Making sustainable, useful science at the complex intersections of genomics, environment, and health

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A. neonatal genetic testing: sustainably useful?

B. heritability: useful?

C. gene-environment interaction in psychology: useful?

D. longituidinal data collection for genetic & environmental exposures: sustainable?

A. PKU neonatal diagnosis

single gene mutation ->
retardation & early death

A. PKU neonatal diagnosis

single gene mutation
-> early diagnosis
-> effective dietary therapy

A. PKU neonatal diagnosis

single gene mutation
-> early diagnosis
-> effective dietary therapy

genetic ≠ unchangeable

A. PKU neonatal diagnosis

single gene mutation
-> early biochem diagnosis
-> dietary amelioration

plus
ongoing struggle to
- **secure health insurance coverage for diet**
- **enlist family & peer support for staying on diet**

A. PKU neonatal diagnosis

single gene mutation
-> early biochem diagnosis
-> lifelong management of chronic condition

including
ongoing struggle
secure health insurance coverage for diet
enlist family & peer support for staying on diet

and
"maternal PKU"

Open Q: Optimism re: genetic diagnosis?

B. Heritability

e.g. Heritability of IQ is 80%

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meaning?

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- **genes have more influence on IQ than environment**

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e.g. Heritability of IQ is 80%

meaning?

- ~~**genes have more influence on IQ than environment**~~
- **variation among means of genetic varieties (averaged across all locations) > variation of means of locations (averaged over all varieties)**

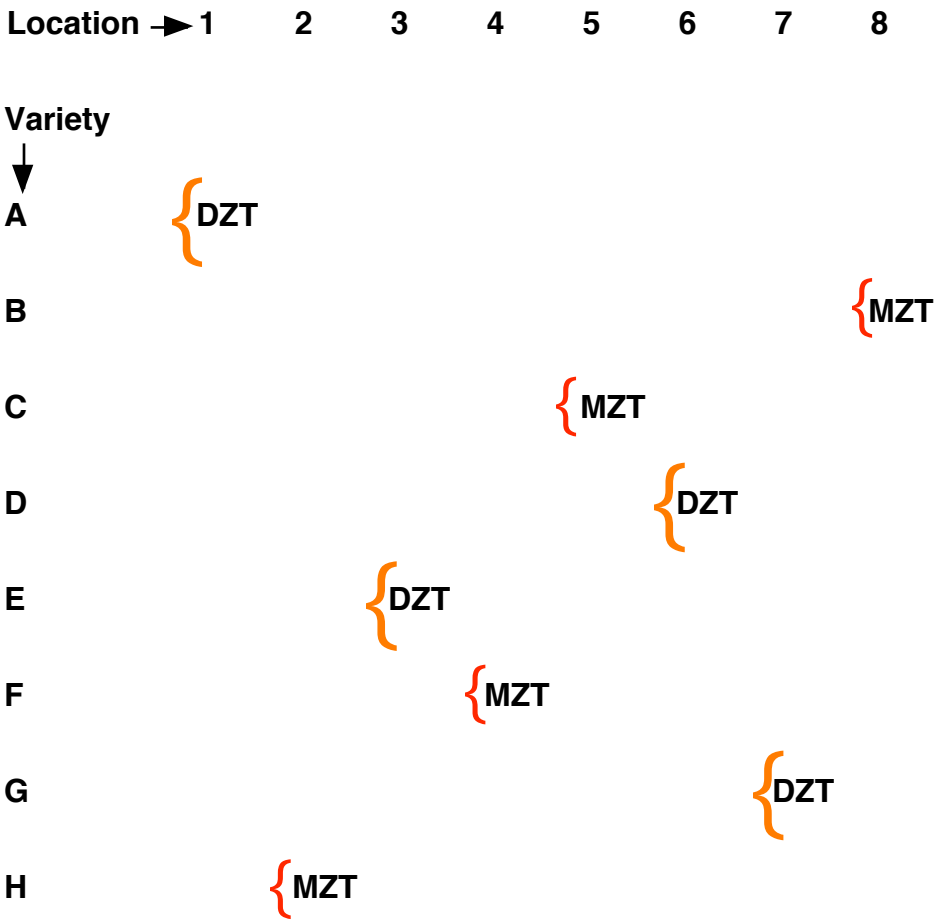
B. Heritability

e.g. Heritability of IQ is 80%

meaning?

