Value of biospecimin collection and biobanking

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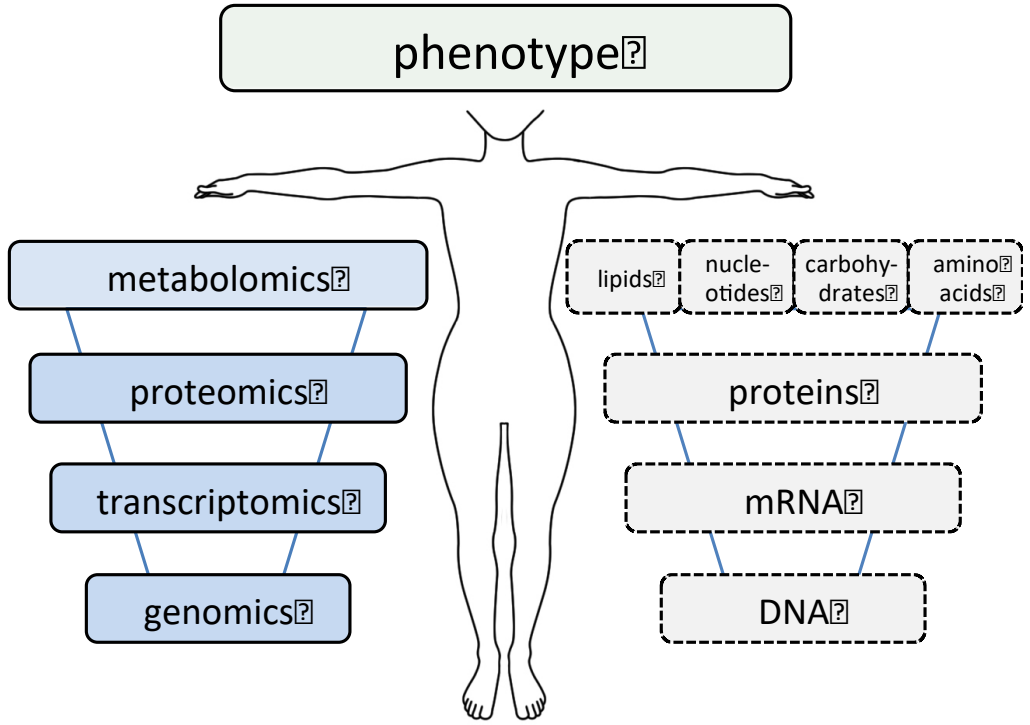
Outline

- Value of collecting biospecimins
  - Prior to development of disease
- Challenges
  - Obtaining and maintaining
    - Getting sample collection ”right”
  - Storage issues
    - Time in freezer, freeze thaw issues, etc
  - Sample depletion (rare phenotypes, etc) vs planned access
- Opportunities



The ideal

Biospecimins and exposure info collected prior to outcomes

AND

age relevant!

LifeGene

Exposure /Events

Home | Kindergarden | Environment | School | Trauma | Substance use | Work | Stress

Children

Teenagers

Adults

Example areas of interest

- Allergies
- Infections
- Behavior

- Neuropsychiatry
- Infections
- Behavior

- Neuropsychiatry
- Muscle pain
- Pregnancies
- Obesity

Collection of data & samples over time

Sampling

- Blood
- Physical data
- Questionnaires

- Blood
- Urine
- Clinical chemistry
- Physical data
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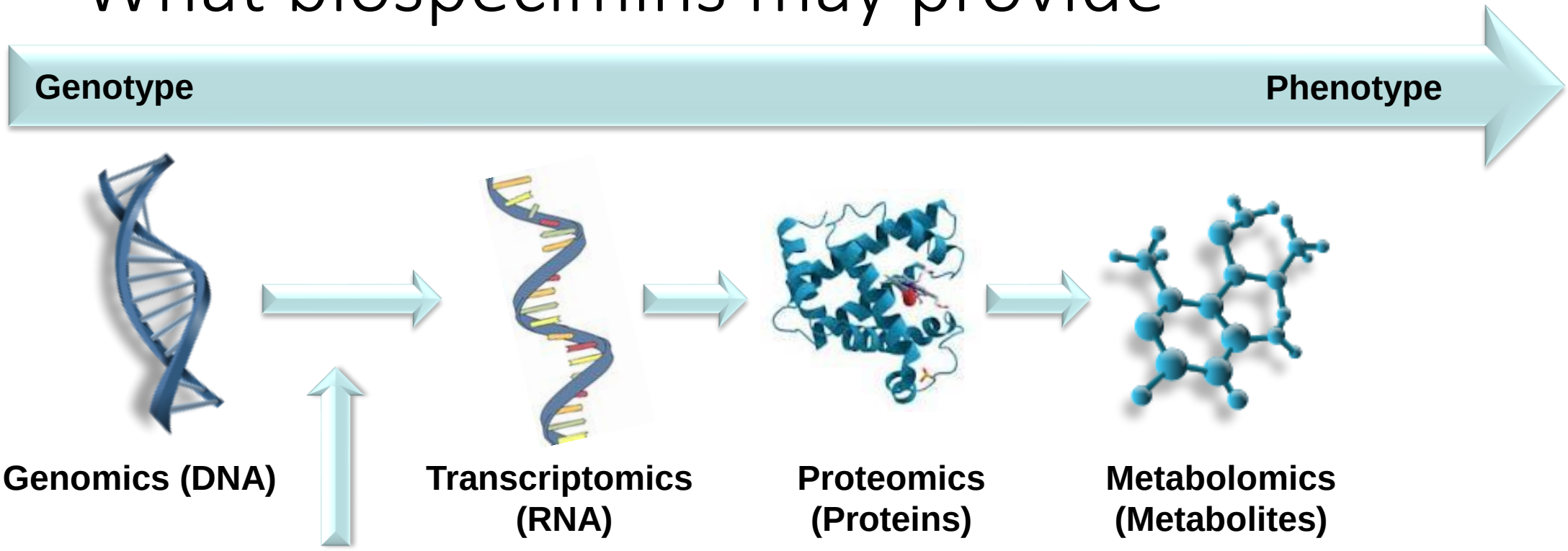
What biospecimins may provide



