

A Brief Overview of Life Course Epidemiology

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April 8, 2013
Oregon Life Course Network Meeting

WHAT is A Life Course?

Life Course, Span or Cycle

- **Life Span/Life Course** – Concept that development and aging form a continuous process from birth to death
- **Life Cycle** - a series of distinct, bounded life stages that are socially or biologically determined
- All have a long-term, multilevel, contextual, and dynamic view of aging

Life Span

- Life-span theories draw attention to the *length of the life of an individual* and to the idea that *processes and trajectories of development and aging are lifelong*
- Life-span researchers are interested primarily in understanding micro-level (endogenous) processes within the aging individual (e.g., the aging brain and mind)

Life Course

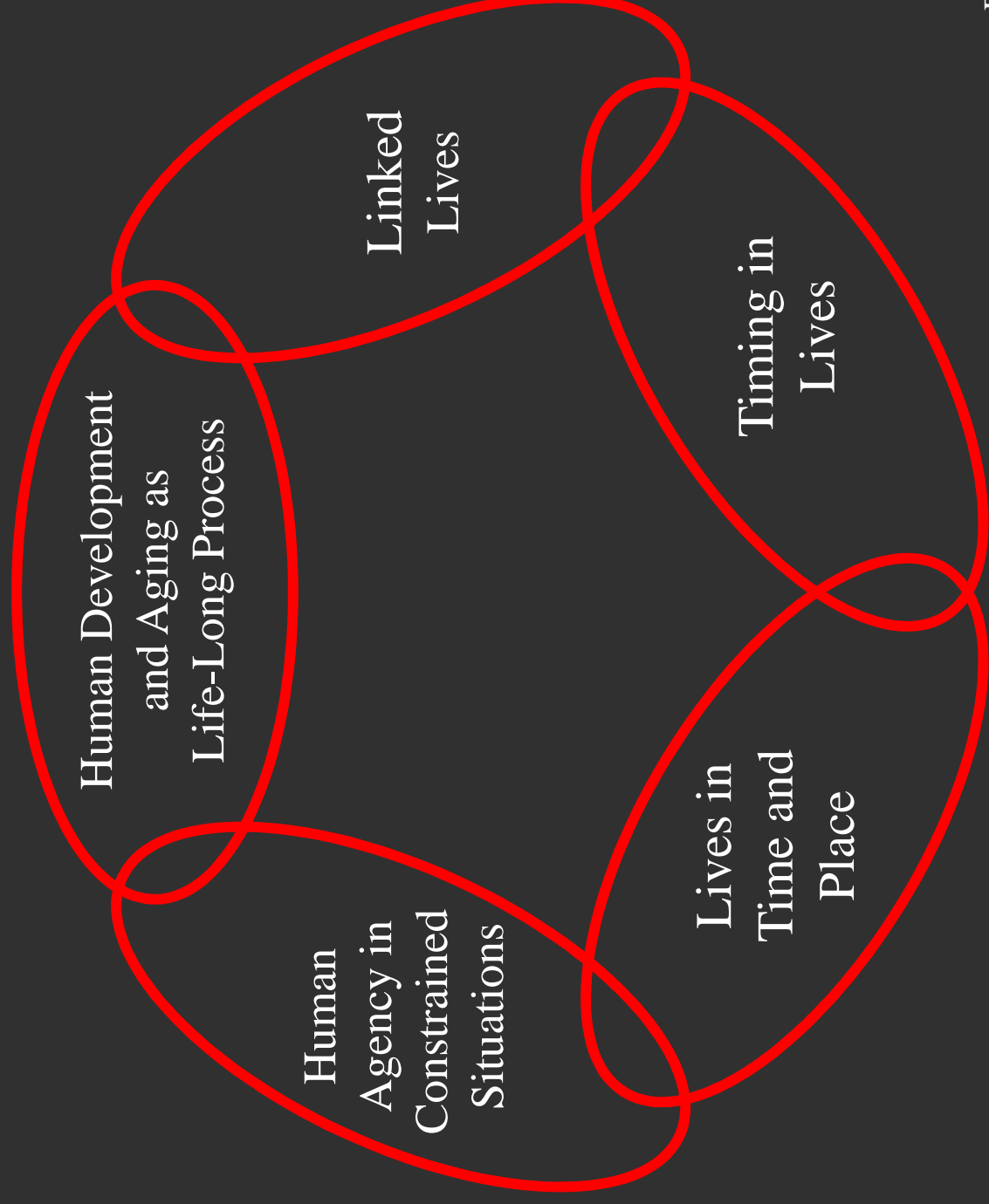
- Life course theories, in contrast, *differentiate between subgroups in society* and focus on the *social pathways* that define the sequence of events, transitions, roles, and experiences in the lives of individuals
- Life course researchers typically analyze macro-level (exogenous) processes that characterize the influence of groups, organizations, and institutions on the individuals within them

TABLE 1.1
*A Selection of Major Themes to Illustrate the Life-Course
 and Life-Span Perspectives*

| Major Themes | |
|--|---------------------------|
| Life Course Perspective | Life Span Perspective |
| Age, cohort, & historical effects | Individual differences |
| Accumulation of (in)equalities | Adaptivity and plasticity |
| Life Course & Life Span Perspectives Linked lives | |
| Differential trajectories and pathways of aging | |

Life Course Principles

Principles of Life Course Theory



Principle of Life-Long Development

Human development and aging are
lifelong processes.

Principle of Human Agency

Individuals construct their own life course through the choices and actions they take within the opportunities and constraints of history and social circumstances.

Principle of Historical Time and Place

The life course of individuals is embedded in and shaped by the historical times and places they experience over their lifetime.

Principle of Timing in Lives

The developmental impact of a succession of life transitions or events is contingent on when they occur in a person's life.

Principle of Linked Lives

Lives are lived interdependently, and social and historical influences are expressed through this network of shared relationships.

Embodiment and Embedding

Under the Skin

- Experience most definitely does get under the skin and is expressed at all levels, from gene expression to behavior.

Embodiment

What we observe as a biological, psychological, behavioral or social characteristic of an individual represents both some inherent predisposition and the ways in which the total environment has been “embodied” into an individual’s body functions or structures from conception onwards

Biological Embedding

- Process where early life experiences influence key biological systems over the long term to produce social gradients
- Biological embedding occurs when:
 - Experience gets under the skin and alters human biological processes;
 - Systematic differences in experience in a socially partitioned environment lead to different bio-developmental states;
 - The differences are stable and long term; and
 - These differences influence health, well-being, learning, and/or behavior over the life course.

Biological Embedding

“Candidate systems” physiological functions link the social environment to aspects of human biology that have the capacity to embed and influence the rest of the life course:

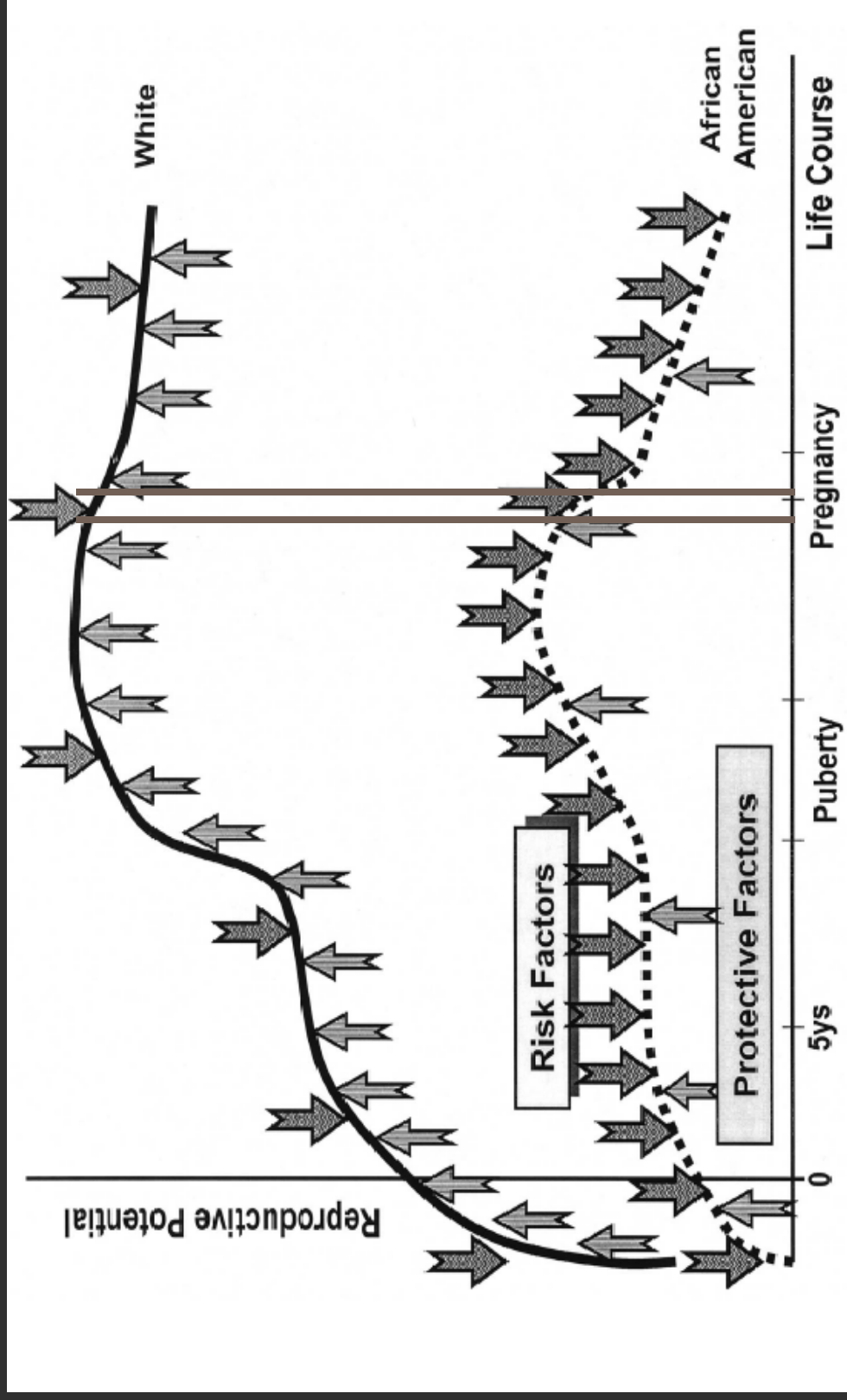
1. Hypothalamic-Pituitary-Adrenal (HPA) axis and its accompanying secretion of cortisol;
2. Autonomic nervous system (ANS) in association with epinephrine and norepinephrine;
3. The development of memory, attention, and other executive functions in the prefrontal cortex; and
4. The systems of social affiliation involving higher-order cerebral connections, mediated by serotonin and other hormones.

