Diabetes Mellitus and Heart Disease Risk Factors in Hawaiians

The Native Hawaiian Health Research Project, RCMI Program*,**

Introduction

Native Hawaiians have the highest mortality rate among the 5 major ethnic groups in Hawaii and the lowest life expectancy among its multiethnic population.[1] Heart disease is the leading cause of death among the people of Hawaii and accounts for greater mortality among Hawaiians than non-Hawaiians, especially among men. In addition, the occurrence of heart disease is estimated to be 44% greater than the national average and affects Hawaiians at a younger age than non-Hawaiians.[2]

The collective interpretation of the vital statistics data strongly suggests that heart disease occurs disproportionately among Hawaiians and contributes to a shorter life expectancy. Despite these troubling figures, accurate prevalence rates of abnormalities of the risk factors for heart disease in Hawaiians are not available. Thus, there is a need to ascertain cardiovascular disease (CVD) risk-factor data among Hawaiians. Such information will allow a more focused effort to prevent heart disease morbidity and mortality.[3]

Guidelines have been established to address major risk factors such as hypertension, hypercholesterolemia, smoking, and diabetes mellitus in an effort to reduce atherosclerotic heart disease. Legislators and funding agencies often ask why there is a need to gather data on Native Hawaiians if control of the major CVD risk factors is already emphasized in clinical practice for Hawaii's multiethnic population. The answer lies in the disproportionately high prevalence of heart disease morbidity and mortality among Hawaiians. In addition, the pathophysiology of atherosclerosis and CVD is exceedingly complex and involves many factors other than those typically labeled major risk factors. Thus, factors ranging from socioeconomic status to genetic background may affect susceptibility to heart disease. The prevalence of abnormalities in CVD risk factors has been found to differ among various populations around the world. Native Hawaiians may possess unique risk-factor profiles of the major contributing disorders or may exhibit a high prevalence of newly identified risk factors such as insulin resistance and elevated fibrinogen levels. The accurate and complete determination of CVD risk-factor rates will provide analysis of the magnitude of these risks among Hawaiians. This information will allow primary care providers to focus resources on the most important of these risk factors. More important, accurate information will provide funding bodies and health agencies with data on which to target their education and awareness programs to prevent the development of these risk factors in future generations of Hawaiians. In addition, the risk factor assessment may potentially allow for the understanding of nonclinical factors, such as cultural identity and social support, that are important in heart disease reduction. Finally, the information gathered has the potential for providing a foundation on which the true attributable risk can be determined for various CVD risk-factor abnormalities in Hawaiians.

This article will provide a review of information currently available on diabetes mellitus and heart disease risk factors in Native Hawaiians and an overview of the Native Hawaiian Health Research (NHHR) Project, a CVD risk factor assessment effort. The NHHR Project is a community-based project, and the process of developing a community partnership for a research effort is highlighted. Also, initial preliminary data from the NHHR Project is presented. The contributors who authored sections of this article are noted and the members of the NHHR Project are listed with an asterisk.

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Diabetes and Cardiovascular Disease Risk among Hawaiians

Marjorie Mau MD and Richard Arakaki MD

The primary form of diabetes mellitus (DM) affecting Native Hawaiians is Type II or non-insulin dependent diabetes mellitus (NIDDM). One of the earliest publications on the prevalence of DM in Hawaiians living in Hawaii is a study of approximately 38,000 gainfully employed individuals between 15 and 65-plus years of age on Oahu. In this study, the prevalence of DM among Native Hawaiians (pure and part-Hawaiians) was reported as 29.9/1000, which is significantly higher than the total study population (18.4/1000).[4] Moreover, among pure Hawaiians, the age-adjusted prevalence rate was reported to be 48.8/1000, the

