

DATA MANAGEMENT & ANALYSIS FOR BIOLOGISTS
APRIL 24TH, 2018

Asking the right questions

(and how conceptual models can help!)

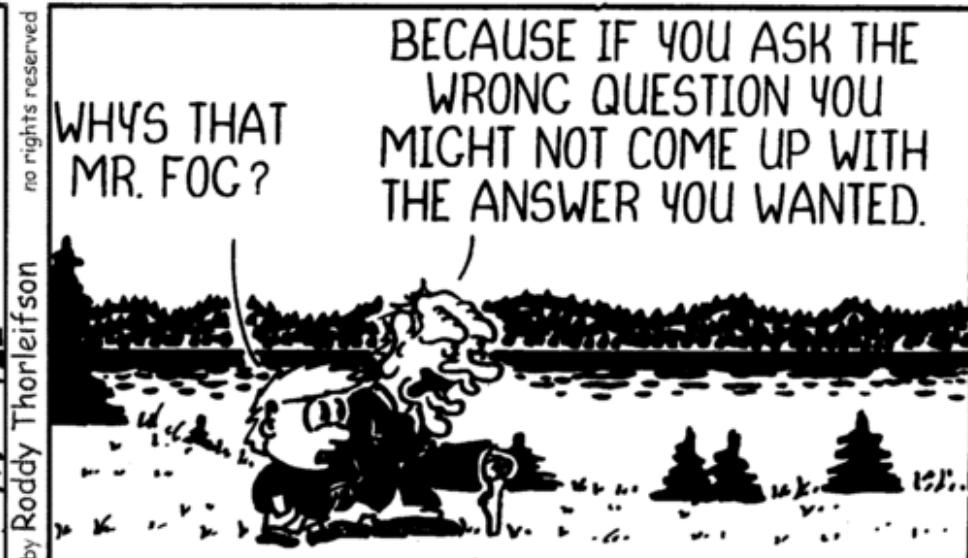
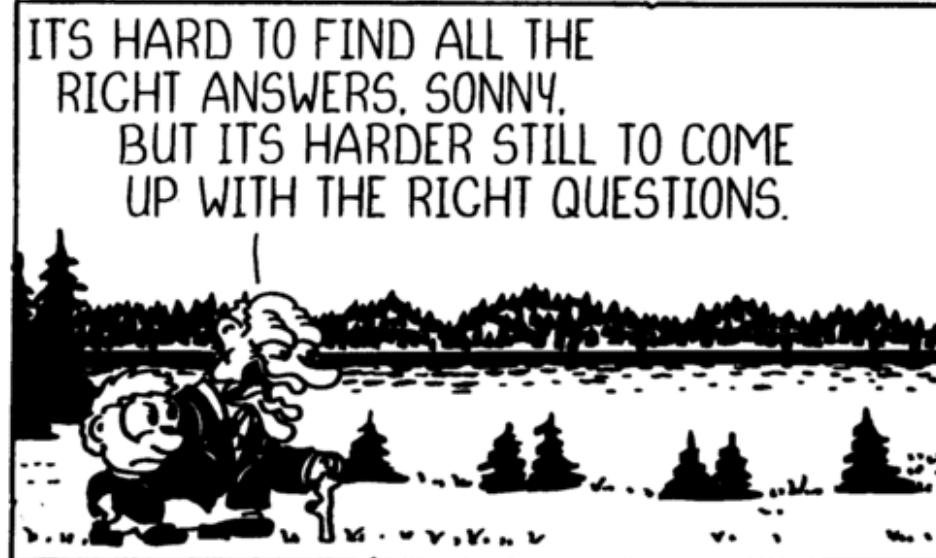
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Outline

- Asking the right questions
- Developmental origins of health and disease (DOHaD)
- DAGs and conceptual models
- An exercise

Asking the right questions



An example

A couple wanted to buy wallpaper for their kitchen but did not have time to measure the dimensions. Instead, they ask their neighbor who recently wall-papered his kitchen and has the same kitchen layout:

“How much wallpaper did you buy for your kitchen?”

The neighbor tells them:

“500 sqft.”

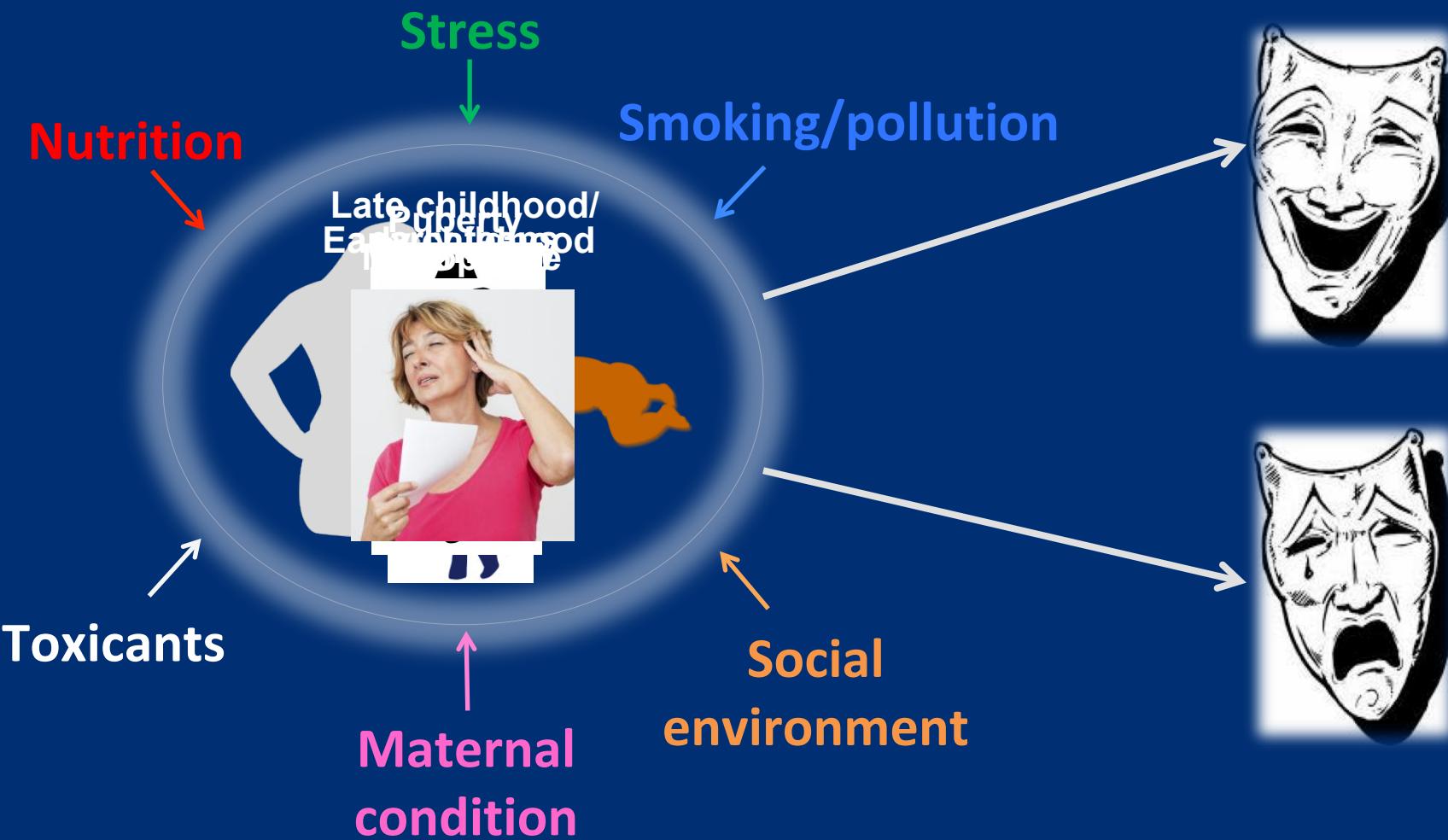
The couple bought 500 sqft of wall paper. After finishing the job, they had 200 sqft left over.

