Investigation of Medicine Adherence in the Samoan Population

by

Samantha Kay Pettersen

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This essay is submitted

by

Samantha Kay Pettersen

on

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and approved by

Essay Advisor:

Samantha Rosenthal, PhD, Assistant Professor, Department of Oral and Craniofacial Sciences, Center for Craniofacial and Dental Genetics, University of Pittsburgh School of Dental Medicine

Essay Reader: Ryan Minster, PhD, MSIS, Assistant Professor, Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh

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Samantha Pettersen MPH

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Abstract

Independent Samoa is approaching a public health crisis with high rates of chronic disease along with disproportionately high rates of obesity. Chronic diseases have underlying genetic factors in the development of disease and cause long term health complications. Chronic diseases like heart disease, hypertension, and hypercholesterolemia require lifestyle adjustments and long-term usage of medicine in order to treat disease symptoms. However, many patients have trouble remaining adherent to needed medicine which can cause health complications and higher health costs in the future. Using data gathered from health-related questionnaires from the Obesity, Lifestyle, and Genetic Adaptations (OLaGA; n. *life* in Samoan) study group, medicine adherence for heart disease, hypertension, and hypercholesterolemia was investigated. The trends for medicine non-adherence for chronic diseases can lead to new knowledge that informs the development of interventions that improve medicine adherence. This research shows that of the study participants with chronic disease, the total non-adherence rate was 24.3%, with hypercholesterolemia having a rate of 33.3% of non-adherence, followed by hypertension (22.3%) and heart disease (22.7%). Females were more non-adherent for heart disease (60%) and hypertension (52.6%) medicines while males were more non-adherent (66.7%) for hypercholesterolemia medicines. With these trends in mind, the existing health intervention programs in Samoa were examined for their ability to address medicine non-adherence, and possible additions to the programs were suggested to increase medicine adherence in Samoa.

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Preface

I would like to thank the following individuals for their help and support was essential in the creation of this document. To Samantha Rosenthal in creating this project from the ground and her unwavering support in every aspect of this document. To Ryan Minster for helping in the details of this project and providing information. To Jon Chernus for his expertise in R which helped me greatly in my data analysis. To Dr. Martha Terry for her expertise in looking at qualitative data.

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1.0 Introduction

Independent Samoa has a high rate of chronic diseases, and estimates have shown that the Samoan population has disproportionately high rates of obesity, along with hypertension and heart disease (Samoa, 2018). These chronic diseases cause long term health complications and high mortality rates. Chronic diseases often have underlying genetic factors in the development of disease, in combination with environmental ones. Chronic diseases like heart disease, hypertension, and hypercholesterolemia require lifestyle adjustments and long term use of medicine in order to manage the symptoms of the disease (Baroletti & Dell'Orfano, 2010; J. A. Cramer, Benedict, Muszbek, Keskinaslan, & Khan, 2008; Gatwood & Bailey, 2014). Medicine adherence, defined as a patient conforming to a medicine regimen, is an important aspect of chronic disease care (Vermeire, Hearnshaw, Van Royen, & Denekens, 2001). Patients that are non-adherent to needed medicines are shown to have poorer health outcomes and may suffer long lasting health consequences (Osterberg & Blaschke, 2005). There is little known about the rates of medicine adherence in lower middle-income countries (LMICs) like Samoa. The goal of this project is to learn more about the rates of medicine adherence through previous research done by the Samoan Obesity, Lifestyle and Genetic Adaptations Study Group (OLaGA). The OLaGA study group has been researching genetic adaptation and health outcomes in the Samoan people via basic health measurements (e.g., height, weight, and blood pressure), health-related questionnaires, and genotyping of research participants; therefore, we have data about the health practices of the Samoan people. Investigating the reasons of medicine non-adherence for chronic diseases can lead to new knowledge that informs the development of interventions that improve medicine adherence. Samoa's Ministry of Health has created a policy plan to reduce the burden of chronic diseases in

the country, informed in part by their research partnerships that aim to understand the origins of obesity and obesity related diseases. Knowledge about the adherence to medicine can help Samoa develop and implement interventions for their goal of strengthening referral systems for management of non-communicable diseases (Samoa, 2018).

2.0 Background of Independent Samoa

Independent Samoa consists of two large islands, Upolu and Savaii, and eight small islets that reside south of the equator, in the Pacific Ocean. The islands are separated into three census regions, Apia urban area, Northwest Upolu, and the rest of Upolu. It is geographically and politically separate from American Samoa, which resides to the east. However, American Samoa and Independent Samoa have similar cultural practices. In 2020, there were around 200,000 people in Samoa, with over 75% living in more rural areas (Population & Demography Indicator Summary, 2022). Samoa has been defined as a lower middle income country by the world bank ("Samoa," 2022). Most of the people in Samoa work in agriculture, and on average, have a 7th grade reading level ("Samoa," 2022). Obesity has been rising in Samoa. In 1978, the obesity prevalence was 27.7% for men and 44.4% for women. In 2013, the rate of obesity in Samoa was 53.1% and 76.7% in men and women, respectively (Samoa, 2018). The Ministry of Health in Samoa has also named cardiovascular diseases as a significant disease burden in Samoa (Samoa, 2018).

2.1 Hospital System in Samoa

The hospital system is comprised of one main hospital and a few district hospitals spread around the two islands. Previously there were 48 doctors for 100,000 people; now there are full time doctors at all district hospitals ("Health systems in Samoa," 2020). As Samoa improves in regard to infectious diseases, the rates of chronic diseases (also known as non-communicable

diseases) are rising. This causes unique strain on healthcare systems (Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, 2011). For example, a study of the rate of people who had hypertension in Samoa and were not diagnosed (Fraser-Hurt et al., 2021) identified that the Samoan healthcare system has obstacles for patients' access to care for non-communicable diseases. Many people reported being unable to pay for healthcare (e.g. medicine or reoccurring testing), feeling no need to get their blood pressure tested, fear of diagnosis, lack of education, or poor communication between the patient and provider (Fraser-Hurt et al., 2021).

Personal perceptions of the Samoan health care system show that many patients have long wait times, with the hospital having little resources and few healthcare staff, and being too expensive (Bollars, Sørensen, de Vries, & Meertens, 2019).

