Introduction to the
Principles and Practice of Clinical Research

APPLICATIONS OF HEALTH DISPARITIES RESEARCH
NIH Clinical Center

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Outline of Presentation

- Define Health Disparities
- Conceptual and Methodological Issues in Health Disparities Research
- Factors Contributing to Health Disparities
- Current Perspectives in Health Disparities Research
- Applications of Health Disparities Principles and Concepts in Clinical Research

Mission

NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.
Healthy People 2020

Overarching Goals

1. Attain high-quality, longer lives free of preventable disease, disability, injury, and premature death;
2. Achieve health equity, eliminate disparities, and improve the health of all groups;
3. Create social and physical environments that promote good health for all; and
4. Promote quality of life, healthy development, and healthy behaviors across all life stages.

PART 1
What are Health Disparities?

Research in Population Health

Population health research examines the health outcomes of a group of individuals, including the distribution of such outcomes within the group.

Research approaches include metrics of health outcomes, patterns of health determinants and policies and programs that link these two.
Health Disparities Terminology

<table>
<thead>
<tr>
<th>HEALTH</th>
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</thead>
<tbody>
<tr>
<td>Disparities</td>
<td>Age</td>
</tr>
<tr>
<td>Variations</td>
<td>Disability status</td>
</tr>
<tr>
<td>Inequalities</td>
<td>Gender</td>
</tr>
<tr>
<td>Inequity</td>
<td>Geography</td>
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<tr>
<td></td>
<td>Race / Ethnicity</td>
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<tr>
<td></td>
<td>Religion</td>
</tr>
<tr>
<td></td>
<td>Socioeconomic Status</td>
</tr>
<tr>
<td></td>
<td>Sexual Orientation</td>
</tr>
</tbody>
</table>

U.S. Healthy People 2020

U.S. Health and Human Services

Healthy People 2020: A health disparity is a “particular type of health difference that is closely linked with social, economic, and/or environmental disadvantage.

Health disparities adversely affect groups of people who have systematically experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; gender; age; mental status; cognitive, sensory or physical disability; sexual orientation or gender identity; geographic location or other characteristics historically linked to discrimination or exclusion.

Health Disparities Research

A broad multi-faceted field that includes basic, applied, clinical, social and behavioral research, as well as translational research addressing significant disparities in the overall health status, rate of disease incidence, prevalence, morbidity, mortality or survival rates – observed in a population or population subgroup.

It includes the causes of such disparities and methods to identify, prevent, diagnose and treat such disparities, with the eventual goal to addressing causes and implementing solutions.
Epidemiology and Health Disparities Research:

Epidemiology = study of the distribution and patterns of health-events, health-characteristics and their causes or influences in well-defined populations.

- Cornerstone method of public health research and practice,
- Helps inform policy decisions and evidence-based medicine by identifying risk factors for disease and targets for preventive medicine and public policies.

Health Disparities Terminology

Social Disparities in Health – disparities in health that is patterned by socioeconomic status (includes race)

Racial and/or Ethnic disparities in health – Divergence in health outcomes that are patterned by race and ethnicity

Biological determinants and health disparities – differential distribution of risk variants in certain populations that put them at unique susceptibility or protection.

Health Disparities Terminology

Healthcare disparities
- Differential access to health care and services
- Differential quality of health care
  - Medical uncertainty and variation
  - Lack of inclusion in clinical trials and evidence-base
  - Discrimination, bias and stereotyping

Resulting in differential health outcomes
- Excludes patient preferences
Healthcare Disparities

- Insurance Status
- Provider practice Pattern
- Transportation
- Geography
- Public Health Infrastructure
- Workforce
- Health Literacy
- Linguistic barriers

Access and Use

- Clinical appropriateness based on patient profile
- Cultural Competence
- Patient safety
- Evidence-based
- Clinical Effectiveness
- Patient-Centeredness
- Timeliness

Costs

- Economic Burden
- Financial Costs of Care

Quality

Determinants of Healthcare Disparities

In healthcare, quality, access, utilization and clinically appropriate care is important.

Quality of Health Care

Doctors provide appropriate health care about half the time

- Alcohol dependence: 11%
- Hip fracture: 33%
- Peptic ulcer: 45%
- Diabetes: 69%
- Lower back pain: 73%
- Prenatal care: 79%
- Breast cancer: 79%
- Cataracts: 79%

Percentage of time

S. Hoffmann, N. J. Austin, et al., The Quality of Health Care Delivered to Adults in the United States, England, Italy, 2005

Social Determinants of Health

The social determinants of health are the circumstances in which people are born, grow up, live, work, and age, as well as the systems put in place to deal with illness. These circumstances are in turn shaped by a wider set of forces: economics, social policies, and politics.