“We bought exactly 500 sqft of wallpaper and now we have extra material that we are not able to return,”
they said to him angrily.

To which the neighbor responded,

“If you had asked me how much wall paper I used to cover my kitchen, then I would have said 300 sqft.”

Developmental Origins of Health and Disease (DOHaD)



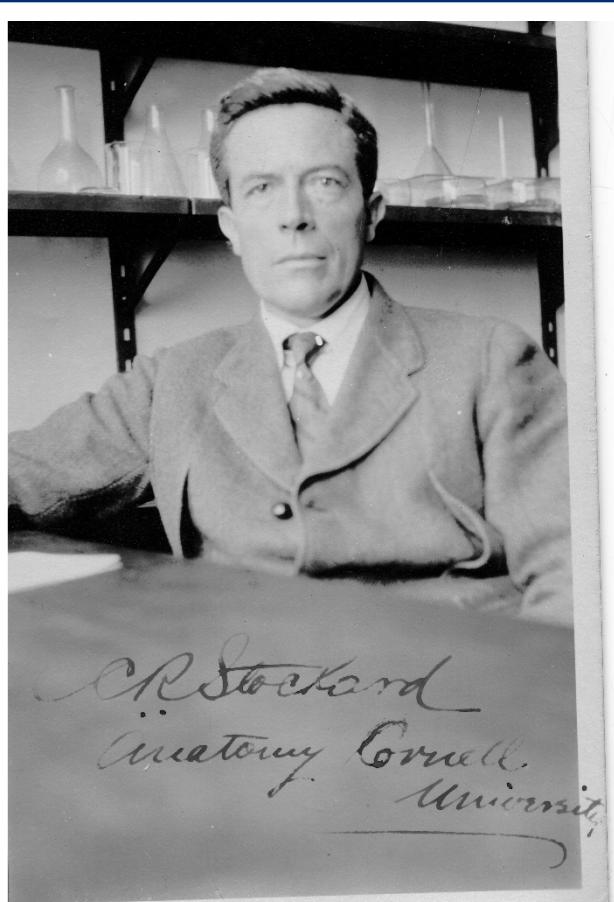
The origins of DOHaD

The Lancet · Saturday 9 : 1

WEIGHT IN INFANCY AND ISCHAEMIC HEART DISEASE

D. J. P. BAREHAM
C. OSMON

MRC Environmental Epidemiology Group,
Southampton, Southampton, South



Charles R. Stockard
Poor early life environment
1879-1933

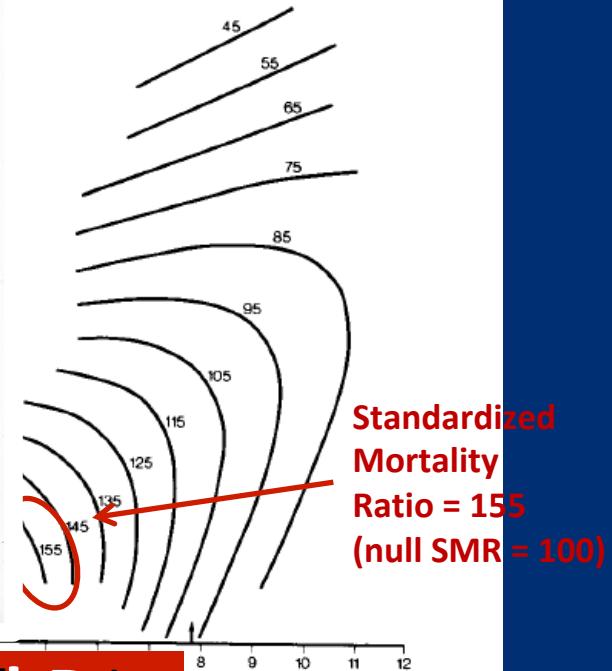
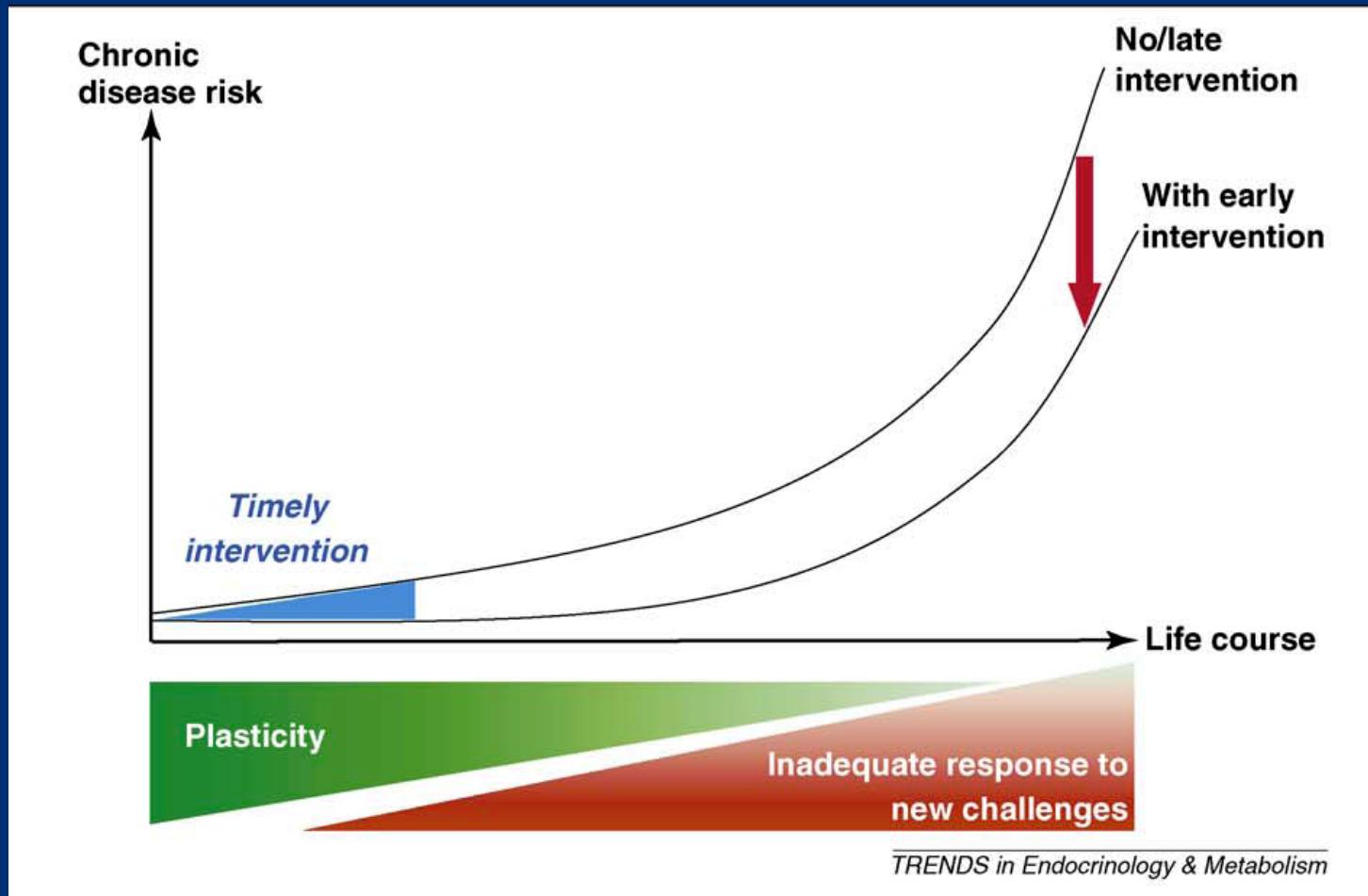


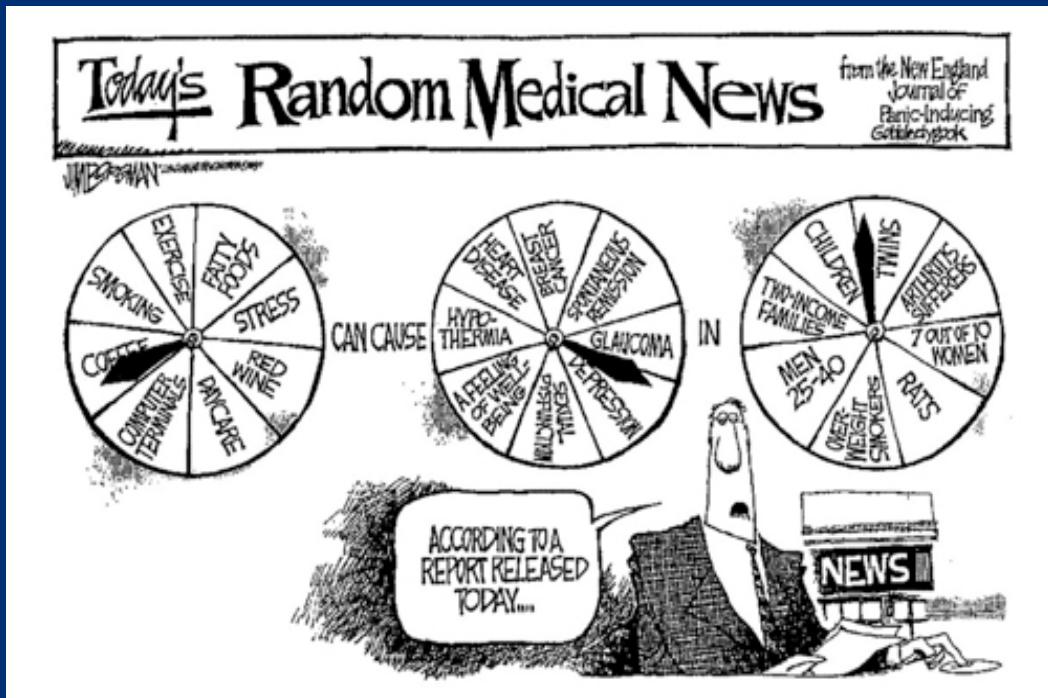
Fig 1—Relative risk of heart disease in men who were breast fed according to birthweight and weight at one year.
Lines join points with equal risk. Arrows = mean weights.