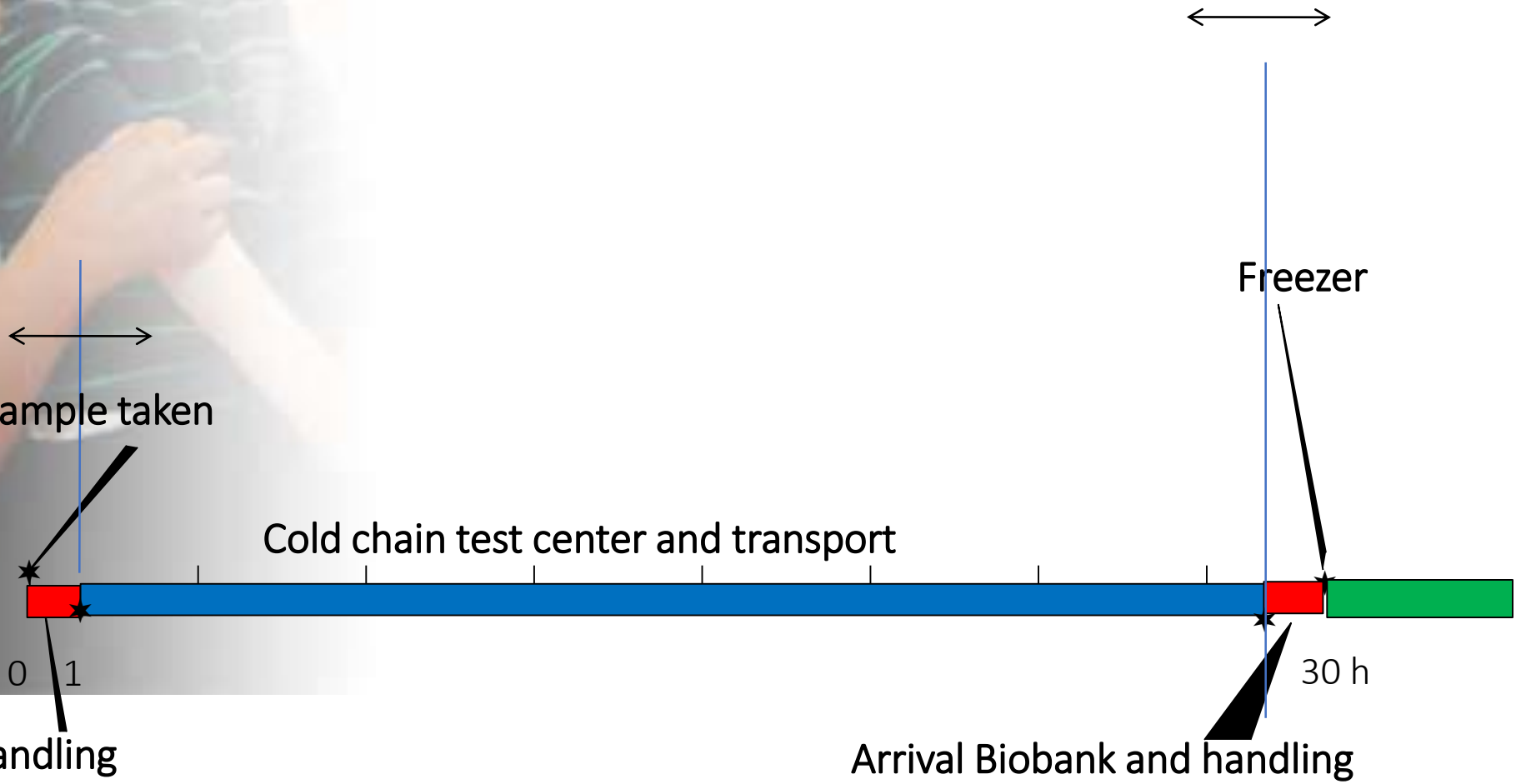
Courtesy of Jessica Prenni

Biospecimins: collected in standardized manner for “omics”: genomics, proteomics, metabolomics, etc.

Sample type	Processing
1 EDTA Whole blood 4ml	→ WBC + diff
1 Li-Hep with Gel plug 8ml	→ Frontend chem.
1 EDTA whole blood 4ml	*DNA extr. + aliquoting*
(1 Citrate 3.8%, 4ml)	*Aliquoting plasma*
1 Li-Hep with gel plug 8ml	*Aliquoting plasma*
2 EDTA 9ml	*Aliquoting plasma*
1 Trace metal tube 7ml	*Aliquoting serum*
1 Urine 9ml	*Aliquoting*

Total of 42 ml blood
39 Aliquots

Arm to freezer within 30 h



LifeGene

Feedback to the participants (on webpage)

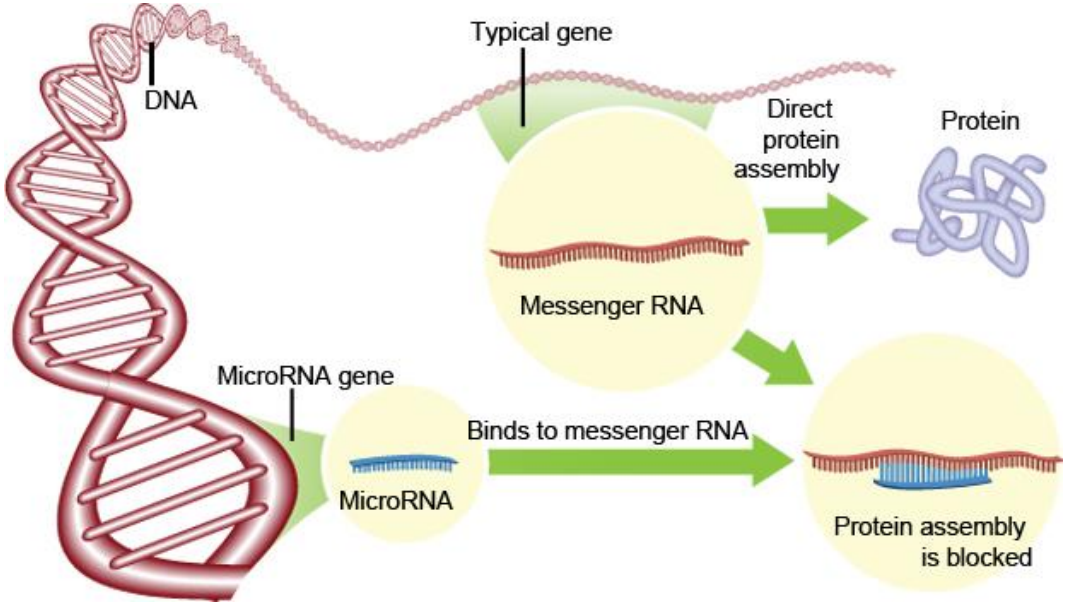
	LifeGene	EpiHealth
Hemoglobin	X	
HbA1c	X	
CRP, sensitive	X	
Cholesterol	X	
Apolipoprotein A1	X	
Apolipoprotein B	X	
Creatinine	X	
Fasting glucose		X
Triglycerides		X
LDL-cholesterol		X
HDL-cholesterol		X

But it is hard to get it right!