2.1.1 Traditional Medicine usage in Samoa

Information on traditional medicine usage by the people of Samoa is hard to find. What is known is that many Samoan people will see a traditional healer to treat a variety of illnesses (Kaholokula, Saito, Mau, Latimer, & Seto, 2008). Traditional healers (*fofō)* in Samoa can be any gender or age. A traditional healer is defined as a person who has culturally-based training to diagnose illnesses and is experienced in the traditional massage *fofō* and/or treating illness with herbal remedies (MacPhearson & MacPhearson, 1990). This training is similar to an apprenticeship where a family member or interested member of the community works with the *fofō* for years; this knowledge transition typically takes around 5 years (MacPhearson & MacPhearson, 1990). The role of a traditional healer takes both the physical and social health of the patient into account during their treatment. The use of a traditional healer is sometimes in

conjunction with visits with a Western medicine doctor (Krosch, 2010). Many Samoan people view illnesses as indigenous to Samoa, *ma'i samoa,* or those from Europe, *ma'i pālagi*. These different illnesses are thought to require different doctors, so it is common for Samoan people to visit either a traditional healer or Western doctor. Many times, if the illness is *ma'i pālagi*, a healer will recommend visiting the Western doctors. There is also belief from Western medicine doctors that the use of *fofō* typically does not interfere with their work and for some chronic or terminal diagnoses like cancer, may be psychologically helpful (MacPhearson & MacPhearson, 1990). Traditional medicine is still commonly used for chronic diseases. It is a common viewpoint in Samoa that chronic diseases like heart disease are ailments that can be immediately relieved and treated more effectively with traditional healing massages (Bollars et al., 2019). This is also an aspect in sociocultural norms impacting the solicitation of healers, with many Samoan people self-diagnosing before seeking out either a traditional healer or Western doctor (MacPhearson & MacPhearson, 1990).

2.1.2 Cultural Views on Health in the Samoas

Many Samoans believe that illness comes from parting from the Samoan way of life (*fa'a sāmoa*) (Puaina, Aga, Pouesi, & Hubbell, 2008). *Fa'a Sāmoa* is a compilation of the Samoan language, practices, and overall culture of Samoans, which is the base guidance of their actions and approaches to the world around them (MacPhearson & MacPhearson, 1990). In an interview of American Samoans, many participants mentioned that when they were young, diseases like diabetes and cancer did not exist. Thus, there is a belief that illnesses such as cancer were brought to Samoa by Westerners (people not originally from Samoa). The daily habits of the American Samoan people also were examined. Many people surveyed agreed that an unhealthy diet along

with tobacco and alcohol use contributed to disease. However, there is also concern that newer refrigerated foods contribute to the "new" illnesses they face today. Interestingly, the knowledge that tobacco and alcohol cause disease is rooted in the idea of these products being "not from Samoa". Traditional products like traditional Samoan cigarettes and kava, a drink considered to be psychoactive, arguably have similar health affects to tobacco and alcohol, but are considered by the Samoan people not to cause disease as traditional cigarettes and kava are "from Samoa" (Hubbell, Luce, & McMullin, 2005).

2.2 Chronic Diseases of Interest

Chronic disease is the term used to define disease that persists for a long time. This terminology indicates diseases that typically take time to be diagnosed, and once diagnosed, usually require long-term treatment (Preventing chronic diseases: a vital investment, 2005). Chronic diseases are a large issue in low and middle income countries (LMICs) as chronic diseases occur at lower ages compared to higher income countries (Preventing chronic diseases: a vital investment, 2005). This issue is compounded by the high rates of infectious diseases in LMICs. Risk factors for chronic diseases include low physical activity, consumption of alcohol or cigarettes, poor diet, high blood sugar, and obesity (Hajat & Stein, 2018). One such chronic disease, cardiovascular disease, is the leading cause of death in many countries. In 2005 it accounted for 30% of all deaths globally (Preventing chronic diseases: a vital investment, 2005). Chronic diseases are often debilitating to those affected due to the need for ongoing medical interventions, which typically affect a person's quality of life. Risk factors like high blood pressure and high cholesterol are labeled as intermediate risk factors for chronic diseases like heart disease

(Preventing chronic diseases: a vital investment, 2005). The Samoan population, in particular, has a high prevalence of chronic diseases. In 2019, 66% of deaths were due to non-communicable diseases ("Global Burden of Disease: Global both sexes , All Ages, 2019, Deaths," 2019). The chronic diseases this essay will examine are heart disease, hypertension, and hypercholesterolemia. The high obesity rates amongst the Samoan population and interconnectedness amongst these chronic diseases make them a priority of investigation.

2.2.1 Heart Disease

Heart disease is an overall term to describe several types of heart conditions (Virani et al., 2021). Heart disease is developed due to a combination of environmental and genetic factors, and the genetic origins of heart disease have begun to be studied more thoroughly. Studies have determined that different forms of cardiovascular disease have different forms of inheritance, either Mendelian or complex (Kathiresan & Srivastava, 2012). Long QT syndrome, which is caused by mutations in genes like *KCNQ1*, *KCNH2*, or *SCN5A*, is one such form of heart disease that is inherited in a Mendelian fashion. Marfan's syndrome, a disease that affects the connective tissue in the body, leading to mitral valve prolapse or heart murmurs, is caused by mutations in the *FBN1* gene (Faivre et al., 2007; M.Alders, 2018) and is also inherited in a Mendelian pattern. Myocardial infarction (MI), however, has complex inheritance, with the genes *PCSK9*, *APOE*, *LDLR*, and *APOB* associated with increased risks of myocardial infarctions, but not necessarily causal for MI (Erdmann, Linsel-Nitschke, & Schunkert, 2010; O'Donnell & Nabel, 2011). In the early stages of heart disease, a patient may have no symptoms. As the condition progresses, some symptoms such as chest pain, chest tightness, shortness of breath, pain or weakness in legs or arms, and pain in the neck, jaw, back, or abdomen may develop (Virani et al., 2021). In the most severe

of cases, heart disease leads to death. Treatment for heart disease typically includes a regimen of antianginal drugs along with disease modifying agents such as hypolipidemic, antithrombotic, and renin-angiotensin blocking therapies (Antman & Braunwald, 2020). The earlier heart disease is diagnosed, the better the results from treatment. Many of these medicines are required for the rest of the person's life, and more medicines may be added or dosage changed following a patient's response to the drugs. Approximately 60% of patients in the United States diagnosed with heart disease exhibit some semblance of medicine non-adherence in the their long term treatment (Baroletti & Dell'Orfano, 2010).

2.2.2 Hypertension

Hypertension, commonly known as high blood pressure, is a condition where the force from blood exerted on the blood vessels is too high leading to thickening of the arteries which can cause a heart attack, stroke, or death. Systolic blood pressure is the pressure on your arteries while your heart beats; diastolic blood pressure is the pressure in the arteries between heart beats. Blood pressure is a ratio of systolic blood pressure to diastolic blood pressure, measured in mmHg (National High Blood Pressure Education, 2004). Family studies have determined that hypertension has some genetic factors, mostly polygenic in nature. However, there are rare cases of severe hypertension that are due to monogenic inheritance (Padmanabhan, Caulfield, & Dominiczak, 2015). Hypertension is diagnosed when a patient's blood pressure is consistently 130/80 mm Hg or higher (Whelton et al., 2018). Typically, people with high blood pressure do not exhibit many symptoms and only find out they have high blood pressure through doctor's visits. However, when symptoms show, often when the blood pressure is dangerously high, a patient may exhibit early morning headaches, irregular heart rhythms, nausea, vomiting, confusion, anxiety,

chest pain, and tremors (Whelton et al., 2018). Complications from untreated hypertension can include heart attack, heart failure, chest pain, kidney damage, and sudden death. Treatment for hypertension includes regular checkups to measure the blood pressure and antihypertensive medicines like thiazide agents, angiotensin-converting enzyme inhibitor long acting dihydropyridine or (ACEi)/ angiotensin II- receptor blocker (ARB) (National High Blood Pressure Education, 2004; "WHO Guidelines Approved by the Guidelines Review Committee," 2021).