Potential impact of DOHaD



Godfrey et al., *Trends Endocrinol Metab* 2010 ; 21:199-205

Challenges



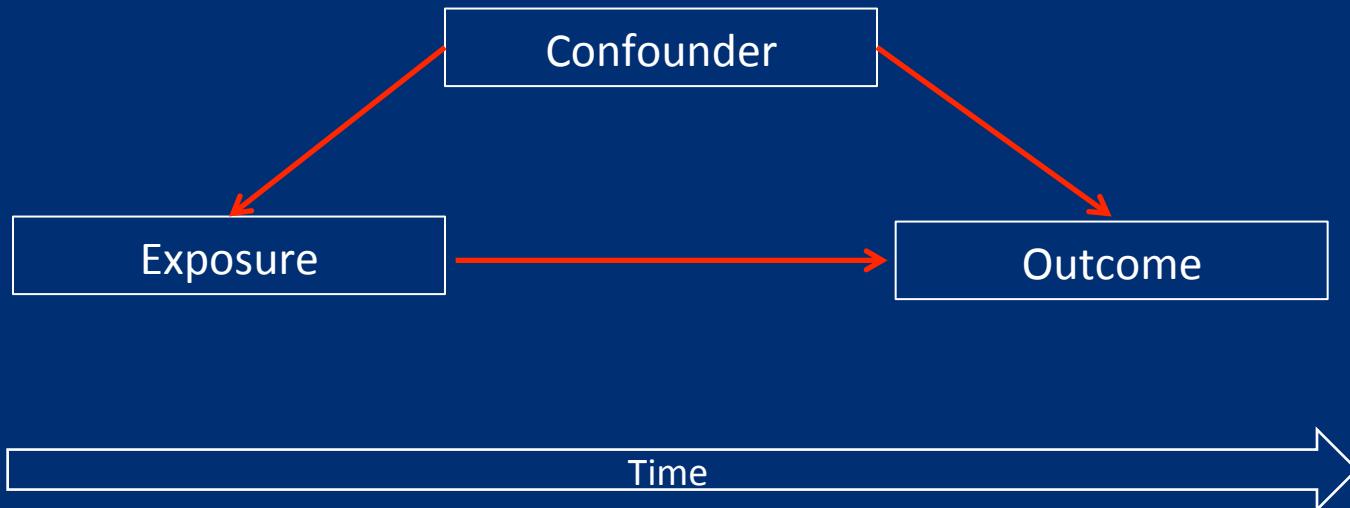
Directed acyclic graphs (DAGs)