The example of transcriptomics

Different RNAs

- RNAs involved in protein synthesis
  - mRNA, tRNA, rRNA
- RNAs involved in regulation
  - miRNA, siRNA, shRNA, lncRNA



Sample preparation – for transcriptomics

- Quality of RNA important!!
- Samples preserved in e.g. RNAlater (mRNA) or EDTA (miRNA)
  - Why most cohorts can’t assess mRNA
- Protocols matter:
  - time to freezer
  - storage time
  - seasonal effects
  - batch effects from analyses

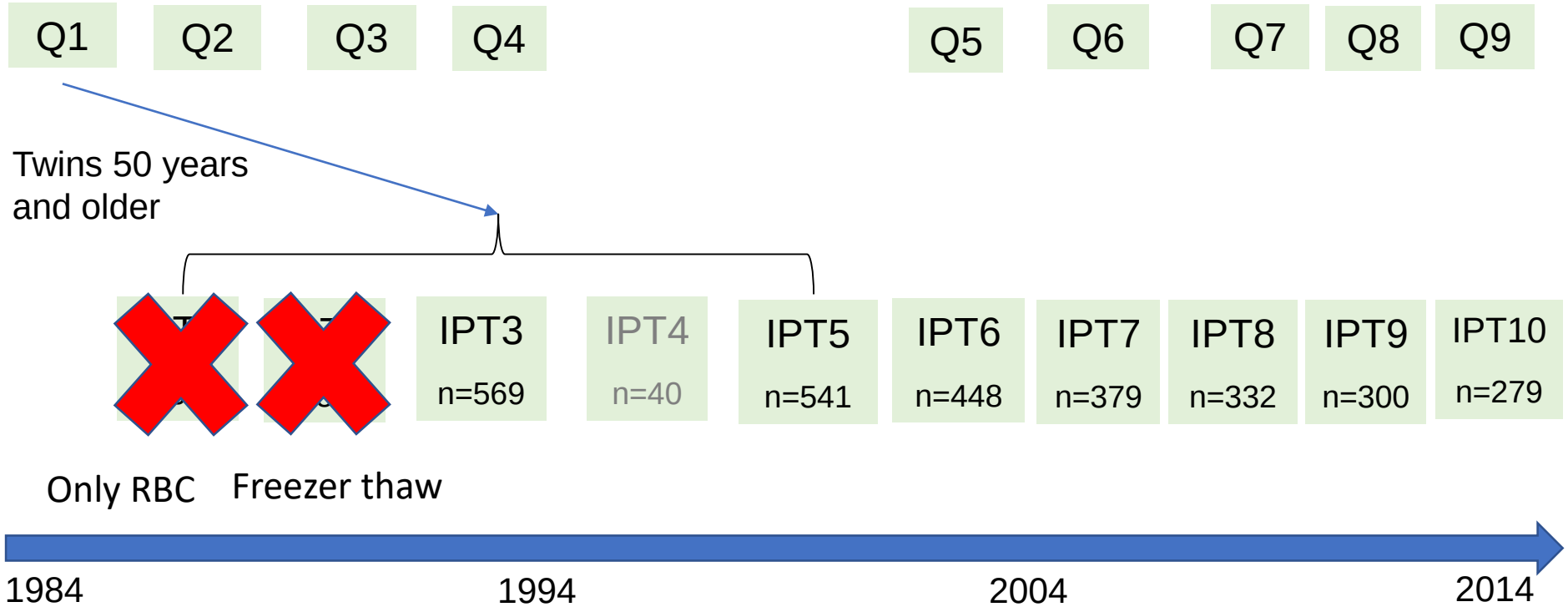
There are other challenges

Experiences from a longitudinal cohort

# SATSA –
# Swedish Adoption Twin/Study of Aging
N=2018

Twins Reared Apart
Twins Reared Together

- 859 individuals participated in at least 1 IPT
- >70% participated in 3 IPTs or more
- Clinical chemistries at all occasions



