

Findings and Future Questions About Biomarker Selection

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BIODEMOGRAPHY

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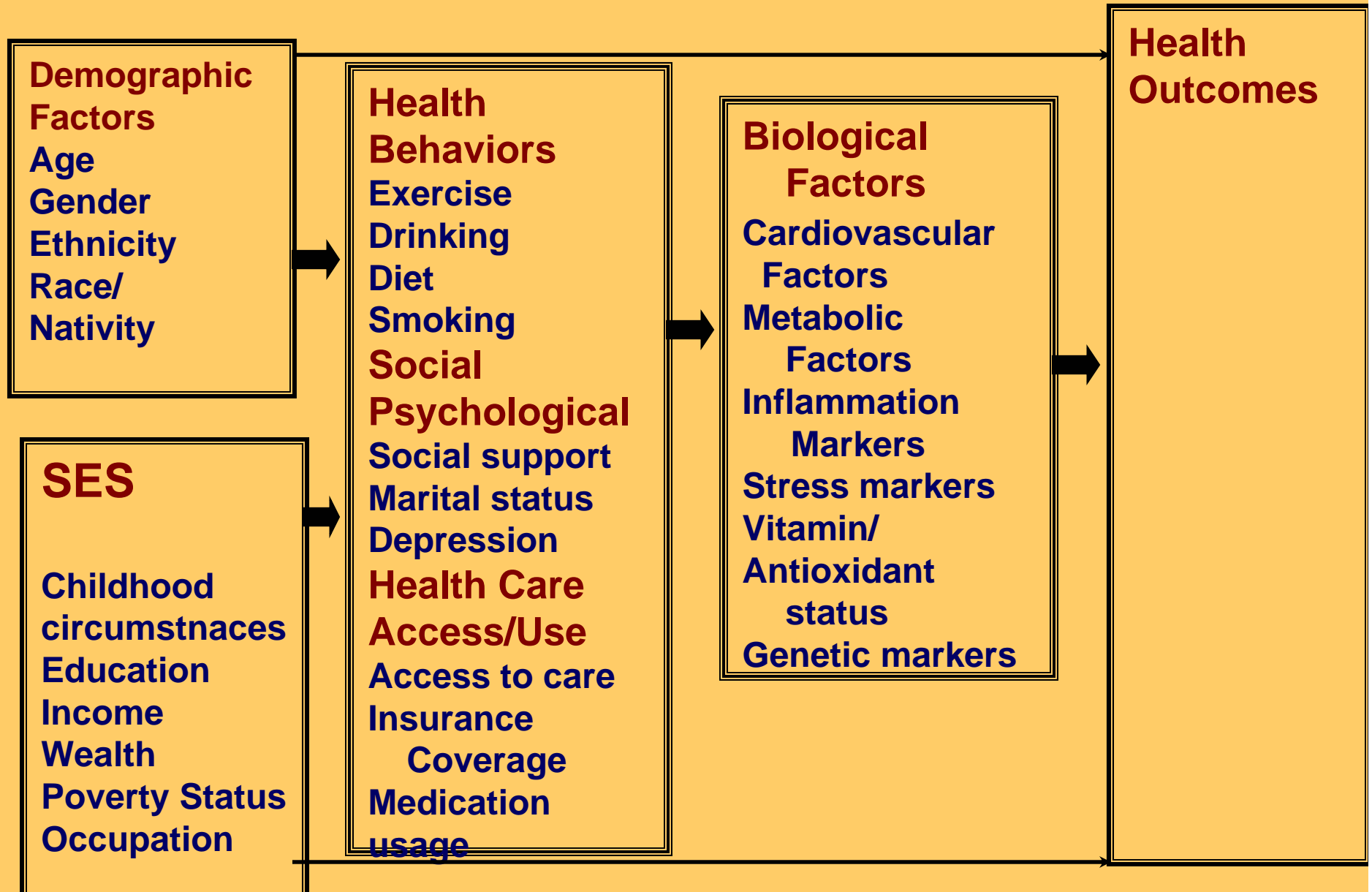
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Center on Biodemography and Population Health

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



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?
- In 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?

- Crimmins, E.M., Alley, D., Reynolds, S.L., Johnston, M., Karlamangla, A., & Seeman, T. 2005. Changes in biological markers of health: Older Americans in the 1990s. *Journal of Gerontology Medical Sciences*, 60, 1409-1413
- Kim, J.K., Alley, D., Seeman, T., Karlamangla, A., & Crimmins, E. 2006. Recent changes in cardiovascular risk factors among women and men. 2006, Journal of Women's Health, 15, 734-746.
- Kim, J.K., Alley, D. Hu, P., Karlamangla, A., Seeman, T., & Crimmins, E. Changes in Postmenopausal Hormone Therapy Use Since 1988. Women's Health Issues. Forthcoming.

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)

	65+	40+
NHANES III 1988-1994	N=4495	N=11448
NHANES 1999-2000/2	N=1196	N=6671

- 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 μ Mol/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

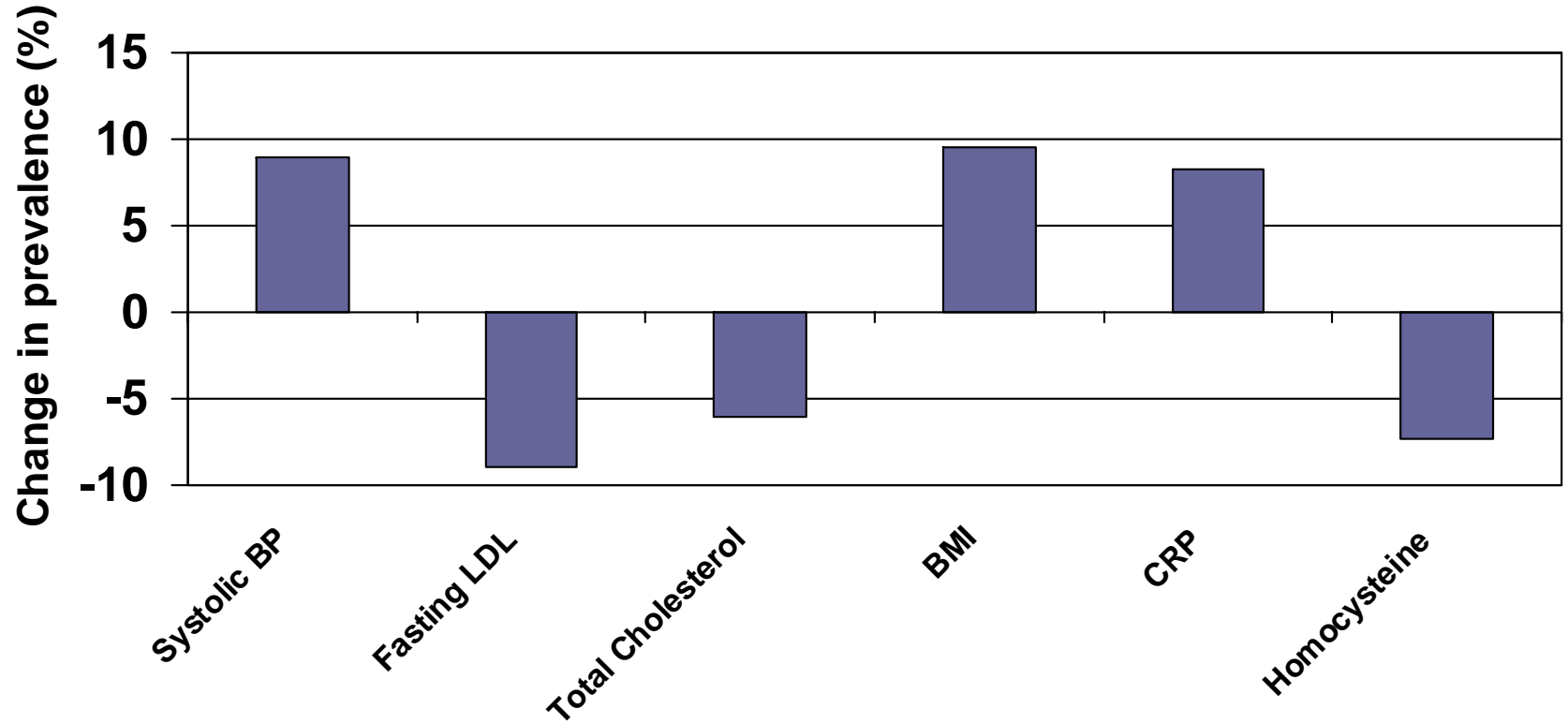
- Change over time in biological markers
 - Each measure divided into two groups
 - At risk / Not at risk
 - Prevalence, defined by clinical cutpoints
 - Summary score of number of risk factors
- Factors influencing trends
 - Logistic regression:
 - How did odds of being in a high-risk group vary by study?
 - Independent variable representing Wave IV compared to Wave III

Trends in Biological Risk **(Persons – 65+ NHANES 1990 – 2000)**

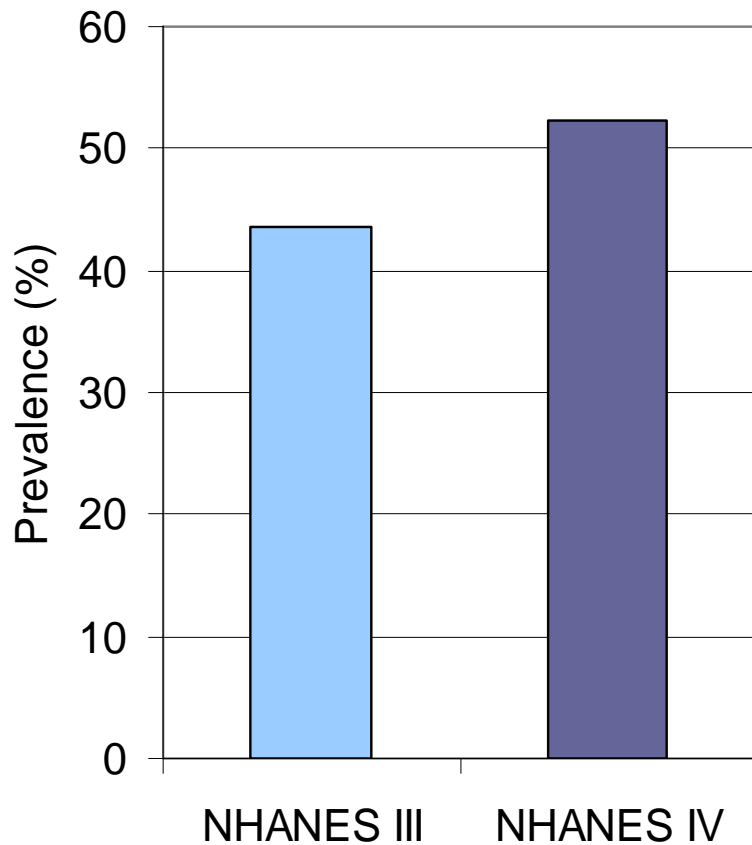
Blood Pressure	Worse
Cholesterol	Better
Weight	Worse
Inflammation	Worse
Homocysteine	Better

Crimmins, E., Alley, D., Reynolds, S., Johnston, M., Karlamangla, A., Seeman, T.(2005) Changes in biological markers of health: Older Americans in the 1990s. Journal of Gerontology: Medical Sciences, 60, 1409-1413.