DAGs

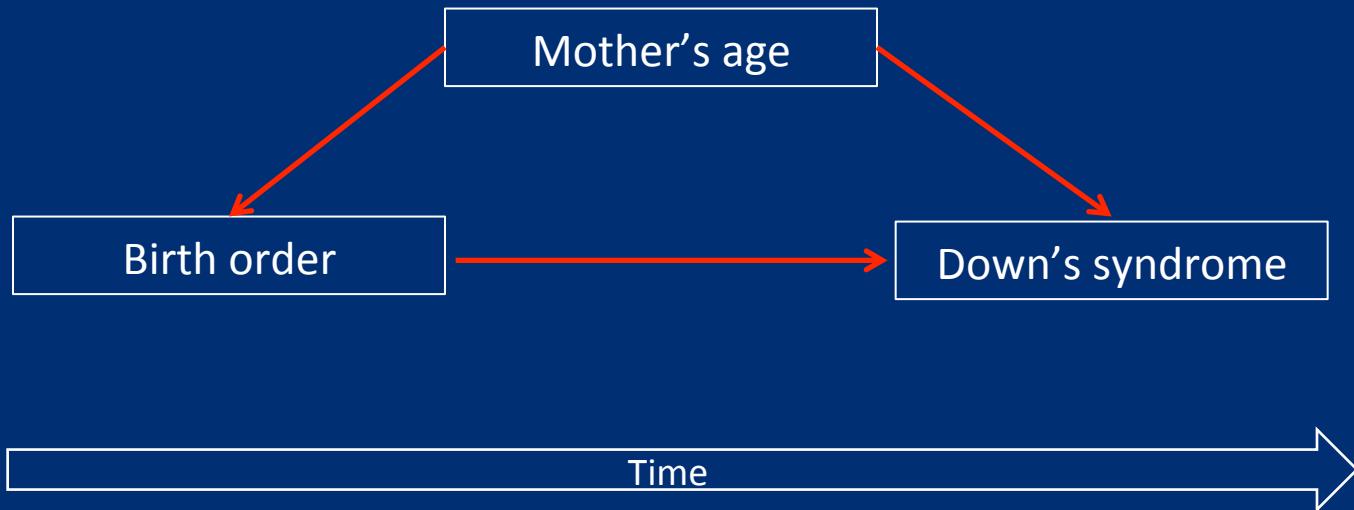
Confounder

A variable that is associated with the exposure and a predictor of the outcome



DAGs

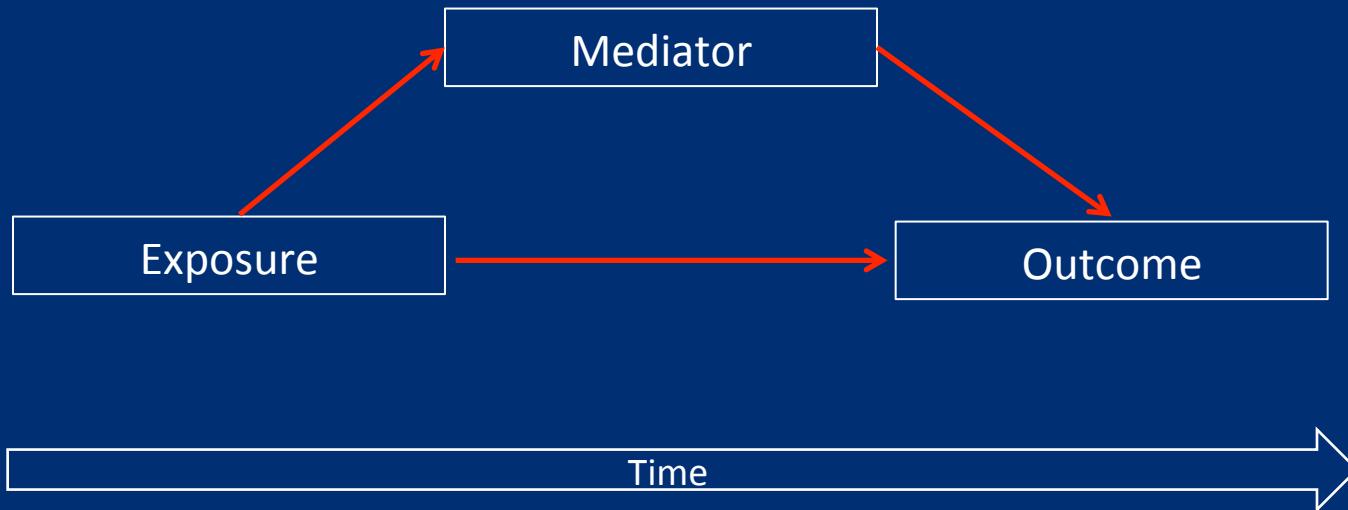
Confounder example



DAGs

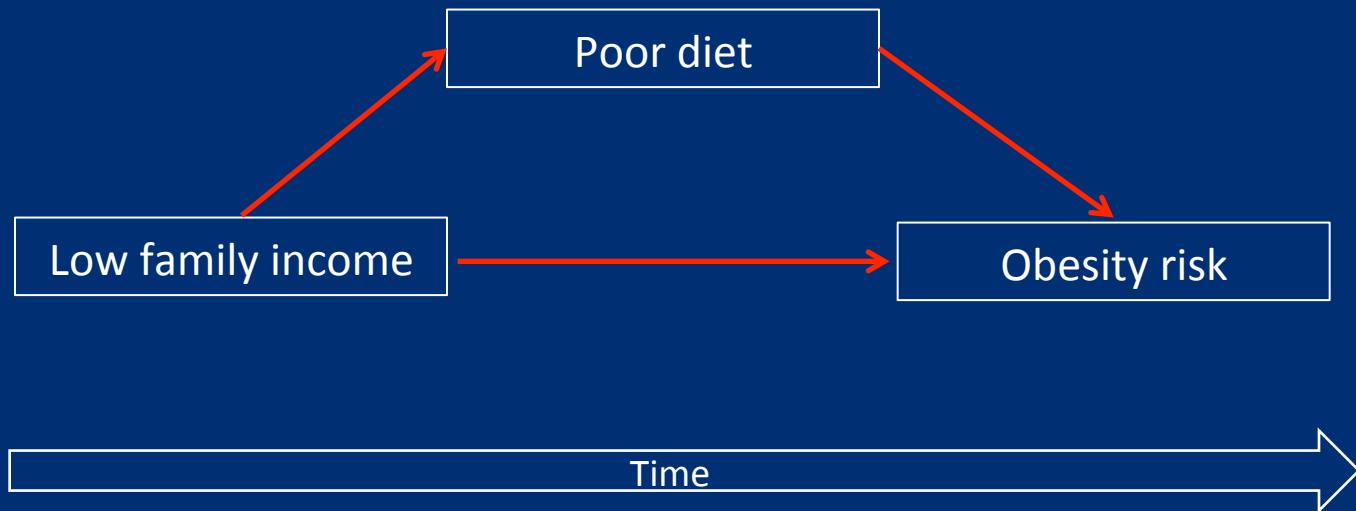
Mediator

A variable on the causal pathway between the exposure and outcome



