



Luxembourg, September, 2009

Life-course perspectives across cohorts: research opportunities and challenges

Chris Power

..... reviews the epidemiological, **social** and **biological** evidence to see which experiences at different stages of the life course may contribute to the development of chronic disease and other aspects of adult health. ...

- Latency: (programming, lag, sleeper) strong effects of discrete events usually in early life.
- Pathway: early environment → life trajectories → adult socio-economic position.
- Cumulative: duration of exposure, accumulation & interaction of risks (vulnerability, susceptibility)

adaptive developmental plasticity and human disease.

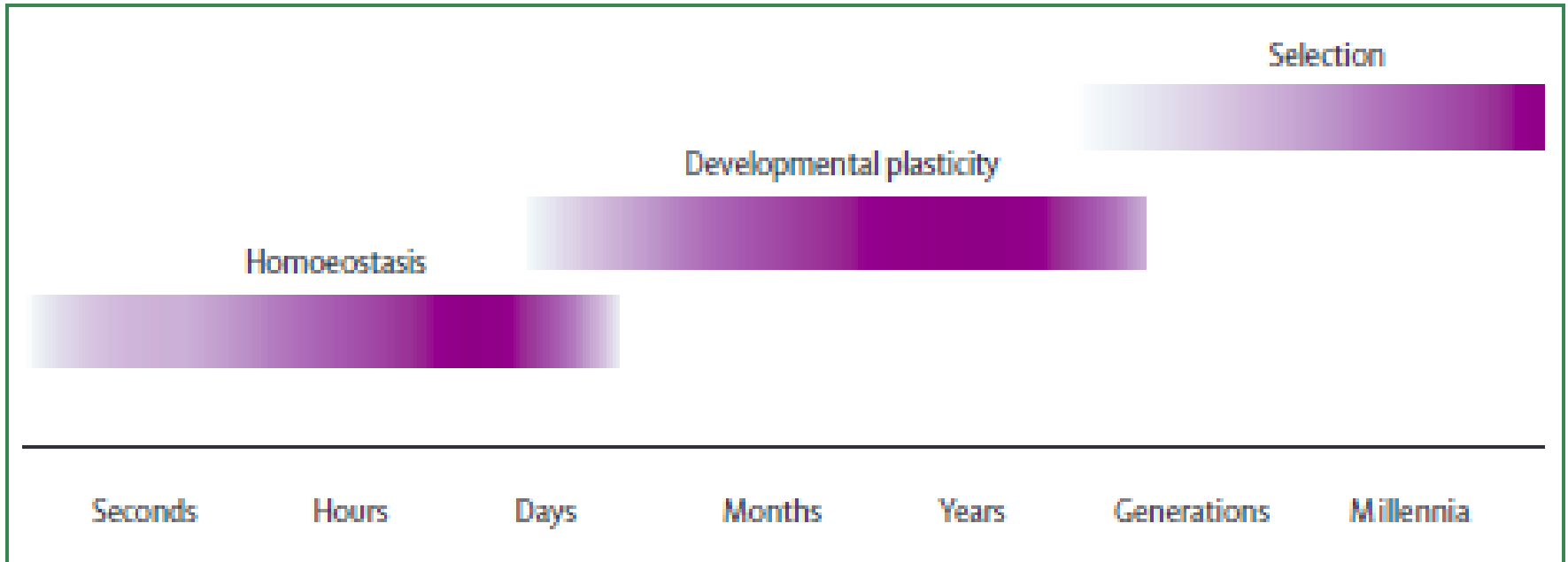
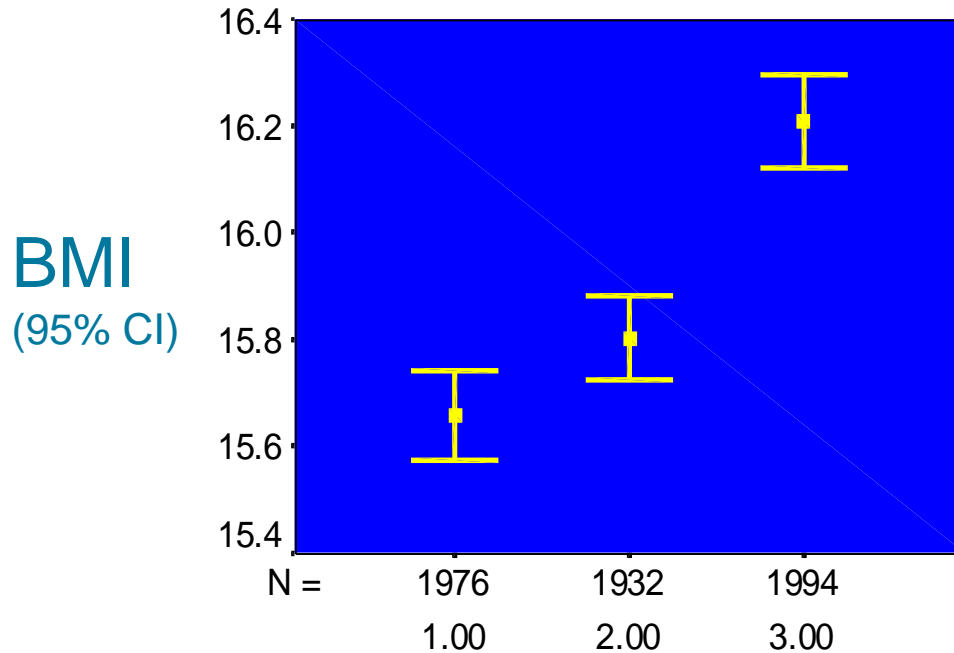


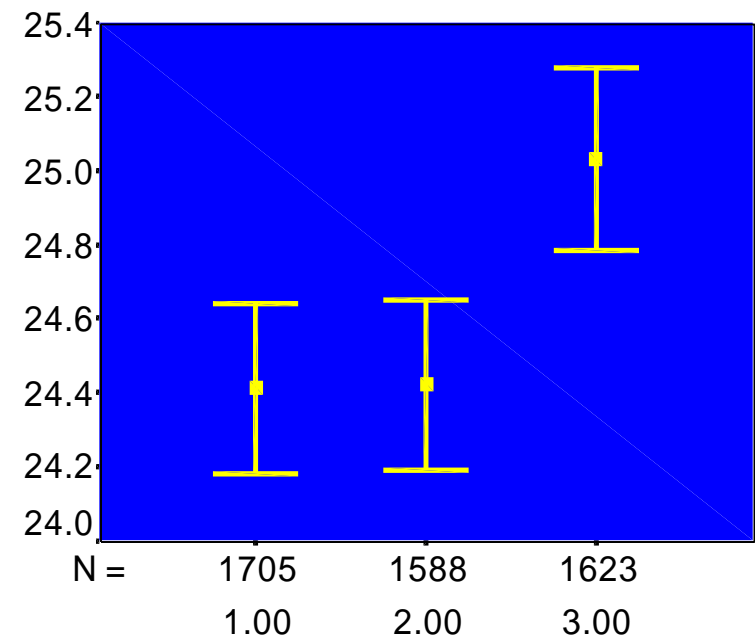
Figure: Modes of human adaptability

(females)

Age 7



Age 33



Birth weight tertile

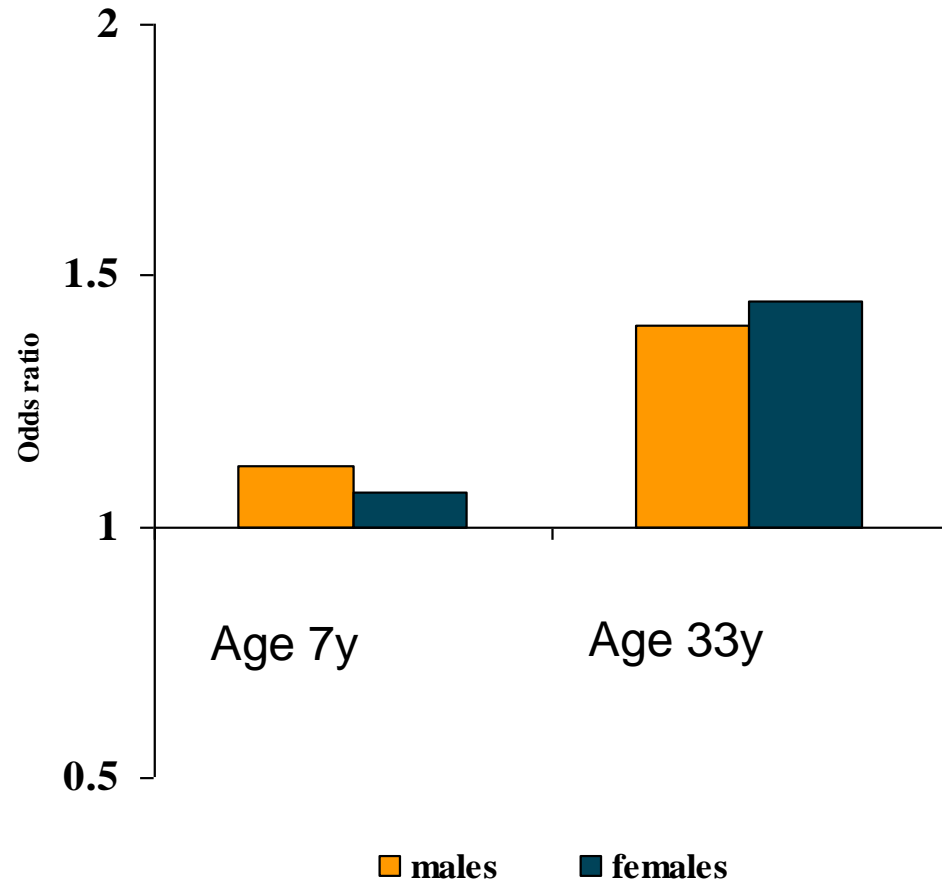
BMI (top 10%) at 7 and 33y (ORs)

