Health Disparities in Diabetes and Obesity: Biological, Clinical, and Nonclinical Factors—An Endocrine Society Scientific Statement

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Background

• Health disparities in disease burden, comorbidities and outcomes exist worldwide

• IOM report: “Unequal Treatment (2002)”
  – Examine health system, provider, and patient factors
  – Ethnic minorities → less access to preventive care, treatment and surgery → delayed diagnosis, advanced disease
  – Persistence of race/ethnic disparities in health and healthcare (type 2 diabetes and complications and thyroid cancer and bone fracture outcomes)

• IOM report: Exploring the Biological Contributors of Human Health: Does Sex Matter? (2001)
  – Highlighted effect of sex on health care disparities
  – Consideration of sex as biological variable, allowing for sex-stratified analyses, reducing sex-based discrimination in health
  – Coronary heart disease in diabetes, thyroid disease, osteoporosis → disproportionately affect women
Objectives

• To provide a scholarly review of the published literature on biological, clinical, and nonclinical contributors to disparities in endocrine disorders
  – Race/ethnic
  – Sex

• To identify current gaps in knowledge as a focus of future research needs
### Scientific Statement Writing Group

<table>
<thead>
<tr>
<th>Name</th>
<th>Area of Expertise</th>
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<tbody>
<tr>
<td>Sherita Hill Golden, MD, MHS (JHU)</td>
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<td>Arleen Brown, MD, PhD (UCLA)</td>
<td>Diabetes disparities, health services research</td>
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<td>Disparities in thyroid disorders, endocrine surgery</td>
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<td>Blair Anton, MLIS, MS (JHU)</td>
<td>Comprehensive literature search skills</td>
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Search Strategy

- Global prevalence data from World Health Organization

- U.S. population-based studies identified through PubMed: MeSH and key word terms
  - Racial, ethnic, and sex differences (specific populations)
  - Specific endocrine disorder or condition

- Identified systematic reviews, meta-analyses, large cohort and population-based studies, original studies

Golden et al., JCEM, 2012
### Definitions of Race/Ethnicity

<table>
<thead>
<tr>
<th>Race/economic groups</th>
<th>Definitions</th>
</tr>
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<tbody>
<tr>
<td>Non-Hispanic Black (NHB)</td>
<td>Individuals of African descent born and/or residing in the US</td>
</tr>
<tr>
<td>Non-Hispanic White (NHW)</td>
<td>Nonminority individuals</td>
</tr>
<tr>
<td>Hispanic-American</td>
<td>Mexican, South American, Cuban, or Puerto Rican descent born and/or residing in US</td>
</tr>
<tr>
<td>Asian-American</td>
<td>South Asian (e.g. Indian), East Asian (e.g. Japanese, Chinese), Southeast Asian (e.g. Cambodian, Vietnamese, Laotian, Thai), Pacific Island (Filipino)</td>
</tr>
<tr>
<td>Native American</td>
<td>American Indians and Alaska Natives</td>
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Golden et al., *JCEM*, 2012
Race/Ethnic Disparities in Diabetes Mellitus
Worldwide Diabetes Prevalence: 346 million individuals
WHO 2010 Statistics

- Countries with highest diabetes prevalence
  - Nauru, United Arab Emirates, Saudi Arabia

- Countries with lowest diabetes prevalence
  - Mongolia, Rwanda, Iceland

- Death from diabetes higher in low- and middle-income countries
Diabetes Prevalence by Race/Ethnicity

- 7.6% Cuban, Central, South American
- 13.6% Mexican American
- 13.8% Puerto Rican American

Centers for Disease Control, National Diabetes Fact Sheet, 2011
Heterogeneity in Diabetes Prevalence in Asian-Americans

*Native Hawaiian/Other Pacific Islander

Biological Factors

• Obesity and body fat distribution
  – 500 million adults ≥20 years were obese in 2010
  – Highest worldwide prevalence—Nauru, Tonga, Cook Island, Micronesia
  – U.S. ranked 5th highest in male obesity (44.2%) and 12th highest in female obesity (48.3%)
Race/Ethnic Differences in Overweight and Obesity

