**Objective:** The high prevalence of diabetes in non-Caucasian populations is reported not only for Native Hawaiians who suffer from high rates of obesity, but also for Japanese with a relatively low body weight. The objectives of this study were to estimate the prevalence of diabetes among participants of the Multiethnic Cohort (MEC) and to examine the association of body mass index (BMI) with self-reported diabetes by ethnicity.

**Design:** Cross-sectional analysis of baseline questionnaire at cohort entry.

**Participants:** 187,439 MEC subjects in Hawaii and California from five ethnic groups.

Main Outcome Measures: Participants completed a 26-page, self-administered survey with questions concerning anthropometrics, demographic, medical, lifestyle, and food consumption behavior. Age-adjusted prevalence of diabetes was calculated by sex and ethnicity and stratified by BMI. Prevalence ratios were determined using logistic regression while adjusting for variables that are known to be related to diabetes. The c statistic was computed to compare models with different confounders.

**Results:** The prevalence of self-reported diabetes in the MEC was 11.6%. The age-adjusted diabetes prevalence ranged from 6.3% in Caucasians to 10.2% in Japanese, 16.1% in Native Hawaiians, 15.0% in African Americans, and 15.8% in Latinos. After adjustment for known risk factors, the prevalence ratio by ethnicity ranged between 2.1 (African American and Latino), 2.8 (Japanese), and 3.0 (Native Hawaiian) as compared to Caucasians. These differences were observed among all BMI categories.

**Conclusions:** Ethnic differences in the prevalence of diabetes persisted after stratification by BMI. The prevalence of diabetes was at least two-fold higher in all ethnic groups than among Caucasians. (*Ethn Dis.* 2009;19:49–55)

**Key Words:** Diabetes Mellitus, Type 2, Obesity, Body mass index, Risk factors, Ethnic groups, Logistic models, Asian Americans, Pacific Islanders

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# INTRODUCTION

Type 2 diabetes is an important cause of mortality and morbidity globally.<sup>1</sup> Increases in obesity and sedentary lifestyle behaviors, early detection and intervention efforts leading to reduction in mortality, and overall longer life expectancy contribute to the increasing prevalence.<sup>2</sup> According to the Behavioral Risk Factor Survey System (BRFSS), the prevalence of diabetes in the United States increased from 4.9% to 6.5% during a nine-year period.<sup>3</sup> Increases were observed in both sexes and in all age and ethnic groups. Overweight, excess energy intake, and physical inactivity have been associated with the rapidly rising numbers of diabetes patients.4,5 The prevalence of diabetes is considerably higher among non-Caucasian ethnic groups than among Caucasians.<sup>6</sup> The effect of body weight and diet appears to differ by ethnic background. Native Hawaiians who suffer from a high rate of obesity have an extremely high risk for diabetes. Persons of Japanese ancestry are also affected by a disproportionately high rate of the disease despite their relatively low body mass index (BMI).7 The Multiethnic Cohort (MEC) Study offers a unique opportunity to examine ethnic differences in the prevalence of diabetes.8 The cohort includes African Americans, Latinos, Japanese Americans, Native Hawaiians, and Caucasians. The objective of this analysis was to estimate the prevalence of diabetes

Address correspondence and reprint requests to: Gertraud Maskarinec, MD, PhD; Cancer Research Center of Hawaii; 1236 Lauhala St; Honolulu, HI 96813; 808-586-3078; gertraud@crch.hawaii.edu among MEC participants according to ethnic group and BMI at cohort entry and at age 21.

# **METHODS**

The Multiethnic Cohort Study of Diet and Cancer was established in 1993 through 1996 to investigate diet and cancer among different ethnic groups in Hawaii and California.8 A concurrent recruitment effort, in Hawaii only, made Native Hawaiians part of the cohort. Persons who reported more than one ancestry were assigned to one of the categories according to the following priority ranking: African American, Native Hawaiian, Latino, Japanese, Caucasian, and other. Of the 215,251 members, 16% were African American, 22% Latino, 26% Japanese, 7% Native Hawaiian, 23% Caucasian, and 6% others. Response rates varied from 20% in Latinos to 49% in Japanese Americans. A comparison of the cohort distributions by educational levels and marital status with corresponding census data for the two geographic areas confirmed that the cohort is representative of the general population.<sup>8</sup> Annual linkages with state death certificate files are used to update vital status information on cohort members.

