Oren Lyons. This is the idea that one must make decisions “on behalf of the seventh generation coming. You who see far into the future,” Lyons continues, “that is your responsibility: to look out for those generations that are helpless, that are completely at our mercy. We must protect them” [34]. Although this is a specifically Haudenosaunee concept, it may have equivalents and applications in many Indigenous communities in the U.S., especially in understanding the requirements of informed consent by tribal nations. Just as individual consent may not be sufficient in the tribal context, because of the risks and harms that may be transferred to the community as a whole, it may not be sufficient to consider consent as something that is given just for the individual, or the community, as it currently is. Consent to participate in research, to share knowledge or information (whether genetic, cultural, environmental, etc.), impacts not only the current generations, but those yet to come. The protections and agreements reached by the current generation are those that future generations will see the impact of, whether for better or worse. Given this cultural sense of responsibility to these generations, as well as to the community as it currently is, it should not be any surprise that it would inspire a need for an in-depth and specific informed consent process.

There are different areas in which greater specificity is required by U.S. tribes for consent to be considered *truly informed*. These include: ownership of data and/or specimens, benefits to the community and/or individual, the methods by which data/specimens are collected, the ways in which data/specimens will be stored, secured, and used, and options for negotiating consent (and for withdrawing from research participation at any time). The consent process must not only cover these concerns to be considered truly informed, but it must also be obtained by the appropriate tribal representatives, in addition to individual participants. It seems largely agreed upon that both individual and collective consents are required and

that upholding tribal sovereignty is critical and to be respected. Tribal IRBs, community review boards and similar bodies are often referenced as authorities to which researchers must apply to receive collective consent, though some authors note that this may vary among tribes, and researchers must take time and care to understand which individuals and authorities they must consult with before beginning their studies [35].

Limitations

Limitations of this literature review include the searching of three databases for articles (we also note that the choice of PubMed and Web of Science as two of the three may have a strong influence toward the biomedical science literature). The articles selected do not include grey literature and, therefore, may exclude many rich voices speaking on this subject, including sovereign tribal nations in the U.S. Also, for the purpose of this literature review, we did not distinguish between Native and non-Native scholars in the selection of articles, thus both perspectives are included and maybe more strongly positioned toward an outsider perspective. Finally, there is the possibility of human error in missing or excluding scholarship. Despite these limitations, we believe that the present literature review provides a good overview of the discussion surrounding informed consent in the tribal context and provides solid answers to the research questions examined.

Future Research

We suggest five areas that warrant additional examination. First, articles reporting on studies in which informed consent was briefly discussed as part of methodology were excluded from this literature review. Further work might be done by reviewing these articles to investigate how informed consent is being applied and self-reported by researchers working with U.S. tribal communities. Second, future research might delve into how informed consent is being discussed outside of the genomic/biomedical context. A few scholars in this review covered perspectives from archaeology, anthropology, linguistics, environmental science/studies, etc. (perhaps because of the databases we chose to use for the current study), but it may be of interest to conduct a search more specific to these fields. Third, another area of importance that needs further attention is the uncertainty about how urban Natives and tribes that are not federally recognized can be protected from unethical research practices.

Fourth, so that we may reveal requirements coming directly from tribal nations, an examination of documents created by U.S. tribal IRBs and community review boards may help us to understand what is being specifically requested from researchers in terms of informed consent at the collective level. Lastly, to encourage scholars to take action for consent to be truly informed in the U.S. tribal context, more immediate next steps may be to use the information found here to support tribal communities in establishing and enforcing their requirements of research.

List Of Abbreviations

U.S. - United States

IRB - Institutional Review Board

IHS - Indian Health Services

ASU - Arizona State University

AI/AN or AIAN - American Indian/Alaska Native

FPIC - Free, Prior, and Informed Consent

MDSA - Material Data-Sharing Agreement

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

Not applicable

Funding

Not applicable

Authors' contributions

Both authors made substantial contributions to the design of the systematic literature review. In particular, CLB conceived and presented the initial idea, helped to manage and supervised the project, and contributed to the interpretation of the results. TG carried out data collection, analysis and synthesis and wrote the first draft of this article, then worked with CLB to edit and refine subsequent drafts. Both authors have approved the final version of this manuscript.

Acknowledgements

First, as visitors to this land, we wish to acknowledge the Duwamish Tribe, the Muckleshoot Tribe, the Suquamish, and other tribes on whose traditional lands we study and work. Second, we are grateful to the University of Washington Information School's Native North American Indigenous Knowledge Initiative for creating an intellectual space for Indigenous Studies to be cultivated and disseminated in the academy. Finally, we wish to acknowledge and thank Leo Egashira and Claire Renaud for their feedback and support on this manuscript.

