

Native Hawaiian preferences for informed consent and disclosure of results from research using stored biological specimens

Abstract: Increasingly, genetic and biomedical researchers are developing protocols to reexamine human tissue specimens that were obtained and stored during clinical care or previous research studies. Although some communities and associations are developing guidelines for human-tissue research, guideline development rarely considers consumer preferences for informed consent and disclosure of results. This study, examining Native Hawaiian preferences for informed consent and disclosure of results (n = 429, 83.2% Native Hawaiian), was modeled after a national study of consumer preferences, allowing comparison between the national sample and the Hawai'i-based sample. The interview schedule included two scenarios on research requiring the re-use of clinically derived and research-derived biological specimens. For each, participants were asked if informed consent should be required: a) in general; b) if the specimen was personally identified; and c) if the specimen was de-identified, or anonymized. Participants were also asked if they would want to know the results of the research and if they would want their doctor to be told. Regardless of how specimens were obtained, 78% of Native Hawaiians would want to be asked for their consent for the re-use of identified specimens and about 35% would want to be consented for the re-use of anonymized specimens. In both cases, Native Hawaiians in the Hawai'i sample were more likely than Whites in the national sample to want an informed consent process. Similar proportions in both samples would want findings from research on stored specimens reported to them (about 90%) and to their physicians (about 80%). These findings call into question the "Common Rule" and the guidelines of the American Society of Human Genetics, which do not require researchers to obtain informed consent for research use of anonymized specimens. **Key Words:** biological specimen banks, Institutional Review Board, minority groups, research ethics, vulnerable populations

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Introduction

Increasingly, genetic and biomedical researchers are developing protocols to reexamine how human tissue specimens that were obtained and stored during clinical care (e.g., from surgery or biopsy) or previous research studies are to be used in future research. To protect subjects from potential harm, institutions have begun to develop recommendations for research that involves stored biological specimens. Current recommendations are not uniformly agreed upon and generally are based on experts' assumptions about the preferences of specimen donors and research participants. Most recommendations do not

take into account preferences of individuals who have donated biological specimens because few studies have made efforts to ascertain preferences of the general population, especially members of non-White minority groups¹.

Only two studies were found that attempted to solicit public opinion about the use of stored biological specimens. A British study by Goodson and Vernon² showed that 18% of survey respondents would not agree to the use of their biological specimens in any type of research. Willingness to donate biological specimens for research among the remaining respondents varied according to the type of research proposed, with 82% being willing to participate in cancer research and only 26% being willing to participate in research on genetic cloning. In addition, 42% of respondents expressed a desire to be informed if their biological specimens would be stored, and 35% would want to be consulted if their biological specimens would be used for further research.

In a U.S.-based study, Wendler and Emanuel¹ interviewed a group of older Americans (90% White) and found that respondents were more likely to require consent for re-use of clinically derived specimens (specimens obtained during previous clinical care) than for re-use of research-derived specimens (specimens obtained during previous research). Respondents were also more likely to require consent for re-use of personally identifiable specimens than for re-use of anonymized specimens. In addition, 88.9% of respondents would want to be informed of research results, and 82.1% would want their physician to be informed of the results. Although non-White respondents made up less than 10% of the sample, an ethnic comparison was performed, and non-White respondents were significantly less likely than White

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respondents to require consent for the use of stored biological specimens in research.

The survey used by Wendler and Emanuel¹ was adapted to examine Native Hawaiian preferences for informed consent and dissemination of results for research that uses stored biological specimens. As a group, Native Hawaiians—descendants of the inhabitants of the Hawaiian archipelago before the arrival of the first foreign visitors in 1778³—have the lowest life expectancy of all major ethnic groups in the state, and have more years of productive life lost than other groups in the state due to heart disease, injuries, cancer, suicide, AIDS, stroke, diabetes, chronic lung disease, and chronic liver disease^{4, 5}.

Although there is a clear need for research on health disparities in this vulnerable population, Native Hawaiians are cautious about participating in research because the research process and the use of research results often do not account for the needs and priorities of the community⁶. As a minority group, Native Hawaiians may also be susceptible to group harm if research reveals harmful genetic or biologic information. In addition, Native Hawaiians have a number of traditional beliefs about the sanctity of tissue and body parts, which may conflict with the demand for research on stored biological specimens and the practice of waiving informed consent, even when biological specimens do not contain personal identifiers⁷.