Participants entered the cohort by completing a 26-page, self-administered mailed questionnaire that included sections on height, body weight (at cohort entry and at age 21), physical activity, tobacco use, medical history, reproductive history, and demographic information, including migrant status, and a food frequency questionnaire.<sup>9</sup> The presence of diabetes, hypertension, heart The objective of this analysis was to estimate the prevalence of diabetes among MEC participants according to ethnic group and BMI at cohort entry and at age 21.

attacks or angina was assessed as follows: "Has your doctor ever told you that you had any of the following conditions?" Physical activity was assessed with questions about the following activities: sleeping; sitting in a car or bus, at work, watching TV, at meals, and at other times; playing strenuous sports; doing vigorous work; or doing moderate activity. Information on the occupation and industry in which the respondent worked the longest was used as a surrogate for occupational physical activity. A summary variable of metabolic equivalents was computed by multiplying the duration for each physical activity with the respective value of that activity based on published values.<sup>10</sup>

Of the 215,251 participants who entered this study, 27,812 were exclud-

ed: 13,992 reported an ethnicity other than the five major groups, 2,541 had incomplete BMI information, and 11,279 did not report their diabetes status. After exclusion, 47,657 partcipants were Caucasians (25.4%), 30,227 were African Americans (16.1%), 13,659 were Hawaiians (7.3%), 54,449 were Japanese (29.1%), and 41,447 were Latinos (22.1%), with a total of 187,439 participants included in this cross-sectional analysis. Categorical variables were created for BMI to indicate underweight (<18.5 kg/m<sup>2</sup>), normal weight  $(18.5-24.9 \text{ kg/m}^2)$ , overweight (25.0-29.9 kg/m<sup>2</sup>), and obesity ( $\geq 30.0 \text{ kg/m}^2$ ). We also created ethnicity-specific categories based on recommendations by the World Health Organization (WHO) with cutpoints for overweight and obesity of 23 and 25 kg/m<sup>2</sup> for Japanese and 26 and 32 kg/m<sup>2</sup> for Native Hawaiians.<sup>11</sup> To obtain prevalence odds ratios (POR) and 95% confidence intervals (CI), we applied logistic regression with the presence of diabetes as outcome and age at cohort entry, sex, BMI, education, physical activity, and total energy intake as independent variables. To compare the ability of models with different confounders to predict diabetes prevalence, we computed the c statistic, a method to assess goodnessof-fit that is based on the area under the receiver operator curve. If the test is perfect, the area under the curve is equal to 1.0; if it performs no better than chance, the area will be .5.

# RESULTS

The age of the 86,205 men and 101,234 women in this analysis ranged from 45 to 78 years (Table 1). The five ethnic groups differed by age, education, anthropometric variables, medical history, and lifestyle behaviors (P < .001). Of the five ethnic groups, the Japanese had the lowest mean BMI, followed by Caucasians, Latinos, and African Americans; Native Hawaiians had the highest mean BMI. The range of BMI at age 21 was considerably smaller. The overall prevalence of diabetes was 11.6%, with a higher ageadjusted prevalence for men than women. Native Hawaiians had the highest prevalence, followed by Latinos, African Americans, Japanese, and Caucasians at 6.3%.