2.2.3 Hypercholesterolemia

Hypercholesterolemia has a large genetic contribution which affects disease risk. Familial hypercholesterolemia (FH) is a monogenic disorder that affects approximately 1 in 250 people, with mutations causing the disease typically occurring in the LDL receptor gene. Polygenic hypercholesterolemia is caused by many underlying genetic factors combined with associated high risk environmental factors such as sedentary lifestyle, and unhealthy diet (Ibrahim, Asuka, & Jialal, 2021). The disease is characterized by high cholesterol levels and increases the risk of coronary heart disease. Measuring deaths directly due to hypercholesterolemia or high cholesterol is almost impossible due to the disease being risk factors for stroke and heart disease, with the former and heart attack often recorded as the immediate cause of death (Ibrahim et al., 2021). A person is diagnosed with high cholesterol when their total cholesterol levels are 240 mg/dL and above (Ibrahim et al., 2021). High cholesterol can cause fatty deposits to develop within blood vessels in the body which can make it difficult for blood to flow though the arteries. This deposits can break off an later form a clot that can result in a heart attack, stroke, or even death (Virani et al., 2021).Like high blood pressure, individuals with high cholesterol do not show symptoms (Ibrahim et al., 2021). Typically, a person is unaware of having high cholesterol until blood tests are done.

Treatment for high cholesterol requires long term use of medicines such as statins, bempedoic acid, cholesterol absorption inhibitors, bile-acid-binding resins, PCSK9 inhibitors, or a combination of these medicines (McPherson, 2018; Tomlinson et al., 2018).

2.3 Medicine Non-Adherence

The World Health Organization has identified medicine non-adherence as a priority health problem (Burkhart & Sabaté, 2003). Medicine adherence is essential in the treatment of chronic disease as non-adherence is associated with poor health outcomes (Osterberg & Blaschke, 2005). In 2003, approximately 50% of people in developed countries adhered to their medicine regimen, and there is no evidence that this rate has increased in the past 20 years (Burkhart & Sabaté, 2003; Kleinsinger, 2018). Non-compliance in situations with chronic disease often cause the patient to experience severe consequences, including worsening of disease conditions and death. Patients who are non-adherent in their medicine regime often fall into a cyclical pattern of medicine regimens. The increasing severity of symptoms due to untreated conditions require an increase of medicine intake. Which, in turn, makes it increasingly hard for patients to comply to their medicine and symptoms will worsen as they are left untreated (Seng, Tan, Yeam, Htay, & Foo, 2020).

Literature describing medicine usage in patients will use the terms “compliance” or “adherence”. Compliance was the original term created in the 1900’s to describe a patient’s non-conforming to practitioner advice. Patients who did not comply were often seen as an untrustworthy and in need of stricter guidance (Chakrabarti, 2014). Currently, adherence is preferred to describe a patient conforming to a medicine regimen. Typically in research studies, adherence is defined as taking 80% or more of prescribed medicine doses (Kleinsinger, 2018).

Compared to compliance, adherence is regarded as a more holistic term, accounting for external issues that may impact patients' abilities to maintain their medicine regimen (Vermeire et al., 2001). The terminology adherence allows for the issue of non-compliance to be viewed as a possible societal failing and not purely the patient's fault. Their meanings are similar, and the change in terminology over time show medicine's movement towards understanding extenuating factors behind a patient's medicine non-adherence. While the distinction between these two terms is important, this paper will use the terms medicine compliance and medicine adherence interchangeably.

2.3.1 Economic Impact of Medicine Non-Adherence

Studies show that the overall cost of healthcare decreases when patients adhere to their medicine regimen. In the United States, there are 125,000 deaths and $100 billion USD in health care costs annually due to medicine non-adherence (Kleinsinger, 2018; Osterberg & Blaschke, 2005). A systematic review of economic costs of medicine non-adherence of various studies across the world, covering the United States, Canada, United Kingdom, Europe, and Asia (Cutler, Fernandez-Llimos, Frommer, Benrimoj, & Garcia-Cardenas, 2018) found that the average cost of non-adherence per patient ranged from $949 to $52,341 USD. In an investigation of disease-specific medicine non-adherence, cardiovascular disease (in this study, defined as hypertension, hypercholesterolemia, and chronic heart failure) showed that the annual cost of non-adherence per patient ranged from $3347 to $19,472 USD. Medical costs were higher for the hypertension and hypercholesterolemia non-adherent groups. The majority of studies in this meta-analysis were in high income countries. The economic impact of medicine non-adherence in LMIC countries has not been researched extensively, however, there has been research to confirm that in Samoa,

priority non-communicable diseases like cardiovascular disease accounts for 23% of all health care spending. Secondary findings from the economic spending research suggest that medicine utilization for non-communicable diseases is low in comparison to other LMICs due to the lower than expected economic spending on medication (Samoa National NCD Cost Analysis Guide, 2017).

2.3.2 Barriers to Medicine Adherence

The World Health Organization identified five factors that interact to determine a patient's level of adherence: socioeconomic factors, condition-related factors, therapy-related factors, patient-related factors, and health system factors (Burkhart & Sabaté, 2003). These factors are summarized below.

2.3.2.1 Socioeconomic Factors:

Socioeconomic factors—socioeconomic status, literacy levels, and education levels, culture, and distance from treatment centers—directly affect a person's medicine adherence. Many treatments are expensive to the patient when available, and in some instances, LMICs have been unable to get the needed medicine for patients. Having a high socioeconomic status has been associated with higher medicine adherence (Gast & Mathes, 2019). The distance to the hospital to retrieve medicine is an issue for medicine adherence. Even if the medicine is free or low cost, the cost of travel can be too much for the patients either through the cost of transportation or loss of wages during the time it takes to get to the hospital (Desrosiers, Ibrahim, & Jacks, 2019).

2.3.2.2 Condition-Related Factors:

Condition-related factors are those specific to the particular illness a patient has, including severity of symptoms, severity of disease, and level of disability associated with the chronic disease. The severity of disease deeply affects a patient's adherence to medicine. Patients with more mild disease tend to adhere to medicine regimens less than patients with moderate or moderately severe disease. The less severe the symptoms, the more a patient is likely to believe they are not sick and do not require medicine. However, patients with severe or terminal disease typically adhere to medicine regimens less than those with moderate or moderately severe disease (J. A. S. B. Cramer, 1991). This is often due to the belief that the symptoms of disease cannot be worse than the side effects of medicine.

