The Life Course Perspective and Longitudinal Methods

Instructor: Rebecca E. Graff, ScD

Friday, February 15, 2019, 8:45am – 10:15am

Mission Hall 1105

Outline

- The life course perspective
  - Example: cardiovascular disease (CVD)
- Model parameterization
- Statistical models for longitudinal data

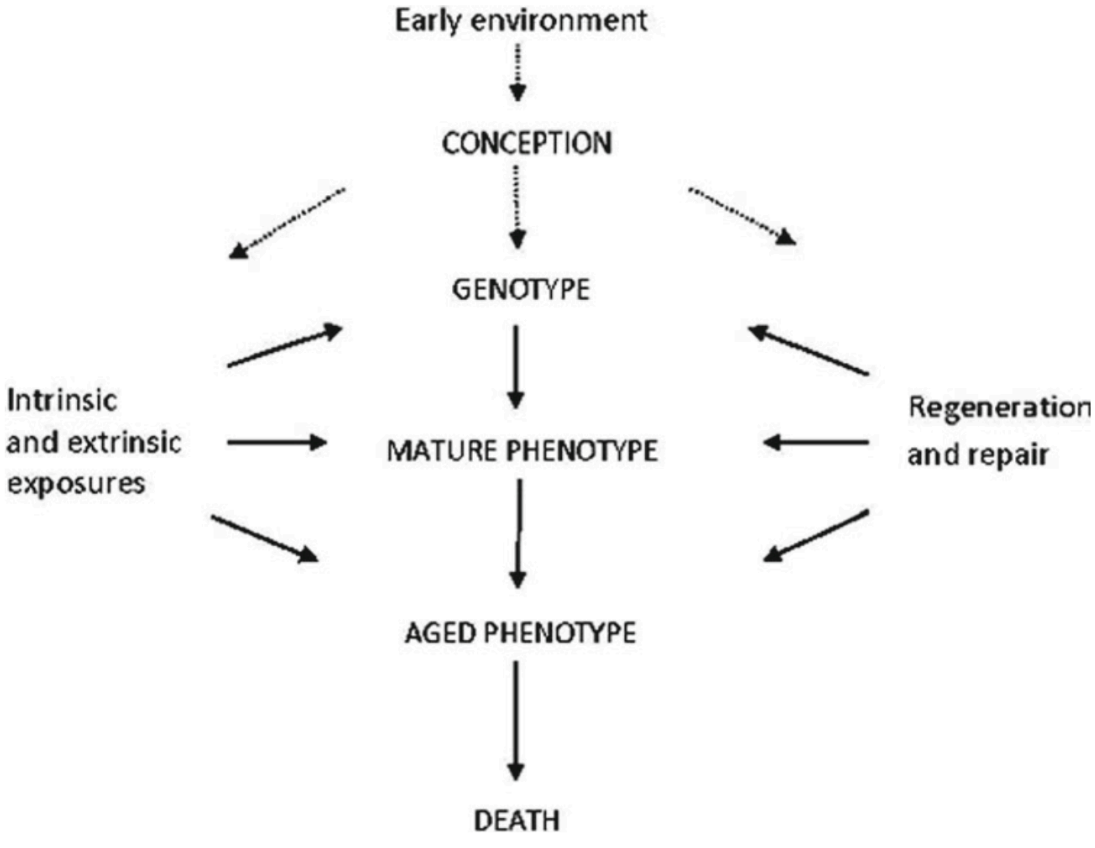
THE LIFE COURSE PERSPECTIVE

The Life Course Approach

- "The study of long-term effects on chronic disease risk of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life."
  - Pathways that operate across an individual's life course
  - Pathways that operate across generations

Ben-Shlomo, Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*. 2002;31(2):285-93.

Life Course Exposure Response Model



The Epidemiology of Aging. Dordrecht, Springer Science+Business Media (2012).

Discussion:

HOW DOES THE LIFE COURSE APPROACH DIFFER FROM OTHER APPROACHES TO EPIDEMIOLOGIC RESEARCH?

Key Conceptual Issues

1. Integrating biological and psychosocial pathways
2. Understanding natural history and physiological trajectory of normal biological systems