- **identical twins are more similar than fraternal twins**

Location →	1	2	3	4	5	6	7	8
Variety ↓								
A	DZT							
B								MZT
C					MZT			
D						DZT		
E			DZT					
F				MZT				
G							DZT	
H		MZT						


Location
1
2
3
4
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6
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8
Variety
A
DZT
B
MZT
C
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D
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E
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F
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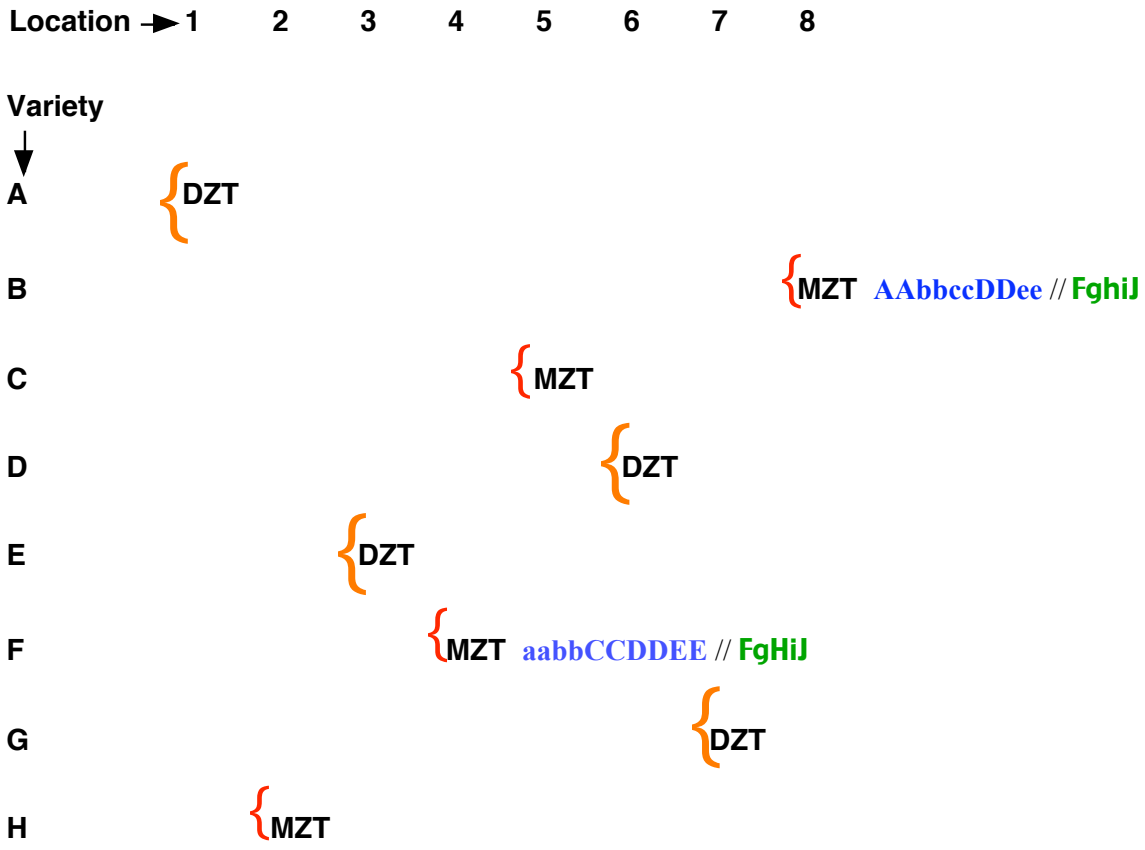

Location → 1 2 3 4 5 6 7 8
Variety
A
DZT
B
MZT AAbbccDDee // FghiJ
C
MZT
D
DZT
E
DZT
F
MZT aabbCCDDEE // FgHiJ
G
DZT
H
MZT

B. Heritability

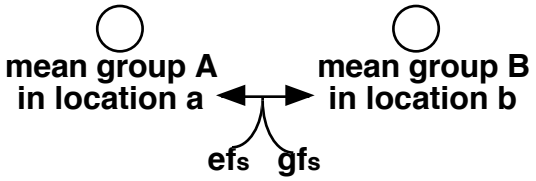
e.g. Heritability of IQ is 80%

useful?

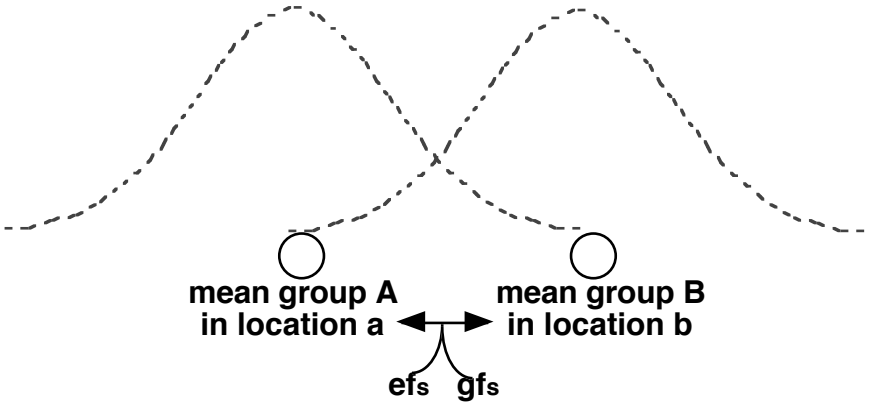
Bridge to next case

Open Q: heterogeneity overlooked—why?