<table>
<thead>
<tr>
<th>Race/Ethnic Group</th>
<th>Percentage BMI≥30 kg/m² (NHANES 2009-2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHWs</td>
<td>34.3%</td>
</tr>
<tr>
<td>NHBs</td>
<td>49.5%</td>
</tr>
<tr>
<td>Mexican-Americans</td>
<td>40.0%</td>
</tr>
</tbody>
</table>

- Grade 2 (BMI≥35 kg/m²) and 3 (BMI≥40 kg/m²) highest in NHBs and Mexican Americans
- NHB and Mexican American women—greater rise in obesity prevalence over last 12 yrs than NHB or Mexican American men or NHW men or women
- Native Americans and Alaska Natives—33.2% obese versus 24.8% of NHWs in 2007 NHIS

Flegal et al., JAMA, 2012; Pleis and Lucas, 2007
## Prevalence of overweight and obesity in Asian-Americans

<table>
<thead>
<tr>
<th>Race/ethnic group</th>
<th>Age-adjusted overweight prevalence (%)</th>
<th>Age-adjusted obesity prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>21.8</td>
<td>4.2</td>
</tr>
<tr>
<td>Filipino</td>
<td>33.0</td>
<td>14.1</td>
</tr>
<tr>
<td>Asian Indian</td>
<td>34.4</td>
<td>6.0</td>
</tr>
<tr>
<td>Japanese</td>
<td>25.9</td>
<td>8.7</td>
</tr>
<tr>
<td>Vietnamese</td>
<td>19.1</td>
<td>5.3</td>
</tr>
<tr>
<td>Korean</td>
<td>27.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Other Asian and Native Hawaiian or other Pacific Islander</td>
<td>29.2</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Narayan et al., *J Am Coll Cardiol*, 2010
Asian individuals develop diabetes at lower body mass index

Race/ethnic differences in body fat distribution

- Asian Americans have more visceral fat at similar BMI and waist circumference compared to NHWs
  - Japanese Americans
  - Filipinos
Biological Factors

- Obesity and body fat distribution

- Glucose metabolism and insulin resistance (compared to NHWs)
  - Greater insulin resistance in minority populations (independent of adiposity)
  - Asian Americans have lower beta cell insulin secretion
  - Glucose metabolic features may differ in Hispanic Americans depending on country of origin
Biological Factors

- Obesity and body fat distribution

- Glucose metabolism and insulin resistance (compared to NHWs)

- Genetics
  - Susceptibility loci associated with type 2 diabetes risk in European populations are also associated with increased risk in minority populations
  - GWAS in non-European populations—novel diabetes-associated SNPs (South and East Asians, NHBs)
  - Overall, genetic architecture of type 2 diabetes similar across race/ethnicity
Non-Biological Factors

- **Acculturation:** “process by which immigrants adopt the attitudes, values, customs, beliefs, and behaviors of a new culture”
  - Hispanic immigrants
  - Asian immigrants

- **Socioeconomic Status**—lower income, education, and occupational status associated with increased diabetes risk

- **Health Behaviors**
  - Physical activity—Less in minorities compared to NHWs
  - Smoking—Native Americans and Alaska Natives have higher rates compared to NHWs
Interface of Clinical/Biological and Environmental Factors: Epigenetics and Early Life Events
Intrauterine Environment

- Fetal undernutrition and stress, maternal stress, maternal obesity → modification of offspring developmental biology

- Low birth weight → insulin resistance, diabetes, abdominal adiposity, CVD risk, elevated cortisol reactivity (esp. NHBs)
  - Nutritional deprivation
  - Placental vascular compromise

- Epigenetic changes in cellular gene expression: fetal adaptation to adverse intrauterine environment

Summary: Take Home Pearls

- Insulin resistance is a key contributor to type 2 diabetes risk in minority populations
  - Prevention target
  - Basic science studies—determine if race/ethnic differences in insulin signaling

- Reduced beta cell function and greater visceral adiposity in Asian-Americans → higher diabetes risk at lower BMI