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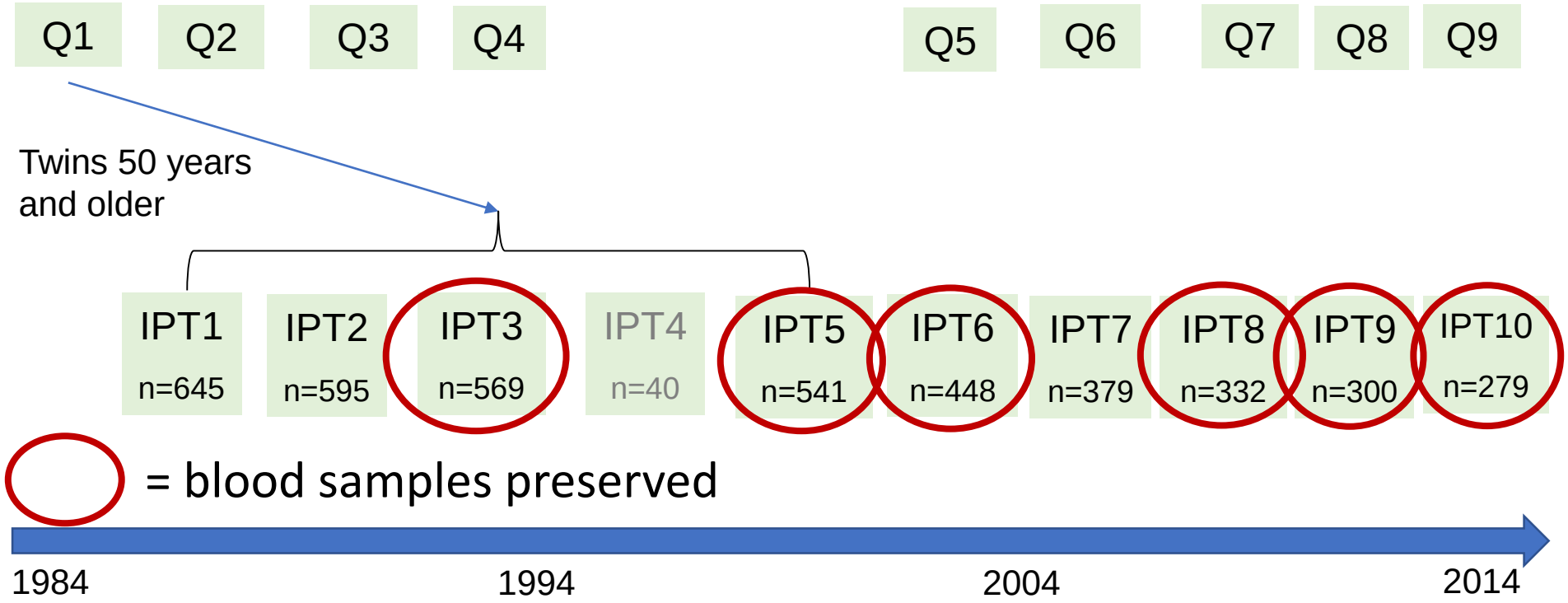
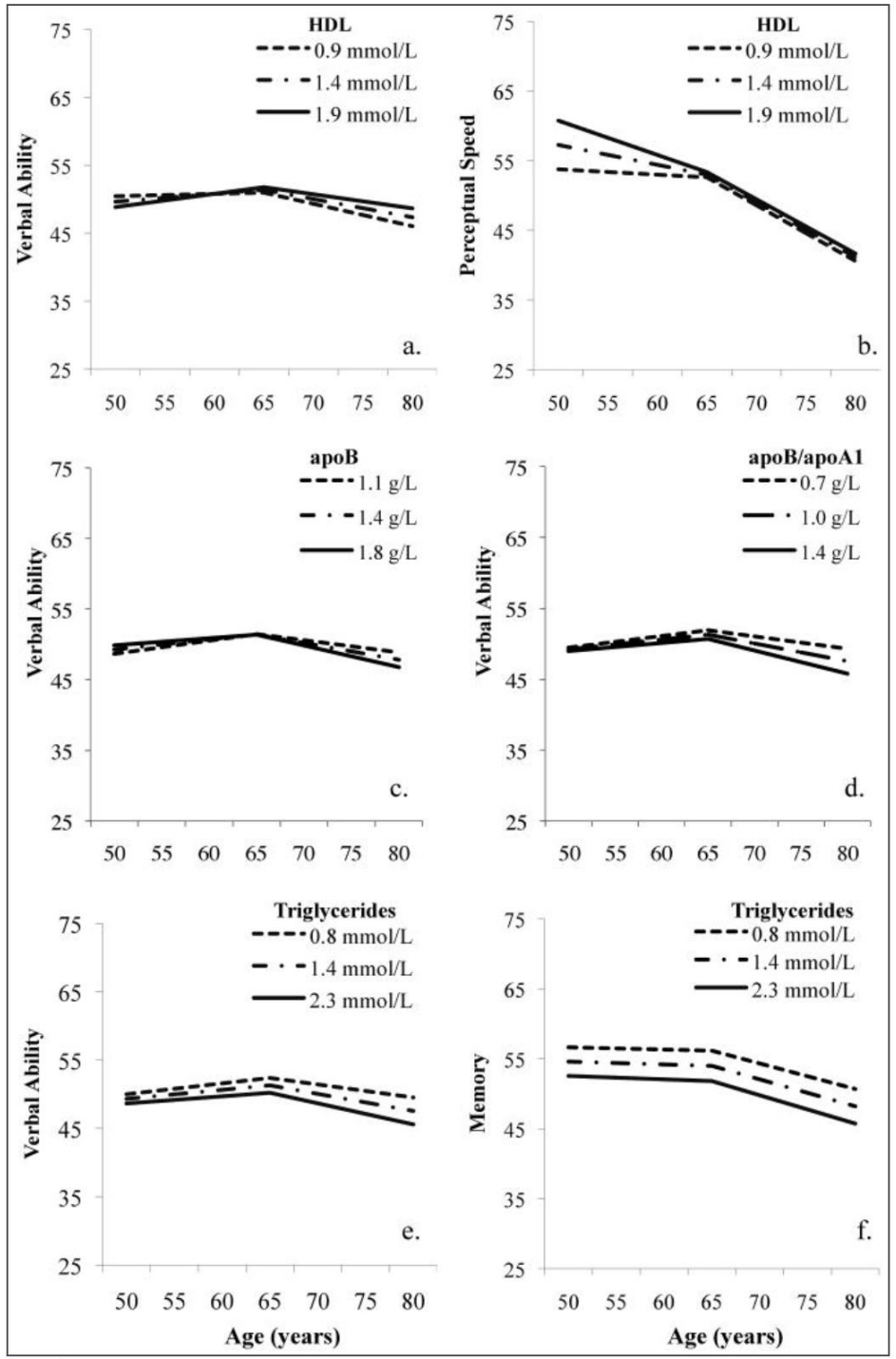
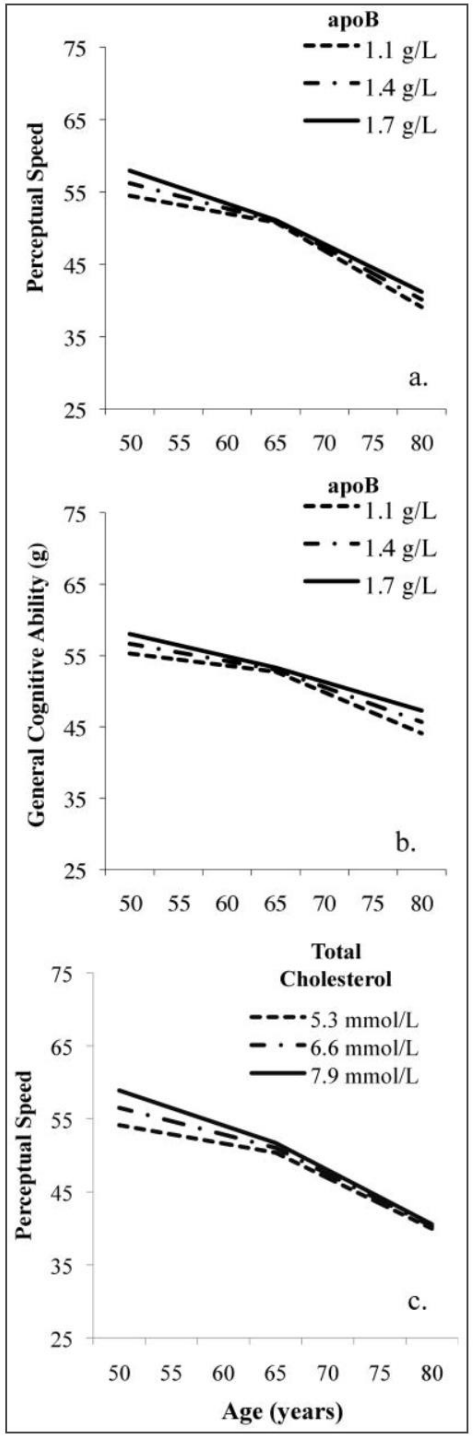