highest for any ethnic group examined. This study suggests that among Hawaiians, particularly pure Hawaiians, DM is highly prevalent. Further supportive evidence was provided by a study of 30 volunteer men on Niihau who were of pure Hawaiian ancestry and were 22 to 64 years of age. Based on fasting glucose levels, the study reported a crude DM prevalence rate of 120/1000. In 1985, the Molokai Heart Study conducted CVD risk factor examinations among 257 residents between the ages of 20 and 59 living on Hawaiian homestead lands on the island of Molokai.[6] In this population-based study, the presence of glucose intolerance was defined as a previous history of diabetes or the presence of 2+ or greater glycosuria. The age-adjusted prevalence of glucose intolerance was reported to be 10% in women and 12% in men. These rates are approximately 4-fold higher than the rates for U.S. white women and men of similar ages.[7] When compared to other at-risk ethnic populations, the prevalence of glucose intolerance reported in the Molokai Heart Study is equal in magnitude to Native Americans living in Tucson, Arizona, and approximately 2.5-fold higher than the U.S. population.[8-9] Concordant with DM prevalence among Hawaiians reported in the Molokai Heart Study is the age-adjusted DM mortality rate, which in 1985 was reported by the Hawaii Health Department to be 29 per 100,000. Compared to the general U.S. population, the DM mortality rate among Hawaiians is 2-fold higher.[10-11]

The prevalence of other CVD risk factors in Hawaiians can be estimated from collected data from the Molokai Heart Study. Based on anthropometric measurements the prevalence of obesity, defined as a body mass index (BMI) greater than 27.5, was reported as slightly more than 60% in both men and women, with approximately 40% of the study cohort being severely overweight defined as a BMI greater than 31.1 in men and 32.2 in women.[12] These prevalence rates for obesity are quite high as compared to the national average, especially among younger Hawaiians in the 20 to 40 age group. Body fat distribution, as measured by waist to hip circumference ratios (WHR) independent of obesity, further categorizes individuals at risk for atherosclerotic vascular disease. In the Molokai Heart Study, a high WHR was measured in both men and women, indicating an increased central or visceral fat distribution and hence an increased risk for noninsulin-dependent diabetes mellitus (NIDDM) and CVD.[13] The prevalence of hypertension (HTN) among Hawaiians in the Molokai Heart Study was found to be comparable to rates reported for U.S. whites.[6] Approximately 24% of women and 26% of men between the ages of 20 and 59 were noted to have HTN. However, individuals in the 40 to 49 age group had approximately 40% prevalence as compared to the 30% rate among U.S. whites.

Biochemical analysis of random blood samples for total cholesterol concentrations among Hawaiians in the Molokai Heart Study revealed that nearly 50% of individuals had levels greater than 200 mg/dl.[6] In addition, the mean HDL-cholesterol levels in Hawaiian participants was reported to be substantially lower than the national average. Cigarette smoking among Hawaiian participants had been found to be slightly more frequent than the national average at approximately 34% for women and 42% for men.

The prevalence of heart disease risk factors in Hawaiians appears to be higher than the national average, especially diabetes mellitus and obesity. Because of certain limitations in the various studies reviewed, the data on CVD risk factors in Hawaiians remain incomplete. However, the previous studies clearly underscore the need to conduct a more complete and accurate assessment CVD risk factors in a representative population of Native Hawaiians across the state of Hawaii.

The RCMI Program as a Mechanism in Establishing the Native Hawaiian Health Research Project: A Community-Based Research Effort

Healani Chang MPH, Danelle Coakley

The NHHR Project is funded by the Research Centers in Minority Institutions (RCMI) Program of the National Centers for Research Resources of the National Institutes of Health. The goal of the RCMI Program is to significantly enhance the capacity for predominantly minority institutions to conduct biomedical and behavioral research. The RCMI program awards grants to institutions to help acquire, enhance, and support the various physical and human resources needed for conducting competitive biomedical research. The University of Hawaii at Manoa instituted the RCMI Program in the Pacific Biomedical Research Center (PBRC) in 1986. In 1990, the RCMI Program fostered the Native Hawaiian Health Research Project in an effort to fulfill a University of Hawaii mandate for clinical research initiatives to benefit the citizens of Hawaii.

The development of the NHHR Project also coincided with a unique opportunity to link research on chronic diseases that disproportionately affect Native Hawaiians, with health care services provided under the Native Hawaiian Health Care Act of 1988. The NHHR project of the university's RCMI Program is working in concert with *Papa Ola Lokahi*, a community-based Hawaiian organization, to address health care promotion, disease prevention, and primary health care services for the Hawaii's indigenous Hawaiian population. Thus, the NHHR Project is a community-based initiative to gather more complete and accurate information on glucose intolerance and cardiovascular risk factors in the Hawaiian population. The guiding principle of this project is a cultural-historical understanding and sensitivity to Native Hawaiian communities, and research initiatives that are culturally consonant with the values, beliefs, and practices of Hawaiians. The continuing goal of this activity has been to improve the health status of Native Hawaiian communities by forming partnerships between the community, their health care professionals, the University RCMI researchers, and *Papa Ola Lokahi*.