2.3.2.3 Therapy-Related Factors:

Therapy-related adherence factors include complexity of medicine, length of treatment, and side effects. It has been shown that the amount of doses per day directly decreases the amount of patient adherence (J. A. S. B. Cramer, 1991). The chronic diseases discussed in this paper—heart disease, hypertension, and hypercholesterolemia—require lifelong medicine or treatment regimens to minimize the effects of the disease. The use of medicine also comes with side effects, a typically undesirable effect on the patient that is secondary to the treatment. The more side effects a patient experiences has been associated with a decrease of medicine adherence (Dibonaventura, Gabriel, Dupclay, Gupta, & Kim, 2012).

2.3.2.4 Patient-Related Factors:

Patient-related factors are those derived from patient perspectives, such as beliefs about illness, confidence, and motivation in management of their disease, and expectations about

outcomes. Communication is a considerable reason for poor medicine adherence. Many patients describe feeling confused about what medicine they are taking and the reason for taking it. This can cause trust issues between the provider and the patient (Bollars et al., 2019; J. A. S. B. Cramer, 1991).

2.3.2.5 Health System Factors:

Health system factors like infrastructure and resource allotments; include a good provider relationship, undeveloped health systems, faulty medicine distribution systems, overworked providers, and lowered ability for the system to educate. Medicine adherence has continual challenges associated with the lowered income status in the country (Burkhart & Sabaté, 2003). Heart disease especially has a low adherence rate in countries with adequate access to health care (Choudhry, 2010). In a resource rich country, the overall adherence to heart disease medicine was 58% (Choudhry, 2010). There is a history of a scarcity of doctors in Independent Samoa, which may have contributed to the country's medicine adherence as a scarcity of doctors creates a scarcity of checkup appointments and the ability to get prescriptions refilled in a timely manner. Being unable to access doctor increases the likelihood of medicine non-adherence. Chronic diseases like hypercholesterolemia requires significant utilization of physician office visits, both to discuss the medicine reaction and to continually measure a person's blood cholesterol levels (Gatwood & Bailey, 2014).

2.4 Medicine Adherence in Samoa

Research about the medicine adherence in LMIC countries is lacking. Typically studies involving medicine adherence are done in resource rich countries (e.g. the United States) (Bowry, Shrank, Lee, Stedman, & Choudhry, 2011). In Samoa, health is typically only discussed within family circles. As the Samoan culture revolves around the family group, individualistic tasks like taking medicine is not seen as a personal issue, but a family commitment. In qualitative interviews with Samoan people, many interviewees focused on the lack of family helping them manage their medicine (Bollars et al., 2019). There are also many barriers associated with access to medicine in Samoa. In Samoa there is a reported lack of knowledge about what medicine people are taking. Often people were quoted as finding it difficult to keep track of all their medicine or not knowing the names and kinds of medicine they are supposed to take. Here, medicines are given in large quantities at health care centers, with medicine name and dosage not labeled on the containers (Bollars et al., 2019). Therefore, the patient is unable to know their exact prescription.

Even with access to medicine, there are underlying beliefs that affect medicine adherence. One such belief is a lack of trust in providers among the Samoan people. Qualitative interviews indicated that some Samoan people believe that the medicine is introducing poison into their body or are concerned that even when they take the medicine they never seem to get better (Bollars et al., 2019). Some people in Samoa view medicine to be taken on an "as needed" basis. Thus, a person may only consider taking medicine when they feel physically ill. Often once a person feels better, they will stop their medicine (Bollars et al., 2019). Many people simply do not like taking the pills prescribed and decide that they will not take them (Bollars et al., 2019).

The health system has caused some issues in medicine adherence. Patients may have a hard time refilling prescriptions. The lack of doctors in Samoa makes it difficult for patients to get

health care and medicine, with some Samoan people expressing upset at the long wait times, sometimes only to find the hospital did not have the needed medicine (Bollars et al., 2019). In the United States, of the patients diagnosed with hypercholesterolemia, only two thirds of patients adhered to medicine after 1 year (J. A. Cramer et al., 2008). Similar to Samoa, this non-adherence is often due to concerns of prescription cost, patient forgetfulness, and patient lack of support (Gatwood & Bailey, 2014).

2.5 Specific Aims

The overall goal of this project is to estimate the medicine non-adherence rates in Independent Samoa from the *Soifua Manuia* ("Good Health") research study, which is comprised of a cohort of 519 research participants and to identify possible methods to improve medicine adherence. There is little data found on the current rates of medicine non-adherence in Samoa and the Pacific Islands in general. Samoa's Ministry of Health has a strong focus on reducing the burden of non-communicable diseases, and medicine adherence will be an important consideration for achieving that goal.

Specific Aim 1: Characterize demographic trends among the *Soifua Manuia* cohort as they relate to medicine adherence.

Specific Aim 2: Describe participants' reasons for medicine non-adherence to identify further learning trends and barriers to access that impact medicine adherence.

Specific Aim 3: Using the trends identified in Specific Aims 2 and 3, develop a culturally appropriate intervention to reduce medicine non-adherence.

3.0 Methods

The data used in this essay were collected by the Obesity, Lifestyle, and Genetic Adaptations (OLaGA) Study Group (Hawley et al., 2020). Anthropometric data and personal health questionnaire responses were collected. The research questions this essay will focus on are related to the trends of medicine non-adherence in Samoa. Specifically, 1. What ages have high medicine non-adherence?, 2. What are the main reasons for not taking medicine?, 3. Are there specific chronic diseases with low medicine adherence?, and 4. Using these trends, can we develop an intervention to increase medicine adherence?

3.1 Dataset

The dataset used for analysis is from the *Soifua Manuia* ("Good Health") study, which aimed to better understand the impact of a missense variant (rs373863828, G>A) in the gene *CREBRF* on cardiometabolic traits. The variant was first identified in a genome wide association study (GWAS) conducted in Samoa in 2010 (Minster et al., 2016), and participants in the present study were recontacted and completed deep phenotyping between 2017 and 2019. In total, the study was able to recruit 519 adults using a biased recruitment strategy targeting 200 GG individuals, 200 AG individuals, and 100 AA individuals, all maximally unrelated. Recruitment criteria included having four Samoan grandparents, being aged 24.5 to 65 years old at the time of the 2010 study, living on the island of Upolu, having no physical or cognitive impairment, and having consented to being contacted again in the original 2010 study. The data collection consisted

of two in-person interviews. The first occurred at participants' homes, where the research assistants collected height and weight data and administered questionnaires covering health information, including previous diagnosis with a chronic illness and treatment regimens. The second occurred at the OLaGA research laboratory seven to ten days after the first. There, measurements such as blood pressure and some serum levels were taken. The interviews were conducted in the Samoan language and then translated into English for research (Hawley et al., 2020). Because the health interviews asked about chronic diseases, this essay focuses on the 103 people that self-reported as having one or more of the following chronic diseases: high cholesterol, high blood pressure, and/or heart disease.