Life Course Perspectives

The Life Course Perspective

- Examines the experiences of human life from beginning to end
- Recognizes that the diversity of individual experience is constrained by her/his location in the social structure
- Incorporates framework of changing social and institutional structures in relation to individuals
- Contributes to understanding, at the population or group level, the roles of *age stratification, cohort and historical period effects, and the accumulation of (in)equalities over time*

Life Course Perspective



Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: a life-course perspective. *Matern Child Health J.* 2003;7:13-30.

Life Course Approach

A life course approach offers a way to conceptualize how underlying socio-environmental determinants of health, experienced at different life course stages, can differentially influence the development of chronic diseases, as mediated through proximal specific biological processes

Life Course Epidemiology

Life Course Epidemiology

- **WHAT it IS**
- ...”the study of the long-term effects on chronic disease risk of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life. It includes studies of the biological, behavioral and psychosocial pathways that operate across and individual’s life course, as well as across generations, to influence the development of chronic diseases.”
- **WHAT it ISN’T**
- “Merely the collection of exposure data across the life course is not synonymous with a life course model of disease causation.”
- (Ben-Shlomo and Kuh, 2002)

Life Course Epidemiology

- WHAT
 - Population-based
 - Draws on multiple disciplinary perspectives
 - Elevates the dimension of time
 - Concerned with dynamic interactions between person and environment

Life Course Epidemiology

- **WHY**
 - Static approaches of ‘modern epidemiology’ (case-control studies, for example) may obscure etiologic processes and intervention points
 - Disease risk begins early in life and accumulates over time
 - Trajectories of risk initiated as early as conception
- **HOW**
 - Design: study persons over time across settings
 - Measures: developmentally sensitive and appropriate
 - Analysis: trajectories, timing

*Structural
Macrosocial
Factors*

*Distal Social
Connections*

Work

*Proximal Social
Connections*

*Individual
Characteristics*

*Genetic
Characteristics*

Pathobiology

Life course

Death

Conception

Lynch JW, 2000

Political Economy Discrimination Institutions
History Culture

Neighborhood Community

Work

Friends

Family

Socioeconomic Behavioural
Psychosocial

Genetics
Human Biology

Pathological Biomarkers

Health Status



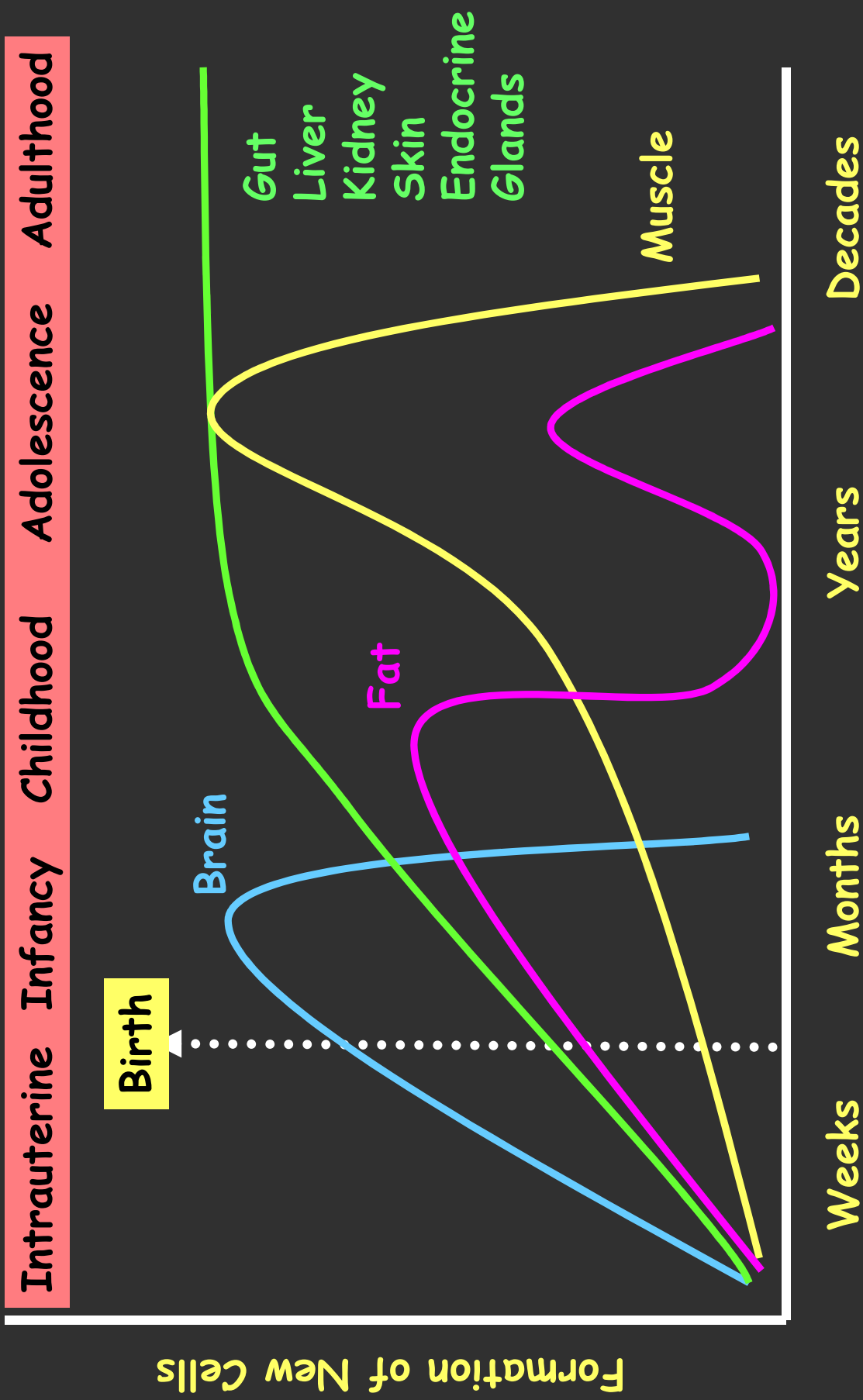
Conceptual Models in Life Course Epidemiology

Life Course Models

| LIFE COURSE MODEL | NOTE |
|---|---|
| CRITICAL PERIOD Models | Focus on importance of timing of exposure |
| <ul style="list-style-type: none"> ▪ With or without later-life risk factors ▪ With later-life effect modifiers | |
| ACCUMULATION of RISK Models | Focus on the importance of exposure over time and the sequence of exposure |
| <ul style="list-style-type: none"> ▪ With independent and uncorrelated insults | |
| <ul style="list-style-type: none"> ▪ With correlated insults <ul style="list-style-type: none"> – Risk clustering – Chains of risk with additive or trigger effects | |