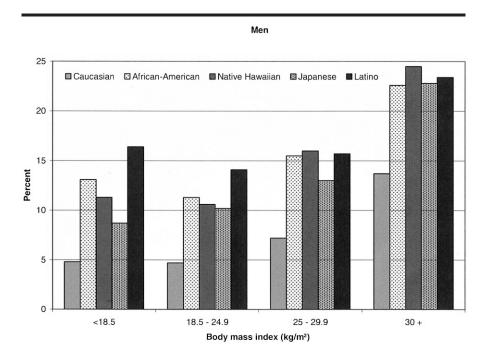
The prevalence of diabetes was significantly higher for all ethnic groups

Characteristic*	Overall	Caucasian	African American	Native Hawaiian	<b>Japanese</b> 54,449	Latino	
Number	187,439	47,657	30,227	13,659		41,447	
Men	86,205	22,194	11,479	6036	26,116	20,380	
Women	101,234	25,463	18,748	7623	28,333	21,067	
Age at study entry, years	$59.8 \pm 8.8$	$58.9 \pm 9.1$	$60.9 \pm 9.0$	$56.4 \pm 8.6$	$60.9 \pm 9.1$	59.6±7.8	
History of diabetes, age-adjusted %	21,825 (11.6)	2847 (6.3)	4664 (15.0)	2032 (16.1)	5772 (10.2)	6510 (15.8)	
History of hypertension, %	73,146 (39.0)	13,898 (29.2)	16,767 (55.5)	6098 (44.6)	21,787 (40.0)	14,596 (35.2)	
History of heart attack or angina, %	15,734 (8.4)	3627 (7.6)	3665 (12.1)	1133 (8.3)	3492 (6.4)	3871 (9.2)	
Weight, pounds	$162 \pm 38$	167±37	179±38	$181 \pm 45$	$141 \pm 28$	166±33	
Men	177±34	$185 \pm 32$	190±35	199±42	157±25	178±30	
Women	$150 \pm 37$	$151 \pm 34$	172±39	167±42	126±23	155±32	
BMI at cohort entry, kg/m <sup>2</sup>	$26.0 \pm 5.1$	25.6±4.9	$27.9 \pm 5.7$	28.4±6.2	$23.9 \pm 3.7$	27.2±4.9	
Men	26.1±4.2	26.0±4.1	$26.7 \pm 4.4$	$28.6 \pm 5.5$	24.7±3.3	26.9±4.0	
Women	$25.9 \pm 5.8$	$25.3 \pm 5.5$	28.6±6.3	$28.3 \pm 6.7$	23.1±3.9	$27.4 \pm 5.5$	
BMI at age 21, kg/m <sup>2</sup>	21.4±3.4	21.4±3.2	21.5±3.6	22.6±4.1	$20.9 \pm 2.8$	21.8±3.7	
Education, years	$13.2 \pm 3.2$	$14.5 \pm 2.7$	13.4±2.8	13.1±2.4	$13.8 \pm 2.6$	10.7±3.8	
Activity per day, MET	$1.62 \pm .3$	$1.62 \pm .3$	$1.57 \pm .3$	1.64±.3	$1.60 \pm .3$	$1.67 \pm .3$	

Table 1. Characteristics of 187,439 participants in the Multiethnic Cohort Study of Diet and Cancer\*

BMI = body mass index, MET = metabolic equivalent.

\* Data are presented as numbers and percentages for categorical variables and means plus or minus standard deviations for continuous variables.



Women

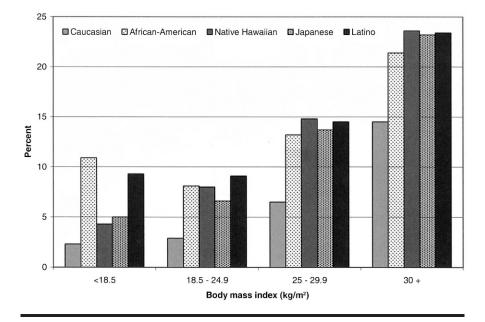


Fig 1. Age-adjusted prevalence of diabetes by ethnicity and BMI category

than for Caucasians across BMI categories (Figure 1). The percentage among obese participants was twice as high as for normal-weight men and three times as high for normal-weight women. For underweight participants, the prevalence tended to be as high, or higher, than in normal-weight subjects. The prevalence of diabetes among Japanese was lower (7.7%, 10.4%, and 14.8%, respectively) when we used the ethnicity-specific BMI cutpoints for normal, overweight, and obese categories compared with the standard categories (8.7%, 13.3%, and 22.2%, respectively); among Native Hawaiians, using the ethnicity-specific categories resulted in an increased prevalence of diabetes (8.8%, 15.7%, and 23.9% compared with 8.0%, 14.1%, 22.4%).

