Ethnic differences in weight gain and diabetes risk: The Multiethnic Cohort Study

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Received 1st June 2010; received in revised form 7 October 2010; accepted 7 October 2010
Available online 28 December 2010

Abstract

Aim. – To improve our understanding of excess body weight and risk for diabetes type 2, the study examined the influence of weight change in the Hawaii component, including 78,006 Caucasians, Japanese Americans and Native Hawaiians, of the Multiethnic Cohort Study.

Methods. – Participants aged 58.5 ± 9.2 years completed a questionnaire at cohort entry (Qx1), including weight at age 21, and a follow-up questionnaire 5 years later (Qx2). After 14 years of follow-up, 8892 incident diabetes cases were identified through self-reports or linkups with the major health plans in Hawaii. Cox regression analysis was applied, stratified by age and adjusted for confounders, to estimate hazard ratios (HRs).

Results. – The mean weight gain from age 21 to Qx1 was 10.5 ± 11.0 kg and, between Qx1 and Qx2, 0.8 ± 5.6 kg. Diabetes risk showed a significant dose–response relationship with weight gain from age 21 (P < 0.0001). The respective HRs for a weight gain of 5–10 kg and greater or equal to 25 kg were 1.8 (95% CI: 1.7–2.0) and 7.7 (95% CI: 7.1–8.4), while weight loss of greater than 5 kg significantly reduced diabetes risk (HR = 0.7; 95% CI: 0.6–0.9). The interaction term of weight change since age 21 with ethnicity was also highly significant (P < 0.0001).

Compared with stable-weight Caucasians, the adverse effects of weight gain were more pronounced in those of Japanese and Native Hawaiian descent. Weight change between Qx1 and Qx2 conferred a smaller risk.

Conclusion. – These findings support the current public-health recommendations for weight control and particularly among ethnic groups at high risk for diabetes.

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Keywords: Type 2 diabetes; Incidence; Epidemiology; BMI; Obesity; Weight gain; Ethnicity; Prospective studies; Longitudinal study; Hawaii

Résumé

Différences ethniques des effets de la prise de poids sur le risque de diabète : données de la cohorte multi-ethnique.

Objectif. – Pour améliorer notre compréhension des liens entre l’excès pondéral et le risque de diabète de type 2 (DT2), nous avons examiné les effets des variations du poids dans la composante d’Hawaii de la cohorte multiethnique qui comportait 78 006 caucasiens, américano-japonais et hawaïens de souche.

Méthodes. – Les participants, âgés de 58,5 ± 9,2 ans ont rempli un questionnaire à l’inclusion dans la cohorte (Qx1) (dans lequel était noté le poids à l’âge de 21 ans) et un questionnaire de suivi cinq ans plus tard (Qx2). Après 14 ans de suivi, 8892 cas incidents de DT2 ont été identifiés par l’auto-déclaration ou grâce aux registres de santé d’Hawaii. Nous avons appliqué la régression de Cox, stratifiée selon l’âge et ajustée pour les facteurs confondants pour calculer le risque relatif.

Résultats. – La prise moyenne de poids entre l’âge de 21 ans et le questionnaire d’inclusion Qx1 était de 10,5 ± 11,0 kg et celle entre Qx1 et Qx2 de 0,8 ± 5,6 kg. Il existait une corrélation entre le risque de survenue du diabète et la prise de poids depuis l’âge de 21 ans (P < 0.0001). Le risque relatif de survenue d’un DT2 était de 1,8 (IC à 95%: 1,7–2,0) pour un gain de poids de 5 à 10 kg et de 7,7 (7,1–8,4) pour un gain de poids supérieur ou égal à 25 kg. Une perte de poids de plus de 5 kg était significativement associée à une réduction de survenue d’un DT2 (RR 0,7 ; 0,6–0,9). Il existait une interaction très significative entre variation du poids et ethnicité (P < 0,0001). Par comparaison aux caucasiens de poids
1. Introduction