- Heterogeneity in diabetes risk within Hispanic and Asian sub-populations

Summary: Take Home Pearls

- Genetic architecture of type 2 diabetes risk similar in European and ethnic minority populations
  - Future GWAS in ethnic minorities (esp. Native Americans, Hispanic-Americans and NHBs)
  - Use of ancestral markers to account for admixture

- Acculturation and health behaviors contribute to diabetes and obesity in ethnic minority populations

- Low birth weight, fetal undernutrition, and maternal-fetal stress → early targets for diabetes preventive intervention

Race/Ethnic Disparities in Diabetic Complications
Microvascular Complications

• Retinopathy
  – Severe retinopathy and visual impairment more common in ethnic minorities

• Nephropathy
  – End-stage renal disease (ESRD) disproportionately affects minority populations (esp. NHBs and Native Americans)
  – ESRD risk higher in Asian-Americans over age 45 yrs
  – NHBs have lower mortality on dialysis compared to NHWs
Macrovascular Complications

• Cardiovascular Disease
  – Lower risk of CVD in minority populations, except Native Americans, compared to NHWs
  – NHBs have higher CVD mortality rate
  – Hispanic-Americans with hyperglycemia have higher post-stroke mortality than NHWs

• Peripheral arterial disease/amputations
  – Higher risk in NHBs and Native Americans than NHWs
  – Lower risk in Asian-Americans than NHWs
  – Studies in Hispanic-Americans mixed
Biological Factors: Race/Ethnic Differences in Glycemic Control

- Ethnic minorities with diabetes have worse glycemic control than NHWs.

- Controversies: HbA1c in minority populations
  - Non-glycemic factors may contribute to higher levels in ethnic minorities
  - Caution in using HbA1c as only measure of diabetes diagnosis and management
  - HbA1c similarly related to micro- and macrovascular complications in NHBs and NHWs.
Race/Ethnic Differences in CVD Risk Factors

- Blood pressure $\rightarrow$ nephropathy, peripheral arterial disease
  - Higher hypertension prevalence in NHBs and Mexican American women than NHWs

- Lipids $\rightarrow$ CVD
  - Minorities generally have more favorable lipid profile (except lower HDL in NHBs)
Genetics and Epigenetics

- Few GWAS analyses on complications in ethnic minorities

- Low birth weight—may be associated with increased nephropathy risk through epigenetics
  - Associated with alterations in anatomical structure and function of kidneys and pancreas in animal models
  - Associated with increased odds of end-stage renal disease in humans
Non-Biological Factors: Health Behaviors

- Self-monitoring of blood glucose
  - Rates lower in NHBs, Hispanic-Americans, and Asian-Americans than NHWs (no differences in Native Americans)

- Physical activity—lower in ethnic minorities than to NHWs
Non-Biological Factors: Access to and Quality of Care

**Poor access to care**

- Factors associated with inadequate access to diabetes specialist care
  - Lower educational attainment
  - Lack of health insurance greater in minorities with diabetes
- Ethnic minorities have worse diabetes-related outcomes even in countries with universal health insurance coverage

**Poor quality of care**

- Uninsured with diabetes receive fewer recommended processes of care, have worse glycemic control, and more diabetic eye disease
- Less aggressive prescribing practices in minority individuals living in countries with universal health insurance coverage
Summary: Take Home Pearls

- Ethnic minorities disproportionately affected by microvascular complications and mortality

- Notable paradoxes
  - CVD mortality higher in NHBs despite lower incidence of disease than in NHWs
  - Survival on dialysis higher in NHBs despite higher rates of end-stage renal disease than in NHWs

- Future basic, translational, and clinical research needed to elucidate mechanisms of survival differences

Golden et al, JCEM, 2012
Sex Disparities in Diabetic Complications
Sex Disparities in Diabetic Complications

• Microvascular complications rates similar in men and women

• Disparities in macrovascular complications
  – Diabetes increases risk of CHD and CHD mortality in women more than men
  – Peripheral arterial disease and diabetes-related lower limb amputations higher in men
Biological and Non-Biological Factors

• Biological Factors
  – Differences in glycemic control, lipids
  – Dimorphic sex hormone status $\rightarrow$ endothelial dysfunction and adipokine activity