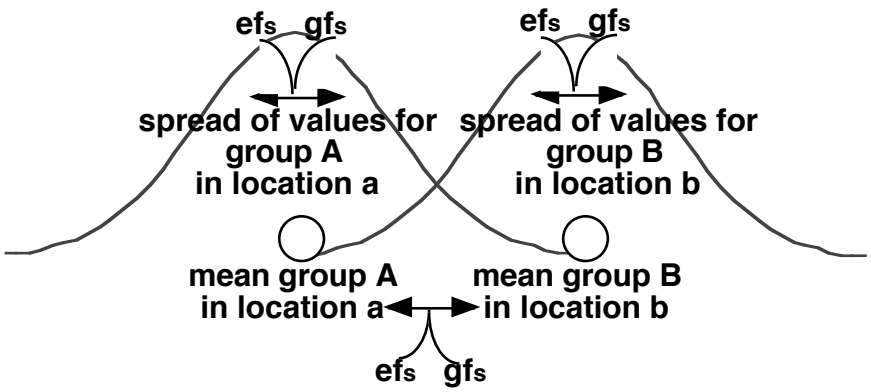
persistence of typological thinking



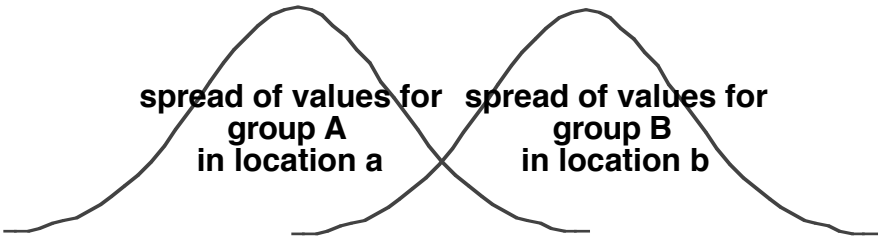
persistence of typological thinking