In light of these considerations, this study addressed the following research questions:

- 1) Do Native Hawaiians want to be asked their consent for research on stored biological specimens?
- 2) Under what conditions should informed consent be required? Should consent be required for the re-use of clinically derived or research-derived specimens? Should consent be required if the specimen has personal identifiers? Is anonymized?
- 3) To whom should research results be disclosed? To specimen donors? To physicians?

Methods

Study Population. Our sampling frame included Native Hawaiians 18 years and older. Participants were recruited through the Native Hawaiian Health Care Systems (NHHCS), agencies established in the early 1990s to provide outreach, health education and limited primary-care services, and to increase Native Hawaiian access to health services on six islands—Hawai'i, Kaua'i, Lāna'i, Maui, Moloka'i, and O'ahu—with the bulk of care provided by Native Hawaiian health professionals and community outreach workers. Together, the NHHCS serve about 10,000 people a year, of whom about 15% are uninsured. Community outreach workers from each NHHCS were trained to recruit participants and administer the survey face-to-face. Informed consent was obtained from each participant, and completed surveys

were confidential. Each participant was given a small incentive (\$5 gift certificate for a local gas station, grocery store, etc.), and each NHHCS received \$10 for each of the first 100 completed surveys. Surveys were completed by 429 individuals from Hawai'i (n = 82), Kaua'i (n = 99), Maui (n = 76), Moloka'i (n = 87), and O'ahu (n = 85).

Survey Development. With permission from Wendler and Emanuel¹, this survey instrument was adapted to include items specific to the Native Hawaiian community, and was pre-tested to assure item clarity. This instrument was selected because it had been tested and found to be feasible in a previous study. Use of this survey instrument also allowed for comparisons between findings from the Native Hawaiian community and findings from the national study.

The survey included the following hypothetical scenarios on research that requires the re-use of clinically derived and research-derived biological specimens:

- 1) "Suppose you had surgery to remove a tumor. The doctor had to remove a tissue specimen so he could study it and find out if you have cancer. The doctor only used up part of the tissue specimen. The rest of the specimen was stored at the hospital. Five years later, a researcher wants to use the stored specimen in a research project to study cancer."
- 2) "Imagine that you were in a cancer research study two years ago. The researcher took a blood or a tissue specimen so he could find out more about why people get sick. The study is over, and the researcher only used up part of the specimen. The rest of the specimen was stored at a lab. Now the researcher wants to use your stored specimen to study something else about cancer, or another disease, like diabetes."

For each scenario, participants were asked if informed consent should be required: a) in general; b) if the specimen was personally identified; and c) if the specimen was anonymized, or stripped of personal identifiers that could link the specimen back to an individual. Participants were also asked if they would want to know the results of the research, and if they would want their doctor to be told.

Statistical Analysis. SPSS 10.0 was used to calculate the percentage of participants in our sample who would require informed consent under each hypothetical scenario. PEPI 4.0 was used to calculate chi-square statistics to test for significant differences in: 1) socio-demographic characteristics of the national and local samples; 2) consent and disclosure preferences of Whites in the national sample and Native Hawaiians in the local sample; and 3) consent and disclosure preferences within each sample where available data allowed for inter-ethnic differences. SPSS 10.0 was used to perform binary logistic regression to examine associations between participant responses and demographic characteristics (age, sex, income, education, and past involvement with medical research).

Approval. The project was reviewed in its conceptual stage by the advisory council of 'Imi Hale—Native Hawaiian Cancer Awareness, Research, and Training Network to solicit feedback and approval to proceed and to assure cultural appropriateness and cultural sensitivity. After funding was received, approval was obtained from the NHHCS Institutional Review Board (IRB). Findings from this study were reported back to administrators of the NHHCS and their feedback was incorporated into the interpretation of the results.