DAGs

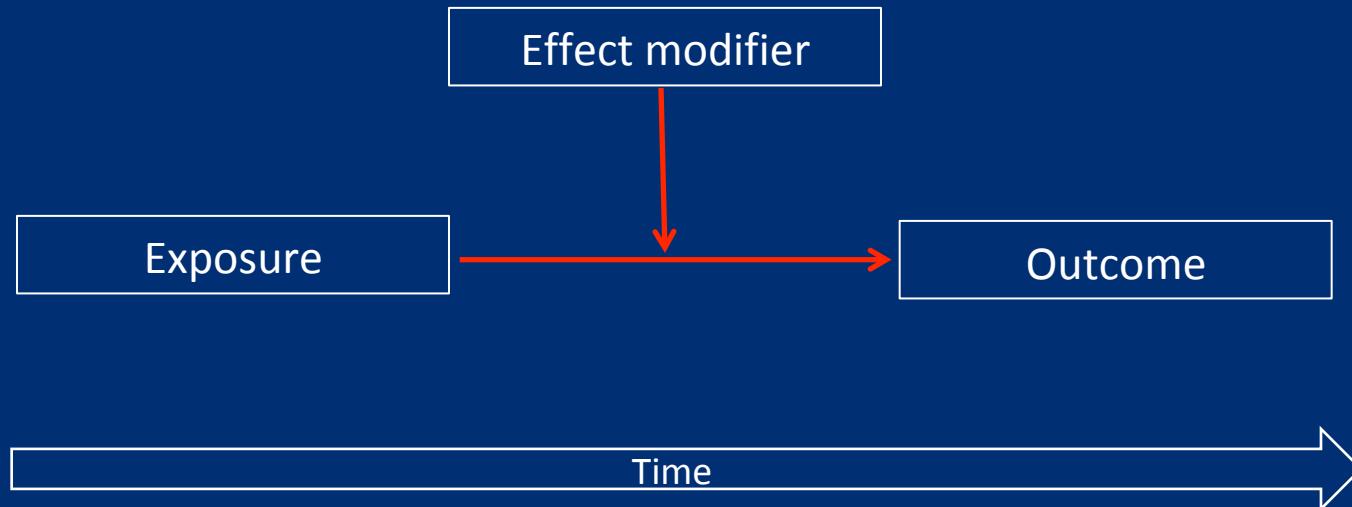
Mediator example



DAGs

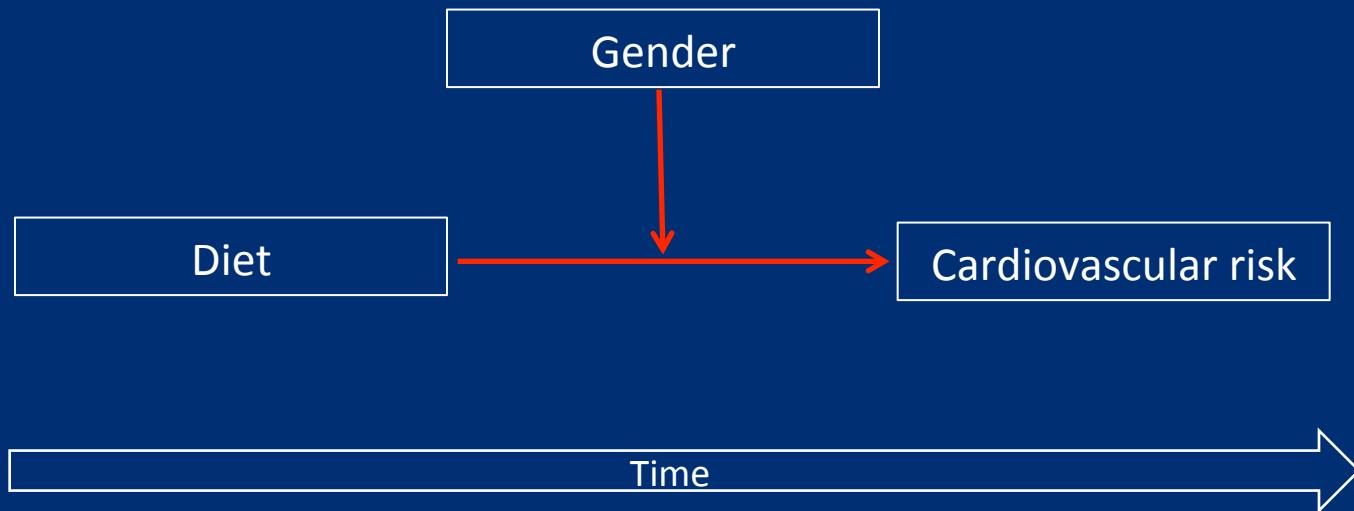
Effect modifier

A variable that changes the nature of the relationship between the exposure and outcome



DAGs

Effect modifier example



Life course epidemiology conceptual models

- “Critical period” models