The specific aim of the NHHR Project is to collect standardized information on the distribution of risk factors for cardiovascular disease in a representative population of adult Hawaiians. The objectives are to determine the prevalence of impaired glucose tolerance and to characterize the smoking behavior, the distribution of serum total cholesterol, HDL-cholesterol and triglyceride concentrations, blood pressure, correlates of adiposity, and insulin levels in the Hawaiian population.

In order to determine the prevalence of any disorder in a given population, a well-defined geographic location and population census is needed first. A community with a large number of Hawaiian residents was required to conduct this project. However, embarking on such a research effort within a community requires a commitment to improving health care regardless of the constraints of budget and limitation of services. Thus, the NHHR Project sought a partnership with a health care organization that would provide support and services to the participants in the study, especially those identified with abnormalities. At the urging of *Papa Ola Lokahi*, the separate Native Hawaiian Health Care organizations of each island were contacted and the research project presented. These 5 uniquely created and defined Native Hawaiian Health Care systems are: *Hoola Lahui Hawaii* representing Kauai and Niihau; *Ke Ola Mamo* representing Oahu; *Na Puuwai* representing Molokai and Lanai; *Hui No Ke Ola Pono* representing Maui; and *Hui Malama Ola Na Oiwi*

representing the island of Hawaii. Each entity has the responsibility of addressing the health care needs of the Hawaiian people it represents. Studies were begun in cooperation with *Hoola Lahui Hawaii* and *Hui Malama Ola Na Oiwi*. The research on Kauai was interrupted by hurricane *Iniki* and is resuming only now. The community of North Kohala has been the focus of research on the island of Hawaii.

A Profile of Research in the North Kohala Community

Kohala is one of the 6 major districts that make up the island divisions of Hawaii. North Kohala is made up of 1,020 square miles within 2 major environmental zones: Windward and leeward. The Kohala mountains form this natural separation allowing Kohala to experience a great variety of environmental conditions. Historically, North Kohala was populated by migrants from Tahiti and is the legendary site of the Kamehameha royal blood line.

After initial contact with the West, missionaries subsequently settled in Kohala where today several congregations still thrive. Originally a subsistence economy, the sugar industry changed this and it became the primary economic presence in Kohala for nearly 100 years. Today Kohala is dependent on the tourist industry concentrated along the South Kohala coast line with its 5 major hotel conglomerates. Community and lifelong residents have expressed their concerns that Kohala is once again in transition, following a closure of one major industry, the sugar mills, and the resurgence of the growing tourist industry and hotel developments. For a changing community, the RCMI project provides a sense of hope to introduce new health-related skills and knowledge in an effort to meet the challenges of the future with a healthier generation of people.

The initial census collection required hiring key community liaisons and up to 12 census takers. The census survey had been a critical step in the building of a community partnership. Highly motivated and active residents conducted a door-to-door census to determine the size of the entire population (Hawaiians and non-Hawaiians) of North Kohala. They assisted in enumerating Hawaiian families living in North Kohala and in identifying the number of adults residing in each household.

A notable benefit of working with existing community organizations was the fortunate event of establishing a collaborative partnership with the local fire department. Firefighter Michael Moriarty and the Kohala Senior Citizen Club created a computerized mapping system to expeditiously locate Kohala residents in emergency situations. The system was called the "The Kohala Dispatcher." With the sytem nearly 80% complete, the RCMI program contributed with additional staffing and together was able to refine and complete the Kohala Dispatcher system.

The census took longer than expected because most census workers had other priorities—their primary employment responsibilities and family commitments. However, we had counted nearly 80% of the population in North Kohala by the end of 1993.

Concurrent with the census collection, the RCMI program had established a research clinic site in the heart of Hawi Town, an ideal location for screening community members for the project. The clinic was subsequently staffed by 2 health technicians and a community coordinator. They received rigorous training in research methods by the core RCMI investigators and assisted in pilot testing the health behavioral questionnaires with neighboring residents.

