Attitudes Towards and Perceptions of Clinical Genetic Testing Among Pacific Islanders Living in the United States and US-Affiliated Pacific Islands (USAPI)

by

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Background: A core value of the ethical, legal, and social implications (ELSI) of genetic research is the concept of public and provider education. Many studies to date have solicited attitudes of the general public in several parts of the world to assess baseline knowledge and attitudes, but there exist several gaps in the literature regarding attitudes towards genetic testing among Pacific Islanders. **Methods:** A survey was developed composed of questions from the literature and shared with Pacific Islander communities in the mainland United States and US-Affiliated Pacific Islands (USAPI). The survey asked participants to provide demographic information, answer true/false questions based on genetic concepts, and share their attitudes and perceptions toward genetic testing, medical family history, and preferences for return of results. **Results:** As a group, the average correct score on the genetic knowledge measure was 77.7%. Participants (*N* = 65) had limited experiences with genetics, including genetic testing (10.8%), genetic counseling (1.6%), and genetic research (1.5%). In the assessment of attitudes toward clinical testing, where, out of a possible 65 points, higher scores correlated with more favorable attitudes towards genetic testing, the average score was 50.38. A majority (84.6%) agreed either somewhat or strongly to the use of genetic testing for early detection of disease. Over 90% agreed, to some extent, that collecting family health history is important for understanding their own or their family's disease risk. Of those sampled, 68.3% would want to receive *any* results if they participated in a health-related research

study, including non-actionable results. Over three-quarters expressed interest in receiving secondary results concerning personal health, regardless of whether it is for an illness that is treatable or untreatable. **Conclusions**: Participants in this study have demonstrated an interest in clinical genetic testing, recognize the value of medical family history for personal health, and endorsed openness to receiving genetic testing results and secondary results both actionable and non-actionable. However, there are still many barriers increasing access to genetic testing in Pacific Islander communities, including basic information such as prevalence of genetic disease among communities.

Table of Contents

List of Tables

List of Figures

Preface

This project, including both thesis and essay, have been close to my heart for almost two years as of the creation of this document. I have invested a great deal of time poring over books on national reports for the islands of Samoa, traveled through pages outlining a day in the life of a traditional healer on the islands, and walked through excepts about the relationship between Christianity and health from Samoan voices. After reading all of these things, sometimes I would find myself lying in bed at night practicing some of the new words I had learned, like *taulāsea* or *matai* on repeat. I drank what I learned for the purpose of writing here now, but more than that I have worked hoping that I could offer something of use to the Samoan community.

However, it is important to acknowledge that (a) I am not of Samoan, or even Pacific Islander, descent and that (b) the attitudes and perceptions recorded in this thesis may not be a representative of what Pacific Islander communities think about genetic testing personally or for their families. Instead, I worked so intimately to get to know Samoa, and of the place of medicine and genetics in Samoa, as a biracial, Black–Latino ("blatino") boy wondering what it would take to make sure communities of color, just like my own, are not left in the shadows of rapidly-evolving medical advances.

While I am a genetics student and have full faith in the ways that genetics can revolutionize human health, the goal of this project is not to induct any community into a climate that it does not wish to be a part of. Instead, I believe with everything I am that communities deserve the chance to *say* exactly what they want to get out of their community health institutions, and that they should at least have the chance to access

services that they desire or that they are otherwise in need of by their own discretion. Rather than turning blindly away from the complex and uncomfortable issues in the clinical setting, I hope that all of our marginalized communities can face the information available head-on and feel both supported and empowered to take charge of their health in light of the facts.

That being said, I am grateful first and foremost to our survey participants. Thank you for the opportunity to learn about your ideas and perceptions about genetics and genetic testing, and for sharing your understanding and perspectives with us. Next, I send my most sincere gratitude to my thesis committee team, for which none of this would have been possible—to my committee chair, Ryan Minster, who has been so conscientious, thoughtful, and humble at every step of the way in this work. To Nicky Hawley and Andrea Durst for your direction and expertise. To Thistle Elias, who has inspired my work in health equity every day and kept it real since the day I met her. To Vickie Bacon, a walking model of genetic counseling and public health genetics in action who has given me very, very large shoes to fill. I'd also like to thank Lacey Heinsberg for keeping us on track and taking initiative when it was needed most, as well as Joshua Naseri and Kit Church for their assistance with survey dissemination.

Finally, my deepest gratitude to my partner, who reminded me of my future when I was not entirely sure I had the stomach to complete this enormous undertaking. Here's to beginning the next phase of our life together.

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1.0 Introduction

The Human Genome Project was born from a concerted attempt to map out the full euchromatic, or protein-coding, sequence of genes in human beings. Starting in 1990, the program finished in 2003, two years shy of the planned estimated fifteen-year timeline (Watson & Cook-Deegan, 1991). The reference sequence gained from the Human Genome Project was updated several times throughout the early 21st century, including a recent 2022 paper addressing a missing 8% of the human genome almost twenty years after the initial completion of the project (Nurk et al., 2022). The information gleaned from the reference genome, and how we use that information, continues to change at an accelerated pace. Mapping of the human genome has allowed researchers to uncover novel genetic targets capable of revolutionizing modern medicine, including targets relevant to drug metabolism, genetic therapies for rare disease, and cancer treatment (Collins, 2001; Hood & Rowen, 2013; McLeod & Evans, 2001).

Founding researchers of the Human Genome Project recognized the need to monitor issues arising at the interface between genetics and public health and developed a program for this purpose. Of the approximately three billion dollars allotted to the project during its thirteen-year run, 3% to 5% of the annual budget was allotted to the ethical, legal, and social Implications (ELSI) of genetics and genomics (Yesley, 2008). The National Human Genome Research Institute (NHGRI) has expressed that the initial goals of its ELSI program have been met but acknowledges the sensitive and complex nature of ELSI topics and the ongoing need for additional research (NHGRI, 2012). The organization has also highlighted several different priority areas, including the need to educate

both the public and professionals, the latter of which may include medical providers who may not be familiar with genetic testing.

The need to address ELSI issues in genetics and genomics, and to do so in an equitable manner, does not fall squarely on NHGRI's shoulders. In the name of progress, it is important that all researchers and policymakers also commit to understanding ELSI in the field of genetics. Many researchers have explored the need for more inclusive and diverse genome-wide studies so that non-European populations benefit from genetic discoveries, while others have focused on identification of baseline genetics education among the public and/or medical providers. This project is rooted in the latter of these two approaches, with a focus on Pacific Islanders living in the United States and United States-Affiliated Pacific Islands (USAPI: the U.S. territories of Guam, American Samoa, and the Northern Mariana Islands and the nations of the Republic of the Marshall Islands, the Republic of Palau, and the Federated States of Micronesia).

Regardless of prior work, there are always gaps to fill as scientists learn about the many global perspectives related to genetic testing and research. For example, while many research groups have attempted to assess genetic knowledge and attitudes towards genetic testing, these exercises have been across a limited scope of racial and ethnic groups. To our knowledge, this project is the first to investigate attitudes and perceptions of genetic testing among Pacific Islanders living in the United States and USAPI, with the goal to use these results to refine the survey instruments for use among citizens of the Independent State of Samoa. Information gathered will be used to create programs and materials to address gaps in genetic knowledge and build confidence and

empowerment to engage with genetics, either for clinical or research purposes, among community members.

1.1 Specific Aims

The specific aims of this project are to:

(a) Examine baseline levels of genetic knowledge among Pacific Islanders living in the United States and among the USAPI

(b) Identify themes and trends in judgment of genetic testing and return of results

(c) Identify current perceptions of medical family history to determine whether participants recognize implications of familial disease for their personal health

2.0 Literature Review

2.1 Bench to Bedside: Setting the Stage for Delivery of Clinical Services

The relationship between research and clinical practice is often referred to as the “Bench to Bedside” pipeline because it denotes the process by which research discoveries occurring in the laboratory (“bench”) translate directly to clinical treatment (“beside”). It is unclear exactly where the phrase first originated, but it has been referenced in editorials of the New England Journal of Medicine in 1968 and in 1974 ("Phagocytes and the “Bench-Bedside Interface”," 1968; Wolf, 1974), indicating that this concept has been a part of scientific consciousness for some time. In modern times, this process has also been referred to as “translational research” (Woolf, 2008).

Though the original phrase is overly simplistic and linear, it has been argued that the movement between research and clinical practice is more cyclical, and the translation of research to use in clinical practice is often not the final destination (Callard, Rose, & Wykes, 2012; Hampton, 2017). Regardless, this concept is an acknowledgement of the intimate relationship between the research development and the treatments that it may introduce (or lack thereof).

2.1.1 Diversity Problems at the Genomic "Bench"

Most genomic research has historically been conducted with populations of European ancestry. There is a wealth of literature citing the lack of diversity in genomic research as a barrier to clinical application (Bentley, Callier, & Rotimi, 2017; Hindorff et al., 2018; Landry, Ali, Williams, Rehm, & Bonham, 2018). Ultimately, what we learn from research is the basis for any benefits gained for clinical use, and for *whom* benefits most readily apply. Using genetic data derived from European ancestry populations in non-European ancestry groups can create erroneous estimates and discovery biases that undermine the relevance of findings.

It is reported that, based on current scientific knowledge, genetic testing in populations of non-European ancestry have a high rate of variants of uncertain significance (VUS), which refers to genetic changes with unknown clinical impact for individuals. Such findings were demonstrated in a database analysis of over 50,000 individuals, both affected and unaffected, who underwent multigene panel testing for hereditary predisposition for cancer. Among African Americans, Asian Americans and Pacific Islander Americans, rates of VUS findings in hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome (LS) were 18.8% and 16.6% respectively, whereas among European Americans the rate of VUS findings was 6.1% (Ndugga-Kabuye & Issaka, 2019). These greater rates of unknowns reflect the gaps that can persist when genomic research fails to prioritize diversity in its accelerated strides.

One of the single most important ways to address the lack of diversity in genomic research tools is to include more diverse populations in both studies and analyses. Even when marginalized participants are included in studies, they are often pruned out of final

analyses in favor of the larger samples sizes and genetic homogeneity afforded by European-ancestry participants (Martin et al., 2019). Inclusion of marginalized and underrepresented participants in genomic research would allow for more robust application of findings and ensure that any clinical benefits derived from genetic testing is accessible to all individuals, regardless of ancestry.

2.1.2 Protections for Participants

Increasing community contributions to research data on a global scale is not without its own set of challenges. Several have hypothesized that this is partly due to a lack of trust in the biomedical community among marginalized groups, tempered by historical scenarios in which these groups were misled, belittled, or otherwise taken advantage of (Garrison, 2013; Hoffman, Trawalter, Axt, & Oliver, 2016). While it is easy to paint broad strokes about opinions towards researchers and, to a larger extent, the medical system entirely, Armstrong, Ravenell, McMurphy, and Putt (2007) determined that levels of physician distrust in the late 1990s varied according to racial/ethnic group geographical location, gender, socioeconomic status, and insurance status. While analyses did not include attitudes towards physician distrust among Asian Americans and Pacific Islanders, the level of variation among those surveyed is a good model for various factors that can contribute to distrust and subsequent abstinence from exposure to physicians and researchers alike.

In what ways can genetic researchers regain trust and show their commitment to equitable gains in public health genetics? Sirugo, Williams, and Tishkoff (2019) highlight the role of ethics committees in assuring compliance to regulations that protect participant

welfare and the need for engagement of community partners at all levels of research to ensure that the needs of the community are being met. Martin et al. (2019) also discuss amending current policies that prevent genetic discrimination (such as the Genetic Information Nondisclosure Act of 2008, or GINA) so that they are more widely protective as well as linking biobanks to share information globally. Prioritizing protections for underserved communities and participant welfare together may increase the willingness of communities to participate in genomic research. Most importantly, as work continues to engage lower-middle income countries (LMIC) in genetic research, investigators must ensure that findings will help increase the health care capacity of these countries and not just benefit high-income countries.

2.2 United States-Affiliated Pacific Islands (USAPI)

The USAPI are a collection of islands located in the Pacific Ocean between Hawai‘i and New Zealand (Figure 1) that includes:

- three U.S. territories, American Samoa, Guam, and the Commonwealth of the Northern Mariana Islands (CNMI), and
- three Freely Associated State (FAS) nations: the Republic of Palau, the Republic of the Marshall Islands (RMI), and the Federated States of Micronesia (FSM). The Federated States of Micronesia are comprised of the states of Pohnpei, Kosrae, Chuuk, and Yap.

Together, these regions have a total population of approximately 465,000 spread across 2,000 islands and millions of square miles of the Pacific Ocean (Aitaoto & Ichiho, 2013; Pacific Islands Regional Climate Assessment, 2016).

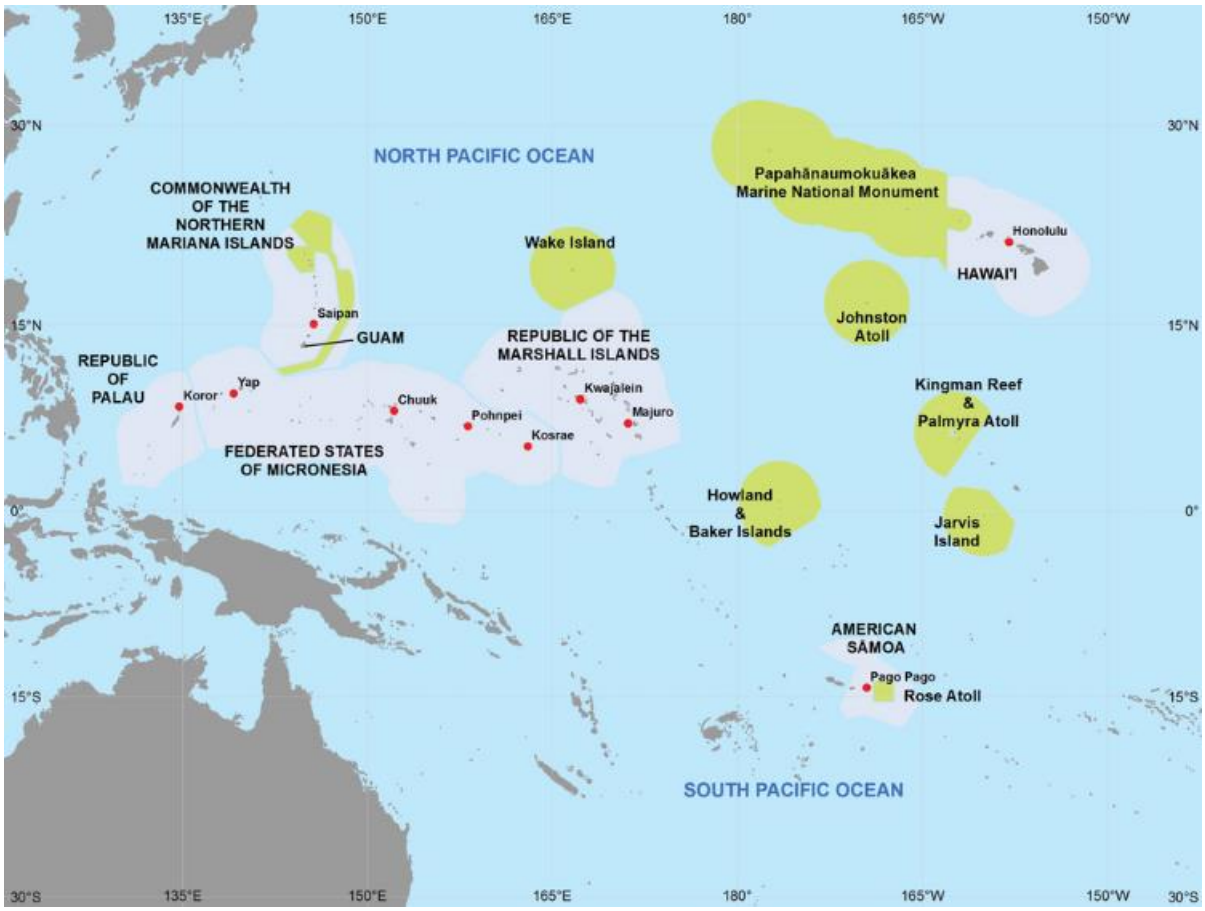

Figure 1. United States-Affiliated Pacific Islands Region (Keener et al., 2018)

2.2.1 United States Territories and Freely Associated States (FAS)

Except for individuals living in American Samoa, those living in U.S. territories are considered U.S. citizens. American Samoans are instead considered U.S. nationals. All U.S. citizens are U.S. nationals, but not all U.S. nationals are U.S. citizens. U.S. nationals

have fewer rights than U.S. citizens. They cannot vote in federal elections or in the state or local elections of the jurisdictions within which they might be residing—an American Samoan living in California, for example, cannot vote in California elections, but a Guamanian can (Cottle, 1995). They also do not have the right to apply for any job for which citizenship is required. However, both groups are protected by the U.S. government.

Freely Associates States are sovereign nations that have entered an international agreement with the United States under the Compact of Free Association (COFA). This international treaty is a financial and military agreement between the U.S. and FAS nations. The RMI and FSM both entered into COFA agreements in 1986, with the Republic of Palau doing so in 1994 (McElfish, Purvis, Riklon, & Yamada, 2019). The United States is responsible for these states in terms of funding and military defense, but FAS nations govern their own foreign policy. Those living in FAS islands are not considered U.S. citizens; they are allowed to live, work, and study in the United States without a visa, but cannot vote and have limited access to U.S. health programs, including Medicare and Medicaid.

In addition to USAPI, there are other Pacific Islander nations not affiliated with the U.S. in the surrounding areas of the Pacific, including the sovereign nations of Fiji, Vanuatu, Tonga, the Solomon Islands, Tuvalu, Niue, the Cook Islands, Nauru, Kiribati, and Tokelau, as well as various non-sovereign territories of the U.S., Australia, New Zealand, France, Great Britain, and Chile. Each territory in the Pacific Islands region belies a diverse culture and complex political history.

2.2.2 Relationships With the United States

The exact relationships between the U.S. and each island are unique and convoluted beyond the scope of this review but, in many cases, there often is a painful history of Western colonization and negligence at the root of these interactions. For example, during World War II in the 1940s, the United States acquired the Marshall Islands as a Trust Territory under a United Nations agreement and, subsequently, took advantage of the islands for nuclear testing. This nuclear research was reportedly done without informed consent of the Marshallese, and materials related to the research were not provided in Marshallese (McElfish, Hallgren, & Yamada, 2015). The consequences from radioactive fallout in the region have been long-lasting for the inhabitants of the Marshall Islands, negatively impacting their health and contaminating indigenous plant and animal life on the islands (Ahlgren, Yamada, & Wong, 2014). Though the U.S. claimed that some of the factors that contributed to extensive fallout damage in the area, such as shifting winds, many in the RMI suspect that the United States inflicted radioactivity on islands inhabitants on purpose to study the scientific effects of radiation (Kupferman, 2011).

Even in modern day, past actions of the United States continue to impact USAPI citizens. Through different methods across its colonial history, the United States has taken “ownership” of different territories but there remain gaps in the care and attention that is given to its U.S. citizens and nationals. Citizens living in U.S. territories are not afforded the same rights as citizens born on the mainland, and some in the literature have argued that the U.S. laws use language that purposefully disenfranchises those living in U.S. territories—what one author refers to as the “Alien–Citizen Paradox” when referring to the effects of colonialism in Puerto Rico on producing this kind of paradox (Román,

1998). Though FAS nations have sovereignty and control over foreign policy, Kupferman (2011) has argued that U.S. control over economic direction has festered dependence and made it more difficult for some USAPI nations to gain a financial foothold. Additional research is needed in the literature that closes the gap between the resources that the United States is currently offering different USAPI territories and what work still needs to be done to better support communities.

Historical patterns of migration into the United States have been associated with many different factors, including the aforementioned nuclear contamination, the search for employment and educational opportunities and, increasingly, climate change and rising sea levels (Ahlgren et al., 2014; Keener et al., 2018; McElfish et al., 2019). As of 2019, the U.S. Census Bureau estimates that there are approximately 1.4 million Native Hawai‘ian and Pacific Islander groups living in the United States, with most living across the western coast of the United States, including Hawai‘i, California, and Washington (U.S. Department of Health and Human Services, 2021).

2.3 Measuring Public Attitudes and Preferences of Genetic Testing and Research

Much of the literature available regarding community views towards genetic testing is centered on European and White American populations, with some notable exceptions that have included an equitable share, if not a majority, of Black and African American communities in the United States. In a 2008 study, Neidich, Joseph, Ober, and Ross (2008) investigated the views of postpartum women living in Chicago about a hypothetical pediatric biobank to learn about views towards goals of research, privacy protections, and

feelings of trust and justice. Of the 239 participants, 82% identified as Black or African American. A more recent study (McCall, Ibikunle, Murphy, Hunter, & Rosenzweig, 2021) investigated motivations for participation in research genetic testing among Black and White Women with breast cancer diagnoses, where 23 of the 47 participants identified as Black or African American.

We are starting to hear more from underrepresented populations about their attitudes towards genetic testing. There is more work to be done to include Black and African American voices in genetics and genomics, and there are even larger gaps in the literature when it comes to attitudes towards genetics and genomics among Native Hawaiians and Pacific Islanders. This section provides an overview of the different questions that researchers have tried to answer about public perceptions of genetics and genomics among Europeans and White Americans. Topics have included surveys of genetic knowledge, conditions for which participants would feel more or less comfortable pursuing genetic testing, and preferences for return of results.

2.3.1 Efforts to Measure Genetic Literacy

Genetic literacy is defined as “sufficient knowledge and appreciation of genetic principles to allow informed decision-making for personal well-being and effective participation in social decisions on genetic issues” (Bowling et al., 2008). While this definition highlights the importance of grasping concepts well enough to make informed decisions and engage with genetic health information, it has been challenging to assess which tools most accurately capture this concept in the context of research (Abrams, McBride, Hooker, Cappella, & Koehly, 2015). Accordingly, Abrams et al. determined that there

may be many elements (e.g. knowledge, familiarity, and skills) that apply to genetic literacy, adding to previous research on a theoretical framework for a hierarchy of knowledge (Smerecnik, Mesters, De Vries, & De Vries, 2011). In effect, no single element of genetic literacy can stand in as a proxy for an individual's ability to fully engage with genetic information.

However, some studies have identified genetic knowledge as an important contribution to one's engagement with genetic health information. Jallinoja and Aro (1999), for example, created one of the first commonly identified measures to assess knowledge of genes and heredity in the Finnish population. In this study, researchers found that participants had ambiguous feelings about genetic testing, and that those with higher academic education had both more acceptance and more skepticism about the possibilities of genetic testing. Those with low genetic knowledge levels were more likely to indicate non-response answers when answering attitude questions about genetic testing (Jallinoja & Aro, 2000).

More recently, Fitzgerald-Butt et al. (2016) have determined that there are few measures available to efficiently assess genetic knowledge in a research setting, citing flaws with the 16-item tool developed by Jallinoja and Aro including its outdated facts and lack of questions on genetic testing. Their research team created and tested a revised tool for measuring genetic knowledge among children and adolescents with congenital heart disease and their parents. Findings indicate that this revised tool predicts knowledge scores well for those below average knowledge levels, and researchers suggest that tools like this can be used to tailor genetic counseling experiences with respect to a patient's knowledge level.

In addition to genetic knowledge, some studies have surveyed public opinion about the heritability of many different physical and psychological qualities as a construct of genetic knowledge. Most notably, Chapman et al. (2017) worked with a collection of specialists to develop an international tool known as the International Genetic Literacy and Attitudes Survey (iGLAS) to measure genetic knowledge and public opinions. The tool includes genetic knowledge portions similar to those above, vignettes and scenarios, as well as a section that asks participants to what degree various traits, including eye color, height, and depression, are thought to be genetic vs. environmental.

2.3.2 Attitudes Regarding Risks, Benefits, and Limitations of Genetic Testing

2.3.2.1 Attitudes Towards Clinical Genetic Testing

Most studies on attitudes towards clinic genetic testing in the literature have focused on whether participants view genetic testing favorably or unfavorably, and with what depth of information participants would want to receive results (e.g. is the disease treatable? Would participants want to know about pathogenic or likely pathogenic variants discovered outside of the original purpose of a clinical test or research study?).

A Dutch research group conducted studies in both 2002 (Henneman, Timmermans, & Van Der Wal, 2006) and 2010 (Henneman et al., 2013) to determine evolving views towards genetic testing in a Dutch population. In the 2002 cohort, 57% of participants expressed concern that people might be forced to have genetic testing in the future, and 44% of participants believed that those living with disabilities might be driven to isolation and exclusion from modern society. Regardless, interest in genetic testing about future disease was about 50% higher when those diseases were preventable, and

only a fifth of the sample likened genetic testing to tampering with nature. In the 2010 cohort, which was demographically similar, participants were more open and optimistic about the promise of genetic testing, with over 50% supporting more investment of funds in genetic research. Concerns about how results would affect insurance also slightly decreased from 42% in 2002 to 36% in 2010.

In both cohorts above, neither knowledge of genetics nor level of education were correlated with attitudes towards the availability and use of genetic testing; rather, those with high familiarity with genetics were more likely to express polar attitudes towards genetics than those with less familiarity, who were more likely to have less-defined opinions on topic questions. This finding is consistent with an earlier study by Jallinoja and Aro (2000), where researchers identified that those with lower education levels have greater challenges in judging statements on genetic attitudes.

A 2013 study (Haga et al., 2013) measured both health literacy using the Short Test of Functional Health Literacy in Adults (S-TOFHLA) and genetic knowledge using previously discussed measures (Jallinoja & Aro, 1999; Morren, Rijken, Baanders, & Bensing, 2007) and analyzed the impact of literacy on attitudes regarding genetic testing, including perceived genetic knowledge and impact of testing on society. Results suggested relatively high genetic knowledge in the sample, positive attitudes towards genetic testing, but similarly found no relationship between the level of knowledge and attitude toward genetic testing.

2.3.2.2 Opinions on Family History as Risk Assessment

Family history has been acknowledged as a valuable tool in clinical risk assessment for genetic disease. In a 2011 statement that was reaffirmed in 2020, the American

College of Obstetricians and Gynecologists (ACOG) espoused the value of family history tailored specifically to practice setting and patient population, and recommended that family history be taken for patients ideally during the period of preconception (The American College of Obstetricians and Gynecologists, 2011). Use of family health history may also help distinguish individuals at high risk for developing disease associated with clinically actionable variants, as there is evidence to suggest high concordance between high risk family history and the identification of clinically significant genetic variants (Bylstra et al., 2021).

Very few studies have surveyed the public directly about how important community members feel family history is in the clinical setting. Vermeulen, Henneman, van El, and Cornel (2014) gauged assessments of family history in a Finnish population, in association with an original study by Henneman et al. (2013), and found that a majority of participants (~59% of the sample, *N* = 964) had not had family history taken in a clinical setting and did not find it necessary to do so. However, those that had a family health history taken for any reason tended to view them as more important than those who did not. For example, this group tended to believe that family health histories might help prevent disease, more often thought family histories should be assessed, and in particular believed that general practitioners should be involved in taking the family health history.