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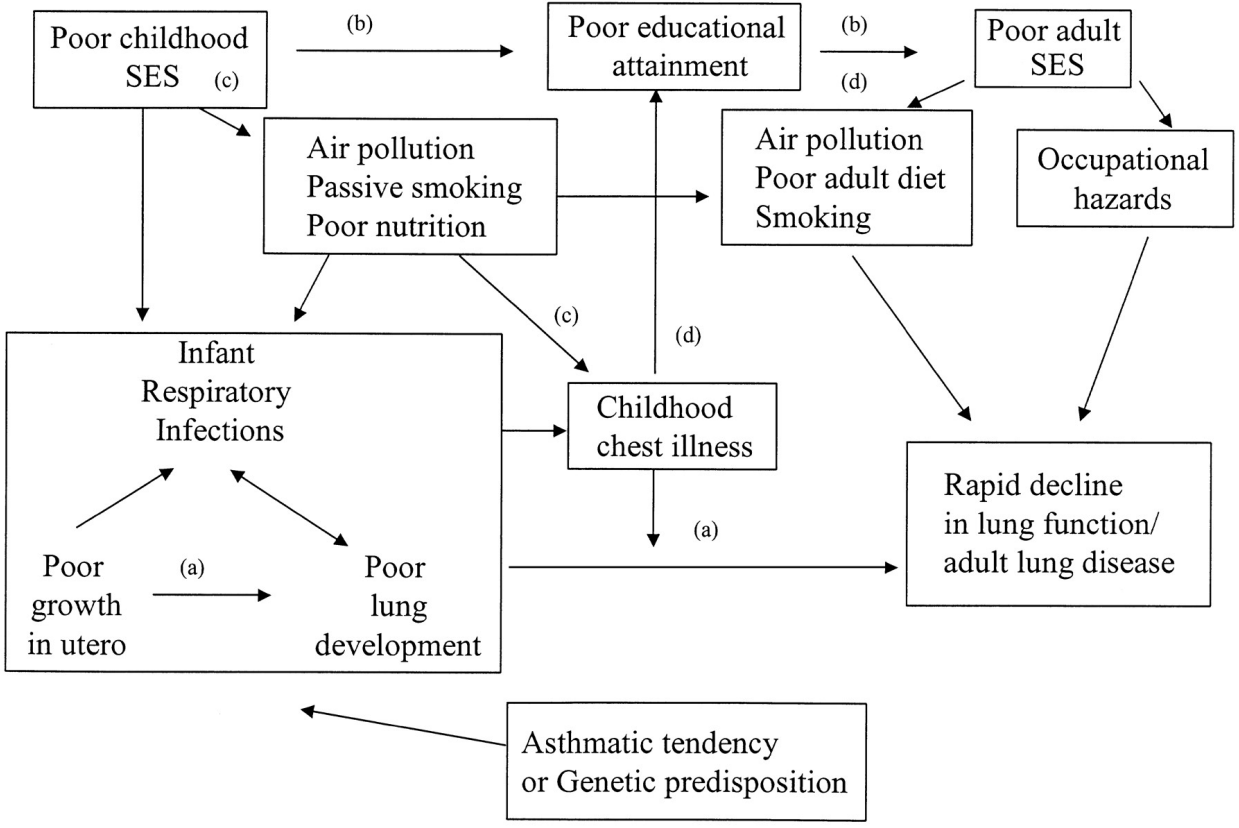
1. Integrating the Biological & Psychosocial



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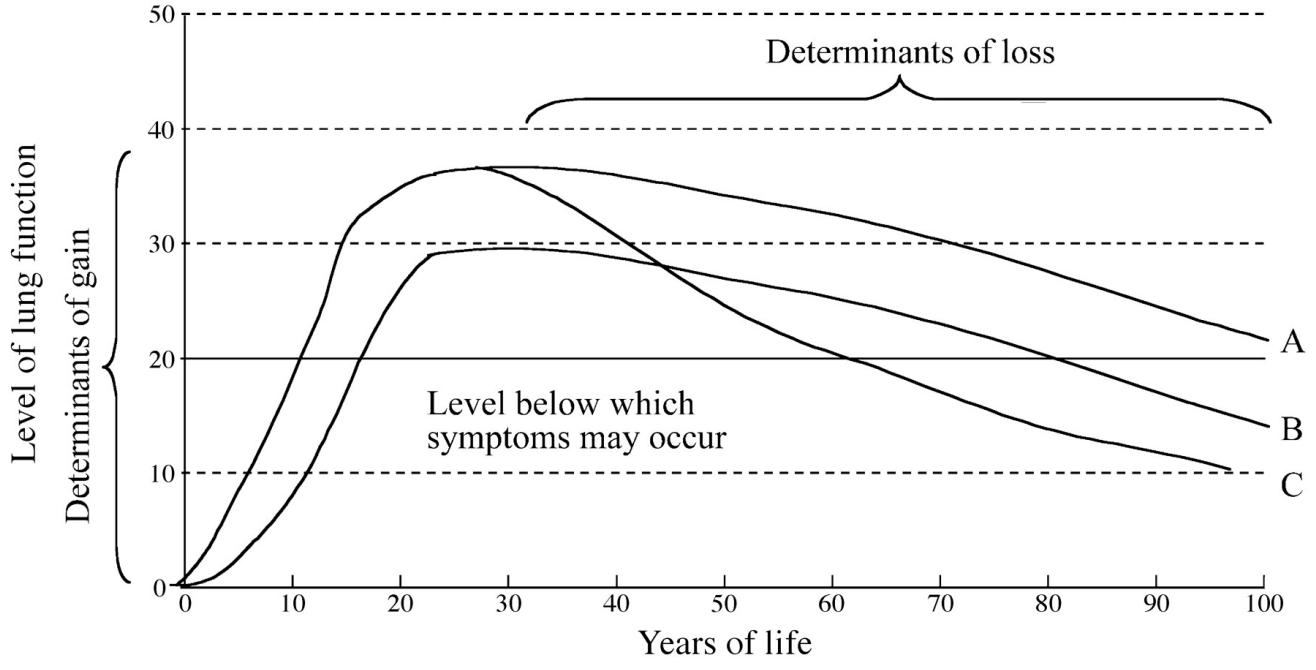
2. Understanding Biological Systems



modified from Strachan D. (1997)

A = normal development and decline; B = exposure in early life reducing lung function potential;
C = exposure acting in mid to later life accelerating age-related decline

Ben-Shlomo, Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*. 2002;31(2):285-93.