Methods

Preliminary Results of the Native Hawaiian Health Research Project

Andy Grandinetti PhD, Healani Chang MPH

Subjects.—This study received approval from the University of Hawaii's Committee on Human Studies, the North Kohala Advisory Board, and the *Hui Malama Ola Na Oiwi* Advisory Board. Approximately 521 Hawaiian individuals over the age of 30 were identified in the census survey which was estimated to enumerate 80% of the population of Hawaiians in North Kohala. Once Hawaiian families were identified, individuals were mailed an invitation to participate and were subsequently contacted by phone to schedule a time to conduct an interview, examination, and blood sampling. All screening protocols were performed at the research site in Hawi beginning in early 1994. Every participant received a detailed explanation of the procedures involved, the risks and benefits, and issues of participant confidentiality related to the research project. An informed consent was obtained prior to the start of the screening protocol. Pregnant women were excluded from the screening.

Questionnaires and Anthropometric Measurements.—A detailed, self-reported ethnic genealogy was obtained to ascer-

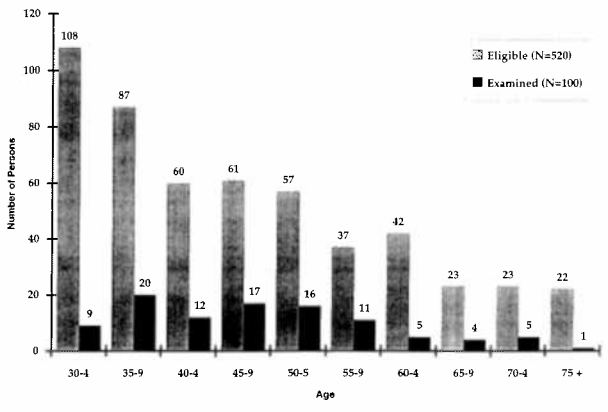

Fig 1.—Age distribution of eligible persons and participants in North Kohala.

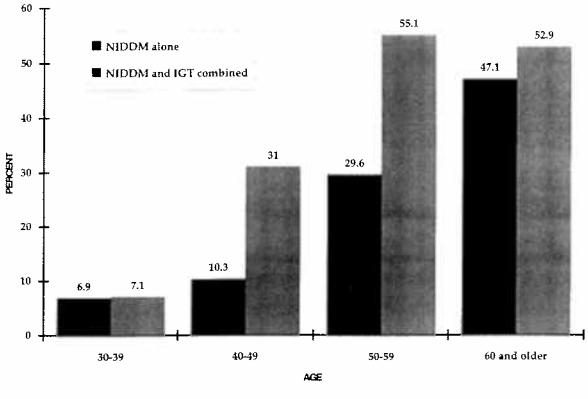

Fig 2.—Age-specific prevalence rates for glucose intolerance among Hawaiians in North Kohala.

tain Hawaiian admixture. Current and past cigarette-smoking history was obtained. Questionnaires about dietary and physical activity history were answered. The food-frequency questionnaire developed by Dr Jean Hankin and validated for other populations in Hawaii was utilized.[14] The physical activity questionnaire was an adapted version of a validated tool used in the Pima Indian studies.[15]

Blood pressure, height, weight, and waist and hip circumferences were obtained in triplicate by standard protocol.[16] Body mass index (BMI) was derived by dividing the mean weight in kilograms by the mean height in meters-squared (Kg/M^2). The waist to hip circumference ratio (WHR) was calculated by dividing the mean waist circumference by the mean hip circumference.

Oral Glucose Tolerance Test.—All individuals scheduled were instructed to maintain a normal diet for 3 days and to fast for 12 to 14 hours prior to the examination. A fasting blood sample was collected which was followed by ingestion of 75 grams of dextrose. Two hours following the oral glucose load, a second blood sample was obtained. Only a fasting blood specimen was obtained on known diabetics (prior history, medication, or a glucose by fingerstick of > 225 mg/dl), and a glucose challenge was not given. All blood samples were rapidly processed by centrifugation and plasma samples were aliquoted in to separate cryotubes. Separate aliquots of plasma were then sent frozen and refrigerated to the research laboratory in Honolulu weekly.

Biochemical Analysis.—Plasma glucose levels were measured by the glucose oxidase method using an autoanalyzer from Yellow Springs Instruments (Yellow Springs, Ill).[17] Plasma total cholesterol, HDL-cholesterol, and triglycerides concentrations were analyzed by beta-estimation and performed by Penn Medical Laboratories of the Med-Atlantic Research Institute, a certified CDC Lipid Research Laboratory in Washington DC.[18] Plasma LDL-cholesterol levels were estimated by calculation using the Freidewald equation.[19]

Statistical analysis.—All variables examined and collected for each participant were analyzed using the SAS (Statistical Analysis System) JMP program procedures. Descriptive statistics such as the mean, standard deviation, and range of different measurements for various anthropometric and biochemical measurements were generated using this program.