The social determinants of health are mostly responsible for health inequities - the unfair and avoidable differences in health status seen within and between countries.

World Health Organization
Social Health

Person’s capacity to fulfill their potential and obligations, the ability to manage their life with some degree of independence (despite a medical condition), and the ability to participate in social activities including work.

Health in this domain can be regarded as a dynamic balance between opportunities and limitations, shifting through life and affected by external conditions such as social and environmental challenges.

Social Health

- Financial health
- Social networks and inclusion
- Community health and cohesion
- Civic engagement
- Food security; access to healthy foods
- Safe neighborhoods to play
- Safe working conditions
- Access to educational opportunities
- Etc.

PART 2
Determinants of Population Health and Health Disparities
PART 3
Conceptual and Methodological Issues
**Health Disparities Terminology**

**Issue #1:**
Defining when a health difference is a disparity

Moral concern about the differences in health status, health outcomes. Value judgments are often made.

<table>
<thead>
<tr>
<th>HEALTH Disparities Variations Inequities</th>
<th>AXIS Age Disability status Gender Geography Race / Ethnicity Religion Socioeconomic Status Sexual Orientation</th>
</tr>
</thead>
</table>

**Language of Health Disparities**

**Health Inequity**

Is it fair that:

**Is it fair that:**

Poor people die younger than rich people.

- It is an unavoidable fact of life.
- Economics should not affect well-being.
- People are responsible for their own well-being.
- If people really want access to high quality care and preventive services, they can get it.

Is it fair that:

Low SES class infants have lower birth rates.

- Preventing lower birth weight among low SES class infants should be a top priority for society.
- Low birth weight may be an indicator of irresponsible parenting.
- Babies are innocent, and their health should not be determined by the social class of their parents.
- It will cost society too much to prevent all undesirable birth outcomes.
**Language of Health Disparities**

Health Inequity

Is it fair that:

Smokers get more lung cancers than non-smokers.

- Smoking is a choice
- Smokers are victims of the tobacco industry
- If people were not so stressed, they would not smoke as much
- Smokers understand the health risks of smoking and should be held accountable for their behavior

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**Health Disparities Definitions**

Health Inequities

Systemic and unjust distribution of determinants of health: i.e. social, economic, and environmental conditions needed for health:

Unjust access to quality education, healthcare, housing, transportation and other resources (e.g. grocery stores, playgrounds, walking spaces)

Unequal employment opportunities and income

Discrimination based upon social status and other factors

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**Issue 2: Unit of Analysis – Between Population Groups**

Reference Group or Comparison Group

Measuring Health Disparities
Measuring Health Disparities

The choice of the reference group will affect the size of the disparity.

Reference Group or Comparison

Quantifying the Health Disparities

Issue #3: Size of population, changing demographics

Population Changes over time
Does it matter whether we are measuring health disparity at a single point in time, or over time?

- Demographic changes
- Immigration changes
- Environmental changes

PART 3
Current Perspectives in Health Disparities Research
Social Disparities in Health

Higher Income, Longer Life

Social Disparities in Health Outcomes

Lower Income Is Linked With Worse Health

Racial or Ethnic Differences in Health Regardless of Income
Examples of health disparities

Life Expectancy at Birth, by Race* and Sex, 1970–2006


Biological Health and Stress

Allostatic load is a multisystem construct theorized to quantify stress-induced biological risk.

Differences in allostatic load may reflect differences in stress exposure and thus provide a mechanistic link to understanding health disparities.
Physical Health and Allostatic Load

Two categories of biomarkers:

Primary Mediators comprises
the substances the body
releases in response to stress
(e.g. Epinephrine, norepinephrine)

Secondary Effects /biomarkers
comprises the results from
the actions of primary
mediators (e.g. elevated BP, HbA1c, lipids)

Variables
Used in the
Allostatic Load
Literature

Commonly used variables:

Physiologic stress response hormones;
e.g. cortisol, epinephrine and norepinephrine,
dopamine, insulin-like growth factors,
Dehydroepiandrosterone sulphate (DHEA-s)

Metabolic markers; e.g. glycosylated
hemoglobin (HbA1c), fasting and postprandial
glucose, and waist hip ratio

Cardiovascular variables; e.g. systolic and
diastolic blood pressure, HDL and total
cholesterol