• Treatment
  – Women with type 2 diabetes less likely to use aspirin
Summary: Take Home Pearls

- Reasons for sex differences remain largely speculative

- Most marked sex differences in diabetic complications are for coronary heart and peripheral arterial disease

- Future basic, translational, and clinical research needed to elucidate differential impact of diabetes on two vascular beds

Conceptual Framework for Endocrine Disparities

BIOLOGIC-ENVIRONMENT INTERACTIONS

Proximate Factors

**Biologic/Genetic Pathways**
Allostatic load, genetics, genetic ancestry, epigenetics

**Biologic/Responses**
Stress, hypertension, obesity, ↑ cholesterol, hyperglycemia

**Individual Risk Behaviors**
Smoking, diet, disease self-management, medication adherence

**Individual Demographics and Social Factors**
Age, socioeconomic status, education, race/ethnicity, acculturation, social support, language barriers

**DISPARATE HEALTH OUTCOMES**
Diabetes Mellitus and Diabetes Complications
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Intermediate Factors

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Individual Demographics and Social Factors
Age, socioeconomic status, education, race/ethnicity, acculturation, social support, language barriers

Physical Context
Neighborhood stability, cleanliness, sidewalks, open space, parks, food availability

Social Context
Collective efficacy, social capital, social network, social cohesion, poverty, racial/ethnic integration, social/economic gradient

Healthcare Context
Access to care, quality of care, provider characteristics, patient-provider relationships, health literacy

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Distal Factors

Social Conditions and Policies
- Poverty, public policy, prejudice, culture, discrimination

DISPARATE HEALTH OUTCOMES
Diabetes Mellitus and Diabetes Complications
# Successful Interventions for Reducing Diabetes Health Disparities

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<tr>
<th>Level of intervention</th>
<th>Successful Components</th>
<th>Outcomes</th>
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<tr>
<td>Patient</td>
<td>Interpersonal connections rather than computer-based</td>
<td>Improved glycemic control and diabetes-related knowledge</td>
</tr>
<tr>
<td></td>
<td>• Face-to-face</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Social networks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Family/peer support groups</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Community health worker Culturally tailored</td>
<td></td>
</tr>
<tr>
<td>Provider</td>
<td>In-person feedback rather than computerized decision-support</td>
<td>Change in provider behavior and improved diabetes outcomes</td>
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<td>Microsystem/health care organization</td>
<td>Disease management • Identification of diabetes population (registries) • Practice guidelines • Health IT to track and monitor patients • Care management*</td>
<td>Improved diabetes outcomes</td>
</tr>
<tr>
<td>Community/health care system</td>
<td>• Culturally tailored patient education and empowerment • Community coalition building and advocacy • Community health workers • Provider audit and feedback • Quality improvement • Case management*</td>
<td>Improved minority health care Reduced racial and ethnic disparities in care</td>
</tr>
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Six cross-cutting themes of successful disparity interventions (RWJ Foundation)

- Target multiple patient barriers rather than single solution
- Culturally tailor interventions
- Use multidisciplinary teams
- Employ interactive, skills based patient training rather than passive learning approaches
- Use patient navigators
- Involve family and community

Take Home Pearls

- Compared to NHWs, NHBs have worse outcomes and higher mortality from certain disorders despite having a lower or similar incidence
  - Coronary heart disease in diabetes

- Obesity is important contributor to diabetes risk in minority populations
Take Home Pearls

• Implications of obesity definitions in different race/ethnic groups → ethnic specific cut-points for central adiposity should be determined to adequately assess metabolic risk

• Little evidence that genetic differences contribute significantly to race/ethnic disparities in diabetes or its complications

• Many current studies fail to specify Hispanic-American and Asian-American subgroups
Take Home Pearls

- Multi-level interventions have reduced disparities in diabetes care → design similar interventions for other endocrine disorders

- Basic science, population-based, translational, and health services studies needed to explore underlying mechanisms contributing to endocrine health disparities
  - Increase representation of ethnic minorities in both clinical and research sectors of endocrinology and diabetes
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