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Troubled by Heterogeneity?

*Control, Infrastructure & Participation in Social
Epidemiology and Life Course Development*

PETER J. TAYLOR

Troubled by Heterogeneity? Control, Infrastructure and Participation in Social Epidemiology and Life Course Development

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This working paper presents the panels of a poster prepared for a conference, “Complex Systems, Health Disparities, and Population Health: Building Bridges,” held at NIH in Bethesda, MD in February 2014. Just as poster presenters hope viewers stop and talk, my aim in sharing the panels as a working paper is to elicit more conversation about different kinds of heterogeneity and the ways they are addressed or suppressed in social epidemiology and life course development. The thinking behind this concern is as follows. The two foundational developments of modern biology—the theories of evolution by natural selection and the genetic basis of heredity—were built from language, arguments, evidence, and practices of controlled breeding in agriculture and the laboratory. The relationship between variation, particularity, or, more generally, heterogeneity and control provides an under-developed angle from which to view modern understandings of heredity and development over the life course and, more generally, in social epidemiology. My guiding contention is that research and application of resulting knowledge are untroubled by heterogeneity to the extent that populations are well controlled. Such control can be established and maintained, however, only with considerable effort or social infrastructure, which invites more attention to possibilities for participation instead of control of human subjects.

Troubled by Heterogeneity?
Control, Infrastructure &
Participation in Social
Epidemiology & Life Course
Development

Copies of panels as pdf at <http://bit.ly/TbHFeb14>

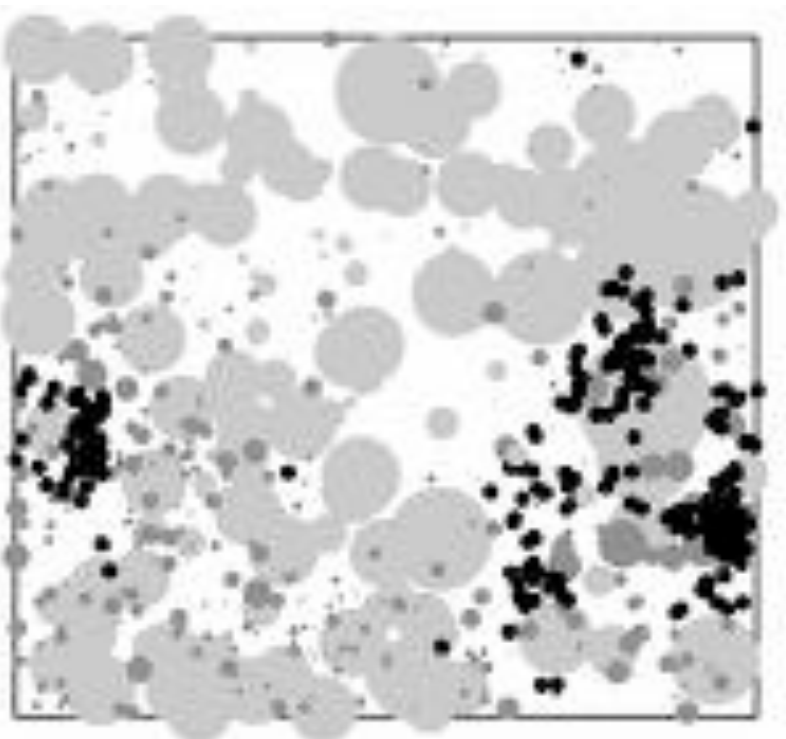
Further discussion welcome--

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*Where do YOU see
heterogeneity as an issue in
health disparities research
and politics?*



“It depends on what you mean by heterogeneity...”

OK ->

A. See taxonomy below

B. Read 1+ vignettes

illustrating some of the heterogeneities listed

C. Discuss with author

Overview

The two foundational developments of modern biology—theories of evolution by natural selection and genetic basis of heredity—were built from language, arguments, evidence, and practices of *controlled* breeding in agriculture and the laboratory.

-> The relationship between *variation*, *particularity*, or, *heterogeneity* and *control* provides an under-developed angle from which to view modern understandings of heredity and development over the life course and, more generally, in social epidemiology.

Guiding contention:

Research and application of resulting knowledge are untroubled by *heterogeneity* to the extent that populations are well *controlled*.

Such control can be established and maintained, however, only with considerable effort or *social infrastructure* -> invites more attention to possibilities for *participation* instead of *control* of human subjects.

This poster = taxonomy of *heterogeneities* + illustrations, raising issues about *addressing* or *suppressing* heterogeneity in social epidemiology and life course development.

