Findings and Future Questions About Biomarker Selection

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BIODEMOGRAPHY
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Demographic Questions about Health

- **Time Trends:**
  - How and why is population health changing?

- **Differentials:**
  - What is the cause of differentials in health and mortality (Age, Socioeconomic Status, Race/Ethnicity, and Sex)
Model of Life Course Health Outcomes

Demographic Factors
- Age
- Gender
- Ethnicity
- Race/Nativity

SES
- Childhood circumstances
- Education
- Income
- Wealth
- Poverty Status
- Occupation

Health Behaviors
- Exercise
- Drinking
- Diet
- Smoking
- Social
- Psychological
- Social support
- Marital status
- Depression
- Health Care
- Access/Use
- Access to care
- Insurance Coverage
- Medication usage

Biological Factors
- Cardiovascular Factors
- Metabolic Factors
- Inflammation Markers
- Stress markers
- Vitamin/Antioxidant status
- Genetic markers

Health Outcomes
Questions Better Understood With Bioindicators

- Is the population healthier or less healthy now than in the past?
- Why is mortality at the oldest ages lower than expected (from the Gompertz curve)?
- Why are health differentials by SES and Race/ethnicity smaller at the older ages?
- Is there a Hispanic paradox in health?
- How do you explain the cohort pattern of mortality decline over the past?
Is the population healthier or less healthy now than in the past?


BACKGROUND: Health trends among older adults in 1990s

- **Improvements** in functioning and disability
  
  **BUT**

- **Increases** in prevalence of some diseases

- **Measurement problems**
  - Self-reported data
  - Limited ability to objectively measure health
  - Other factors may affect trends
Why look at trends in biomarkers?

- Can be objectively measured
- Provide pre-clinical information in younger age groups
- Potential opportunities for intervention
- Increasingly easier in population-based studies
DATA

- National Health and Nutrition Examination Survey (NHANES)

<table>
<thead>
<tr>
<th></th>
<th>65+</th>
<th>40+</th>
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<tbody>
<tr>
<td>NHANES III</td>
<td>N=4495</td>
<td>N=11448</td>
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<td>1988-1994</td>
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<tr>
<td>NHANES</td>
<td>N=1196</td>
<td>N=6671</td>
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<td>1999-2000/2</td>
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- Questionnaires
- Clinical Examinations
- Laboratory Tests
Biological risk factors

- **Cardiovascular**
  - Systolic BP (>140 mmHg)
  - Diastolic BP (>90 mmHg)

- **Inflammatory**
  - C-reactive protein (>4 mg/dL)

- **Dietary**
  - Homocysteine (>15 µMol/L)

- **Metabolic**
  - HDL cholesterol (< 40 mg/dL)
  - Fasting LDL cholesterol (>160 mg/dL)
  - Total cholesterol (> 240 mg/dL)
  - Fasting triglycerides (>200 mg/dL)
  - Glycated hemoglobin (> 6.4%)
  - Body mass index (>30 kg/m²)
METHODS

- Change over time in biological markers
  - Each measure divided into two groups
    - At risk / Not at risk
    - Prevalence, defined by clinical cutpoints
    - Summary score of number of risk factors

- Factors influencing trends
  - Logistic regression:
    - How did odds of being in a high-risk group vary by study?
    - Independent variable representing Wave IV compared to Wave III
## Trends in Biological Risk

*(Persons – 65+ NHANES 1990 – 2000)*

<table>
<thead>
<tr>
<th>Biological Marker</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>Worse</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Better</td>
</tr>
<tr>
<td>Weight</td>
<td>Worse</td>
</tr>
<tr>
<td>Inflammation</td>
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<td>Homocysteine</td>
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</table>

Trends in biological markers in 65+ population: Change in % High Risk Category
Increased Systolic blood pressure

28% increased risk of high systolic blood pressure after controls for age and gender.
Reasons for increased Systolic blood pressure

- Diagnosis
- Medication
- Medication ineffective
- Undiagnosed

NHANES III
NHANES IV
Decreases in Cholesterol

35% decreased risk of high total cholesterol after controls for age and gender
Reasons for decreased Cholesterol

![Bar chart showing different reasons for decreased cholesterol: Diagnosis, Medication, and Medication ineffective. The chart compares NHANES III and NHANES IV.]
Homocysteine: Reasons for trend

Model 1

Model 2: Folate
Trends in biomarkers in 40+ population by gender
Trends in Biological Risk Mixed

- Getting better:
  - Decrease in lipids related to more effective medication
  - Decrease in homocysteine results from folate supplementation

- Getting worse:
  - Increase in hypertension related to more risk uncontrolled by drugs
  - Increase in CRP related to increased obesity, more chronic conditions, increase in HRT
Why is mortality increase at the older ages lower than expected?