Discussion:

WHAT ARE THE PRIMARY CONCEPTUAL LIFE COURSE MODELS?

Conceptual Life Course Models

Table 1 Conceptual life course models

Critical period model
with or with out later life risk factors
with later life effect modifiers
Accumulation of risk
with independent and uncorrelated insults
with correlated insults
'risk clustering'
'chains of risk' with additive or trigger effects

Ben-Shlomo, Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*. 2002;31(2):285-93.

1. Critical Period Model

- "Exposure acting during a specific period has lasting or lifelong effects on the structure or function of organs, tissue and body systems which are not modified in any dramatic way by later experience."
- Versus sensitive periods
- Effect modification

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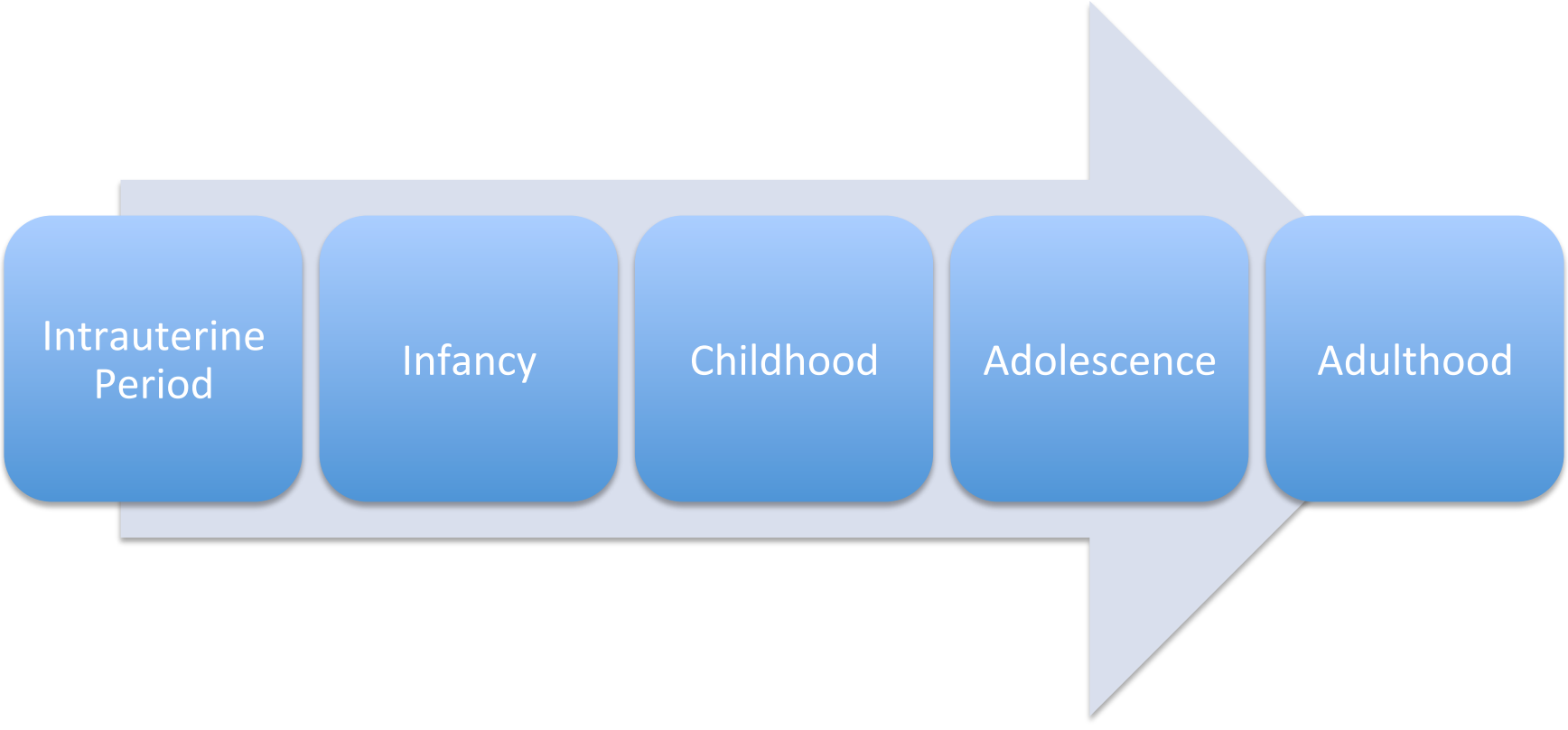
Programming

- Definition
- Developmental plasticity
- Organ systems are most susceptible during phases of rapid growth

Possible Critical Periods



Discussion:

WHAT ARE SOME EXAMPLES OF ASSOCIATIONS BETWEEN OLDER ADULT HEALTH AND EXPOSURES IN DIFFERENT KEY PERIODS?