Nevertheless, valuable information from baseline biospecimins on longitudinal outcomes

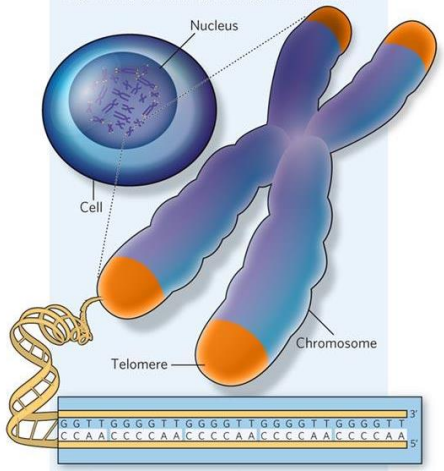
Cognitive change as a function of baseline lipid and lipoprotein levels in women (left panel) and men (right panel)

Reynolds et al., 2010 *Hum Mol Genet*

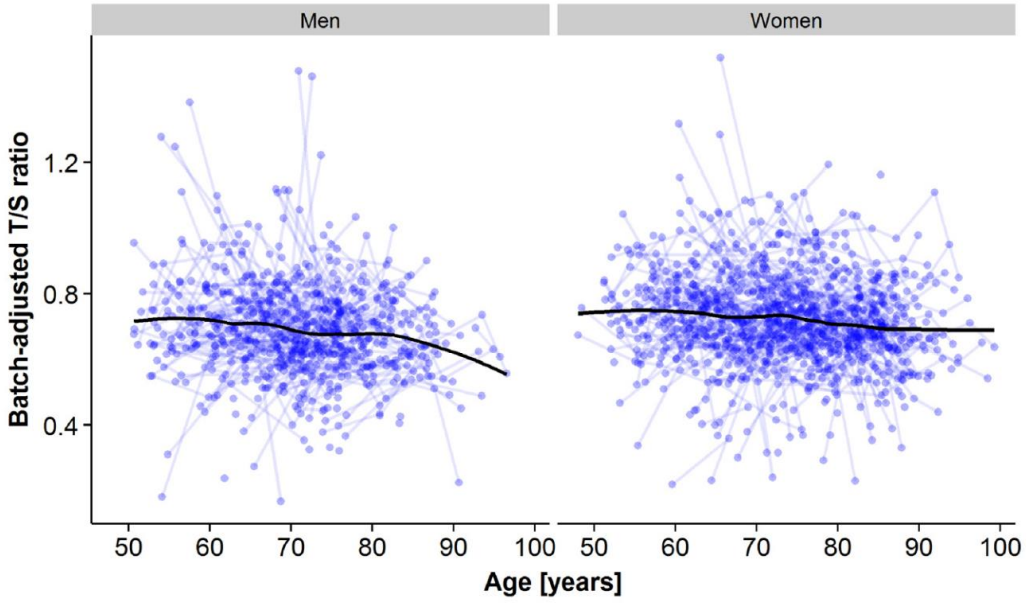


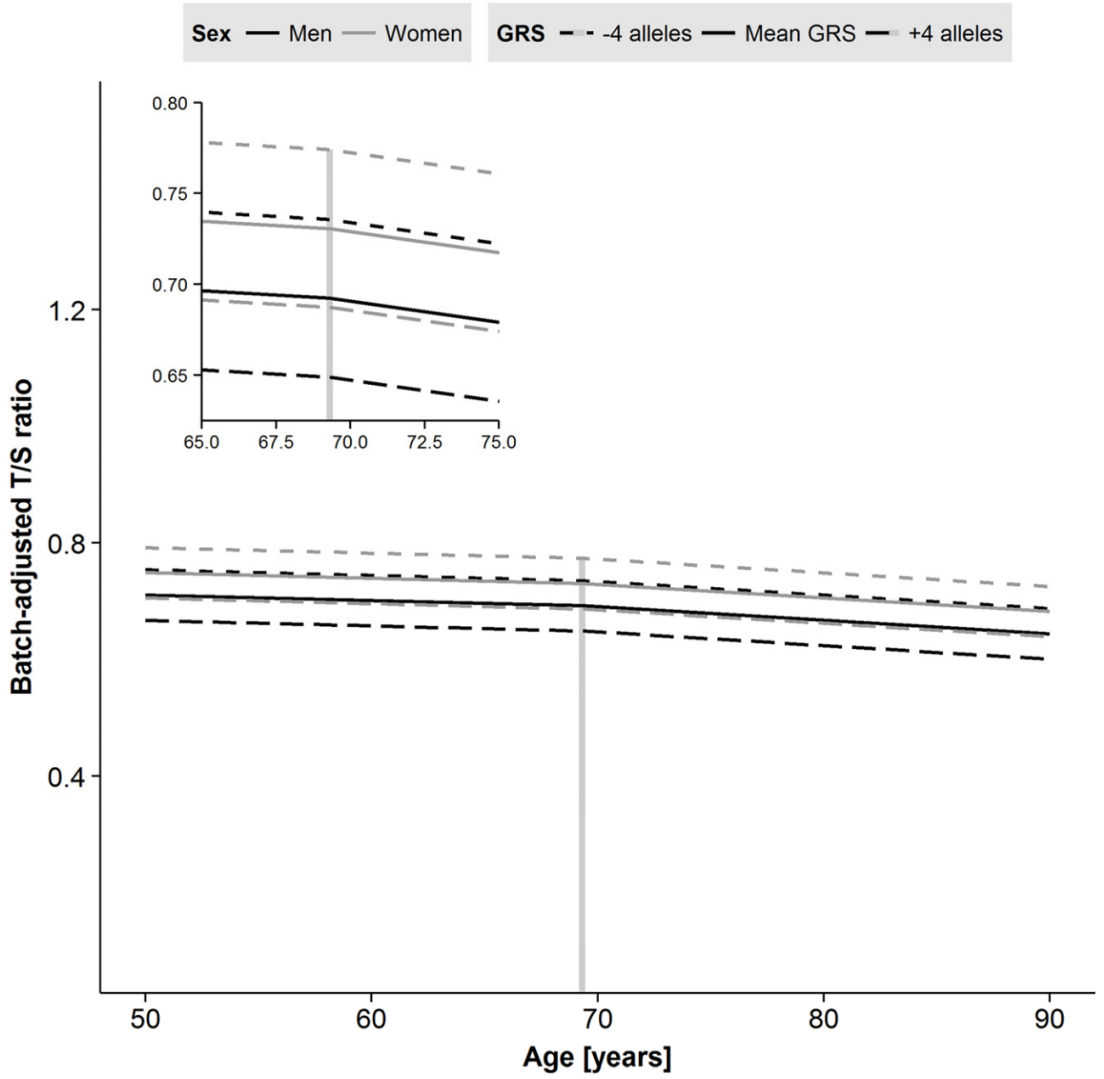
Other considerations

Cross-sectional effects / mean differences often greater than longitudinal



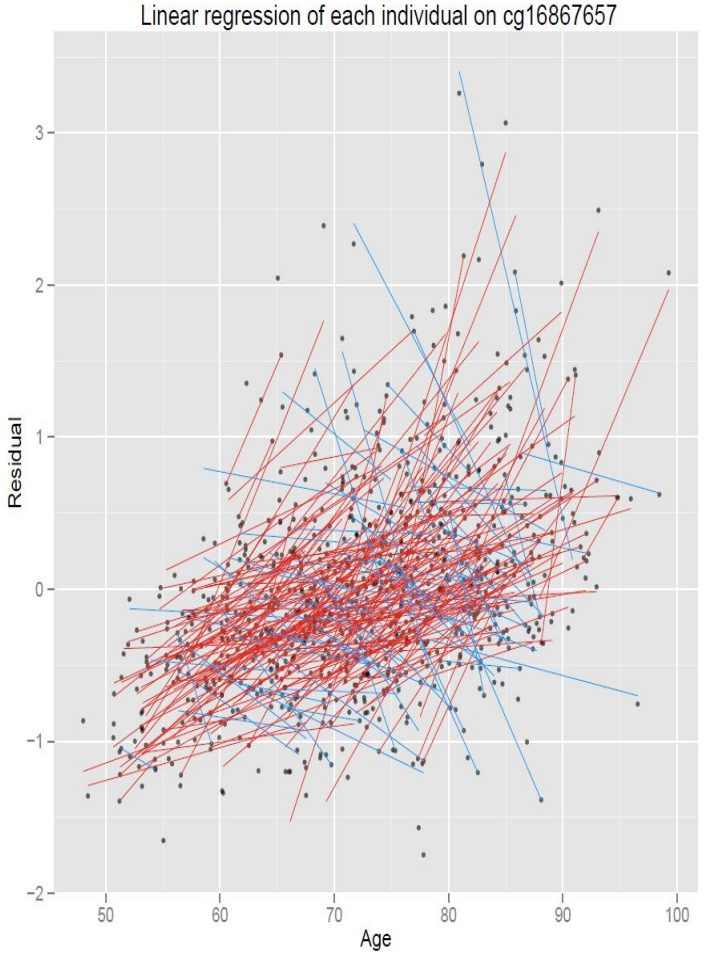
Longitudinal vs Cross-sectional: lessons from telomeres