In an American cohort, Thompson et al. (2015) conducted a qualitative study of 32 African American women, half of whom had a personal cancer history, to define family, to learn about health communication styles within families, and to identify whether participants or their family members actively collected family health history. The results of the study suggested that participants were unaware of whether family members had health

histories or reported that no one did; when reflecting on family members that they might ask, participants often cited family matriarchs as being most informative. Interestingly, many families reported denial about some health conditions, which researchers attributed to a need to avoid stress and anxiety associated with a medical diagnosis.

2.3.3 Return of Results

As the population has growing access to genetic testing methodologies, including whole exome sequencing (WES, targeted sequencing of the coding regions of DNA to find variants of clinical significance), there is continuing debate about how much detail testing results should be returned and in what way to patients and to research participants alike. One such study, administered by Saastamoinen et al. (2020), sought to identify if attitudes towards genetic testing might differ among adults when compared to attitudes towards testing in their children in a Finnish population. The survey, created independently by the research group, included 15 questions, each related to preferences about attitudes towards testing, cascade screening, and secondary findings. Both adults and their adolescent children were surveyed and, generally, the group found that there were higher levels of concern for the impact of genetic information gathered from testing in children compared to themselves.

In the research arena globally, there do not appear to be any clear laws or policies that dictate how researchers are expected to coordinate the return of results to research participants (Thorogood, Dalpé, & Knoppers, 2019). Several studies have consulted researchers to generate discourse around how return of results might work for participants in their own communities (Mwaka et al., 2021; Ochieng et al., 2021).

In an extensive systematic review, Vears et al. (2021) identified stakeholder perspectives for return of genomic results and found that those engaging with testing are interested in return of their results and that researchers and clinicians are willing to provide these results. They also found that stakeholders are more interested in those results that have the potential to change clinical management. Similarly, Love-Nichols et al. (2021) found that in the aortopathy population, participants were also motivated to receive genetic results, particularly those that were considered to be “actionable”. The study also found that, though most preferred in-person results disclosure, up to 75% found phone call disclosure permissible. Findings showing support for return of “medically actionable” results are in line with The American College of Medical Genetics and Genomics (ACMG) stance that information about “medically actionable” genetic variants should be reported to patients in a clinical setting, beyond the general purpose of testing; that list currently sits at 73 genes (Miller et al., 2021).

While it is important to consider how an excess of information may burden individuals from a psychosocial or practical perspective, some have argued that to restrict the information shared with participants and/or patients may be considered paternalistic and assumes that the average person is unable to decide for themselves how to use results from genetic testing (Fernandez, 2008). With proper consent on the risks and benefits of obtaining this kind of information, Fernando argues that that it is necessary to create comprehensive plans for return of genetic results. This is further complicated by differences in “personal utility” and “perceived utility”: individuals may perceive that certain results are beneficial to them even when there is no known practical use for the information gleaned (Vears et al., 2021).

Many researchers have explored the need for more inclusive and diverse genome-wide studies so that non-European populations benefit from genetic discoveries, while others have focused on identification of baseline genetics education among the public and/or medical providers. To our knowledge, this project is the first to investigate attitudes and perceptions of genetic testing among Pacific Islanders living in the United States and USAPI territories, with the goal to use these results to refine survey measures for use among citizens of the Independent State of Samoa. Information gathered will be used to create programs and materials to address gaps in genetic knowledge and build confidence and empowerment to engage with genetics, either for clinical or research purposes, among community members.

The specific aims of this project are to (a) gauge baseline levels of genetic knowledge among Pacific Islanders living in the United States and among USAPI, (b) identify themes and trends in judgment of genetic testing and return of results, (c) identify current perceptions of medical family history to determine whether participants recognize implications of familial disease for their personal health and (d) determine if there are relationships between demographic information, such as education level, income, or age, and attitudes towards clinical genetic testing or preferences for return of results and secondary findings.

3.0 Manuscript

3.1 Background

The Human Genome Project was born from a concerted attempt to map out the full euchromatic, or protein-coding, sequence of genes in human beings. Starting in 1990, the program finished in 2003, two years shy of the planned estimated 15-year timeline (Watson & Cook-Deegan, 1991). The reference sequence gained from the Human Genome Project was updated several times throughout the early 21st century, including a recent 2022 paper addressing a missing 8% of the human genome almost 20 years after the initial completion of the project (Nurk et al., 2022). The information gleaned from the reference genome, and how we use that information, continues to change at an accelerated pace. Mapping of the human genome has allowed researchers to uncover novel genetic targets capable of revolutionizing modern medicine, including targets relevant to drug metabolism, genetic therapies for rare disease, and cancer treatment (Collins, 2001; Hood & Rowen, 2013; McLeod & Evans, 2001).

Regardless of prior work, there are always gaps to fill as scientists learn about the many global perspectives related to genetic testing and research. Most genomic research has historically been conducted with European ancestry populations. There is a wealth of literature citing the lack of diversity in genomic research as a barrier to clinical application (Bentley et al., 2017; Hindorff et al., 2018; Landry et al., 2018). Ultimately, what we learn from research is the basis for any benefits gained for clinical use, and for *whom* benefits most readily apply. Given that research discoveries occurring in the laboratory (“bench”)

translate directly to clinical treatment (“bedside”), missing data among marginalized and indigenous communities can negatively impact the availability of clinical genetic services. Using genetic data derived from European ancestry populations in non-European ancestry groups can create erroneous estimates and discovery biases that undermine the relevance of findings, including a high rate of variants of uncertain significance (VUS).

Additionally, while many research groups have attempted to assess genetic knowledge and attitudes towards genetic testing, these exercises have been across a limited scope of racial and ethnic groups. Much of the literature available regarding community views towards genetic testing is centered on European and White American populations, with some notable exceptions including studies that have focused on Black and African American communities in the United States (Kibler & Brisco, 2006; McCall et al., 2021; Neidich et al., 2008). Topics have included surveys of genetic knowledge, conditions in which participants would feel more or less comfortable pursuing genetic testing, and preferences for return of results.

Some studies have identified genetic knowledge as an important contribution to one’s engagement with genetic health information. Jallinoja and Aro (1999), for example, created one of the first commonly identified measures to assess knowledge of genes and heredity in the Finnish population. In this study, researchers found that participants had ambiguous feelings about genetic testing, and that those with higher education had both more acceptance and more skepticism about the possibilities of genetic testing. Those with low genetic knowledge levels were more likely to indicate non-response answers when answering attitude questions about genetic testing (Jallinoja & Aro, 2000). Abrams et al. (2015) determined that there may be many elements (e.g., knowledge, familiarity,

and skills) that apply to genetic literacy, adding to previous research on a theoretical framework for a hierarchy of knowledge (Smerecnik et al., 2011). In effect, no single element of genetic literacy can stand in as a proxy for an individual's ability to fully engage with genetic information.

Most studies on attitudes towards clinical genetic testing in the literature have focused on whether participants view genetic testing favorably or unfavorably, and in what situations participants would want to receive results (e.g., is the disease treatable? Would participants want to know about pathogenic or likely pathogenic variants discovered outside of the original purpose of a clinical test or research study?). A 2013 study (Haga et al., 2013) measured both health literacy using the Short Test of Functional Health Literacy in Adults (S-TOFHLA) and genetic knowledge using previously discussed measures (Jallinoja & Aro, 1999; Morren et al., 2007) and analyzed the impact of literacy on attitudes regarding genetic testing, including perceived genetic knowledge and impact of testing on society. Results suggested relatively high genetic knowledge in the sample, positive attitudes towards genetic testing, but similarly found no relationship between the level of knowledge and attitude toward genetic testing.

Very few studies have surveyed the public directly about how important community members feel family history is in the clinical setting. Vermeulen et al. (2014) gauged assessments of family history in a Finnish population, in association with an original study by Henneman et al. (2013), and found that a majority of participants (~59% of the sample, *N* = 964) had not had family history taken in a clinical setting and did not find it necessary to do so. However, those that had a family health history taken for any reason tended to view them as more important than those who did not. In some cases, individuals may not

have the means to develop family health histories: in a 2015 study investigating the role of family health history in a cohort of African American women with cancer, participants were unaware of whether family members had health histories or reported that no one did; many families reported denial about some health conditions, which researchers attributed to a need to avoid stress and anxiety associated with a medical diagnosis (Thompson et al., 2015).

In an extensive systematic review, Vears et al. (2021) identified stakeholder perspectives for return of genomic results and found that those engaging with testing are interested in return of their results and that researchers and clinicians are willing to provide these results. They also found that stakeholders are more interested in those results that have the potential to change clinical management. Similarly, Love-Nichols et al. (2021) found that in the aortopathy population, participants were also motivated to receive genetic results, particularly those that were considered to be “actionable”. The study also found that, though most preferred in-person results disclosure, up to 75% found phone call disclosure permissible. Findings showing support for return of “medically actionable” results are in line with The American College of Medical Genetics and Genomics (ACMG) stance that information about “medically actionable” genetic variants should be reported to patients in a clinical setting, beyond the general purpose of testing; that list currently sits at 73 genes (Miller et al., 2021).

While many of these studies have set the foundation for what questions to ask of communities, there is clear deficit of research to investigate how Pacific Islander communities feel about the prospects and/or pitfalls that they perceive of genetic testing. In the name of progress, it is important that all researchers and policymakers also commit to

ELSI in the field of genetics. Many researchers have explored the need for more inclusive and diverse genome-wide studies so that non-European ancestry populations benefit from genetic discoveries, while others have focused on identification of baseline genetics education among the public and/or medical providers. To our knowledge, this project is the first to investigate attitudes and perceptions of genetic testing among Pacific Islanders living in the United States and USAPI territories, with the goal to use these results to refine survey measures for use among citizens of the Independent State of Samoa. Information gathered will be used to create programs and materials to address gaps in genetic knowledge and build confidence and empowerment to engage with genetics, either for clinical or research purposes, among community members.

The specific aims of this project are to (a) gauge baseline levels of genetic knowledge among Pacific Islanders living in the United States and among USAPI, (b) identify themes and trends in judgment of genetic testing and return of results, (c) identify current perceptions of medical family history to determine whether participants recognize implications of familial disease for their personal health and (d) determine if there are relationships between demographic information, such as education level, income, or age, and attitudes towards clinical genetic testing or preferences for return of results and secondary findings.

3.2 Methods

3.2.1 Survey Design

For context, the Yale University School of Public Health and the University of Pittsburgh School of Public Health have been collaborating for several years with researchers on the Samoa Islands (and some individual researchers at each institution even longer than that) to better understand the relationship between physical health markers, lifestyle changes over the end of the 20th century, and genetic markers among Samoans. The spectrum of studies that have come out of these studies are referred to as “OLaGA”, which stands for “Obesity, Lifestyle, and Genetic Adaptation” and, in the Samoan language means “life” or “the process of living”. The research team includes Samoan researchers who live and work directly from the islands and take full responsibility for many research activities on the islands. In total, the research team has recruited and interacted with thousands of Samoan participants over the time frame of decades and continues to disseminate its research activities to the community via Facebook.

The survey was created as part of this ongoing collaboration between the two universities consisting of approximately seven members, including two principle investigators who have worked directly with the Independent State of Samoa as part of the OLaGA team, the director and the associate director of the Public Health Genetics and Genetic Counseling programs respectively at the University of Pittsburgh, a post-doc with the Human Genetics department, and three master’s level students with a combination of training in Human Genetics and Public Health. The focus of the subcommittee was to create and manage projects associated with analysis of the Ethical, Legal, and Social

Implications (ELSI) genetic research in the OLaGA cohort. As part of first steps in this endeavor, it was necessary to create a survey capable of measuring attitudes towards genetic testing, clinical and research aspects of testing, and preferences for sample handling and return of results. Though the focus of the current study is of those attitudes in Pacific Islanders living in the United States and USAPI, an additional goal is to compare these findings to data on attitudes and perceptions of genetic testing using the same survey among Samoans living in the Independent State of Samoa, including those that have worked with the OLaGA team previously and those of the general population who have not. Additional feedback about the survey was solicited from the greater OLaGA research team, including Samoan team members in Samoa.

The survey was developed and managed using REDCap electronic capture tools, a secure, web-based platform to support research studies, hosted through Yale University (Harris et al., 2019; Harris et al., 2009). The survey captured demographic information about participants, including level of education, marital status, income, and baseline experiences with genetic testing, research participation, and health literacy. Questions asking participants about their attitudes towards genetic testing are a combination of different tools that have been previously used to measure public attitudes towards genetic testing and research. Information about what literature was used to inform each of the question blocks and approximately how large each questionnaire section is can be found in Table 1 below. The survey is a mix of true/false, sliding scale, multiple choice, and Likert scale questions with some opportunities to fill-in-the-blank for those questions where participants may wish to clarify an answer selection. Some grammatical edits were made to questions taken from the prior literature for clarity, but the overall integrity of questions

has been maintained. Finally, each section was given a primer to provide foundational information prior to participation to clarify complex genetic concepts. These primers also underwent edits and were trimmed with a goal of achieving an average reading level of the 8th grade using the Simple Measure of Gobbledygook (SMOG) Index Readability Formula (Mc Laughlin, 1969); primers for all sections can be found in Appendix B.3.

The survey currently exists in two formats, an English version and a Samoan version; all translations were completed with the assistance of Samoan research team members. For the purposes of this thesis, the survey was disseminated in an English format. A copy of the complete survey in English is available in Appendix B.3. Though there are a total of nine sections in the complete survey, only those relevant to clinical testing will be reviewed in this study; results from attitudes on genetic research will be explored in later projects. The current study was approved by Yale University's Human Investigations Committee (Protocol #2000030094; PI: Nicola Hawley) with whom the University of Pittsburgh has an Institutional Review Board (IRB) Authorization Agreement that covers this research.

Table 1. Reference Literature by Survey Section

Section	Associated Author(s)	Number of Questions by Section (151 Total)
Genetic Knowledge	Fitzgerald-Butt et al., 2016	18
Heritability Estimates	Chapman et al., 2017	8
Attitudes Towards Clinical Genetic Testing	Haga et al., 2013	14
Family History	Vermeulen et al., 2014	8

Attitudes Towards Genetic Research	Haga et al., 2013 Neidich et al., 2008 Kibler & Brisco, 2006	33
Motivations For and Concerns About Participation in Genetic Research	Goodman et al., 2019 Sanderson et al., 2016	27
Return of Results and Secondary Findings	Love-Nichols et al., 2021 Saastamoinen et al., 2020	20
Sample Storage	Neidich et al., 2008 (trust statements only)	15
Sharing of Research Data	N/A	8

3.2.2 Study Participants

Eligibility criteria for the study required that participants were (i) of Pacific Islander decent, (ii) residents of the mainland United States or any USAPI, and (iii) over the age of 18 years. In the current study, Pacific Islander descent included Carolinian, Chamorro, Chuukese, Fijian, Guamanian, Hawaiian, Kosraean, Marshallese, Niuean, Palauan, Pohnpeian, Papua New Guinean, Samoan, Tokelauan, Tongan, and Yapese as well as an “Other” option for those identifying as any Pacific Islander group not listed.

Dissemination of the survey began in February of 2022 through joint efforts by the research team. A reference list for contacts to disseminate the survey included both professional networks among research team members and national Pacific Islander groups endorsing missions associated with health, pollical advocacy coalitions, and other academic groups. Contact was primarily initiated either through email or through social network groups such as Facebook and Twitter and included a block of text explaining the study (Appendix B.1) as well as a flyer (Appendix B.2). The survey was also posted on

the research team's Facebook page and advertised to Facebook users identifying as Pacific Islander. Though the survey is still being disseminated and responses are still being collected, the cut-off date for analysis purposes for this study was on April 25th, 2022.

3.2.3 Data Analysis

All data analysis was completed using STATA/SE 17.0 (StataCorp, 2021). Tables summarizing demographic and response percentage information were created using Microsoft Excel. Participants were included in analyses if they completed any part of each italicized section in Table 1; sample sizes for each question are noted in tables to reflect non-responsiveness where applicable. Data analysis was such that each section, with the exception of the return-of-results portion of the survey, was given a composite score assessing affinity towards the subject with higher scores indicative of mastery (knowledge scores) or favorable attitudes (Clinical Attitudes Score, Family History Score).

First, knowledge scores were calculated based on the number of true/false questions correct out of 18. Each correct answer was worth one point; incorrect answers or non-responses were not worth any points. Similar to previous studies (Fitzgerald-Butt et al., 2016), participants were only included in knowledge score analyses if they answered at least 14 questions, which represents approximately three-quarters of completion.

Additionally, scores were assigned to represent attitudes towards clinical testing (hereby referred to as "Clinical Attitudes Score") where higher scores are associated with more favorable attitudes towards testing and lower scores are associated with more reserved attitudes towards testing. These questions had Likert scale responses with five different point values: Strongly Disagree (1), Slightly Disagree (2), Neither Agree Nor

Disagree (3), Slightly Agree (4), and Strongly Agree (5). For questions demonstrating more reserved attitudes (e.g. “If a disease cannot be treated, I don't want a genetic test”), point values were inverted such that individuals strongly agreeing with this statement would earn a “1”. Although there are 14 questions total in this section, one question retained from a study from the literature (Haga et al., 2013) was omitted from scoring as it is unclear, based on phrasing, whether it represents a favorable or reserved attitude (“The possibility of a genetic test will change one's future"). As a result, the most favorable possible score a participant could achieve is a 65; conversely, the most reserved score possible was a 13.

Scores regarding attitudes towards the importance of medical family history were assigned in a similar fashion as Clinical Attitude Scores. Of the eight questions included in this section, only five were used to calculate scoring (hereby referred to as “Family History Scores”); this is because (a) both questions “I can easily recall the health history of most of my relatives” and whether participants have ever actively collected medical family history may not be indicative of how important a participant believes medical family history is for their or their family’s health and (b) a final question about participation in a genetic research study about family history is not directly related to collection of medical family history in a clinical sense. There is a single reserved stance question (“Family health history does not have the power to predict my personal health outcomes”) with inverted scoring. The total possible Family History score is 25; the lowest possible score is 5.

Finally, a similar score was calculated in this project based on the 4-item BRIEF Health Literacy Screening Tool, a validated measure of self-reported health literacy

associated with reading and understanding of medical materials, both written and verbal (Haun, Luther, Dodd, & Donaldson, 2012). Higher scores indicate greater self-perceived health literacy and lower scores indicate reduced self-perceived health literacy. The tool is comprised of three questions that have Likert scale responses, “Always” (1), “Often” (2), “Sometimes” (3), “Occasionally” (4), and “Never” (5). A fourth question changes responses slightly to “Not at All” (1), “A Little Bit” (2), “Somewhat” (3), “Quite a Bit” (4), and “Extremely” (5). Point values are indicated in parentheses. The maximum score possible is a 20; the minimum score is 4. Please refer to Table 3 for more details.

3.3 Results

3.3.1 Demographic Information

After pruning of incomplete survey responses and ineligible participants who lived outside of the United States and USAPI territories, the total sample size was 65 participants. A summary of demographic information is available in Table 2 below. The sample overwhelmingly identified as female (75.4%); for clarification, “Unknown” responses include occasions where individuals responded to the free text box provided with a response unrelated to their gender, including entry of geographical locations. There was an overrepresentation of Samoan participants in the sample, who represented approximately 55.4% of the sample (N = 36). Geographical location of residence among participants also reflected this trend as those from American Samoa represent 48% of the total sample size (N = 35).

Table 2. Demographics

N = 65	*N* (%)
Gender	
Female	49 (75.4)
Male	11 (16.9)
Trans Female	1 (1.5)
Non-Binary	1 (1.5)
Unknown	3 (4.6)
Pacific Islander Identity	
Carolinian	4 (4.9)
Chamorro	8 (9.8)
Fijian	2 (2.4)
Guamanian	2 (2.4)
Hawaiian	7 (8.5)
Marshallese	3 (3.7)
Palauan	5 (6.1)
Papua New Guinian	1 (1.2)
Samoan	36 (55.4)
Tokelauan	2 (2.4)
Tongan	4 (4.9)
Current Residence	
American Samoa	35 (48.0)
Commonwealth of Northern Mariana Island	6 (8.2)
Guam	5 (6.9)
Hawai‘i	4 (5.5)
Mainland USA	6 (8.2)
Palau	3 (4.1)
Republic of the Marshall Islands	6 (8.2)
Age	
18-29	15 (23.1)
30-39	21 (32.3)
40-49	17 (26.2)
50-59	6 (9.2)
60+	6 (9.2)
Education	
No formal education	1 (1.5)
Less than primary school	1 (1.5)
Primary school	2 (3.1)
Secondary school	16 (24.6)
College/University	35 (53.9)

Postgraduate degree	10 (15.4)
Annual Household Income	
$20,000 or less	23 (35.4)
$20,001-$40,000	15 (23.1)
$40,001-$60,000	11 (16.9)
$60,001+	16 (24.6)
Marital Status	
Never married	21 (32.3)
Married	30 (46.2)
Separated	1 (1.5)
Divorced	5 (7.7)
Widowed	4 (6.2)
Cohabitating	4 (6.2)
Children	
Yes	41 (63.1)
No	24 (36.9)

The majority of participants were between the ages of 30 and 49 (together representing 58.5% of the sample), married (46.2%) and had children (63.1%). Approximately 69.3% of survey participants attained a college degree or postgraduate education, though there is some spread in annual household income; the majority earned less than $20,000 annually (35.4%).

There was also a wide range of job sectors represented in the sample. Participants were allowed to fill in an open response for their job position; these have been broadly categorized by the student researcher according to job sector represented. Most participants identified as supervisors or managers, though many of those indicating so did not necessarily specify their own fields of expertise. These job positions have been categorized as “Business/Management” below (Figure 2). Jobs categorized as “Miscellaneous” include those with job titles too general to be categorized into any others; the only job position qualifying for this specification was “Advocate”.

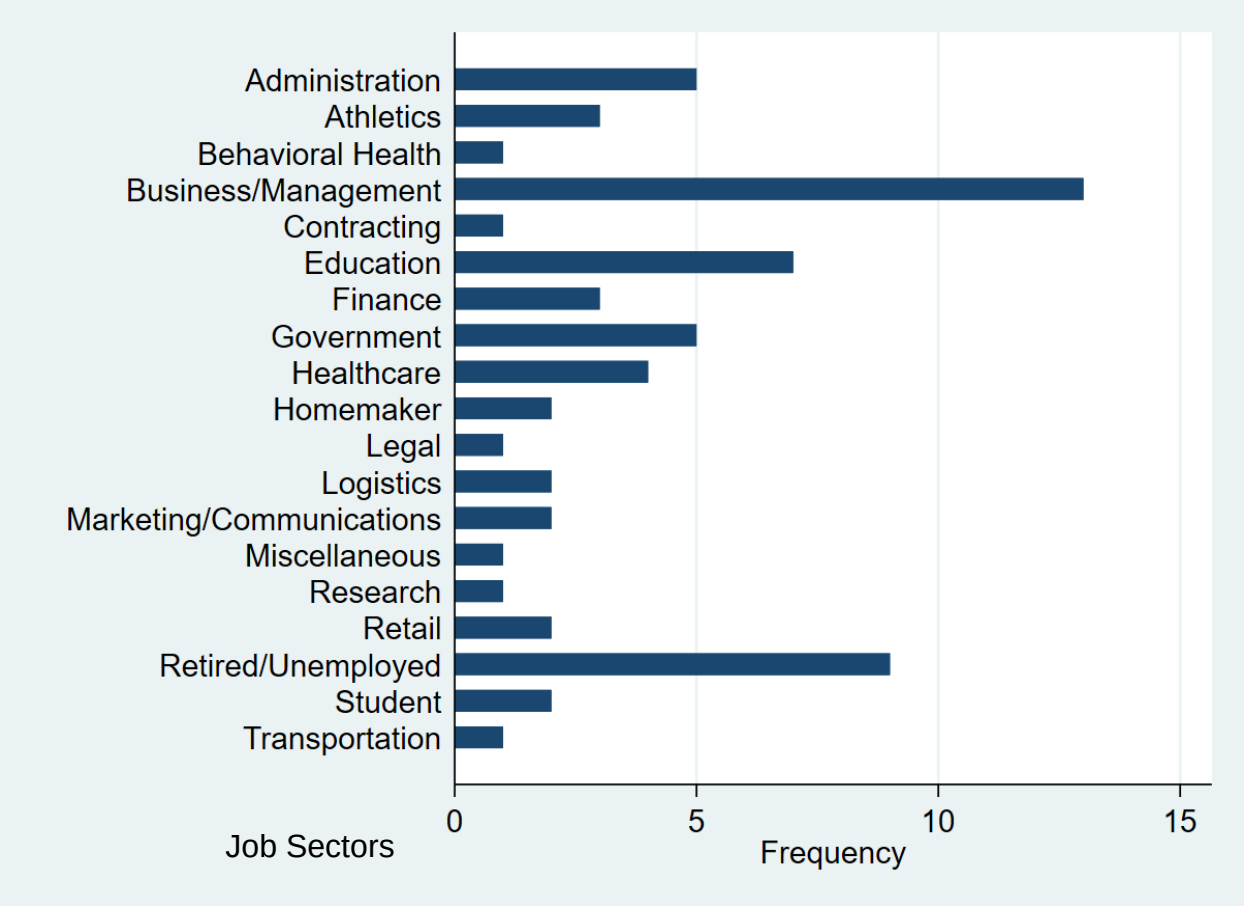

Figure 2. Job Sector Representation

3.3.2 Patterns by Section

3.3.2.1 Baseline Clinical Experiences

The goal of learning about participant clinical experiences was to determine what prior experiences individuals had with genetics to determine if there may be influences of these experiences on knowledge, comfort with clinical genetic testing, or family history. To begin, participants characterized their difficulties understanding medical information according to several different formats, including written medical instructions, verbal medical instructions, and confidence in handling these tasks alone (Table 3). The majority

endorsed feelings of confidence with reading materials (66.2%), understanding written medical instructions (60.9%), verbal medical instructions (59.4%), and filling out medical forms on their own (50.8%). However, a sizeable proportion of participants also reported some difficulties with reading and understanding medical instructions. Approximately 23.1% reported either occasionally or sometimes needing assistance reading health materials, 32.8% reported either occasionally or sometimes having difficulty understanding written medical instructions, another 34.4% reported either occasionally or sometimes having difficulty understanding verbal medical instructions, and finally 41.6% reported reduced confidence in filling out medical forms.