Trends in biological markers in 65+ population: Change in % High Risk Category

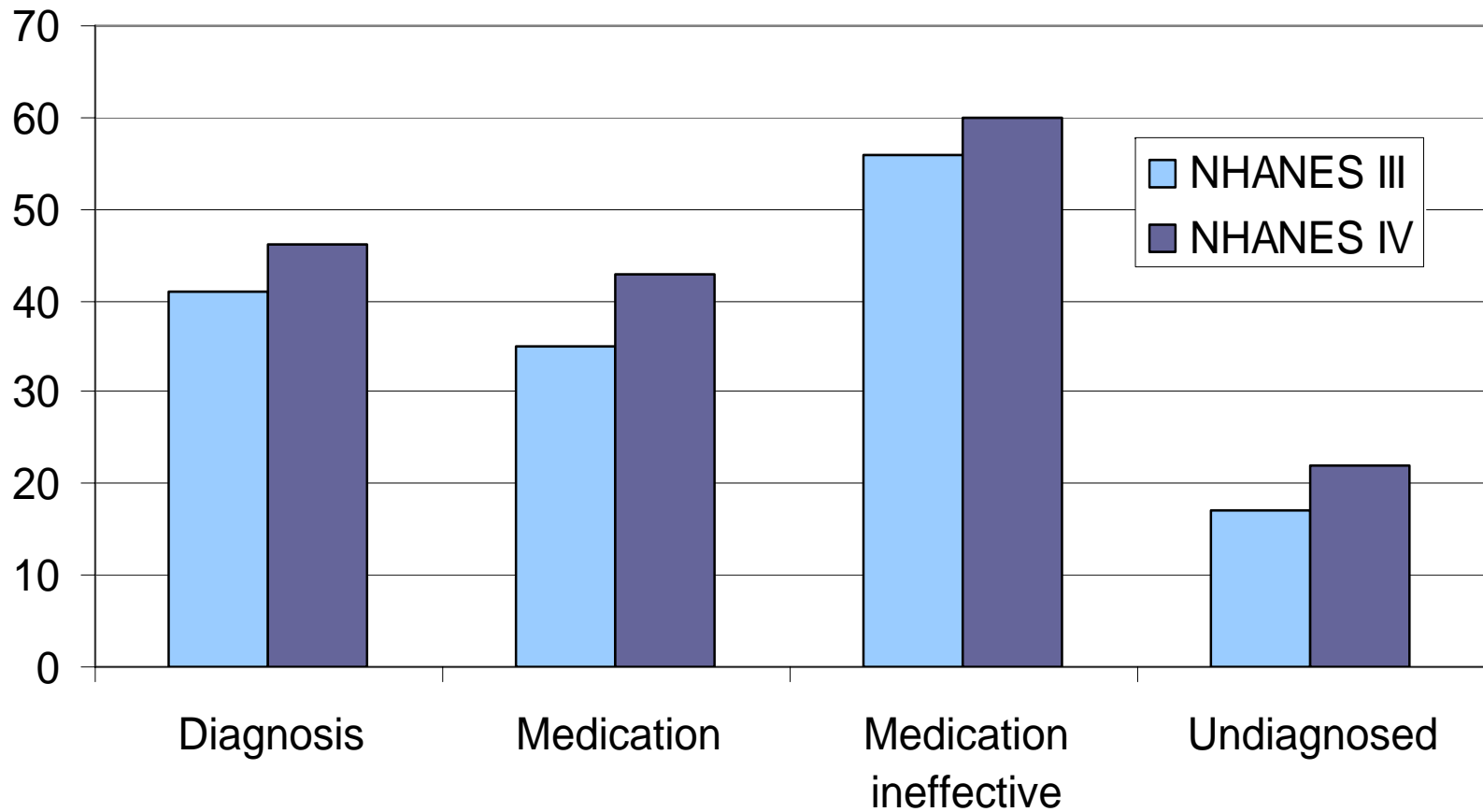


Increased Systolic blood pressure

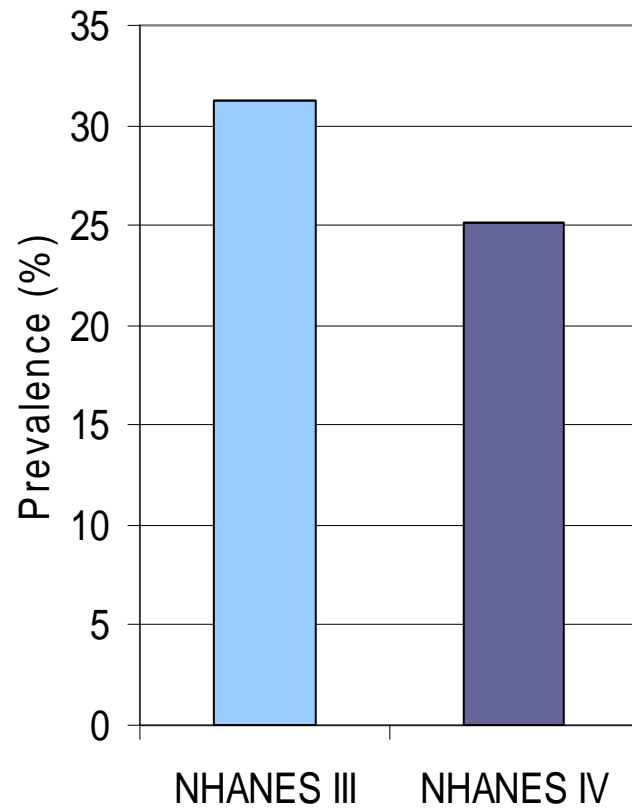


28% increased risk of high systolic blood pressure after controls for age and gender