adjustments:

parental BMI,
birthweight,
breastfeeding,

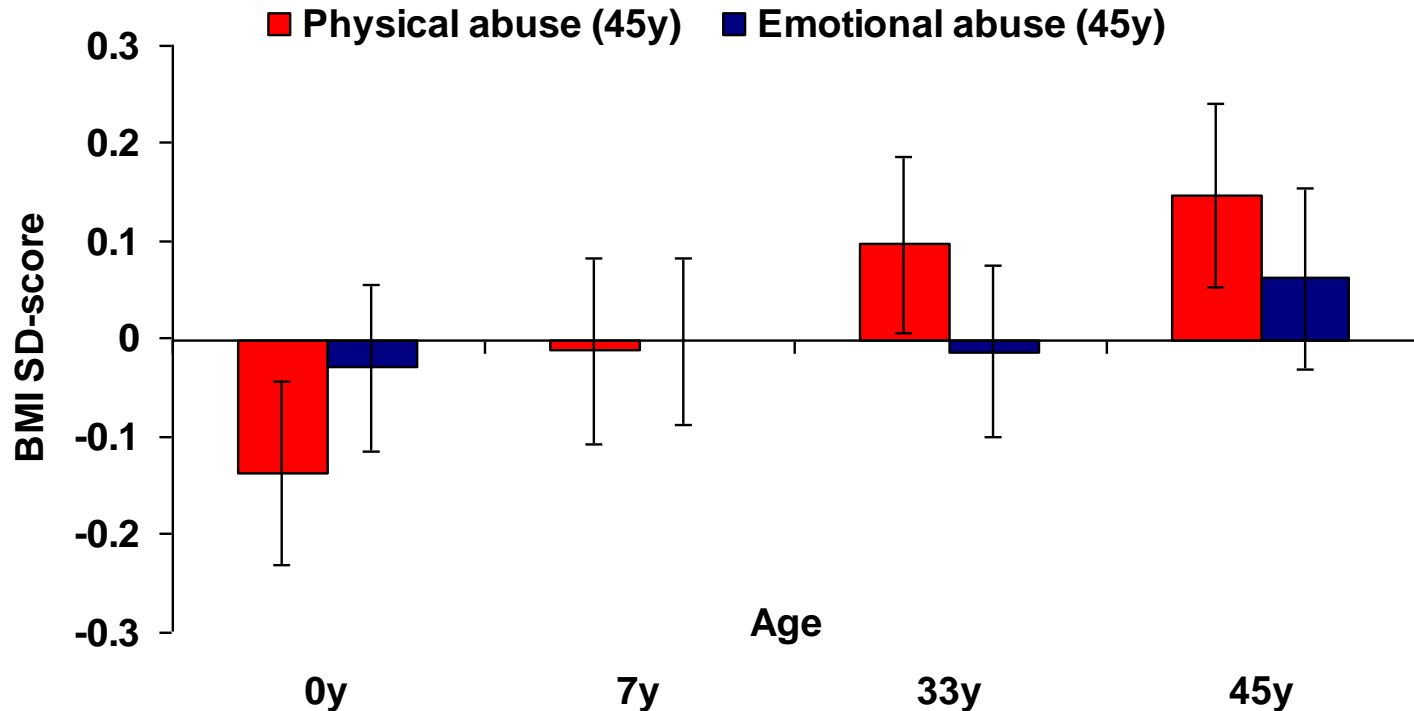
social class at
birth, 7yr & 33y,
qualifications,