- “Accumulation of risk” models

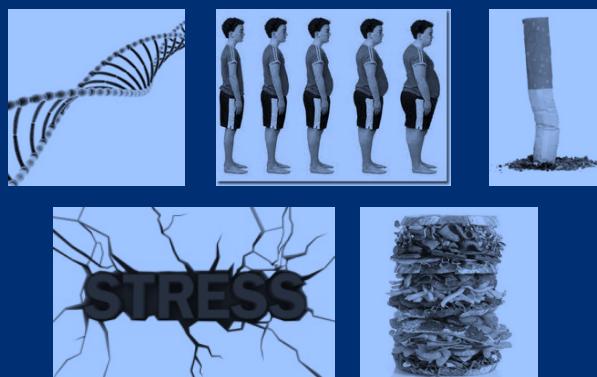


Life course epidemiology conceptual models

- “Critical period” models



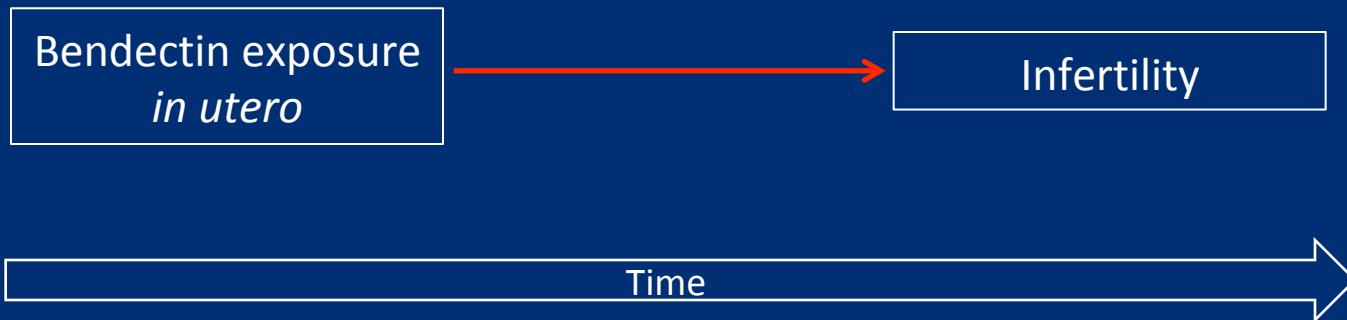
- “Accumulation of risk” models



Critical Period Models:

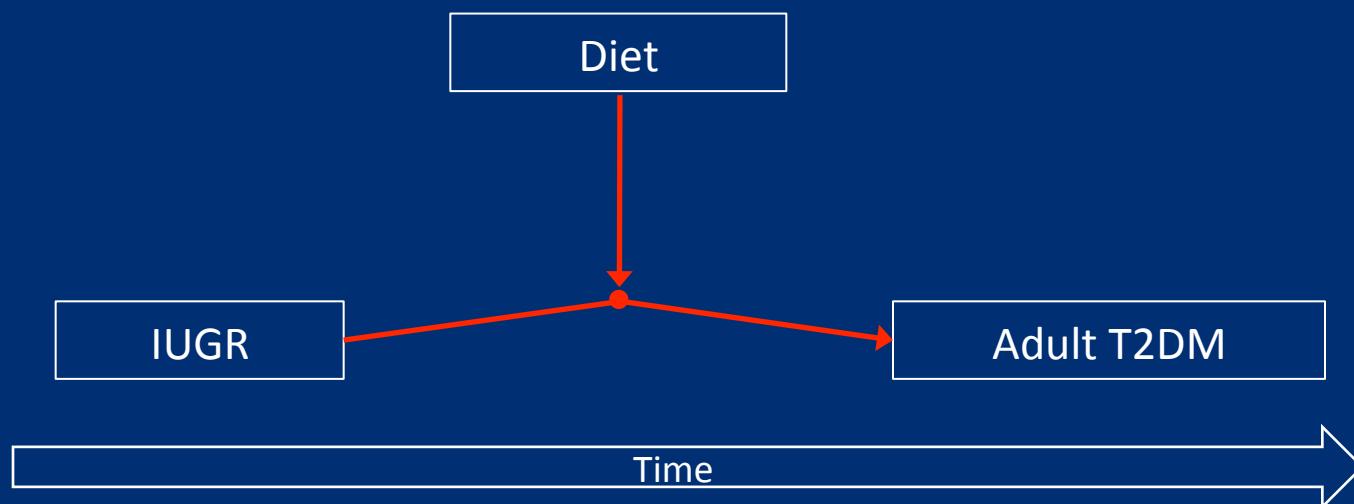
“Critical period with no later modifiers”