Reasons for increased Systolic blood pressure

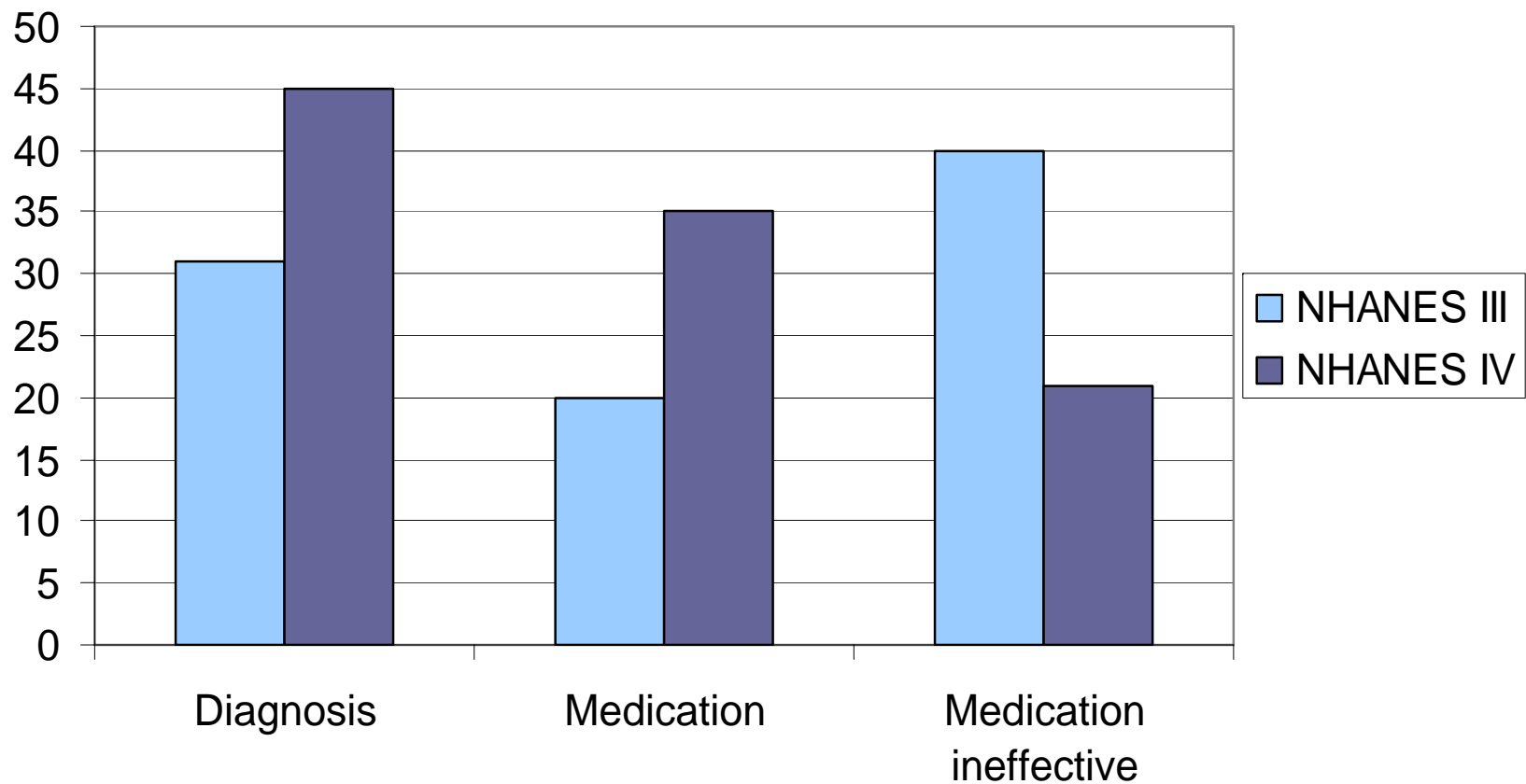


Decreases in Cholesterol

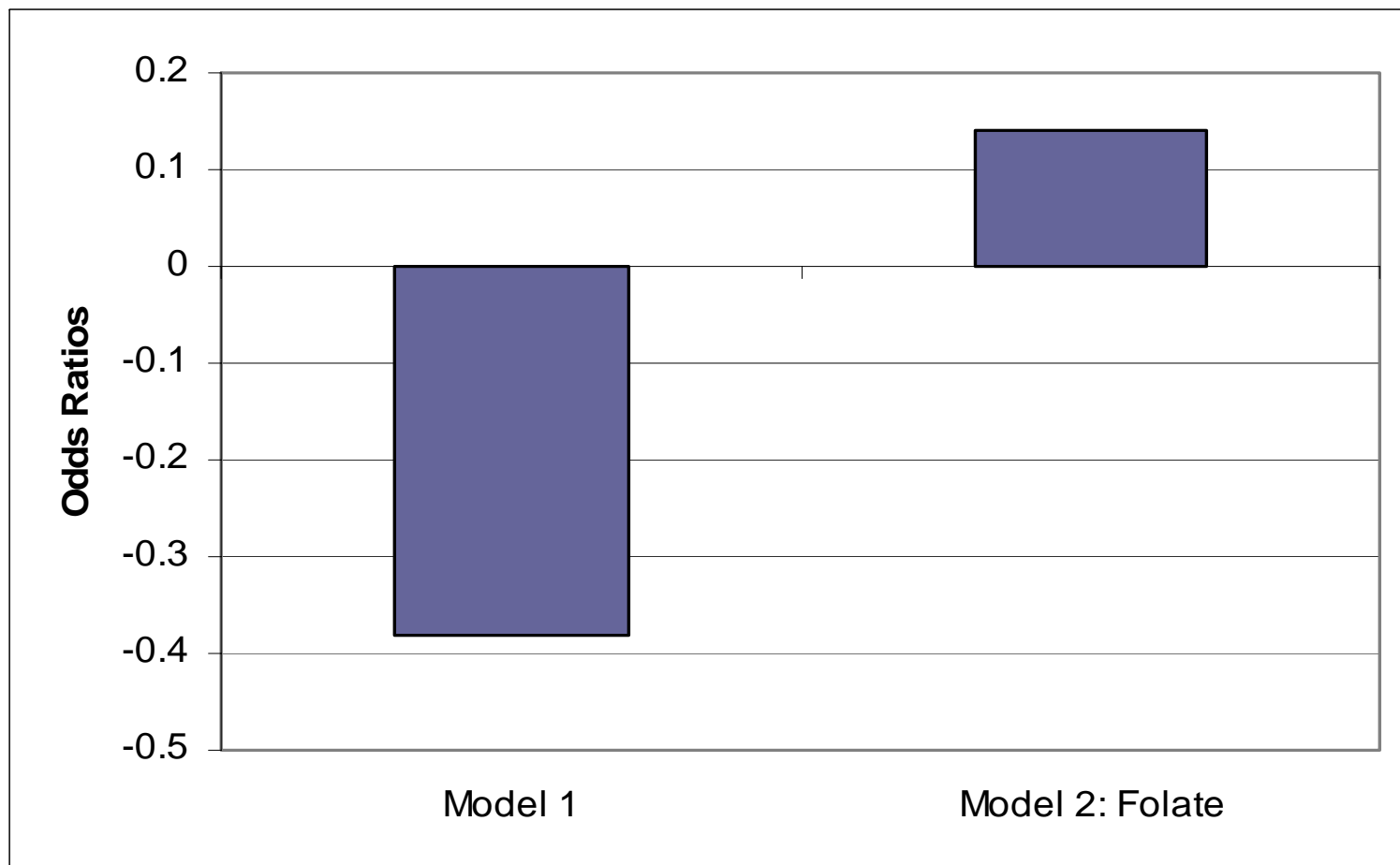


35% decreased risk of high total cholesterol after controls for age and gender

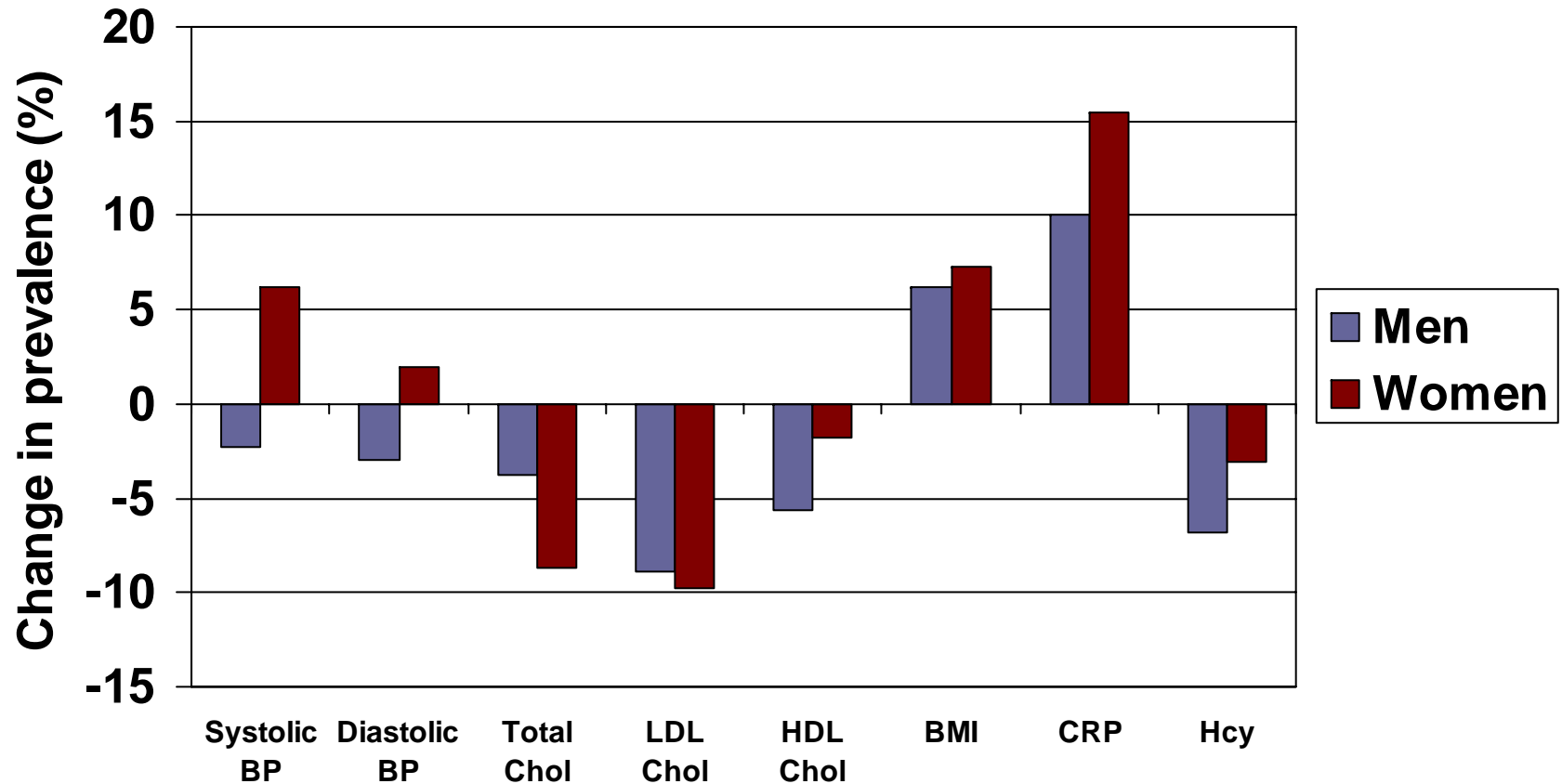
Reasons for decreased Cholesterol



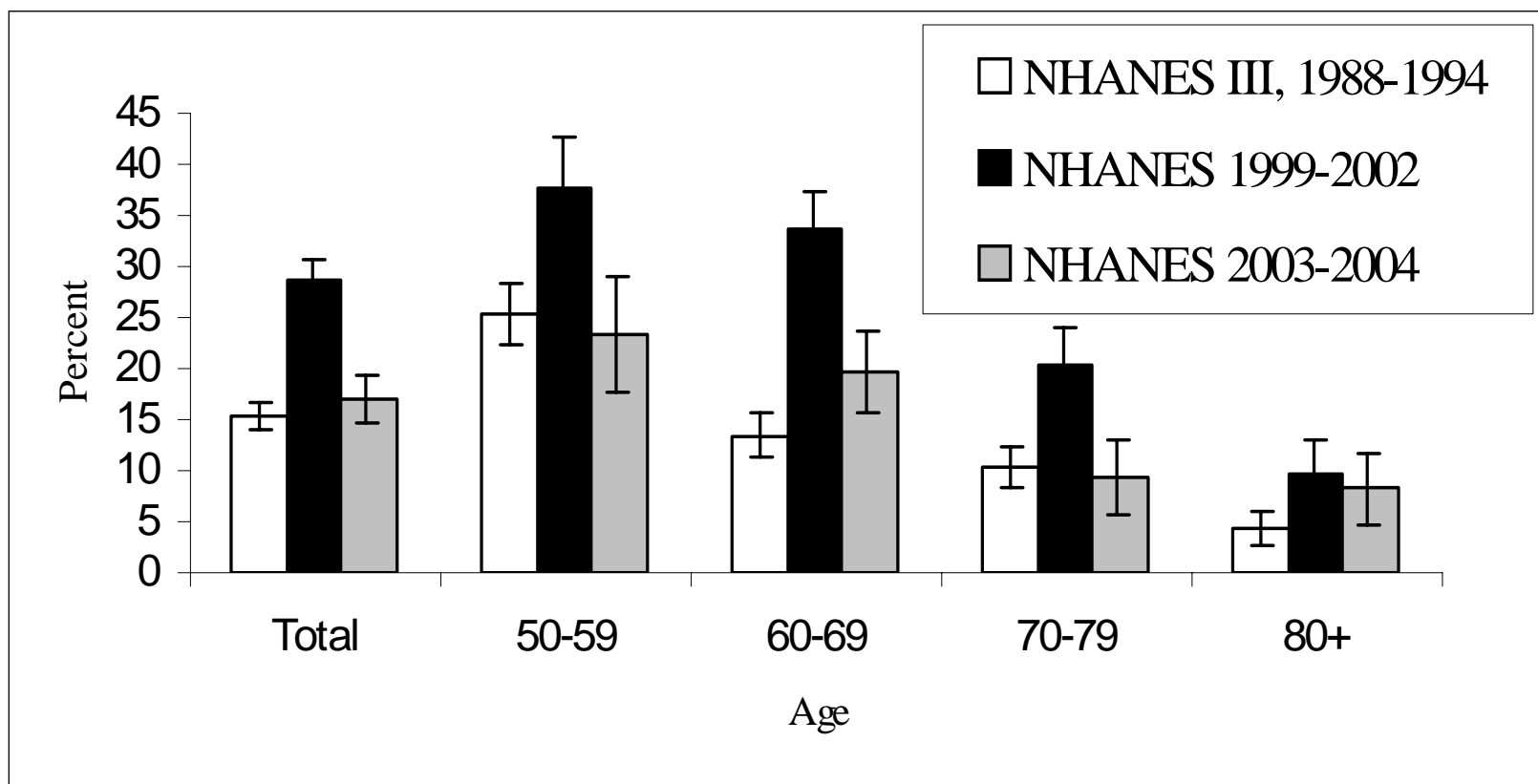
Homocysteine: Reasons for trend



Trends in biomarkers in 40+ population by gender



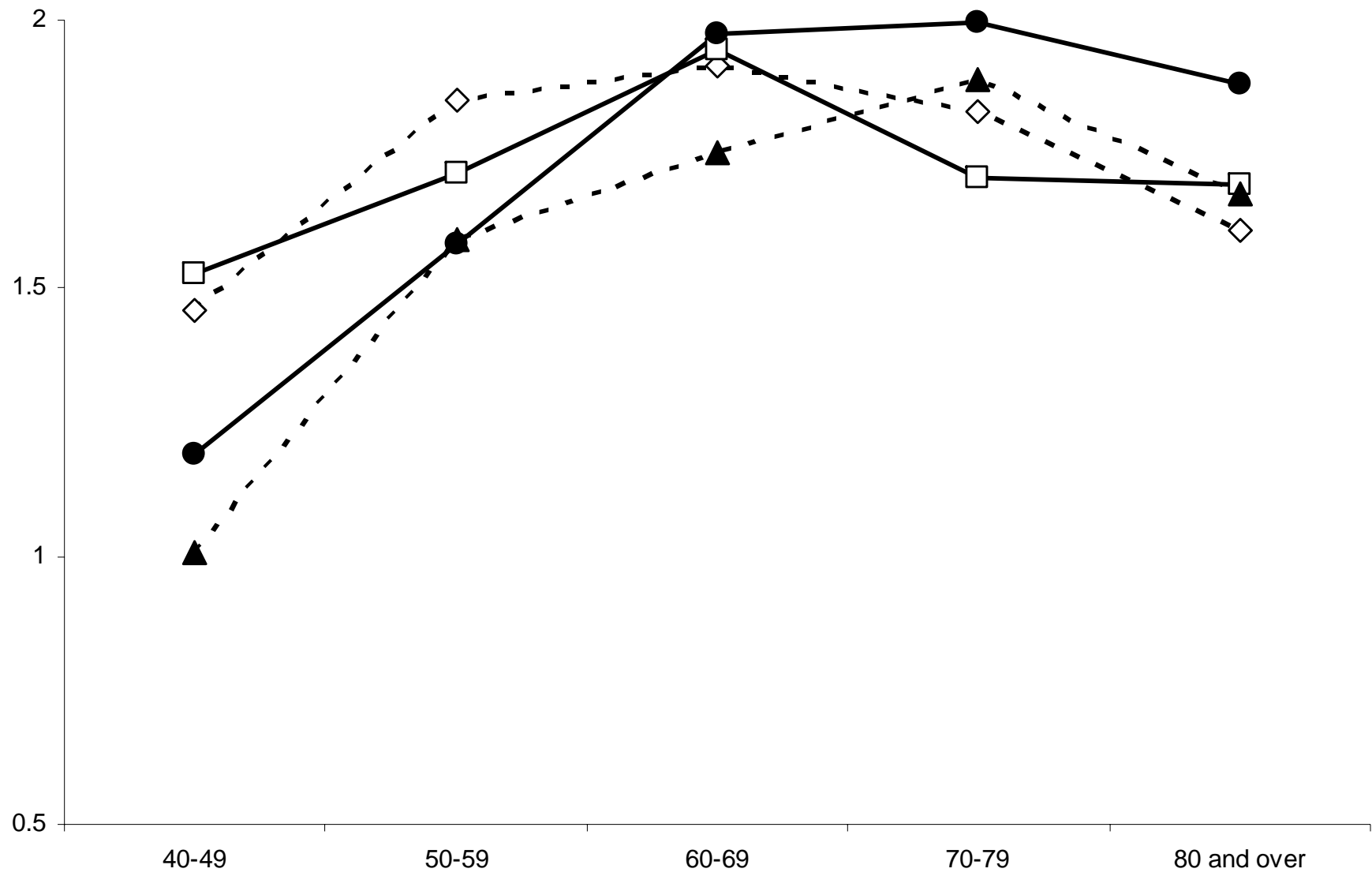
Percentage of Postmenopausal Women, 50 Years or Older Using Postmenopausal Oral Hormone Therapy in 1988-1994, 1999-2002, 2003-2004: NHANES III and NHANES 1999-2004