Results

Table 1 presents socio-demographic characteristics for our sample and for the national sample surveyed by Wendler and Emanuel¹. As expected, 83.2% of our sample was Native Hawaiian and only 7.5% was White, while 90.5% of the national sample was White. The national study targeted older adults, many of whom had participated in research and provided biological specimens that were stored for future research. Our study targeted Native Hawaiian adults of all ages; thus, our sample was considerably younger than the national sample with a mean age of 42.5 years, compared to 65.2 years in the national sample (not shown in

table). A smaller percentage of respondents in the national sample had a household income of less than \$25,000 per year (21.2% vs. 38.7%), while 20.8% of the national sample reported an annual household income in excess of \$75,000 per year (not shown in table). In the national sample, a greater proportion had attended graduate school (32.3% vs. 7.9%). Finally, almost half of the participants in the national sample had previously participated in research, compared to only 16.1% of the Hawai'i sample.

Table 2 presents the proportion of respondents who would require informed consent for the re-use of identified and anonymized specimens, both clinically derived and research-derived. Native Hawaiians in the Hawai'i sample were significantly more likely than Whites in the national sample to require informed consent for re-use of clinically derived tissue, regardless of whether specimens were identified or anonymized ($p < .01$). Likewise, for research-derived tissue, Native Hawaiians in the Hawai'i sample were significantly more likely than Whites in the national sample to require informed consent for both identified specimens and anonymized specimens ($p < .01$). Within samples, there were small differences in proportions requiring informed consent (e.g., in the Hawai'i sample, Native Hawaiian re-

Table 1. Characteristics of the Hawai'i sample, compared with those in the national study by Wendler and Emanuel (2002)

| Characteristic | Hawai'i sample | National sample |
|---|------------------|------------------|
| | (N=429) n (%) | (N=504) n (%) |
| Sex^a | | |
| Male | 118 (27.5) | 197 (39.1) |
| Female | 310 (72.3) | 307 (60.9) |
| Ethnicity^a | | |
| Hawaiian | 357 (83.2) | 0 |
| White | 32 (7.5) | 456 (90.5) |
| Black and Hispanic | 0 | 30 (6.0) |
| Other | 40 (9.3) | 10 (2.0) |
| Age Group (years)^a | | |
| 18-34 | 145 (33.8) | 0 |
| 35-49 | 139 (32.4) | 0 |
| 50-64 | 98 (22.8) | 169 (33.5) |
| 65+ | 40 (9.3) | 335 (66.5) |
| Household Income | | |
| \$0 - 24,999 ^a | 166 (38.7) | 107 (21.2) |
| \$25K + | 237 (55.2) | 278 (55.2) |
| Education^a | | |
| Some high school, diploma, or GED | 156 (36.4) | 138 (27.4) |
| Tech school, some college, or college degree | 230 (53.6) | 202 (40.1) |
| Some grad education or graduate degree | 34 (7.9) | 163 (32.3) |
| Participated in medical research^a | 69 (16.1) | 246 (48.8) |

^a $p < .01$

Table 2. Frequency and percentage of respondents who would require informed consent: Comparison within and between samples^a

| | Hawai'i sample (N=429) | | National sample (N=504) | |
|------------------------------------|-----------------------------|------------------|----------------------------|--------------------------------|
| | Native Hawaiians (n=357) | Whites (n=32) | Whites (n=456) | Blacks and Hispanics (n=30) |
| | n (%) | n (%) | n (%) | n (%) |
| Clinically-derived specimen | | | | |
| Identified | 278 (77.9) | 21 (65.6) | 306 (67.1) | 15 (50.0) |
| Anonymized | 125 (35.0) | 9 (28.1) | 120 (26.3) | 6 (20.0) |
| Research-derived specimen | | | | |
| Identified | 278 (77.9) | 22 (68.8) | 131 (28.7) | 8 (26.7) |
| Anonymized | 132 (37.0) | 8 (25.0) | 50 (11.0) | 4 (13.3) |

^aInter-ethnic differences within studies were not statistically significant. However, differences between Native Hawaiians in the Hawai'i sample and Whites in the national sample were significant for all four conditions ($p < .01$).

spondents were more likely than White participants to require informed consent), but these differences were not statistically significant.

Table 3 shows preferences for dissemination of research findings. Looking across the two samples, similar proportions would want research findings disclosed to their physicians (82.1%). Although differences were small, respondents from the Hawai'i sample (90.7%) were significantly more likely than respondents from the national sample (88.8%) to want to personally know about research findings ($p < .05$). Inter-ethnic differences were negligible and not shown in the table.