3.2 Statistical Analyses

All data analysis was performed using R (version 4.1.2) (Appendix A). Descriptive statistics for age, chronic disease status, sex, census region, and medicine adherence were calculated. The rates of adherence and non-adherence were calculated in subsets of individuals with particular chronic diseases (heart disease, hypertension, and hypercholesterolemia), stratified by sex and age. Adherence was defined by answering "yes" to the survey question asking if the participant currently taking medication for a chronic disease. Participants who were partially adherent (i.e., had multiple diagnoses and were taking medications for some but not all diagnoses) were categorized as adherent except when assessing the relationship between number of diagnoses and full medicine adherence. The chronic disease rates were compared to the rates of U.S. Pacific Islanders from (Bitton, Zaslavsky, & Ayanian, 2010). Descriptive statistics were also generated for reasons given for medicine non-adherence. Factors common to high non-adherence rates were

analyzed. The dataset included questions such as: years from date of diagnosis, the number of chronic diseases a participant had, self-reported health, and the usage of traditional medicine and healers.

4.0 Results

4.1 Demographic Data

The *Soifua Manuia* cohort had 103 participants who had one or more of the following chronic diseases: high blood pressure, heart disease, and high cholesterol ("chronic disease sample"). Participants in the chronic disease sample were between 35.5 and 71.1 years old, with a median of 57.5 years and a mean of 56.8 years old. (Table 1, Figure 1). The sample was 39.8% male and 60.2% female (Table 1). The average years of education attended is 11 years with a median of 12 years and a range of 5 to 19 years. Participants resided in the three census regions as follows: 30.1% in Urban Apia, 37.9% in Northwestern Upolu, and 32% in the Rest of Upolu. The occupation of participants were also noted, with a majority of respondents with a chronic disease being unemployed or working on plantations (Table 1).

Table 1 Demographics of Chronic Disease Sample (n=103)

Age	
Mean	56.8 Years
Median	57.5 Years
Range	35.5- 71.1 Years
Sex	
Male	41 (39.8%)
Female	62 (60.2%)

Education	
Mean	11 years
Median	12 years
Range	4-19 years
Census Region	
Apia Urban Area	31 (30.1%)
Northwest Upolu	39 (37.9%)
Rest of Upolu	33 (32.0%)
Occupation (n=102)*	
Unemployed	61
Skilled Labor	4
Semi-Skilled Labor	1
Plantation work	19
Menial/Custodial	3
Clerical	3
Management	4
Education	1
Health Worker	1
Clergy/Mayor	3
Small Business Owner	2

*One participant did not respond to occupation question within survey.

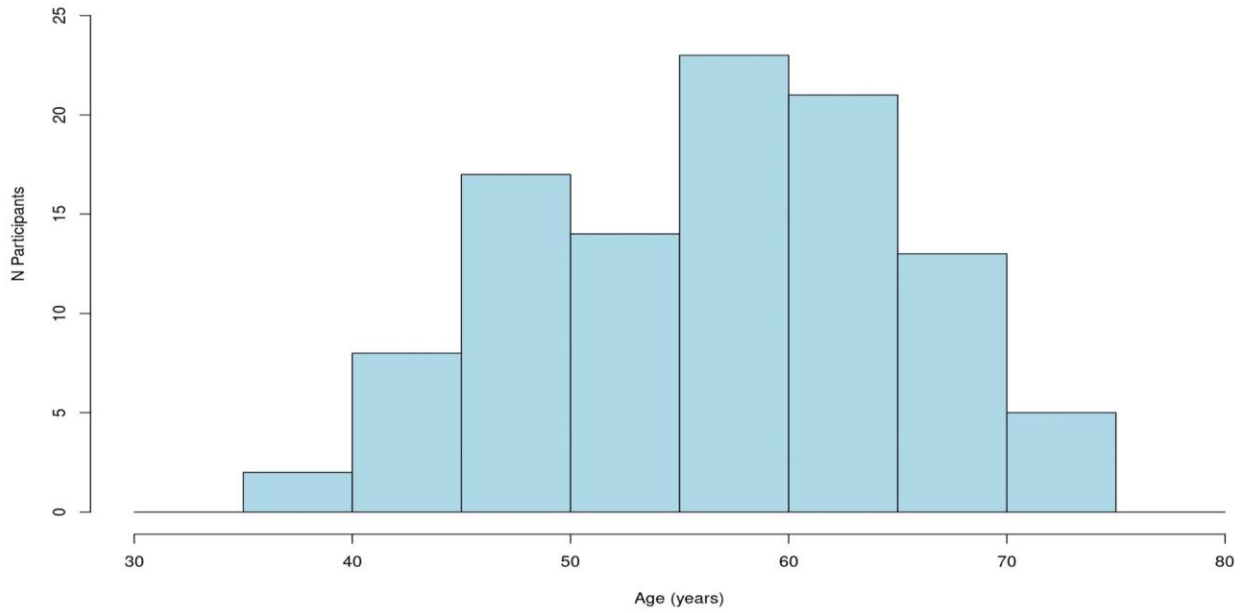

Figure 1 Age Disturbution in Chronic Disease Sample

4.2 Chronic Disease Data

The rates of chronic disease within the population were 4.2%, 16.4%, and 1.7% for heart disease, hypertension, and hypercholesterolemia, respectively (Table 2). Comparatively, reported rates of chronic disease in U.S Pacific Islanders for heart disease, hypertension, and hypercholesterolemia were 2.3%, 20.6% and 29.6% (Bitton et al., 2010) (Table 2). Chronic disease stratified by sex shows that females had higher rates of hypertension (63.5%), and heart disease (51.9%) (Table 3). Men had a higher rate of hypercholesterolemia at 55.6% compared to women, while women were more represented among individuals with heart disease and hypertension (Table 3).