E.g., Cardiovascular Disease

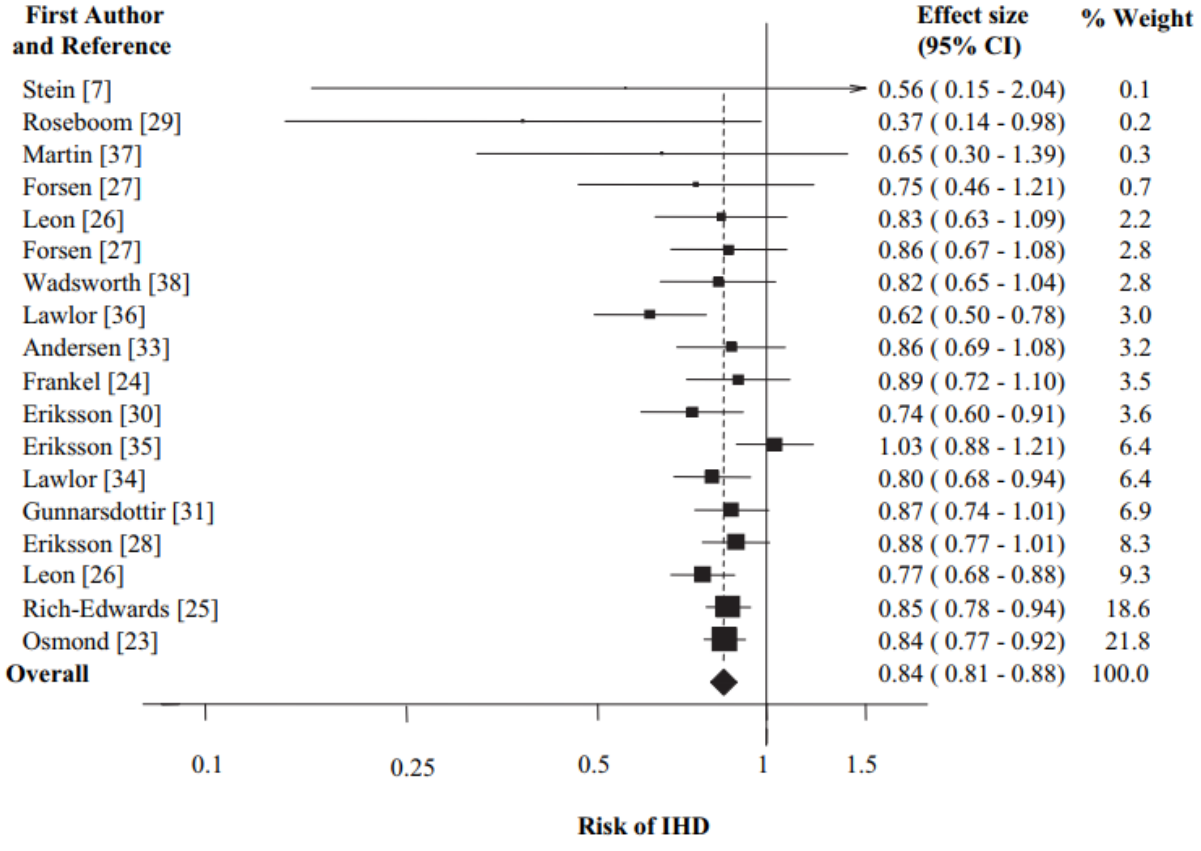
Life Course Risk Factors

- Maternal health, development, and diet before and during pregnancy
- Parental history of cardiovascular disease
- Intrauterine growth retardation
- Childhood:
  - Socioeconomic deprivation
  - Stress
  - Poor growth
  - Short leg length
  - Obesity
  - Certain infections
  - Diet
- Late adolescence:
  - Blood pressure
  - Serum cholesterol
  - Smoking
  - Little physical activity
- Adulthood:
  - Blood pressure
  - Serum cholesterol
  - Obesity
  - Job insecurity and unemployment
  - Short stature
  - Binge alcohol drinking
  - Diabetes and components of syndrome X
  - Elevated fibrinogen, acute phase reactants
  - Certain infection

Fetal Origins Hypothesis

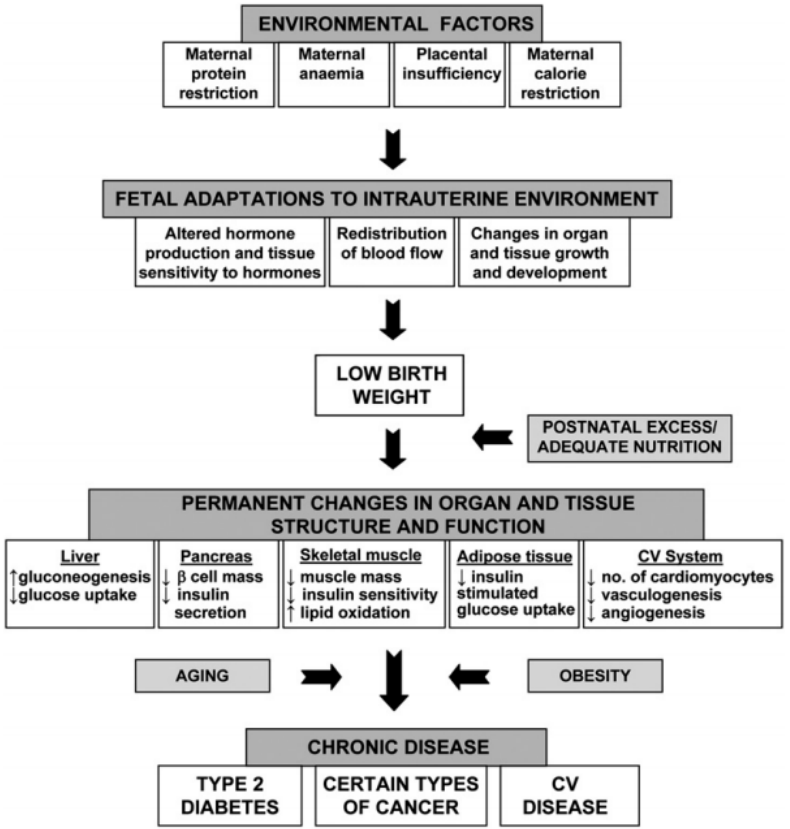
- Import of gestational period
- Key characteristics
- I.e., Barker hypothesis, fetal programming hypothesis, thrifty phenotype hypothesis
- Caveat: measured exposure is typically size at birth
  - Inexact proxy for fetal growth

