Type 2 Diabetes in Native Hawaiians according to Admixture: The Multiethnic Cohort

Gertraud Maskarinec, Yukiko Morimoto, Simone Jacobs, Andrew Grandinetti, Marjorie Mau, Laurence N. Kolonel
Prevalence of obesity*, ages 20+, age standardized
Both sexes, 2008

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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Background

- Overweight and obesity have been associated with rapidly rising numbers of diabetes patients.
- Incidence and prevalence of type 2 diabetes are particularly high among Asians and Pacific Islanders even in groups with low rates of obesity.
- Persons with multiethnic backgrounds appear to be more likely to have excess body weight.
- The distribution of visceral and subcutaneous fat differs across ethnic groups and may be related to the development of chronic diseases.
Multiethnic Cohort Study

- Baseline, 26 page self-administered questionnaire in 1993-1996
- Validated food frequency questionnaire
- Sent to residents of Hawaii and Los Angeles County
- Subjects’ names were obtained through drivers’ license records, voter registration records and Medicare files
- Follow-up questionnaires after 5 years, updated body weight
- In 2001-2006, 67,594 cohort members (49.7% of eligible) contributed blood and urine samples to biospecimen repository
- 215,251 adult men & women ages 45-75 years were recruited
  - Japanese American (26.4%)
  - White (22.9%)
  - Latino (22.0%)
  - African American (16.3%)
  - Native Hawaiian (6.5%)
  - Other ancestry (5.8%)
Timeline for Data Collection in MEC

- Qx1
- Qx2
- Qx3
- Qx4
- Med. Inventory
- Medicare Claims
- HI Health Plans
- CA Hospital Discharge

Cohort entry
Obesity in the Multiethnic Cohort

- **Haw**: Men 35, Women 35
- **J-A**: Men 7, Women 7
- **Cauc**: Men 15, Women 20
- **A-A**: Men 23, Women 38
- **Latino**: Men 22, Women 30

The chart above illustrates the obesity rates among different ethnic and gender groups in the Multiethnic Cohort study. The obesity rates are indicated in percentage points.
Overweight/Obesity by Ethnic Admixture
Albright et al. Obesity 2008

Men

Women

% Overweight
% Obese
Diabetes Prevalence in Men
Maskarinec et al. Ethnicity & Disease 2009
Diabetes Prevalence in Women

Maskarinec et al. Ethnicity & Disease 2009
MEC Diabetes Prevalence over Time

Caucasian
Native Hawaiian
Japanese American
African American
Latino

Qx1, Qx2, Qx3, Meds, Medicare, HI Claims, CA Hospital
Dietary Indices and Diabetes

Jacobs et al. Diabetologia 2014

Fig. 1 HRs and 95% CI of T2D of the highest compared to the lowest dietary pattern category in men (n=41,818) and in women (n=47,267)
### MEC Population in Hawaii

*Maskarinec et al. Diabetes 2009*

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>N</th>
<th>Follow-up time (years)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>35,042</td>
<td>12.2</td>
<td>5,566</td>
</tr>
<tr>
<td>Japanese</td>
<td>44,513</td>
<td>11.9</td>
<td>6,557</td>
</tr>
<tr>
<td>Native Hawaiian</td>
<td>14,346</td>
<td>11.5</td>
<td>2,806</td>
</tr>
<tr>
<td>Other</td>
<td>9,997</td>
<td>11.8</td>
<td>1,357</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>103,898</strong></td>
<td><strong>11.9</strong></td>
<td><strong>16,286</strong></td>
</tr>
<tr>
<td>Time</td>
<td>N</td>
<td>Diabetes cases</td>
<td>Prevalence (%)</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>---------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Follow-up questionnaire (1999-2003)</td>
<td>86,732</td>
<td>9,964</td>
<td>11.5</td>
</tr>
<tr>
<td>Medication questionnaire (2003-2006)</td>
<td>39,787</td>
<td>4,425</td>
<td>11.1</td>
</tr>
<tr>
<td>Linkage with HMSA (2007)*</td>
<td>67,467</td>
<td>11,375</td>
<td>16.9</td>
</tr>
<tr>
<td>Linkage with Kaiser (2007)</td>
<td>20,539</td>
<td>4,003</td>
<td>19.5</td>
</tr>
</tbody>
</table>