- An exposure acting during a specific timeframe has lifelong effects on physiology that are not altered by later experiences



Critical Period Models: “Critical period with modifiers”

- An exposure acting during a specific timeframe has lifelong effects on physiology that can be modified by later experiences

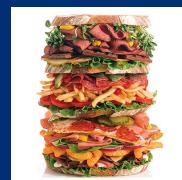


Life course epidemiology conceptual models

- “Critical period” models

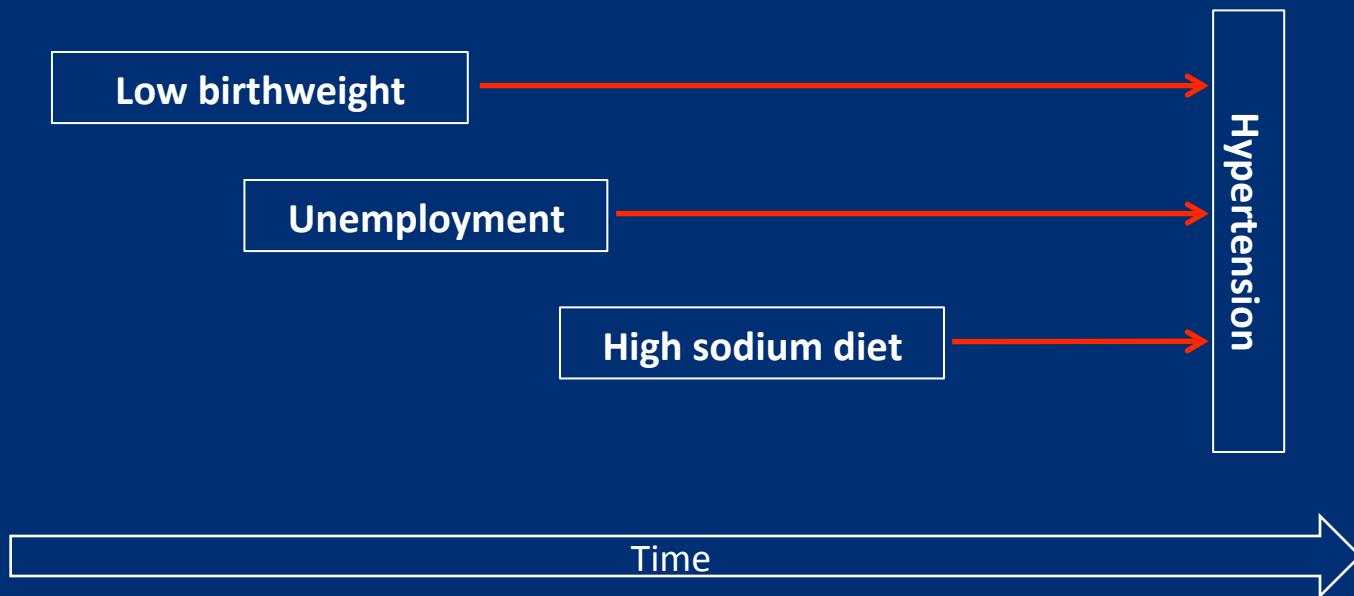


- “Accumulation of risk” models



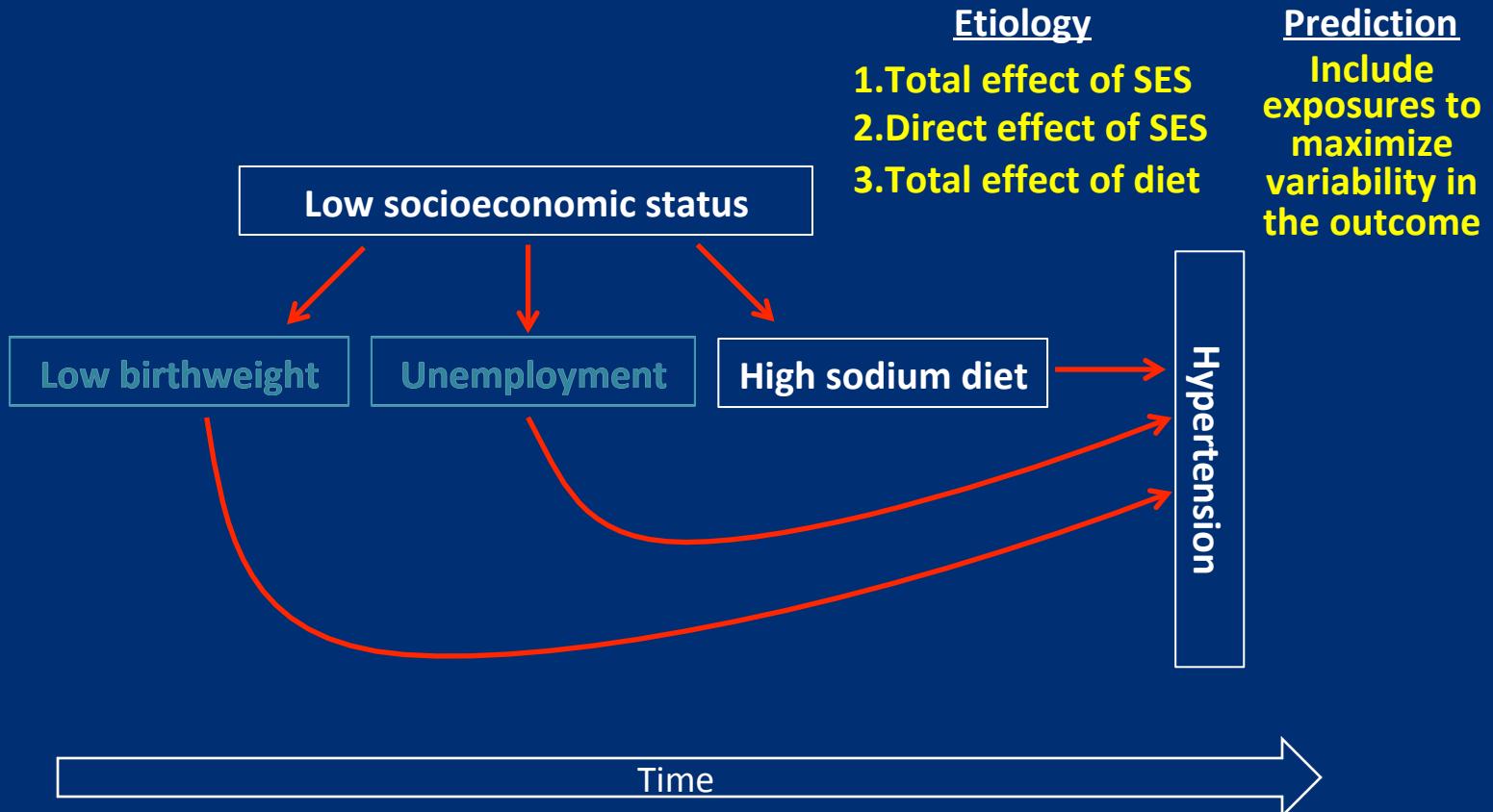
Accumulation of Risk Models: “Independent Risk Exposures”