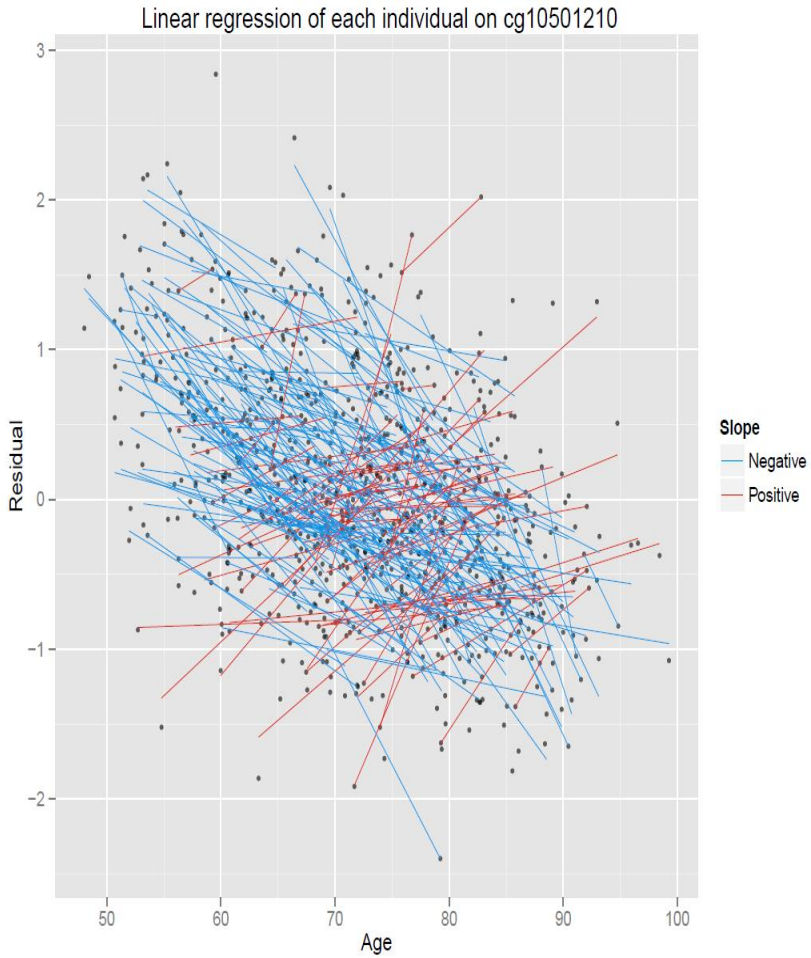


Berglund et al., 2016, *Aging*

Methylation: 2 age related sites

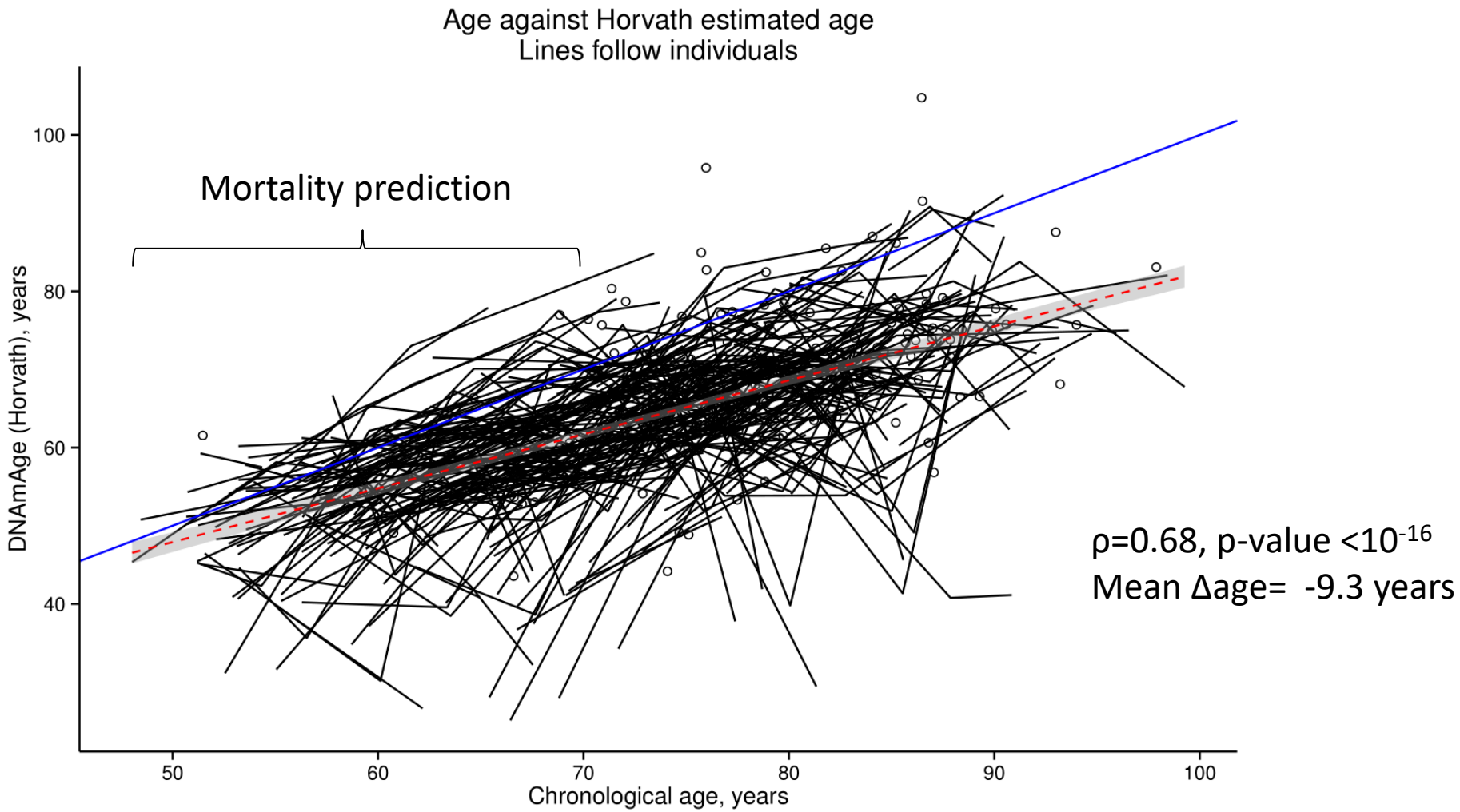


mean	Positive	Negative
0.026	205 (71.4%)	82 (28.6%)