Table 3. Confidence in Understanding Medical Information

Need Help Reading Materials (*N* = 65)	*N* (%)
Always	2 (3.1)
Often	5 (7.7)
Sometimes	9 (13.9)
Occasionally	6 (9.2)
Never	43 (66.2)
Difficulty Understanding Written Instructions (*N* = 64)	
Always	2 (3.1)
Often	2 (3.1)
Sometimes	11 (17.2)
Occasionally	10 (15.6)
Never	39 (60.9)
Difficulty Understanding Verbal Instructions (*N* = 64)	
Always	1 (1.6)
Often	3 (4.7)
Sometimes	11 (17.2)
Occasionally	11 (17.2)
Never	38 (59.4)
Confidence Filling Out Medical Forms by Self (*N* = 65)	
Not at all	3 (4.6)
A little bit	2 (3.1)
Somewhat	9 (13.9)

Quite a bit	18 (27.7)
Extremely	33 (50.8)

Notably, participants have had very few exposures to genetics with respect to both clinical and research experiences (Table 4). Approximately 89.2% of respondents cited never having had genetic testing, with the remaining who had genetic testing split between testing directly from their healthcare provider (4.6%) and direct-to-consumer (DTC) testing only (6.2%). Though genetic testing was administered to a select few, only one person in the sample ever received genetic counseling. Likewise, only one person, a different participant, had previously participated in genetic research.

Table 4. Prior Experiences with Genetics

	N (%)
Genetic Testing (*N* = 65)	
Yes, healthcare provider	3 (4.6)
Yes, DTC Only	4 (6.2)
No	58 (89.2)
Genetic Counseling (*N* = 64)	
Yes	1 (1.6)
No	63 (98.4)
Research Study (*N* = 65)	
Yes	1 (1.5)
No	64 (98.5)

3.3.2.2 Knowledge Score

General knowledge scores were attained for each participant based on the number of correct responses out of 18 true/false questions; a summary of each question and the sample percentage correct can be found in Table 5. The average score was approximately 14 correct answers out of 18 (77.7%), with a standard deviation of 2.02. The

median score was also 14. The lowest score was 9 out of 18 answered correctly while the highest score was 18. This includes participants who answered more than 14 questions but less than 18; in this case, non-responses were treated as incorrect answers. For 10 of the 18 questions in this section, 80% or more of participants answered correctly. Questions that were particularly challenging: whether or not identical twins have different sets of genes (with 36.9% indicating that this is correctly false) and whether parents pass both sets of chromosomes onto their children (with 27.7% answered correctly false).

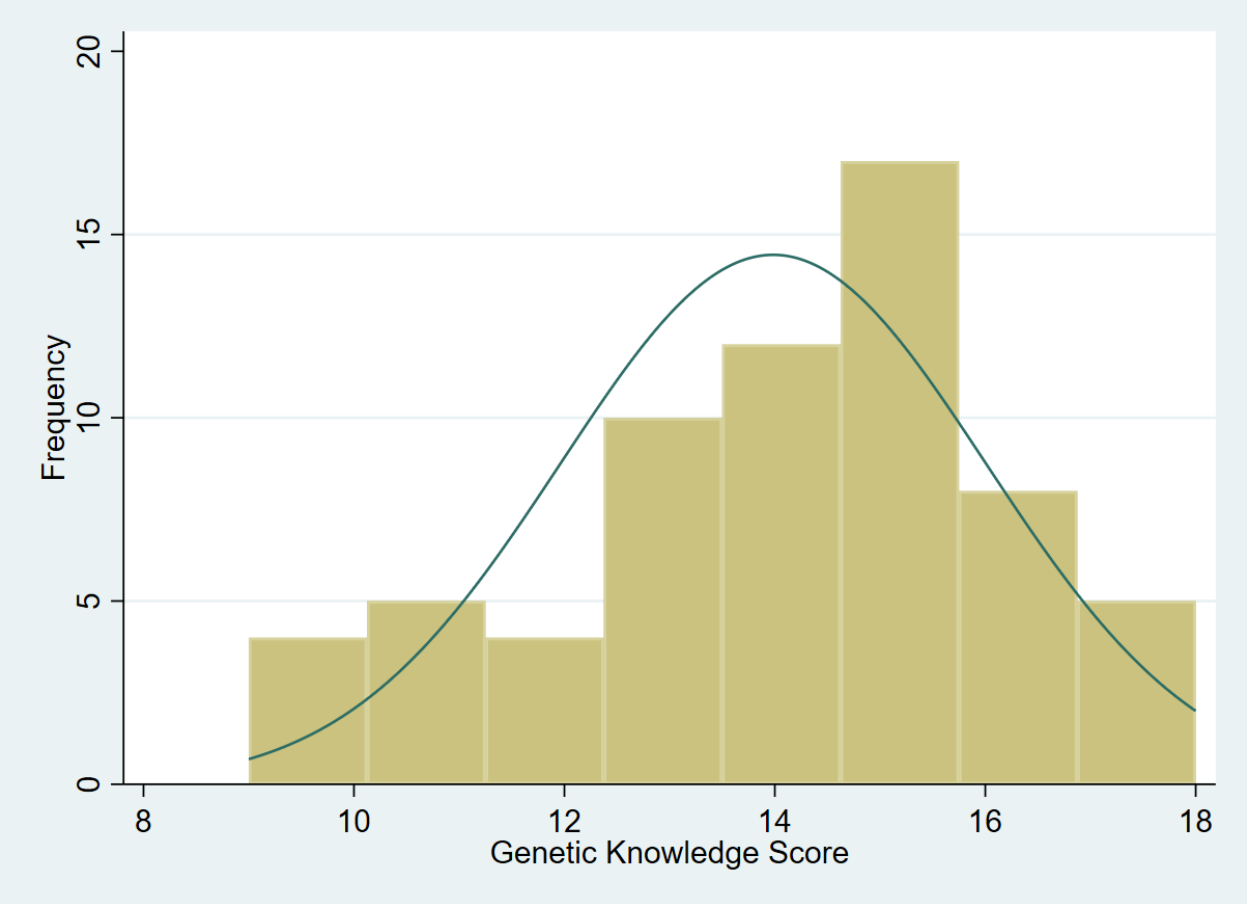

Figure 3. Histogram of Genetic Knowledge Scores

Table 5. Genetics Knowledge Response Percentages

N = 73	Question Type*	Percentage Correct
Some diseases are caused by genes, environment, and lifestyle. (T)	Applied	100.0%
A gene is a disease. (F)	Applied	90.8%
You can see a gene with the naked eye. (F)	Applied	86.1%
Healthy parents can have a child with an inherited disease. (T)	Applied	96.9%
A person with an altered (mutated) gene may be completely healthy. (T)	Applied	64.6%
All serious diseases are inherited. (F)	Applied	90.8%
Genes are instructions for making proteins, which help the body grow and work properly. (T)	Basic	60.0%
The child of a person with an inherited disease will always have the same disease. (F)	Applied	84.6%
A gene is a piece of DNA. (T)	Basic	93.8%
Altered (mutated) genes can cause disease. (T)	N/A	76.9%
Genes are inside of cells. (T)	Basic	89.2%
A chromosome contains many genes. (T)	Basic	86.2%
Genes determine traits such as height, eye color, and facial appearance. (T)	Applied	90.8%
A person has thousands of genes. (T)	Basic	69.2%
Identical twins have different sets of genes. (F)	Applied	36.9%
Humans have 20 pairs of chromosomes. (F)	Basic	64.6%
Parents pass both copies of each chromosome to their child. (F)	Basic	27.7%

A genetic test can tell you if you have a higher chance to develop a specific disease. (T)	Applied	89.2%
		Avg Score: 77.7%

*Based on factor loadings from Fitzgerald-Butt et al. (2016) where "basic" refers to items "that are facts about genetics, such as number of genes and chromosomes..." and "applied" refers to items "pertaining to the relationship of genes and genetic testing with health and disease".

3.3.2.3 Attitudes Towards Clinical Testing

Out of a total score of 65, the average Clinical Attitudes score was 50.38 with a standard deviation of 8.82. The median score was 52. The lowest score was 29 and the highest score was 65. These values represent generally positive attitudes about clinical uses of genetic testing. It is a measure of participant interest in learning about genetic testing and likelihood that they might be willing to sharing results with family members.

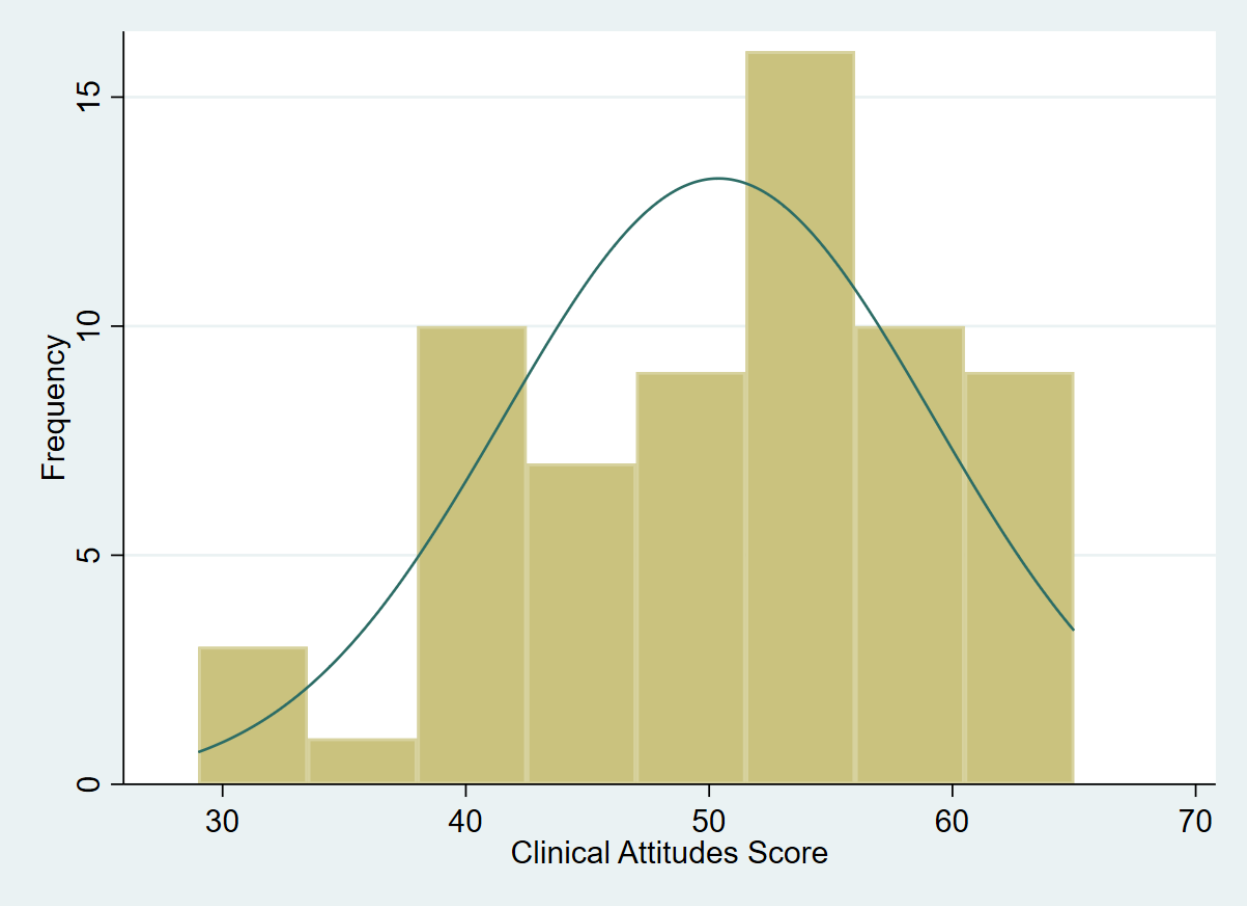

Figure 4. Histogram of Clinical Attitudes Scores

Full response information regarding attitudes towards clinical testing are recorded in Table 6 below. Questions are divided by favorable and reserved attitudes. Generally, participants were supportive of favorable statements, particularly those statements favoring the use of genetic testing for clinical health purposes. For example, a vast majority (84.6%) agreed either somewhat or strongly to the use of genetic testing for early detection of disease, and most would share the results of genetic testing with their children (87.7%) and their siblings (86.2%). For every statement indicative of a favorable response, approximately three-quarters of participants agreed to some degree.

Responses for reserved views are more mixed across the sample. A quarter of participants (23.4%) agreed to some extent that they would *not* want a genetic test for a disease that could not be treated, and a further 28.1% neither agreed nor disagreed. Only about half of the sample (50.8%) believed that their families should be informed about the results of their genetic testing to some extent. About 46.2% and 37.5% worried about how genetic testing could negatively impact their health insurance and employment respectively. Finally, three-quarters of the sample (76.9%) believed that the possibility of a genetic test could change one's future.

Table 6. Attitudes Towards Genetic Testing by Question

	N	Strongly Disagree (%)	Somewhat Disagree (%)	Neither Agree/Disagree (%)	Somewhat Agree (%)	Strongly Agree (%)
Favorable						
I approve of using genetic testing for early detection of diseases	65	6.2	3.1	6.2	29.2	55.4
I would inform my children about the results of my genetic test for a specific disease	65	---	4.6	7.7	21.5	66.2
I would be interested in genetic testing that can give me a medical diagnosis	65	1.5	9.2	7.7	23.1	58.5
I want to know whether my disease is hereditary (passed on from parents to children)	64	3.1	1.6	6.3	17.2	71.9
I would inform my siblings about the results of a genetic test for a specific disease	65	4.6	1.5	7.7	18.5	67.7
I would be interested in a genetic test to help me decide if a treatment is helpful for me	64	9.4	1.6	10.9	10.9	67.2
I would be interested in genetic testing that would give me information that I could use to lower my risk of developing a disease	64	3.1	3.1	9.4	15.6	68.8
Reserved						
The possibility of a genetic test will change one's future*	65	1.5	3.1	18.5	27.7	49.2

If a disease cannot be treated, I don't want a genetic test	64	40.6	7.8	28.1	10.9	12.5
I don't want a genetic test to tell me that I am at risk for a certain disease	64	40.6	7.8	31.3	12.5	7.8
I worry about the consequences of genetic testing for being able to get health insurance	65	21.5	4.6	27.7	18.5	27.7
I worry about the consequences of genetic testing for the chances of finding a job	64	34.4	6.3	21.9	15.6	21.9
If I had a genetic test done, my family does not need to know about the result	63	36.5	14.3	17.5	11.1	20.6
The idea of a genetic test frightens me	65	26.2	10.8	35.4	16.9	10.8

* Not included in composite Clinical Attitudes Score

3.3.2.4 Attitudes Towards Family History

Out of a total score of 25, the average Clinical Attitudes score was 18.91 with a standard deviation of 2.14. The median score was 19. The lowest score was 13 and the highest score was 21. These values are intended to represent how important participants feel medical family histories are for personal and family health. Given the mean score, it appears that participants place some importance on medical family histories though few had previous experiences with collecting family history (27.7%, Table 8). Noteworthy is that, despite overall positive attitudes, almost half agreed to some extent that family health history did *not* have the power to predict power health outcomes (question 3 in Table 7).

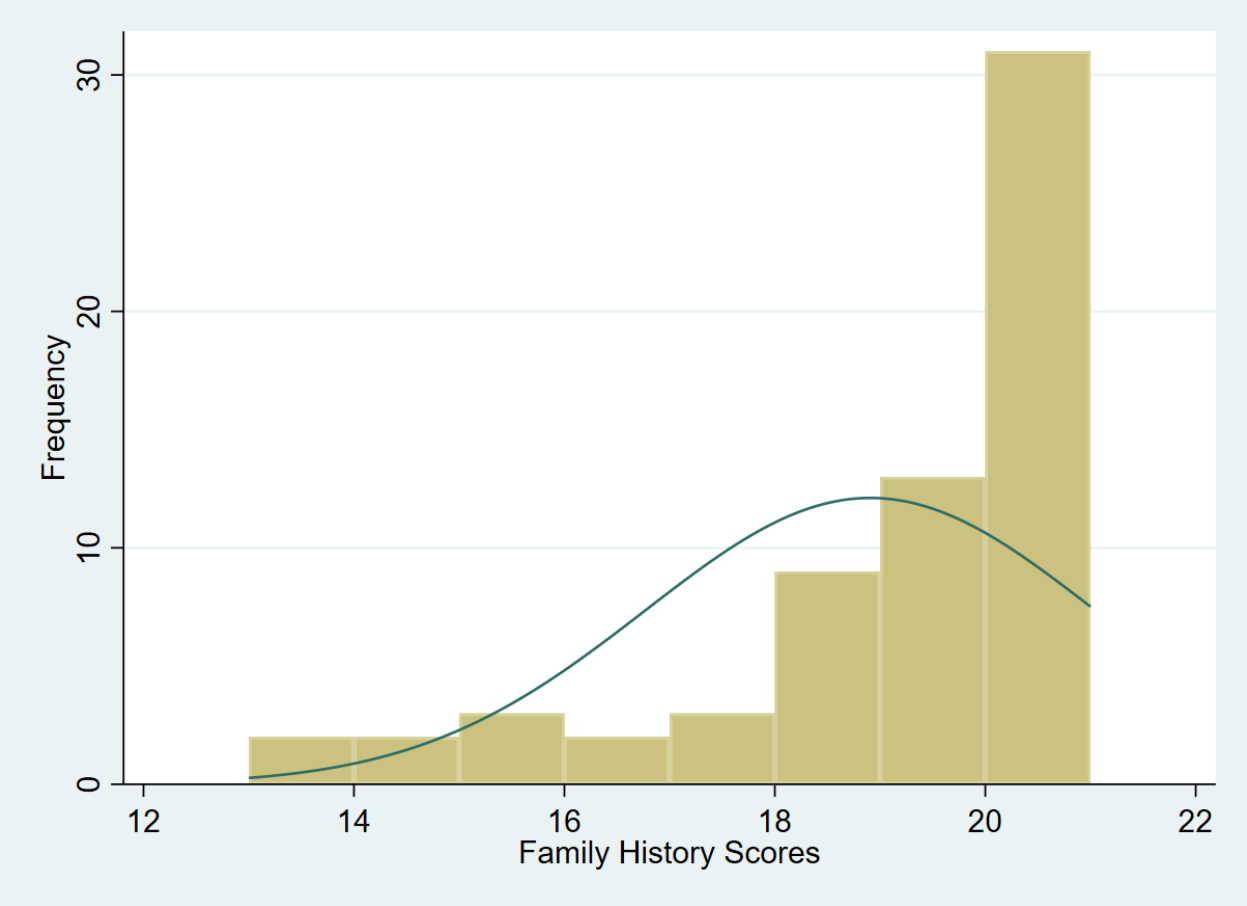

Figure 5. Histogram of Family History Scores

Table 7. Attitudes Towards Family History

	N	Strongly Disagree (%)	Somewhat Disagree (%)	Neither Agree/Disagree (%)	Somewhat Agree (%)	Strongly Agree (%)
My doctor should be required to collect family health information in clinical practice	64	4.7	3.1	23.4	26.6	42.2
I can easily recall the health history of most of my relatives*	65	12.3	18.5	18.5	23.1	27.7
Family health history does not have the power to predict my personal health outcomes**	64	17.2	15.6	18.8	26.6	21.9
Family health history collection can help me reduce risks for heritable diseases (diseases that run in my family)	65	1.6	3.1	9.2	30.8	55.4
Collecting family health history is helpful for understanding my own disease risk	65	---	3.1	6.2	15.4	75.4
Collecting family health history is helpful for understanding my family's disease risk	64	---	3.1	4.7	17.2	75.0

*Not included in Family History Score
**Only inverted statement

Table 8. Experience Collecting Medical Family History

	N	Yes (%)	No (%)
Have you ever actively collected health information from your relatives for the purposes of developing a family health history?	65	27.7	72.3

Similar to the views on medical family history, the majority of participants also expressed interest in participation of genetic studies focused on family health histories (Table 9) with 38.5% being “Very Likely” to participate and 40% “Likely” to participate in this kind of research.

Table 9. Interest in Family History Research Study

	N	Very Unlikely (%)	Unlikely (%)	Unsure (%)	Likely (%)	Very Likely (%)
If you were approached by researchers and asked to take part in a study that involved giving family health history for genetic research, how likely would you be to participate?	65	1.5	7.7	12.3	40.0	38.5

3.3.2.5 Attitudes Towards Return of Results

The goal of this section was to determine how strongly participants felt about receiving both genetic testing results and secondary results for which there are clear guidelines for treatment and management (e.g., hereditary breast and ovarian cancer) versus those that are non-treatable (e.g., degenerative diseases, such as Alzheimer's disease or Huntington Disease). Interestingly, most participants were in favor of receiving genetic testing results from health-related research, regardless of whether they could do something about them (68.3%). An additional quarter was in favor of receiving genetic testing results that they could do something about (27%). Participants then selected, among three individuals that might share their genetic testing results with them, who they would prefer to do so. While the sample generally felt a generous level of comfort with all three, the greatest proportion (72.3%) endorsed being contacted by a genetics specialist.

Table 10. Preferences for Return of Results

If you decided to participate in genetic testing for health-related research purposes, would you want your results returned to you? (*N* = 63)	Response (%)

Yes, I would want to receive any results related to my health (even if the result would tell me about a health risk that I could not do anything about)	43 (68.3)
Yes, I would want to receive results that I could do something about	17 (27.0)
No, I would not want to receive any results	3 (4.8)
If you participated in health research, who should be able to contact you and tell you your genetic results? (*N* = 65*; check all that apply*)	
Member of Research Team (%)	34 (52.3)
Genetics Specialist (%)	47 (72.3)
My Doctor (%)	37 (56.9)

Finally, participants demonstrated interest in receiving secondary findings, more so than genetic testing results gathered from health-related research. For example, compared to the 68.3% who indicated in Table 10 that they would want to receive any result, including those they could not do something about, 76.9% indicated that they would still like to hear about secondary results for an illness that is untreatable (Table 11).

Table 11. Preferences for Secondary Findings Information by Type

Would you like to hear about secondary findings concerning your health, if they were for an illness that is… (*N* = 65)	Yes (%)	No (%)	Unsure (%)
Treatable?	83.1	9.2	7.7
Untreatable?	76.9	9.2	13.9
Hereditary?*	84.6	10.8	4.6

*"...a disease you do not have, but that you could pass on to your children."

3.3.3 Data Analysis

The bolded Pearson values in Table 12 highlight those variables for which there was a statistically significant correlation between the two at the $\alpha = 0.05$. There was a statistically significant positive correlation between annual income and both Genetic Knowledge Scores ($r = 0.2707$, $p = 0.029$) and Clinical Attitudes Scores ($r = 0.3792$, $p = 0.002$): as annual income rose, so too did the number of correct answers on the Genetic Knowledge portion of the survey, as well as positive attitudes towards clinical testing. However, *r* values are moderate, suggestive of a weak correlation. In addition, there was a statistically significant positive correlation between Clinical Attitudes Scores and Family History Scores ($r = 0.4071$, $p = 0.001$). Those who expressed favorable views towards the prospects of genetic testing also tended to recognize medical family history as meaningful for one's personal health. Finally, there was a significant positive correlation between health literacy comfort and knowledge score ($r = 0.3082$, $p = 0.013$). For those variables that were significantly correlated, a scatterplot and linear regression analysis was performed; these can be observed in Figures 6, 7, 8, and 9 below.