- Risk factors for disease are independent and unrelated



Accumulation of Risk Models: “Risk Clustering”

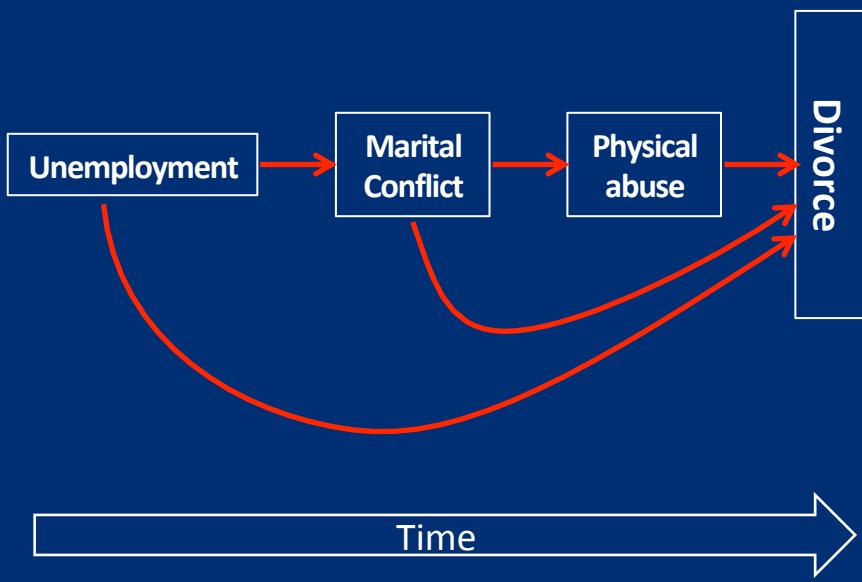
- Risk exposures that are related tend to occur in concert



Accumulation of Risk Models: “Chains of risk”

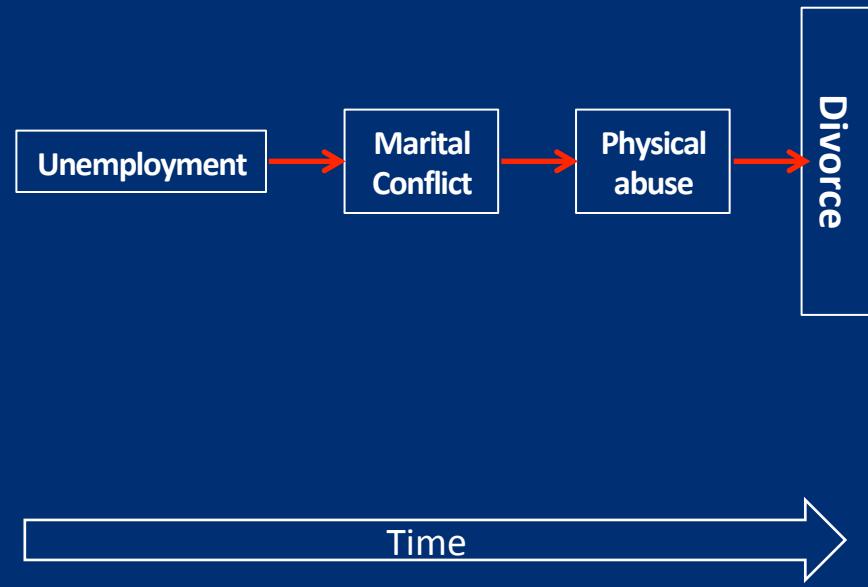
*Chains of risk with **additive effects***

- Each exposure in a chain of risk increases likelihood of subsequent exposures, and may also have an independent additive effect on later disease risk



*Chains of risk with **trigger effect***

- Only the final link has a marked effect



Summary of life course epidemiology conceptual models

Critical Period Models

- No later modifiers
- Later modifiers

Accumulation of Risk Models

- Uncorrelated risk exposures
- Risk clustering
- Chains of risk with additive effects
- Chains of risk with trigger effect



- Model selected for your study are based on *a priori* knowledge.
- Models inform data analysis and interpretation of results.
- Models are not mutually exclusive.

Exercise

In a population of hyenas, you are interested in the relationships of the following independent variables:

- human exposure
- gender
- body size
- social rank

with the outcome aggressive behavior in hyenas.

Some assumptions:

- Human exposure affects aggressive behavior of hyenas
- Gender is a determinant of a rank
- Rank is a determinant of aggression
- Rank is acquired at birth, but otherwise, it is not earned or influenced by body size or human exposure status

Exercise

Please draw conceptual models for the following scenarios:

- The relationship between human exposure and aggressive behavior, and potential effect modification by gender.
- The association of gender with aggressive behavior that does not operate through rank
- Interaction between sex and rank, in relation to aggressive behavior

Assumptions:

- Human exposure affects hyenas' aggression
- Gender is a determinant of a rank
- Rank is a determinant of aggression
- Rank is acquired at birth, but otherwise, it is not earned or influenced by body size or human exposure status