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

Mean Number of High-Risk Cardiovascular Risk Factors by Sex and Age: NHANES III and IV



- -◇- - Men NHANES III —□— Men NHANES IV
- -▲- - Women NHANES III —●— Women NHANES IV

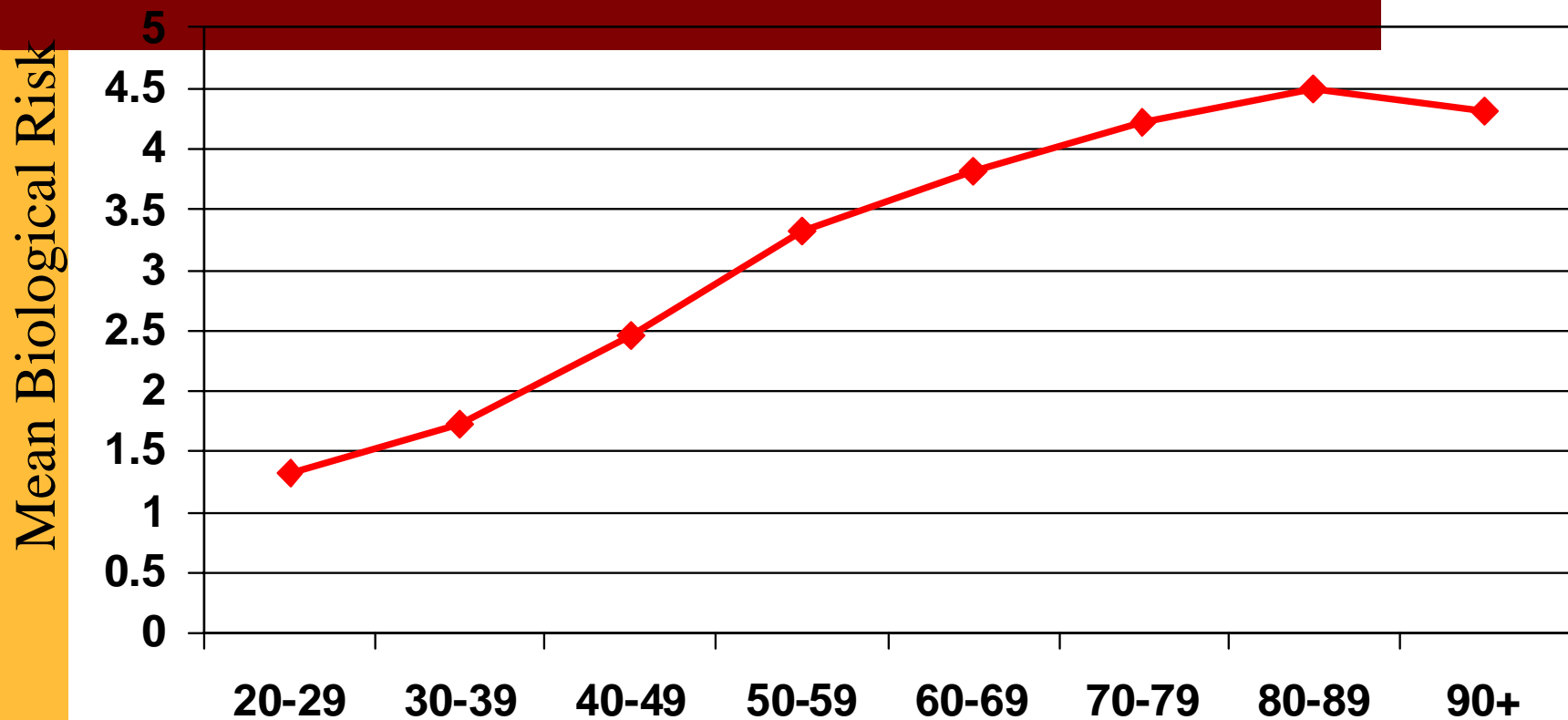
Why is mortality increase at the older ages lower than expected?

- **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

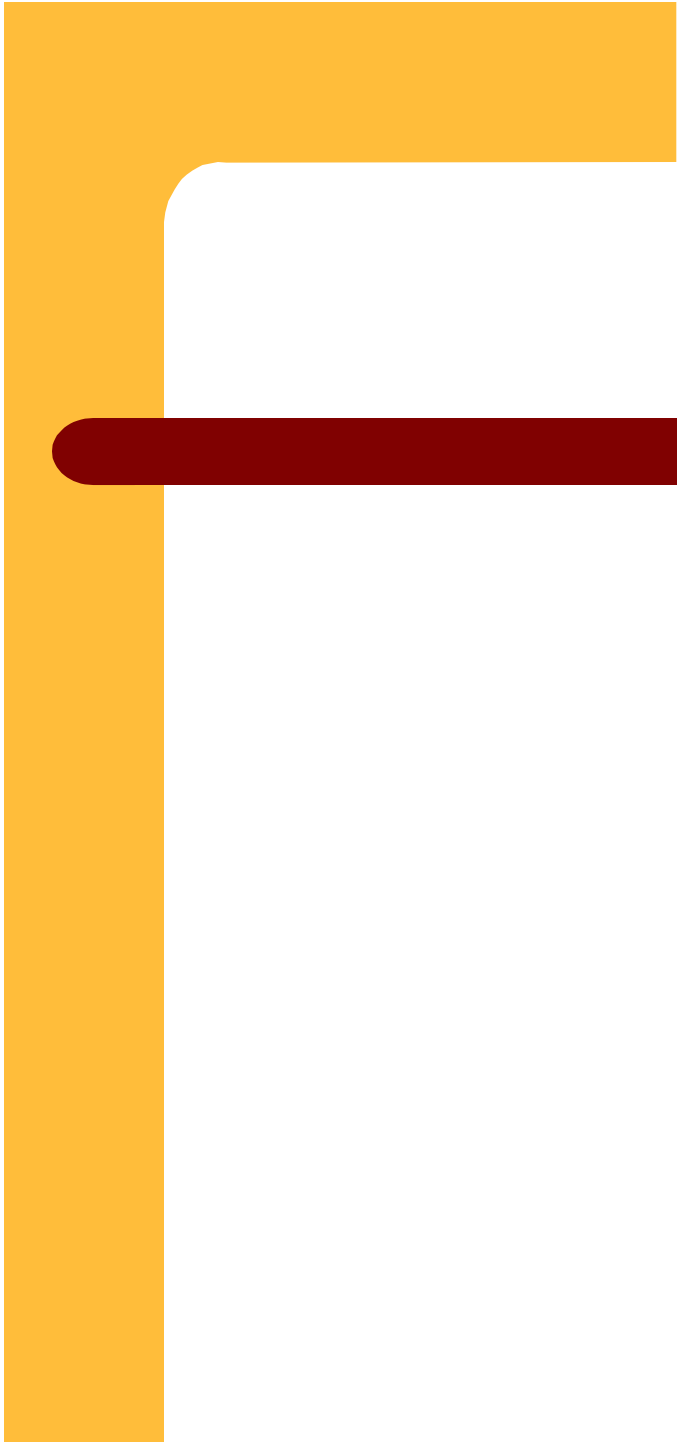
Mean Biological Risk by Age



“Age Differences in Allostatic Load: An Index of Frailty,” 2006, E. A. Kimmins, M. Johnston, M. Hayward, T. Seeman, in Zeng Yi et al., Longer Life and Healthy Aging, Springer; Dordrecht, Netherlands, pp. 111-126.

Why are health differentials by SES smaller at older ages?

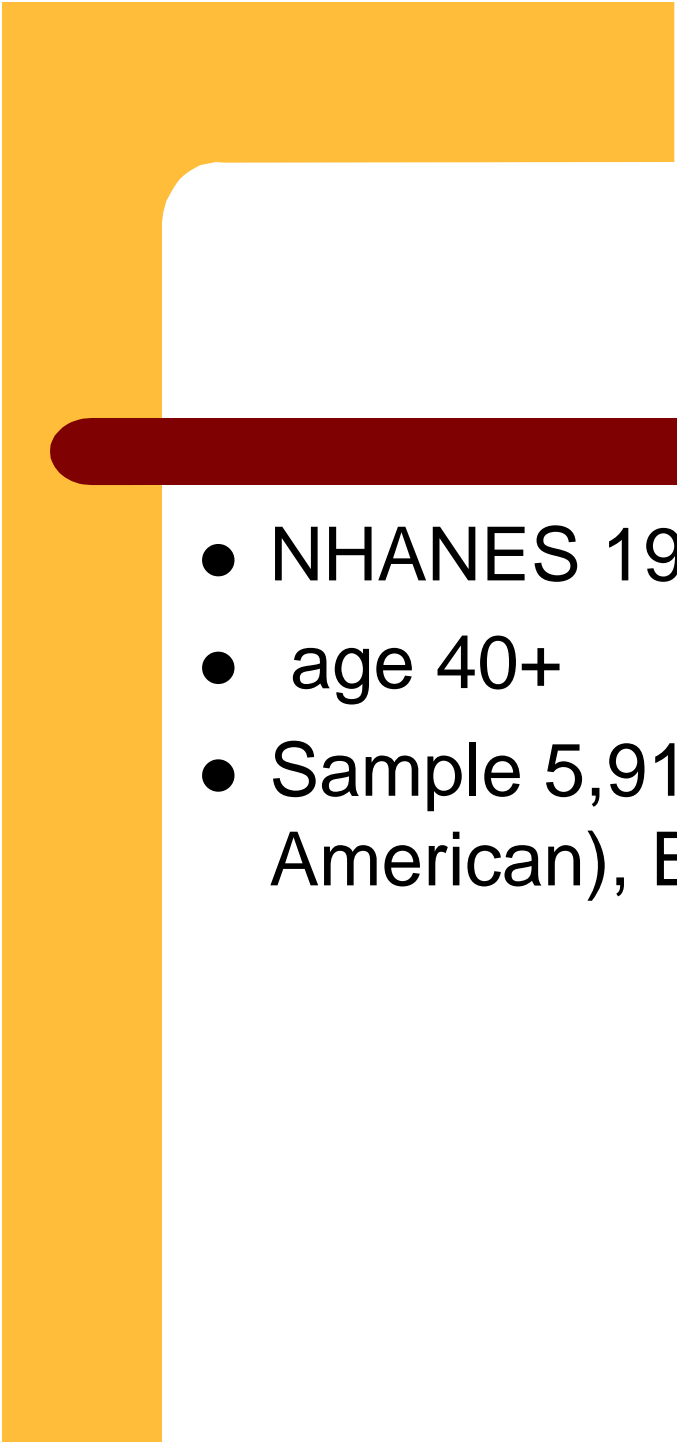

- **Number of biological risk factors increases earlier in life for those who are poor (or black)**
- **Population levels of biological risk are similar for rich and poor at the oldest ages**