Table 12. Correlation Matrix for Quantitative Variables of Interest

		Age	Annual In-come	Health Literacy	Knowledge Score	CA Score	FH Score
Age	Pearson Correlation	1.000	0.0918	−0.0476	−0.0909	−0.0943	0.1723
	Sig. (2-tailed)	---	0.467	0.707	0.472	0.455	0.170
	N	65	65	65	65	65	65
Annual Income	Pearson Correlation	0.0918	1.000	0.1678	**0.2707***	**0.3792****	0.1622
	Sig. (2-tailed)	0.467	---	0.181	0.029	0.002	0.197
	N	65	65	65	65	65	65
Health Literacy	Pearson Correlation	−0.0476	0.1678	1.000	**0.3082***	0.1213	0.0983
	Sig. (2-tailed)	0.707	0.181	---	0.013	0.336	0.436
	N	65	65	65	65	65	65
Knowledge Score	Pearson Correlation	−0.0909	**0.2707***	**0.3082***	1.000	0.1249	0.0358
	Sig. (2-tailed)	0.472	0.029	0.013	---	0.322	0.777
	N	65	65	65	65	65	65
CA Score	Pearson Correlation	−0.0943	**0.3792****	0.1213	0.1249	1.000	**0.4071****
	Sig. (2-tailed)	0.455	0.002	0.336	0.322	---	0.001
	N	65	65	65	65	65	65
FH Score	Pearson Correlation	0.1723	0.1622	0.0983	0.0358	**0.4071****	1.000
	Sig. (2-tailed)	0.170	0.197	0.436	0.777	0.001	---
	N	65	65	65	65	65	65

*Correlation statistically significant at $p < 0.05$
**Correlation statistically significant at $p < 0.01$
CA = Clinical Attitudes
FH = Family History

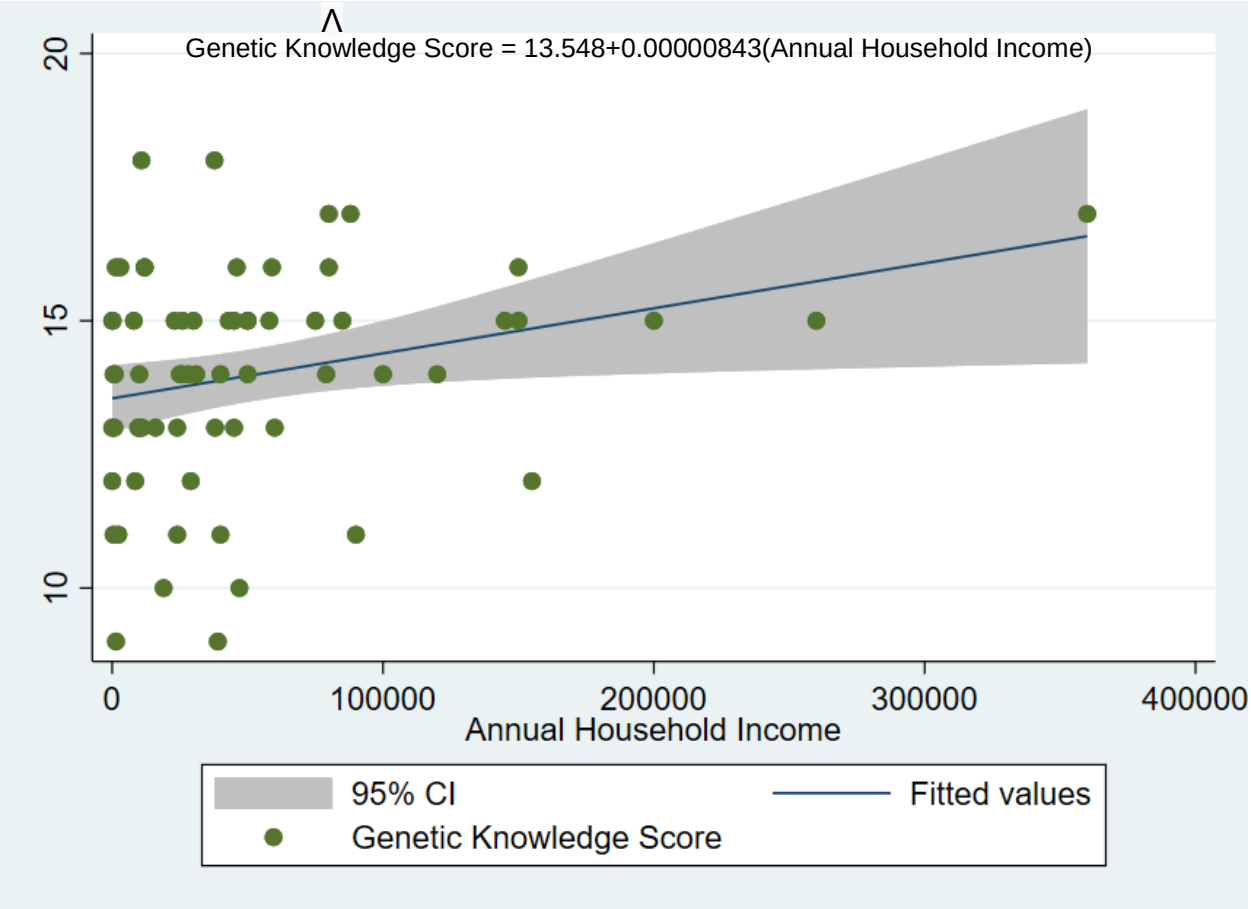

Figure 6. Scatterplot of Annual Household Income x Genetic Knowledge Scores

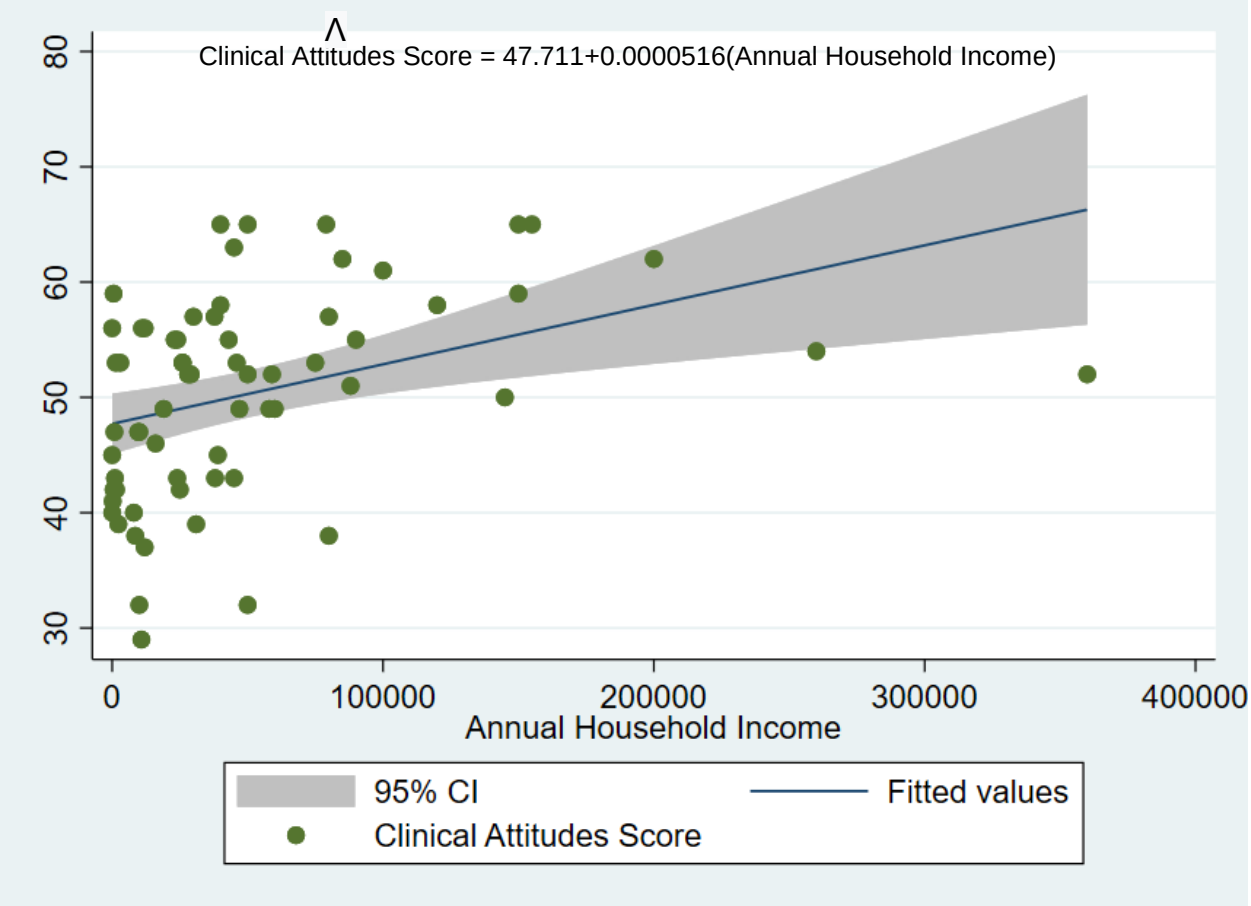

Figure 7. Scatterplot of Annual Household Income x Clinical Attitudes Scores

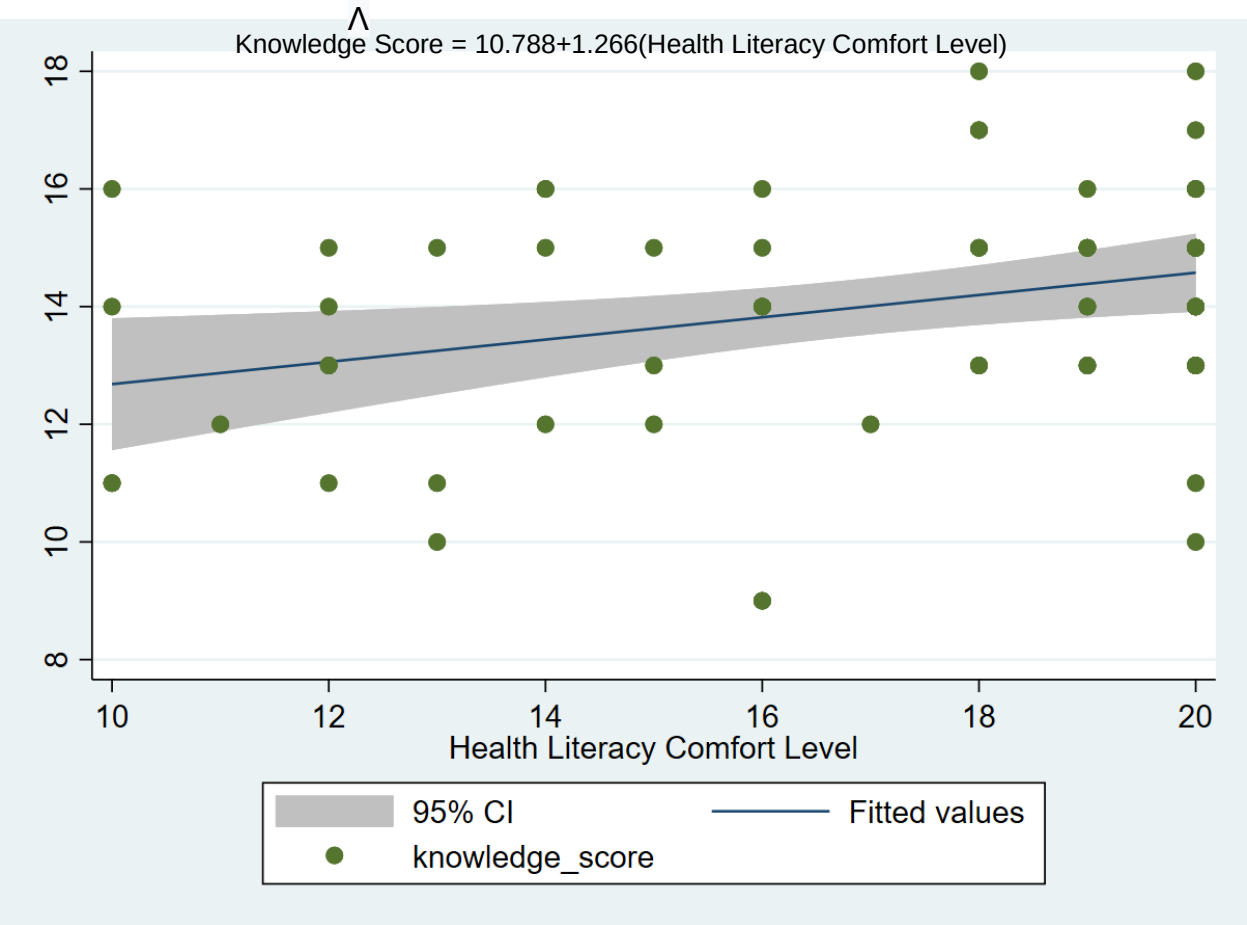

Figure 8. Scatterplot of Health Literacy Comfort Levels x Clinical Attitudes Scores

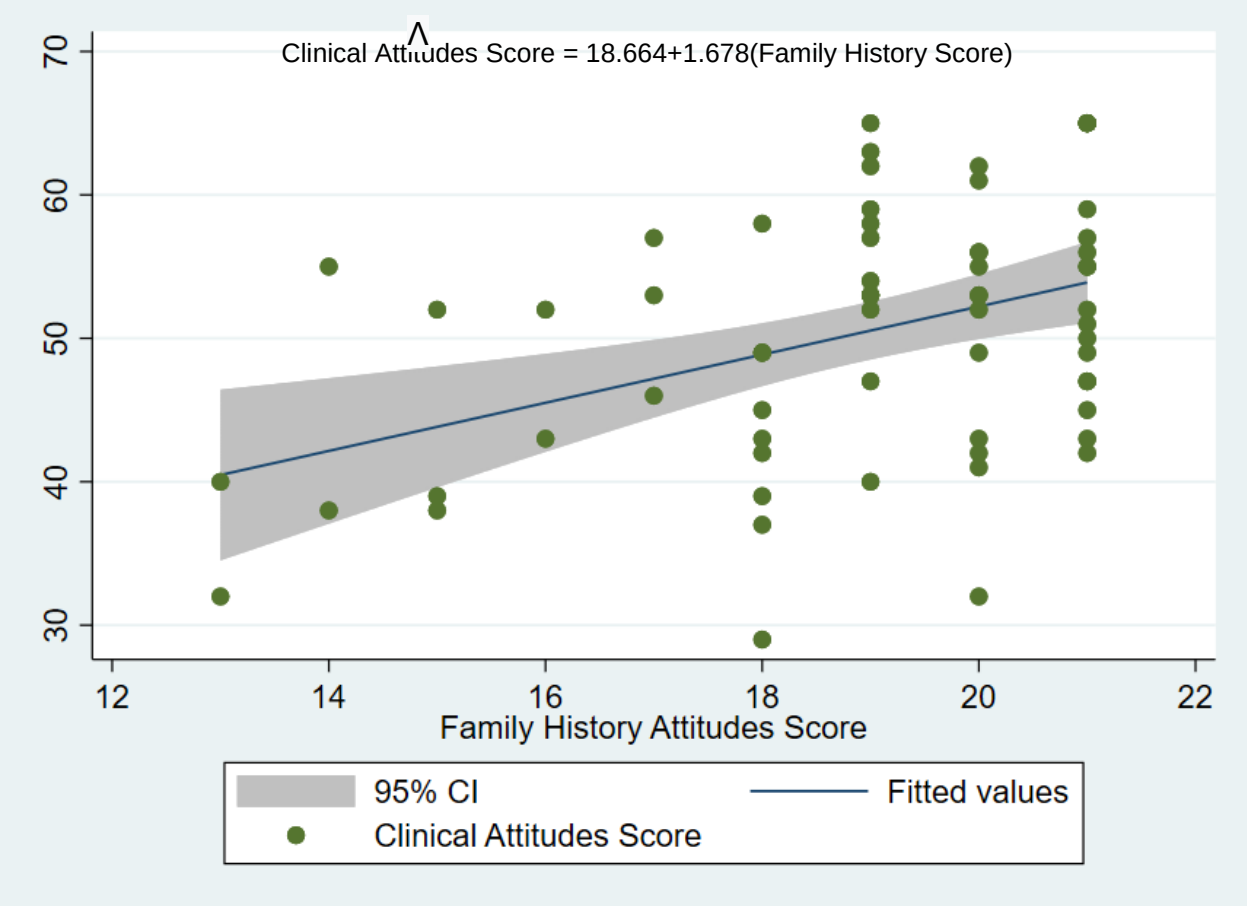

Figure 9. Scatterplot of Family History Scores x Clinical Attitudes Scores

3.4 Discussion

To the student researcher's knowledge, this project is the first survey of its kind to learn about the personal attitudes and perspectives of Pacific Islanders about genetic testing, and so adds to the current gap in literature around Pacific Islander attitudes and knowledge regarding genetic services and issues. Based on the information gathered from the clinical-based survey questions, participants seemed to have favorable views towards clinical genetic testing, valued the use of medical family histories and understood

the implications of this information for their own health, and expressed interest in testing even in the context of genetic conditions for which there is no present treatment.

The number of complex issues to consider as part of ELSI research is summarized in a 2021 paper by Ascencio-Carbajal, Saruwatari-Zavala, Navarro-Garcia, and Frixione (2021). Sub-criteria for social issues as they pertain to genetic research includes “access to services under the principle of justice” and “education and dissemination”. Though there is still much more to learn, the perspectives shared from our Pacific Islander communities in this survey is a critical piece of ELSI research because it (a) establishes whether participants may find clinical genetic services useful for their health and (b) identifies current genetic knowledge and attitudes levels, presenting opportunities to address questions and create educational materials of both current and future participants.

3.4.1 Demographics

With respect to demographics, there are several interesting characteristics of the sample, namely (a) a skew towards female participants, with over three-quarters represented, and (b) a majority of American Samoan representation, with almost half of participants identifying as such. While the latter point is likely a consequence of dissemination methods and use among communities that research group contacts were more familiar with, the gender skew is an unexpected result. However, this skew is reflected in similar measures of attitudes towards genetic testing, particularly among studies with smaller sample sizes. These studies, often with less than 500 participants, saw female representation closer to 70% (Goodman, Johnson, Bowen, Wenzel, & Edwards, 2019; Haga et al.,

2013; Saastamoinen et al., 2020). While studies acknowledge some differences by gender, very few examine the reasons for these disparate proportions.

While this paper is not an intimate study of health literacy among participants, and most participants demonstrated relatively high levels of comfort with medical information, it is interesting that a sizeable amount reported “Occasionally” or “Sometimes” having difficulty understanding verbal (34.4%) and written (32.8%) medical instructions. This is not entirely surprising given the complex relationships between health literacy, medical communication, and health outcomes. When it comes to health literacy, the focus is often placed on the patient; however, it is important to consider how institutions can better adjust their communication styles, including vocabulary usage, speech pacing, and teach-back methods, to better clarify complex medical instructions. For example, there are many methods institutions may be able to take to better tailor services to patients, including assessments of baseline patient literacy, use of multi-format materials, structured letters, and methods to solicit feedback from patients (Ratna, 2019; Vermeir et al., 2015).

Very few participants in this study report experiences with genetic testing (10.8%), genetic counseling (1.6%), and genetic research studies (1.5%). This pattern may be attributed, at least in part, to the fact that there are limited genetic services available in the USAPI territories and nations, with a vast majority of respondents living in USAPI. There is little literature outlining the state of genetics in Pacific Island territories. As it pertains to genetic counseling, for example, a paper by Abacan et al. (2019) suggests that, globally, there are very few trained GCs working outside of the Americas and Europe based on 2017 data, but it is unclear how USAPI territories and nations fit into this picture. This lack of data is likely due to gaps in the genetic research that hinder usage of invalid clinical

data received from non–Pacific Islander groups. Current research is perhaps more focused on foundational biological studies to first characterize the genetic architecture of some of these communities (Friedlaender et al., 2008)

3.4.2 Genetic Knowledge Scores

With respect to Genetic Knowledge Scores, this sample did exceptionally well, with an average score of 14.0 correct out of 18. However, it is important to note that this sample may not be representative of the typical education level reflected in the general USAPI population. Though many in the literature have learned about attitudes and perceptions of genetic testing in different communities, there is great heterogeneity among how exactly each research team came to this conclusion. Since the Genetic Knowledge survey was based on a design by Fitzgerald-Butt et al. (2016), comparisons can truly only be made with that sample. While the average score for that sample was 12.6 out of 18, it is important to note it included both adults and young adult/adolescents (ages 15-25). It was also conducted among individuals with congenital heart disease at a US clinic, along with their parents, with a total sample size of 661 between the studies two IRB protocols. Therefore, it is difficult to draw conclusions from the direct comparison between the two groups.

Patterns of question accuracy are similar to patterns observed in this paper. For example, the sample in the Fitzgerald-Butt et al. (2016) survey, the questions “Identical twins have different sets of genes” and “Parents pass both copies of each chromosome to their child” average percentages of 41% and 28.7%, which isn’t too far off from the percentage correct in this sample (36.9% and 27.7%). Interestingly, 64.6% of participants

correctly answered that humans do not have 20 chromosomes compared to the sample in Fitzgerald-Butt et al. (2016), who answered this question correctly, on average, only 26.7% of the time.

3.4.3 Attitudes Towards Clinical Testing

A majority of the sample endorsed favorable attitudes towards (a) clinical genetic testing, (b) uses of medical family history for clinical purposes and (c) return of results from both genetic research studies and secondary findings regardless of context. For example, regarding favorable responses, over 75% participants agreed, to some degree with the use of genetic testing for clinical reasons and would share their own testing results with their children or siblings. However, this is not to say that participants would accept genetic testing whole-heartedly: the same majority proportion seen towards favorable attitudes is not reflected in reserved responses. In this section, there was a high rate of uncertainty, with most responding that they neither agreed nor disagreed. A quarter of participants (26.1%) disagreed with worry about how genetic testing might impact one's health insurance, and only 37% disagreed that a genetic test frightens them.

The highest proportion of participants agreed with the reserved statement, "The possibility of a genetic testing could change one's future" at 76.9% of the sample. However, though Haga et al. (2013) categorized this as a "reserved" statement, there is there is some ambiguity around its phrasing. It can be argued that "possibilities" typically has a more positive connotation, at least in daily speech. It is unclear what proportion of participants thought this was a positive possibility, such as possibilities for treatment and

lifestyle changes) and what proportion viewed these possibilities as negative (such as negatively impacting familial relationships, health insurance, or job prospects).

On reflection of the two categories of clinical attitudes, it is important to note that statements classified as “reserved” were also more likely to elicit more uncertainty, as a greater proportion of the sample responded “Neither Agree nor Disagree” in this section. Words used in the section, such as “possibility”, “worry”, “idea” may have been more closely associated with lack of a straight-forward answer compared to some of the words reflected in favorable attitudes which are, overall, more active (e.g., “I approve…”, “I want…”, “I would be interested…”). Rather than reserved, perhaps these questions could be more accurately categorized as “uncertain” attitudes.

3.4.4 Attitudes Towards Family History

Sample attitudes towards family history taking were mostly positive. Over 92% of participants agreed to some degree with the statement that “Collecting family health history is helpful for understanding my family’s disease risk.” And 68.8% believed, to some degree, that their doctors should be required to collect family health information. The majority of participants also expressed interest in genetic research that required them to submit a medical family history. Most questions demonstrated similar trends in positive perception towards family history. However, there were two statements that introduced some challenges towards the interpretation of results.

The first was a statement about how easy individuals found it to recall the health history of their own relatives. This was not included in analysis because it does not fairly represent participant assessment one way or another. While a person who can recall their

family health history may find such information important (and hence why they may have committed it to memory), an inability to do so does not necessarily indicate that this information is important. There may be other more complex reasons for individuals being unable to recall family health history. Individuals may not learn about it in the first place due to family systems where individuals avoid spontaneously disclosures of their health information, and situations where family or having other things to worry about.

The second statement of concern asked of participants whether they agreed with the statement “Family health history does *not* have the power to predict my personal health outcomes”. A surprising 48.5% of participants agreed, to some degree, with this statement. However, in the same sample, 90.8% agreed, to some extent, that collecting family health history would be helpful for understanding their own disease risk. One interpretation is that, because this is the only negatively-phrased statement in a series of positively-phrased statements, some participants selected statements of agreement because they read that “Family health history *does* have the power to predict my personal health outcomes” or were otherwise moving quickly through a series of positively-framed statements. Alternatively, the difference between this question and others may be associated with how participants interpreted the meaning of the statement and feelings of agency over their own personal health outcomes. Regardless of the explanation, this question was included in final analyses, though it may have contributed largely insignificant analyses that included Family History Scores.

3.4.5 Return of Results

Finally, we asked participants how they felt about the types of results that they could receive from genetic testing, categorized into two broad categories: results that were explicitly as part of health-related genetic research and secondary finding results in any context. Here, there may be an important distinction to be made between “actionable” vs. “non-actionable” and “treatable” vs. “non-treatable”. Affirmative responses for the first question were divided into two possibilities: receiving all results related to health (even if the result would tell the participant about a health risk that they could not do anything about) and results that the participant would accept only if they could do something about. In this case, the latter response endorses receiving *actionable* findings (i.e., “that I could *do something about*). In contrast, secondary findings about a disease that is treatable may not necessarily be actionable (if, for example, it is unaffordable for a patient).

Sixty-eight percent of the sample expressed interest in receiving both actionable and non-actionable results from health-related genetic research, while 27% were only interested in results that they could do something about. This trend continued on the topic of secondary findings, without context: while 83.1% were in favor of receiving secondary results for treatable illness, 76.9% were in favor of receiving secondary findings for even untreatable illnesses. On the topic of who should be disclosing results, most agreed (72.3%) that this should be a job for a genetic specialist. In the context of this question, this may refer to a Medical Geneticist, Genetic Counselor, or someone with special training in the interpretation of genetic testing results.

3.4.6 Analysis Reflection

The primary analysis method for the current data was the use of correlation studies to determine if there were relationships between demographic information, such as age or annual income, and any of the calculated scoring systems (Genetic Knowledge, Clinical Attitudes Scores, and Family History Scores). While it would have been informative to learn about the relationship between attitudes and categorical demographic variables, such as ethnic identity, there was not a large enough proportion amongst the many categorical variables to conduct these kinds of analyses. Most statistical analyses outside of the current research were vastly insignificant from a statistical point-of-view and were not included in this study.

Previous studies have suggested that higher knowledge scores do not necessarily correlate with more positive attitudes (Haga et al., 2013; Jallinoja & Aro, 1999, 2000), which is also the case of the current study. However, there were some statistically significant trends with annual household income and other variables. Those with higher income levels tended to have more favorable attitudes towards genetic testing; this is in line with at least one previous study that measured attitudes towards genetic testing among African American women (Wright, Newhall, Barcelona, & Taylor, 2020). There was also a positive correlation between annual income and knowledge scores. This may be related to the fact that the sample is highly educated, and this correlation may be a reflection of that. However, most of these trends are weak, likely as a result of the small sample size.

3.4.7 Limitations

The current study has a number of important limitations. First, the survey was administered online only. As a result, the integrity of data collection is not as stable as other methods. For example, there is no way to ensure that any one participant has not completed the survey twice. The sample size is also very small and lacks representativeness. Given that most participants identify as Samoan (specifically those currently residing in American Samoa), the sample lacks a diverse set of Pacific Islander views. The sample was greatly overrepresented by both female-identifying participants and highly educated participants. This may have influenced observed patterns in other parts of the survey. The different job sectors among the sample also demonstrates apparent gaps in perspectives as there is a high proportion of participants working in office sector positions. Given the disproportionate representation of so many variables, the depth of data analysis and comparisons between groups were limited. This may have been a result of the method of survey dissemination, including which communities we were able to push the survey out to.

An additional limitation is that there were no community members directly involved in the creation of the survey or as part of the research process. Part of this is due to the preliminary nature of the survey and its administration to a heterogenous group in an online-only format. While this may have been permissible at this first stage to learn about Pacific Islander perspectives, it does create challenges for the contextualization of responses among different ethnic groups (an additional reason why these analyses are not included, other than small sample sizes among territories). Given that the goal is to use this information to create educational materials, it will certainly be important to consult

community members to contextualize these results and determine the most respectful way to proceed in a way that builds capacity among individual Pacific Islander communities.

Finally, while the primers were our method of setting the stage so that participants were clear on what concepts they were addressing, it is possible that they may have introduced response bias. For example, take the following primer for Family History questions, which can be found in Appendix B.4.3:

> *"Your family health history is a collection of health information about you and your family. Sometimes multiple family members can have similar health problems. This could be due to you and your family members:*
>
> *1.Sharing the same environment, and/or*
>
> *2.Sharing the same lifestyle (like diet), and/or*
>
> *3.Sharing the same genetic variants.*
>
> *Your family health history can help you and your doctor better understand your risk for certain health problems. The next questions ask how you feel about your family health history."*

In some ways, the above may have demonstrated some bias towards the use of medical family history as a tool to "understand…risk for certain health problems." Even though primers feature several reminders that we are looking for the ***participant's*** perspective and that there are no right or wrong answers, some primers may have influenced participants to answer the way they thought they were expected to answer based on the above, for example.

3.4.8 Future Research

While this survey allowed us to gather feedback from Pacific Islander voices for the first time, there is still much work needed to refine these results and use of this survey in other communities. There are also several responses in this survey specific to genetic research that were not discussed. It may be useful to analyze these results in a separate paper and determine if there are any relationships between participant viewpoints between clinical versus research genetic testing.

First, it is vital that we increase the sample size to bolster representation of every community and allow for more detailed analyses. Several weaknesses in data analysis were due to the small sample size. Given that the survey is still open, we are still striving towards a goal of surveying 1000 participants. Additionally, it may be helpful to consider adding a qualitative aspect to the survey that allows participants to clarify their positions. This is true for minority responses as much as for majority responses; this would allow participants to add detail about which parts of genetic testing might be frightening, for example. Adding this kind of information might be done either through the survey or by having participants consider joining a focus group with the research team. This extra step would perhaps justify a smaller sample size.