In comparison with Caucasians, the sex- and age-adjusted PORs for the other ethnic groups ranged from 1.66 to 3.08; the lowest POR was among Japanese (Table 2). Adding BMI to the model reduced the range to 2.11-2.63 and increased the c statistic from .644 to .695. A model with BMI, age, and sex alone showed a c statistic of .674, indicating the strong association between BMI and ethnicity. After additional adjustment for education, physical activity, and total energy intake, the PORs remained above 2 for all ethnic groups, and the c statistic rose to .703. As indicated by the 95% CIs, Japanese had a significantly lower POR than Native Hawaiians and Latinos. An interaction term between BMI and ethnicity revealed that, in comparison with Caucasians, BMI influenced diabetes prevalence significantly less in African Americans, Native Hawaiians, and Latinos (P<.001), while the interaction term was not significant for Japanese (P=.82).

Although a higher BMI at age 21 predicted a higher prevalence of diabetes for all ethnic groups, the difference between lowest and highest categories was less than for BMI at cohort entry. Diabetes prevalence was 9.1%, 10.7%, 19.7%, and 30.1% for underweight, normal weight, overweight, and obese subjects, respectively. As compared with the c value of .695 for model 2 in Table 2, c was only .674 when BMI at age 21 was the dependent variable. The respective PORs for African Americans, Native Hawaiian, Japanese, and Latinos were 2.70, 2.79, 1.85, and 2.85. In a logistic model with BMI at age 21, the PORs for overweight and obesity were 1.91 (95 CI 1.69-2.16) and 3.56 (95 CI 3.15-4.02), as compared with 2.31 (95 CI 2.05-2.61) and 4.68 (95 CI

The most noteworthy finding is the elevated diabetes prevalence of similar magnitude across the four non-Caucasian groups.

4.14–5.30) with BMI at cohort entry as outcome.

# DISCUSSION

This analysis observed a higher prevalence of diabetes among persons from five ethnic groups with overweight and obesity when compared with those of normal weight. The most noteworthy finding is the elevated diabetes prevalence of similar magnitude across the four non-Caucasian groups. When stratified by BMI, ethnic differences in diabetes prevalence were observed even among normal-weight and underweight participants. Inclusion of BMI in the logistic model raised the POR for Japanese, whereas the PORs for African Americans, Native Hawaiians, and Latinos declined. After additional adjustment for covariates, the prevalence of diabetes remained at least twice as high among African Americans, Japanese, Native Hawaiians, and Latinos as compared with Caucasians, although the POR was slightly lower for Japanese than for Native Hawaiians and Latinos. The association of diabetes with BMI at age 21 was weaker than for BMI at cohort entry.

The ethnic differences in diabetes prevalence agree with previous reports. In Hawaii, Native Hawaiians and Japanese reported a much higher diabetes prevalence than Caucasians (11.5% and 9.2% vs 5.6%).<sup>12</sup> The prevalences in California were 6.7% for Caucasians, 15.9% for African Americans, and 8.9% for Hispanics.<sup>13</sup> In comparison with the 2001 BRFSS, the PORs in the MEC analysis were higher for all ethnic groups except for Native Hawaiians. In the BRFSS, they were 1.6 for Asians, 1.9 for African Americans, 1.9 for Hispanics, and 3.0 for Pacific Islanders as compared with Caucasians.<sup>14</sup> The relatively small population of Asians in the BRFSS may have been younger and more recent immigrants than the second- and third-generation Japanese Americans in the MEC. As in our study, adjustment for BMI made the high rate of diabetes in Asians more apparent.