Critical Period

Critical Periods of Cell Development



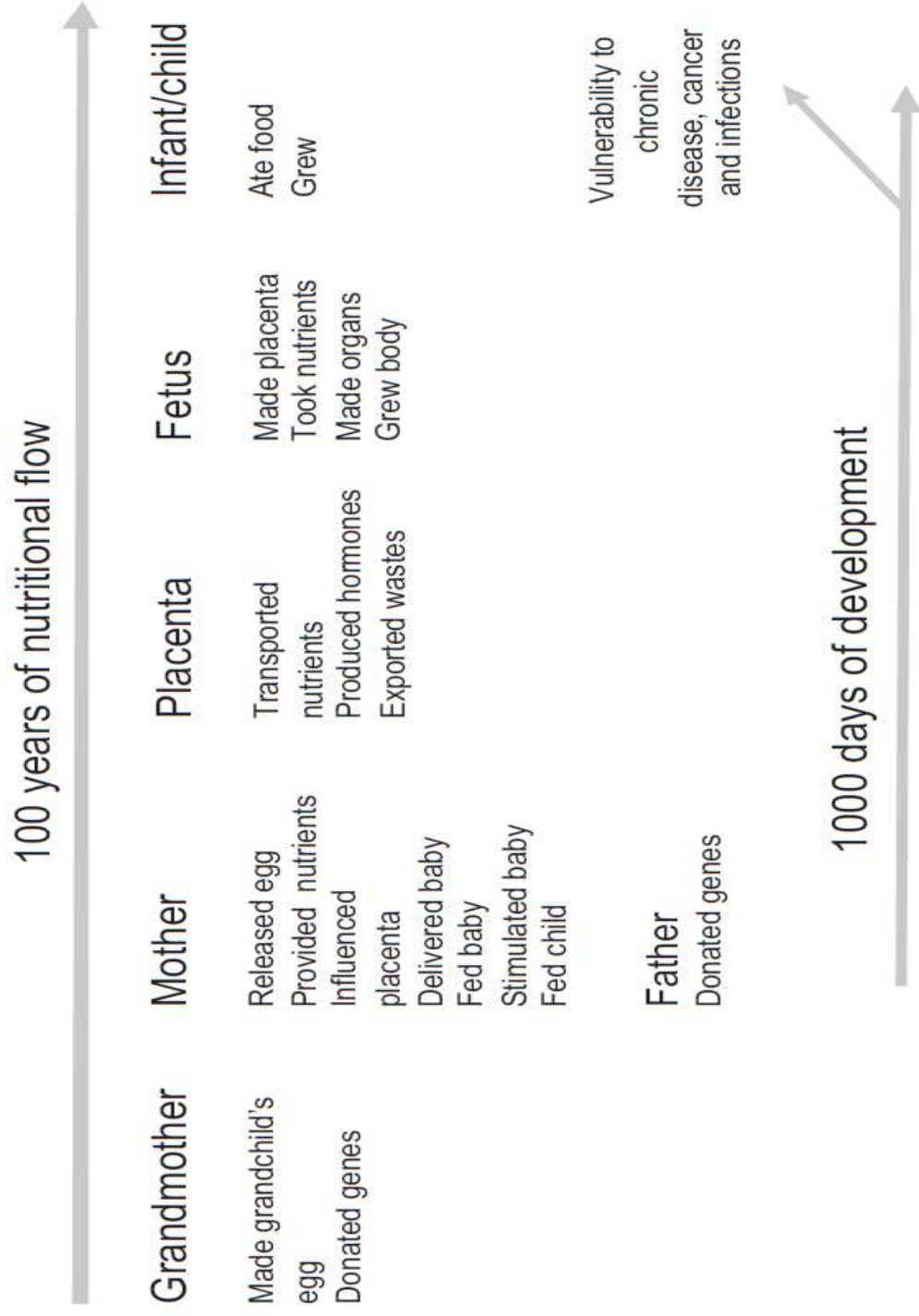


Fig. 2 – The transgenerational roots of chronic disease.

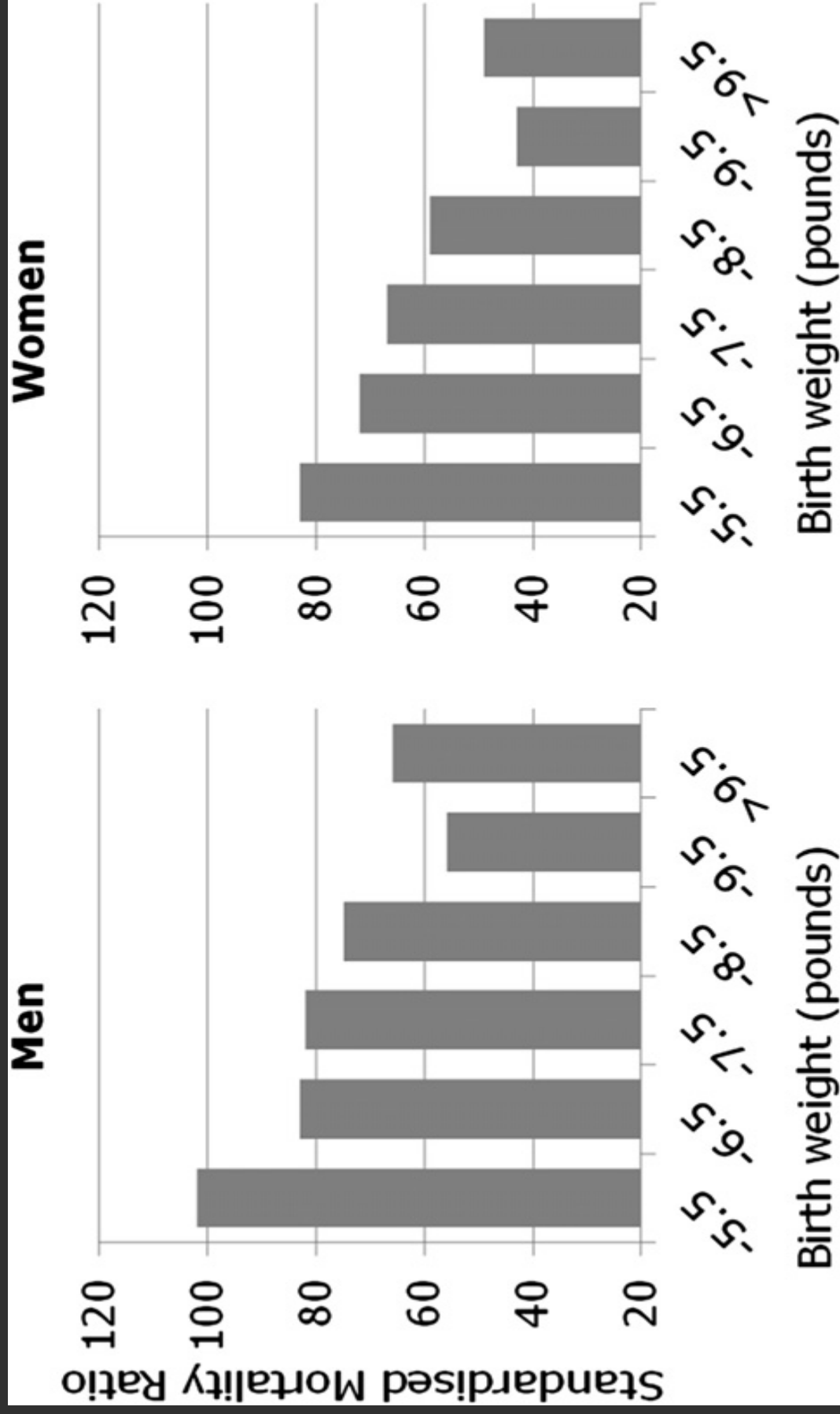
Life Course Models: CRITICAL PERIOD

- Critical Period Models emphasize timing of exposure
- Exposure at a specific period in life course can have lasting effects on the structure or function of organs, tissues and body systems
 - Also called ‘Biological Programming’ or ‘Latency Model’
 - Basis of “Developmental Origins of Adult Disease” hypothesis
- **EXAMPLES:**
 - Limb development in relation to maternal thalidomide use
 - Fracture across the epiphysis (growth plate) when bone is growing during childhood and adolescence

Life Course Models: CRITICAL PERIOD

- Term ‘Critical Period’ usually reserved for exposures occurring during known periods of unalterable biological development.
- Insults can affect structure or function or both
- Compensatory functional effects may hide structural limitations
- Effects of insults during critical period may only become ‘critical’ for those who experience some other exposure(s)

Mortality from Coronary Heart Disease in 15,726 Men and Women in Hertfordshire.