activity, diet &
smoking at 23y



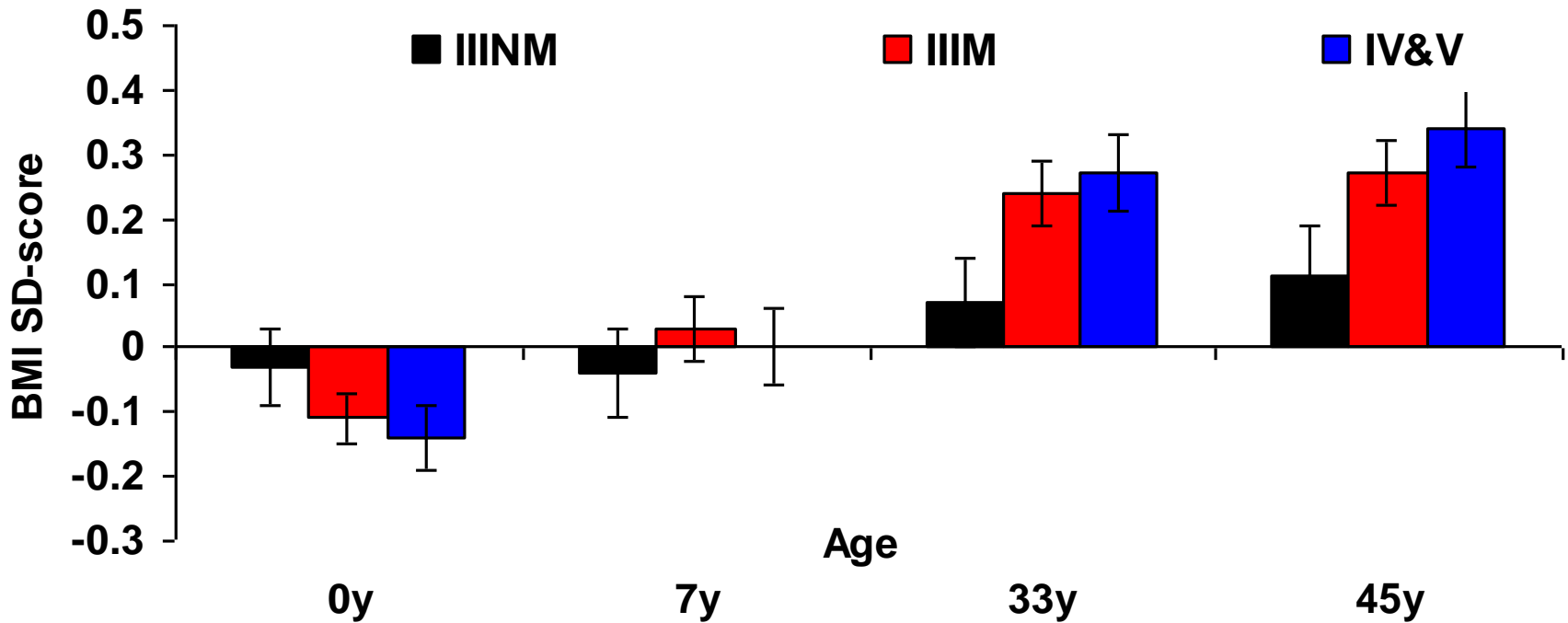
Physical & emotional abuse

child – adult BMI sd-score

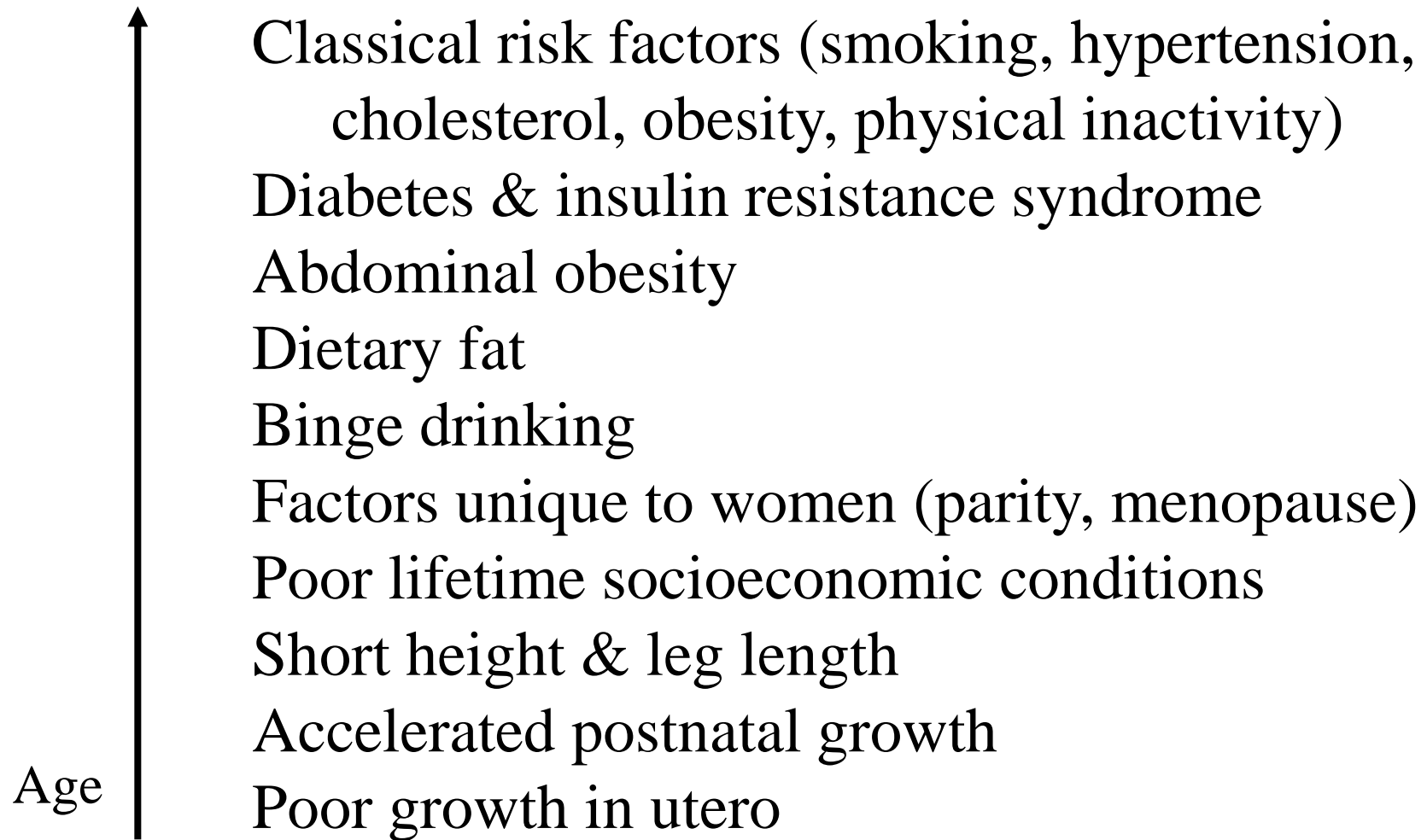


Difference in mean sex-standardised SD-scores (exposed v unexposed)
BGA used for 0y; BMI other ages.

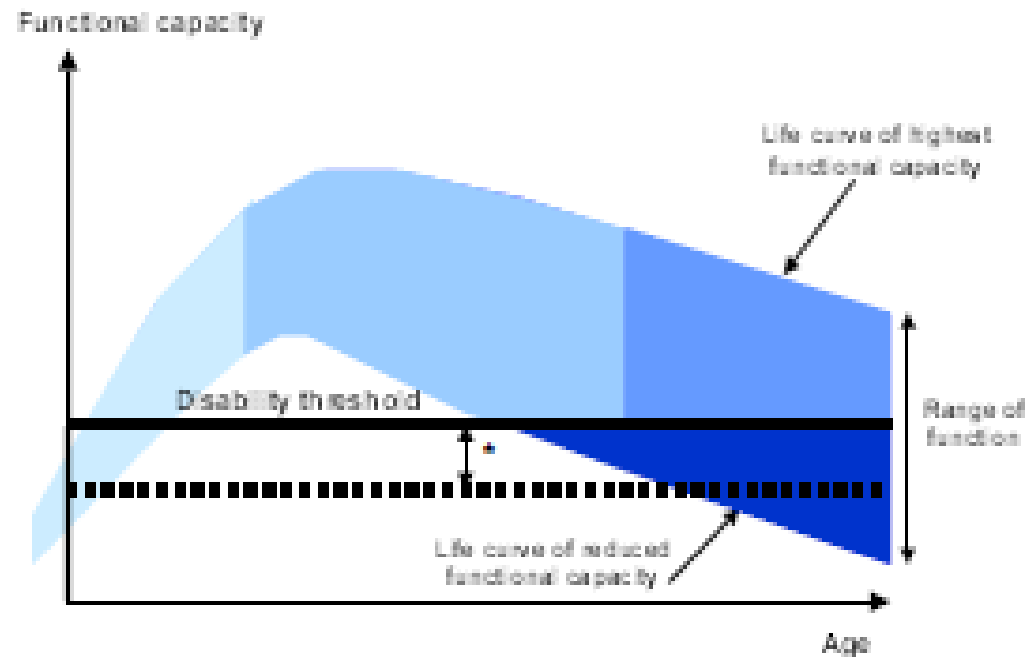
child – adult BMI sd-score







Difference in mean sex-standardised SD-scores (exposed v unexposed)
BGA used for 0y; BMI other ages.



Maintenance of functional capacity



*changes in external environment can lower disability threshold

-  Early life interventions to ensure the highest possible functional capacity
-  Adult life interventions aimed at slowing down the decline
-  For those in older age above the disability threshold, revisiting previous interventions
-  For those in older age below the disability threshold, interventions are aimed at improving the quality of life

Stein & Moritz
WHO Ageing & Health 1999

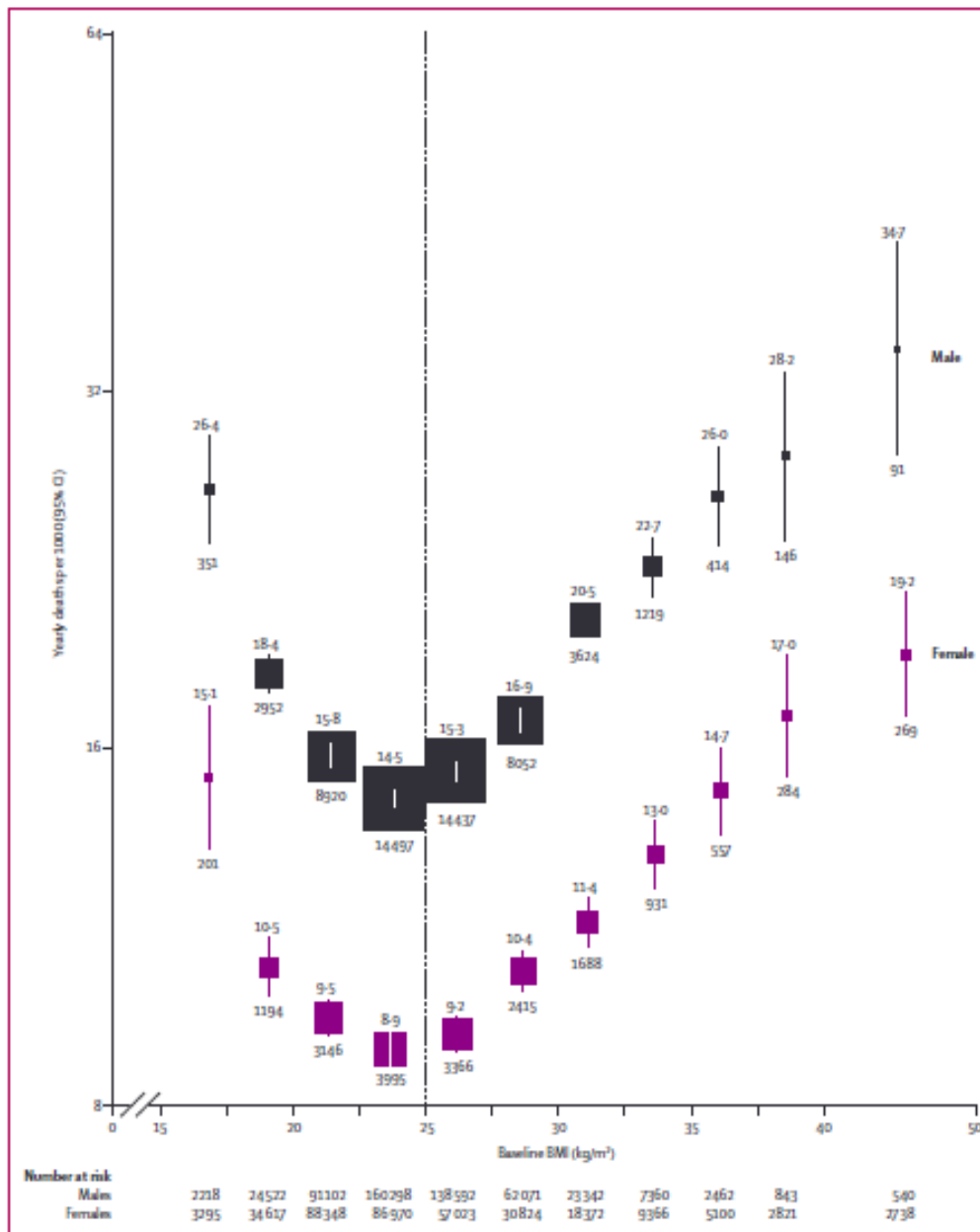
bringing cohorts together

- replicate findings (standardise methods).
 - different life stages (ages) → when do influences exert effect(s)
- pooling data → increase sample-size → investigate issues otherwise unable to address
 - sub-groups
 - precision of estimates
 - genetic studies
- longitudinal phenotypes are essential to understand biological development
- investigate changing influences and consequences over time.