The global burden of diabetes continues to rise particularly among ethnic groups other than Caucasian [1–3]. Native Hawaiians suffer from extremely high rates of obesity and diabetes. However, despite their relatively low body weight, people of Japanese ancestry are also disproportionately affected by diabetes [4]. For the more than 44,000 Japanese Americans, 14,000 Native Hawaiians and 35,000 Caucasians in the Hawaii component of the Multiethnic Cohort (MEC) Study, a previous analysis had found diabetes risk estimates of 2.1, 4.1 and 9.5 for a body mass index (BMI) of 22.0–24.9, 25.0–29.9 and greater or equal to 30.0 kg/m², respectively, compared with less than 22 kg/m² [5]. However, the risk was highest for Japanese Americans (46% for men and 51% for women) and lowest for Native Hawaiians (28% for men and 35% for women); nevertheless, the MEC was a representative sample of the population, as evidenced by comparisons of educational levels and marital status with the corresponding census data [14]. After excluding non-eligible subjects (10,028 prevalent diabetes cases, 8797 other ethnic groups, 6202 with missing covariates, 855 unconfirmed diabetes cases and 10 with either no follow-up information or diabetes information at baseline), 78,006 subjects (37,482 men and 40,524 women) were ultimately eligible for the present analysis. The study was approved by the Committee on Human Studies at the University of Hawaii and by the Institutional Review Board at Kaiser Permanente Hawaii.

2. Methods

2.1. Study population

The MEC Study was established from 1993 through 1996 to examine diet and cancer among different ethnic groups in Hawaii and California [14]. The current analysis was limited to the Hawaii component due to the availability of diabetes-incidence data from major local health plans [5]. The Hawaii component of the MEC comprised 103,898 individuals belonging to three main ethnic groups (Native Hawaiians, Caucasians and Japanese Americans). Subjects aged 45–75 years entered the cohort by completing a 26-page, self-administered mailed survey (Qx1), which asked about demographics, medical conditions, and current height and weight, as well as weight at age 21, lifestyle factors and the usual diet over the past several years [15]. Response rates were highest for Japanese Americans (46% for men and 51% for women) and lowest for Native Hawaiians (28% for men and 35% for women); nevertheless, the MEC was a representative sample of the population, as evidenced by comparisons of educational levels and marital status with the corresponding census data [14]. After excluding non-eligible subjects (10,028 prevalent diabetes cases, 8797 other ethnic groups, 6202 with missing covariates, 855 unconfirmed diabetes cases and 10 with either no follow-up information or diabetes information at baseline), 78,006 subjects (37,482 men and 40,524 women) were ultimately eligible for the present analysis. The study was approved by the Committee on Human Studies at the University of Hawaii and by the Institutional Review Board at Kaiser Permanente Hawaii.

2.2. Case ascertainment

The detailed follow-up and categorization of diabetes cases, as reported previously, was only available for the Hawaii component of the MEC [5]. Incident cases were identified through three sources:

- a short follow-up questionnaire (Qx2), sent to all MEC members in 1999–2003 to update information on medical conditions, which achieved a response rate of 84%;
- a medication questionnaire, including diabetes drugs administered in 2001–2007, available for 38% of the 103,898 subjects;
- and the MEC database which, in July 2007, was linked to the institutional review board (IRB) to identify diabetes cases.

After excluding 855 cases that were self-reported in the questionnaire, but not confirmed by a health insurance plan, 2337 of the 8892 incident cases were first identified in the Qx2, 1029 through the medication questionnaire and 5526 by one of the health plans. From the time that the MEC was initiated, annual linkages with state and national death-certificate files have been performed to obtain information on vital status.
2.3. Statistical methods