*Number of MEC subjects provided to HMSA minus Kaiser members, health plan membership not established for non-cases
Diabetes Incidence, Hawaii MEC

Maskarinec et al. Diabetes 2009

Cases/1,000 person years

- Caucasian
- Japanese American
- Native Hawaiian

Men

Women
Diabetes Risk by BMI Category

Maskarinec et al. Diabetes 2009

Hazard ratio

- Caucasian
- Native Hawaiian
- Japanese American

BMI Categories:
- <22
- 22.0-24.9
- 25.0-29.9
- 30+

Hazard ratios increase with BMI category for all groups, with the highest risk in the 30+ category for all groups.
# MEC Population-Focus on Asians

Maskarinec et al. Asia Pacific J Public Health 2014

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>N</th>
<th>Cases</th>
<th>Incidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>31564</td>
<td>2231</td>
<td>9.9</td>
</tr>
<tr>
<td>Japanese</td>
<td>36712</td>
<td>5522</td>
<td>21.1</td>
</tr>
<tr>
<td>Filipino</td>
<td>3871</td>
<td>634</td>
<td>21.3</td>
</tr>
<tr>
<td>Chinese/Korean</td>
<td>1632</td>
<td>201</td>
<td>17.9</td>
</tr>
<tr>
<td>Part-Asian</td>
<td>694</td>
<td>103</td>
<td>16.3</td>
</tr>
<tr>
<td>Mixed Asian</td>
<td>8480</td>
<td>1529</td>
<td>24.9</td>
</tr>
<tr>
<td>Native Hawaiian</td>
<td>4772</td>
<td>799</td>
<td>22.8</td>
</tr>
<tr>
<td>Other</td>
<td>1473</td>
<td>199</td>
<td>19.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>89198</strong></td>
<td><strong>11218</strong></td>
<td><strong>10.6</strong></td>
</tr>
</tbody>
</table>

*per 1,000 person-years
# Diabetes Incidence by Hawaiian Admixture

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>N</th>
<th>Cases</th>
<th>Incidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>White only</td>
<td>32,641</td>
<td>2,321</td>
<td>5.8</td>
</tr>
<tr>
<td>Hawaiian &amp; White</td>
<td>2,712</td>
<td>410</td>
<td>13.4</td>
</tr>
<tr>
<td>Hawaiian only</td>
<td>1,974</td>
<td>366</td>
<td>17.4</td>
</tr>
<tr>
<td>Hawaiian &amp; Other</td>
<td>4,385</td>
<td>774</td>
<td>15.3</td>
</tr>
<tr>
<td>Hawaiian &amp; Asian</td>
<td>2,916</td>
<td>597</td>
<td>18.4</td>
</tr>
<tr>
<td>Asian</td>
<td>44,634</td>
<td>6,738</td>
<td>12.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>89,262</strong></td>
<td><strong>11,206</strong></td>
<td><strong>10.5</strong></td>
</tr>
</tbody>
</table>

*per 1,000 person-years
## Diabetes Incidence by BMI & Hawaiian Admixture

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Normal (&lt; 25 kg/m²)</th>
<th>Overweight (25-30 kg/m²)</th>
<th>Obese (≥ 30 kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White only</td>
<td>2.0</td>
<td>7.3</td>
<td>19.3</td>
</tr>
<tr>
<td>Hawaiian &amp; White</td>
<td>3.7</td>
<td>12.4</td>
<td>26.3</td>
</tr>
<tr>
<td>Hawaiian only</td>
<td>6.5</td>
<td>13.2</td>
<td>30.8</td>
</tr>
<tr>
<td>Hawaiian &amp; Other</td>
<td>5.5</td>
<td>14.2</td>
<td>30.9</td>
</tr>
<tr>
<td>Hawaiian &amp; Asian</td>
<td>8.7</td>
<td>18.9</td>
<td>35.0</td>
</tr>
<tr>
<td>Asian</td>
<td>8.2</td>
<td>19.9</td>
<td>37.6</td>
</tr>
</tbody>
</table>

*per 1,000 person-years*
Diabetes Risk by Hawaiian Admixture

HR

<table>
<thead>
<tr>
<th></th>
<th>Basic model</th>
<th>Plus BMI</th>
<th>Plus BMI, diet and lifestyle factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawaiian &amp; White</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawaiian only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawaiian &amp; Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawaiian &amp; Asian (C, F, J, K)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Diabetes Incidence, KP in California
Karter et al. Diabetes Care 2013