cause-specific mortality in 900,000 adults

57 prospective studies

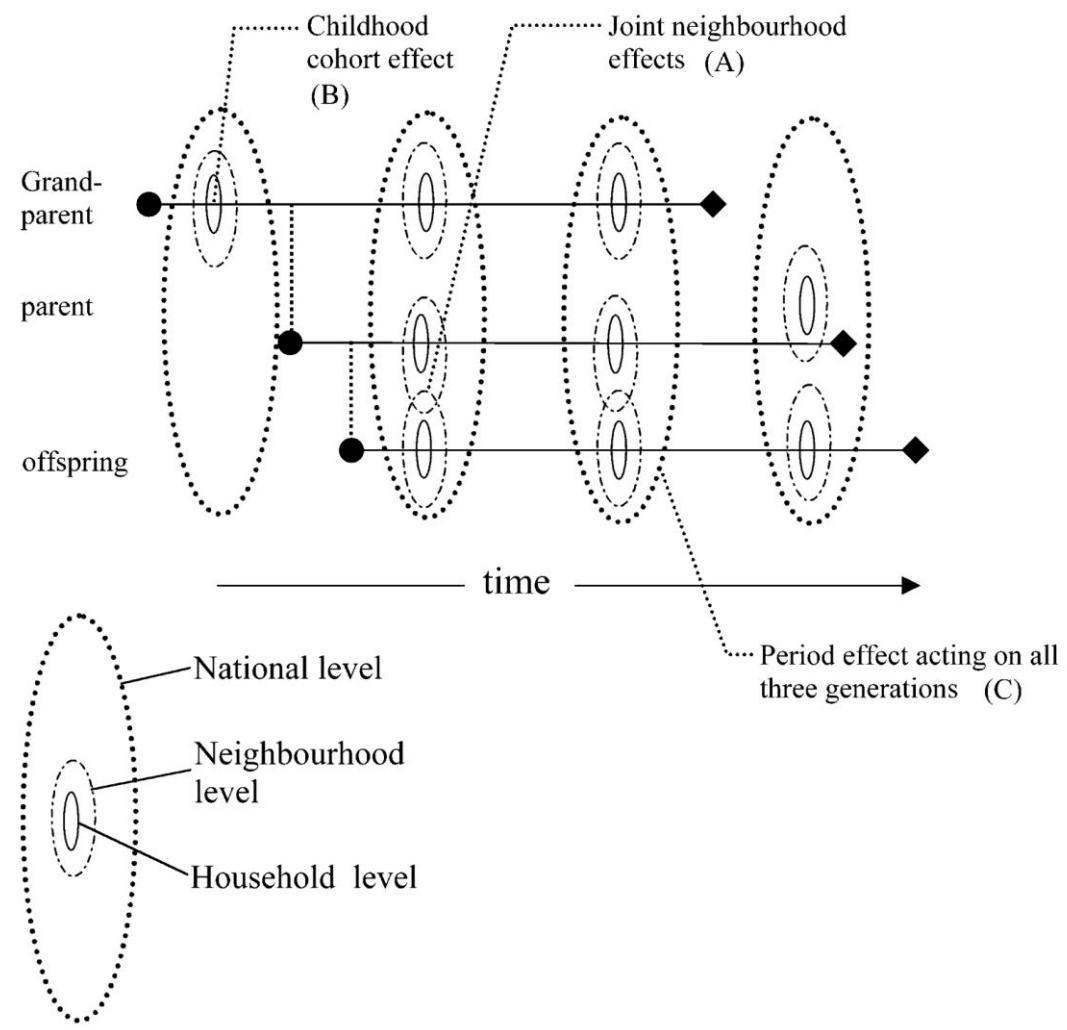
Prospective Studies Collaboration
Lancet 2009



bringing cohorts together

- replicate findings (standardise methods).
 - different life stages (ages) → when do influences exert effect(s)
- pooling data → increase sample-size → investigate issues otherwise unable to address
 - sub-groups
 - precision of estimates
 - genetic studies
- longitudinal phenotypes are essential to understand biological development
- investigate changing influences and consequences over time.

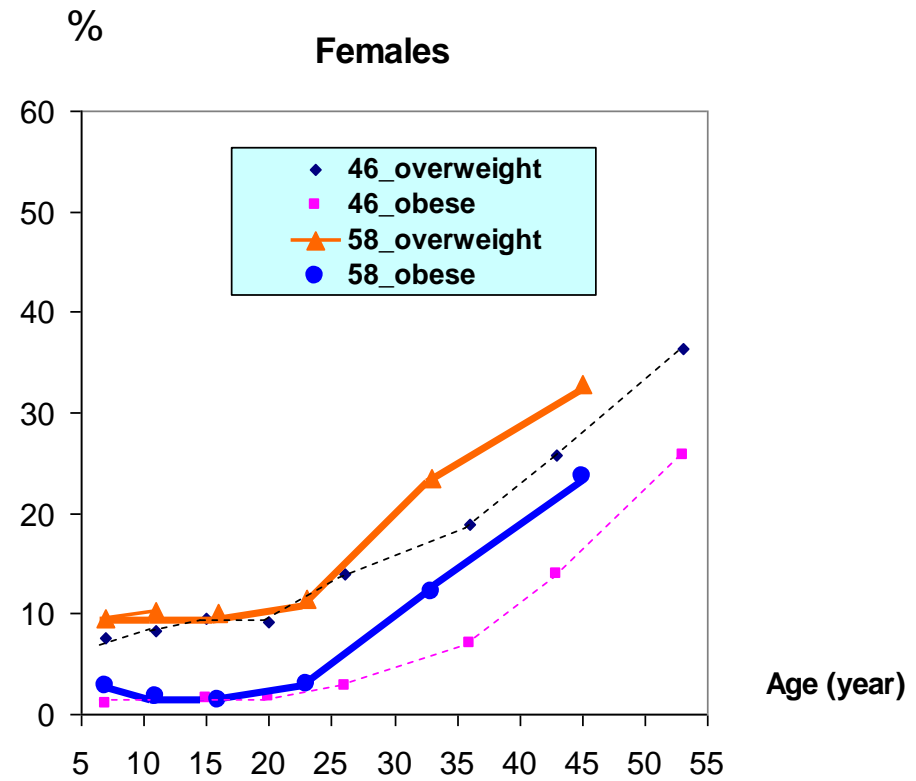
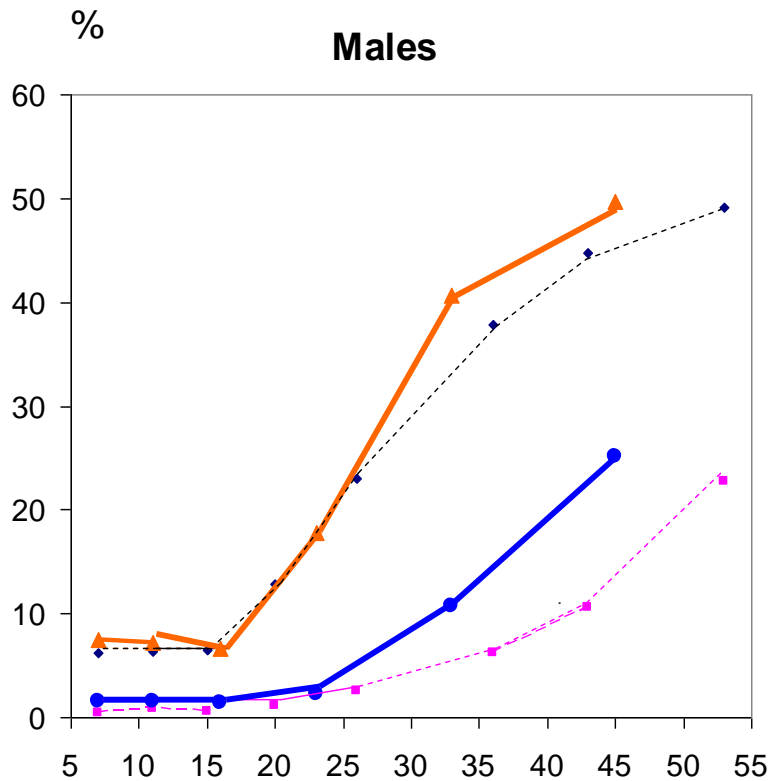
Multi-generational schema: influences of hierarchical and life course exposures on disease risk across three related individuals



A = Joint neighbourhood effect of exposure on parent and offspring; B = Childhood cohort effect on grandparent;
 C = Period effect influencing all three generations