Birth Weight and CVD



Huxley R, Owen CG, Whincup PH, et al. Is birth weight a risk factor for ischemic heart disease in later life?. *Am J Clin Nutr*. 2007;85(5):1244-50.

Possible Mechanisms of Action



Matin-Gronert MS, Ozanne SE. Mechanisms linking suboptimal early nutrition and increased risk of type 2 diabetes and obesity. *J Nutr*. 2010;140(3):662-6.

Effect Modification by Adult Obesity

	Age-adjusted cumulative incidence of coronary heart disease in % (number of cases)				p
	All men	BMI tertile			
		Lowest	Middle	Highest	
All men	..	9·1 (34)	12·3 (49)	11·1 (45)	0·46
Birthweight tertile					
Lowest	11·6 (46)	10·8 (14)	9·4 (13)	16·4 (19)	0·12
Middle	12·0 (44)	9·0 (13)	14·6 (18)	12·6 (13)	0·70
Highest	9·1 (38)	7·3 (7)	12·6 (18)	7·5 (13)	0·70
p	0·03	0·51	0·47	0·0005	..

Table 1: **Age-adjusted cumulative incidence of coronary heart disease by birthweight and BMI tertiles**

Frankel S, Elwood P, Sweetnam P, et al. Birthweight, body-mass index in middle age, and incident coronary heart disease. *Lancet*. 1996;348(9040):1478-80.

Catch-up Growth

- Rapid growth during any phase of development when an identified constraint has been removed
- In infancy, associated with CVD risk factors by early childhood

Anthropometrics by Catch-up Growth

TABLE 2. Comparisons of anthropometric and body composition values for normal children and AGA catch-up children at 9 years of age[1]

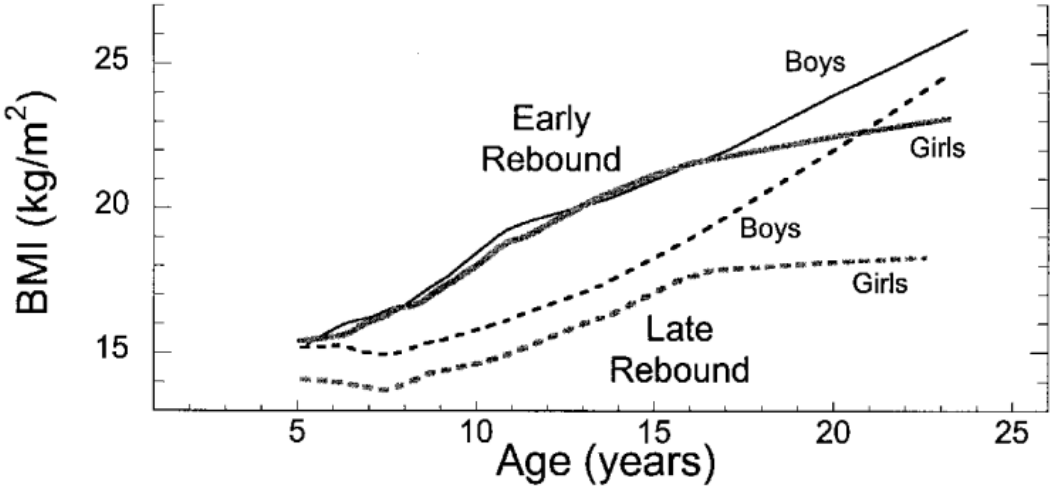
Variables	Normal	Catch-up	*t*	*P*
Birth weight (g)	3205	2982	3.39	0.001
Weight (kg)	28.6	32.4	−4.24	0.000
Height (cm)	132.1	135.8	−3.87	0.000
BMI (kg/m^2)	16.39	17.47	−2.39	0.018
Waist circumference (cm)	56.65	59.70	−3.03	0.003
Hip circumference (cm)	63.38	66.77	−2.55	0.012
Sum skinfolds* (mm)	53.90	65.41	−3.30	0.001
BMC (g)	902.73	959.36	−2.38	0.019
Fat weight (kg)	7.32	9.76	−3.62	0.000
LTM (kg)	20.17	21.58	−3.22	0.002
% fat	24.99	28.74	−2.62	0.010

[1] Sum skinfolds, triceps, biceps, subscapular, suprailiac, thigh, calf; BMC, bone mineral content; LTM, lean tissue mass.

Cameron N, Demerath EW. Critical periods in human growth and their relationship to diseases of aging. *Am J Phys Anthropol*. 2002;Suppl 35:159-84.