mean	Positive	Negative
-0.027	199 (69.3%)	88 (30.7)

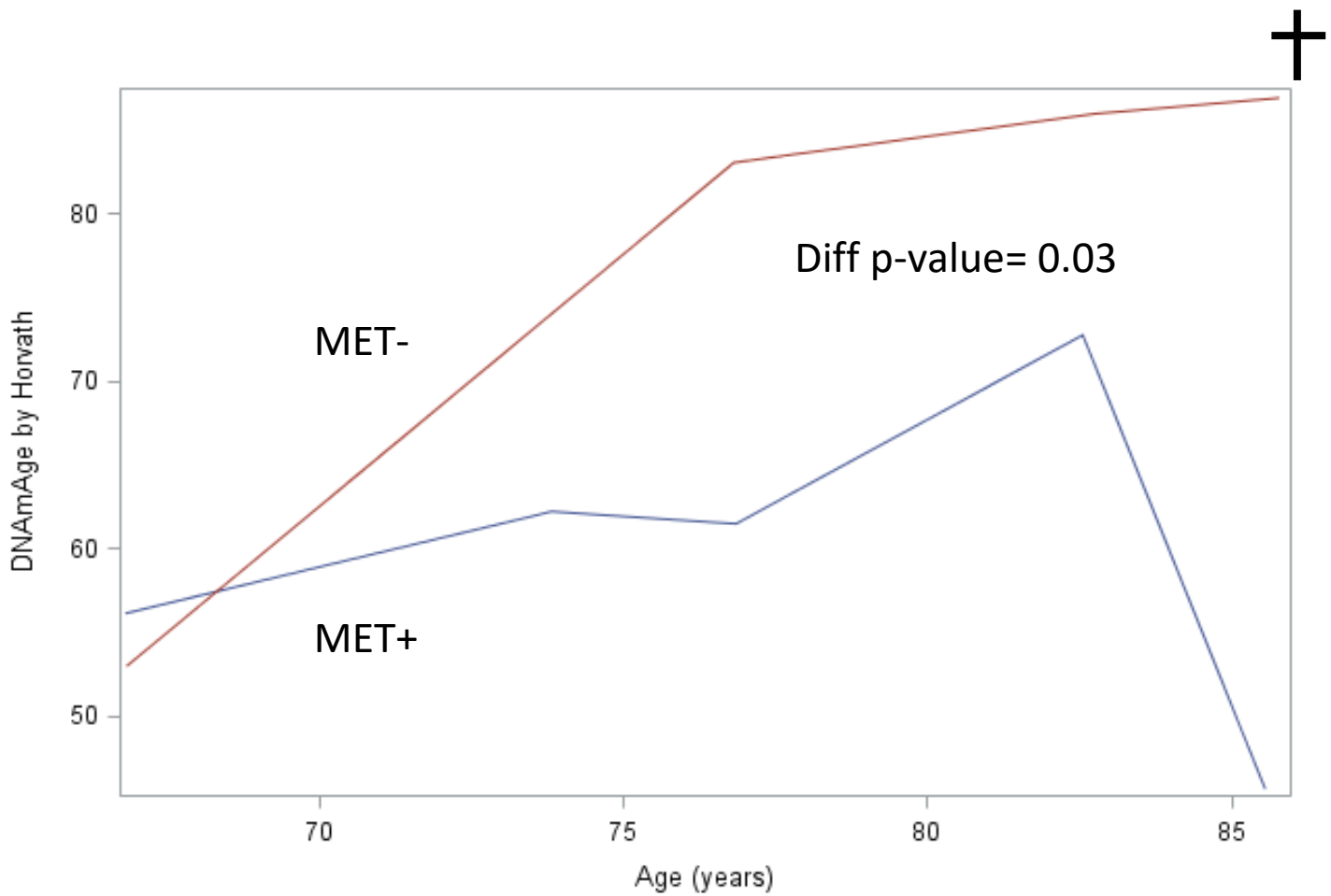
Biological age prediction: the epigenetic clock x-sectional data as basis perhaps not best?