Authors' information

Clarita Lefthand-Begay, MS, PhD
Assistant Professor
Information School
University of Washington, Box 352840, Seattle, WA 98195-2840

Email: Clarita@uw.edu
ORCID iD: https://orcid.org/0000-0001-5882-8108

Tasha Gross

Graduate Student

Information School, University of Washington

1112 N.E. 41st St, Cedar Apts W310A, Seattle, WA 98105

Email: ngross3@uw.edu

ORCA iD: https://orcid.org/0000-0002-3139-7042

References

1. Sterling RL. Genetic Research among the Havasupai: A Cautionary Tale. AMA Journal of Ethics. 2011;13:113–7. doi:10.1001/virtualmentor.2011.13.2.hlaw1-1102.
2. Winters A. Trespass to Culture: The Bioethics of Indigenous Populations' Informed Consent in Mainstream Genetic Research Paradigms. American Indian Law Review. 2016;41:231–51.
3. Champagne D. Centering Indigenous Nations within Indigenous Methodologies. Wicazo Sa Review. 2015;30:57–81. doi:10.5749/wicazosareview.30.1.0057.
4. James R, Tsosie R, Sahota P, Parker M, Dillard D, Sylvester I, et al. Exploring pathways to trust: a tribal perspective on data sharing. Genetics in Medicine. 2014;16:820–6. doi:10.1038/gim.2014.47.
5. Garrison NA, Hudson M, Ballantyne LL, Garba I, Martinez A, Taualii M, et al. Genomic Research Through an Indigenous Lens: Understanding the Expectations. Annual Review of Genomics and Human Genetics. 2019;20:495–517. doi:10.1146/annurev-genom-083118-015434.

6. Hodge FS. No Meaningful Apology for American Indian Unethical Research Abuses. Ethics & Behavior. 2012;22:431–44. doi:10.1080/10508422.2012.730788.
7. Chadwick JQ, Copeland KC, Branam DE, Erb-Alvarez JA, Khan SI, Peercy MT, et al. Genomic Research and American Indian Tribal Communities in Oklahoma: Learning From Past Research Misconduct and Building Future Trusting Partnerships. American journal of epidemiology. 2019;188:1206–1212.
8. Trennert RA. Indian Sore Eyes: The Federal Campaign to Control Trachoma in the Southwest, 1910-40. Journal of the Southwest. 1990;32:121–49. https://www.jstor.org/stable/40169723. Accessed 17 Sep 2020.
9. Whitener RJ. Research In Native American Communities in the Genetics Age: Can the Federal Data Sharing Statute of General Applicability and Tribal Control of Research be Reconciled? Selected Works of Ron J Whitener. 2010. https://works.bepress.com/ron_whitener/1/. Accessed 17 Sep 2020.
10. Garrison NA. Genomic Justice for Native Americans: Impact of the Havasupai Case on Genetic Research. Science, Technology, & Human Values. 2013;38:201–23. https://www.jstor.org/stable/23474493. Accessed 17 Sep 2020.
11. Pensabene C. A Canyon Full of Woes: The Havasupai Tribe Illustrates the Need for Cultural Competency in Genetic Research. Alb Gov't L Rev. 2014;7:637. https://heinonline.org/HOL/Page?handle=hein.journals/aglr7&id=659&div=&collection=.
12. Mello MM, Wolf LE. The Havasupai Indian Tribe Case — Lessons for Research Involving Stored Biologic Samples. New England Journal of Medicine. 2010;363:204–7. doi:10.1056/NEJMp1005203.
13. Palosaari N. Intellectual Property Rights and Informed Consent in American Indian Communities: Legal and Ethical Issues. American Indian Law Review. 2016;41:125–65. https://www.jstor.org/stable/26492256. Accessed 17 Sep 2020.
14. Garrison NA, Barton KS, Porter KM, Mai T, Burke W, Carroll SR. Access and Management: Indigenous Perspectives on Genomic Data Sharing. Ethnicity & Disease. 2019;29 Supp:659–68. doi:10.18865/ed.29.S3.659.
15. Miller RJ. Consultation or Consent: The United States' Duty to Confer with American Indian Governments. ND L Rev. 2015;91:37. https://heinonline.org/HOL/Page?handle=hein.journals/nordak91&id=41&div=&collection=.
16. Mengden WH. Indigenous People, Human Rights, and Consultation: the Dakota Access Pipeline. American Indian Law Review. 2017;41:441–66. https://www.jstor.org/stable/26492269. Accessed 17 Sep 2020.
17. Sahota PC. Body Fragmentation: Native American Community Members' Views on Specimen Disposition in Biomedical/Genetics Research. AJOB Empirical Bioethics. 2014;5:19–30. doi:10.1080/23294515.2014.896833.
18. Rao R. Informed Consent, Body Property, and Self-Sovereignty. Journal of Law Medicine and Ethics. 2016;44:437. https://repository.uchastings.edu/faculty_scholarship/1535.