Age of Adiposity Rebound

- Second rise in the BMI curve that occurs between ages ~5-7 years
- Inversely associated with adult adiposity



Freedman DS, Khan LK, Serdula MK, et al. BMI rebound, childhood height and obesity among adults: the Bogalusa Heart Study. *Int J Obes Relat Metab Disord*. 2001;25(4):543-9.

Age of Maturation

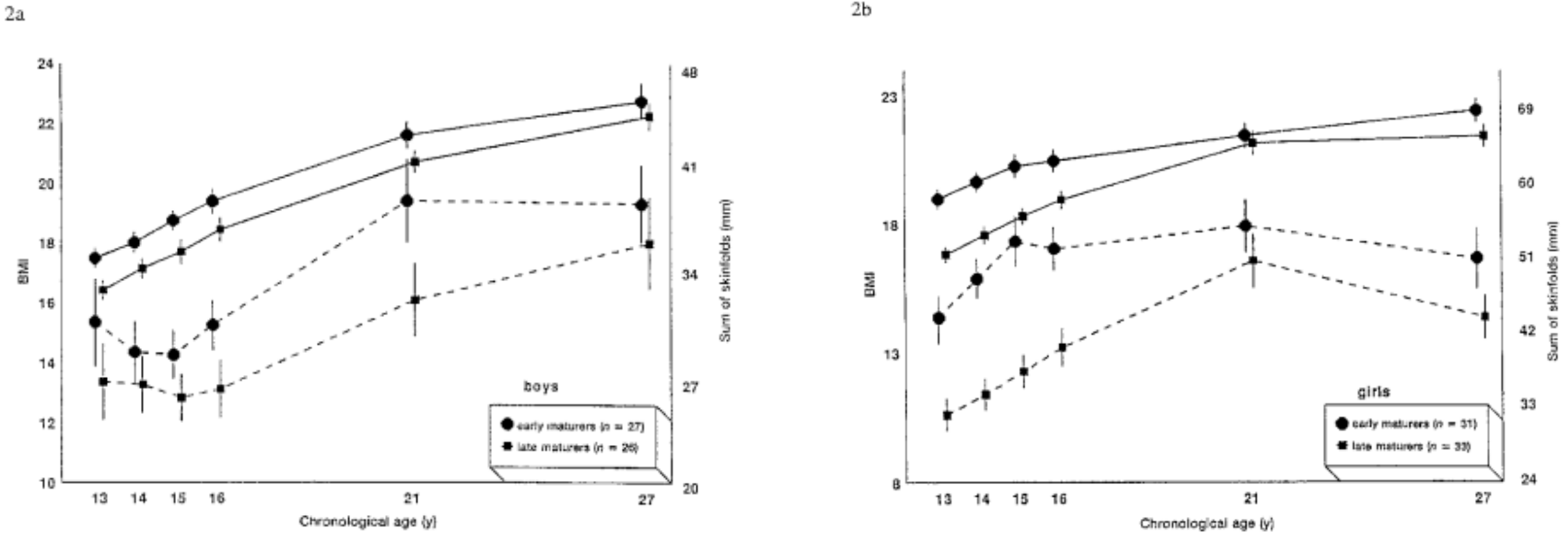


Fig. 2. **a:** Mean (± SE) of body mass index (BMI; in kg/m^2, solid lines) and sum of four skinfold thicknesses (dotted lines), measured six times between 13–27 years of age for early- and late-maturing boys, based on age of peak height velocity. y, years. From Van Lethe et al. (1996a). **b:** Mean (± SE) of BMI (in kg/m^2, solid lines) and sum of four skinfold thicknesses (dotted lines) measured six times between 13–27 years of age for early- and late-maturing girls, based on age at menarche. From Van Lethe et al. (1996a). Reproduced with permission by the American Journal of Clinical Nutrition. ©Am J Clin Nutr. American Society for Clinical Nutrition.

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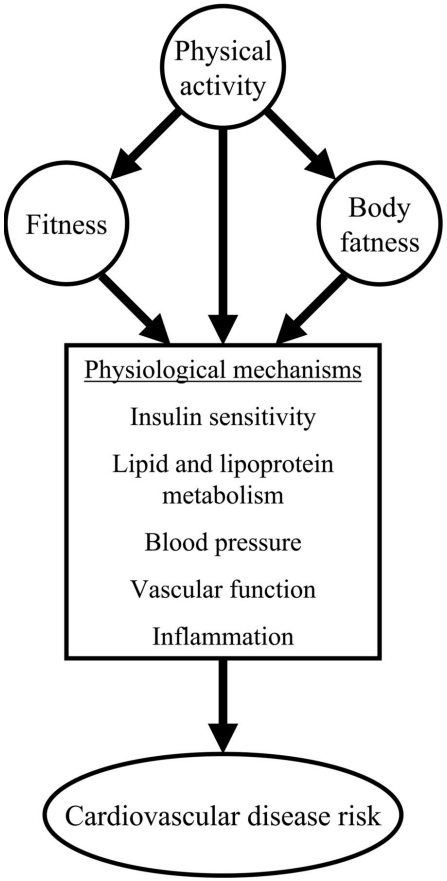
Physical Activity in Adulthood



Gill JM, Malkova D. Physical activity, fitness and cardiovascular disease risk in adults: interactions with insulin resistance and obesity. *Clin Sci (Lond)*. 2006;110(4):409-25.