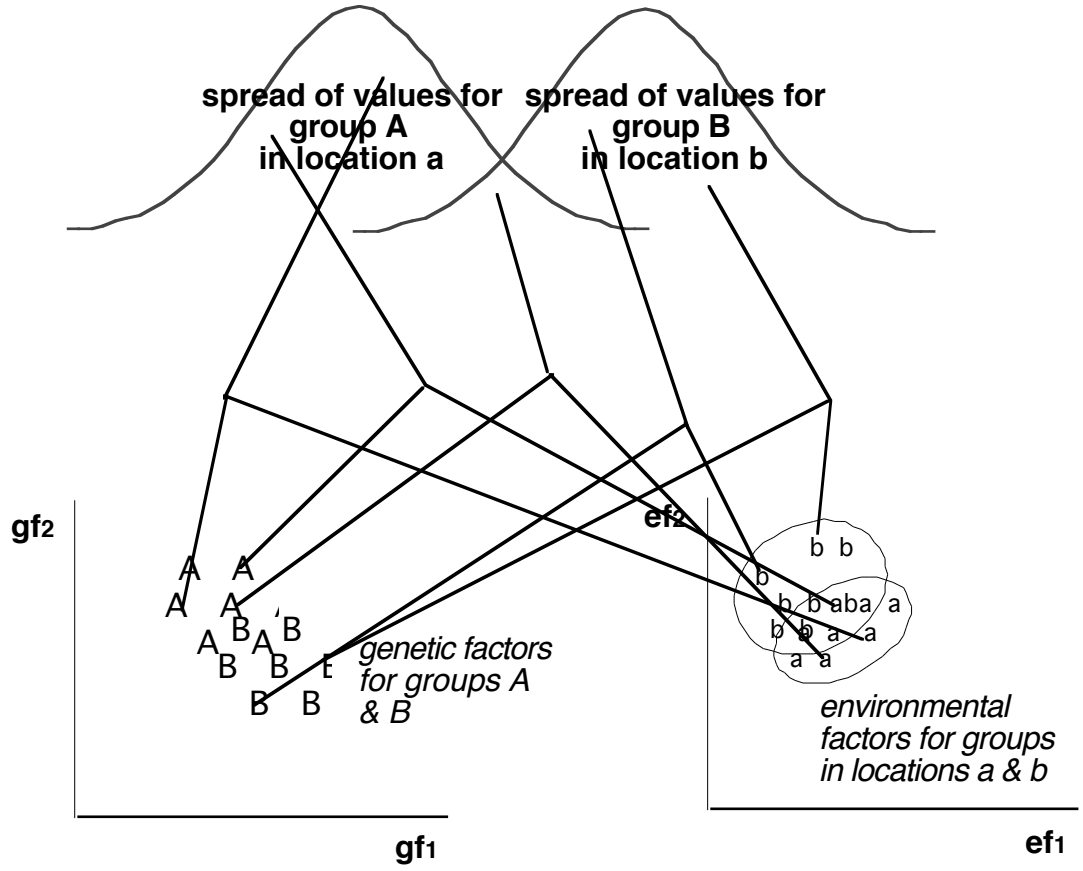
persistence of typological thinking



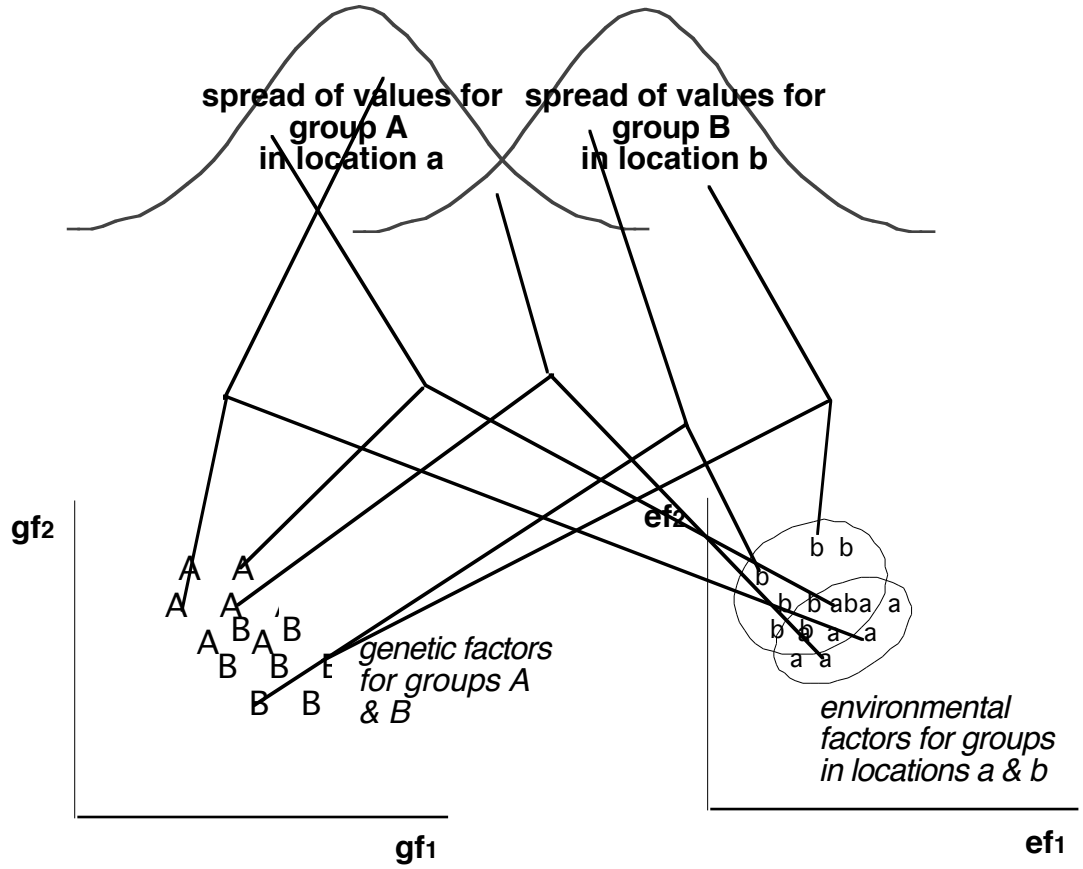
From typological thinking to recognizing possible heterogeneity