Inflammation markers; e.g. albumin, C-
reactive protein, interleukin-6, tumor necrosis
factor

Measures of organ function; e.g. creatinine
function, homocysteine

Cumulative Biological Risks: Metabolic Score* by
Education

Metabolic Score = sum (glyco. Hemoglobin, ADL and
HDL cholesterol, waist:hip ratio)

**Biological Determinants of Health**

1. **Endogenous**
   (a) Genetic
   (b) Immunological defenses, including nutritional status
   (c) Intrinsic biological attributes, age, sex
   (d) **Epigenetic** – determined largely by biological and physical environmental challenges (which may be passed on from generations)

2. **Exogenous**

**Cardiovascular Score** by Education

Cardiovascular Score = sum (Systolic and Diastolic BP, resting heart rate)

Seeman et al, Soc Sci & Med
Developmental Origins of Health and Disease

**Concept:** biologic capacity of normal developing organisms to be *durable*ly changed by environmental exposures without change in the inherited genome

**Process:** 'developmental programming'

**Exposures:** nutrients, O2, chemicals, toxins

**Pathways:**
- Δ organ structure (permanent)
- Δ cell/organ function (± reversible)
- Δ regulatory system setpoints

**Impact:** Vulnerability to development of chronic disease in later life

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Key Points

Developmental programming

- first recognized because it created socioeconomically-based health disparity
- is a major *mechanism* by which
  - Socio-economic/psychosocial stressors become biologically embedded within a population
  - developmentally-based health disparities can be transmitted to future generations

Biology of Developmentally-Programmed Health Disparities

*Birthweight as a surrogate measure of Fetal Growth*

*OUTCOMES at 50+ yrs*

- HTN
- CAD
- Obesity
- Diabetes

*Courtesy: S. Bagby, MD*
Life Course Epidemiology: Two models

Cumulative risk model
• Chronic stressors can lead to cumulative dysregulation or damage across lifecourse.

→ Critical period model
• Early life experiences can durably modify biology by changing development.
• These modifications interact with later behaviors or exposures to influence health.


Altered Organ Structure/Function

“Critical Windows” of Organ Development

<table>
<thead>
<tr>
<th>Embryo</th>
<th>Fetus</th>
<th>Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from Conception</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placenta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas (insulin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney (functional units)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Heart</td>
<td></td>
<td></td>
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<tr>
<td>Heart cell maturation</td>
<td></td>
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</tr>
</tbody>
</table>

Courtesy: S. Bagby MD
### Mechanisms of Fetal Programming

<table>
<thead>
<tr>
<th>Organ</th>
<th>Change</th>
<th>Associated Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>↓ Nephron #</td>
<td>HTN, renal risk</td>
</tr>
<tr>
<td>Pancreas</td>
<td>↓ Islet β cell #</td>
<td>Δ Insulin secretion</td>
</tr>
<tr>
<td>Muscle</td>
<td>↓ muscle mass</td>
<td>↓ Basal met rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ Exercise capacity</td>
</tr>
<tr>
<td>Heart</td>
<td>↓ myocyte #</td>
<td>↑ Risk CHF</td>
</tr>
<tr>
<td>Liver</td>
<td>↓ lobule, cell #</td>
<td>Δ lipid metabolism</td>
</tr>
<tr>
<td>Vascular</td>
<td>↓ microvasc dens</td>
<td>↑ vasc resistance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ ischemia risk</td>
</tr>
</tbody>
</table>

### Developmental Origins of Disease

**Asymmetric Growth Restriction**
- Thin (Wt:Ht ratio)
- Blood flow redistribution
  - ↓ kidney, liver, pancreas
  - ↓ abdomen’ girth
  - Heart/brain ‘sparing’
- Low arm circumference
  - ↓ muscle mass
- Can occur without low birth weight

*Courtesy: S. Bagby, MD*

### Time Course of Renal Development

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Gestation</th>
<th>Human 5 - 35 wks</th>
<th>Rat or Pig</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
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<td>2</td>
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<td>3</td>
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<tr>
<td>4</td>
<td>4</td>
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<td>4</td>
</tr>
</tbody>
</table>

*Courtesy: S. Bagby, MD*
New Nephrons Form in Concentric Layers during Gestation

- Condensing Mesenchyme
- Comma Shaped Bodies
- Glomeruli
- Outer Nephrogenic Layer
- Branching Morphogenesis → Nephrogenesis

In Term Births:
Birth Weight Predicts Nephron Number

Δ = 230,000 nephrons per kg increase in birth weight

Hughson et al., Kid Internat (2003) 63, 2113

What Conveys Risk of HTN-Renal Disease in Low Birth-weight Offspring?