While this was an abbreviated way to learn about Pacific Islander attitudes in a broad sense, it may be more important to consider the attitudes of individual territories; to consider the consequences of anything learned in this study as being helpful to the Pacific Islander community as a whole is abstract and unwieldy. Though each is bound by an affiliation to the United States, each community is unique and managed by different sets of policies and health care oversight according to geographical and geopolitical

boundaries. Therefore, it might be useful to focus on a specific area or geographical community when considering patterns in attitudes and perceptions of genetic testing. That being said, we hope that these findings will eventually serve as useful control data for surveys among specific Pacific Islander communities. For example, some citizens of the Independent State of Samoa have historically participated in OLaGA studies and may offer differing perspectives about research and clinical genetic testing based on that exposure. Furthermore, how might these views differ from those of the general population who have not had exposure to the research team?

There are many gaps in the literature when it comes to the perspectives of non-Western communities. While this study brushed only the surface of participant comfort with health materials, there may yet be an important intersection between health literacy and education in the field of genetic health care. Future studies should consider using a reliable tool to measure both genetic and health literacy and analyze the relationship between medical literacy and education of genetic concepts. There is also potential to learn from health care providers in these regions to learn about their patient-provider interactions, which has important implications considering that in Samoa, this may differ between clinic settings and traditional medicine settings.

3.5 Conclusion

In summary, this survey of Pacific Islander communities in the United States and among USAPI demonstrates that attitudes towards clinical genetic testing are mostly favorable, and that participants recognize the potential for testing to improve clinical

outcomes of many diseases. Individuals in these communities may find genetic testing information desirable, regardless of its actionability. There may be additional need to investigate attitudes about actionability and other topics (e.g., non-paternity, consanguinity) associated with genetic testing in more detail. Participants were quite knowledgeable about genetic topics, and most expressed high levels of comfort receiving medical information, which may someday include genetic information. Participants demonstrated interest in using genetic information to manage their health, and mostly seemed to value sharing this information among their families. Regardless of the interest, however, there are clear barriers when it comes to the translation of basic research to clinical practice in non-Western communities. There is a great need to direct resources to better understand both the genetic architecture and societal attitudes towards genetics of Pacific Islander communities for the sake of health equity on a global scale.

4.0 Research Significance to Genetic Counseling and Public Health

In gathering information about how different communities, particularly those historically underrepresented in the literature, feel about genetic testing, this research holds an important place in forwarding the goals of both Public Health and Genetic Counseling. Gathering public knowledge and attitudes about genetics and genomics gives some of the biggest clues about how to proceed, even if it is not the first step in the process, because it clarifies whether the public perceives a need for, or at the very least an openness to, genetics engagement.

According to the Ten Essential Public Health Services (EPHS), communities should “inform, educate, and empower people about health issues” (Center for Disease Control and Prevention, 2021); however, it would be inefficient to attempt to do this unless you first understand the public’s baseline understanding on the topic of interest. An additional point of the EPHS is that communities should “Link people to needed personal health services and assure the provision of health care when otherwise unavailable”. One possibility is that this survey can be used to gather information that can be used by community policymakers and leaders to consider how they might consider the provision of services for genetic health if their public is interested in gaining access to these services.

Of course, there are critical questions to answer before approaching that reality in many parts of the world, including what the prevalences for different genetic diseases are—even the most basic information is still unknown. However, screening paradigms can be useful for the detection of unrecognized individuals who may be at increased susceptibility to poor clinical outcomes without early intervention. In fact, population-level

screening is already occurring in the United States in the form of newborn screening, one of the most successful public health programs in the country (McCandless & Wright, 2020). Not only that, but there is increasing discussion about the value of population-level screening for Tier 1 genomic conditions, including hereditary breast and ovarian cancer, familial hypercholesterolemia, and Lynch syndrome (Abul-Husn et al., 2021; Buchanan et al., 2020; Foss et al., 2022). While we are not yet at a place to implement these screening methods, the fact that these conversations are happening here and not elsewhere (including Pacific Islander communities) represents a real threat to health equity and, subsequently, *public* health. Ideally, this survey is one way to get members of the public in on the conversation to make sure they are being heard and considered in the push for novel clinical paradigms.

Reflecting on models for genetic service provision, Rigter et al. (2014) reviewed three different case studies for the development of genetic services in three different areas, a county in the United Kingdom (Exeter), South Sweden, and Spain. Results from that study found that there were several topics important to address to facilitate creation of genetic service programs; those that stand out in the context of this project include perceived needs of the region (including stakeholder priorities, awareness, and methods for surveillance) as well as the availability of genetic counseling.

This is where genetic counseling fits into this research: as we consider education and how to support communities that perceive a need for genetic services, genetic counselors are uniquely positioned to assist with the education process. This includes both the general public as well as non-genetic health care providers. Given the training of the genetic counselor, and adaptability to work as part of multi-disciplinary teams, genetic

counselors are uniquely positioned to bridge the gaps between access to genetic services. As previously stated, genetic counseling is not available diffusely on the global scale (Abacan et al., 2019). What will it take for the field to reach communities that are still left in the dark, including Pacific Islander communities? That is not to say that it is an easy task, or that all communities would endorse a need for genetic services.

The answers to such questions require an intimate examination of the barriers that exist to access and how current models of service delivery should be adapted to accommodate different communities. At its core, this project is an endeavor of education and empowerment for our communities and for our patients. It is important to both the public health and genetic counseling to continue to prioritize ways to increase access and shift focus to historically marginalized voices to deliver equitable health care for all.

5.0 Public Health Essay

5.1 Background

5.1.1 The Public Health Burden of Cardiovascular Disease

Noncommunicable diseases (NCD), also called chronic diseases, are the leading cause of global deaths and account for approximately 71% of all deaths annually (World Health Organization, 2021b). Though chronic disease is primarily associated with developed, high-income countries, over three-quarters of this proportion were due to the high rates of death to NCDs that occur in low- and middle-income countries in 2016 (World Health Organization, 2021a). The estimated cumulative cost of NCDs between 2011 and 2030 totals roughly $47 trillion dollars (Kaiser Family Foundation, 2019).

Of the main NCDs contributing to global deaths and disability (which include cancer and diabetes), cardiovascular disease (CVD) is currently creating the greatest disease burden. CVD is a class of several different conditions that can negatively impact heart structure and function, including coronary artery disease (CAD), atherosclerotic heart disease (ASCVD), and ischemic stroke, among many others. An estimated 17.9 million people died globally due to CVD complications in 2016 (World Health Organization, 2021a). In the United States alone, it accounts for approximately 655,000 deaths each year (Virani et al., 2020). The economic burden of CVDs is also substantial due to the costs of treatment and associated disability. In 2017, the estimated cost of CVD in the US was $555

billion; by 2035, that cost is estimated to grow to $1.1 trillion if current health patterns persist (Khavjou, Phelps, & Leib, 2016).

The public health burden of CVD mostly impacts low- and middle-income countries (LMIC) that may lack the infrastructure to properly adapt to increasing effects of NCDs (Owolabi, Miranda, Yaria, & Ovbiagele, 2016). Current epidemiological transitions occurring in LMICs associated with increases in NCDs are due to increasing prevalence of risk factors such as hypertension, diet, obesity, and decreased physical inactivity in these countries (Bowry, Lewey, Dugani, & Choudhry, 2015).

The impact of these changes can be exemplified by health outcomes in the Independent State of Samoa. Located in the Pacific Ocean, in a region known as Oceania, Samoa is an LMIC with a population of approximately 197,000. The leading cause of death in Samoa was ischemic heart disease in both 2009 and 2019, increasing by 14.9% over that ten-year period (Institute for Health Metrics and Evaluation, 2019). Rapid urbanization in the past few decades has caused a significant increase in mean BMI among Samoans, placing them at high risk for a number of NCDs, including CVD, obesity, and type 2 diabetes mellitus (Hawley et al., 2012). There is increasing interest in how biological factors, including genetics, may interact with the environmental change that is occurring in LMICs such as Samoa.

Risk factors for CVD include both behavioral factors and medical predispositions. Behavioral risk factors include poor diet, tobacco use, alcohol consumption, and sedentary lifestyle. Medical predispositions for CVD include hypertension, obesity, diabetes, and hereditary hyperlipidemias. Frontline prevention efforts are focused on lifestyle changes. While lifestyle changes show benefit for the most motivated individuals

(Riccardi, Vaccaro, Costabile, & Rivellese, 2016), those with genetic susceptibility to some types of dyslipidemia (e.g., familial hypercholesterolemia) may not be able to manage their lipid levels using lifestyle changes alone (Center for Disease Control and Prevention, 2022). It has been suggested that statin therapy may be more effective in managing lipid levels for those with inherited forms of dyslipidemia (Mega et al., 2015).

However, significant gaps exist in methods to identify individuals who would most benefit from statin therapy. Novel interventions are needed to identify individuals with genetic susceptibility to CVD earlier. By approaching prevention from all angles, we will get closer to reducing the global public health and economic burden of CVD. This can be particularly important for those individuals in which diet and lifestyle changes alone will not significantly lower lipid levels and subsequent risk of CVD events.

5.1.2 Dyslipidemias

Dysregulation of lipid levels, either genetic or environmental in etiology, is referred to as dyslipidemia. Dyslipidemias are caused by errors in lipoprotein metabolism, and these errors can lead to imbalances of lipids in blood serum. Affected individuals may see increases in low-density cholesterol (LDL-C, often referred to as “bad cholesterol”) and triglycerides (TC), and decreases in high-density cholesterol (HDL-C, often referred to as “good cholesterol”). Increased LDL-C and decreased HDL-C are both correlated with the development of atherosclerosis and adverse cardiovascular events, such as myocardial infarctions (MI) and stroke (Berliner et al., 1995).

5.1.2.1 Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is the most common inherited cause of dyslipidemia. Those affected have elevated LDL-C plasma levels from birth due to genetic mutations that affect proteins responsible for LDL-C metabolization. According to a recent meta-analysis by Hu et al. (2020), the overall prevalence of FH in the global general population is approximately 1 in 250. Despite this relatively high prevalence, the condition is vastly underdiagnosed and undertreated. Most patients with the condition are not aware of their FH status until their first cardiovascular event occurs, which may often be sudden and severe.

Presentation of suspected FH is characterized by a combination of key features in affected individuals, including (Youngblom, Pariani, & Knowles, 2014):

I. Extreme hypercholesterolemia, defined as elevated LDL-C levels above the thresholds of 190 mg/dL in adults and 160 mg/dL in children at baseline OR total cholesterol levels above 310 mg/dL in adults and 230 mg/dL in children
II. Physical manifestations, including xanthomas (fatty deposits of cholesterol that build up under the skin, most commonly occurring in the tendons, elbows, and buttocks) corneal arcus (white, gray, or blue opaque rings in the cornea) and atherosclerosis (accumulation of fatty buildup in the arterial wall)
III. Personal and/or family history of premature coronary artery disease or other cardiovascular diseases

At present, three sets of criteria are accepted for the clinical diagnosis of FH: the MedPed criteria of the US, the Simon Broome criteria of the UK, and the Dutch Lipid Clinic

Network (DLCN) criteria of the Netherlands (Al-Rasadi et al., 2014). The MedPed criteria uses age and family history of FH diagnosis to determine designated cholesterol cutoff points. The Simon Broome criteria considers a number of clinical features, including cholesterol blood concentration, presence of tendon xanthomas, and family history to determine the presence of “definite” or “probable” FH in the patient. Finally, the DLCN criteria uses a point value system based on family history, clinical history, physical exam, and cholesterol levels to offer a “definite”, “probable”, or “possible” diagnosis of FH. While the DLCN and Simon Broome criteria are relatively similar, the DLCN criteria requires that at least one other clinical feature is present in addition to the presence of a functional mutation in the LDL receptor gene (*LDLR*). Of these, the DLCN criteria is the most widely used FH diagnosis criteria tool (Alonso, Perez De Isla, Muñiz-Grijalvo, Diaz-Diaz, & Mata, 2018).

5.1.1.2 The Genetics of FH

Most criteria for FH diagnosis are based on the presentation of elevated LDL-C levels above a phenotypic threshold, in combination with select clinical features and family history. However, the reasons for hyperlipidemia in FH may be a result of either a monogenic or polygenic genetic etiology.

Monogenic FH is most commonly caused by mutations in loci associated with one of three identified genes important for LDL-C metabolism: low-density lipoprotein receptor (*LDLR*), apolipoprotein B (*APOB*), and proprotein convertase subtilisin/kexin type 9 (*PCSK9*). These mutations are inherited in an autosomal dominant fashion, and penetrance close to 100% (De Castro-Oros, Pocovi, & Civeira, 2010). Clinical symptoms associated with FH tend to compound if individuals carry mutations on both alleles for these

genes. As an example, the standard total cholesterol range in the general population is less than 200 mg/dL. Homozygous FH (hoFH), while rare (~1 per 1,000,000), results in total cholesterol levels between 650 and 1,000 mg/dL. Heterozygous FH (heFH) is much more common in the general population (estimated at a prevalence of 1 in 250); these individuals tend to have total cholesterol levels in the range of 350 mg/dL to 550 mg/dL (Pejic, 2014).

In polygenic FH, patients may show a clinical phenotype indicative of hyperlipidemia, but the genetic influence on disease is attributed to many different loci (over 100) exerting small effect sizes on disease. Of those individuals diagnosed with clinical FH *that do not have a monogenic FH indication*, polygenic causes are responsible for an estimated 80% of individuals diagnosed with clinical FH (Sharifi, Futema, Nair, & Humphries, 2017). There is also great phenotypic heterogeneity among individuals with FH mutations. For example, while xanthomas are a key feature of FH, <20% of individuals with FH mutations present with them (Alonso et al., 2018).

Clinical presentation of FH is based on total cholesterol and LDL-C cutoffs. If an affected individual meets clinical criteria, they may consider diagnostic testing for pathogenic genetic variants associated with FH, such as the *LDLR, APOB,* or *PCSK9* genes. However, many patients are not aware of their FH status until later in life, and often after their first CVD event (Alonso, Perez de Isla, Muniz-Grijalvo, & Mata, 2020)**.** There is a lack of intervention tools that could be used to identify individuals most at risk for complex diseases, such as CVDs. Such tools should take into account both individual lifestyle risk factors and genetic susceptibility to developing disease compared to the general population.

5.1.3 The Genetics of Obesity and CVD in Samoa

Environmental influences of globalization, including ultra-processed foods and increased sedentary behaviors, are part of the model that has led to rising NCDs in the region. However, Samoans face greater rates of obesity compared other populations in the Pacific. A 2010 study conducted using members health plan based in Hawai‘i (total *N* = 119,563) showed an obesity rate of 50% among Samoans (*N* = 169), up 13% from the next highest group, Puerto Ricans, in the sample (Juarez, Samoa, Chung, & Seto, 2010). Furthermore, Samoans reported greater numbers of poor physical health days (5.4) and poor mental health days (4.4) over 30 days compared to other racial/ethnic groups living in the Pacific. Though the study results were derived from a sample based in Hawai‘i, these disparities suggest that there may be some genetic differences that contribute to obesity in Samoans compared to other Pacific Islanders.

Using a discovery cohort of over 3,000 Samoans, Minster et al. (2016) identified a SNP missense variant (rs373863828) that has a minor allele frequency of 0.259 in the Samoan population, despite being quite rare in populations outside the Pacific (Karczewski et al., 2020). The A allele in this genotypic region was positively associated with increased obesity risk, with odds ratios of 1.305 and 1.441 in discovery and replication cohorts respectively. This suggests that there is some genetic variation in the Samoan population affecting energy metabolism and subsequent BMI levels. However, the team found that these associations primarily only suggested a link to the variant and obesity/adiposity; the same positive association was not found with blood serum lipid levels.

A follow-up study by Carlson et al. (2020) moved forward to characterize the genetic architecture of fasting serum lipid levels in the same 2010 discovery cohort using

GWAS analysis and found a significant association signal for LDL-C and total cholesterol at rs1160985, an intronic variant in *TOMM40*, a gene in close proximity to *APOE*. The research team also discovered association for HDL-C at rs289708, a variant in a gene known as *CETP*. This study was the first of its kind to characterize the genetic contributions to LDL-C and HDL-C in Samoans, and also showed that some of the genetic architecture uncovered in the study among Samoans is shared with other populations.

5.1.4 The Samoan Islands

5.1.4.1 Overview of Samoa

The Samoan Islands are a chain of islands located in the Oceanic subregion known as Polynesia, located in the Pacific Ocean. It consists of two territories: The Independent State of Samoa (also known as "Samoa") and the unincorporated U.S. territory of American Samoa; their populations are approximately 198,000 and 55,000 respectively (World Bank, 2020). Samoa is democratic, predominantly Christian nation consisting of two main islands, Upolu and Savai'i, the former of which houses the largest proportion of the population as well as nation's urban capital, Apia. The country was under New Zealand control until 1962, at which time it gained independence as "Western Samoa"; this name was formally changed to the Independent Island of Samoa in 1997 (Lowry, 2016).

Samoa is considered to be an LMIC, with a gross domestic product (GDP) per capita of approximately $4,500 as of 2019 (Lansford, 2021). Economic growth has increased steadily over the past few decades, particularly as the country created a formal tourism policy and additional policies in the 1990s to support the private sector. However, the country faced many setbacks due to natural disasters, including cyclones that ravaged

the country in the early 1990s, and several catastrophes in the late 2000s, including losses as part of the global economic recession in 2009 and a destructive tsunami in September of that same year.

5.1.4.2 *Fa‘asāmoa*

Fa‘asāmoa is a word that refers to the Samoan way of life, of culture and of spirit. In spite of some western influences, the nation has worked to preserve its *fa‘asāmoa.* Generally, Samoan villages are organized into extended family structures known as an *‘āiga*, and each *‘āiga* with its own village chief, or *matai*, who makes larger decisions on behalf of the village (Lansford, 2021). The arrangement of *‘āiga potopoto*, or extended family structures, in villages also determines how land is divided, with land typically being inherited through the generations. This village structure also exemplifies the importance of family in Samoan society; family comes first in *fa‘asāmoa*, and individuals are expected to behave in a manner that honors the family (Scroope, 2017). According to one author, social expectations around family are so important to Samoan culture that individuals may choose “what is best for the family over what is best for individual health” (Hardin, 2018).

5.1.4.3 The Globalization of the Samoan Islands

The Independent State of Samoa is considered an LMICs due to the current epidemiological shift that is occurring in the region. However, American Samoa has experienced a more significant degree of urbanization and development than Samoa and is considered an upper-middle income country. Economic growth was not as substantial in the mid-20th century due to reduced infrastructure among the islands to support large jets until the mid-1980s, as well as low priority to develop policies related to tourism at the

time. There was also a concern of losing *fa'asāmoa* in the face of increased tourism. However, natural disasters occurring in the early 1990s catalyzed the formation of a formal economic development policy in 1992 (Lowry, 2016).

Over the past several decades, rapid globalization has contributed to urbanization of the region, technological advances, and improved health care. Increased globalization and the aforementioned changing trade and tourism policies have bolstered the economy; however, these advances have also led to Western food imports that are cheap, high in calories, and ultra-processed. A complex interplay between this urbanization, occupational transitions, budgets, national GDP, and political and economic influences of trade have provided opportunities for high availability of nutrients high in salt, sugar, and fat and increased sedentary living (Seiden, Hawley, Schulz, Raifman, & McGarvey, 2012).

Additionally, traditional subsistence fishing and farming has been increasingly replaced over the past several decades by higher calorie, higher fat diets and sedentary behavior as the Samoan islands have transitioned from plant-based food and farming to meat and processed foods. Physical activity associated with farming and sustenance behaviors has also declined (Fox, Feng, & Asal, 2019). Keighley, McGarvey, Turituri, and Viali (2006) also suggest that farming is associated with lower BMI and percentage of body fat among Samoans, and that loss of this activity may further exacerbate increased adiposity. Given the higher rate of urbanization in American Samoa, there is a more significant presence of obesity and cardiovascular risk factors in this territory compared to Samoa (Hawley et al., 2012).

5.1.4.4 The Role of Healthcare and Traditional Medicine

Despite Western influences, *fa'asāmoa* has persevered in many facets of daily living. One such facet includes the use of traditional medicine, also sometimes referred to as complementary and alternative medicine (CAM). The World Health Organization defines traditional medicine as the "sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness" (World Health Organization, 2022).

Traditional medicine practice includes the exercise of skills that are passed down through generations of knowledge, though practices may vary from country to country. In Samoa, this type of care is delivered by local healers, *taulāsea* or *fofō*, when individuals encounter illness. *Fofō* refers to local healers that practice massage techniques for wellness while *taulāsea* refers to local healers with some training to prescribe herbal medication and diagnose illness (Krosch, 2010). Remedies prescribed for those receiving CAM may include a number of different medicinal plants and specific means of administration incorporated as folk medicine, which is practiced in the household, or those administered by traditional healers (Whistler, 2006).

Historically, disease in the islands has been perceived as two different subtypes: those diseases indigenous to the community, or *mama'i sāmoa,* and those diseases, both communicable and non-communicable, brought to the islands from outsiders, called *mama'i papālagi* (Macpherson & Macpherson, 1990). This duality is a similar parallel between the division in health care approaches in the country: traditional Samoan and

modern medical clinics that have come to the islands. Despite the difference in approach to health care offered by the two, there is reportedly no apparent animosity between them because of these distinct categories of malady. *Mamaʻi sāmoa* are considered a concern for local healers and *mamaʻi papālagi* are considered as a concern for Western medicine; in effect, there is a division of labor between the two systems depending on the ailment affecting the individual (Macpherson & Macpherson, 1990).

This coexistence of the two approaches to healthcare suggests that CVD care and the uptake of genetic services will be strongly guided by Samoan views of the role of healthcare and the intersection of these expectations with traditional medicine. Moreover, Samoa does not have a universal health care system or insurance benefit programs, and most health care spending is provided by the government, who provided approximately 88% of health care spending in 2010 (Boslaugh, 2013). Specialized care not otherwise available on the islands of Samoa must be received elsewhere, though both Samoa and New Zealand offer programs that can support travel overseas for specialty care.

5.2 Specific Aims

The literature suggests that there is an elevated risk for CVDs in LMICs; this is exemplified by Samoa and American Samoa, two middle-income polities where NCDs are rising and CVDs are the leading cause of death (Institute for Health Metrics and Evaluation, 2019). Rapid globalization in the region over the past several decades has led to changes in diet and physical activity that has increased population susceptibility to CVD risk factors including hypertension and obesity. Few studies have identified novel

applications of genetics to create health policies that would allow early intervention for those who are most at risk of CVD in Samoa. LDL-C has long been established as a risk factor for CVD (Kannel, 1971); this association is supported by the presence of early cardiac events in those with hyperlipidemias such as FH.

With this in mind, the purpose of this essay is to characterize the impact of LDL-C on CVD risk in Samoa using the same 2010 discovery cohort data used in Hawley et al. (2014), Minster et al. (2016), and Carlson et al. (2020). The specific aims to accomplish this task are to clarify the relationship between LDL-C blood serum lipid levels and a number of different independent variables, including: census region, BMI, activity level, and cardiovascular event.

The goal of this essay is not to suggest that variant susceptibility to obesity or CVDs makes those diseases inevitable in the Samoan population. The search for biological and genetic influences of NCDs here serve only to explore ways to intervene in the delivery of health care and inform models aimed at prevention and early intervention. Public health policies should continue to investigate environmental interventions to improve population health, including changes to diet or activity.

5.3 Methods

5.3.1 Study Recruitment

Inclusion criteria for the sample were that (1) participants are between the ages of 24.5 years and 65 years and (2) had Samoan ancestry as identified by self-report of having four Samoan grandparents, (3) were non-pregnant, (4) did not exhibit any severe physical or cognitive limitations that would prevent them from completing either questionnaires or anthropometric activities, and (5) could complete the study interview section in Samoan. After exclusion of any participants who did not meet inclusion criteria, the final sample size was *N* = 3,475 (Hawley et al., 2014). In the current study, the number was reduced to *N* = 2,937 after removing any null data for LDL-C measures in the sample.

Participants were recruited between February and July of 2010. During this time, the research team visited different villages scattered throughout the four main census regions of Independent Samoa (Figure 10): on the island of ‘Upolu, investigators recruited from nine villages in the urban central of Apia (AUA), eight villages in the northwest ‘Upolu region (NWU), and eight villages in the rest of ‘Upolu (ROU), except for the eastern region of ‘Upolu, which was still recovering from a catastrophic tsunami that hit the island in 2009 (Hawley et al., 2014). Recruitment also occurred at eight villages on the rural island of Savai‘i (SAV), for a total of 33 different villages. During each visit, the Samoan Bureau of Statistics allowed the team to collect data for about two or three days before moving on.

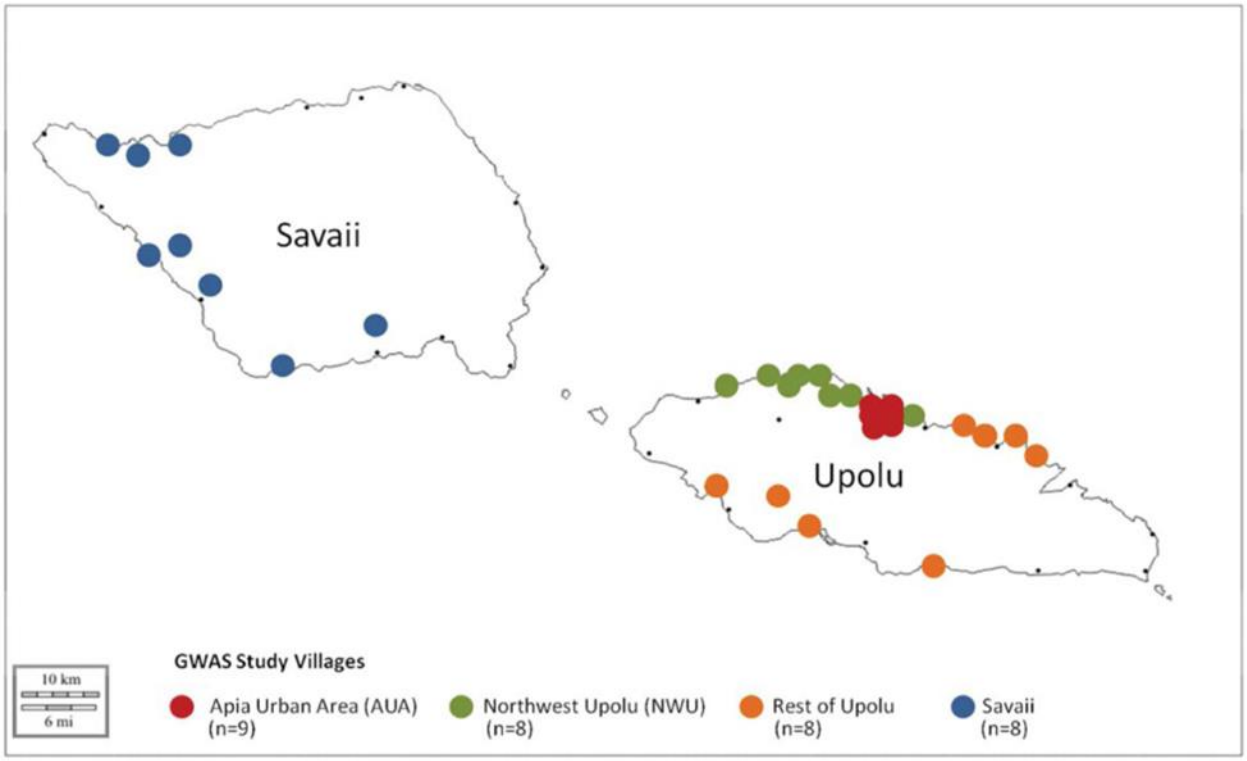

Figure 10. The Independent State of Samoa

Village leaders and study orators assisted in the recruitment of participants at large recruitment centers in villages, explaining the purpose of the study and facilitating participation (Hawley et al., 2014). Once participants were consented, researchers collect information using a number of different measure tools, including questionnaires and surveys, anthropometric measures, serum sampling, and DNA samples. Questionnaires were administered in Samoan, and included questions that investigated participant health history and behaviors (including physical activity, diet, and smoking frequency). Anthropometric measures of interest in the study include height, weight, circumference of the hip, abdomen, and calf. Serum sampling of fasting blood lipid levels were taken to determine total cholesterol, LDL-C, HDL-C, and triglycerides. Finally, DNA samples provided

genotypes of each participant for the use of analysis regarding genotype and environment exposures.