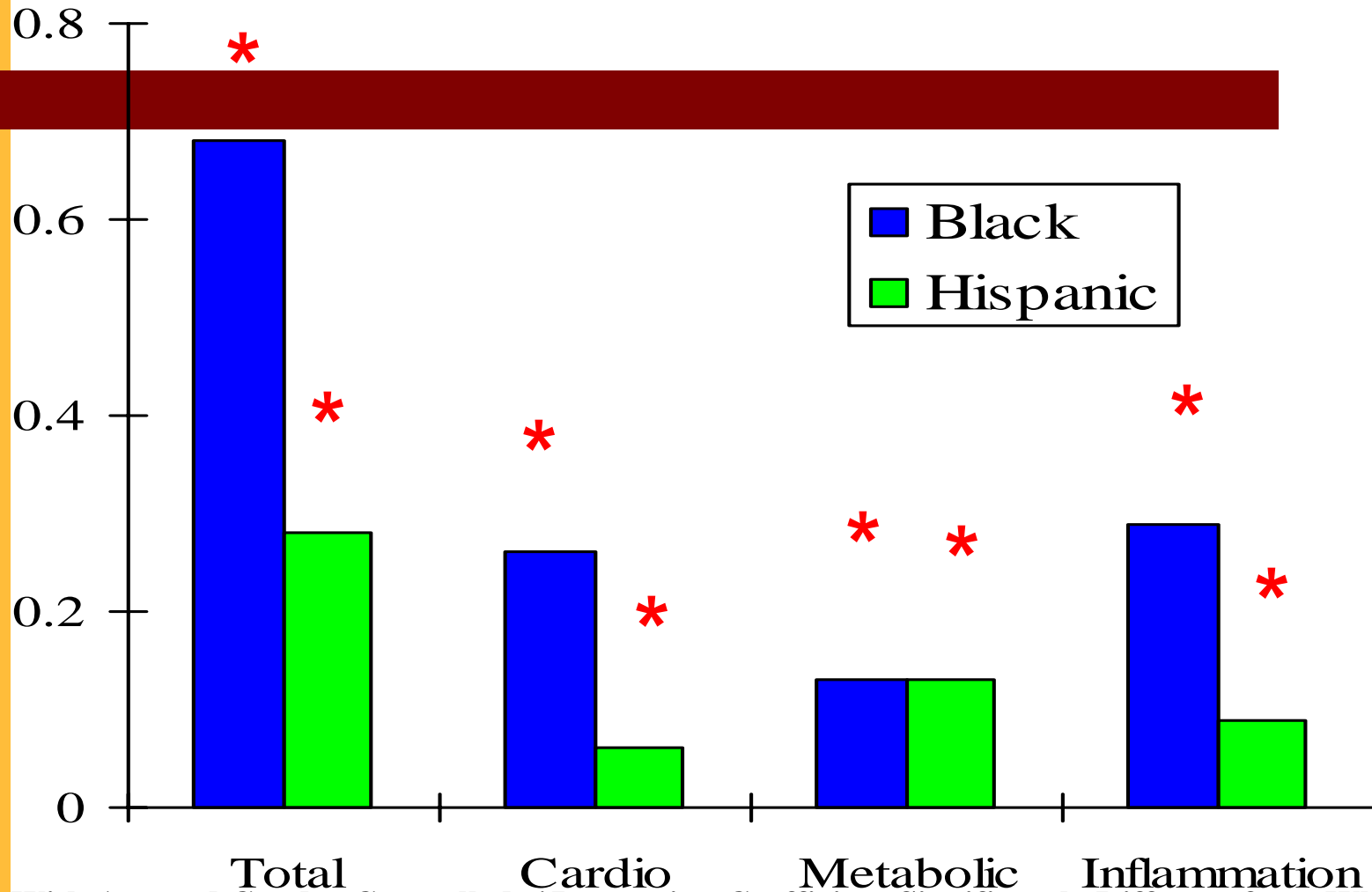
Is there a Hispanic Paradox?

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

Crimmins, E.M, Kim, J.K., Alley, D.A., Karlamangla, A., Seeman, T.(2007). Hispanic Paradox in Biological Risk Profiles. American Journal of Public Health, July.

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- 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

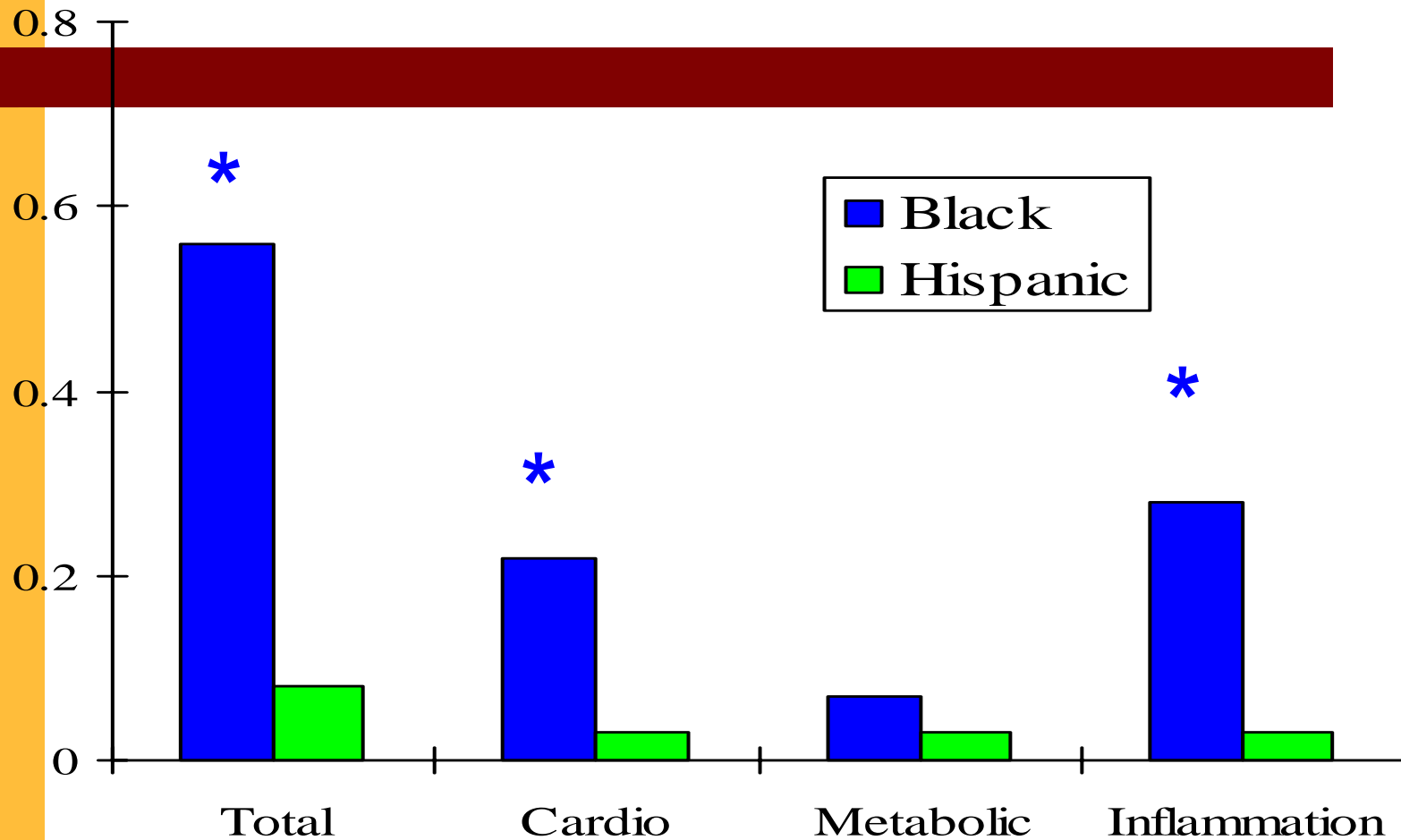


With Age and Gender Controlled; *Regression Coefficient Significantly Different from White

“Hispanic Paradox”? NO

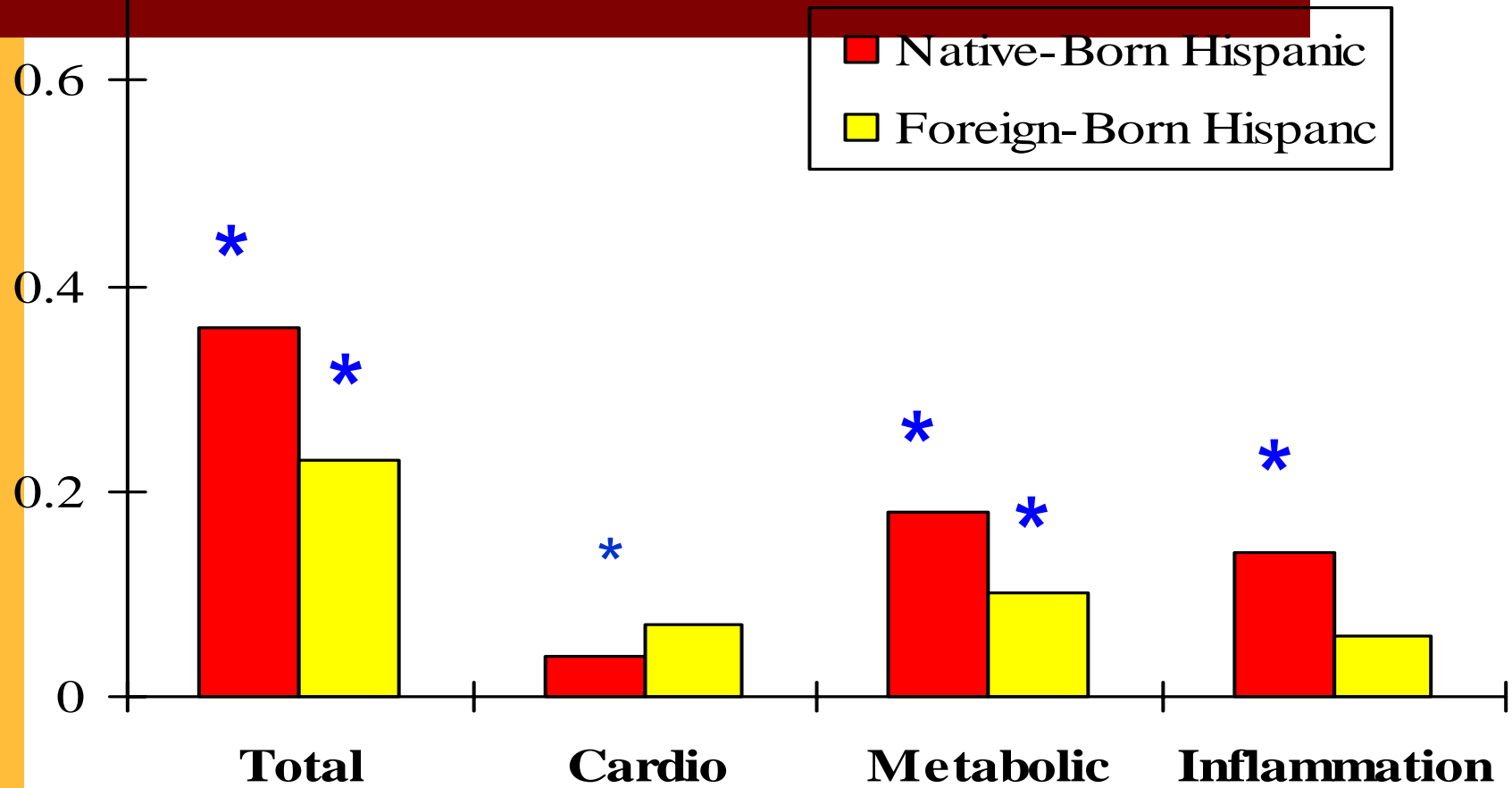
- **With age and gender controlled**
- **Hispanics are higher in biological risk than NH whites – All three types**
- **Lower than Blacks – “Black” paradox**
- **Next - Controls for low ed and poverty**