All statistical analyses were performed using SAS statistical software, version 9.2 (SAS Institute Inc., Cary, NC, USA). Self-reported weight changes between age 21 and Qx1 (T1) as well as changes from Qx1 to Qx2 (T2) were computed. For the former, seven categories were created (>5 kg weight loss; ≤5 kg as stable weight; and weight gains of 5–10, 10–15, 15–20, 20–25 and ≥ 25 kg). These categories were limited to the sample sizes for T1 and T2 were 37.4 ± 9.2 years (Table 1). The mean age at cohort entry for all Hawaii MEC Study members was 58.5 ± 9.2 years. Mean time periods for Cox proportional-hazards regression models were used to estimate diabetes risk in relation to categories of weight change using ±5 kg as the reference category. Hazard ratios (HRs) and 95% confidence intervals (CI) were calculated, using follow-up time as the underlying time metric [16], while controlling for age at Qx1 by stratification. Because of previously established associations, all models were adjusted for gender, ethnicity (Japanese Americans and Native Hawaiians vs Caucasians; overall model only), and levels of physical activity (quintiles) and education (13–15 and > 15 years). Models for weight change during T1 also included BMI category at age 21 (23.0–24.9, 25.0–29.9 and ≥ 30.0 kg/m² vs < 23.0 kg/m²). T2 models included BMI category at Qx1 (25.0–29.9 and ≥ 30.0 kg/m² vs < 25.0 kg/m²) and excluded diabetes cases diagnosed at Qx2. Because of missing values, the sample sizes for T1 and T2 were 75,590 and 61,982 individuals, respectively. Linear trend tests were performed by fitting a model with weight-change categories as a single ordinal variable, while stratifications were performed by ethnicity, BMI at age 21 (<23 kg/m² vs ≥ 23 kg/m² because of the low mean BMI at that age) and BMI at Qx1 (<25 kg/m² vs ≥ 25 kg/m²). Also, a T1 model was fitted for weight change that adjusted simultaneously for BMI at age 21 and at Qx1. No major violations of the proportional-hazards assumption were observed when examined by Kaplan–Meier survival curves [17].

3. Results

Of the 8892 incident diabetes cases, 1870 were Caucasian, 5230 were Japanese American and 1792 were Native Hawaiian (Table 1). The mean age at cohort entry for all Hawaii MEC Study members was 58.5 ± 9.2 years. Mean time periods for T1 and T2 were 37.4 ± 9.2 years (n = 75,590) and 5.5 ± 0.8 years (n = 61,982), respectively. The mean weight gain was 10.5 ± 11.0 kg during T1 and 0.8 ± 5.6 kg during T2. Japanese Americans were the leanest group at each time point and reported the greatest weight gain from age 21 to Qx1, while Native Hawaiians had the highest BMI at each time point and reported the least weight gain from age 21 to Qx1. No major violations of the proportional-hazards assumption were observed when examined by Kaplan–Meier survival curves [17].

Table 1
Incident cases of diabetes and baseline characteristics of the Hawaii component of the Multiethnic Cohort Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Caucasian</th>
<th>Japanese American</th>
<th>Native Hawaiian</th>
<th>All (n = 78,006)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (n = 15,590)</td>
<td>Women (n = 15,111)</td>
<td>Men (n = 17,147)</td>
<td>Women (n = 19,267)</td>
</tr>
<tr>
<td>Cases (%)</td>
<td>7.2</td>
<td>5.0</td>
<td>16.1</td>
<td>12.8</td>
</tr>
<tr>
<td>Non-cases (%)</td>
<td>92.8</td>
<td>95.0</td>
<td>83.9</td>
<td>87.2</td>
</tr>
<tr>
<td>Age (years; %)</td>
<td>45–54</td>
<td>44.7</td>
<td>47.1</td>
<td>32.8</td>
</tr>
<tr>
<td></td>
<td>55–64</td>
<td>27.7</td>
<td>26.7</td>
<td>27.9</td>
</tr>
<tr>
<td></td>
<td>≥ 65</td>
<td>27.6</td>
<td>26.2</td>
<td>39.3</td>
</tr>
<tr>
<td>Education (years; %)</td>
<td>≤ 12</td>
<td>19.5</td>
<td>23.6</td>
<td>39.4</td>
</tr>
<tr>
<td></td>
<td>13–15</td>
<td>29.0</td>
<td>34.3</td>
<td>28.8</td>
</tr>
<tr>
<td></td>
<td>&gt; 15</td>
<td>51.5</td>
<td>42.1</td>
<td>31.8</td>
</tr>
<tr>
<td>BMI at Qx1 (%)</td>
<td>&lt; 25 kg/m²</td>
<td>75.7</td>
<td>73.9</td>
<td>26.9</td>
</tr>
<tr>
<td></td>
<td>25–30 kg/m²</td>
<td>40.7</td>
<td>36.7</td>
<td>21.4</td>
</tr>
<tr>
<td></td>
<td>≥ 30 kg/m²</td>
<td>12.3</td>
<td>12.6</td>
<td>5.8</td>
</tr>
<tr>
<td>BMI (kg/m²) at age 21</td>
<td>22.3 ± 2.8</td>
<td>20.4 ± 2.6</td>
<td>21.6 ± 2.6</td>
<td>20.1 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>at Qx1</td>
<td>25.8 ± 3.9</td>
<td>24.6 ± 4.9</td>
<td>24.7 ± 3.3</td>
</tr>
<tr>
<td></td>
<td>at Qx2</td>
<td>26.6 ± 4.1</td>
<td>25.6 ± 5.2</td>
<td>25.3 ± 3.5</td>
</tr>
<tr>
<td>Weight change (kg)</td>
<td>age 21 to Qx1 (T1)</td>
<td>11.1 ± 11.2</td>
<td>11.3 ± 11.8</td>
<td>9.0 ± 8.6</td>
</tr>
<tr>
<td></td>
<td>Qx1 to Qx2 (T2)</td>
<td>1.0 ± 6.4</td>
<td>1.4 ± 6.0</td>
<td>0.2 ± 4.6</td>
</tr>
<tr>
<td>Physical activity (METS)</td>
<td>1.7 ± 0.3</td>
<td>1.6 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>1.6 ± 0.2</td>
</tr>
<tr>
<td>Total energy intake (kcal)</td>
<td>2316 ± 891</td>
<td>1824 ± 689</td>
<td>2293 ± 833</td>
<td>1823 ± 674</td>
</tr>
</tbody>
</table>