From typological thinking to recognizing possible heterogeneity



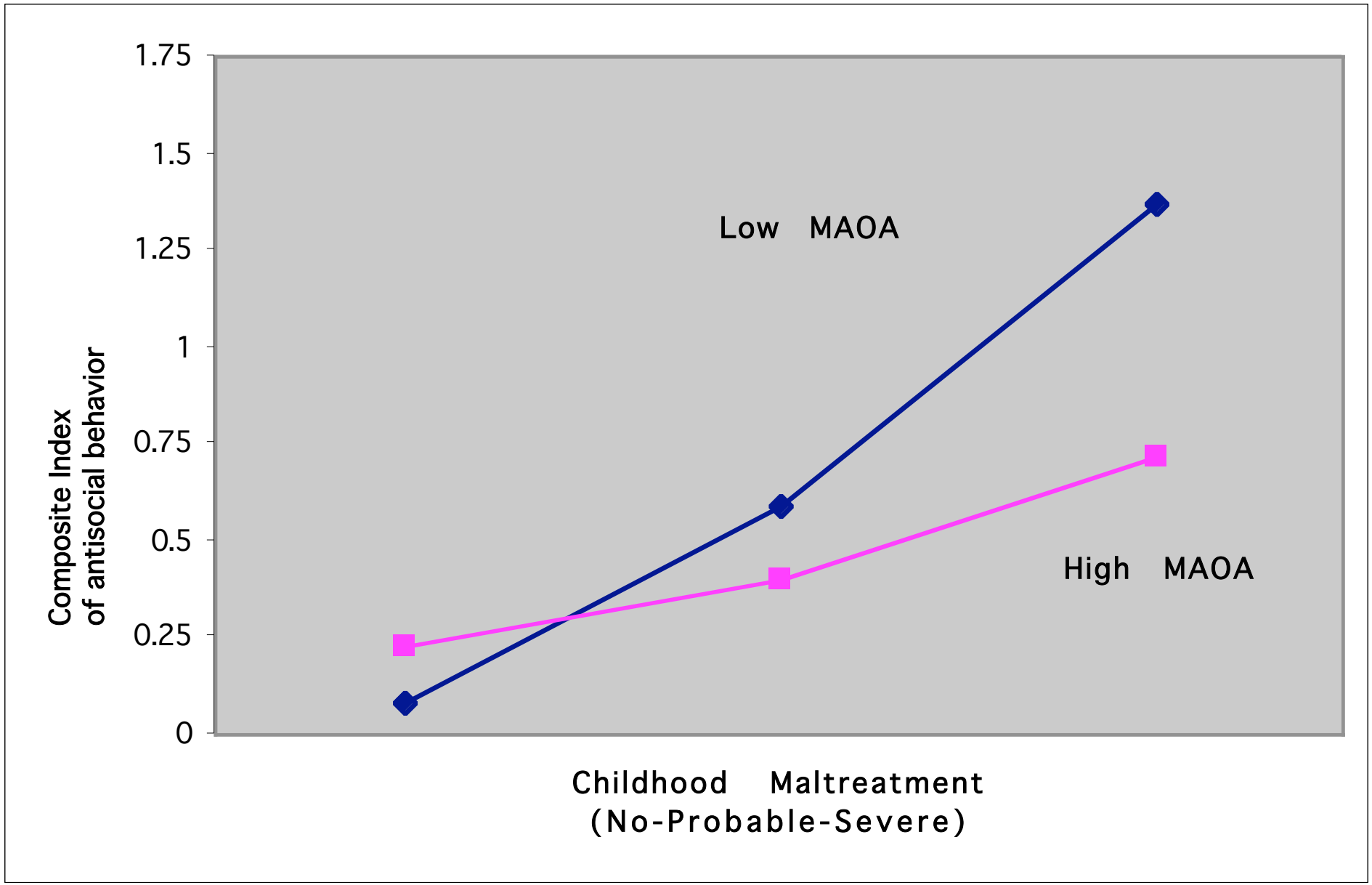
From typological thinking to recognizing possible heterogeneity



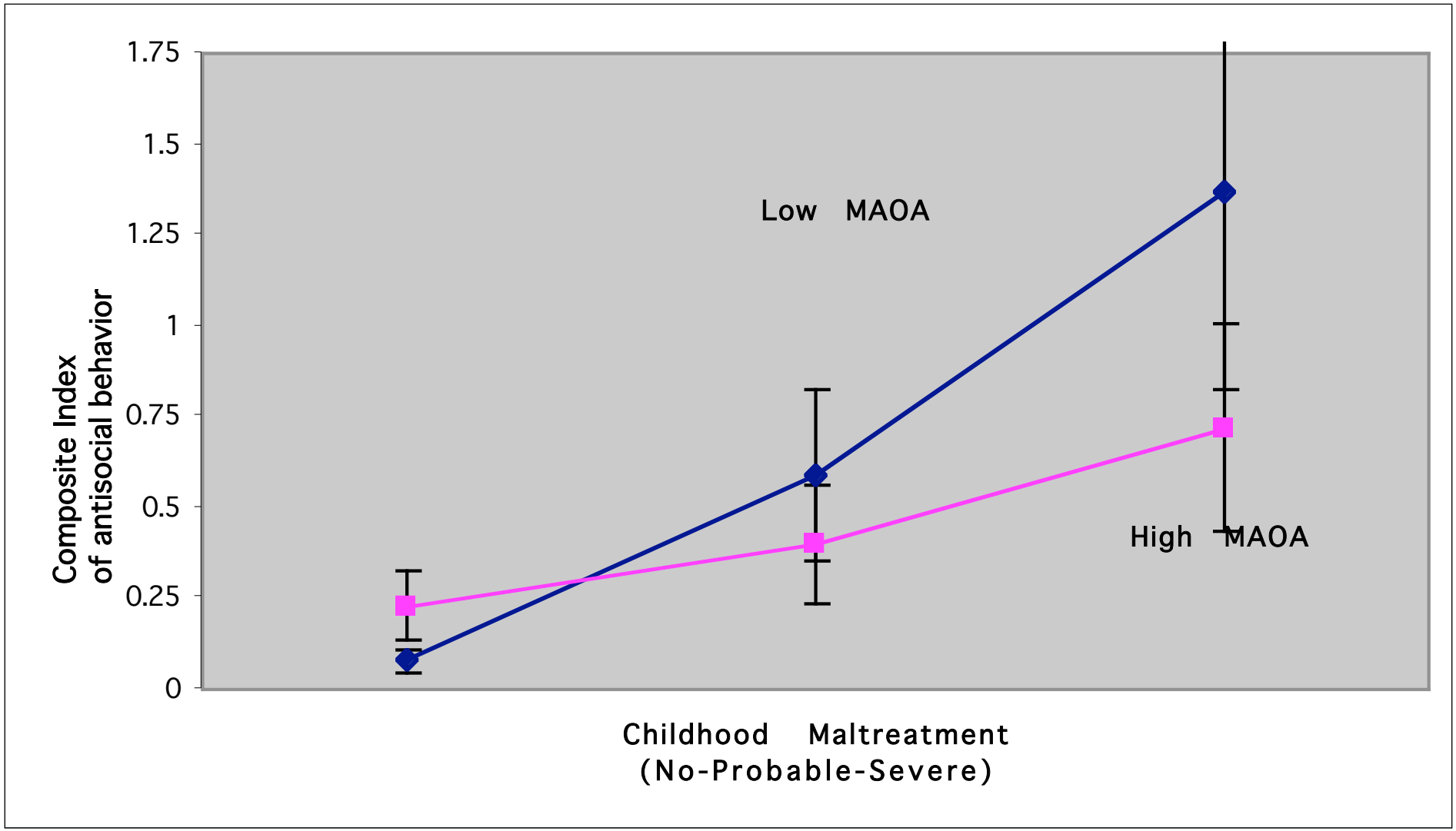
Open Qs: How to expose these factors?