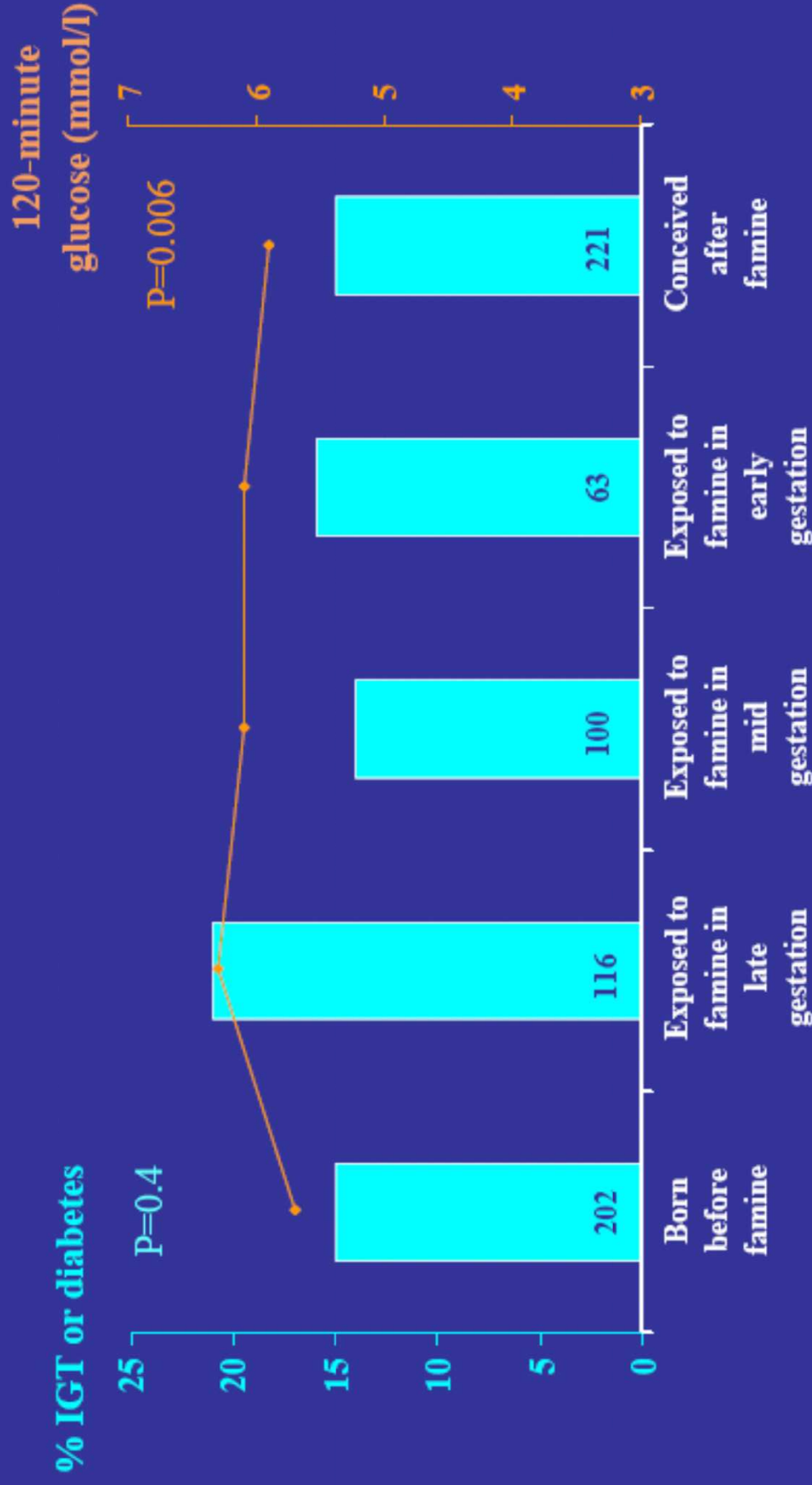


Life Course Models: CRITICAL PERIOD

- SENSITIVE Period Models - Period of time when an exposure(s) has a stronger effect (positive or negative) on disease risk or development than at other times
- Outside of this developmental period, the effect of the particular exposure will be weaker
- Influence of these exposures may be modified by later-life exposures
- **EXAMPLES:**
 - Poverty during periods of important childhood social transitions such as school entry
 - Energy imbalance and overweight just prior to puberty

Dutch Hunger Winter

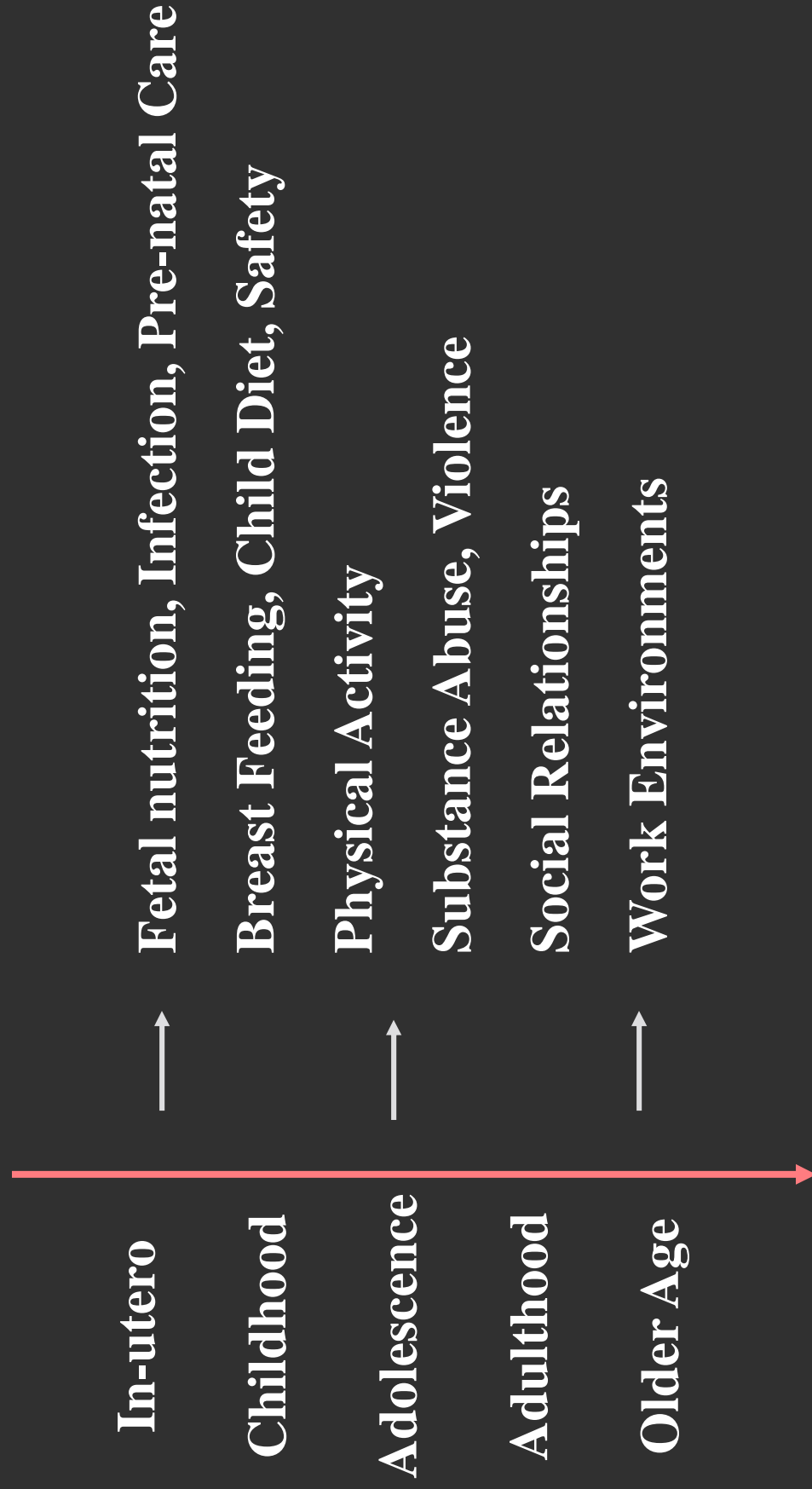
702 men and women aged 50 years



Ravelli ACJ et al Lancet 1998;351:173-7

Accumulation of Risk

Health-Related Exposures Over the Lifecourse



Life Course Models: ACCUMULATION of RISK

- Accumulation of Risk Models focus on the total amount and/or sequence of exposure
 - Exposures or insults gradually accumulate through episodes of illness and injury, adverse environmental conditions, and health damaging behaviors
 - Accumulation of different types of negative exposures (e.g., environmental, socioeconomic, and behavioral) may cause long term damage

Life Course Models: ACCUMULATION of RISK

- **Dose-Response**
 - Health damage increases with duration and/or number of detrimental exposures
 - Example: Additive effects of experiencing low socioeconomic position across different life stages influence risk of adult health outcomes
- **Clustering of Exposures**
 - Example: Children from poorer socioeconomic backgrounds are more likely to be of low birth weight, have poorer diets, more exposed to passive smoking and have fewer opportunities for physical activity
- **Chains of Risk**
 - One negative exposure increases the subsequent risk of another ...
 - Example: Becoming overweight in childhood may cause reduced physical activity in adolescence