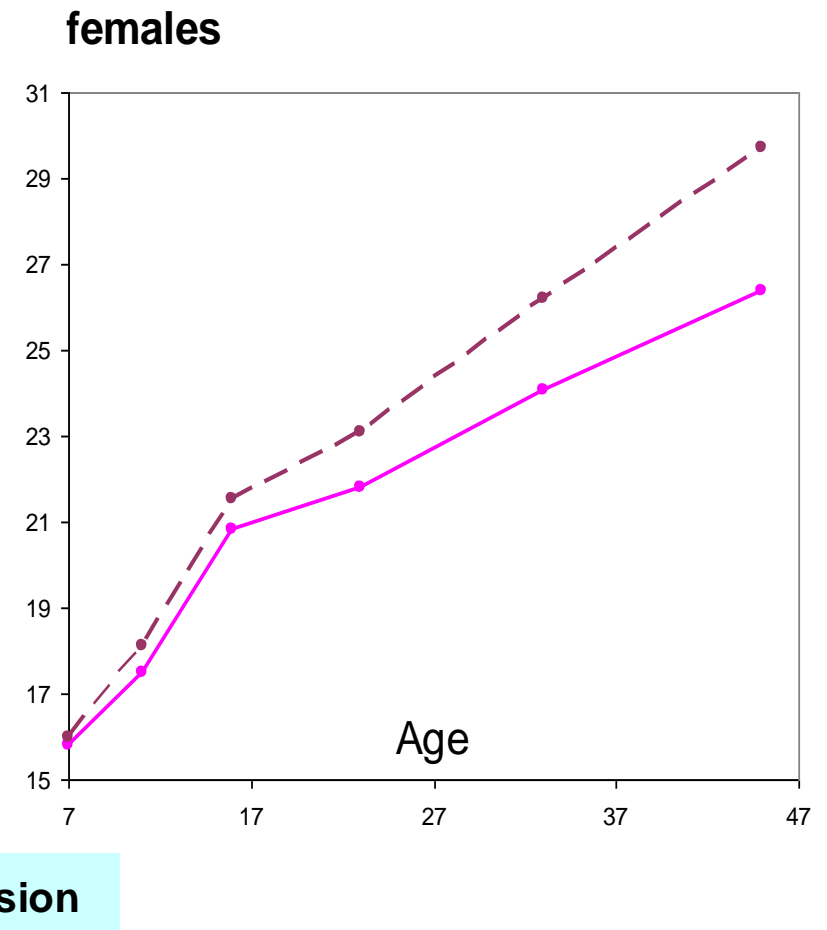
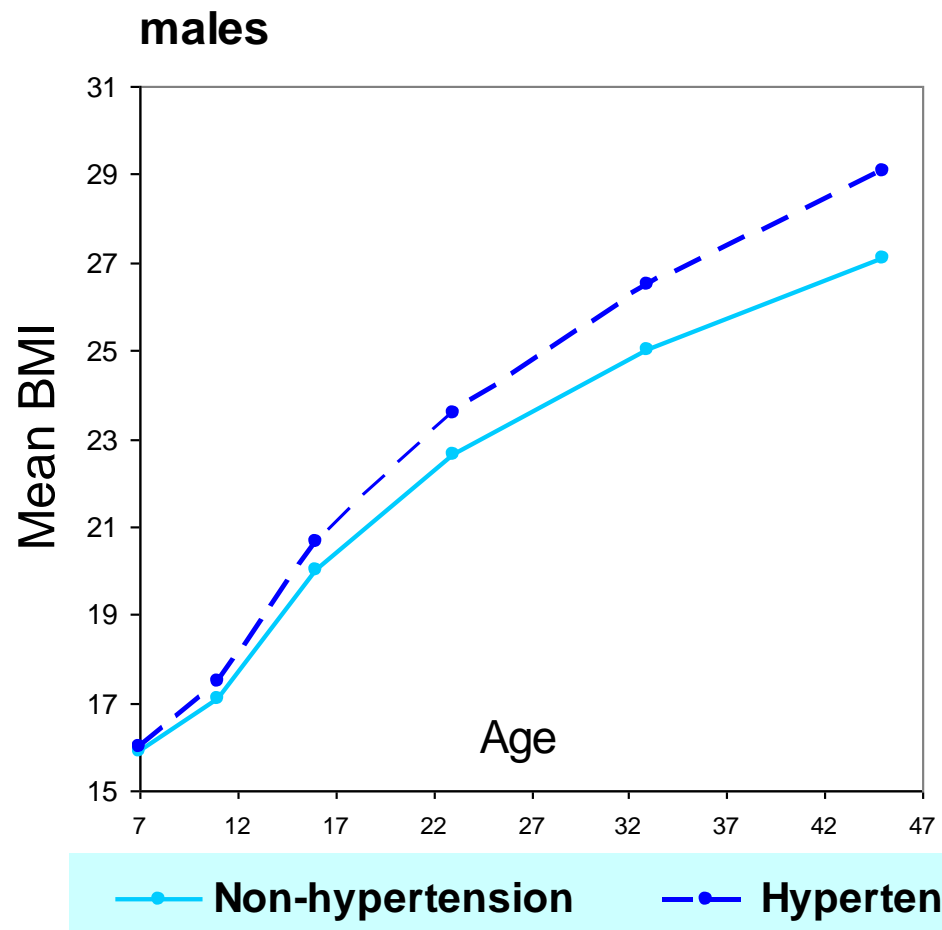
Ben-Shlomo & Kuh 2002
 International Journal of
Epidemiology

1946 and 1958 cohorts

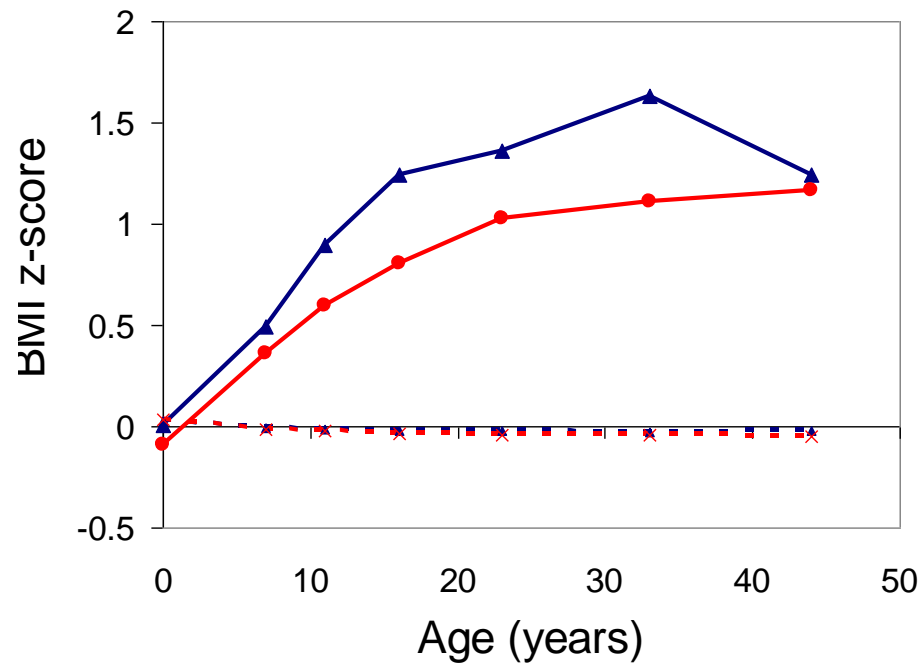
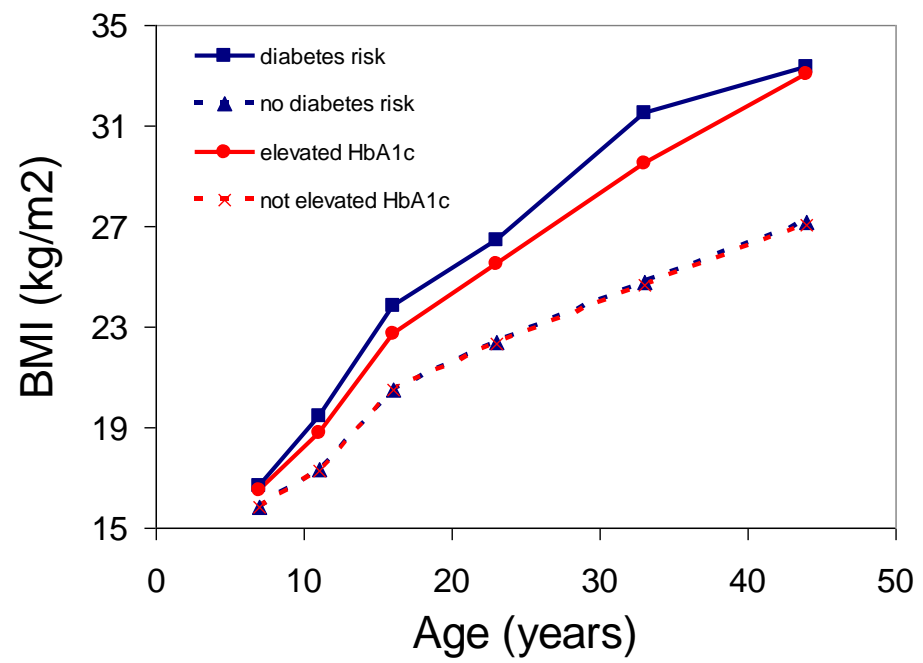


Hypertension at 45y:

BMI trajectory



BMI & SD-BMI trajectories



bringing cohorts together

- replication /combination
 - changing influences & consequences over time
 - co-operation/consortia
 - capacity building: skills base
 - governance structures
 - funding
- depends on
 - overlapping information
 - comparability in meaning
 - sensitivity to context
 - management
 - expertise in study design, phenotypes, genetics, genetic epidemiology, biostatistics.
 - data sharing – security, confidentiality
 - resources for collation & monitoring

- By bringing together cohorts born at different times, studied over different periods of life
- Scientific gains for understanding the origins of functional capacities, disease and disease progression
 - Trick will be to retain the richness of individual studies, whilst gaining levels of comparability; to develop research capacity so that the full potential can be exploited.