C. Gene-environment interaction in human psychology

Caspi, A., et al. (2002)
"Role of Genotype in the Cycle of Violence in Maltreated Children."
Science 297: 851-854.


1.75
1.5
1.25
1
0.75
0.5
0.25
0
Composite Index
of antisocial behavior
Low MAOA
High MAOA
Childhood Maltreatment
(No-Probable-Severe)

Childhood Maltreatment	MAOA	
	low	high
No or Probable	low anti-social	low anti-social
Severe	HIGH ANTI-SOCIAL	low anti-social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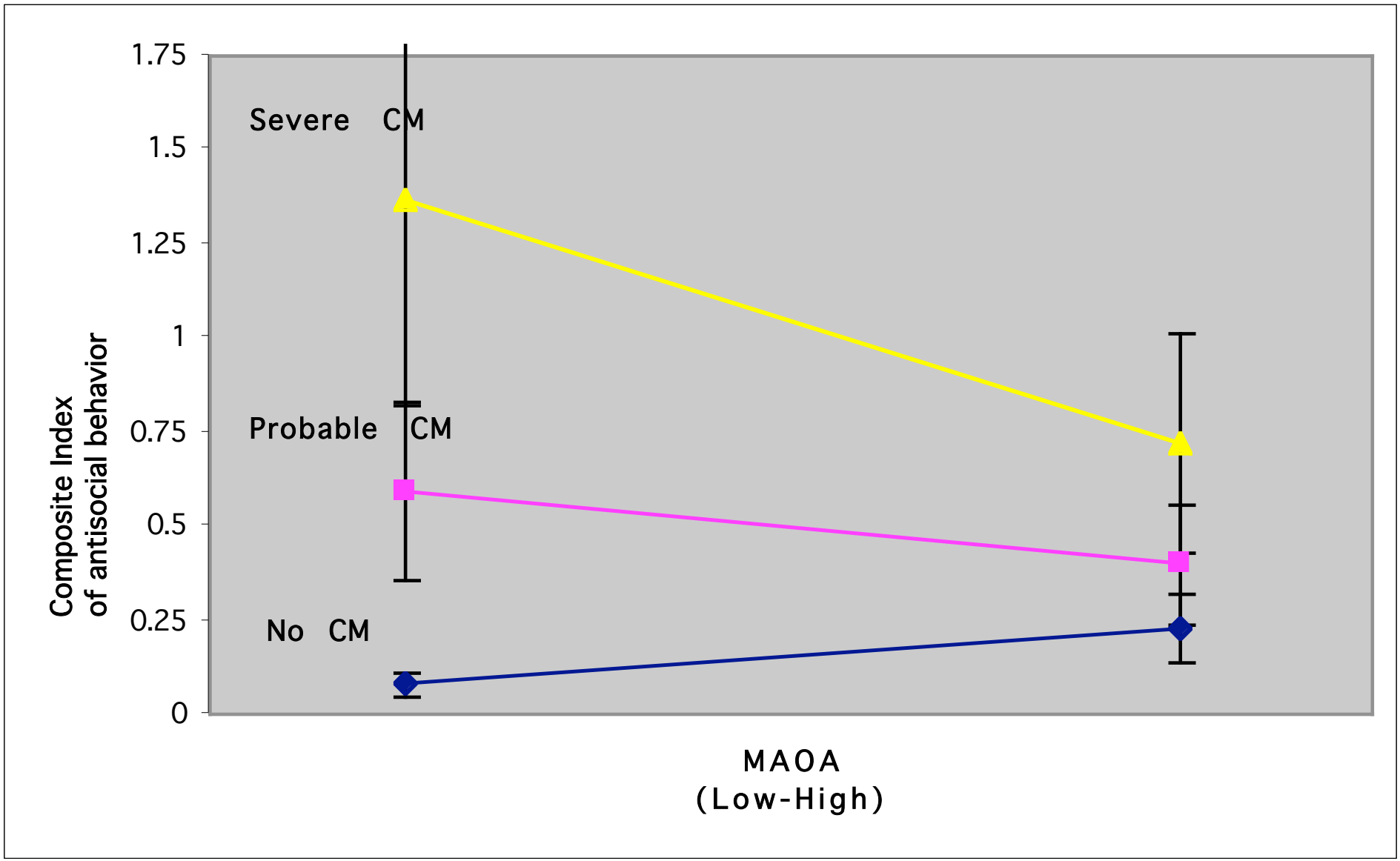