Data are presented as means ± SD unless otherwise specified.

a Excluded from the 103,898 members of the Hawaii component were: 10,028 prevalent diabetes cases; 8797 other ethnicity; 6202 with missing covariates; 855 unconfirmed diabetes cases; and 10 with either no follow-up information or diabetes information at Qx1.
b Calculated with those included in the first (n = 75,590) and second analyses (n = 61,982).

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Table 2

Weight change and diabetes risk in the Hawaii component of the Multiethnic Cohort Study.

<table>
<thead>
<tr>
<th>Weight change (kg)</th>
<th>All</th>
<th></th>
<th>Caucasian</th>
<th></th>
<th>Japanese American</th>
<th></th>
<th>Native Hawaiian</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>HR^a</td>
<td>95% CI</td>
<td>n</td>
<td>HR^a</td>
<td>95% CI</td>
<td>n</td>
</tr>
<tr>
<td>Between age 21 and</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qx1^b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5</td>
<td>134</td>
<td>0.74</td>
<td>0.61–0.88</td>
<td>18</td>
<td>0.56</td>
<td>0.34–0.92</td>
<td>90</td>
</tr>
<tr>
<td>± 5</td>
<td>1062</td>
<td>1.00</td>
<td></td>
<td>147</td>
<td>1.00</td>
<td></td>
<td>807</td>
</tr>
<tr>
<td>5–10</td>
<td>1525</td>
<td>1.82</td>
<td>1.68–1.97</td>
<td>221</td>
<td>2.05</td>
<td>1.67–2.53</td>
<td>1147</td>
</tr>
<tr>
<td>15–20</td>
<td>1275</td>
<td>3.74</td>
<td>3.44–4.06</td>
<td>261</td>
<td>4.60</td>
<td>3.76–5.64</td>
<td>775</td>
</tr>
<tr>
<td>20–25</td>
<td>1163</td>
<td>4.90</td>
<td>4.50–5.33</td>
<td>313</td>
<td>6.55</td>
<td>5.38–7.97</td>
<td>554</td>
</tr>
</tbody>
</table>

P for trend < 0.0001 < 0.0001 c < 0.0001c < 0.0001c

Between Qx1 and Qx2^b

|                   |     |      |            |     |      |            |     |      |            |
|                   | n   | HR^a | 95% CI     | n   | HR^a | 95% CI     | n   | HR^a | 95% CI     |
|                   |     |      |            |     |      |            |     |      |            |
| > 5               | 532 | 0.98 | 0.89–1.07  | 126 | 0.88 | 0.73–1.07  | 262 | 3.07 | 2.66–3.54 |
| ±5                | 4011| 1.00 |           | 719 | 1.00 |           | 2717| 3.05 | 2.81–3.32 |
| 5–10              | 699 | 1.31 | 1.21–1.42  | 193 | 1.30 | 1.11–1.52  | 346 | 4.01 | 3.53–4.57 |
| ≥10               | 328 | 1.59 | 1.41–1.78  | 127 | 1.66 | 1.37–2.00  | 84  | 4.46 | 3.55–5.59 |