Diagnostic bias is a serious concern in many diabetes investigations. However, a Hawaii study among a rural population that measured fasting glucose and administered an oral glucose test in 1452 participants supports our findings.<sup>15</sup> Native Hawaiians, Japanese, and Filipino participants had an approximately threefold higher prevalence of diabetes and of impaired glucose

tolerance compared with Caucasians. Each of these groups also had significantly higher means for fasting and twohour post-challenge glucose levels than Caucasians. The similarity in prevalence of abnormal glucose tolerance among each of the non-Caucasian ethnic groups was striking, considering the significantly higher BMI observed among part-Hawaiian participants. While insulin resistance has been observed to precede the development of type 2 diabetes and be closely associated with obesity, type 2 diabetes in nonobese Japanese was reported to be preceded by decreased insulin secretion.<sup>16</sup> Therefore, different etiologic pathways for type 2 diabetes have been proposed that range from the obesityassociated insulin resistance seen in the Pimas and Native Hawaiians to the non-obese impaired insulin secretion observed in Japanese, Korean, and Vietnamese populations.<sup>16–18</sup>

While the obese type of type 2 diabetes is associated with increased fasting blood glucose, hyperinsulinemia, and insulin resistance of the peripheral target tissues accompanied by declining beta-cell function, the non-obese type initially manifests itself with decreased insulin secretion despite normal fasting blood glucose. This inability of pancreatic beta-cells to secrete sufficient insulin was well described in Japanese.<sup>19–21</sup> Its importance is evident from reports that diagnosis by fasting blood sugar alone misses 25% of cases of type 2 diabetes in Asians and 66% of cases in

Ethnicity	Model 1		Model 2		Model 3		Model 4	
	POR	95%CI	POR	95%CI	POR	95%CI	POR	95%CI
Caucasian	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
African American	2.74	2.61-2.88	2.27	2.16-2.39	2.18	2.06-2.30	2.20	2.08-2.33
Native Hawaiian	3.08	2.89-3.27	2.48	2.33-2.64	2.37	2.22-2.53	2.40	2.24-2.57
Japanese	1.74	1.66-1.82	2.11	2.01-2.21	2.07	1.97-2.18	2.10	1.99-2.21
Latino	2.91	2.77-3.04	2.63	2.51-2.75	2.39	2.27-2.52	2.44	2.31-2.57
c statistic	.644		.695		.702		.703	

POR = prevalence odds ratio, CI = confidence interval

\* Obtained by logistic regression. Model 1 adjusted for sex and age; model 2 added body mass index; model 3 added education and physical activity level; model 4 added total energy intake.

one study of elderly Japanese American men.<sup>22,23</sup> Thus, Asians may be at higher risk for diabetes at lower levels of BMI in part because of a reduced response of beta-cells to even mild insulin resistance. These observations prompted the recommendation of different BMI cutpoints to define overweight and obesity in Asians and Pacific Islanders.<sup>11</sup> As shown in our data, the use of ethnicityspecific criteria lowered the prevalence in Japanese and increased it in Native Hawaiians.

One surprising finding of our study was that the prevalence of diabetes among underweight participants in some ethnic groups was similar to or higher than among normal-weight participants in the same ethnic group. Some participants may have had type 1 diabetes, which is not associated with BMI. However, given the age structure of the MEC, we expect more than 90% of cases to be type 2 diabetes. Another possibility is that type 2 patients may have experienced weight loss, intentional, because of therapeutic changes in lifestyle factors, or unintentional, because of disturbed glucose metabolism. However, diabetes medications more often result in weight gain. Finally, the use of self-reported body weight may have resulted in underreporting that would have reduced the association with diabetes. It is noteworthy, however, that another recent cohort study in Japan reported significantly higher incidence rates of diabetes among underweight persons compared with normal-weight persons.24

A limitation of this study is the selfreported disease status reported in a selfadministered questionnaire, in effect relying on diagnoses in variable clinical settings in Hawaii and Los Angeles. Although the World Health Organization recommended use of the oral glucose tolerance test as the gold standard criterion in 1985,<sup>25</sup> few clinicians use this approach and rely more on fasting and casual glucose levels for diagnosis. The American Diabetes Association recently revised the diagnostic criteria with a recommendation for greater reliance on fasting plasma glucose levels.<sup>26</sup> Detection bias by healthcare providers may have also occurred because they may consider certain groups, eg, Pacific Islanders, at higher risk of diabetes and be more likely to order diagnostic tests. In addition, there is a possibility of selection bias, as persons willing to participate in a prospective cohort may be healthier or more concerned with their health compared with the general population.