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

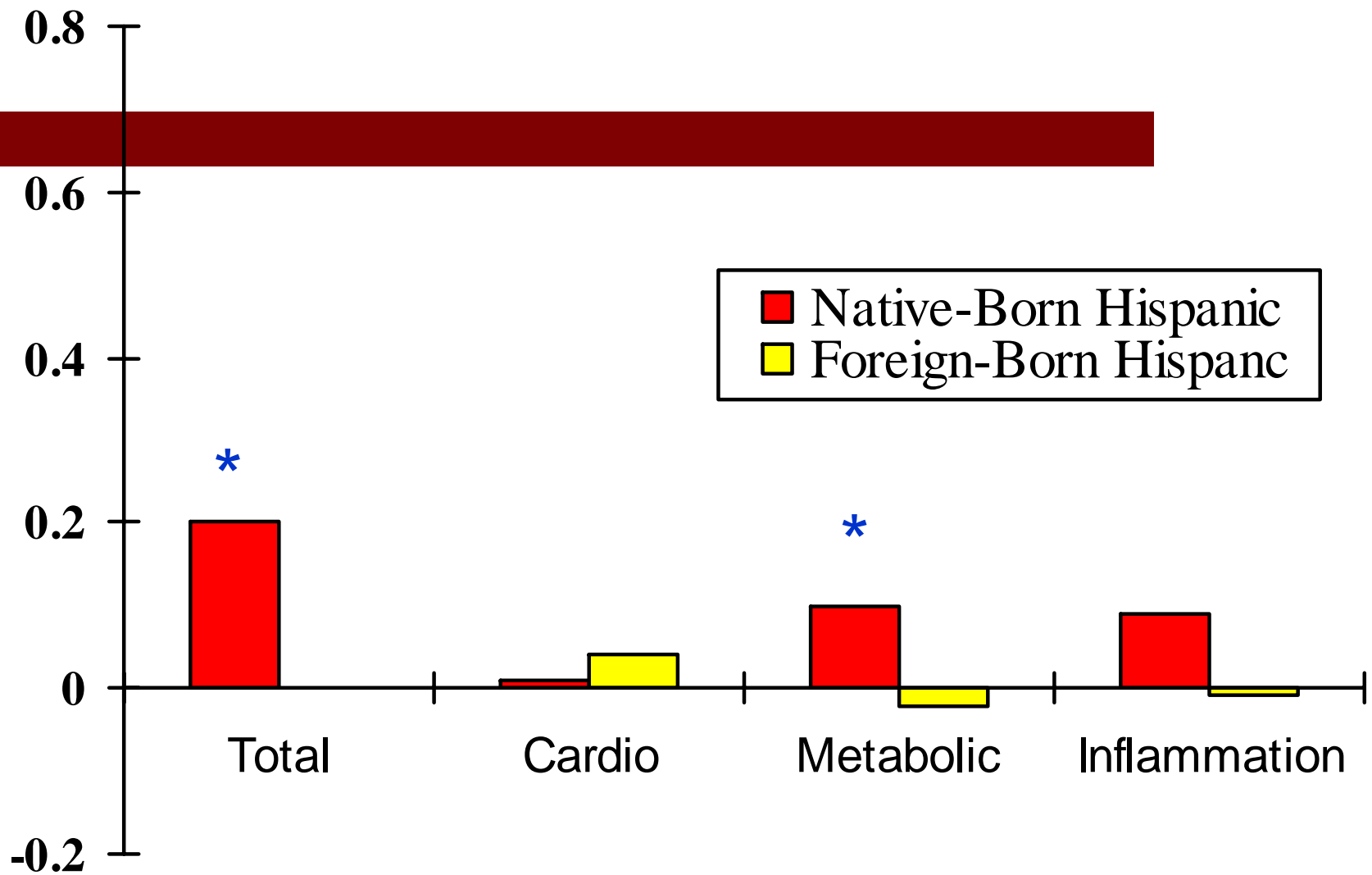


With Age and Gender Controlled; *Regression Coefficient Significantly Different from White

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

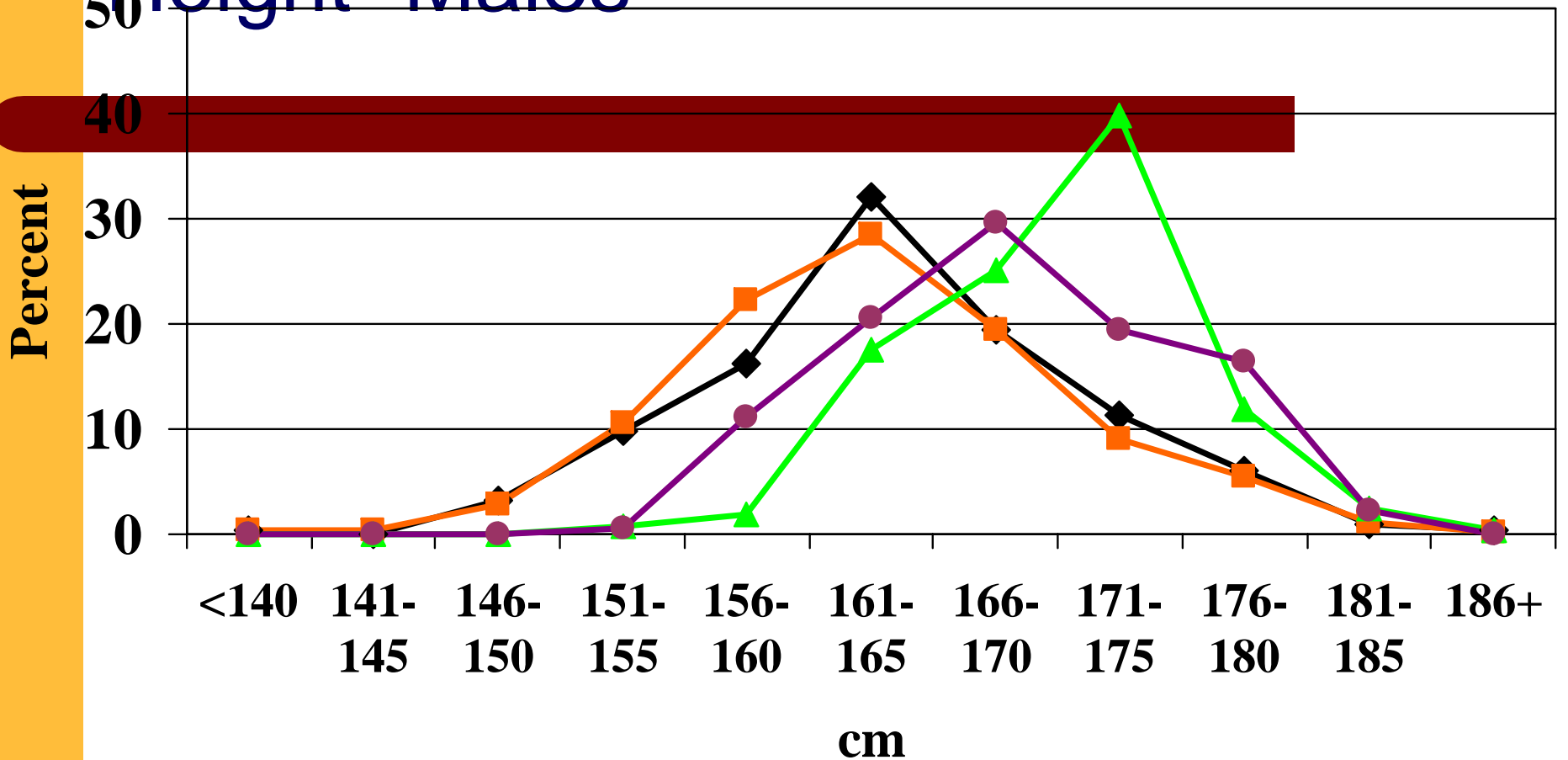
Are foreign-born Mexican Americans a group selected for good health?

- **Crimmins, E.M., Soldo, Beth J., Kim, Jung Ki, Alley, Dawn E. Using Anthropometric Indicators for Mexicans in the United States and Mexico to Understand the Selection of Migrants and the “Hispanic Paradox”. Social Biology, forthcoming.**