19. Drabiak-Syed K. Lessons from Havasupai Tribe v. Arizona State University Board of Regents: Recognizing Group, Cultural, and Dignity Harms as Legitimate Risks Warranting Integration into Research Practice. J Health & Biomedical L. 2010;6:175. https://heinonline.org/HOL/Page?handle=hein.journals/jhbio6&id=183&div=&collection=.
20. Smith-Morris C. Asserting Communalism. In: Smith-Morris C. Indigenous Communalism: Belonging, Healthy Communities, and Decolonizing the Collective. Rutgers University Press; 2020. p. 105-122. doi:10.2307/j.ctvscxrb6.
21. Hiratsuka V, Brown JK, Hoeft TJ, Dillard DA. Alaska Native people's perceptions, understandings, and expectations for research involving biological specimens. International Journal of Circumpolar Health. 2012;71:18642. doi:10.3402/ijch.v71i0.18642.
22. Harding A, Harper B, Stone D, O'Neill C, Berger P, Harris S, et al. Conducting research with tribal communities: sovereignty, ethics, and data - sharing issues. Environmental Health Perspectives. 2012;120:6-. https://link.gale.com/apps/doc/A278773895/PROF?u=wash_main&sid=zotero&xid=615b7d6c. Accessed 17 Sep 2020.
23. Williams RL, Willging CE, Quintero G, Kalishman S, Sussman AL, Freeman WL. Ethics of Health Research in Communities: Perspectives From the Southwestern United States. The Annals of Family Medicine. 2010;8:433–9. doi:10.1370/afm.1138.
24. After Havasupai litigation, Native Americans wary of genetic research. American Journal of Medical Genetics Part A. July 2010;152A:fm ix-fm ix. doi:10.1002/ajmg.a.33592.
25. Tauali`i M, Davis EL, Braun KL, Tsark JU, Brown N, Hudson M, et al. Native Hawaiian Views on Biobanking. J Canc Educ. 2014;29:570–6. doi:10.1007/s13187-014-0638-6.
26. Angal J, Petersen JM, Tobacco D, Elliott AJ, Network PA in S and S. Ethics Review for a Multi-Site Project Involving Tribal Nations in the Northern Plains. Journal of Empirical Research on Human Research Ethics: An International Journal. 2016;11:91–6. doi:10.2307/90012137.
27. Tsosie KS, Yracheta JM, Dickenson D. Overvaluing individual consent ignores risks to tribal participants. Nature Reviews Genetics. 2019;20:497–8. https://link.gale.com/apps/doc/A596653039/HWRC?u=wash_main&sid=zotero&xid=6a3195a3. Accessed 17 Sep 2020.
28. Villegas M. What's Love Got to Do With It? Stewarding a Healing Vision at the National Congress of American Indians Policy Research Center. Journal of American Indian Education. 2016;55:99–119. doi:10.5749/jamerindieduc.55.2.0099.
29. Claw KG, Anderson MZ, Begay RL, Tsosie KS, Fox K, Garrison NA. A framework for enhancing ethical genomic research with Indigenous communities. Nature Communications. 2018;9:1–7. doi:10.1038/s41467-018-05188-3.
30. Chadwick JQ, Tullier MA, Wolbert L, Coleman C, Branam DE, Wharton DF, et al. Collaborative implementation of a community-based exercise intervention with a partnering rural American Indian community. Clinical Trials. 2019;16:391–8. doi:10.1177/1740774519839066.

31. Shaw JL, Robinson R, Starks H, Burke W, Dillard DA. Risk, Reward, and the Double-Edged Sword: Perspectives on Pharmacogenetic Research and Clinical Testing Among Alaska Native People. Am J Public Health. 2013;103:2220–5. doi:10.2105/AJPH.2013.301596.
32. Abadie R, Heaney K. “We can wipe an entire culture”: fears and promises of DNA biobanking among Native Americans. Dialectical Anthropology. 2015;39:305–20. https://www.jstor.org/stable/43895157. Accessed 17 Sep 2020.
33. Caplan AL, Moreno JD. The Havasu ‘Baaja tribe and informed consent. The Lancet. 2011;377:621–2. doi:10.1016/S0140-6736(10)60818-5.
34. Lopez B, Lyons O. The Leadership Imperative: An Interview with Oren Lyons. *Manoa.* 2007;19(2):4-12. doi:10.1353/man.2008.0008.
35. Kuhn NS, Parker M, Lefthand-Begay C. Indigenous Research Ethics Requirements: An Examination of Six Tribal Institutional Review Board Applications and Processes in the United States. Journal of empirical research on human research ethics. 2020;15(4):279-291. doi:10.1177/1556264620912103.