5.3.2 Data Analysis

Data was collected and all statistical analyses were performed using RStudio (v.1.3.1093-1), with statistical significance set at $p < 0.05$. Individuals were pruned from analyses if they were missing LDL-C values since all analyses involved comparisons across groups based on LDL-C. All descriptive statistics were compiled using Microsoft Excel.

Primary questions to be answered in the current essay included whether:

- There were differences in LDL-C by census region
- There were differences in sample mean LDL-C between those reporting a previous heart attack and those who did not
- There is an association between BMI and LDL-C such that the population correlation coefficient is not equal to zero
- There is an association between daily time spent sitting and LDL-C such that the population correlation coefficient is not equal to zero

Differences in LDL-C by census region were evaluated using a one-way ANOVA. Differences in LDL-C by heart attack history was evaluated using a two-sample *t* test. Linear regression was carried out to test both the association of LDL-C and BMI and LDL-C and daily time spent sitting in the population.

5.3.3 Study Demographics

The total sample size for the preliminary data analysis was *N* = 2,937; of these, approximately 59.7% identify as female. Tables 13 and 14 below describe summary demographics and values for variables of interest in the analysis, including LDL-C.

Table 13. Number of Participants by Region, Gender

Total *N* = 2397	*N* (%)
Census Regions	
AUA	621 (21.1%)
NWU	790 (26.9%)
ROU	830 (28.3%)
SAV	696 (23.7%)
Gender	
Female	1753 (59.7%)
Male	1184 (40.3%)

Table 14. Descriptive Statistics for Age, BMI, LDL-C, and HDL-C

	Mean (SD)	Min	Median	Max
Age (years)	45.2 (11.2)	22.7	45.5	70.1
BMI (kg/m^2)	33.4 (6.65)	18	32.8	62.2
LDL-C (mg/dL)	130 (34.2)	21	129	324
HDL-C (mg/dL)	45.4 (11.0)	14	44	107

As a reminder, the reference (normolipidemic) value for LDL-C is between 50 mg/dL and 100 mg/dL and the reference (normolipidemic) value for HDL-C is > 45 mg/dL. Polynesian cutoffs for BMI overweight and obesity are ≥ 26 kg/m^2 and ≥ 32 kg/m^2 respectively (cite PMID: 10578208). The more rural regions of ROU and SAV are more strongly represented in the data (28.3% and 23.7% for a total of 52%) compared

to the semi-urban region of NWU (26.9%) and AUA (21.1%). Furthermore, the mean age of 45.2 years reflected levels of participation based on those eligible for inclusion; of the total sample, 42.2% of those 60 years to 64 years of age participated compared to 16.1% eligible among 24.5 years to 29 years of age. Researchers hypothesize that older participants may have been more likely to participate due to increased availability from lack of employment (Figure 11).

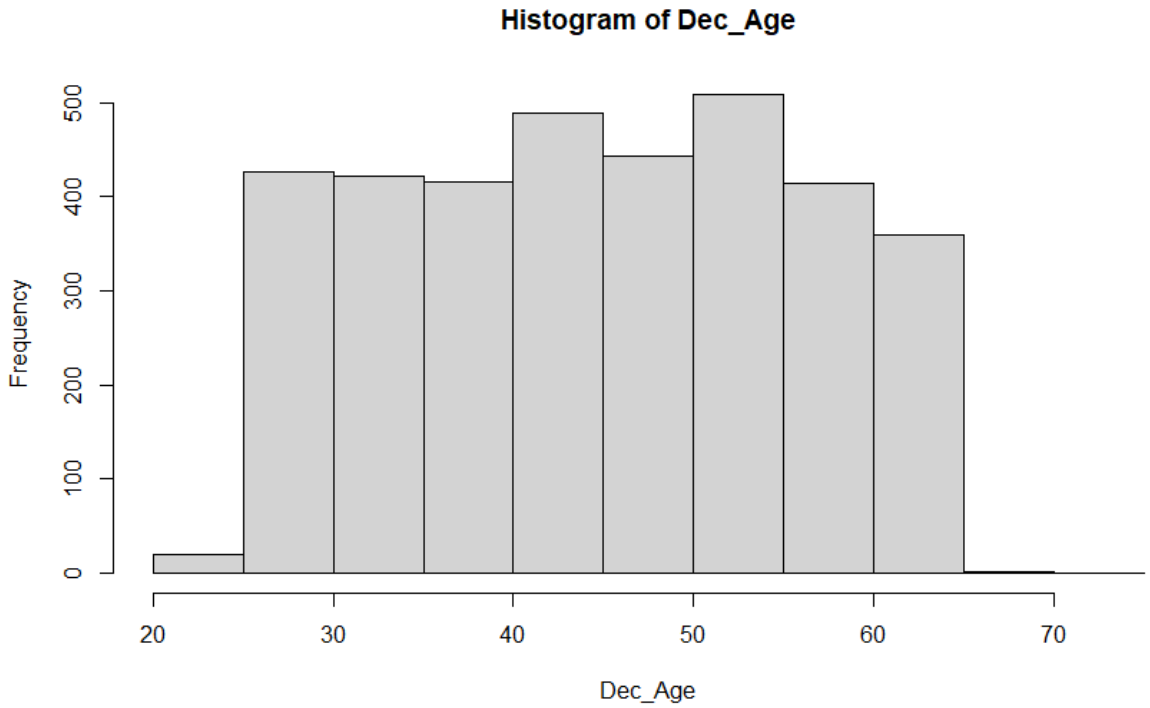

Figure 11. Histogram of Participants' Ages

5.3.4 Trends in Visualization

Overall, preliminary visualization did not reveal any strong relationships between LDL-C and independent variables representative of risk factors for elevated LDL-C,

including obesity, age, or gender. Categorizations of thresholds for LDL-C are indicated in five different categories: Optimal (below 100 mg/dL), Near/Above Optimal (100 to 129 mg/dL), Borderline High (130 to 159 mg/dL), High (160 to 189 mg/dL), and Very High (above 190 mg/dL) (Lee & Siddiqui, 2021). A frequency histogram of LDL-C shows that approximately three-quarters of the sample had LDL-C fasting blood lipid levels above the recommended healthy threshold of 100 mg/dL (Figure 12).

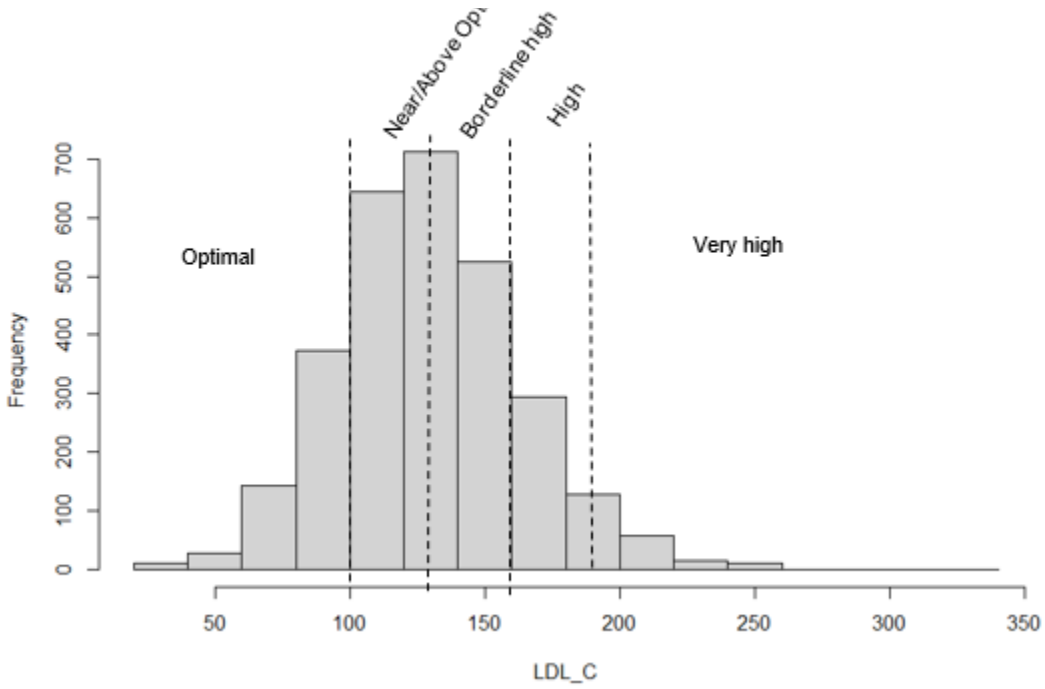

Figure 12. Histogram of LDL-C Levels

BMI did not strongly correlate with age, though there appeared to be a slight positive trend: as Samoans increase in age, only slightly do they also increase in BMI (Figure 13). There were no significant differences in BMI by gender (Figure 14). There appeared to be a weak positive correlation between LDL-C and age, but no notable

patterns appeared on reflection of LDL-C levels by gender (Figure 15, Figure 16). Finally, with respect to heart disease diagnosis, there were no significant patterns in LDL-C levels between the two groups (Figure 17). Initial trends suggested that there would not be any statistically significant differences with respect to groups in stage one of the preliminary analysis to observe differences in LDL-C, leading to some changes in research questions in later stages.

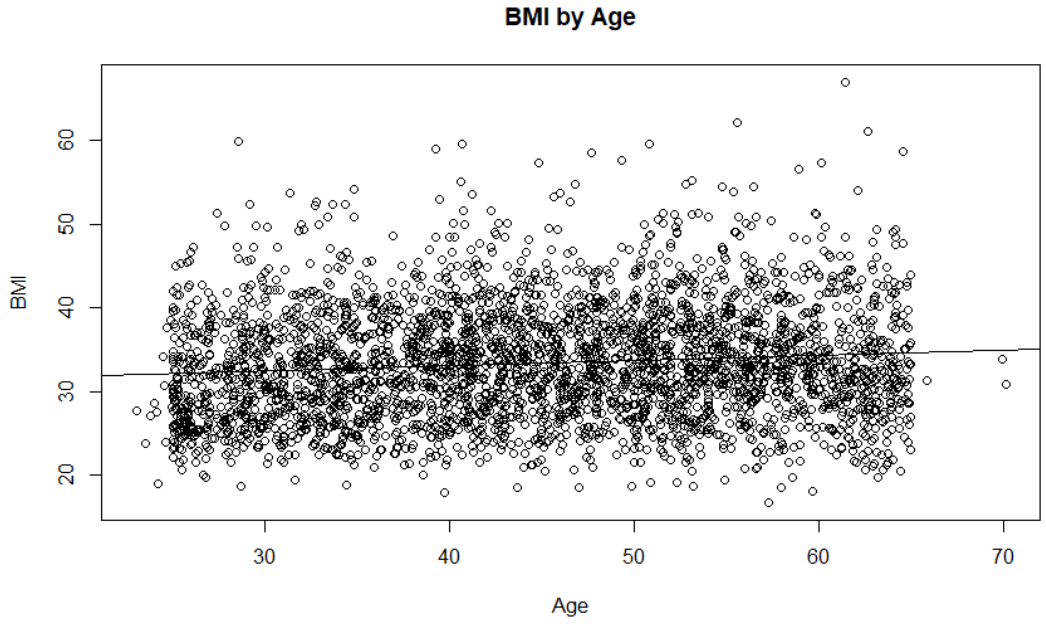

Figure 13. Scatterplot of BMI by Age

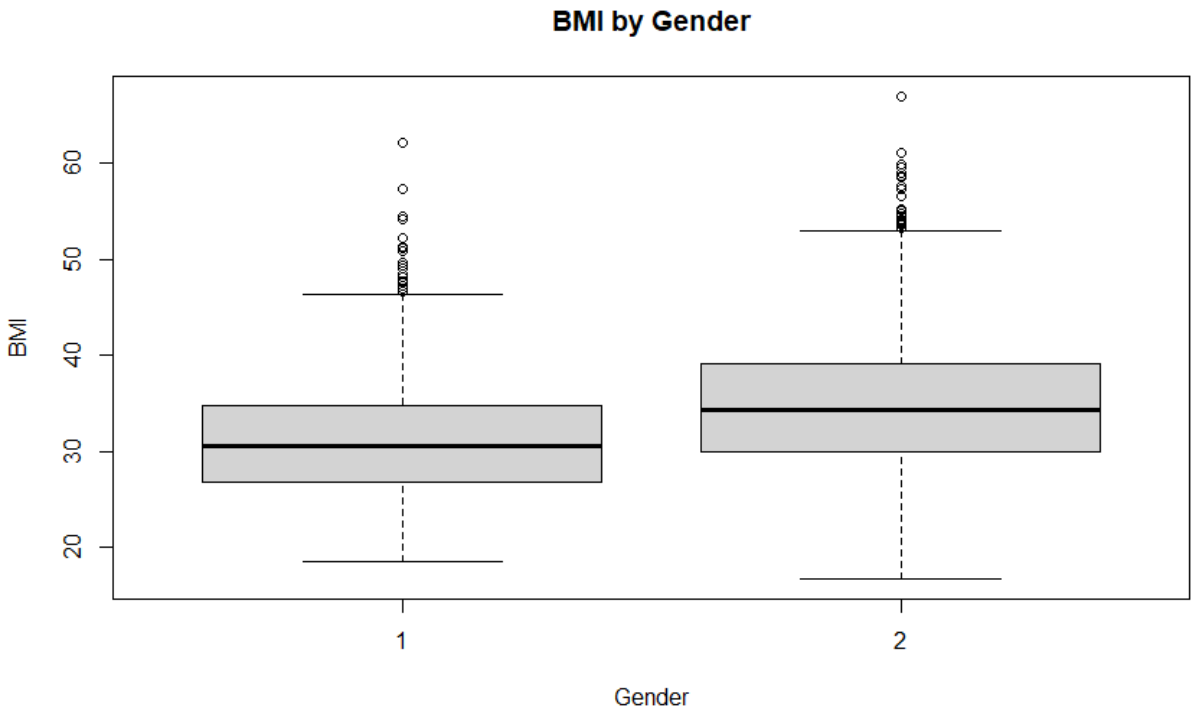

Figure 14. BMI by Gender (1 = Male, 2 = Female)

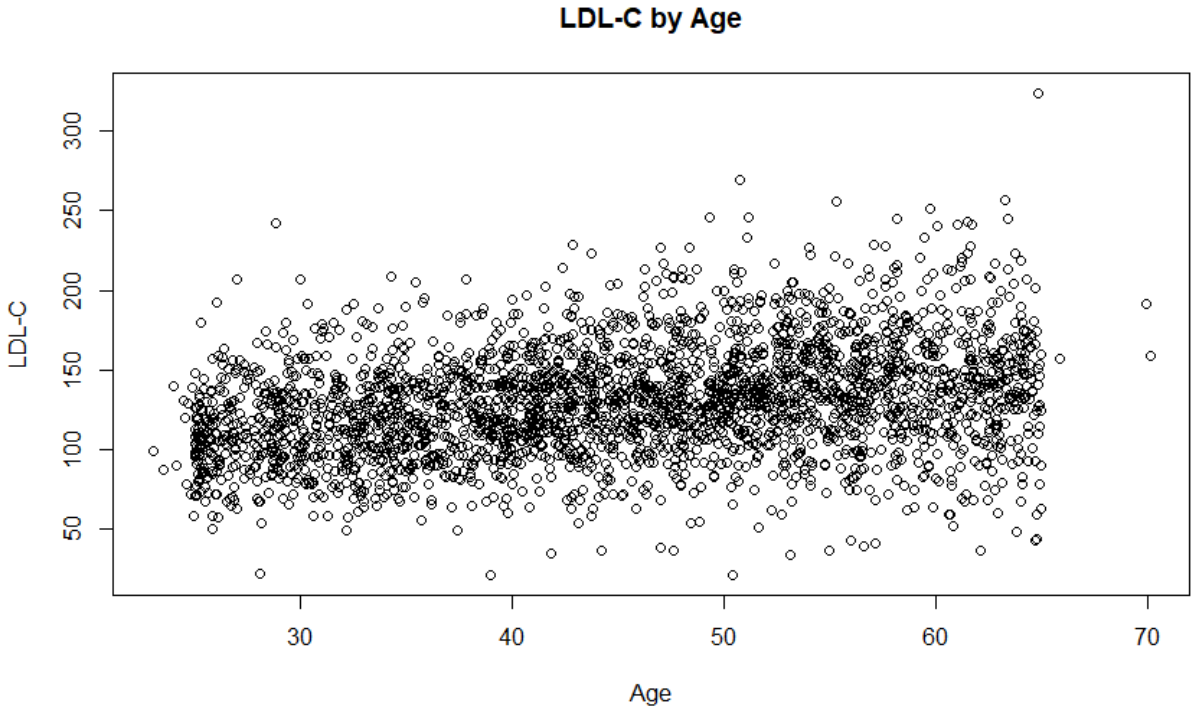

Figure 15. LDL-C by Age

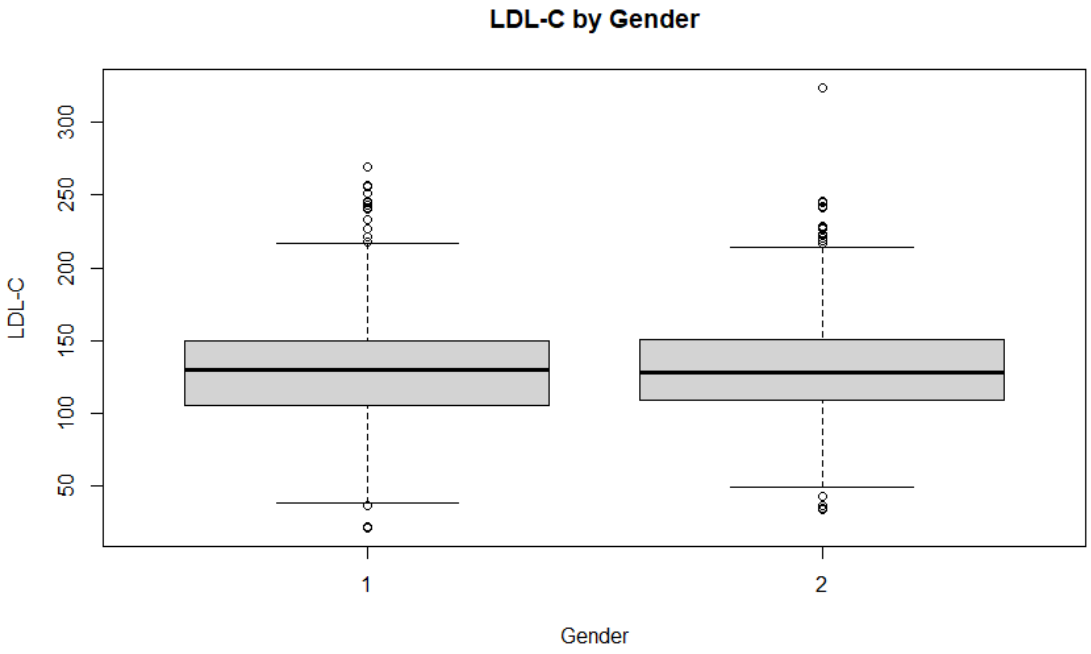

Figure 16. LDL-C by Gender (1 = Male, 2 = Female)

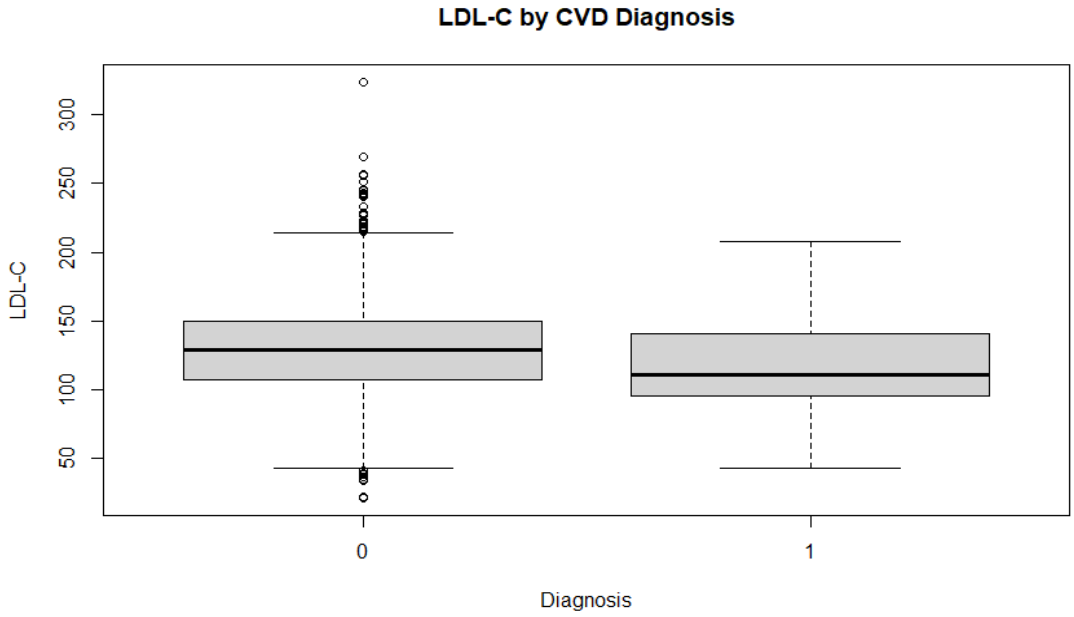

Figure 17. LDL-C by CVD Diagnosis (0 = No, 1 = Yes)

5.3.5 Analyses

5.3.5.1 Analysis #1: One-Way ANOVA

The first analysis was a one-way ANOVA to determine if there were statistically significant differences in mean LDL-C for at least one of the four census regions from the others. For preliminary analysis, this test was carried out to determine if a meaningful difference exists, with further examination into which region is showing the difference at a later stage. Statistical testing led to an F value of 5.575 with 3 degrees of freedom for $p = 8.22 \times 10^{-4}$. With this result, we reject the null hypothesis at $\alpha = 0.05$. If the null hypothesis were true, we would expect results as or more extreme that this less than 1% of the time. We have evidence to suggest that the population mean LDL-C level is different for at least one of the census regions in the study.

Table 15. Mean LDL-C Levels by Census Region

Census Region	Mean LDL-C Levels (mg/dL)
AUA	129.5
NWU	127.9
ROU	128.5
SAV	134.5

AUA = Apia Urban Center
NWU = Northwest ‘Upolu
ROU = Rest of ‘Upolu
SAV = Savai‘i

Table 16. Tukey HSD Results (ANOVA)

Census Regions	Difference	95% CI Lower Limit	95% CI Upper Limit	Adjusted P-Value
NWU–AUA	−1.590783	−6.2882561	3.106691	0.8201281
ROU–AUA	−1.026165	−5.6735538	3.621225	0.9417009
SAV–AUA	4.96642	0.1313508	9.801488	0.0414401*
ROU–NWU	0.564618	−3.7891482	4.918384	0.9872325
SAV–NWU	6.557202	2.0036383	11.110766	0.0012481**
SAV–ROU	5.992584	1.4907055	10.494463	0.0035277**

*Statistically significant at p < 0.05
**Statistically significant at p < 0.01

Table 15 shows the mean LDL-C levels by each of the four census regions; Table 16 demonstrates the significance in difference between each of the census regions, including the raw difference, the 95% confidence intervals for each, and their respective *p* values. Based on Table 16, the greatest difference in mean LDL-C is between Savai‘i and the census regions on ‘Upolu. The difference is most pronounced between SAV and ROU with a total difference of 5.99, a 95% confidence interval between 1.491 and 10.494, and $p = 0.0035$.

5.3.5.2 Analysis#2: Two-Sample *t* Test

In the next analysis, a two-sample *t* test was used to determine if the mean LDL-C among those reporting a previous heart attack ($N = 33$) different from the mean LDL-C of those not reporting a previous heart attack ($N = 2452$, subtracting null values in the data). A test for equal variances revealed $p = 0.0193$, below $\alpha = 0.05$. A follow-up two-sample *t* test for unequal variances revealed a *t* statistic of 0.0655 and $p = 0.948$. At $\alpha = 0.05$, we do not reject the null hypothesis. We do not have evidence to suggest that the mean LDL-C among those reporting a previous heart attack is different from the mean LDL-C of those not reporting a previous heart attack.

5.3.5.3 Analysis #3: Correlation/Linear Regression (LDL-C vs BMI)

In the third analysis, a simple correlation was used to determine if there was a statistically significant linear association between BMI and LDL-C levels. Pearson's coefficient was $r = 0.12$, with a test statistic of $t = 6.55$. The p value for the test statistic was 1.2×10^{-11}, indicating a statistically significant relationship between the variables and confirming the suspicion of a weak, positive correlation between LDL-C and BMI (Figure 18). If there was no correlation between the two variables, we would expect results as or more extreme than this less than 1% of the time. Simple linear regression was performed and the estimated linear regression line was LDL-C = 108.5 + 0.643 × BMI.