Luxembourg, September, 2009

bringing cohorts together

A New Era of Cardiovascular Disease Epidemiology

Bruce M. Psaty, MD, PhD

Donna Arnett, PhD

Gregory Burke, MD, MS

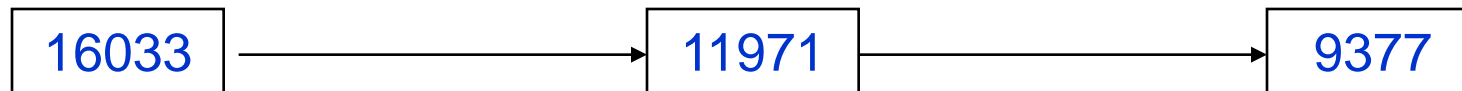
CARDIOVASCULAR EPIDEMIOLOGY HAS A RICH, COLLABORATIVE, and productive history. Beginning in 1948, the Framingham Heart Study was instrumental in identifying, for instance, high blood pres-

sure to those used in SHARe will make available to community both the CArE genotype and phenotype data on about 50,000 participants in 9 Nat Lung, and Blood Institute (NHLBI)-funded or spring of 2008. SHARe and CArE are indeed sources. The expectation is that the widespread of these data to the scientific community will accelerate high-quality scientific findings in genomics. The success of making data widely available

“The effort to generalize from the genome assembly of base pair data to the epidemiological analyses of genotype phenotype data represents a bold experiment.”

“problems with data analysis interpretationsome potential risks associated with the large scale release of genotype-phenotype data”.

- all births one week in March 1958 (N~17000)
- nationwide coverage (England, Wales, Scotland)
- followed at ages 7, 11, 16, 23, 33, 42 years.
- disease risk assessed at age 45y in a biomedical survey



Alive/ in Britain 2003

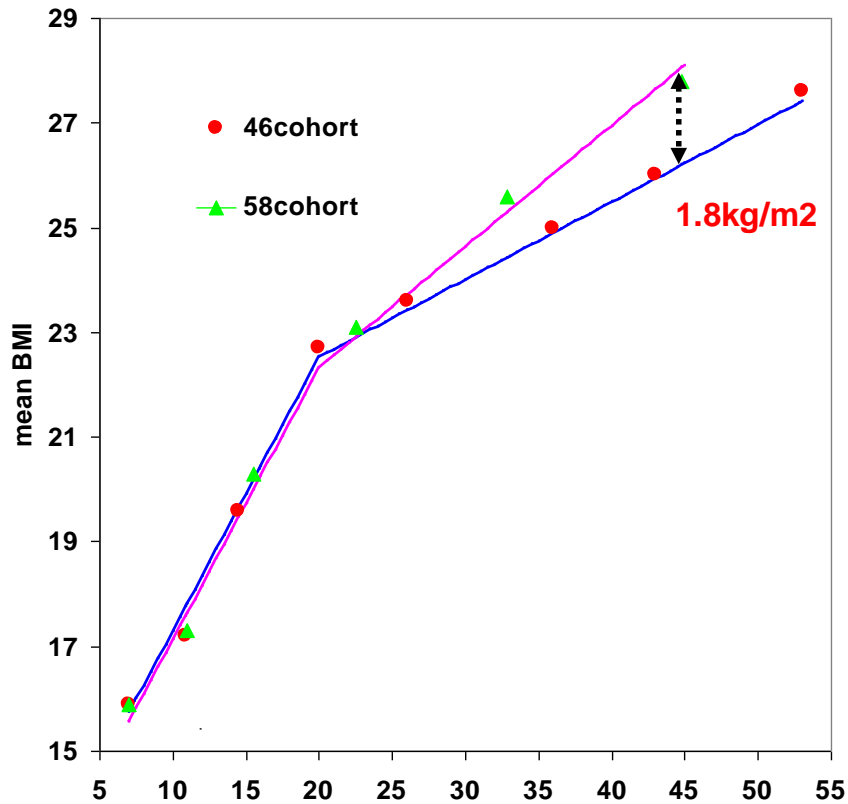
Invited for biomedical

Biomedical interviews

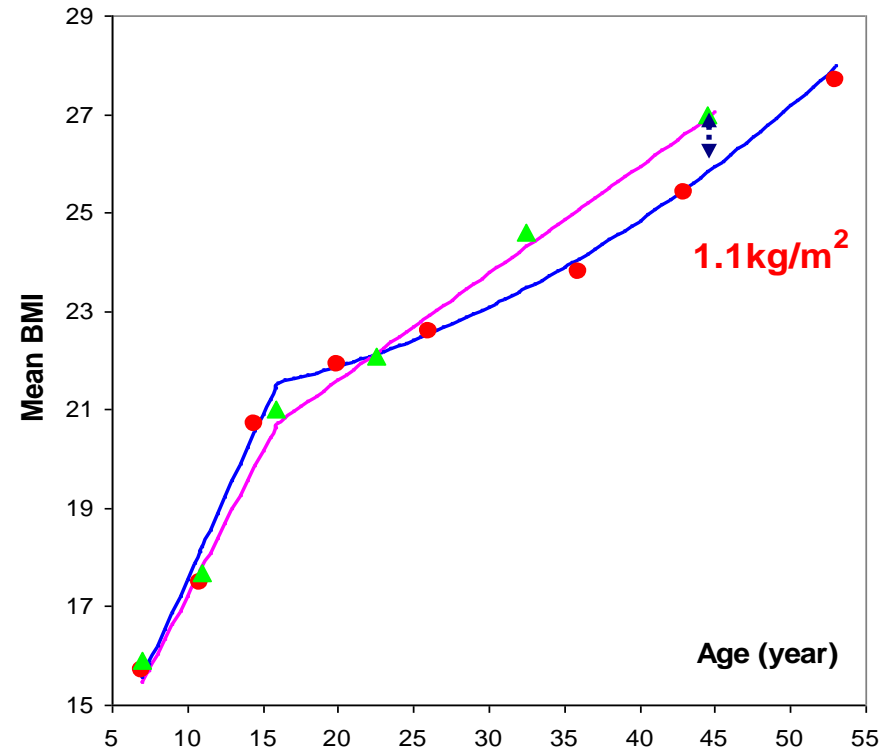
BMI trajectories

1946 and 1958 cohorts

Males



Females



Dots - observed mean BMI

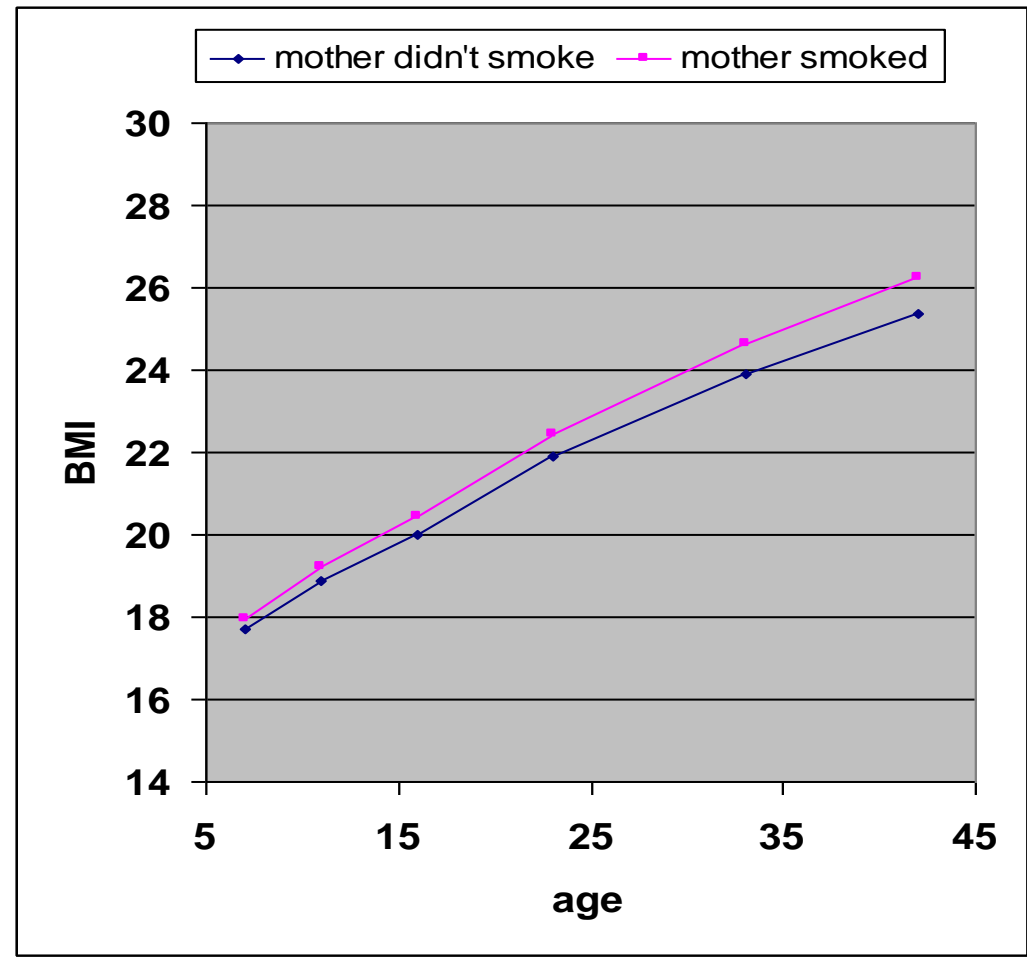
Solid lines - estimated BMI trajectories