Table 2 Prevalance of Chronic Diseases in Soifua Manuia study and U.S. Pacific Islanders (Bitton et al., 2010)

Chronic Disease	***Soifua Manuia* Study (n=519)**	**U. S. Pacific Islanders (n= 2609) (Bitton et al., 2010)**
Heart Disease	4.2%	2.3%
Hypertension	16.4%	20.6%
Hypercholesterolemia	1.7%	29.6%

Table 3 Prevalance of Chronic Disease by Sex in Chronic Disease Sample

Chronic Disease	**Male**	**Female**
Heart Disease (n=22)	40.9%	59.1%
Hypertension (n=85)	36.5%	63.5%
Hypercholesterolemia (n=9)	55.6%	44.4%

4.3 Non-Adherent Data

There were 25 medicine non-adherent participants ranging in age from 35.5 to 69.6 years old (mean=53.6) (Table 4). Of those non-adherent participants, 44.0.% are male and 56.0% are female and have between 7 and 19 years of education is (mean=11.52) (Table 4). Census regions most represented were Northwest Upolu and Rest of Upolu, with 36% of participants residing in each region. Among non-adherent participants, females were more non-adherent for heart disease and hypertension medicines (60% and 52.6%, respectively), while males were the more non-adherent for hypercholesterolemia medicines (66.7%) (Table 5). The total non-adherence rate was

24.3%, with hypercholesterolemia having the highest rate (33.3%) of non-adherence, followed by heart disease (22.7%) and hypertension (22.3%) (Table 5)

Table 4 Demographic Data for Non-Adherent Chronic Disease Sample (n=25)

Age (years)	
Mean	53.6
Median	53.2
Range	35.5 - 69.6
Sex	
Male	11 (44.0%)
Female	14 (56.0%)
Education (years attended)	
Mean	11.52 years
Median	12 years
Range	7-19 years
Census Region	
Apia Urban Area	7 (28.0%)
Northwest Upolu	9 (36.0%)
Rest of Upolu	9 (36.0%)
Occupation	
Unemployed	14
Skilled Labor	1
Semi-Skilled Labor	0

Plantation work	7
Menial/Custodial	0
Clerical	0
Management	0
Education	1
Health Worker	0
Clergy/Mayor	1
Small Business Owner	1

Table 5 Disease-specific Rates of Non-adherence

Chronic Disease	**n non-adherent (%)**	**n female non-adherent (%)**
Heart Disease (n=22)	5 (22.7%)	3 (60%)
Hypertension (n=85)	19 (22.3%)	10 (52.6%)
Hypercholesterolemia (n=9)	3 (33.3%)	1 (33.3%)

The chronic diseases of interest are hypercholesterolemia, heart disease and hypertension. Although the health surveys also included questions about diabetes mellitus, extensive work on this phenotype in this cohort had already been performed, so diabetes was excluded for this essay.

Table 6 Diagnosis Distribution and Medicine Adherence

Chronic disease diagnoses	**n participants**	**n participants fully adherent**
1 diagnosis	91	66 (72.5%)
Hypertension	74	55
Heart disease	14	10
Hypercholesterolemia	3	1

2 diagnoses	11	8 (72.7%)
Heart Disease and Hypertension	6	4
Hypertension and Hypercholesterolemia	4	3
Heart Disease and Hypercholesterolemia	1	1
3 diagnoses	1	1 (100%)
Heart Disease, Hypertension, and Hypercholesterolemia	1	1

Table 7 Years Since Diagnosis

Disease and Adherence	**Mean years since diagnosis**	**Median years since diagnosis**
High cholesterol		
Adherent	1.3	1
Non-adherent	1.3	2
Heart Disease		
Adherent	3.52	4
Non-adherent	11.4	10
Hypertension		
Adherent	5.38	3
Non-adherent	4.44	3

The most prevalent reason (34%) for non-adherence was “doctor recommended stopping of medicine. The reasons of “side effects”, “long wait times at hospital” and “didn’t think they needed it” were the next most common reason to stop medicine at 22% of responders choosing each answer (Figure 2). No data was available for reasons for stopping cholesterol medicines, so data in Figure 2 only represent individuals diagnosed with heart disease and hypertension.

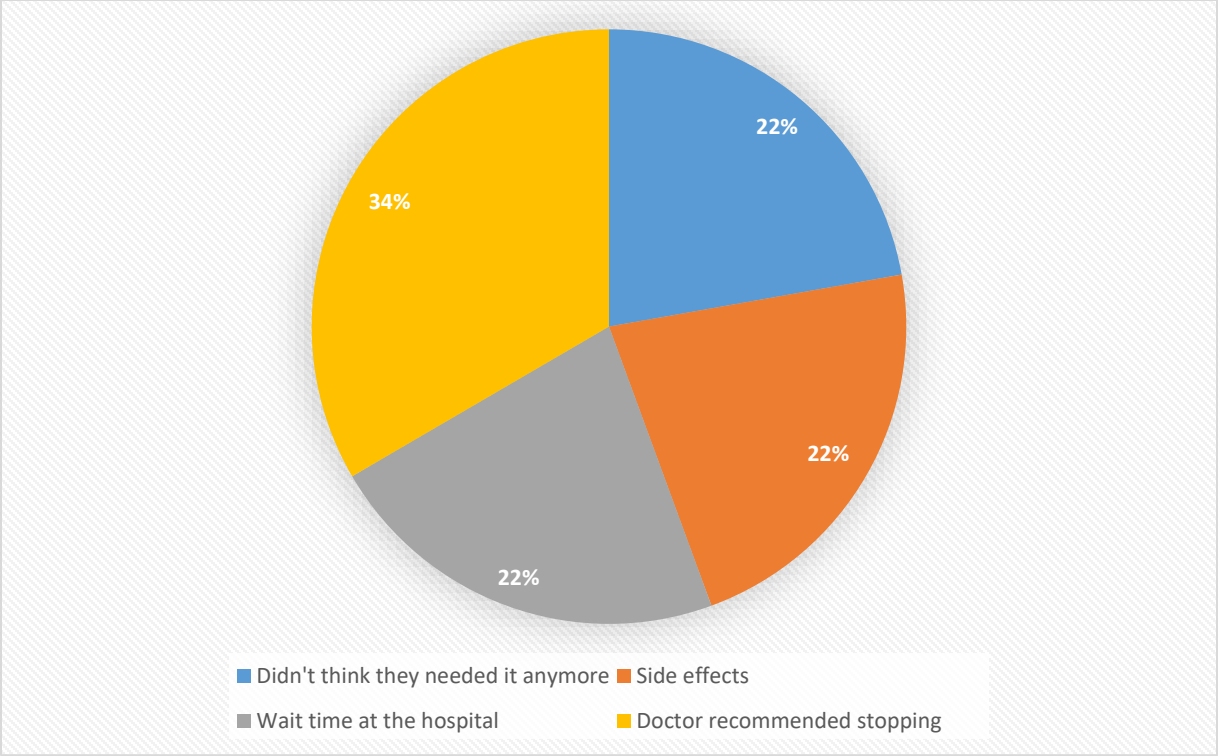

Figure 2 Quantitative Reasons for being Non-adherent to Prescribed Medicine

Participants reported their health status on a scale ranging from "Very Poor" to "Excellent" (Table 8). Participants in the adherent group were the only ones to respond that their health was poor. The use of traditional healers and medicine was investigated participants labeled as adherent were more likely to have seen a traditional healer and to also be taking traditional medicine (Table 9).