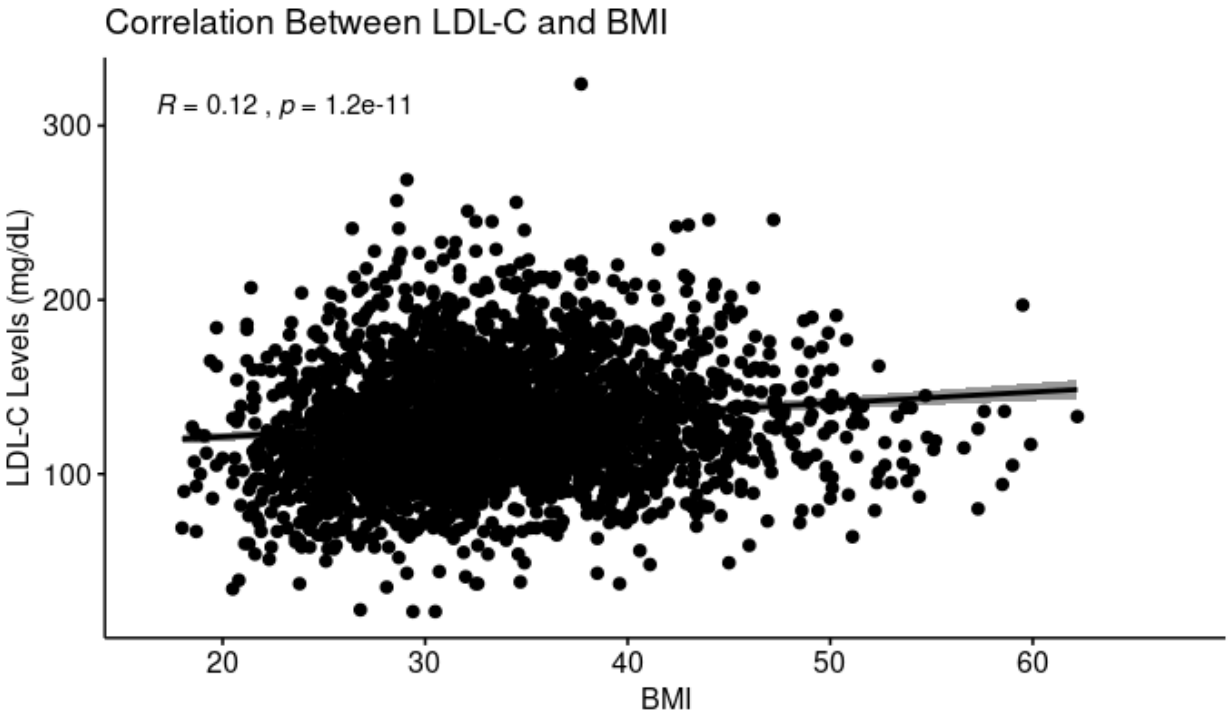

Figure 18. Correlation Analysis: LDL-C x BMI (kg/m2)

5.3.5.4 Analysis #4: Correlation/Linear Regression (LDL-C vs Sitting Minutes)

Finally, I attempted to determine if there was a statistically significant linear association between daily time spent sitting and LDL-C levels. There was no meaningful correlation between the two variables, with a Pearson's coefficient of −0.01 and $p = 0.58$. however, a scatterplot revealed a more surprising result (Figure 19). The reasoning behind this graph can be found in the discussion section to follow.

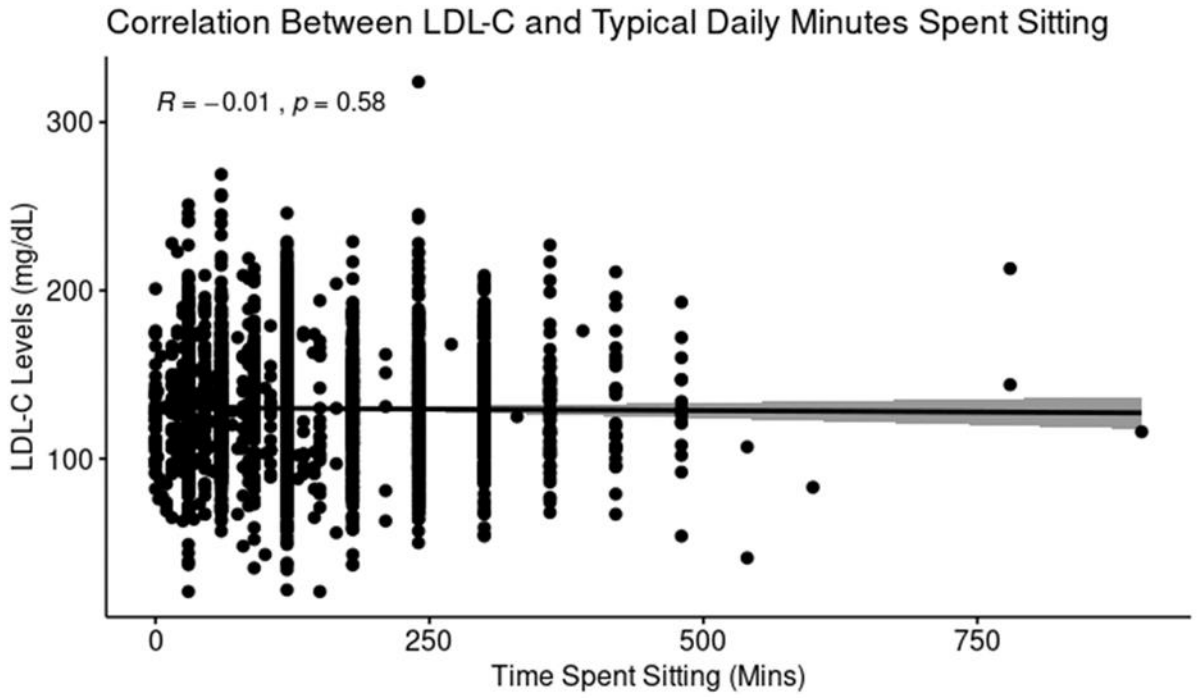

Figure 19. Correlation Analysis: LDL-C x Typical Daily Minutes Sitting

Table 17. Summary Table of Analyses and Results

Analysis	Hypothesis Test	Degrees of Freedom	Test Statistic	*p* value
LDL-C vs. Census Region	ANOVA	3	5.575	**8.22×10^{-4}***
LDL-C vs. Heart Attack History	Two-sample *t* test (unequal variance)	32.5	0.0655	0.948
LDL-C vs. BMI	Correlation/Linear Regression		6.55	**1.2×10^{-11}***
LDL-C vs. Daily Sitting Minutes	Correlation/Linear Regression		NULL	

5.4 Discussion

The current preliminary data analysis has revealed very few relationships in significance and weak correlations. The most impactful finding in this preliminary study was the significant finding that LDL-C level differences may exist by census region, with those from Savai'i (more rural that the Apia Urban Region) having higher mean levels of LDL-C. While the influences on mean LDL-C among participants are likely complex, one possible influence on this difference between LDL-C may be related to differing diets between the regions: neo-traditional diets of the Samoan Islands have historically included many native foods, including bananas, taro, seafood, and coconuts (Dibello et al., 2009). Of these, coconuts may have an unexpected influence on LDL-C levels: A 2020 meta-analysis found that increased coconut oil consumption significantly increased levels of LDL-C compared to non-tropical vegetable oils (Neelakantan, Seah, & Van Dam, 2020). It is possible that the difference in mean LDL-C between regions may be related to differences in

regional diets, including the consumption of more traditional Samoan diets in some regions compared to others.

The findings of the current study supported some associations between LDL-C and risk factors known in the literature, but the effect sizes were much smaller than anticipated. However, these results offer many answers about variables in need of fine-tuning as well as those that may not be worth pursuing for future research. Furthermore, the lack of greater statistical power in these results does not negate the public health mission to increase and sustain community well-being. There are members of the sample with LDL-C blood serum lipid levels above the threshold for familial hypercholesterolemia who may or may not be received medical attention, and many more below the threshold who have elevated LDL-C levels (Figure 12). There may still be ways to intervene that can help participants decrease LDL-C levels and maintain those levels for cardiovascular health that we have yet to understand.

Initially, the goal was to also include more in-depth analyses of the relationship between daily sitting minutes, a proxy for activity level, and LDL-C levels. However, the observed pattern (Figure 19) occurred because, though the variable was reported quantitatively, many participants were unable to report accurate measurements beyond approximately 100 min. There are some limitations to report on self-reported measures of physical activity to be discussed that may affect any opportunity to include independent measures of physical activity in future studies. This is particularly disappointing as it means that these variables will not be suitable in future analyses, and we will be unable to identify associations between this measure of sedentary activity, a known risk factor in the development of CVDs, and LDL-C levels.

5.4.1 Limitations

There are several limitations of the data, both (1) in the discovery cohort and (2) in the analysis of the data in this preliminary phase. Regarding data collection limitations, the data may not be representative of the population due to selection bias. The increased participation of older individuals and elders, as a result of increased availability, decreased the representativeness of the sample. However, researchers managing the original discovery cohort did provide age-specific, sex-specific prevalence estimates and age-adjusted risk of disease based on the 2011 Samoan census. Such adjustments will be required before this preliminary data is useful. The team also had to make conscientious choices not to include some villages, including southeastern ‘Upolu, due to a 2009 tsunami that was still impacting recovery in the region (Hawley et al., 2014). The data set lacks additional information from that region, and it is currently unknown by the student researcher how populous areas along the coast are.

Time constraints in data collection may have further exacerbated the inability to capture data on individuals who were not able to participate within the two-to-three-day window of recruitment; this is especially true for full-time workers in villages. Finally, the data, at the time, encompassed a relatively new epidemiological approach to observing the Samoan population. Considering that Samoa is an LMIC, many of the first steps required to inform genetic awareness and build capacity in the region are in development (or pre-development) phase. It is relatively recent that the team is beginning to look at genotype-phenotype correlations and the ethical, legal, and social implications (ELSI) of genetic data in the Samoan Islands. There is a need for research that investigates findings in the literature to increase precision and bolster the foundation of current findings.

Regarding limitations in analyses, Figure 19 is a demonstration of how the use of self-reported typical daily minutes sitting will not be an accurate way to complete linear regression analysis. In fact, the use of accelerometers in future studies suggest that participants may have underestimated their activity levels; moving forward, self-reported measures of physical activity cannot be used in analyses. Additionally, many of the tests performed in this preliminary analysis may be more informative if quantitative variables are binned as binary traits above and below a “disease” threshold. For example, the relationship between LDL-C by BMI (Figure 18) might have more statistical power if the sample is divided by participants above Polynesian cutoffs for BMI obesity and those below Polynesian cutoffs for BMI obesity. Finally, the use of RStudio is novel and complex, and there is a moderate potential for systematic error in analyses due to developing knowledge on the use of the program.

5.4.2 Future Directions

The results of the essay here provide plenty of leads for next steps to modify variables in new ways and reassess statistical significance. In future research with this dataset, there is still work to do regarding the additional aims of the study. Future analyses may consider the addition of both the Material Lifestyles Scores (MLS) and statistical analyses computed using sentinel SNPs in the Samoan population.

The MLS, also known as the household asset score, is calculated as the sum of a number of durable goods that are owned by participants, including: stove type, refrigerator, portable stereo, stereo, television, videocassette recorder, landline phone, carpet, car/4-wheeled motorized vehicle, couch, European-style home, plumbing, freezer, and

washing machine. With a maximum possible score of 14 points, the MLS is a composite measure of socioeconomic status. The addition of the variable to the dataset will allow for an analysis to determine the statistical relationship between the MLS and LDL-C, since the literature reflects associations between increased modernization and the prevalence of NCDs.

Carlson et al. (2020) also discovered sentinel SNPs for both LDL-C and HDL-C—rs1160985 and rs289708 respectively. These offer additional opportunities to look for genotype-phenotype correlations between these SNPs and observed LDL-C and HDL-C levels. Additionally, the focus of this data analysis focused on LDL-C as the primary dependent variable. HDL-C has been suggested to confer some protection against the development of CVD (Ali, Wonnerth, Huber, & Wojta, 2012); follow-up analyses could explore the literature more in-depth and add additional analyses looking at HDL-C in the Samoan population, particularly with the inclusion of analyses that incorporate rs289708.

Appendix A Internal Review Board Approval Documents

Yale

Human Research Protection Program
Institutional Review Boards
FWA00002571
25 Science Park – 3rd Fl., 150 Munson St.
New Haven CT 06520-8327

Telephone: 203-785-4688
http://www.yale.edu/hrpp

April 8, 2021

APPROVAL OF SUBMISSION VIA EXPEDITED REVIEW

Approval Date: 3/29/2021

Investigator:	Nicola Hawley
Type of Review:	Initial Study
Title of Study:	Examining genetic literacy and capacity for engagement in genetic research among Pacific Islanders
IRB Protocol ID:	2000030094
Submission ID:	2000030094

Research activities associated with this submission are approved and may begin consistent with the terms of IRB approval.

The IRB notes that the PI is sponsoring this multi-center trial and that Yale serves as coordinating center. The Committee reminds the Investigator of their obligations as a sponsor coordinating a multi-center trial. These responsibilities include, but are not limited to, ensuring ongoing IRB approval at other study sites, monitoring adverse events and reporting to the IRB, the FDA, Sponsor, and other bodies that monitor the conduct of the study and retaining copies of this documentation. Approval from the Samoan Ministry of Health Research Committee and the American Samoa Department of Health IRB must be obtained and submitted to the Yale IRB via IRES modification prior to commencing human research activities in Samoa.

The PI is reminded that human subjects research activities cannot commence at the University of Pittsburg until a reliance agreement is approved. Please continue to work with the HRPP External Relations Team at external.reviews@yale.edu.

The PI is reminded to submit a modification when the funding subcontract from the University of Pittsburg is approved to add the grant information to the IRES Funding section.

The IRB understands that non-English speaking patients will be recruited and requires submission and approval of a Samoan version of the consent form (as well as all questionnaires given to subjects) before they are recruited into the study. If languages in addition to Samoan and English are required for consenting a subject(s), materials in

those languages must be developed and submitted. This IRB determination does NOT constitute institutional approval for initiating or resuming in-person research during the COVID-19 pandemic. All research studies that require in-person interactions with research participants whether on campus or off campus (including a research participant's home) require approval from the Human Subject Research Committee (HSRC).

If your research requires in-person interactions with research participants, and you do not already have HSRC approval for this study, you must submit your safety plans through EHS Integrator (https://ehsis.yale.edu/EHSIntegrator/Registration) as soon as possible.

Please read the guidance regarding research activation and reactivation on the Yale website during the COVID-19 pandemic: General Guidelines for Human Subjects Research | Research at Yale. It is your responsibility to comply with institutional requirements, CDC guidelines, state of Connecticut guidelines, and other applicable policies.

See the next pages for important reminders and the list of IRB approved documents.

IMPORTANT REMINDERS:

- This research does not require IRB continuing review.
- You are obligated to submit the following to the IRB:
    - **Modifications**: Changes must be submitted with a modification and approved by the IRB prior to implementation except to eliminate immediate hazards to participants. This includes changes to study procedures, informed consent documents, recruitment activities or study personnel.
    - **Reportable New Information:** Information that requires prompt reporting to the IRB must be done so within 5 days of the PI becoming aware of the event (see Policy 710: Reporting Unanticipated Problems Involving Risks to Subjects or Others, including Adverse Events). This includes potential serious noncompliance, continuing noncompliance, and unanticipated problems to subjects or others.
    - **Closure request** (to end the IRB's oversight) when:
        i. The protocol is permanently closed to enrollment,
        ii. All subjects have completed all protocol related interventions and interactions, and
        iii. Analysis of private identifiable information is completed.
- In conducting this activity, you should refer to and follow the Investigator Manual (HRP-103) as applicable, which can be found in the IRB Library within the IRB system.

IRB APROVED DOCUMENTATION:

• Consent ELSI Objective 2 3.0.pdf, Category: Consent Form;
• ELSI Questionnaire Objective 2.pdf, Category: Study questionnaires, measures, focus groups/interview questions;
• ELSI Questionnaire Objective 1.pdf, Category: Study questionnaires, measures, focus groups/interview questions;
• SubmissionForm_GeneticLiteracy v3.0.doc, Category: IRB Submission Form;
• Consent ELSI Objective 1 3.0.pdf, Category: Consent Form;
• ELSI Questionnaire Objective 3.pdf, Category: Study questionnaires, measures, focus groups/interview questions;
• Semi-Structured Interview Agenda (Objective 3), Category: Study questionnaires, measures, focus groups/interview questions;
• Consent ELSI Objective 3 3.0.pdf, Category: Consent Form;
• Flyer Advertising Text Objective 2.pdf, Category: Recruitment Materials;
• Facebook Advertising Text Objective 2.pdf, Category: Recruitment Materials;
• Social Behavioral_ELSI_Jan25.pdf, Category: IRB Protocol;
• 450ch1internationalresearchfinal_GeneticLiteracy.doc, Category: Other;

Please keep this letter with your copy of the approved protocol documents.

Yale

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October 25, 2021

APPROVAL OF SUBMISSION VIA EXPEDITED REVIEW

Approval Date: 10/25/2021

Investigator:	Nicola Hawley
Type of Review:	Modification / Update
Title of Study:	Examining genetic literacy and capacity for engagement in genetic research among Pacific Islanders
IRB Protocol ID:	2000030094
Submission ID:	MOD00045921

Research activities associated with this submission are approved and may begin consistent with the terms of IRB approval.

The modification request to revise the questionnaire measures to be used in each of the aims, per your request submitted October 14, 2021, is approved.

See the next pages for important reminders and the list of IRB approved documents.

IMPORTANT REMINDERS:

- This research does not require IRB continuing review.
- You are obligated to submit the following to the IRB:
    - **Modifications**: Changes must be submitted with a modification and approved by the IRB prior to implementation except to eliminate immediate hazards to participants. This includes changes to study procedures, informed consent documents, recruitment activities or study personnel.
    - **Reportable New Information:** Information that requires prompt reporting to the IRB must be done so within 5 days of the PI becoming aware of the event (see Policy 710: Reporting Unanticipated Problems Involving Risks to Subjects or Others, including Adverse Events). This includes potential serious noncompliance, continuing noncompliance, and unanticipated problems to subjects or others.
    - **Closure request** (to end the IRB's oversight) when:
        i. The protocol is permanently closed to enrollment,
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IRB APROVED DOCUMENTATION:

- ELSI Questionnaire Objective #1.pdf, Category: Study questionnaires, measures, focus groups/interview questions;
- ELSI Questionnaire Objective #2.pdf, Category: Study questionnaires, measures, focus groups/interview questions;
- ELSI Questionnaire Objective #3.pdf, Category: Study questionnaires, measures, focus groups/interview questions;

Please keep this letter with your copy of the approved protocol documents.

Appendix B Survey Materials

Appendix B.1 Initiation Email for Dissemination

To Whom It May Concern,

My name is Frank Swann, and I am a genetic counseling graduate student at the University of Pittsburgh's Graduate School of Public Health, working together with the Yale School of Public Health as part of my thesis project!

I wanted to reach out to let you know about a new research project from our group and ask if you might be willing to help us distribute a survey link to some of your contacts?

We were recently awarded an NIH grant to examine genetic literacy among Pacific Islander populations in the US, US-affiliated Pacific Islands (USAPIs), and in Samoa. There have been many calls in the genetic literature recently for increased representation of historically underrepresented populations but, as we know from our work in Samoa, there are likely unique considerations for this group that should be explored. With the grant we are expanding some of our ongoing capacity building activities in Samoa and American Samoa, but we have also developed a survey for Pacific Islanders resident in the US and USAPIs.

The survey assesses general knowledge about genetics, attitudes toward testing in clinical settings, and potential barriers and facilitators to genetic testing as part of research. We are hoping that the information generated will be useful to guide those who are considering attempting to recruit Pacific Islanders into genetic studies as well as potential participants, if we can generate educational materials to help them weigh decisions about participation.

The survey link is here: https://poa-redcap.med.yale.edu/surveys/?s=WHTF8C7XMAPHCD3E

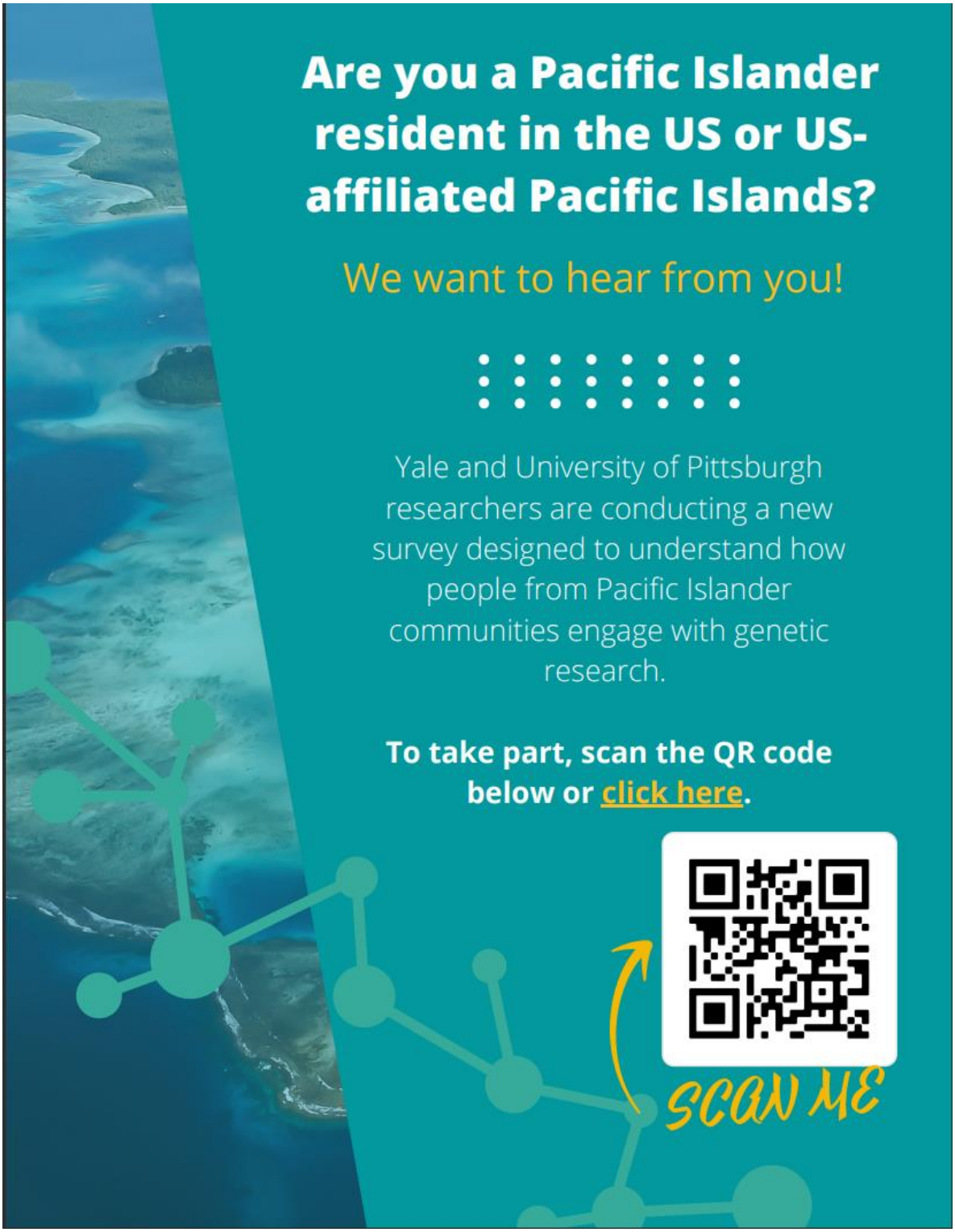
We have been reaching out to our contacts and have also advertised the survey on our Facebook page (https://www.facebook.com/YaleOlaga). We would be so grateful if you could pass the link to anyone in your networks who you think might be interested in completing the survey - the only eligibility criteria are identifying as a Pacific Islander and being resident in the US/USAPIs.

I know you have great connections with our USAPI community on a national scale, and that your goals of achieving wellness in and advocating for these communities align with our own, and it would be wonderful if you could share this survey link or point others towards our social media.

You can reach me at frs19@pitt.edu, where I would be happy to answer any questions that you may have about the project. Alternatively, if there is someone is in your organization that I should reach out to specifically with this request, I would very much appreciate if you can point me in the right direction!

Thank you,
Frank

Appendix B.2 Flyer Invitation



Appendix B.3 REDCAP Complete Survey

Appendix B.3.1 Screening Questions

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ELSI Online Screening Questions

Please complete the questions below to determine whether you are eligible to participate in the study.

Thank you!

Do you identify as having Pacific Islander ethnicity?	◯ Yes ◯ No
Are you at least 18 years of age?	◯ Yes ◯ No
To which Pacific Islander groups do you belong:	☐ Carolinian ☐ Chamorro ☐ Chuukese ☐ Fijian ☐ Guamanian ☐ Hawaiian ☐ Kosraean ☐ Marshallese ☐ Niuean ☐ Palauan ☐ Pohnpeian ☐ Papua New Guinean ☐ Samoan ☐ Tokelauan ☐ Tongan ☐ Yapese ☐ Other
Please specifiy:	_____
Current place of residence:	◯ Mainland USA ◯ Hawaii ◯ American Samoa ◯ Guam ◯ Commonwealth of the Northern Mariana Islands ◯ Federated States of Micronesia ◯ Republic of the Marshall Islands ◯ Palau ◯ Other
Please specify:	_____

If you are resident in the mainland US, please provide your state of residence:	◯ Alabama ◯ Alaska ◯ Arizona ◯ Arkansas ◯ California ◯ Colorado ◯ Connecticut ◯ Delaware ◯ Florida ◯ Georgia ◯ Idaho ◯ Illinois ◯ Indiana ◯ Iowa ◯ Kansas ◯ Kentucky ◯ Louisana ◯ Maine ◯ Maryland ◯ Massachusetts ◯ Michigan ◯ Minnesota ◯ Mississippi ◯ Missouri ◯ Nebraska ◯ Nevada ◯ New Hampshire ◯ New Jersey ◯ New Mexico ◯ New York ◯ North Carolina ◯ North Dakota ◯ Ohio ◯ Oklahoma ◯ Oregon ◯ Pennsylvania ◯ Rhode Island ◯ South Carolina ◯ South Dakota ◯ Tennessee ◯ Texas ◯ Utah ◯ Vermont ◯ Virginia ◯ Washington ◯ West Virginia ◯ Wisconsin ◯ Wyoming
Which of these best describes the general area where you live?	◯ Large city center (urban) ◯ Suburb near a large city (outlying area that surrounds larger cities and metropolitan areas) ◯ Small city/town ◯ Rural area (countryside)

Thank you so much for agreeing to take our survey! We anticipate this survey will take approximately 30 minutes. Upon completion of the questionnaire measures today you will have the chance to opt into a raffle to win one of five $100 gift cards.

Appendix B.3.2 Demographics

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ELSI Demographics

Please complete the survey below.

Thank you!