BMI 7-42y

smoke vs. non-smoke

F: 7y 0.3 kg/m²
42y 0.9 kg/m²

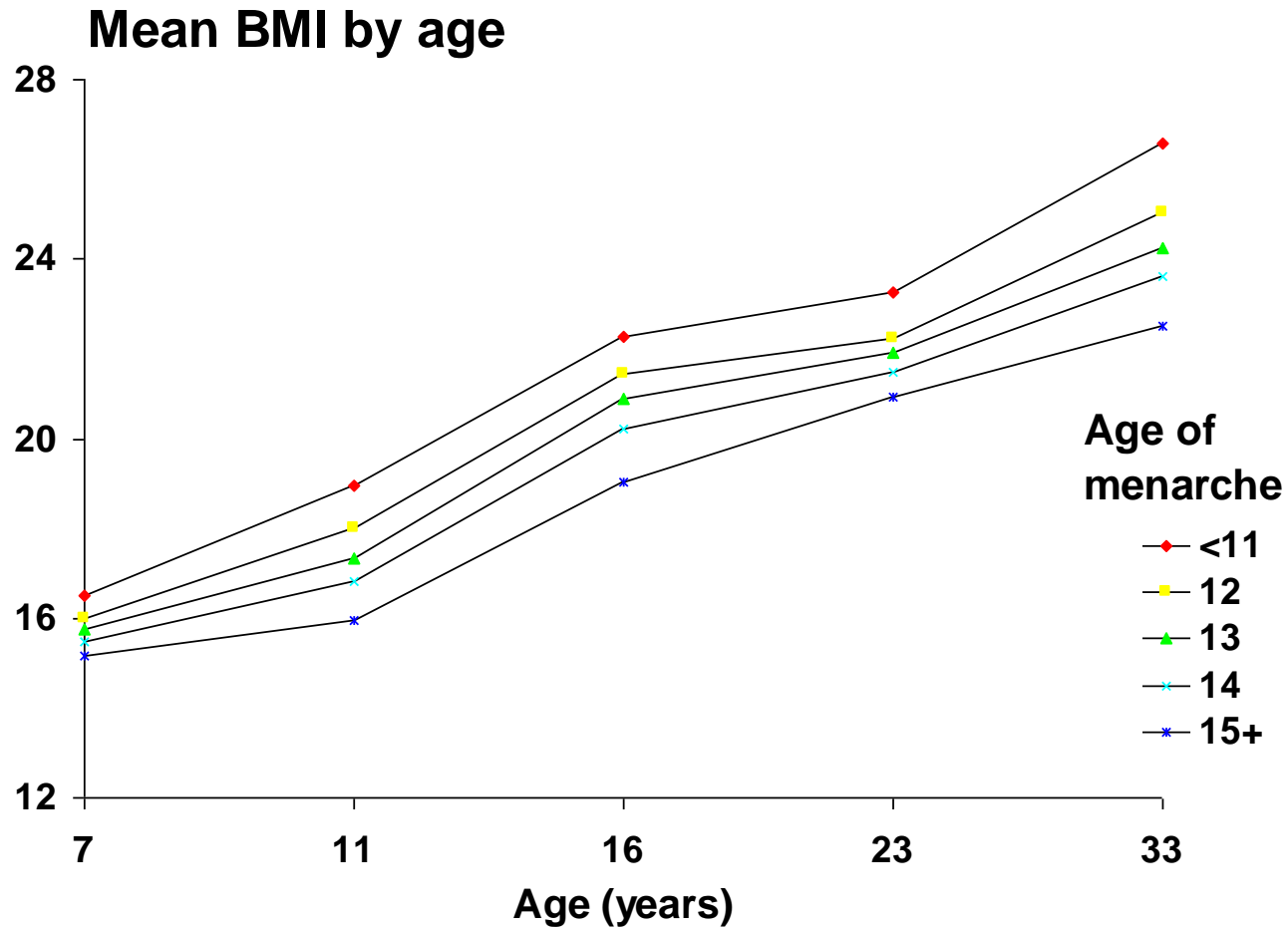
M: 7y 0.3 kg/m²
42y 0.9 kg/m²



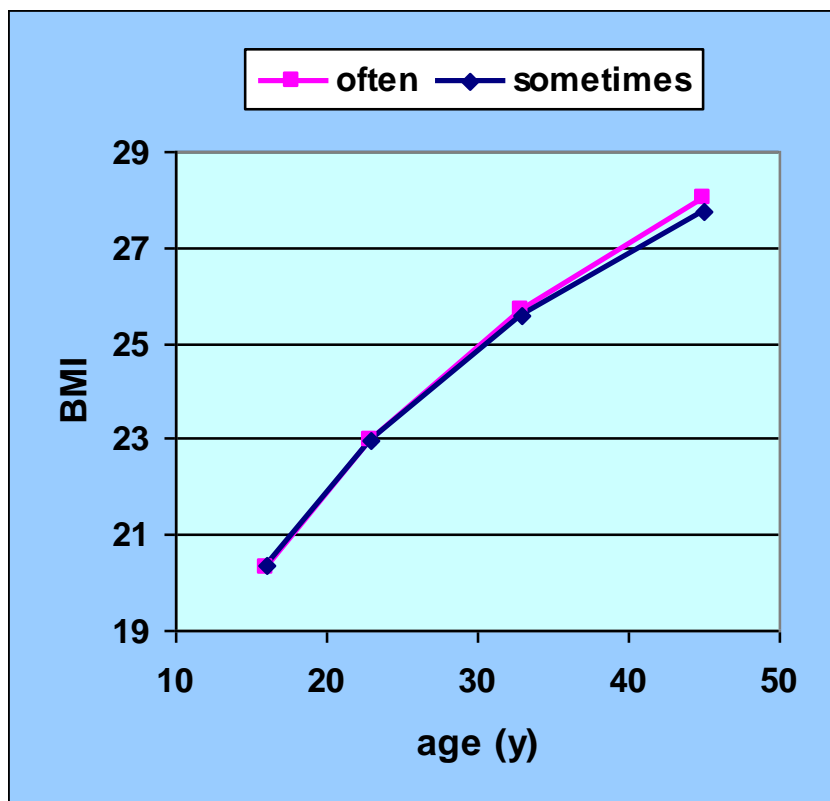
Females (n=5905)