2. Accumulation of Risk

- Cumulative insults during the life course increase risk
- Independent vs. clustered insults
- Additive effect vs. trigger effect

Challenges of a Life Course Approach

- Data availability
- Study design
  - Historical cohorts
  - Case-control studies
  - Experiments
- Analysis

MODEL PARAMETERIZATION

Discussion:

HOW IS EXPOSURE MOST COMMONLY MODELED IN EPIDEMIOLOGICAL STUDIES?

Discussion:

HOW DID THE INVESTIGATORS MODEL “SOCIAL CLASS” IN THE MISHRA PAPER?

Summative Score

$$\text{Exposure} = \sum S_j$$

- Corresponds to accumulation of risk

Early Life Score

Exposure = S_{early}

- Corresponds to critical period hypothesis

Interactions

$$\text{Exposure} = S_{\text{early}} + S_{\text{later}} + S_{\text{early}}S_{\text{later}}$$

- Corresponds to critical period hypothesis with effect modification at later time point

Also

- Average score
- Various functional forms
- Weighting different time points
- Covariates
- Etc.

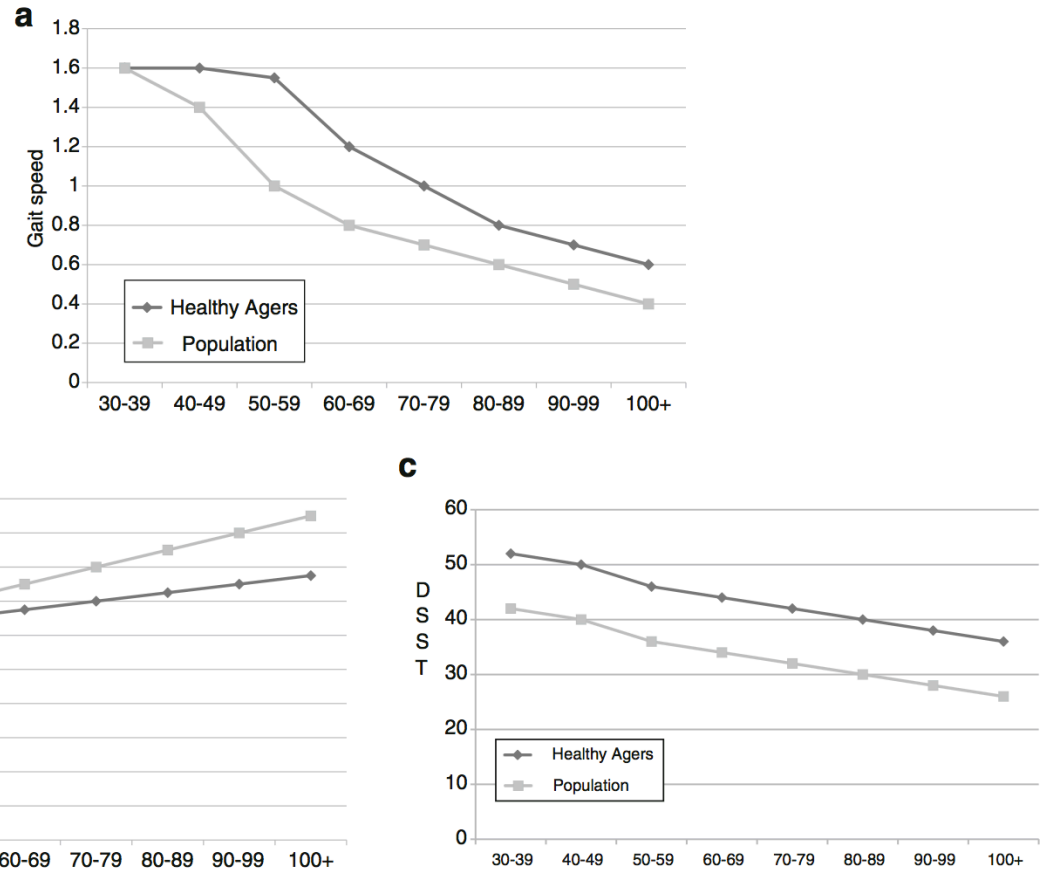
"It is highly advantageous to have an understanding of the biological mechanisms underlying the effect of exposures on specific health outcomes upon which to base statistical modelling"

Mishra G, Nitsch D, Black S, et al. A structured approach to modelling the effects of binary exposure variables over the life course. *Int J Epidemiol*. 2009;38(2): 528-37.

Outcomes

- Achievement of advanced old age
- Specific health conditions
- Decline vs. maintenance of function
- Mortality

Trajectories of Outcome



The Epidemiology of Aging. Dordrecht, Springer Science+Business Media (2012).

Discussion:

HOW DID HULMÁN AND COLLEAGUES GET AT AGE TRENDS?

Discussion:

HOW DID HULMÁN AND COLLEAGUES GET AT SECULAR TRENDS?