With which gender identity do you most identify?	_____
How old are you in years?	_____
What is your relationship status?	◯ Never married ◯ Currently married ◯ Separated ◯ Divorced ◯ Widowed ◯ Cohabiting
What is the highest level of education you received?	◯ No formal schooling ◯ Less than primary school ◯ Primary school completed ◯ Secondary school completed ◯ College/University completed ◯ Postgraduate degree
What is your job title?	_____
What is the primary language spoken in your home?	◯ English ◯ Samoan ◯ Tongan ◯ Marshallese ◯ Chamorro ◯ Other
Please specify:	_____
Do you have children? (biological or adopted)	◯ Yes ◯ No
What is your annual household income? (include all sources of income from work, family abroad, pensions, etc.)	_____ (US Dollars)

Appendix B.3.3 Health Conditions

Confidential

ELSI Health Conditions

Have you or your family members ever been diagnosed with any of the following conditions? Please check all that apply.	You	Someone in your family
Asthma	☐	☐
Diabetes	☐	☐
High Blood Pressure (Hypertension)	☐	☐
Obesity	☐	☐
Heart Disease	☐	☐
Problems with memory or clear thinking (e.g. dementia, Alzheimer's)	☐	☐
Infertility	☐	☐
Mental health problems (e.g. depression)	☐	☐
Cancer	☐	☐
Birth defects	☐	☐

Do you currently smoke cigarettes?	○ Yes ○ No
Have you ever had problems with excessive drinking?	○ Yes ○ No
Have you ever had problems with sleep? (e.g. insomnia, sleep disordered breathing, excessive daytime sleepiness)	○ Yes ○ No
Have you ever undergone genetic testing?	☐ Yes - I received testing from a healthcare provider ☐ Yes - I purchased a testing kit (23 and Me, or other providers) ☐ No
Have you ever received genetic counseling?	○ Yes ○ No
Have you ever participated in a scientific research study that involved providing genetic data?	○ Yes ○ No
How often do you have someone help you read hospital materials?	○ Always ○ Often ○ Sometimes ○ Occasionally ○ Never

How often do you have problems learning about your medical condition because of difficulty understanding written information?	◯ Always ◯ Often ◯ Sometimes ◯ Occasionally ◯ Never
How often do you have a problem understanding what is told to you about your medical condition?	◯ Always ◯ Often ◯ Sometimes ◯ Occasionally ◯ Never
How confident are you filling out medical forms by yourself?	◯ Not at all ◯ A little bit ◯ Somewhat ◯ Quite a bit ◯ Extremely

Appendix B.3.4 Genetic Knowledge and Heritability Estimates

Confidential

ELSI Genetic Questionnaire

Genetic Knowledge

These true/false questions will help us understand what you know about genetics. Please answer without Googling!

	True	False
Some diseases are caused by genes, environment, and lifestyle	○	○
A gene is a disease	○	○
You can see a gene with the naked eye	○	○
Healthy parents can have a child with an inherited disease	○	○
A person with an altered (mutated) gene may be completely healthy	○	○
All serious diseases are inherited	○	○
Genes are instructions for making proteins, which help the body grow and work properly	○	○
The child of a person with an inherited disease will always have the same disease	○	○
A gene is a piece of DNA	○	○
Altered (mutated) genes can cause disease	○	○
Genes are inside of cells	○	○
A chromosome contains many genes	○	○
Genes determine traits such as height, eye color, and facial appearance	○	○
A person has thousands of genes	○	○
Identical twins have different sets of genes	○	○
Humans have 20 pairs of chromosomes	○	○
Parents pass both copies of each chromosome to their child	○	○

A genetic test can tell you if you have a higher chance to develop a specific disease	○	○

On a scale of 0-100, please give your best guess about how important genetic differences are in explaining individual differences in the following characteristics/conditions:

Height	0 (Not at all)	50	(Completely) 100
			(Place a mark on the scale above)
School achievement	0 (Not at all)	50	100 (Completely)
			(Place a mark on the scale above)
Eye color	0 (Not at all)	50	100 (Completely)
			(Place a mark on the scale above)
Depression	0 (Not at all)	50	100 (Completely)
			(Place a mark on the scale above)
Motivation	0 (Not at all)	50	100 (Completely)
			(Place a mark on the scale above)
Diabetes	0 (Not at all)	50	(Completely) 100
			(Place a mark on the scale above)
Obesity	0 (Not at all)	50	100 (Completely)
			(Place a mark on the scale above)
Heart disease	0 (Not at all)	50	100 (Completely)
			(Place a mark on the scale above)

Appendix B.3.5 Attitudes Towards Clinical Testing

ELSI Genetic Questionnaire

Did you find those questions hard? In a recent survey of US adults, none of these questions were answered correctly by everyone. Don't worry, some of our researchers got a couple wrong too! Here's some information to help you answer some of the questions that come next.

WHAT IS A GENE?

Genes are the instructions for how our bodies work. Our genes can be found in our cells, where they are packaged in 'chromosomes'. Most of us have 23 pairs of chromosomes. We inherit one of each pair from our mother and one from our father. That's why some diseases run in families, because they can be passed from parent to child. Our whole collection of genes is our 'genome'.

HOW ARE OUR GENES RELATED TO HEALTH?

Genes are made of DNA. DNA has four building blocks. For genes to work correctly, the building blocks, or "DNA sequence", must be in the right order. When there is a difference in the sequence, this is a 'gene variant'. A gene variant may cause the gene to give different instructions to the body. A gene variant might make a disease more likely, and another might make a disease less likely.

Our environment can also change the way our genes work. In some cases our genes can stop giving instructions. In others, it can cause the instructions to no longer be correct. This can impact our health.

Many health conditions are related to our genes. Sometimes just a single gene variant is enough to cause disease. Most diseases (like diabetes and heart disease) are caused by a combination of gene variants and the environment.

You can look back at this information as you answer the survey questions.

Attitudes Toward Clinical Genetic Testing

A genetic test is a test that looks for gene variants. Samples of blood or spit (saliva) are collected for these tests. Your doctor can use a genetic test to understand your risk of disease or make decisions about your care.

The following questions ask about genetic testing used in medical care.

	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
I approve of using genetic testing for early detection of diseases	○	○	○	○	○
The possibility of a genetic test will change one's future	○	○	○	○	○
If a disease cannot be treated, I don't want a genetic test	○	○	○	○	○
I would inform my children about the results of my genetic test for a specific disease	○	○	○	○	○
I would be interested in genetic testing that can give me a medical diagnosis	○	○	○	○	○

I don't want a genetic test to tell me that I am at risk for a certain disease	○	○	○	○	○
I want to know whether my disease is hereditary (passed on from parents to children)	○	○	○	○	○
I would inform my siblings about the results of a genetic test for a specific disease	○	○	○	○	○
I worry about the consequences of genetic testing for being able to get health insurance	○	○	○	○	○
I worry about the consequences of genetic testing for the chances of finding a job	○	○	○	○	○
I would be interested in a genetic test to help me decide if a treatment is helpful for me	○	○	○	○	○
If I had a genetic test done, my family does not need to know about the result	○	○	○	○	○
The idea of a genetic test frightens me	○	○	○	○	○
I would be interested in genetic testing that would give me information that I could use to lower my risk of developing a disease	○	○	○	○	○
Surprise - we just want to make sure you are still with us. Please select the "Totally agree" button for this question!	○	○	○	○	○

Appendix B.3.6 Family History

Confidential

ELSI Genetic Questionnaire

Family History

Your family health history is a collection of health information about you and your family. Sometimes multiple family members can have similar health problems. This could be due to you and your family members:
Sharing the same environment, and/or
Sharing the same lifestyle (like diet), and/or
Sharing the same genetic variants.

Your family health history can help you and your doctor better understand your risk for certain health problems.

The next questions ask how you feel about your family health history.

	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
My doctor should be required to collect family health information in clinical practice	○	○	○	○	○
I can easily recall the health history of most of my relatives.	○	○	○	○	○
Family health history does not have the power to predict my personal health outcomes.	○	○	○	○	○
Family health history collection can help me reduce risks for heritable diseases (diseases that run in my family).	○	○	○	○	○
Collecting family health history is helpful for understanding my own disease risk.	○	○	○	○	○
Collecting family health history is helpful for understanding my family's disease risk	○	○	○	○	○

Have you ever actively collected health information from your relatives for the purposes of developing a family health history?

○ Yes
○ No

If you were approached by researchers and asked to take part in a study that involved giving family health history for genetic research, how likely would you be to participate?

○ Very Likely
○ Likely
○ Unlikely
○ Very unlikely
○ Unsure

Appendix B.3.7 Attitudes Towards Genetic Research

ELSI Genetic Questionnaire

Genetic Research

Health researchers are scientists who study the role of genes in health. In some cases, that information can be used to help diagnose, treat, or prevent disease. Participating in genetic studies involves giving a blood, spit, or other type of sample.

Genetic testing done as part of health research is different from clinical genetic testing. Some ways that it is different include:

1. Genetic research is considered more exploratory than clinical testing.
2. Results of genetic research are usually not given back to participants.
3. It is often unknown whether genetic test results will be helpful in improving health.

The next questions ask about your views on genetic (DNA) research. There are no right answers - only your beliefs and opinions.

General attitudes towards genetic (DNA) research

	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
I think the development of DNA research is hopeful for the treatment of diseases	○	○	○	○	○
God determines wellness, not the results of research	○	○	○	○	○
I think that the development of DNA research is a positive medical progress	○	○	○	○	○
Focusing on genes and biology ignores the role that poverty, inequality, and other social causes play in determining illness	○	○	○	○	○
Genetic research won't benefit all communities equally	○	○	○	○	○
Researchers are not concerned about the welfare of human participants	○	○	○	○	○
Genetic findings will be used to discriminate against minority/marginalized communities	○	○	○	○	○
Genetic research will benefit persons of all economic status	○	○	○	○	○

Knowledge about the genetic background of diseases will help people to live longer	○	○	○	○	○
Genetic research is not useful when health systems are not equipped to offer genetic testing or personalized treatment	○	○	○	○	○
Researchers are motivated by their own career goals	○	○	○	○	○
Researchers are motivated by their desire to help people	○	○	○	○	○
Genetic research will benefit persons of all races and ethnicities	○	○	○	○	○

Likelihood of Participation in Genetic Research

The next questions ask about how likely you would be to take part in health research studies that involve genetic testing. They also ask whether you would allow your children to participate.

In general, if you were approached by researchers and asked to take part in a genetic research study, how likely would you be to participate?

- ○ Very Likely
- ○ Likely
- ○ Unlikely
- ○ Very unlikely
- ○ Unsure

Please tell us the reason for your response: _____

You are doing great! Thank you so much for taking the time to complete this survey. You are about 50% done!

In general, if you were approached by researchers who wanted to enroll your child in a genetic study, how likely would you be to give your permission for them to participate?

- ○ Very Likely
- ○ Likely
- ○ Unlikely
- ○ Very unlikely
- ○ Unsure

Please tell us the main reason for your response: _____

Most cats have 4 legs, but please check the box next to the number 22 so we know you are still with us.

- ☐ 3
- ☐ 22

If you were asked, would you consider participating, and/or would you consider allowing your child to participate, in genetic research that was specifically focused on the following:

	I would consider participating	I would consider allowing my child to participate
Asthma	☐	☐

Diabetes	☐	☐
Blood pressure	☐	☐
Obesity	☐	☐
Heart Disease	☐	☐
Memory and clear thinking (e.g. dementia, Alzheimer's Disease)	☐	☐
Sleep	☐	☐
Fertility	☐	☐
Alcoholism	☐	☐
Cigarette smoking	☐	☐
Mental Health (e.g. depression)	☐	☐
Cancer	☐	☐
Birth defects	☐	☐
Preterm (early) birth	☐	☐
Ancestry/Geneaology	☐	☐

If you were asked to give a genetic sample, would you rather provide a blood sample (from a blood draw) or a saliva (spit) sample?	◯ Blood ◯ Saliva (spit) ◯ Either would be OK ◯ I would not participate/provide a sample

Some research that focuses on childhood diseases uses tissues from birth. Would you be willing to give a sample of:

	Yes	No
Umbilical Cord Blood	◯	◯
Placenta Tissue	◯	◯

If you were making the decision to participate in a research study, how important would the following be to you?

	Very important	Somewhat important	Not very important	Not at all important
The reputation of the research institution or researcher	◯	◯	◯	◯
The value of incentives (for example, gift cards or cash)	◯	◯	◯	◯
That it does not cost me anything to participate	◯	◯	◯	◯
The research must be meaningful to me personally	◯	◯	◯	◯
The research will improve my health	◯	◯	◯	◯
The research will provide information I can use to improve my health	◯	◯	◯	◯

The research will provide information about me I didn't know	○	○	○	○
The research could benefit my family	○	○	○	○
The research could benefit people I know	○	○	○	○
The research could benefit society	○	○	○	○
People I know have participated or are participating	○	○	○	○
The research focuses on a medical condition that is of importance to me and/or my family	○	○	○	○
That my community was consulted in the design of the research study	○	○	○	○
That someone in my government had reviewed the study and allowed it to proceed	○	○	○	○
I will receive a personal report about my individual genetic risks and/or benefits	○	○	○	○
Data and samples are stored securely	○	○	○	○
The research team includes scientists that come from my own community	○	○	○	○
Another reason (please specify below)	○	○	○	○

Please specify: _____

Below is a list of concerns that people have raised about participating in genetic research. Please tell us how important each of these things would be if you were making a decision to participate:

	Very important	Somewhat important	Not very important	Not at all important
Concerns related to potential privacy issues about my data	○	○	○	○
Concerns related to not knowing how I will feel about my results	○	○	○	○

Concerns related to learning about my disease risk from genetic test results	○	○	○	○
Concerns related to the quality and reliability of the testing lab and the results	○	○	○	○
Concerns about the time commitment required	○	○	○	○
Will not benefit my community equitably (others will benefit more)	○	○	○	○
Concerns that my data will be used for other purposes without my knowledge	○	○	○	○
Concerns that the biological specimens I provide (blood or saliva) will not be stored securely	○	○	○	○
Concerns about whether the research team are trustworthy	○	○	○	○
Other concerns	○	○	○	○

Please specify: _____

Appendix B.3.8 Return of Results and Secondary Finding Preferences

Confidential

ELSI Genetic Questionnaire

Return of Results

Sometimes people who take part in research studies can choose to get certain genetic test results returned. The next questions ask about if and how you would prefer to receive results of genetic testing done for research purposes.

If you decided to participate in genetic testing for health-related research purposes, would you want your results returned to you?	○ Yes, I would want to receive results that I could do something about ○ Yes, I would want to receive any results related to my health (even if the result would tell me about a health risk that I could not do anything about) ○ No, I would not want to receive any results
This is another attention check question - please select the box that says "grass"	☐ grass ☐ sky

Please tell us if you would want to receive the results from your participation in genetic research for the following:

	Yes	No
Asthma	○	○
Diabetes	○	○
Blood Pressure	○	○
Obesity	○	○
Heart Disease	○	○
Memory and Clear Thinking (e.g. dementia, Alzheimer's Disease)	○	○
Sleep	○	○
Fertility	○	○
Alcoholism	○	○
Cigarette smoking	○	○
Mental Health Conditions (e.g. depression)	○	○
Cancer	○	○
Birth defects	○	○
Preterm (early) birth	○	○
Ancestry/Genealogy	○	○

If you participated in health research, who should be able to contact you and tell you your genetic results? (Check all that apply)	☐ Member of the research study team ☐ Genetics specialist ☐ My doctor

Secondary findings are results that are not related to the original purpose of the research. For example, suppose you join a research study that is looking at genes related to heart disease. When the researchers look at your DNA, they do not find a gene variant related to heart disease. But, they do find evidence that you are at risk for a health condition that they were not looking for, like diabetes. This is an example of a secondary finding.

Would you like to hear about secondary findings concerning your health, if they are related to an illness that IS treatable? (Select One):	◯ Yes ◯ No ◯ Unsure
Would you like to hear about secondary findings concerning your health, if they are related to an illness that is NOT treatable? (Select One):	◯ Yes ◯ No ◯ Unsure
Would you like to hear about secondary findings if they were related to a disease you do not have, but that you could pass on to your children? (Select One):	◯ Yes ◯ No ◯ Unsure

There are only two sections left! Almost done! Thank you so much!

Appendix B.3.9 Sample Storage and Sharing Preferences

Confidential

ELSI Genetic Questionnaire

Sample Storage

When you give a sample (like blood, spit, or other) for genetic research, your sample is sent to the location where specialized laboratory work can be done. This may mean that samples are moved outside of the community that gave them. An example would be sending samples from Tonga to the United States for research to be done.

After the research study is finished, there are often left-over samples. Different actions can be taken with these samples. The samples could be stored for future use or destroyed. The samples can be stored for different lengths of time. They could be used again by the same researchers or different researchers.

Sometimes when samples are stored they are 'de-identified.' This means that any information that might link the sample to you is removed. Instead, the sample is given a study ID number. The original researchers have access to the records that link your information to the study ID number, but this is kept separate from the samples.

The next questions ask about how you would prefer your sample to be handled if you took part in genetic research.

It is often unclear who 'owns' your samples after you donate blood or spit for research. Who do you think the samples belong to? (Select One):	◯ Me, the participant ◯ The research team ◯ The institution (for example, university or hospital) that the researchers work for ◯ Someone else
As the participant, I want the option to withdraw my sample from the study.	◯ Yes ◯ No
Please specify:	_____
If some of your sample remains after the main research question has been asked, what would you prefer happened to it? (Select One):	◯ The remaining sample should be thrown out/destroyed ◯ Any remaining sample should be returned to me ◯ Researchers should be allowed to keep remaining samples for a set period of time ◯ Researchers should be allowed to keep remaining samples indefinitely
How long should researchers be able to keep the remaining samples?	_____
If researchers are allowed to keep your remaining samples, how would you prefer they use your sample? (Select All That Apply):	☐ To answer future questions related to the original study's aims only (for example, if the original study looked at one gene related to heart disease, remaining samples may be used to look at other genes related to heart disease) ☐ To answer future questions related to other health conditions ☐ To answer future questions about other behaviors or environmental factors related to health (for example, exposure to environmental toxins, cigarette smoking or alcohol use)
Are there any special considerations/beliefs about biological samples (blood, saliva, placenta) in your community that genetic researchers should be aware of when they think about best practices for collection and long term storage?	_____

How much do you agree with the following statements about permitting access to the samples by other researchers?	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
Access to my samples should be restricted to only the original research team that collected them	○	○	○	○	○
After their use for the original research question, my de-identified samples can be shared with other researchers as long as they are asking questions about the same health condition as the original researchers	○	○	○	○	○
After their use for the original research question, my de-identified samples can be shared with other researchers for the purpose of looking at other health conditions or environmental/behavioral factors that could impact health	○	○	○	○	○
After their use for the original research question, my de-identified samples can be shared with other researchers for the purpose of looking at non-health related questions, like ancestry/genealogy	○	○	○	○	○

How much do you agree with the following statements about who has the authority to permit access to the samples to other researchers?	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
If my samples are being used for other research questions, someone should recontact me personally to ask my permission or give me the option to opt out	○	○	○	○	○
The original research team should be able to make decisions about who else has access to my samples	○	○	○	○	○

If a researcher wants to use my samples for other research questions, I would be comfortable with representatives from my community (a research review board, for example) making decisions on behalf of me and all of the other participants in the original study	○	○	○	○	○

Do you trust health researchers to use your samples only for the purposes to which you consented?

○ Yes
○ No
○ Unsure

Do you trust health researchers to keep your samples and medical information confidential or private?

○ Yes
○ No
○ Unsure

Appendix B.3.10 Preferences for Sharing of Research Data

ELSI Genetic Questionnaire

Sharing of Research Data

When genetic information is studied, it provides us with a lot of information, or data. Some examples of this data include:
The sequences of some or all of your genes
The variants that are found in your genes
How many copies of a particular gene variant you have

These data are usually linked to other information about you that you gave to the researchers. This other information could include:
Age
Education level
Health information
Information about your lifestyle

Usually, the data from all participants in a research study are combined into one set of data, this is what we mean when we use the term "the dataset" below; your data combined with that of other participants in the study. This dataset can sometimes be shared with other researchers (if you gave permission when you joined the study).

When the data is shared with others, it is usually de-identified. This means that any extra information that might link your genetic data to you is removed. However, each person has their own unique set of genetic information. This means that there is always some risk that your genetic data could be linked to you. This risk increases with the amount of information researchers have about you.

The next questions ask you to think about data that might be generated from a research study you participate in. Think about your opinions on who should be responsible for and have access to the study dataset, which would include your de-identified data.

How much do you agree with each of the following statements about permitting access to the data set to other researchers?

	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
Access to the data set should be restricted to only the original research team that collected them	○	○	○	○	○
After their use for the original research question, the data set, including my deidentified data, can be shared with other researchers as long as they are asking questions about the same health condition as the original researchers	○	○	○	○	○

After their use for the original research question, the data set, including my deidentified data, can be shared with other researchers for the purpose of looking at other health conditions, environmental or behavioral factors	○	○	○	○	○
After their use for the original research question, the data set, including my deidentified data, can be shared with other researchers for the purpose of looking at non-health related questions, like ancestry/genealogy	○	○	○	○	○
Data can be shared with organizations responsible for overseeing the conduct of research in my community, for example a Department or Ministry of Health	○	○	○	○	○

How much do you agree with the following statements about who has the authority to permit access to the data set to other researchers?	Totally agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Totally disagree
If my de-identified data are being used for other research questions, someone should recontact me personally to ask my permission or give me the option to opt out	○	○	○	○	○
The original research team should be able to make decisions about who else has access to the data set, including my de-identified data	○	○	○	○	○

If a researcher proposes to use the data set, including my de-identified data, for other research questions, I would be comfortable with representatives from my community (a research review board, for example) making decisions on behalf of me and all of the other participants in the original study	○	○	○	○	○

Appendix B.4 Survey Primer Text

Appendix B.4.1 Genetic Knowledge

These true/false questions will help us understand what you know about genetics. Please answer without Googling!

[…SURVEY SECTION…]

Did you find those questions hard? In a recent survey of US adults, none of these questions were answered correctly by everyone. Don't worry, some of our researchers got a couple wrong too! Here's some information to help you answer some of the questions that come next.

WHAT IS A GENE?

Genes are the instructions for how our bodies work. Our genes can be found in our cells, where they are packaged in 'chromosomes'. Most of us have 23 pairs of chromosomes. We inherit one from our mother and one from our father. That's why some diseases run in families. Our whole collection of genes is our 'genome'.

HOW ARE OUR GENES RELATED TO HEALTH?

Genes are made of DNA. DNA has four building blocks. For genes to work correctly, the building blocks, or "DNA sequence", must be in the right order. When there is a difference in the sequence, this is a 'gene variant'. A gene variant may cause the gene to give different instructions to the body. A gene variant might make a disease more likely, and another might make a disease less likely.

Our environment can also change the way our genes work. In some cases our genes can stop giving instructions. In others, the instructions are no longer correct. This can impact our health.

Many health conditions are related to our genes. Sometimes just a single gene variant is enough to cause disease. Most diseases (like diabetes and heart disease) are caused by a combination of gene variants and the environment.

You can look back at this information as you answer the survey questions. If you need to, just click to read again.

Appendix B.4.2 Attitudes Toward Clinical Genetic Testing

A genetic test is a test that looks for gene variants. Samples of blood or spit (saliva) are collected for these tests. Your doctor can use a genetic test to understand your risk of disease or make decisions about your care. The following questions ask about genetic testing used in medical care.

[…SURVEY SECTION…]

Appendix B.4.3 Family History

Your family health history is a collection of health information about you and your family. Sometimes multiple family members can have similar health problems. This could be due to you and your family members:

1.Sharing the same environment, and/or

2.Sharing the same lifestyle (like diet), and/or

3.Sharing the same genetic variants.

Your family health history can help you and your doctor better understand your risk for certain health problems. The next questions ask how you feel about your family health history.

[…SURVEY SECTION…]

Appendix B.4.4 Genetic Research

Health researchers are scientists who study the role of genes in health. In some cases, that information can be used to help diagnose, treat, or prevent disease. Participating in genetic studies involves giving a blood, spit, or other type of sample.

Genetic testing done as part of health research is different from clinical genetic testing. Some ways that it is different include:

1. Genetic research is considered more exploratory than clinical testing.

2. Results of genetic research are often/usually not given back to participants.

3. It is often unknown whether genetic research test results will be helpful in improving health.

The next questions ask about your views on genetic research. There are no right answers - only your beliefs and opinions.

[…SURVEY SECTION…]

The next questions ask about how likely you would be to take part in health research studies that involve genetic testing. They also ask whether you would allow your children to participate.

[…SURVEY SECTION…]

Appendix B.4.5 Motivations for Participation in Genetic Research

[…SURVEY SECTION…]

- No Primer -

Appendix B.4.6 Return of Results

Sometimes people who take part in research studies can choose to get certain genetic test results returned to them. The next questions ask about if and how you would prefer to receive results of genetic testing done for research purposes.

[…SURVEY SECTION…]

Secondary findings are results that are not related to the original purpose of the research. For example, suppose you join a research study that is looking at genes related to heart disease. When the researchers look at your DNA, they do not find a gene variant related to heart disease. But, they do find evidence that you are at risk for a health condition that they were not looking for, like diabetes. This is an example of a secondary finding.

[…SURVEY SECTION…]

Appendix B.4.7 Sample Storage

When you give a sample (like blood, spit, or other) for genetic research, your sample is sent to the location where specialized laboratory work can be done. This may mean that samples are moved outside of the community that gave them. An example would be sending samples from Tonga to the United States for research to be done.

After the research study is finished, there are often left-over samples. Different actions can be taken with these samples. The samples could be stored for future use or destroyed. The samples can be stored for different lengths of time. They could be used again by the same researchers or different researchers.

Sometimes when samples are stored, they are ‘de-identified.’ This means that any information that might link the sample to you is removed. Instead, the sample is given a study

ID number. The original researchers have access to the records that link your information to the study ID number, but this is kept separate from the samples.

The next questions ask about how you would prefer your sample to be handled if you took part in genetic research.

[…SURVEY SECTION…]

Appendix B.4.8 Sharing of Research Data

When genetic information is studied, it provides us with a lot of information, or data. Some examples of the data include:

- The sequences of some or all of your genes
- The variants that are found in your genes
- How many copies of a particular gene variant you have

These data are usually linked to other information about you that you gave to the researchers. This other information could include:

- Age
- Education level
- Health information
- Information about your lifestyle

Usually, the data from all participants in a research study are combined into one set of data, this is what we mean when we use the term “the dataset” below; your data combined

with that of others in the study. This dataset can sometimes be shared with others (if you gave permission when you joined the study).

When the data is shared with others, it is usually de-identified. This means that any extra information that might link your genetic data to you is removed. However, each person has their own unique set of genetic information. This means that there is always some risk that your genetic data could be linked to you. This risk increases with the amount of information researchers have about you.

The next questions ask you to think about data that might be generated from a research study you participate in. Think about your opinions on who should be responsible for and have access to the study dataset, which would include your de-identified data.

[…SURVEY SECTION…]

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