In the national study, Wendler and Emanuel¹ reported that older and non-White respondents were less likely to require consent than younger and White respondents. Similarly, the data were examined for possible associations between socio-demographic characteristics and consent preferences. Findings shown in Table 4 suggest that age and gender are associated with preferences for informed consent. First, regression analysis showed a negative association between age and the desire to be asked for consent for the re-use of identified specimens, i.e., older respondents were significantly less likely than younger respondents to require consent, for both clinically derived specimens (odds ratio, 0.98; 95% confidence interval, 0.97-0.99) and research-derived specimens (odds ratio, 0.98; 95% confidence interval, 0.96-0.99). For anonymized specimens, males were

significantly more likely than females to require being asked for consent for both clinically derived specimens (odds ratio, 0.49; 95% confidence interval, 0.29-0.83) and research-derived specimens (odds ratio, 0.59; 95% confidence interval, 0.35-0.99). None of the other socio-demographic variables were statistically significant.

Discussion

This study was constrained by dependence on a convenience sample, which included individuals participating in programs provided by the NHHCS. The national sample was also, in part, a convenience sample (including individuals who had previously participated in research) and was restricted to older adults. Thus, findings from neither study can be generalized to the U.S. population. Future studies should use more rigorous sampling methods, which can be achieved by adding appropriate items to national random-sample surveys such as the Behavioral Risk Factor Surveillance Survey.

Despite this limitation, findings are presented because very few studies have been published on consumer preferences regarding informed consent and disclosure of results from research using stored biological specimens. In general, Native Hawaiians in this sample wanted to be consented for research that uses stored biological specimens and appraised of research findings. Within this sample, older individuals and males were less likely to require

Table 3. Frequency and percentage of respondents who would require disclosure of research results: Comparison between samples

| | Hawai'i sample (n=429) | National sample (n=504) |
|---|---------------------------|----------------------------|
| | n (%) | n (%) |
| Would want to know results ^a | 389 (90.7) | 448 (88.9) |
| Would want MD to know results | 352 (82.1) | 414 (82.1) |

^a $p < .05$

Table 4. Socio-demographic characteristics associated with preference for informed consent among respondents in the Hawai'i sample

| Independent variables ^a | Clinically derived specimen | | Research-derived specimen | |
|------------------------------------|-----------------------------|----------------------------|----------------------------|----------------------------|
| | Identified OR (95% CI) | Anonymized OR (95% CI) | Identified OR (95% CI) | Anonymized OR (95% CI) |
| Age | .98 (.97-.99) ^b | 1.00 (.98-1.01) | .98 (.96-.99) ^b | .99 (.97-1.01) |
| Gender | .68 (.36-1.29) | .49 (.29-.83) ^b | .78 (.41-1.46) | .59 (.35-.99) ^b |
| Education | 1.04 (.88-1.24) | 1.13 (.97-1.32) | .95 (.80-1.23) | 1.04 (.99-1.21) |
| Income | .96 (.78-1.18) | .92 (.77-1.11) | .96 (.78-1.17) | .97 (.80-1.16) |
| Medical research | 1.05 (.54-2.06) | 1.73 (.96-3.12) | 1.11 (.57-2.17) | 1.37 (.75-2.49) |

^a Age was a continuous variable; education and income were ordinal variables, where a higher value meant more education and greater income; gender and medical research were categorical variables, with male and "no" serving as the reference values, respectively.

^b $p < .05$

informed consent. The age-related trend may be due to a cohort effect, in that younger individuals are more aware of risks and benefits of research. The gender difference may stem from the fact that men tend to underutilize the health care system and therefore may be less comfortable asserting themselves in a medical research situation.

When Native Hawaiian preferences were compared to findings from a national study conducted by Wendler and Emanuel¹, three similarities were identified. First, at least two-thirds of respondents in both studies indicated they would want to be asked permission for research use of personally identified specimens that had been gathered during clinical care. Second, members of both samples were less likely to require consent for research using anonymized specimens than for research using identified specimens. Finally, more than 85% of both samples would want to review research results, even if the clinical significance of findings was uncertain.

Two notable differences were observed. First, participants in the Hawai'i sample wanted to be asked for consent for re-use of any stored biological sample, whether it had been obtained during clinical care or a previous research study, whereas respondents from the national sample were less likely to require informed consent for the re-use of research-derived specimens. Second, larger proportions of the Hawai'i sample wanted to be asked for consent for the re-use of anonymized specimens, whether clinically or research-derived.