Sequential Cross-Sectional Analysis

- Evaluation of risk factor distributions in the same age group over time

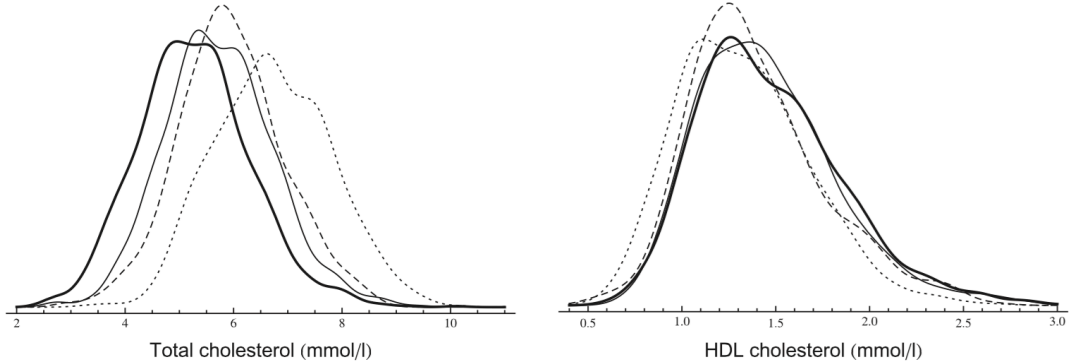


Figure 1 A,B. Sequential cross-sectional analysis (age group: 57–61 years). Smooth kernel distributions of cardiovascular risk factors (probability density functions are displayed) in men (A) and women (B) (dotted line: phase 3, dashed line: phase 5, solid line: phase 7, thick line: phase 9).

Hulmán A, Tabák AG, Nyári TA, et al. Effect of secular trends on age-related trajectories of cardiovascular risk factors: the Whitehall II longitudinal study 1985-2009. *Int J Epidemiol*. 2014;43(3):866-77.

Quantile Regression

- Explanatory variable: calendar year
- Outcome variable: quantiles of risk factors
- Result: assessment of linear trends

Hulmán A, Tabák AG, Nyári TA, et al. Effect of secular trends on age-related trajectories of cardiovascular risk factors: the Whitehall II longitudinal study 1985-2009. *Int J Epidemiol*. 2014;43(3):866-77.

Year of Birth x Age Interactions

- Inclusion of interaction terms in mixed effects models

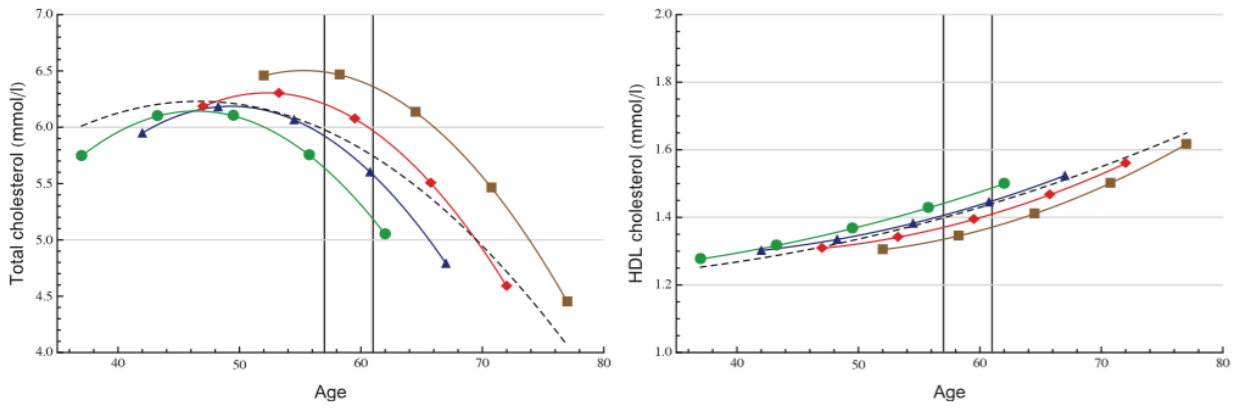


Figure 2A, B. Longitudinal trajectory analysis. Age-related trajectories (in years) of cardiovascular risk factors in men (A) and women (B) with adjustment for four different birth cohorts: 1933 (■), 1938 (◆), 1943 (▲), 1948 (●) and unadjusted (– – –).

Hulmán A, Tabák AG, Nyári TA, et al. Effect of secular trends on age-related trajectories of cardiovascular risk factors: the Whitehall II longitudinal study 1985-2009. *Int J Epidemiol*. 2014;43(3):866-77.

STATISTICAL MODELS FOR LONGITUDINAL DATA

Discussion:

WHAT STATISTICAL MODELS ARE VIABLE FOR LONGITUDINAL DATA?

Generalized Linear Models

- Prediction of a response variable based on a linear combination of observed predictor variables
  - Linear regression: continuous outcomes
  - Logistic regression: binary outcomes
  - Poisson regression: outcomes of count
- No inherent component of time

Survival Analysis

- Evaluation of duration of time until outcome occurs according to explanatory variables (failure time data)
  - Parametric survival model: hazard function is specified
    - Proportional hazards
    - Accelerated failure time model
  - Cox proportional hazards model: estimation of hazard function from the data (semi-parametric)

Longitudinal Analysis

- Characterization of change in the response variable over time according to explanatory variables (repeated measures)
  - Generalized estimating equations (marginal effects models): estimation of population averages
  - Mixed effects models (random effects models): estimation of individual effects

Next Week:

LECTURE: CHRONIC DISEASES AND DISORDERS OF AGING

HOMEWORK: OUTLINE OF DEBATE ARGUMENTS, (PRESENTATION SLIDES)