Results

Of the 521 eligible adult Hawaiian residents of North Kohala, more than half of the participants were between 30 and 50 years of age (Fig 1). To date, slightly less than half of the eligible persons have participated in the NHHR project screening examination. These participants are somewhat older than the eligible population identified; consequently, the crude prevalence rates reported below must be interpreted with caution, since they may in part reflect the underlying age bias.

Based on the first 101 persons examined, the observed age-specific prevalence rates of diabetes mellitus among Hawaiian participants is 19.6%. The criteria used to establish NIDDM in participants were: History of NIDDM with current use of medication or a fasting plasma glucose value greater than 140 mg/dl or a 2 hour plasma glucose value greater than or equal to 200 mg/dl by 75 gm OGTT.[20] Interestingly, among those individuals found to have NIDDM, 45% were unaware of their condition before their participation in the NHHR health screening project. Approximately 14% of the participants were found to have impaired glucose tolerance (IGT) which was ascertained by a fasting plasma glucose level less than 140 mg/dl and a 2 hour glucose value between 140 to 200 mg/dl. Individuals with IGT are considered to be at increased risk for NIDDM and heart disease.[21] Overall, the prevalence of glucose intolerance (NIDDM and IGT) in NHHR project participants is 33% (Fig 2). The association of obesity with NIDDM has been well documented. A similar association is observed for the 101 NHHR participants. The median BMI for all study participants was 30 kg/m^2 and 76% had a BMI $\geq$ 27.5 kg/m^2. Furthermore, central body fat distribution was also observed in high proportion of NHHR participants. Almost half of all individuals (44%) had central adiposity as determined by WHRs (greater than 0.8 for women, 0.9 for men). Analysis of the detailed questionnaire of dietary intake is not available for this preliminary report.

Hypercholesterolemia is a major risk factor for CVD and this risk was examined in NHHR participants by analysis of fasting plasma cholesterol concentrations. Total cholesterol levels in excess of 200 mg/dl were observed in 79 of 166 participants. These findings are similar to that reported in the Molokai Heart Study. Analysis of plasma triglyceride, HDL-cholesterol, and LDL-cholesterol levels are not available for this report.

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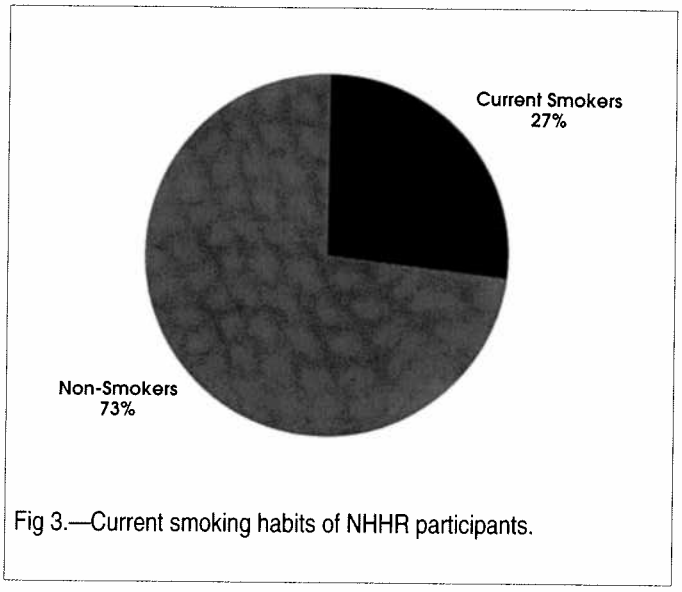

Fig 3.—Current smoking habits of NHHR participants.