It is possible that participants in the Hawai'i sample did not discriminate between clinically and research-derived samples because Hawai'i-based interviewers did not adequately articulate the difference between the two methods for obtaining tissue specimens to the participants. However, this explanation is unlikely, as interviewers were well trained for the task and each interviewer conducted approximately one-quarter of his/her data collection under the direct supervision of the first author. An alternate explanation could be the fact that the Hawai'i sample and the national sample were significantly different in nearly

every socio-demographic characteristic. In the national study, specific characteristics, including age, were found to be associated with a reduced likelihood of requiring consent¹. Testing this hypothesis in the Hawai'i sample, younger respondents were more likely than older respondents to require consent for identified samples. However, none of the other socio-demographic characteristics on which the two samples differed were significantly associated with consent preferences.

Thus, it is likely that preferences differed between the Hawai'i sample and the national sample because of ethnic differences, i.e., the national sample was predominantly White, while our sample was predominantly Native Hawaiian. Several factors set Native Hawaiians apart from other ethnic groups, including the fact that the indigenous peoples of Hawai'i have a history of discrimination and abuse, resulting in a generalized distrust of research⁶. Additionally, some Native Hawaiians maintain traditional beliefs that require certain ritual practices surrounding tissue and body parts, especially of the deceased, and specifically forbid the desecration of placentas, bones, hair, fingernails, and excrement. While western minds may view these biological specimens as inconsequential and disposable, Native Hawaiians believe that they contain *mana* or the very life force of the individual⁷. As such, an increase in research on stored biological specimens, without attention to Native Hawaiian cultural beliefs, practices, and preferences for informed consent and dissemination of research results, may be unsettling to many Native Hawaiians.

The finding that Native Hawaiians wish to be informed and asked for consent for the re-use of stored biological specimens calls into question the U.S. federal government's "Common Rule" (CFR §46.101) and the guidelines of the American Society of Human Genetics⁸, which do not require researchers who use stored biological specimens to contact donors and obtain informed consent for research use of anonymized specimens. These policies have been justified by the claim that if donors cannot be identified, they cannot be harmed. Following this rule, most IRBs generally expedite their review of studies using human samples of hair, nail

clippings, deciduous or permanent teeth, gingival dental plaque/calculus, sweat, saliva, amniotic fluid, sputum, placenta, or skin-mucosal-buccal cells (CFR §46.110).

As noted by Sade⁹, however, only individuals who have had a chance to weigh risks and benefits of a specific research project can judge whether they may be harmed. This may be especially true for research that makes ethnic comparisons, as individuals of an ethnic group with unfavorable characteristics may be harmed if they are rendered unemployable or uninsurable or are socially stigmatized by research findings^{1,10}. Sade⁹ argues that the concept of autonomy and the tenets of informed consent mean that people must be asked if they want to participate in research (including research on stored specimens) and that people must be given adequate information to make this decision. Recommendations to waive the consent process, even if the majority of Americans are in favor of waiving it, would compromise the very principles upon which human subjects protections are based.

In light of this, the results of this study build a strong case for the adoption of a more conservative approach to the issue of informed consent, such as that recommended by the U.S. National Institutes of Health—Department of Energy Working Group on Ethical, Legal and Social Implications of the Human Genome Project, which stipulates that informed consent should be obtained whenever research involves a biological specimen for which the donor can be identified¹¹. Proponents of this type of policy view the informed consent process as a “right” of all research participants. This would require that investigators take the time to educate potential participants about the risks and benefits of specimen-related research and obtain informed consent for the use of stored specimens^{1,9}. Data from this study suggest that members of the Native Hawaiian community would be in agreement with this type of policy and would prefer for researchers to obtain informed consent whenever possible.

Acknowledgements

This study was funded by a grant from the Oregon Health and Sciences University (Thomas Becker, PI). Acknowledgements are tendered to Dr. Wendler, who gave permission to use his study as a model. Many thanks to the community outreach staff at the Native Hawaiian Health Care Systems—Velma Becraft, Mona Cardejon, Michelle Ka’aihue, Leimomi Shearer, and Val Starkey—and to the 429 individuals who participated in this study.

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