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**

Height - Males



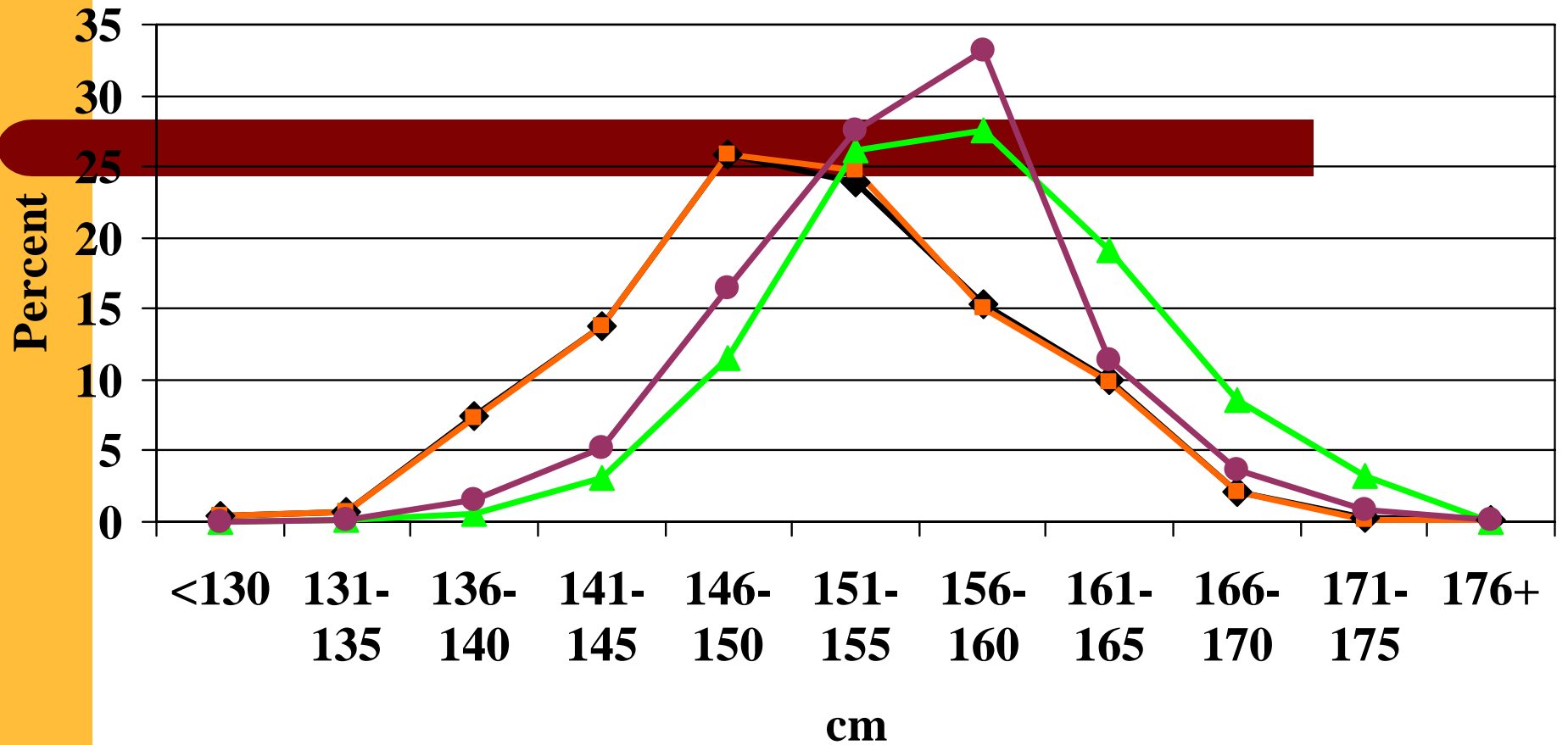
◆ Mexicans in Mexico

■ Return Migrants to Mexico

▲ US-born Mexican-Americans

● Foreign-born Mexican-Americans

Height - Females



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

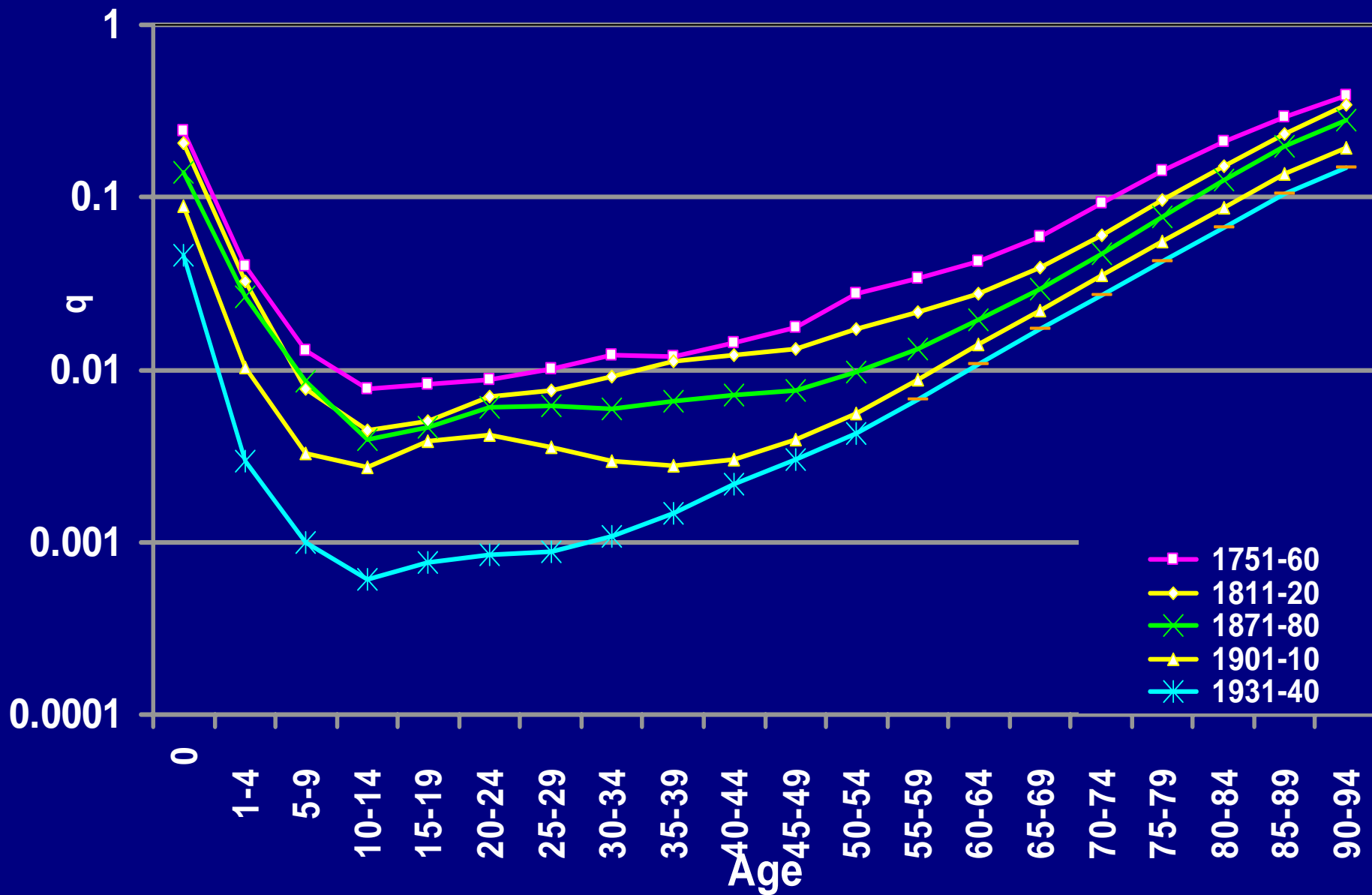
Explain Cohort Pattern of Mortality decline over past centuries

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

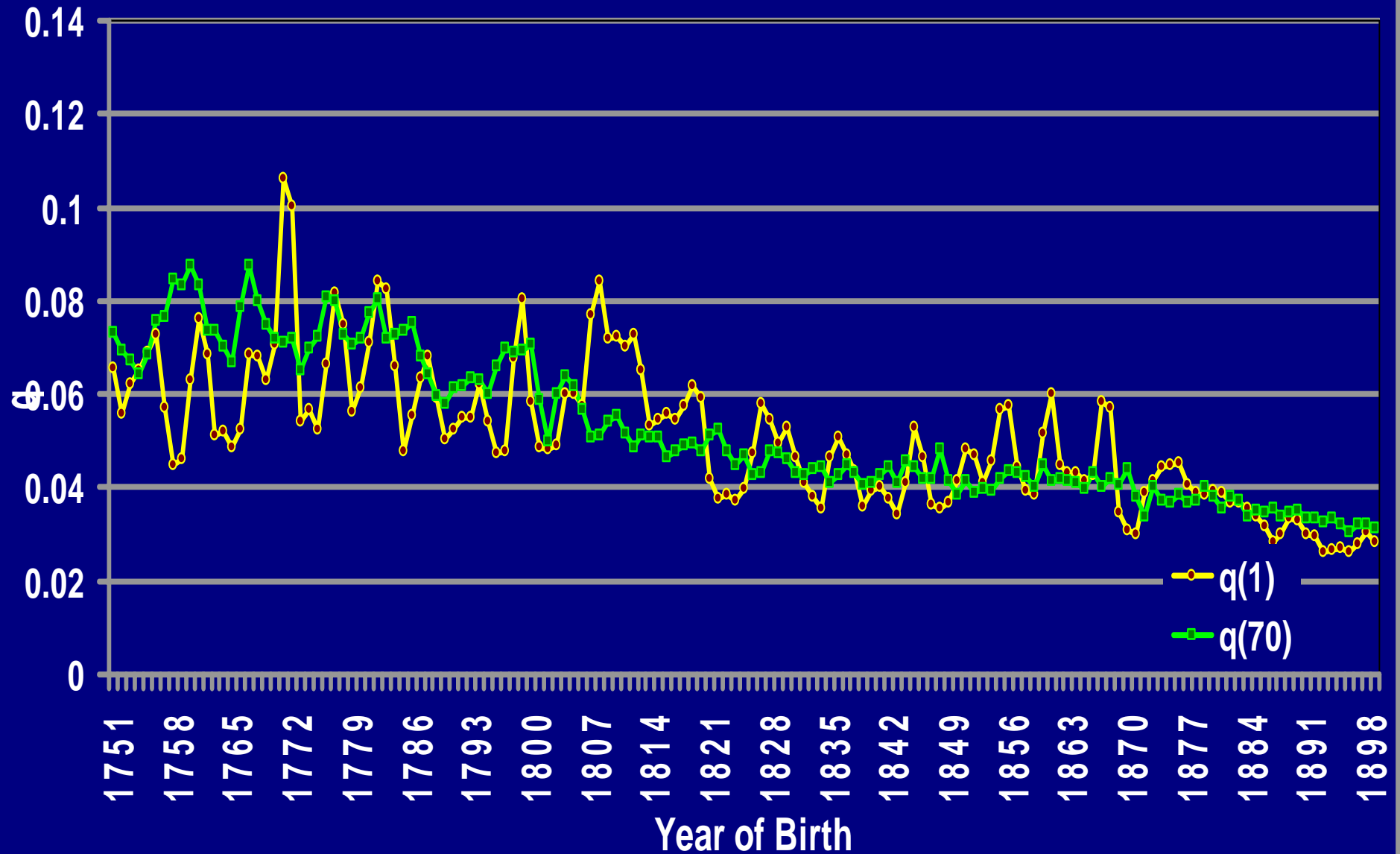
Finch & Crimmins. (2004). Inflammatory exposure and historical changes in human life-spans. Science, 305, 1736-1739.

Crimmins & Finch. (2006). Infection, Inflammation, Height, and Longevity. Proceedings of the National Academy of Sciences, 103, 498-503.

Cohort Mortality: Sweden (1751-1940)



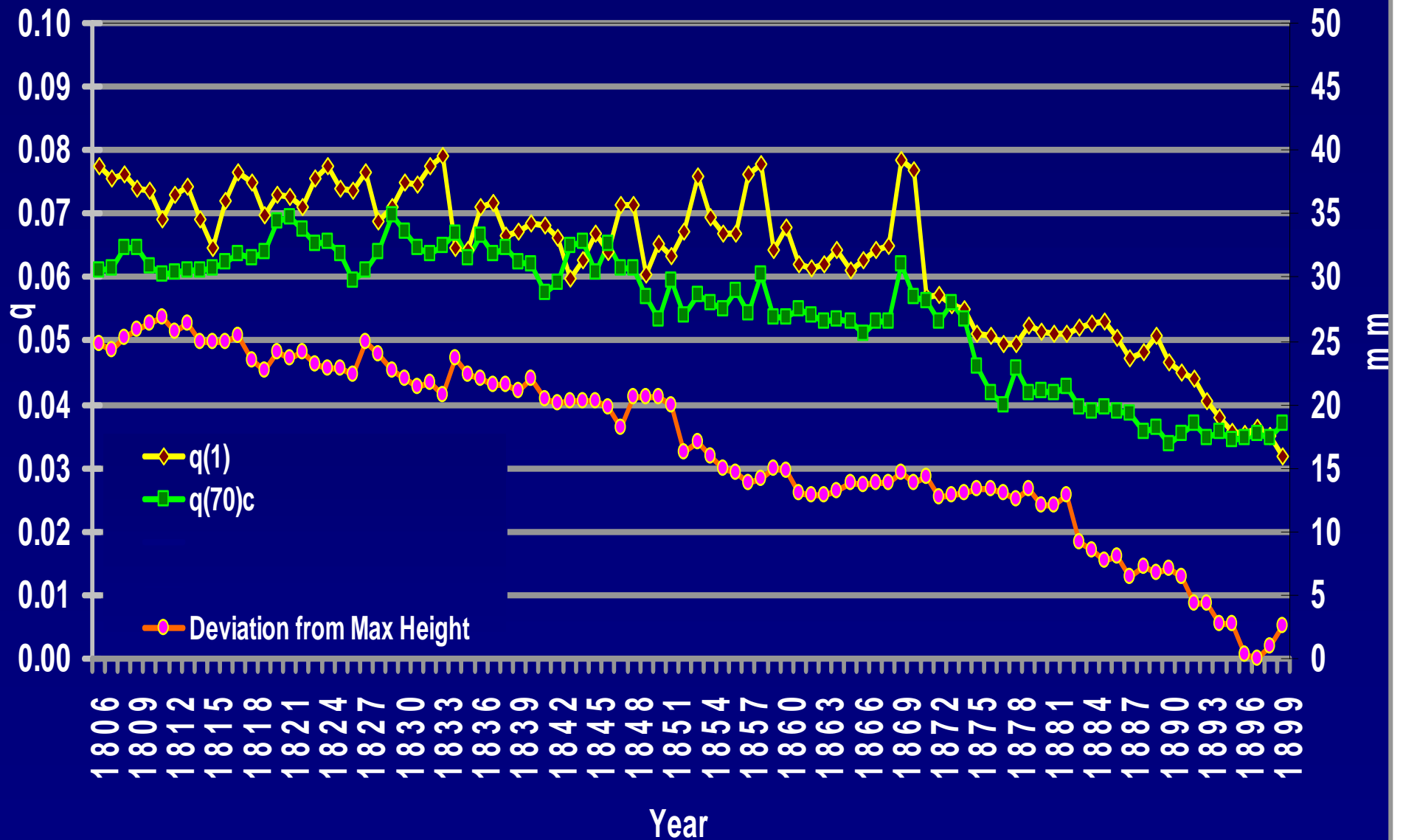
Cohort Mortality: Sweden (Cohorts born 1751-1899)