- Biological risk in population does not continue to increase with age.
- People with high risk die younger leaving a population that is “healthier” at the older ages.
Summary Indicator of Biological Risk – Measured High Levels

- Cardiovascular Risk Factors
  Blood Pressure (Systolic and Diastolic), Pulse
  - Metabolic Syndrome
    Obesity, Total Cholesterol, Glycated Hemoglobin
  - Markers of Inflammation
    C-Reactive Protein, Fibrinogen, Albumin
Mean Biological Risk by Age

Why are health differentials by SES smaller at older ages?

- Number of biological risk factors increases earlier in life for those who are poor (or black)

- Population levels of biological risk are similar for rich and poor at the oldest ages
Is there a Hispanic Paradox?

- Do Hispanics have biological risk as low as non Hispanic Whites?
- How does risk differ with controls for SES?

- NHANES 1999-2002
- age 40+
- Sample 5,912 – Hispanics (mainly Mexican American), Blacks, NH whites
Effects of Race/Ethnicity on Number of Biological Risk Factors

With Age and Gender Controlled; *Regression Coefficient Significantly Different from White
“Hispanic Paradox”? NO

- With age and gender controlled
- Hispanics are higher in biological risk than NH whites – All three types
- Lower than Blacks – “Black” paradox
- Next - Controls for low ed and poverty
Effects of Race/Ethnicity on Number of Biological Risk Factors

With Age, Gender, SES controlled; *Regression Coefficient Significantly Different from White
Effects of Hispanic Nativity on Number of Biological Risk Factors

With Age and Gender Controlled; *Regression Coefficient Significantly Different from White
Native-born versus foreign-born Hispanic Americans

- Both have more biological risk than non-Hispanic whites (without controls)
- The two nativity groups – NB and FB - do not differ from each other
- With controls for SES – Neither group differs from NH whites
Effects of Nativity on Number of Biological Risk Factors

With Age, Gender, SES Controlled; *Regression Coefficients Significantly Different from White
Only Hispanics of Mexican Origin:

- Native born - Still higher whites overall biological risk - cardiovascular and metabolic (not inflammation) – Not very different from Blacks
- Native born - With controls for SES – differences stay same
- Foreign Born – Look worse than non-Hispanic whites but not when SES controlled
- With controls for SES –
  - Foreign-born same as NHwhites (paradox)
  - Native born worse FB
Are foreign-born Mexican Americans a group selected for good health?

MHAS and NHANES

- Compare childhood health among Mexicans who migrated and those who stayed in Mexico
- Height as an indicator of childhood health and nutrition
- Migrants are taller than those who did not migrate
The diagram shows the distribution of heights for males in different groups:

- **Mexicans in Mexico**
- **Return Migrants to Mexico**
- **US-born Mexican-Americans**
- **Foreign-born Mexican-Americans**

The x-axis represents height in centimeters, ranging from less than 140 cm to 186 cm. The y-axis represents the percent distribution. The graph indicates different peaks and trends among the four groups, reflecting variations in height distributions.
Explain Cohort Pattern of Mortality decline over past centuries

- Many countries show cohort pattern of mortality decline after 1750
- The cohorts with lower mortality while young, experienced lower mortality while old

Cohort Mortality: Sweden (1751-1940)
Cohort Mortality: Sweden (Cohorts born 1751-1899)
Hypothesis: Inflammation is a link between conditions in youth and adulthood

- As infection declined.
- Survivors of cohorts with lower mortality experienced lower levels of inflammation throughout their lives.
- Lower inflammation meant less vascular damage – a slowing in the rate of aging.
- Lower inflammation meant more energy for growth.
Change of mean height at age 20-21: France

Source: 1. Tables de mortalite francaises pour les XIX siecles et projections pour le XXI siecle-Jaques Vallin and France Mesle, tableau-II-C-2
Testing the Hypothesis: With Hillard Kaplan and Michael Gurven

Mortality Among the Tsimane and Sweden 1843

- Tsimane Bolivia
- Sweden 1843

Age Groups:
- <1
- 5-10
- 15-20
- 25-30
- 35-40
- 45-50
- 55-60
- 65-70
- 75+
Prevalence of High Risk CRP (>3mg/L) in Bolivia and the U.S.
Years Lived with High CRP for Those Living to Specified Age
New Project

- The world we evolved in is not the world we live in
- We evolved to live in a highly infectious and nutritionally scarce environment
Summary: Introduction of Biological Markers

- Provides answers (hypotheses) to potential mechanisms causing trends and differentials.
- Provides more objective measurement of relatively early health problems.
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