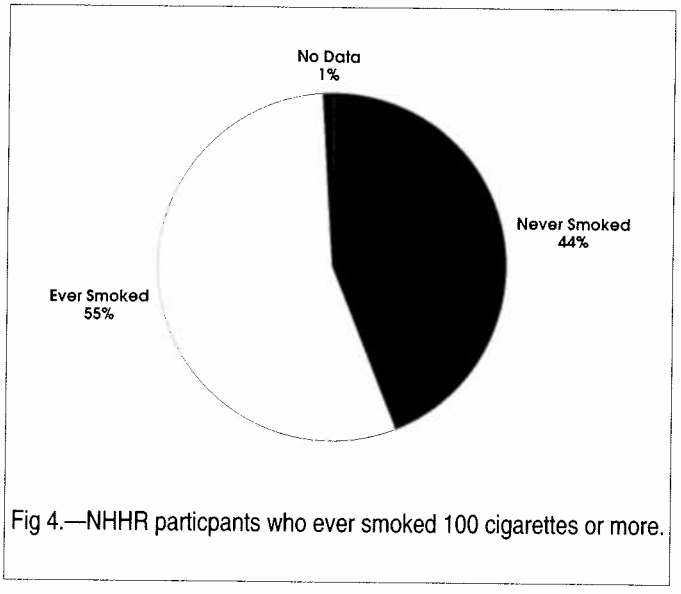

Fig 4.—NHHR particpants who ever smoked 100 cigarettes or more.

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Smoking habits were also assessed in this preliminary analysis. Twenty-seven percent of 101 NHHR participants were current smokers, a somewhat smaller proportion than was reported in the Molokai study (Fig 3). Approximately half of the participants admitted to having smoked at least 100 cigarettes during their lifetimes (Fig 4).

Hypertension, another important CVD risk factor, was also prevalent in NHHR participants. Thirty-eight percent of all participants met study criteria for hypertension (a systolic pressure greater than 140, diastolic pressure greater than 90, or a history of hypertension).[22] Of those reporting a prior history of hypertension, 60% had either a high systolic blood pressure or diastolic blood pressure, an indication their hypertension was not well controlled. Moreover, 38% of the known hypertensives were not taking antihypertensive medications at the time of NHHR screening.

Analysis of the extensive questionnaire on current and past leisure and occupational activity levels was not yet available for this preliminary report; however, a list of the 10 most common activities participated in at least 10 times in a lifetime was compiled (Fig 5). Only 3 of these 10 activities are considered to adequately sustain aerobic activity that is sufficient to reduce the occurrence of CVD and NIDDM.

Discussion

The preliminary findings of the NHHR Project appear to support and confirm the findings of other studies that there is a high prevalence of NIDDM in Native Hawaiians. The use of well-established and rigorous methods to obtain data has allowed this project to ascertain additional information which will provide explanations of the disproportionately high prevalence of CVD in Hawaiians. The discovery of undiagnosed NIDDM and IGT in NHHR participants provides new information of the cryptic nature of glucose intolerance and the risk for CVD and NIDDM in Hawaiians. However, data collection and analysis is incomplete and premature interpretation of the preliminary findings may be unwise.

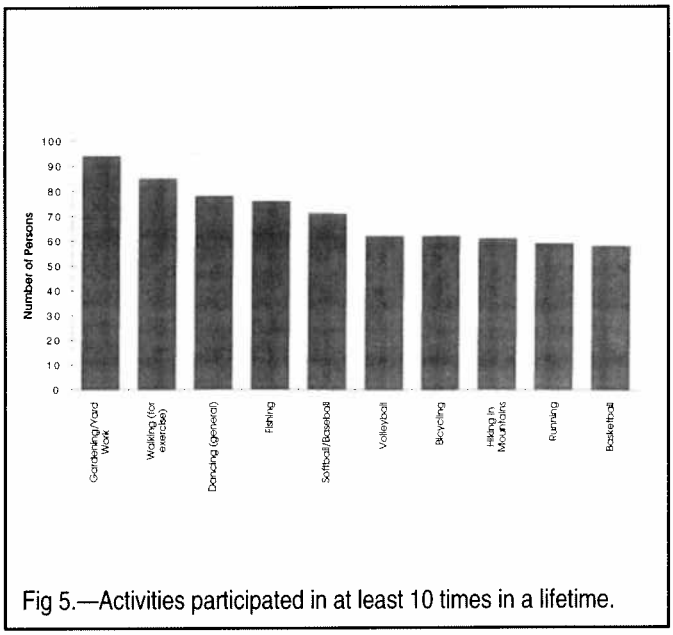

Fig 5.—Activities participated in at least 10 times in a lifetime.