ρ=0.68, p-value $<10^{-16}$

Mean Δage= -9.3 years

Biological age prediction in twinpair discordant for metformin treatment



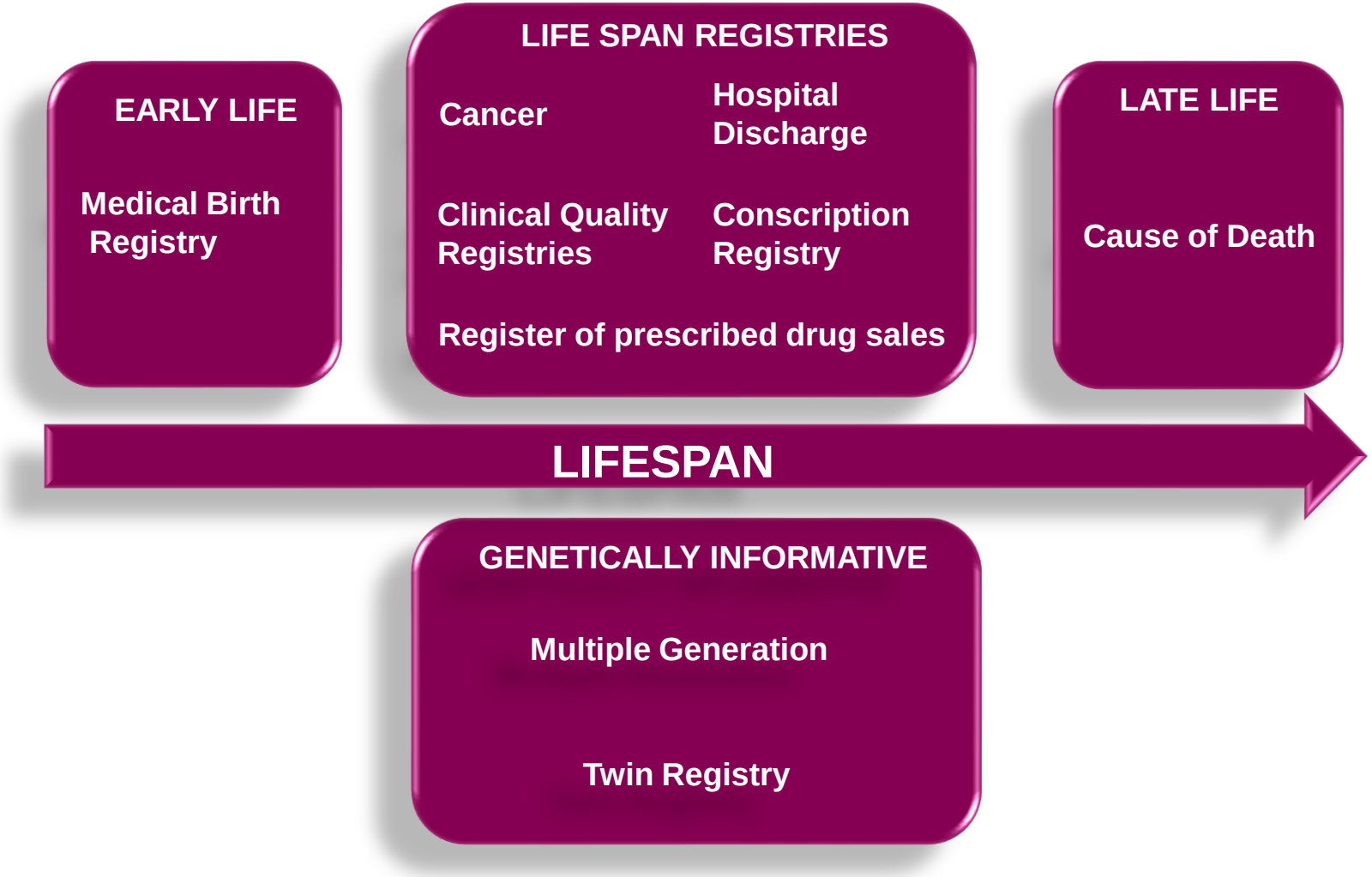
Back to important considerations

- Getting sample collection right
- Maintaining sample collections
  - Partitioning samples for various uses
    - Limiting freeze thaw cycles for some samples
    - Interest in samples from rare cases vs total population
    - ”Saving” e.g. 10-20% of samples for access after 10-20 years
  - Financial considerations
- ELSI
  - GDPR (new European regulations)
    - Original consent vs re-consent vs opt-out, etc.

Opportunities!

Just look at the cohort list for this meeting!

Nordic countries: well situated with national registries



And biobanks:
KI Biobank has become a rich source of samples

604 287 donors, 6 967 951 available samples (460 644 DNA), 183 studies
479 454 withdrawals for research (from 187 998 donors)
Some extensive cohorts…

- Swedish Twin Registry 50 000 donors
- LifeGene prospective, 0-50y, 40 000 donors
- EpiHealth prospective, 45-75y 25 000 donors
- Stockholm Prostate cancer prospective, 110 000 donors
- Karma Breast cancer prospective, 77 000 donors
- BBMRI.se sample collection register, bbmriregister.se
- + Mayo Clinic biobank cohort sharing > 50 000 donors

Thank you!

Support

- NIH
  AG 04563, AG 10175
  AG 08724, AG 08861, AG 037985
  NS 141483, ES 10758, DK 066134
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