P for trend < 0.0001 < 0.0001c < 0.0001c < 0.0001c

^a Adjusted for ethnicity (overall model only), gender, physical activity (quintiles), education (12–15 and > 15 years vs ≤ 12 years) and body mass index (at age 21 or cohort entry).

^b Qx1 at cohort entry in 1993–1996; Qx2 in 1999–2003.

^c Derived by fitting a model with weight-change categories as a single ordinal variable for each ethnic strata separately.

change (HR = 0.74; 95% CI: 0.61–0.88). The respective HRs for those who gained 5–10 kg and greater or equal to 25 kg were 1.82 (95% CI: 1.68–1.97) and 7.74 (95% CI: 7.13–8.41), with a clear dose–response relationship (P < 0.0001). Weight loss during T2 did not lower diabetes risk, while a weight gain of greater than 10 kg increased diabetes incidence significantly by 60%, with no differences by ethnicity (P for interaction = 0.89).

As the interaction term of weight change since age 21 and ethnicity was highly significant (P < 0.0001), ethnic-specific analyses were conducted, using Caucasians with stable weight as the reference group (Table 2). Each weight-gain category conferred a higher risk of diabetes, with weight gain of greater or equal to 25 kg associated with an HR of 11.57 (95% CI: 9.65–13.88) in Caucasians, 18.50 (95% CI: 15.44–22.17) in Hawaiians and 30.59 (95% CI: 25.31–36.97) in Japanese Americans. Weight loss of greater than 5 kg was associated with a 44% lower diabetes risk in Caucasians. However, when this association was examined in Japanese Americans (using stable-weight Japanese Americans as reference), the HR for weight loss was 0.70 (95% CI: 0.56–0.87) while, in Native Hawaiians (using stable-weight Hawaiians as reference), the HR was 0.89 (95% CI: 0.58–1.38) (data not shown).

In addition, as a strong interaction was found between weight gain and BMI at age 21 (P = 0.0001), an analysis stratified by BMI at age 21 (< 23 kg/m² and ≥ 23 kg/m²) was conducted, again using Caucasians with stable weight as the reference group (Fig. 1). Because of the higher absolute diabetes risk in Japanese Americans and Native Hawaiians, the incidence of diabetes exceeded that for Caucasians across all weight-gain categories. The HRs associated with weight-gain categories for participants with a BMI less than 23 kg/m² at age 21 were considerably higher than for those with a BMI greater or equal to 23 kg/m² at age 21. For the low BMI group, the HRs for the highest category were 16.7, 30.1 and 47.0 for Caucasians, Native Hawaiians and Japanese Americans, respectively, whereas for the greater or equal to 23 kg/m² group, the HRs ranged from 7.0 to 14.7.

The interaction of BMI at Qx1 with weight change during T2 (Fig. 2) was not statistically significant (P = 0.23). Nevertheless...
those with a BMI greater or equal to 25 kg/m² experienced little additional risk due to weight gain, whereas the risk estimates among normal-weight participants were increased for weight gains greater or equal to 10 kg in all ethnic groups (HR = 2.6, 6.8 and 10.8 for Caucasians, Native Hawaiians and Japanese Americans, respectively).

Simultaneous adjustment for BMI at age 21 and BMI at Qx1 attenuated the diabetes risk estimates for weight change during T1, but the associations remained significant. The HR for a weight gain of greater or equal to 25 kg was 4.3 (95% CI: 3.8–4.8) for all participants compared with those with stable weight, and 6.1 (95% CI: 5.0–7.5), 15.8 (95% CI: 12.8–19.4) and 10.1 (95% CI: 8.3–12.3) for Caucasians, Japanese Americans and Native Hawaiians, respectively, compared with stable-weight Caucasians. BMI at age 21 and BMI at Qx1 both increased diabetes risk significantly.