1.75
1.5
1.25
1
0.75
0.5
0.25
0
Severe CM
Probable CM
No CM
Composite Index
of antisocial behavior
MAOA
(Low-High)

Open Qs:
Can genome-typing be useful for:

* public policy?
* personalized therapy?

D. Longituidinal data collection for genetic & environmental exposures

A Tale of (More Than ?) Two Cohorts – from Canada

By **Dr. John Frank, Scientific Director,**
CIHR-Institute of Population & Public Health

Professor, Dept. of Public Health Sciences,
University of Toronto

Senior Scientist, Institute for Work and Health,
Toronto

November 16 -19, 2005

CIHR IRSC

Canada

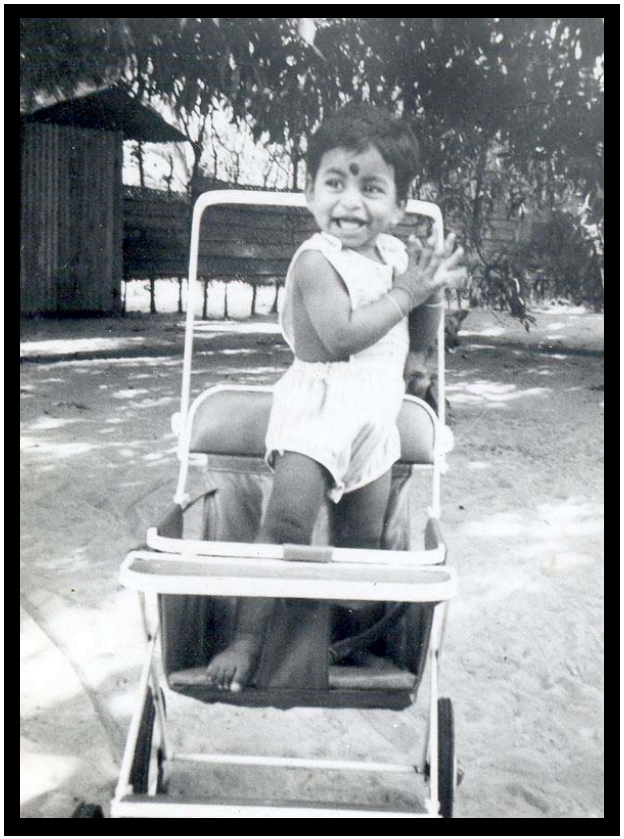
Why study gene-environment interactions?

- Most disease burden is jointly determined by interaction of individual genetic endowments and complex sequence of environmental factors
- These gene-environment interactions require decades to fully manifest over the life course
- Diseases and conditions of later life occur in some and not others because of intense interactions between particular genetic constitutions and particular sequence of social and physical environments

CIHR IRSC

Canada

Why study gene-environment interactions? cont'd



- BUT…little is known about underlying causes of these conditions and why they are now increasing in frequency – for e.g. asthma
- Requires study of these sequential events in large numbers of people over time, on whom baseline genetic and repeated environmental exposures are taken, to:
  - understand the causal pathways; and,
  - develop disease prevention strategies

Studying Genetic and Environmental Contributions to Disease Causation: An Uneven Playing Field

Measurement Attribute	Genetic Exposure Measures	Environmental Exposure Measures
Time-varying?	No – one sample per lifetime is enough (unless gene expression arrays are used)	Yes – new samples needed whenever exposure changes
Data Collection Costs	Cheap (on a sample)	Expensive (real-time assays)
Sample Storage (for later analysis)	Easy (buccal swab, buffy coat)	Difficult (e.g. air/water/diet samples)
Data Analysis Costs	Getting cheaper by the day	Getting Costlier (as awareness of chemical/physical/biological complexity increases)
Overall Ease & Cost of Accurate Ascertainment	**Easy / Cheap**	**Difficult / Costly**

Comparison of "Huge, Data-Thin" Cohorts (e.g. U.K. BioBank) And "Small, Data-Thick" Cohorts (e.g. Southampton)

Cohort Attribute	Huge – Thin	Small – Thick
Cost Per Subject due to:	Low (e.g. < $500. / data-wave)	High (if > $1,000. / data-wave)
Sample Size due to choice of:	500,000+	< 30,000
Exposures	Cheap-to-collect/store measures – e.g. genetic	Expensive, balanced mix of environmental and genetic measures
Outcomes	Cheap-to-collect administrative data – e.g. hospitalizations for diagnoses/deaths (dichotomous) → ↑ **SS.**	Expensive, directly measured bi-chemical physiologic, imaging, functional outcomes (often continuous) → ↓ **SS.**
Leading "Exposure-Measure Bias"	Large environmental exposure error >> genetic factor errors	"Better balanced errors" for environmental versus genetic factors
Leading to:	**Biased main effects and interaction results**	**Less biased results**

Asymmetry political, economic & cultural as well as technical

roots for real
your ancestry discovered

HOME

Your Ancestral Motherline

Would you like to find out from which people your personal maternal lineage is descended?