Table 8 Self Reported Health by Adherent and Non-adherent Groups

	Self-Reported Health (n=103)				
Adherence Group	Excellent	Very Good	Good	Poor	Very Poor
Adherent (n=78)	6	17	48	6	1
Non-adherent (n=25)	2	8	15	0	0

Table 9 Traditional Healer and Medicine Use by Adherent and Non-adherent groups

	Adherence Group	
Use	Adherent (n=78)	Non-adherent (n=25)
Not currently using traditional medicine and never seen a traditional healer	64 (82.1%)	24 (96.0%)
Currently using traditional medicine or has seen a traditional healer	11 (14.1%)	1 (4.0%)
Currently using traditional medicine and has seen traditional healer	3 (3.8%)	0

5.0 Conclusions and Implications

Participants diagnosed with chronic disease were an average age of 56.8 years old. This lower average was expected as in LMICs the age of chronic disease diagnosis trends younger than those in higher income countries (Preventing chronic diseases: a vital investment, 2005). The trends of chronic disease in this sample show that amongst the people with a chronic disease, females had higher rates of hypertension (63.5%) and heart disease (59.1%), while males had higher rates of hypercholesterolemia (55.6%). The rate of chronic disease in this sample shows a large difference in rates of chronic disease when compared to another study that had a comparatively larger sample of United States Pacific Islanders (Bitton et al., 2010). For instance, the rates of hypertension and hypercholesterolemia in the sample are 16.4% and 1.7% respectively. The rates in the U.S. Pacific Islanders for the same diseases are 20.6% for hypercholesterolemia and 29.6% for hypertension.

The rates of medicine non-adherence in Independent Samoa have not been reported previously. Therefore, there is little to compare the total rate of non-adherence (24.3%) found in the preliminary data. In comparison to United States data for heart disease non-adherence (60%) (Baroletti & Dell'Orfano, 2010), Samoan medicine adherence rates are lower. This comparison is thought to be skewed because of the difference of incomes and populations between the United States and Samoa, and there a few studies in medicine adherence more suitable for comparison.

The average age of people who have chronic disease in the chronic disease set was 56.8 years old, and participants who were non-adherent to their medication had an average age of 53.6 years old. These averages follow a typical trend in research as in LMICs chronic diseases tend to show up at younger ages than for those in higher income countries. Rates for non-adherence in

hypertension are relatively even between males and females (48.1% and 51.9%, respectively). However, disease specific non-adherence does show some sex-specific trends. Females tend to be more non-adherent for medicines for heart disease (60%) and hypertension (52.6%), while males tend to be more non-adherent for hypercholesterolemia medicine (66.7%).

The average education level in the non-adherence group is slightly higher than the overall chronic disease group (means 11.52 years and 11 years, respectively), which is interesting as research shows that higher levels of education typically lead to higher medicine adherence (Vermeire et al., 2001). This difference of education may be due to the small sample size of the research. Previous research shows that the more chronic diseases a person has, the less likely they are to be adherent to their medication (J. A. S. B. Cramer, 1991, however, these data do not support those findings (Table 6). Again, sample size and recall bias may be impacting this trend, as well as a minimal number (n=3) of diseases being asked about in the *Soifua Manuia* cohort. Medicine adherence generally decreases with more chronic disease diagnoses as it becomes difficult for patients to keep track of medicines when they have multiple prescriptions and directions for administration to keep track of. More non-adherent people live Northwest Upolu and Rest of Upolu, which may suggest a lack of resources in these regions or geographic barriers to staying adherent to medicine (e.g., large distance to clinics that fill medicine). Further research of geographic location of hospitals, patients, and health centers may shed more light upon medicine adherence barriers created by location.

Interestingly, participants adherent to medicine were more likely to have ever gone to a traditional healer for treatment and/or more likely to be taking traditional medicine for their diagnoses than non-adherent participants (17.9% vs. 4.0%, respectively).

Medicine adherent individuals were more likely to report poor health. This may be due to psychosocial factors behind medicine and a Samoan belief that if you are not taking medicine, you are "well".

This analysis shows that the main reason for being non-adherent is due to "doctor recommended stopping", which may not qualify as true non-adherence. The remaining reasons for non-adherence — "side effects", "long wait times at hospital" and "didn't think they needed it" — were reported at equal frequencies (22%). These reasons are against doctor recommendations (Vermeire et al., 2001) and are possible targets to introduce interventions. Because few options were available for a person to choose in the survey, free form answers show more thinking into the beliefs of the Samoan people in relation to health and medicine. Within the free form responses, there seems to be dissatisfaction with hospital, and a few participants mentioned the wait time for medicine at the hospital. There is also confusion about how long they need to take their medicine. One participant commented that they did not take their medicine because "The disease cure from the medicine". Quite a few people responded that their doctor said that they no longer needed the medicine. This comment may require some follow up as we are studying chronic diseases that typically require lifelong medicines or lifestyle changes, it would be unusual for a doctor to stop prescribing this medication. Some suggestions for further investigation would be to access the medical records of the Samoan people to cross reference self-reported behavior with doctor's notes.

The dataset was not collected specifically to answer medicine non-adherence, therefore, there are some limitations of the study due to secondary use of data. There are limitations that may exist due to confusion during survey administration. The survey asked specifically for a doctor's diagnosis of their disease which may have confused participants due to their usage of traditional

healers and requirement to remember if they have been officially diagnosed with illness. Also in Samoa, there is lower access to doctors be able to be diagnosed with a chronic disease in comparison to the United States, where most medicine adherence research has been done ("Health systems in Samoa," 2020). There are also many other chronic diseases that may be of importance in medicine adherence research. For example, a high prevalence type 2 diabetes, has been reported in this population, but was excluded from this work (Hawley et al., 2020), and a number of other chronic diseases were not assessed in the survey. Another limitation is that the sample was selected to maximize rs373863828 genotype ratios and may not be a representative sample of Samoans with chronic disease. Furthermore, the overall chronic disease sample (n=103) is relatively small, and likely underestimates chronic disease prevalence as the diseases of interest frequently lack overt symptoms until disease becomes severe. Thus, clinical visits are required to identify and diagnose these conditions, and throughout the study duration, Samoa had very few doctors available ("Health systems in Samoa," 2020; Ibrahim et al., 2021). Hypercholesterolemia in particular may be underestimated (1.7% sample vs 29.6% US Pacific Islanders), and non-adherence for cholesterol medications was difficult to assess as the survey did not include why medication was not being taken. Survey responses may be affected by translation from Samoan to English. Future directions should more closely examine the motivation for non-adherence for these and other priority diseases identified in Samoa's 2018 policy goals.