Chains of Risk

- “Pathways model”
- Social, biological, and psychological chains of risk are possible and involve “mediating” factors and often “modifying” factors
- Sequence of linked exposures - one bad experience or exposure leads to another and then another – that raise disease risk

Life Course Models: ACCUMULATION of RISK

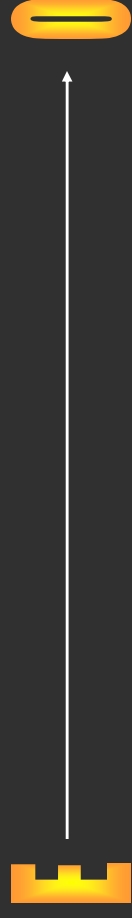
- Life course epidemiology tests the extent and effect of cumulative damage to biological systems as the number, duration or severity of exposures increase, and as body systems age and become less able to repair damage

In epidemiology, life course models posit different types of risk factor associations over time, which presumably suggest different causal paths to disease

Early-Life Exposures and Risk for Adult Outcomes



- Latency model



- Pathway models

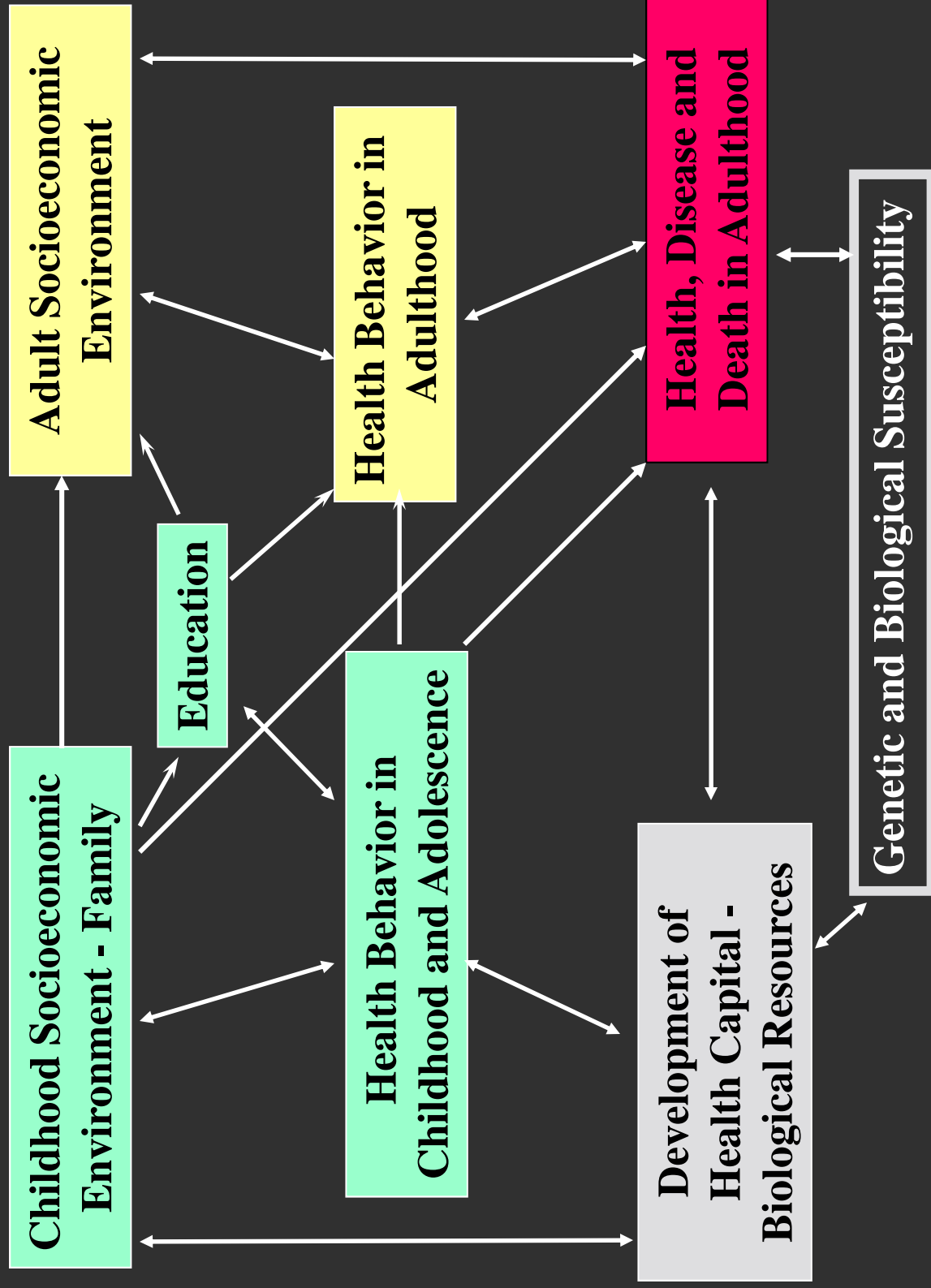


- Accumulation

- Mediation



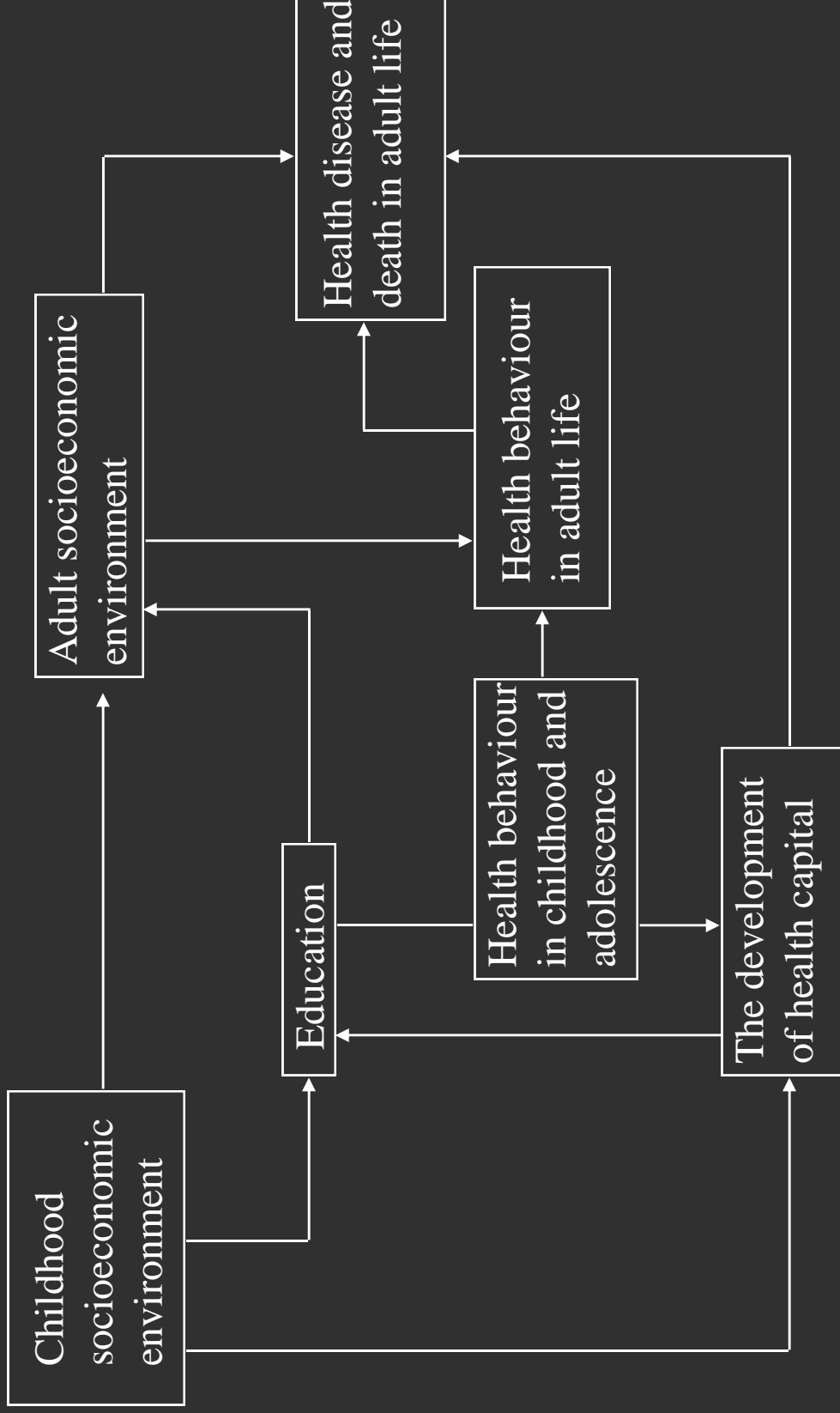
Social Pathways



Social Pathways

- “Because most factors associated with early child development are a function of socioeconomic status, differences in early child development form a socioeconomic gradient.”