Most of us can trace our family history for a few generations - possibly down to our great-great-grandparents - but certainly not thousands of years into the distant past, when Europe and other continents were settled by prehistoric tribes and peoples.

Others of us have little knowledge of even fairly recent ancestors and suspect that they may hark from an exotic land - but until now have had no way of knowing for sure.

As shown in the BBC's documentary "Motherland - A Genetic Journey" and PBS's recent film "African American Lives" modern genetics shows us a way to address these questions. In the genetic material in each of us, a mass of historic information is encoded, with which experts can for the first time gain clues to our past ancestors. Over the last ten or so years, groundbreaking work by geneticists has shown that mitochondrial DNA (mtDNA) - which is passed from mother to child unaltered for many generations - is a very reliable tool for discovering personal family history.

The Roots for Real mtDNA tracing service uses a small sample of your mtDNA - easily obtained by a simple home saliva test. With it, we match you to people around the world who share your own very specific motherline - people who are in effect distant cousins. The Roots for Real service is based on up-to-date genetic knowledge and processes, is carried out in highly qualified laboratories, and uses the largest available global geographic database of human mtDNA.

National cohort studies

-> Q: overcoming these asymmetries?

National cohort studies

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Extensions of scorecard.org?

Scorecard
THE POLLUTION INFORMATION SITE

Investigate Pollution Topics

TOXICS
- Toxic Chemical Releases
- Lead Hazards
- Superfund

AIR
- Smog and Particulates
- Hazardous Air Pollutants

WATER
- Clean Water Act
- Watershed Indicators

AGRICULTURE
- Animal Waste

ENVIRONMENTAL JUSTICE
- Community Center
- En Español

HEALTH HAZARDS
- Chemical Profiles
- Health Effects
- Regulations

ZIP TO YOUR COMMUNITY
GO

SEARCH SCORECARD
GO

Pollution in Your Community

Get an in-depth pollution report for your county, covering air, water, chemicals, and more.

Your Zip Code: GET REPORT

More Facts on Pollution

Get answers to the most commonly asked questions on nationwide pollution.

- Who's polluting?
- What pollutants do the most harm?
- Where is the worst pollution?
- Compare communities and states.
- Search by company, location, or ch

Take Action: Oppose EPA's efforts to weaken pollution reporting

Tell EPA not to weaken pollution reporting!

We think American citizens have a right to know what toxic chemicals are being released into their communities. But the EPA recently proposed to limit the information that companies are required to disclose about the hazardous chemicals they release into our environment. By reducing the reporting requirements of its Toxics Release Inventory program, the EPA would take away an important tool for protecting public health and reducing industrial pollution.

There is no justification for weakening this successful program, other than to please

USE THIS INFORMATION

Learn how Scorecard visitors use this information to protect and educate their communities.

WAYS YOU CAN HELP

- Tell EPA not to weaken pollution reporting!
- Email this page to a frien
- Sign up for email update

Your Email Address:

SIGN UP

ABOUT THIS SITE

Find out more about Green Media Toolshed, which sponsors Scorecard. By giving a donation, you will suppo information and action for a cleaner environment.

Scorecard.org

builds on various laws & government-mandated databases

-> Open Q:

prospects for epidemiologically relevant information being sustained?

Extensions of scorecard.org

longituidinal

Extensions of scorecard.org

- longituidinal
- interface with local organizing

  -> grassroots pressure to sustain environmental data collection & centralized data bases?

  -> Open Q: "self-surveillance"?

-> Open Q: agent-oriented focus in social epidemiology?

traditional emphasis on exposures impinging on subjects

->

elucidate people's resilience and reorganization of their lives and communities in response to social patterns

Critical and constructive roles of social studies of science

Highlight or Open Questions

-> Open Q:

How to engage w/ scientists?

Open Qs:

Optimism re: genetic diagnosis?

Heterogeneity overlooked—why?

How to expose heterogeneous factors?

Can genome-typing be useful for:
*** public policy?**
*** personalized therapy?**

Prospects for epidemiologically relevant information being sustained?

Longituidinal "self-surveillance"?

Agent-oriented focus in social epidemiology?

How to engage scientists on open Qs?

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How to engage scientists on open Qs?

Qs, Insights, Discussion points:
On paper // Pair-share // Whole group discussion