Toward a Systems Science Approach to Eliminating Health Disparities in Indigenous Populations

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National Heart, Lung, and Blood Institute

International Indigenous Health Symposium
October 14, 2016
Imagine the NIH in 2025 - Diversity – Source of Our Excellence: What If? Diversity of NIH Grantees Reflected a Diverse Nation

**NIH PI Grantees**
- White, 71.0%
- Hispanic, 3.5%
- Black, 1.1%

**US Population**
- White, 72.4%
- Hispanic, 16.3%
- Black, 12.6%
Toward a Systems Science Approach to Eliminating Health Disparities

- Diverse, Global, Networked Scientific Community
- **Health Inequities and Mission-driven Public Health Impact**
- Seizing Unprecedented Opportunities
The Health Inequity Challenge: “Unfinished Business” in Public Health Impact

Locally,
Nationally,
Globally.
Variation in Life Expectancy and Health Inequities: Place Matters – Effects of Income and Geographic Region: Men

Bottom income quartile

Top income quartile

- Higher income was associated with greater longevity.
- Association between LE and income varied substantially across areas.
- Differences in LE were correlated with health behaviors and local area characteristics.

Health Inequities – A Complex, Multi-level Problem

Systems Science & the Socio-ecological Model

<table>
<thead>
<tr>
<th>Classic Approach</th>
<th>Systems Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reductionist</td>
<td>Holistic; Integrated Systems</td>
</tr>
<tr>
<td>Uni-dimension data</td>
<td>Multi-dimensional data</td>
</tr>
<tr>
<td>Single-discipline lab</td>
<td>Multidiscipline teams</td>
</tr>
<tr>
<td>Individual molecules</td>
<td>Pathways &amp; networks</td>
</tr>
<tr>
<td>Descriptive models</td>
<td>Predictive modeling</td>
</tr>
<tr>
<td>Molecular assays</td>
<td>High-output assays</td>
</tr>
<tr>
<td>Molecules OR Cells OR Tissues OR Populations OR Social Context</td>
<td>Molecules AND Cells AND Tissues AND Populations AND Social Context</td>
</tr>
</tbody>
</table>

Barabasi A. NEJM 2007;357:404-7

NIH National Heart, Lung, and Blood Institute
CVD, Diabetes & Lung Diseases - Greatest Causes of Mortality; Yet Modifiable Risk Factors Greatest Contributors in Oceania

Mortality Over Time as Percentage of Overall Harm from Non-Communicable Diseases

Risk Factors Contributing to Non-Communicable Disease Mortality

- Dietary Risks
- High Body Mass Index
- High Fasting Plasma Glucose
- High Systolic Blood Pressure
- Tobacco Smoke
- Air Pollution
- High Total Cholesterol
- Low Physical Activity
- Low Glomerular Filtration Rate
- Alcohol and Drug Use
- Occupational Risks

Global Health Data Exchange. As of 2013; refreshed July 2016
Mortality from Diabetes in Oceania Highlights Differences and Disparities Across the Region

Mortality Rate from DM Higher Over Time in Samoa as Compared to Oceania and the World

Annual Mortality Rate (per 100,000 people)

Differences and Disparities in Mortality Rate from DM

Global Health Data Exchange. As of 2013; refreshed July 2016
Native Hawaiians/Pacific Islanders

- 70% more likely to die from heart disease than whites.
- 70% more likely to be diagnosed with heart disease than whites.
- More prevalent risk factors for heart disease than whites.

### Age-adjusted percentages of coronary heart disease among persons 18 years of age and over, 2012

<table>
<thead>
<tr>
<th>Native Hawaiian/Pacific Islander</th>
<th>Non-Hispanic White</th>
<th>Native Hawaiian/Pacific Islander / Non-Hispanic White Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.3*</td>
<td>6.2</td>
<td>1.7</td>
</tr>
</tbody>
</table>

### Age-adjusted percentage of persons 18 years of age and over who have high blood pressure, 2012

<table>
<thead>
<tr>
<th>Native Hawaiian/Pacific Islander</th>
<th>Non-Hispanic White</th>
<th>Native Hawaiian/Pacific Islander / Non-Hispanic White Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>36.5</td>
<td>23.4</td>
<td>1.6</td>
</tr>
</tbody>
</table>
Indigenous Leaders Engaged in Transformational Change: Eliminating Health Disparities in Native Hawaiians & Pacific Islanders