The proper emphasis of this report is to demonstrate that an accurate assessment of diabetes and CVD risk factors are possible with a community-based research effort. The passage of the Native Hawaiian Health Care Act and the creation of *Papa Ola Lokahi* and the Native Hawaiian Health Care Systems have established a new protocol for all community-based initiatives. There are, however, very few models of successful collaboration between Native Hawaiian communities and researchers at the university; thus, the development of a partnership between the RCMI Program and the Hawaiian community should be considered as forging new ground. The results presented in this article, however preliminary, must then be considered as a successful and revisited model of community-based research. For the RCMI researchers, the experience so far has been a learning process in uncovering which types of approaches to every aspect of clinical research will work in certain communities. We have learned that the community directs the flow of information about its health concerns, and sometimes federal and university-related deadlines are not applicable. Through the continued cooperative effort of the community of North Kohala, the *Hui Malama Ola Na Oiwi*, other Native Hawaiian health care organizations, and the RCMI Program, definitive information that is needed about the health status of Hawaiians will become available in the near future. In addition, future collaborative efforts to develop intervention and prevention programs should be on the horizon.

References

1. Look MA. *A mortality study of the Hawaiian people.* Honolulu, Hawaii: Research and Statistics Office; 1982. Hawaii State Department of Health1-18.
2. *State of Hawaii, Native Hawaiian Health Data Book.* Honolulu, Hawaii: Papa Ola Lokahi: 1992.
3. Elliot WJ. Cardiovascular risk factors: Which ones can and should be remedied? *Postgrad Med.* 1994; 96:49-61.
4. Sloan NR. Ethnic distribution of diabetes mellitus in Hawaii. *JAMA.* 1963;183:123-128.
5. Bassett DR, Rosenblatt G, Moellering RC, Hartwell AS. Cardiovascular disease, diabetes mellitus and anthropometric evaluation of Polynesian males on the island of Niihau. *Circulation.* 1963;34:1088-97.
6. Curb JD, Aluli NE, Kautz JA, Petrovitch H, Knutsen SF, Knutsen R, O'Conner HK, Conner WE. Cardiovascular risk factor levels in ethnic Hawaiians. *Am J Public Health.* 1991; 81:164-167.
7. *National center for health statistics: Current estimates from the national health interview survey.* Washington, DC: U.S. Govt Printing Office; 1989.
8. Valway S, Freeman W, Kaufmann S, Welty T, Helgerson SD, Gohdes D. Prevalence of diagnosed diabetes mellitus among American Indians and Alaskan Natives. *Diabetes Care.* 1987;16(Suppl 1):271-276.
9. Diabetes 1993 Vital Statistics. Ed: Moy CS. American Diabetes Association..
10. Department of Health annual report, State of Hawaii. Hawaii Health Surveillance Program 1988.1990: 96-113.
11. Miike LH. *Current health status and population projections of Native Hawaiians living in Hawaii.* Washington DC: Office of Technology and Assessment; April 1987; U.S. Congress.
12. Aluli NE. Prevalence of obesity in a Native Hawaiian population. *Am J Clin Nutr.*1991; 53:1556S-60S.
13. Kissebah AH, Freedman DS, Peuris AN. Health risks of obesity. *Med Clin N Am.*1989;73:111-138.
14. Yano K, Reed DM, Curb JD, Hankin JH, Albers JJ. *Arteriosclerosis.* 1986;6:422-433.
15. Kriska AM, Bennet PH. An epidemiological perspective of the relationship between physical activity and NIDDM: From activity assessment to intervention. *Diab Metab Rev.* 1992;8:355-372.
16. Lohman TG; Roche AF, Martorel R, eds. *Anthropometric Standardization Reference Manual.* Champaign, Illinois: Human Kinetics Books; 1988; 3-9,44-47.
17. Kunst A, Draeger B, Ziengenhorn; Bergenmeyer HU, Verlag C, Weiheim FRG, eds. *Methods of Enzymatic Analysis.* 1983;6:178-185.
18. Lipid Research Clinic Program. DHEW Publication (NIH) 1974, 75-628,Washington DC.
19. Friedewald WT, Levy RI, Fredrickson DS. Clin Chem. 1972, 18:499-502.
20. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes. 1979;28:1039-1057.
21. Marris MI. Impaired glucose tolerance diabetes. 1987;36:523-34.
22. The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). Arch Intern Med. 1993; 153:154-183.