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

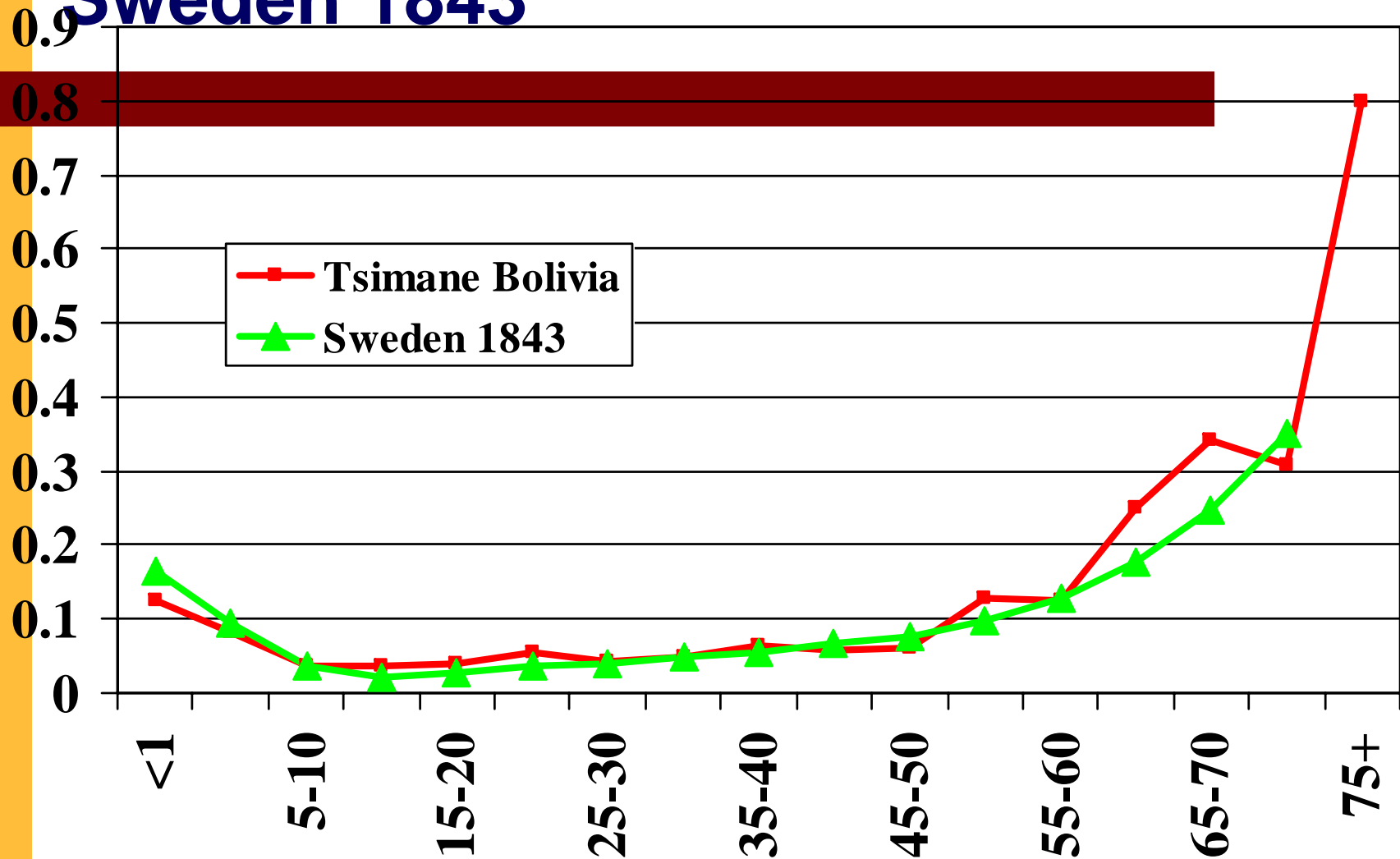


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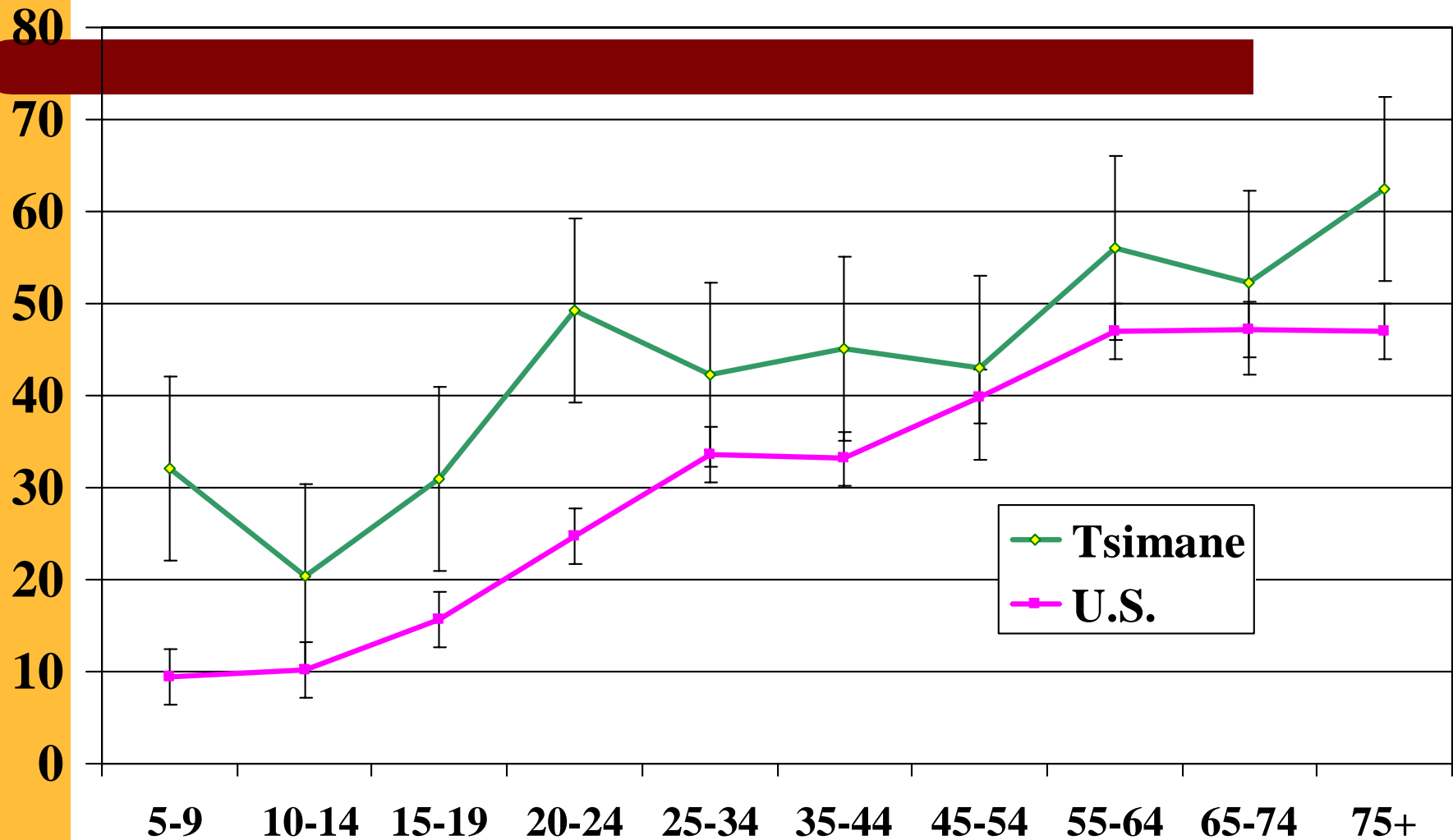
Testing the Hypothesis: With Hillard Kaplan and Michael Gurven

- Gurven, M., Kaplan, H., Winking, J., Finch, C., Crimmins, E. “Inflammation Levels in Two Epidemiological Worlds”, Journal of Gerontology: Medical Sciences (forthcoming).

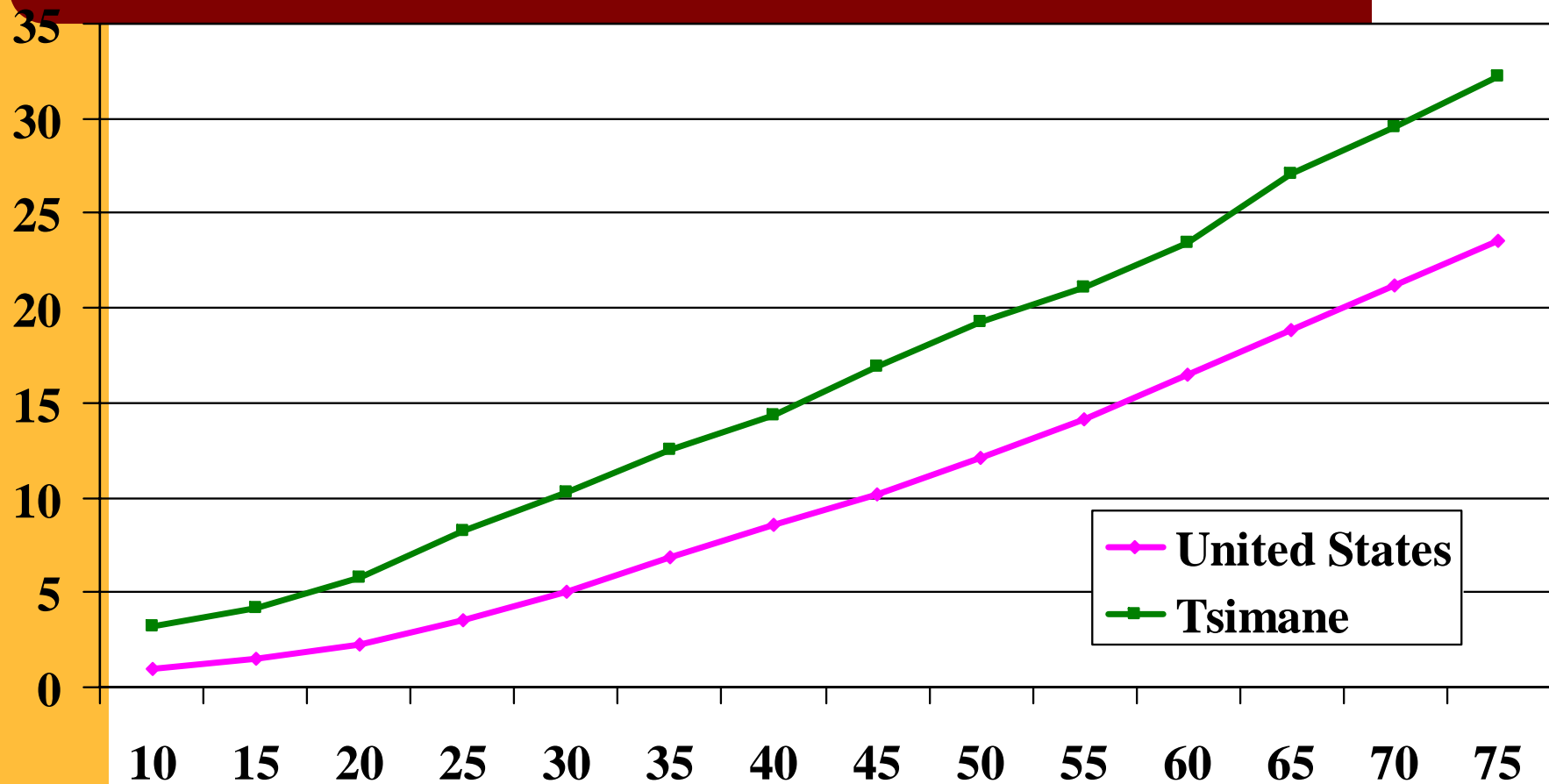
Mortality Among the Tsimane and Sweden 1843



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.

Acknowledgements

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 - Dawn Alley, Jung Ki Kim, Arun Karlamangla,
 - Teresa Seeman, Sandra Reynolds, Caleb Finch, Hillard Kaplan, Michael Gurven
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