Figures

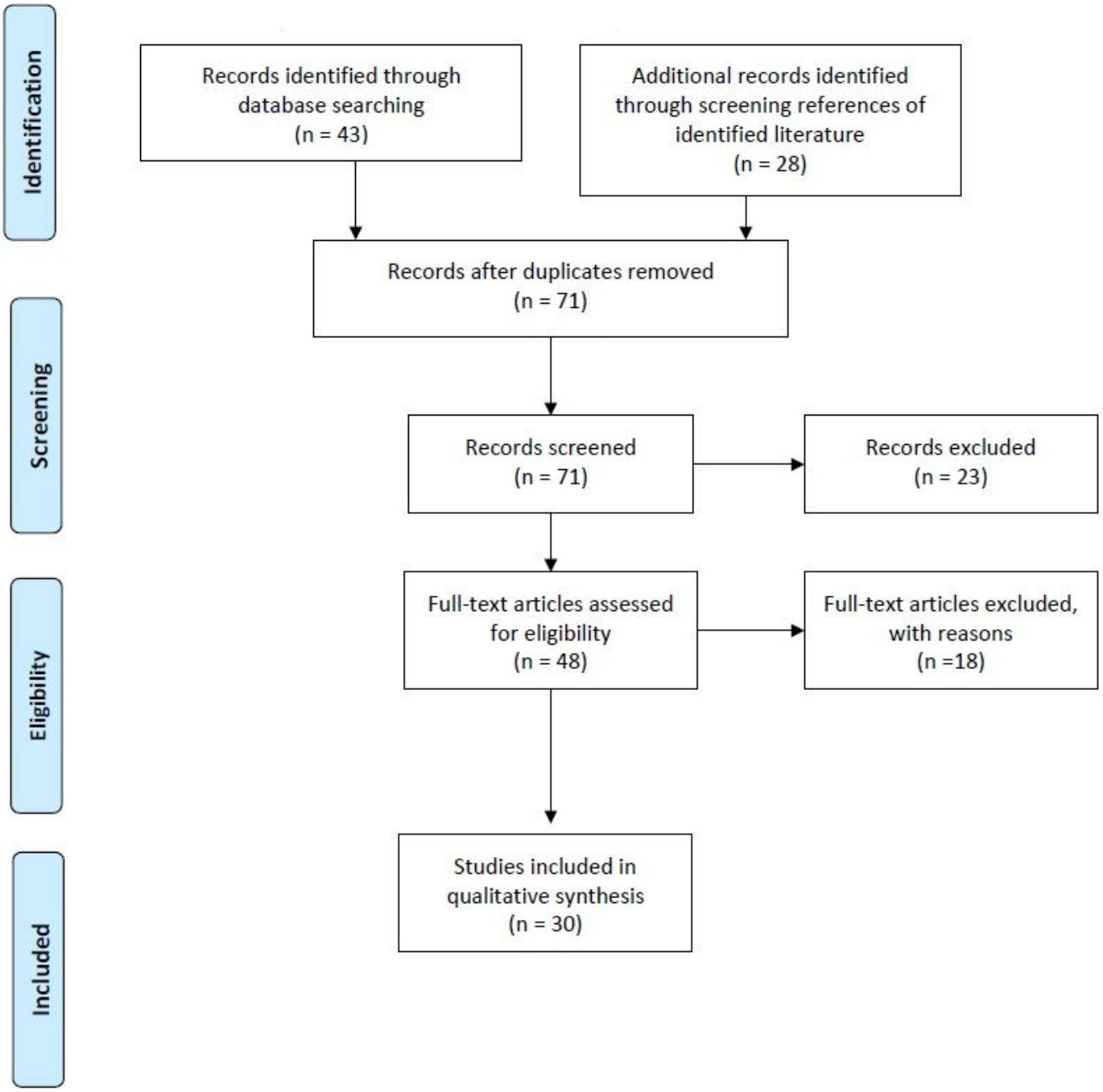

Figure 1

Flow Diagram of literature selection process for a review on informed consent using Flow diagram of the study selection process using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, Moher et al.2009).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Appendix.docx

- PRISMA2009checklistsubmit.docx