adj. for social class, mothers BMI,
birth-weight, breast-feeding

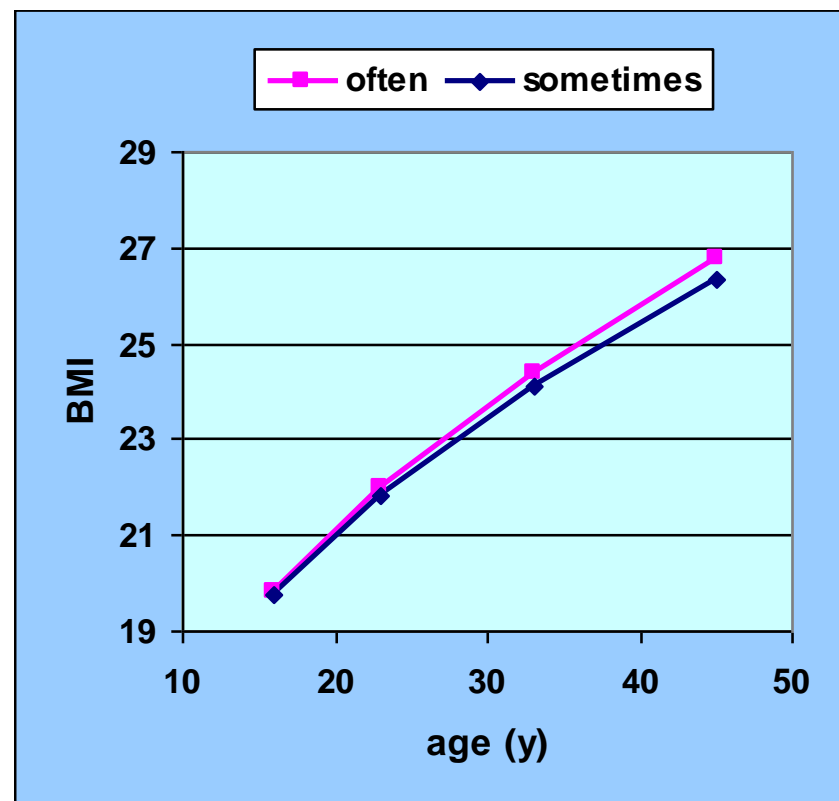
Parsons, 2005



males



females



often vs. sometimes

M: 16y 0.08 kg/m² 45y 0.25 kg/m²

F: 16y 0.05 kg/m² 45y 0.43 kg/m²

diff between slopes: sig males & females

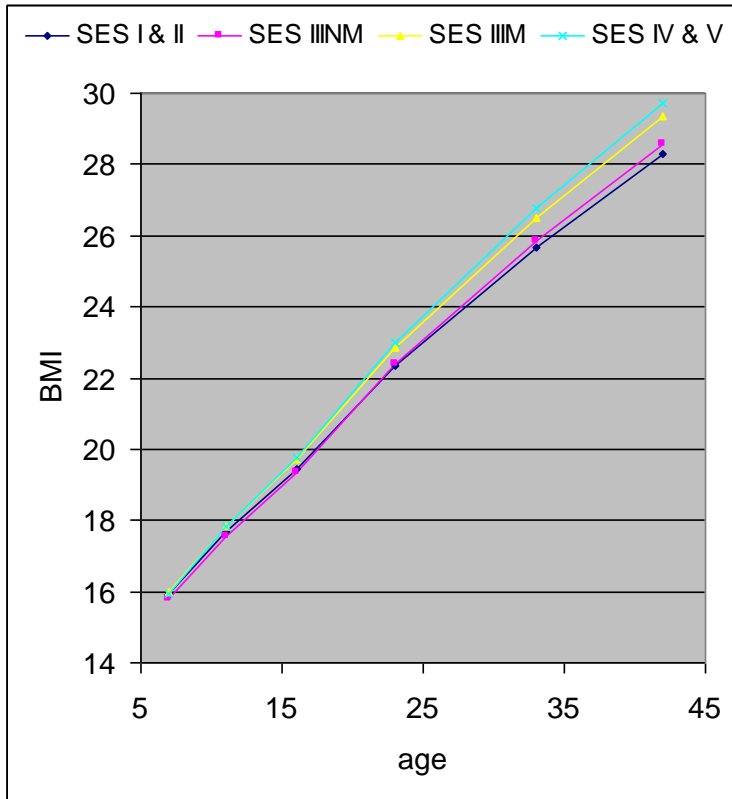
bringing cohorts together

- replication of findings (standardisation of methods).
- pooling data → increase sample-size → allows investigation of issues otherwise unable to address
 - sub-groups
 - precision of estimates
 - genetic studies
 - » longitudinal phenotypes are essential to understand biological development
- allowing us to investigate changing influences and consequences over time.

- **Magnitude of disease risk associated with gene variants**
- **Contribution of gene variants to the occurrence of disease**
- **Magnitude of disease risk associated with gene-gene and gene-environment interactions**
- Human genome epidemiology studies depend on high quality phenotypic data
- Longitudinal phenotypes are essential to understand biological development from a life course perspective

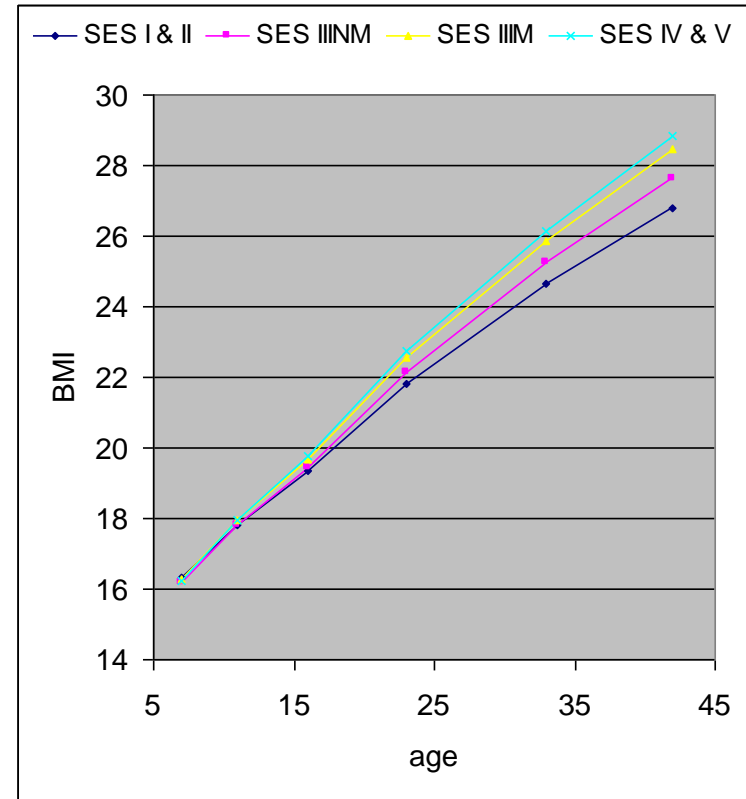
Males

n=7718



Females

n=7327



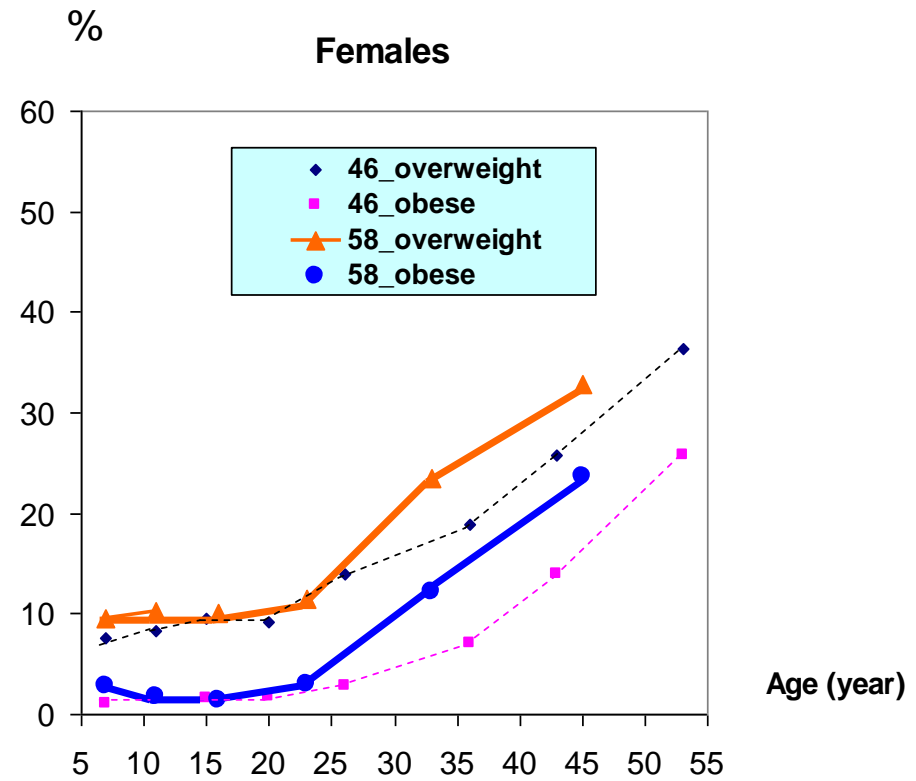
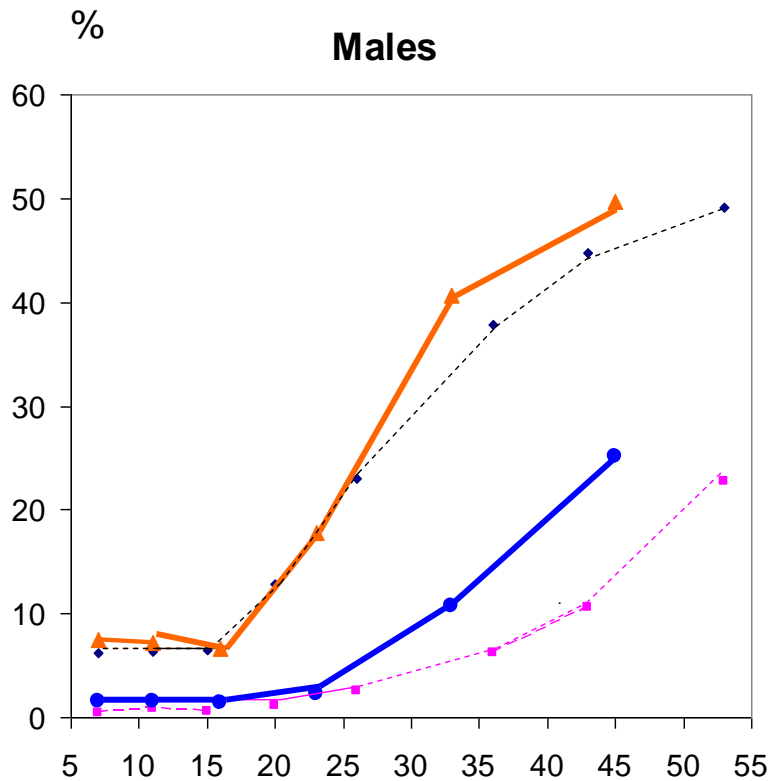
IV&V vs. I&II

M: 1.4 kg/m²

F: 2.1 kg/m² at 42y

Parsons, 2005

1946 and 1958 cohorts



..... Such an approach explores evidence for both programming during **critical periods** of growth and development and the **cumulative** risk attached to a number of different exposures throughout the life course.