Another issue is the sparse data available on co-morbid conditions that may be associated with BMI. Unfortunately, the MEC did not collect other measures of adiposity at baseline. Since the effect of excess body weight appears to be due to excess abdominal fat, in particular the visceral fat component,<sup>27</sup> BMI may inadequately assess adiposity. In the EPIC/Potsdam study, waist circumference was the most predictive anthropometric variable, but the difference from BMI was small.<sup>28</sup> Among Native Hawaiian women, it was reported that waist-to-hip ratios are an independent determinant of glucose tolerance.<sup>29</sup> Because of the cross-sectional nature of this study, a lower BMI could be the result of a healthier lifestyle as a consequence of being diagnosed with diabetes. If one considers that diabetes patients are advised to control their diet and to be physically active, risk estimates for incident cases of diabetes may have been higher than the PORs in this report.

The MEC population offered considerable strengths for a diabetes study. It is a large, population-based study with a high response rate. Persons of five different ethnic backgrounds living in two distinct locations completed the same questionnaire.<sup>8</sup> Furthermore, the number of participants with Japanese and Native Hawaiian background far exceeded previous comparative reports.<sup>14,15</sup> The test-based results from the Kohala study provide confidence that the ethnic differences are not due to diagnostic bias.<sup>15</sup>

This study confirmed previous reports of high diabetes rates among non-Caucasian populations. Contrary to some studies, we found that diabetes prevalence in all ethnic groups was related with similar strength, although slightly weaker in Japanese, to obesity as in Native Hawaiians.<sup>30</sup> The importance of diabetes as a risk factor for cardiovascular disease was demonstrated in another MEC investigation; the presence of diabetes significantly increased mortality due to acute myocardial infarction and other heart diseases.<sup>31</sup> Given the six- to seven-fold higher diabetes mortality rates for Native Hawaiians as compared with Caucasians,<sup>32</sup> the incidence among Native Hawaiians may be even higher than prevalence data suggest. The twofold higher prevalence among Japanese Americans in Hawaii and in Los Angeles than in Hiroshima<sup>33</sup> suggests that the occurrence of diabetes in migrants rises as a result of changing environments and lifestyles.6

Although changes in lifestyle leading to chronic overnutrition, impaired insulin signaling, and relative insulin deficiency are of major importance in the etiology of type 2 diabetes, genetic susceptibility contributes to the development of metabolic disturbances on the pathway to disease.<sup>34</sup> Ethnic disparities in disease occurrence also support a possible genetic etiology. Genetic studies have employed both candidate gene and genome-wide association studies and have implicated eleven genes or gene regions in the etiology of type 2 diabetes mellitus.<sup>35</sup> Of these, the strongest association, with an odds ratio of 1.37, has been reported for TCF7L2. The mechanism how this locus confers diabetes susceptibility is unclear, but it has been shown to encode a transcription factor that is involved in the Wnt signaling pathway. All eleven of these genes/gene regions were identified in Northern European populations, and

### DIABETES AND BODY MASS INDEX - Maskarinec et al

little is known about genetic variations of these regions in Asian and Polynesian populations. Furthermore, the relatively small risk estimates suggest that it is unlikely that variants of any single gene loci will account for the ethnic variability in our population. While recent work in Japan has identified two candidate gene loci on chromosomes 7p and 11p, the strength of association with diabetes was not reported.36 Therefore, further research is needed to ascertain the role of these gene regions in explaining the high prevalence of diabetes observed among Japanese Americans. Moreover, no data currently exist on the variability of any of these susceptibility loci among Hawaiians or any other Polynesian populations. The high diabetes prevalence across minority populations with significantly different BMIs warrants further investigation into etiologic pathways, body fat distribution, and genetics. As the incidence and prevalence of type 2 diabetes continue to rise, current strategies related to diabetes diagnosis and prevention may require modifications in order to consider the importance of sex and ethnicity related to diabetes risk.

### **ACKNOWLEDGMENTS**

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- Acquisition of data: Henderson, Kolonel
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