CVD Risk -- Diabetes in Hawaii by Race/Ethnicity, BRFSS 2014

<table>
<thead>
<tr>
<th>DOH Race-Ethnicity</th>
<th>Diabetes</th>
<th>Estimated Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>17,000</td>
<td>5.0</td>
</tr>
<tr>
<td>Native Hawaiian</td>
<td>17,000</td>
<td>12.6</td>
</tr>
<tr>
<td>Chinese</td>
<td>5,500</td>
<td>13.0</td>
</tr>
<tr>
<td>Filipino</td>
<td>24,500</td>
<td>13.0</td>
</tr>
<tr>
<td>Japanese</td>
<td>30,700</td>
<td>13.6</td>
</tr>
<tr>
<td>Black</td>
<td>n/r</td>
<td>n/r</td>
</tr>
<tr>
<td>Native Alaskan/ American Indian</td>
<td>n/r</td>
<td>n/r</td>
</tr>
<tr>
<td>Other Asian</td>
<td>n/r</td>
<td>n/r</td>
</tr>
<tr>
<td>Other Pacific Islander</td>
<td>3,800</td>
<td>14.8</td>
</tr>
<tr>
<td>Other</td>
<td>2,400</td>
<td>9.0</td>
</tr>
</tbody>
</table>

Native Hawaiians & Pacific Islanders are one of the highest risk populations for cardiometabolic diseases in the US.

Translating Discovery Science into Public Health Impact: From ‘Nucleotides-to-Neighborhoods’

Bench Research
- Discovery Science
  - Animal Studies
- Preclinical

Bedside
- 1st Human Studies
- Controlled Observations
- Phase I/II Trials

Patients
- Phase III Trials
- Guideline Development

Practices
- Phase IV Trials
- Comparative Effectiveness Research

Real World
- Implementation and Dissemination Science

Discovery Science T1 Translation to Humans T2 Translation to Patients T3 Translation to Clinical Practices T4 Translation to Real World Settings

A Systems Approach to Health Inequities:
What if we systematically leveraged a network of community partners and resources in knowledge-exchange to reduce health inequities?

Community Health Workers

Primary Care Physicians

Home Health Setting

Schools / Community Resources

Pharmacies & Clinics

mHealth/Wearable Sensors
Converting Data-2-Knowledge for Community Health Impact: Duke Health System Maps/Targets Diabetes ‘Hot Spots’

- Integrative, multi-component systems analysis
  - EMR-linked data warehouse
  - Geographic Information Systems
    - Socio-economic (female head-households)
    - Environmental factors (food access)

- Health System Platform
  - Innovative strategies to target fundamental change interventions
  - Patient-centered, value-added community-level healthcare

Miranda, Ferranti, Strauss, Neelon, Califf. *Health Affairs* 2013;32:608-1615
DPP-like intervention improves weight loss, BP, exercise capacity, physical activity frequency, and Fat in Diet Score across all groups.

Kaholokula JK, …and M K Mau MK. TBM 2014;4:149–159
Translating Discovery Science into Public Health Impact: From ‘Nucleotides-to-Neighborhoods’

**Biomedical Model**

**Bench Research**
- Discovery Science
  - Animal Studies
- Preclinical

**Bedside**
- 1st Human Studies
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**Real World**
- Implementation and Dissemination Science

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The Ecosystems of Cardiovascular Health Inequities: Multi-Level, Bio-Social Determinants

Environment/‘Exposome’
- Racism
- Inactivity
- Diet
- Psychosocial Stress
- Social Network
- Social Deprivation
- Neighborhood Features

The Bio-Social Interface

Biological Interface Systems
- Microbiome
- Immune System
- Epigenome

Systems Biology/Medicine/Public Health

Genomic Variation

Population History

Hypertension

Stroke
Heart Failure
Kidney Failure

Obesity
Diabetes

NIH National Heart, Lung, and Blood Institute
Understanding Ancestral Population History: Cultural-Genetic Influences on Health

• Pacific Islands populated from waves of migration from SE Asia.
• First people to Near Oceania >40,000 BP
• Early waves (3000 BP) of migrants populated Remote Oceania
• Subsequent waves of Papuan ancestry.

High prevalence (>80%) of obesity in Samoans.
Common variant (0.25) in the CREBREF gene strongly associated with BMI.
CREBREF missense variant is rare (<0.001) in other populations.
Positive selection for fat storage; metabolic advantage during famine.
What If? Molecular Markers and Imaging Tools Provided Better Refinement of Patient Subsets for Targeted, Tailored Interventions?

Promise of Precision Medicine

[Image of a silhouetted figure with the text: Right Drug, Right Dose, Right Time, Right Person]

NIH National Heart, Lung, and Blood Institute
Among Papua New Guinea, Iruna have the highest frequency (34%) of poor metabolism variants; compared with Europeans (3%).

Poor metabolism of the anti-platelet drug – clopidogrel – to active form reduces clinical efficacy in preventing CVD events.
What if we embedded within minority-serving health systems rich data collection of behaviors, mHealth sensor data, patient-centered outcomes, and environmental factors, into shared data commons platforms…

Built Environment
Physical Activity
Nutrition
Geospatial
Psychosocial
Genomics
Proteomics
Metabolomics

….and applied deep analytics with creative cultural insight to predict, prevent and preempt chronic disease?