Pathways between Childhood Socioeconomic Circumstances & Adult Health



Socioeconomic Life Course Models

- A. Accumulation model hypothesizes that early and later adverse socio-economic experiences have a cumulative, dose–response effect on later outcomes
- B. Latent model (or critical period) suggests that adverse socioeconomic circumstances during childhood have an independent, detrimental effect on health, over and above current circumstances
- C. Pathway models (chains of risk) emphasize the importance of trajectories across the life course and are proposed if the influence of childhood SEP is attenuated after taking into account later conditions

Parents Occupation and Education

+ Own Education

+ Occupation

+ Income

+ Wealth

Cumulative Socioeconomic Disadvantage

Socioeconomic Status over the Life Course and Allostatic Load in Northern Swedish Cohort, 1981-2008

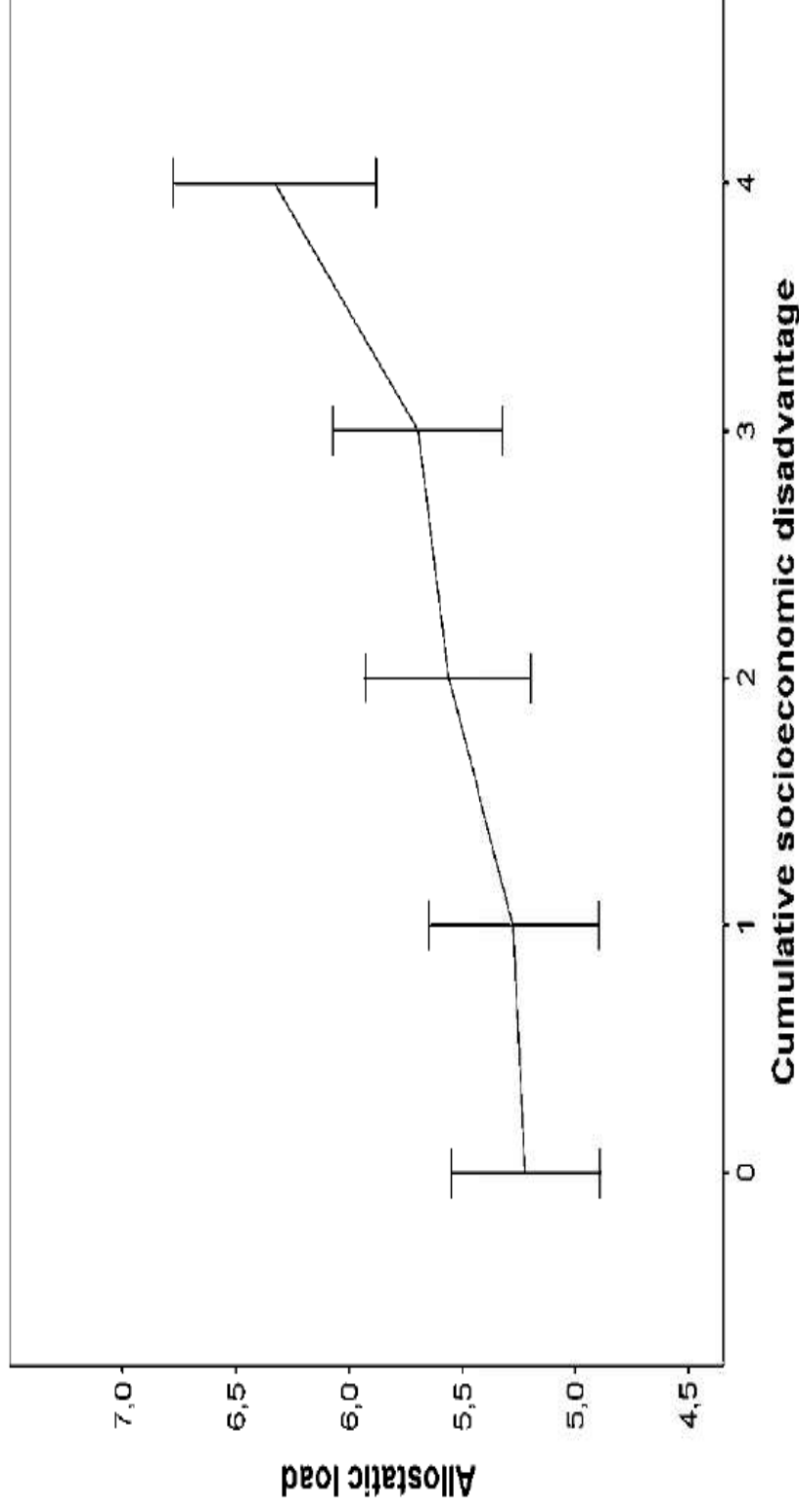


Figure 1 Allostatic load (mean, 95% CI) by cumulative socioeconomic disadvantage, ie, the cumulative number of times with low socioeconomic status at 16, 21, 30 and 43 years.

Table 4Odds ratio (95% confidence interval) of chronic kidney disease, cumulative social class and area socioeconomic status^a

| | | African-Americans | | | | |
|--|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|
| | | Whites | | | | |
| Adjusted for: | Age | Model 2: confounders | Model 3: Model 2 + DM, HTN | Age | Model 2: confounders | Model 3: Model 2 + DM, HTN |
| <i>Cumulative working class</i> | | | | | | |
| All periods | 1.4 (1.0, 2.1) | 1.4 (0.9, 2.0) | 1.3 (0.9, 1.9) | 2.1 (1.4, 3.1) | 1.9 (1.3, 2.9) | 1.8 (1.2, 2.7) |
| Some periods | 1.4 (1.0, 1.9) | 1.3 (1.0, 1.9) | 1.2 (0.9, 1.7) | 1.5 (1.0, 2.4) | 1.4 (0.9, 2.2) | 1.3 (0.8, 2.2) |
| No periods | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. |
| <i>p</i> for trend | 0.04 | 0.07 | 0.17 | <0.01 | <0.01 | <0.01 |
| <i>Cumulative low area SES tertile</i> | | | | | | |
| All periods | 1.4 (0.8, 2.4) | 1.2 (0.7, 2.2) | 1.1 (0.6, 2.0) | 1.5 (0.9, 2.4) | 1.3 (0.8, 2.0) | 1.1 (0.7, 1.9) |
| Some periods | 1.3 (0.9, 2.1) | 1.3 (0.8, 2.1) | 1.2 (0.8, 2.0) | 1.3 (0.8, 2.1) | 1.2 (0.7, 1.9) | 1.2 (0.8, 1.9) |
| No periods | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. | 1.0 Ref. |
| <i>p</i> for trend | 0.20 | 0.53 | 0.69 | 0.09 | 0.38 | 0.66 |

First column within each race stratum, marked "age-adjusted", is adjusted only for age.

Model 2: adjusted for age at visit 1, gender, cumulative exposure to working class and low area SES tertile, father farming, and center.

Model 3: Model 2 + diabetes mellitus (DM) and hypertension (HTN) at visit 1.

^a Chronic kidney disease (CKD) defined as GFR < 45 ml/min/1.73 m², or a hospital discharge diagnosis of CKD.

Socioeconomic Life Course Models

D. Social mobility models divided into intra- and inter-generational

- Inter-generational mobility refers to a change in social class between generations, often measured by comparing parental social class to own social class in adulthood
- Intra-generational mobility is the movement between different social classes in adulthood, such as the first and last occupation
- No consensus regarding the health consequences of social mobility
- Evidence shows mobile individuals eventually experience levels of health between those of their current social position and position of origin (closer to the current social position)