6.0 Public Health Significance and Intervention Recommendation

6.1 Public Health Significance

Medicine non-adherence in Samoa has not been well researched. Low and middle income countries like Samoa are suffering from high rates of chronic disease in addition to the fight against infectious diseases. Untreated chronic diseases will incur higher associated medical costs than chronic disease that are treated with medicine. In this study, I estimated the baseline levels of non-adherence in the Samoan population from the *Soifua Manuia* study cohort. In Samoa chronic diseases are overtaking infectious disease to be the leading cause of death, with hypertension and heart disease designated as priority non-communicable diseases. The Samoan Ministry of Health has created the National Noncommunicable Disease Control Policy 2018-2023 to provide guidance on design of care in Samoa. This policy outlines how to best help Samoa by decreasing non-communicable diseases, improve the life of people with non-communicable diseases, and created evidence-based interventions. The research described in this essay may assist in the development of patient education/selfcare guidelines for prevention and control of NCDs and develop protocols for NCD management (Key action 3.4.1 of the NCD control policy) (Samoa, 2018). The trends from the *Soifua Manuia* dataset show that there is more non-adherence in younger ages, of those with higher education, and those who live in more rural settings. There is also data to suggest that the more years from diagnosis a patient is and if they might have more than one chronic disease also influence higher rates of non-adherence. As determined in the literature review and further seen in this analysis, there are cultural beliefs around health also may be contributing to medicine non-adherence in Samoans.

6.2 Intervention

An intervention to reduce medicine non-adherence needs to focus on the needs and concerns of the Samoan population. Participants in the *Soifua Manuia* study group report concerns about the long wait times to receive medicine. There are also trends that suggest people are more likely to be medicine non-adherent when they have more than one chronic disease diagnosis, are younger, and have increased time from diagnosis to present (i.e., survey completion). Much of the population is spread in rural villages around Samoa and work plantation jobs, which may cause issues in leaving work to receive medicine.

Samoa has acknowledged that chronic diseases are a growing problem, and there a few programs already in Samoa that are targeting chronic diseases.

Examples include:

The Non-communicable Disease clinic in Apia, Samoa is located within the building Matagialalua, which is well known to the Samoan people. It previously focused preventing complications of diabetes through education and counseling as well as providing pharmaceutical services (Samoa, 2018). It recently changed its name to focus more broadly on the education of common non-communicable diseases.

The Integrated Community Health Awareness Program (ICHAP) was a health outreach program created by the Ministry of Health (Samoa, 2018). ICHAP recruited many partners including the Samoa Red Cross, National Health Service, and Ministry of Women, Community and Social Development. This program originally focused on health education about infectious disease and non-communicable diseases, with its 2015 outreach focusing on HIV and Tuberculosis. Due to collaboration among many stakeholders, the program developed was able to

overcome cultural and religious stigma about health issues. This program has been implemented in a variety of settings including schools, villages, prisons, and churches.

Package of Essential NCD Interventions (PEN Fa'asamoa) (Samoa, 2018) was originally developed as toolkit by the World Health Organization Package of Essential Non-communicable disease interventions (PEN) (WHO package of essential noncommunicable (PEN) disease interventions for primary health care, 2020). The Ministry of Health has adapted the program to suit Samoan needs. Specifically, the changes focus on using the governance structure of Samoan villages to help find and follow up high risk patients. After a trial period, the program was expanded in 2016-2017 to all health districts within the country. For the focus of Medicine Adherence, protocol one of PEN focuses on the prevention of heart attacks through management of hypertension through three pillars— non-communicable disease early detection, non-communicable disease management, and non-communicable disease awareness in the community. Notably, one objective of the PEN program focuses on increasing adherence for non-communicable disease treatment and management protocols. This program relies on the women's committee members from the Ministry of Women, Community and Social Development to provide outreach in the community for people diagnosed with non-communicable diseases to gain support from their family and community. This is in the form of members going to the home of a designated high-risk patient and follow-up sessions after a doctor's appointment. An individual with a non-communicable disease or part of a high-risk family (determined by medical checks and family history) will have four visits a year from the women's committee.

Any intervention for medicine non-adherence in Samoa will require cultural considerations of health and medicine. The programs that are available have good aspects and outcomes to use for a medicine adherence intervention. ICHAP was able to reach 700 people in 2018 with their

HIV and tuberculosis program (Integrated Community Health Approach Program (ICHAP) Survey: Behavioral Surveillance from MoH Outreach Programming, 2018). Its ability to easily be launched in many settings makes it a great education tool. The PEN Fa'asamoa was also able to screen about 90% of the targeted population in their villages in 2015 (PEN Fa'a Samoa expansion 2016- 2017, 2016). This program has been deemed a success and will be expanded to many more villages from 2020 to 2025 ("Samoa Returns to Community-based Approach to Contain Rise of Non-communicable Diseases," 2021). However, there is concern about the strain on community partners in the continued monitoring of medicine adherence. As time from diagnosis increases, patients are more likely to become medicine non-adherent, resulting in additional visits by the women's committee. For example, non-adherent participants with heart disease were diagnosed an average of 11.4 years prior to survey (Table 7). This burden on the women's committee is difficult to calculate, but is likely to increase with increasing prevalence of non-communicable diseases in Samoa. It may help to have electronic systems that set alerts for patients missing appointments or missing refills of prescriptions, but this will require additional infrastructure development. ICHAP has been able to reach and educate many groups about non-communicable diseases. It would be useful to develop risks of medicine non-adherence material to send to communities that may have not been exposed to education like this. Its ability to react more rural villages and schools will set a stage for medicine adherence. Along with these programs it is suggested that the Samoan Ministry of Health use a program like what Kaiser Permanente has done to increase medicine adherence for hypertension to 80%. This includes electronic health record tracking with alerts to mark at risk patients and outreach so all patients have documentation of their health measurements, as well as access to chronic case managers that can help patients treat their disease and disease specific health education classes (Kleinsinger, 2018). Another option

would be to have a system like the Pennsylvania Project, which was a pharmacy led medicine adherence project where the pharmacists screened for risk of medicine non-adherence and provided counseling to those patients deemed high risk. This led to approximately $300 (USD) per patient annual health cost savings (Pringle, Boyer, Conklin, McCullough, & Aldridge, 2014). Samoa has a strong culture of community to provide support systems to chronic disease patients and has various education programs about medicine non-adherence. However, to further improve medicine adherence, a program that has health service provider screening could provide data and alerts about possible high-risk patients. Such documentation about their health data could help demonstrate to the Samoan people how conditions like hypercholesterolemia may exist even when the symptoms are not obvious. Like the Kaiser Permanente program, changing the education to be more disease specific may be beneficial to reduction of medicine non-adherence. This obviously comes with increased costs of health care, however, long term preventative measure for medicine non-adherence will help reduce care costs for chronic diseases in the future.

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Appendix A R Markdown for Investigation into Chronic Disease and Medicine Adherence in the Soifua Manuia (Good Health) Study

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