Low Nephron Number?

1Am J HTN 1988 1:335-47;
2Am J Kid Dis 1994 23: 171

Nephron Dosing

Brenner Hypothesis1,2

Courtesy: S. Bagby, MD
Mismatch

END STAGE RENAL DISEASE (ESRD)

High Cardiovascular Risk

Chronic Kidney Disease (CKD)
Reduced GFR (late stage)

HTN ↓ Salt Excretion

Progressive nephron loss;
Fewer and fewer functional nephrons

Focal Glomerular Sclerosis

Courtesy: S. Bagby, MD

Fewer Nephron Units Promotes Hypertension

IN BP OUT

IN BP OUT

Courtesy: S. Bagby, MD

How important are developmental and epigenetic processes to U.S. disparities between “racial” and ethnic groups?
Trends in Low Birth Weight (LBW)

Trends in Very Low Birth Weight (VLBW)

Major US health disparities:
Disproportionate burden of poor health outcomes among individuals experiencing low SES and African Americans

<table>
<thead>
<tr>
<th>Early life</th>
<th>Adulthood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>Heart attack</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>Stroke</td>
</tr>
<tr>
<td>IUGR</td>
<td>Diabetes</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
</tr>
</tbody>
</table>
**Developmental Origins of Adult Health**

Environmental Stressors

- Low SES, Racism, Discrimination, Nutrition etc.

Developmental response

- Biological Changes

Long-term chronic illness and effects

Activation of the HPA axis in stressful intrauterine conditions

Overexposure of the fetus to glucocorticoids

- Under-nutrition
- Over-nutrition
- Exposure to toxins

Ref.: Developmental response to intrauterine stress

Courtesy of C. Kuzawa PhD


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**Incident ESRD patients; Rates by age & Rates by race/ethnicity (1980 – 2004)**

Incident ESRD patients, rates by age adjusted for gender & race, rates by race & ethnicity adjusted for age & gender. For Hispanic patients we present data beginning in 1996, the first full year after the April 1995 introduction of the revised Medical Evidence form, which contains more specific questions on race & ethnicity.

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**MYH9 is a major-effect risk gene for focal segmental glomerulosclerosis**


Genetic variation at the MYH9 locus substantially explains the increased burden of FSGS and hypertensive ESKD among African Americans.

Disparities in Chronic Kidney Disease and ESRD

A risk allele for focal segmental glomerulosclerosis (FSG) in African Americans is located within a region containing APOL1 and MYH9

2010 International Journal of Nephrology

- Found APOL1 variants associated with non-diabetic glomerular disease in African American populations
- Stronger associations than with European Americans
- Higher prevalence of this gene than anticipated in the population

Proposed pathogenesis of MYH9-associated nephropathy.

35% African Americans
1% European Americans

Bostrom M.A., and Freedman B I CJASN 2010;5:1107-1113

©2010 by American Society of Nephrology

Association of duration of residence in the southeastern United States with chronic kidney disease may differ by race: the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study

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Health Disparities

**Thesis 1:**
An individual’s biological health embodies exposures arising from their societal, political, cultural and environmental context, thereby producing population rates and distributions of health.

- Poverty and adverse life effects have harmful effects on health
- Psychosocial stressors are socially patterned

Health Disparities

**Thesis 2:**
Social stratification and inequalities
- Arises from and reinforces unequal distribution of resources
- Linked with social disparities – education, income, employment etc.
- Creates the persistent social gradient in a number of indices including health status, clinical encounters, access and health outcomes.
Health Disparities

**Thesis 3:**
Differences in population health, that creates health disparities **are the result of socially patterned gradients in health**, mediated by physiology, behavior, psychosocial pathways and gene-environment expression, that affect the development, growth and regulation of our body’s biological systems, organs, and cells, culminating in disease risk, morbidity or mortality.

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**Elements that are desirable in conducting health disparities research**

A scientifically rigorous and transparent strategy for measuring health disparities

- Across multiple dimensions of the population
- Across multiple health indicators
- Across time

**Appropriate Data Sources**

Review of the relevant dimensions of health that is pertinent to the individual or community

- Social environment
- Intervening variables, e.g. life course trajectories

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**National Institute on Minority Health and Health Disparities**

[www.nimhd.nih.gov](http://www.nimhd.nih.gov)

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