Health Trajectories

Generally had the best risk factor and health profiles

Advantaged Childhood

Advantaged Adulthood

Some evidence for enduring childhood effects on risk factors and some outcomes

Disadvantaged Childhood

Disadvantaged Adulthood

Generally had the worst risk factor and health profiles

Employment Trajectory and Health Risk Factors, HeSSup Study, Finland, 1998-2003

Table 3 Changes over 5 years in smoking intensity, alcohol consumption, physical activity, body weight and sleep duration by employment trajectory and sex (estimated marginal means and standard errors, adjusted for age and, when significant, for the interaction between trajectory and age in case)

| Sex | Employment Trajectory | Smoking intensity (cigarettes/day) | Alcohol intake (g/week) | Body weight (kg) | Physical activity (MET h/week) | Sleep duration (h/day) |
|--------------|-------------------------|------------------------------------|-------------------------|------------------|--------------------------------|------------------------|
| Men | | | | | | |
| | Stable | -1.73 (0.29) | 4.7 (2.0) | 2.77 (0.12) | -4.62 (0.68) | -0.050 (0.013) |
| | Upward | -1.30 (0.91) | -23.1 (8.1) | 1.87 (0.39) | -5.95 (2.39) | 0.189 (0.045) |
| | Unstable | -3.28 (1.77) | 3.5 (13.8) | 1.48 (0.68) | -5.63 (4.18) | 0.032 (0.077) |
| | Downward | -0.48 (0.80) | 13.7 (6.3) | 3.39 (0.35) | -7.98 (2.15) | -0.140 (0.039) |
| | Chronic unemployment | -1.19 (1.15) | 29.3 (12.1) | 2.28 (0.63) | -11.4 (3.89) | -0.078 (0.072) |
| | <i>P</i> for difference | 0.510 | 0.001* | 0.015 | 0.279 | <0.001 |
| Women | | | | | | |
| | Stable | -1.43 (0.21) | -1.5 (1.1) | 2.48 (0.11) | -2.74 (0.52) | -0.005 (0.012) |
| | Upward | -1.64 (0.65) | -3.1 (4.1) | 2.72 (0.38) | -5.42 (1.93) | 0.174 (0.045) |
| | Unstable | -0.34 (0.86) | 7.6 (5.5) | 2.40 (0.51) | -4.87 (2.59) | -0.118 (0.061) |
| | Downward | -0.78 (0.51) | -4.2 (2.9) | 2.74 (0.38) | -8.48 (1.37) | -0.267 (0.033) |
| | Chronic unemployment | 1.85 (1.24) | 4.8 (8.5) | 2.42 (0.84) | -3.23 (4.02) | -0.242 (0.093) |
| | <i>P</i> for difference | 0.054 | 0.373* | 0.906 | 0.002* | <0.001* |

*adjusted for age

Operationalization of Life Course Epidemiology

Disease Causation in a Life Course Perspective

- Disease and disability likely result from the complex interplay of critical and sensitive period, and trajectory and accumulation processes
- These general life course conceptual models are simplistic representations of complex life course processes – however, even simple models can be difficult to distinguish empirically

Ideal Life Course Study

- Longitudinal study
- Follows a birth cohort into adulthood and, ideally, across generations
- Investigators collect extensive information on the physical and social environments and on psychosocial or behavioral and biological measures
- Researchers repeat these measures for the same individuals at short intervals over time

Reality for Life Course Epidemiology

- Most life-course literature comes from Europe, where investigators have had access to high-quality longitudinal databases rich in contextual information
- In the United States, many life-course studies rely on retrospective approaches, including case-control and retrospective cohort studies with long recall period, and associated biases, for early exposures
- Life-course research, regardless of location, often depends on record linkage, natural experiments, or historical cohorts with limited follow-up across life stages

TABLE 3 Examples of Major Health-Focused Longitudinal Databases: United States

| Name of Study, Lead Agency | Initial Sample | Follow-up |
|---|---|--|
| Alameda County Study, ⁹⁹ NIA | 6928 noninstitutionalized Alameda County residents, aged ≥ 21 y at entry in 1965 (≥ 16 y if married) | 1965, 1974, 1994, and 1995 |
| Coronary Artery Risk Development in Young Adults (CARDIA), ¹⁰⁰ NHLBI | 5115 black and white men and women aged 18–30 y at entry in 1986, in 4 major US cities | 7 waves over 20 y |
| Framingham Heart Study, ¹⁰¹ NHLBI | Original cohort: 5209 men and women aged 30–62 y in 1948 in Framingham, MA; offspring (1971): 5124 adult children and spouses in 1971; third generation (2005): 4095 adult grandchildren of original participants | Every 2 y until present |
| Health and Retirement Study (HRS), ¹⁰² NIA | >22 000 men and women aged ≥ 50 y in 1988 | Biennially to present |
| Midlife Development in the United States (MIDUS), ¹⁰⁵ NIA | 7000 men and women aged 25–74 y in 1995 (MIDUS I) | Second wave ~ 10 y later (MIDUS II) |
| National Longitudinal Study of Adolescent Health (ADD Health), ¹⁰⁴ NICHD | ~ 90 000 students in grades 7–12 in 1994 at 145 schools; more than ~ 20 000 students and their parents interviewed at home | Reinterviewed at ages 18–26 and 24–32 y |
| Nurses' Health Study (NHS), ¹⁰⁵ NIH | Original cohort: ~ 122 000 married registered nurses, aged 30–55 y in 1976; NHS II: 116 686 women aged 25–42 y in 1989 | Biennially to present |

NIA indicates National Institute on Aging; NHLBI, National Heart, Lung and Blood Institute; NICHD, Eunice Kennedy Shriver National Institute of Child Health and Human Development; NIH, National Institutes of Health.

TABLE 4 Examples of Other Longitudinal Databases: United States

| Name of Study, Lead Agency | Initial Sample | Follow-up |
|---|---|---|
| Early Childhood Longitudinal Study Birth Cohort (ECLS-B), ¹⁰⁶ Department of Education | 14 000 children born in 2001 | Data collection at birth, 9 mo, 2 y, preschool age, and entry to kindergarten |
| Early Childhood Longitudinal Study Kindergarten Cohort (ECLS-K), ¹⁰⁶ Department of Education | Nearly 4 million kindergartners enrolled in 1998–1999 | Additional data collection in 1st, 3rd, 5th, and 8th grades |
| National Longitudinal Survey of Youth (NLSY79), ¹⁰⁷ Bureau of Labor Statistics | 12 686 men and women aged 14–22 y in 1979 | Interviewed annually through 1994, and biennially to present |
| NLSY79 Children and Young Adults, ¹⁰⁷ Bureau of Labor Statistics | Ongoing enrollment of NLSY79 women's offspring, beginning in 1986 | Biennially to present |
| NLS Original Cohorts, ¹⁰⁷ Bureau of Labor Statistics | 5159 women aged 14–24 y in 1968; 5063 women aged 20–44 y in 1967; 5225 men aged 14–24 y and 5020 men aged 45–59 y in 1966 | Women: biennially to present; men: interviews ceased in 1981 |
| Panel Study of Income Dynamics (PSID), ¹⁰⁸ National Science Foundation | 4800 families in 1968 core sample; ~7400 families by 2005 | Annually 1968–1996, biennially to present |

TABLE 5 Examples of Major Longitudinal Health-Focused Databases: Europe

| Name of Study | Initial Sample | Follow-up |
|---|---|---------------------------------------|
| Avon Longitudinal Study of Parents and Children (ALSPAC) ¹⁰⁹ | >14 000 mothers enrolled during pregnancy in Bristol, United Kingdom, during 1991 and 1992 | Ongoing |
| 1970 British Birth Cohort Study ¹¹⁰ | ~17 200 infants born in England, Wales, Scotland, and North Ireland in a week in April 1970 | 6 follow-ups, 1975–2004 |
| Millennium Cohort Study (MCS) ¹¹¹ | 18 818 infants born in the United Kingdom over a 12-mo period in 2000–2001 and living in selected UK wards at 9 mo of age | 4 waves between June 2001 and present |
| National Child Development Study (NCDS) ¹¹² | 17 500 infants born in England, Scotland, and Wales in a week in March 1958 | 7 waves to the present |
| Newcastle Thousand Families Study ¹¹³ | All 1142 infants born to mothers in Newcastle Upon Tyne, United Kingdom, May–June 1947 | At ages 15, 22, 32, 50, and 54 y |
| Population, Cancer, Cause of Death, and Hospital Discharge Registries | Population-wide registries in the Scandinavian countries, linkable through the personal identification code | NA |
| Understanding Society Study ¹¹⁴ | Household members aged ≥ 10 y in 40 000 households across the United Kingdom | Annually from 2009 |

NA indicates not applicable.