4. Discussion

This analysis of three ethnic groups in Hawaii detected a strong effect of weight gain over more than 25 years, after taking into account BMI at age 21 and at cohort entry, when the mean age of participants was close to 60 years. A weight gain of 5–10 kg between age 21 and cohort entry doubled diabetes risk, and a gain of greater or equal to 25 kg was associated with an eightfold higher risk, while weight loss of greater than 5 kg reduced the risk by 25%. Compared with stable-weight Caucasians, the adverse effects of weight gain were more pronounced in participants of Japanese and Native Hawaiian descent. Similarly, the association between weight gain and diabetes was stronger for those with a BMI less than 23 kg/m² at age 21 compared with those with a BMI greater or equal to 23 kg/m². Weight gain during the 5.5 years of follow-up after cohort entry conferred a 60% increased risk, but weight loss during this interval was not associated with diabetes incidence, probably because older participants might have already experienced weight loss due to ageing and chronic health conditions.

Although modeling BMI at age 21 and at cohort entry attenuated the risk estimates for weight change slightly, each variable remained a significant predictor of diabetes risk. Also, the association between diabetes risk and weight gain was strongest in initially normal-weight participants—those with a BMI less than 23 kg/m² at age 21—thus underscoring the importance of maintaining low body weight throughout life. In addition, as hypothesized, the association between weight gain and diabetes was more pronounced in participants of Japanese descent. The prevailing theory is that excess BMI and weight gain have stronger effects in people of Asian descent due to their relatively higher proportion of body fat and, in particular, their tendency to accumulate visceral fat [18]. Visceral fat, but not abdominal subcutaneous fat, has been shown to be a risk factor for insulin resistance in Japanese Americans [19]. Furthermore, mechanistic studies indicate decreased insulin secretion during the early stages of diabetes development among Japanese, but not among Caucasian subjects [8], which suggests that Japanese subjects may not be able to compensate for insulin resistance through increased insulin production as seen in Caucasians.

In our present analyses, the diabetes risk estimates for Native Hawaiians were in between those for Caucasians and Japanese Americans, which may be explained by the ethnic admixture of this group. In the baseline questionnaire that allowed for more than one ethnicity, more than 95% of Caucasians or Japanese Americans indicated only one ethnic background whereas, among Native Hawaiians, 53% reported some Caucasian ancestry and 54% some Asian ancestry [20]. In addition, ethnic differences in food and nutrient intakes might also contribute to the different diabetes risks: for example, Caucasians consume more dairy foods than do the other groups; Japanese Americans eat more legumes, vegetables and rice; and Native Hawaiians report high intakes of fat, meat and calories in general [14,21].

Our findings agree with previous reports from Caucasian populations that found higher diabetes risks associated with weight gain [9,10,12,22–24]. In the NHS, the relative risks for diabetes among women with weight gains of 5.0–7.9 kg and 8.0–10.9 kg were 1.9 and 2.7, respectively, compared with women of stable weight since age 18 [22]. Similar risk estimates were reported in a community-based study in California [23], British men [10], the Johns Hopkins Precursors Study [12] and NHANES I [9]. During the 10-year follow-up for NHANES I, a 5- to 8-kg weight gain doubled diabetes risk, and a gain of greater than 20 kg quadrupled it [9]. Also comparable to our present findings is...
that weight gain or fluctuation of at least 10 lb (4.5 kg) between ages 40 to 60 years significantly increased the diabetes rate by 40% [23]. In addition, in agreement with our present stratified results, weight gain in Pima Indian women was related to diabetes incidence only in those who were not initially overweight [24]. Similarly, another report observed that, among middle-aged men with a BMI greater or equal to 28 kg/m², any further weight gain made little difference in their risk of diabetes [10]. Also in the NHANES I report, stratification by weight status at baseline made little difference [9].