New cases per 1,000 person-years

Self-identified race/ethnicity

- White
- African Am
- Latino
- Nat American
- Chinese
- Japanese
- Filipino
- South Asians
- Pacific Islander
- All Asians
- All API

API subgroups

Other race/ethnic groups

Aggregated API
Type 2 Diabetes in East Asians: Similarities & Differences with Populations in Europe & US
Ma et al. Annals of the New York Academy of Science 2013
Possible Biologic Mechanisms

- Impaired insulin secretion may have a greater impact on diabetes incidence than insulin resistance
  - Morimoto et al. Diabetologia 2013
    - Population-attributable fractions in Japanese
      - Impaired insulin secretion (IIS): 51%
      - Insulin resistance (IR): 14%
      - IIS plus IR: 13%

- Ethnic differences in the stabilization points of insulin sensitivity and insulin response to maintain the normal blood glucose levels
  - Kodama et al. Diabetes Care 2013
    - Due to high insulin sensitivity, a limited capacity for insulin secretion may have evolved
    - Low β-cell function may contribute to the high diabetes risk in persons of Asian ancestry

- Ethnicity-specific differences in fat distribution and adipokines
  - Visceral fat has stronger association with IR than subcutaneous fat
  - Asians have higher proportion of visceral fat than Caucasians
  - Adipokines may be mediators for higher visceral fat on disease risk
Visceral vs. Subcutaneous Fat
Lim et al. Nutrition and Diabetes 2011

Figure 2. An example MRI scan of L4/L5 vertebral inter-space for visceral and subcutaneous fat
# Visceral vs. Subcutaneous Fat

Lim et al. Nutrition and Diabetes 2011

## Participant Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Japanese (n=30)</th>
<th>White (n=30)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participant Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Age-adjusted mean</td>
<td>63.6</td>
<td>63.6</td>
</tr>
<tr>
<td>Weight, kg</td>
<td></td>
<td>62.2</td>
<td>69.2</td>
</tr>
<tr>
<td>Height, m</td>
<td></td>
<td>1.54</td>
<td>1.61</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td></td>
<td>26.5</td>
<td>27.1</td>
</tr>
<tr>
<td>DXA total fat mass, kg</td>
<td></td>
<td>25.5</td>
<td>28.8</td>
</tr>
</tbody>
</table>

## Body Fat Distribution

<table>
<thead>
<tr>
<th></th>
<th>Age- and total fat-adjusted mean</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>DXA trunk-to-periphery fat ratio</td>
<td>1.41</td>
<td>1.11</td>
</tr>
<tr>
<td>MRI % subcut fat/abdo area</td>
<td>33.4%</td>
<td>30.2%</td>
</tr>
<tr>
<td>MRI % liver fat</td>
<td>5.8%</td>
<td>3.8%</td>
</tr>
<tr>
<td>MRI fatty liver (&gt; 5.5%)</td>
<td>51%</td>
<td>24%</td>
</tr>
</tbody>
</table>
Leptin by Ethnicity & BMI Category

African American
Caucasian (reference)
Native Hawaiian
Latino
Japanese American

(normal/mL)

Normal weight  Overweight  Obese
Adiponectin by Ethnicity & BMI

(μg/mL)

[Graph showing adiponectin levels by ethnicity and BMI categories: Caucasian (reference), Native Hawaiian, Latino, African American, Japanese American. The x-axis represents normal weight, overweight, and obese categories, and the y-axis represents adiponectin levels in μg/mL. The graph indicates a decrease in adiponectin levels with increasing BMI for all ethnic groups.]

Caucasian (reference)
Native Hawaiian
Latino
African American
Japanese American
Conclusions

- Individuals with Asian ancestry (Japanese, Filipino, and Chinese/Korean) share a 2.5 times higher risk of developing type 2 diabetes than whites.
- Native Hawaiians and multiethnic persons are at intermediate risk but type of admixture is important.
- Body fat distribution may be responsible for excess risk in Asians after controlling for lifestyle risk factors.
- Adipokines and other biomarkers may play a role in differential diabetes risk.
- Additional factors, e.g., insulin sensitivity and insulin resistance, probably contribute to high diabetes risk.
Acknowledgments

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  UM1CA164973
  (PI: Le Marchand/Wilkens/Henderson)

- The diabetes project was funded by
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