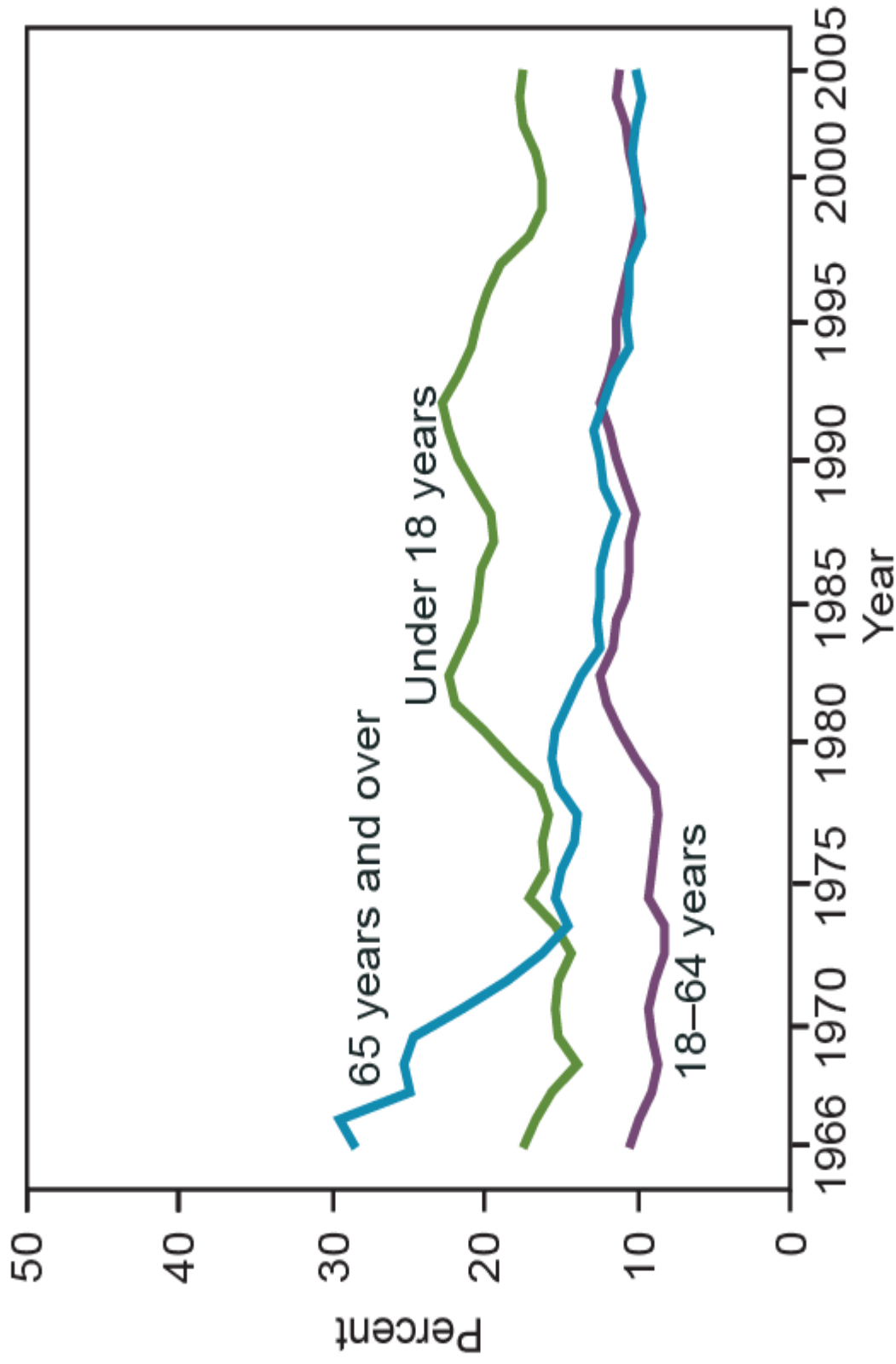
What Now?

“Living conditions cannot simply be left to fluctuate as people pass through childhood and their reproductive and working years and into old age, because health and quality of life at any one stage is affected by prior circumstances and events. ...

“The life course may be regarded as combining biological and social elements which interact with each other. Individuals’ biological development takes place within a social context which structures their life chances, so that advantages and disadvantages tend to cluster cross-sectionally and accumulate longitudinally.”

Bartley M, et al, 1997

Poverty rates

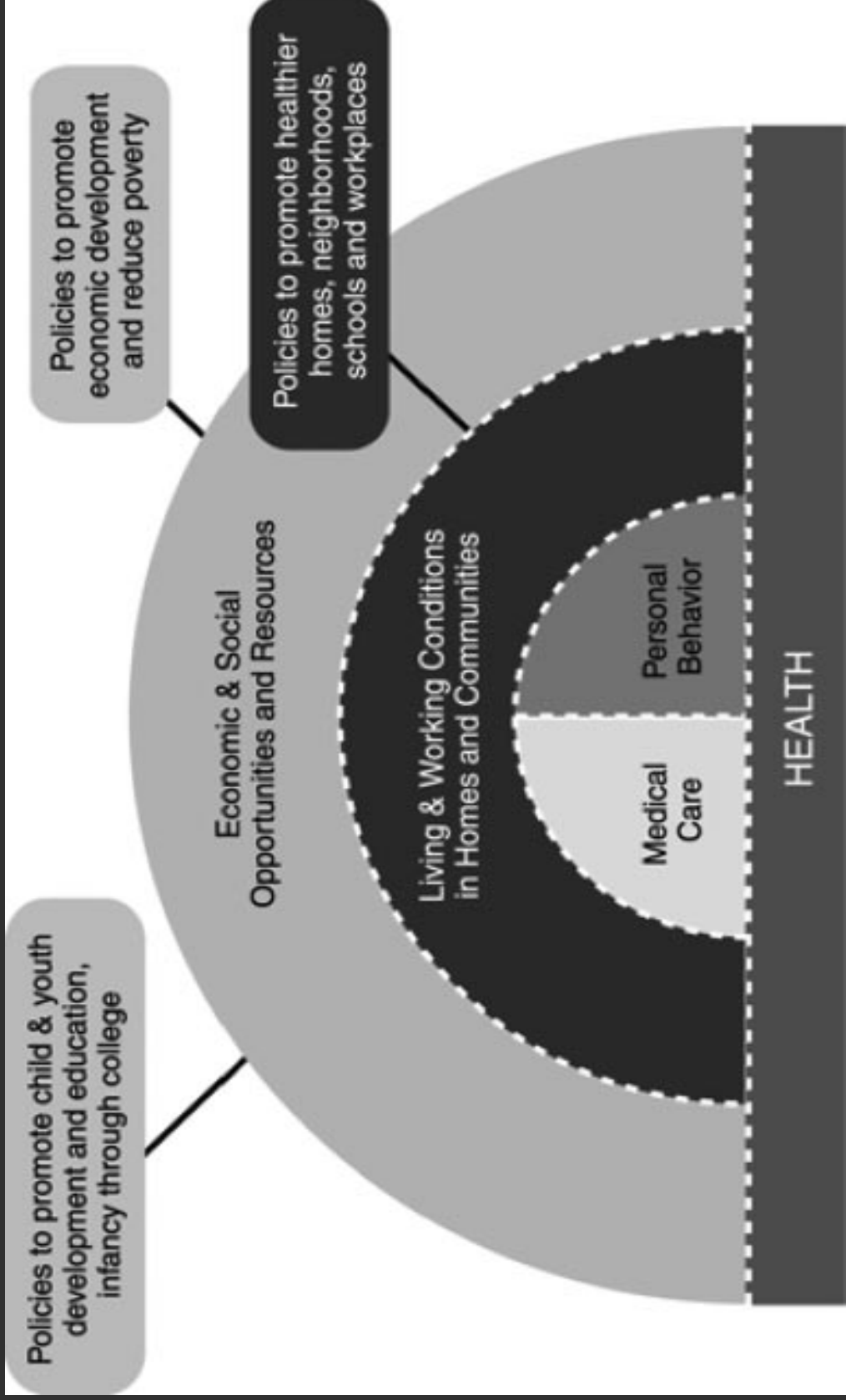


SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2007*, Figure 4. Data from the U.S. Census Bureau.

Policy Implications

- Intervening early in life
 - Prevent, reduce exposures with latent effects
 - Avoid negative chains of events
- Interrupting pathways
 - Prevent (reduce the likelihood of) specific negative health outcomes
 - Is it possible to entirely overcome the health consequences of social adversity early in life?
 - Multiple adverse health consequences in adulthood
 - Multiple pathways

Influences on Health: what shapes the conditions that shape health?



10 Tips for Better Health

Health Perspective

1. Don't smoke. If you can, stop. If you can't, cut down.
2. Follow a balanced diet with plenty of fruit and vegetables.
3. Keep physically active.
4. Manage stress by, for example, talking things through and taking time to relax
5. If you drink alcohol, do so in moderation.
6. Cover up in the sun, and protect children from sunburn.
7. Practice safer sex.
8. Take advantage of disease screening opportunities.
9. Drive safely
10. Learn First Aid ABC : airways, breathing, circulation

Social Perspective

1. Don't be poor. If you can, stop. If you can't, try not to be poor for long.
2. Don't have poor parents.
3. Own a car.
4. Don't work in a stressful, low paid manual job.
5. Don't live in damp, low quality housing.
6. Be able to afford to go on a foreign holiday and sunbathe.
7. Practice not losing your job and don't become unemployed.
8. Take up all benefits you are entitled to, if you are unemployed, retired or sick or disabled.
9. Don't live next to a busy major road or near a polluting factory.
10. Learn how to fill in the complex housing benefit/asylum application forms before you become homeless and destitute.

Questions?