Few previous investigations have included people of ethnic backgrounds other than Caucasian. Three reports included participants of Asian descent—one from Japan [11], one from China [13] and the NHS, which included 801 Asians [7]—and one study focused on Pima Indians [24]. A report of male Japanese employees showed a 14% greater diabetes risk with weight gain of greater than 2 kg [11]. The 801 women of Asian descent in the NHS had a twofold higher incidence rate than did Caucasians. Also, for each 5-kg increase in weight, risk estimates differed significantly by ethnicity, with 1.84 for Asians and 1.37 for Caucasians (P < 0.05) [7]. Among middle-aged Chinese women in Shanghai, a weight gain of greater than 0.75 kg/year since age 20, which corresponded to approximately 20 kg in total, was associated with a risk of 12.7 compared with those with no weight gain [13]. Among Pima Indian men, the age-adjusted diabetes incidence was 56.7/1000 person-years in those with an annual weight gain of greater or equal to 3 kg compared with 16.9/1000 person-years in those who lost weight [24].

Several limitations of this investigation need to be borne in mind. Body weight at all points in time relied on self-reports. In particular, weight at age 21 may have been recalled incorrectly after more than 25 years. There is evidence, however, that remote weight earlier in life can be recalled with some accuracy, as shown in elderly subjects [25], the NHS [26], a follow-up of American adults [27] and the Newton Girls’ Study [28]. Unfortunately no information on body weight between the three time points was available. For this reason, the possible effect of weight fluctuation could not be investigated in the present study. Also, no information on the reasons for weight loss was collected, such as whether it was voluntary or involuntary. Weight loss particularly during T2 may have been involuntary as a result of disease or ageing. Furthermore, as BMI is not an accurate estimate of body fat and because the proportion of body fat differs with ethnicity [29,30], it is possible that the true ethnic differences are of a different magnitude. It would have been preferable to examine other anthropometric measures such as waist circumference. Also, risk estimates for T1 were based exclusively on new cases diagnosed after cohort entry and excluded the 10,028 self-reported prevalent cases.

Although all cases of diabetes were confirmed by a health plan [5], detection bias is possible, given that those who are obese or of high-risk ethnic backgrounds may be more likely to undergo testing for diabetes. Such a bias would overestimate the association between BMI and diabetes. Also, there was no information on type of diabetes. However, given the median age of 59 years at Qx1, more than 90% of diabetes cases were most likely type 2.

On the other hand, this study also had several important strengths, foremost of which were its prospective nature, with 14 years of follow-up, and the inclusion of three ethnic groups that vary widely in both BMI and diabetes risk. Other strengths include the large sample size and the ascertainment of diabetes status through linkups with documented health plans [5]. Although diabetes at Qx2 was self-reported, only those cases confirmed by health-plan linkages in 2007 were included in the analysis.

5. Conclusion

In the present study, a strong dose–response relationship was observed between weight gain and diabetes risk in all the studied ethnic groups. Data from this analysis indicate that weight gain over time leads to increases in diabetes risk, particularly among lean individuals, and Native Hawaiians and Japanese Americans. The implications of these findings are that even low levels of weight gain can lead to increased diabetes risk, and that lifestyle modifications leading to weight loss are effective for lowering diabetes risk. Our observations support the current recommendations to reduce the risk of diabetes by preventing weight gain throughout adulthood, and to encourage weight loss in overweight and obese individuals. This advice is even more important for Japanese Americans and Native Hawaiians who, compared with Caucasians, appear to develop diabetes at a higher rate across all weight and weight-gain categories. Future analyses need to explore the possible causal mechanisms that might be promoting greater diabetes risk with equal weight gain in some populations, such as dietary preferences, body-fat distribution and weight fluctuations.

Conflict of interest statement

The authors have not declared any conflicts of interest.

Acknowledgements

The Multiethnic Cohort Study was supported by NCI grant R37CA54281 (PI: Dr L.N. Kolonel), the recruitment of Native Hawaiians was funded by grant DAMD 17-94-T-4184 (PI: Dr A. Nomura) and the diabetes project was funded by R21 DK073816 (PI: Dr G. Maskarinec). S.M.S. was supported by a postdoctoral training fellowship in Nutrition & Behavioral Cancer Prevention in a Multiethnic Population, funded by R25 CA090956 (PI: Dr G. Maskarinec). The authors also wish to thank Mark M. Schmidt and Aileen Uchida at the Kaiser Permanente Center for Health Research in Honolulu, HI, and Deborah Taira Juarez and Krista Hodges, at HMSA–Blue Cross Blue Shield of Hawaii, for their assistance in linking the cohort with the health plans.

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