Taxonomy of heterogeneities (=complexities to be addressed in theory & practice)

Static	<ol style="list-style-type: none"> 1. There is an <i>assortment</i>, each a separate type ("cabinet of curiosities") 2. <i>Mixture</i> of types (e.g., allelic heterogeneity & locus heterogeneity in genetics) 3. Trait = <i>composite</i> of types (analogy: the 3 components of a triathalon)
Variational	<ol style="list-style-type: none"> 4. There is noise or error, but that is <i>deviation from the type</i> or essential trajectory 5. Variation in a set of traits involves a <i>composite of variance/covariance structures</i> (statistical heterogeneity)
	<ol style="list-style-type: none"> 6. There is <i>variation, not types</i>
Dynamic	<ol style="list-style-type: none"> 7. <i>Possibility of underlying heterogeneity</i>: When similar responses of different individual (e.g., genetic) types are observed, it is not necessarily the case that similar conjunctions of risk or protective factors have been involved in producing those responses 8. Variation produces <i>qualitative changes in results</i> from standard theory based on uniform units (e.g., theory about Malthusian population growth, tragedy of the commons, prisoner's dilemma)
	<ol style="list-style-type: none"> 9. Heterogeneity in <i>pathways of development</i> Variants, from Taylor (2005): <ol style="list-style-type: none"> 9a. <i>Intersecting processes</i>--Processes operating at different spatial and temporal scales that cut across the boundaries of the situation under consideration and restructure its "internal" dynamics. 9b. <i>Unruly complexity</i>--arises whenever there is ongoing change in the structure of situations that have built up over time from heterogeneous components and are embedded or situated within wider dynamics. 9c. <i>Heterogeneous construction</i>--researchers establish knowledge and technological reliability through practices that are developed through diverse and often modest practical choices. This is the same as saying the researchers are involved in contingent and ongoing mobilizing of diverse materials, tools, people, and other resources into webs of interconnected resources.
Dynamic-participatory	<ol style="list-style-type: none"> 10. <i>Participatory restructuring</i> of the dynamics (intersecting processes, unruly complexity, or heterogeneous construction) that generated the data.
	<ol style="list-style-type: none"> 11. <i>Transversal engagement</i>--Participatory restructuring through multiple points of engagement, occurring in tension with deployment or withholding of trans-local knowledge and resources.

Heterogeneity #1

An assortment

In an essay on "The Analytical Language of John Wilkins," Borges (1964) mentions a "doctor Franz Kuhn" referring "to a certain Chinese encyclopaedia entitled 'Celestial Empire of benevolent Knowledge'. In its remote pages it is written that the animals are divided into: (a) belonging to the emperor, (b) embalmed, (c) tame, (d) sucking pigs, (e) sirens, (f) fabulous, (g) stray dogs, (h) included in the present classification, (i) frenzied, (j) innumerable, (k) drawn with a very fine camelhair brush, (l) et cetera, (m) having just broken the water pitcher, (n) that from a long way off look like flies."

(http://alamut.com/subj/artiface/language/john_wilkins.html. Michel Foucault brought attention to this passage in Borges in the opening to his The Order of Things.)



Heterogeneity #2, Mixture of types

Cases: PKU, Rats, Aspirin, CCTV, Genetic & Allelic heterogeneity, Life Events & Difficulties

If the population in question contains a mix of different types that are identified and separable, then identification of a subject's type allows them to be treated or investigated separately and differently.

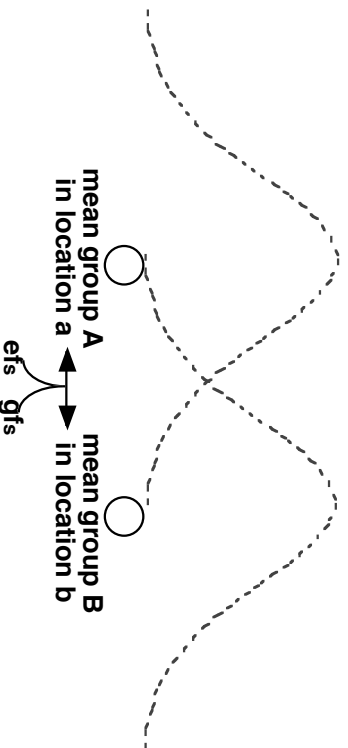
- Phenylketonuria (PKU) is a condition associated with a single genetic locus, but there are different mutations within that locus. People with PKU are a mix of people with different mutations or genetic subtypes.
- "Maternal PKU" arises when a fetus gestates in high-phenylalanine conditions that occur when a PKU mother was not **insufficiently compliant** with the diet (where compliance may be influenced by a variety of factors; see #9a). If maternal PKU is considered a form of PKU, then the population of children with the deleterious symptoms of PKU is a mix of those with a genetic condition that was not followed by the special diet and those without the genetic condition who have.
- A certain population of light-eyed, yellow rats consisted of two strains, each bred separately from some ancestral founding group. The "two strains of light-eyed, yellow rats, each of which bred true by itself... produced nothing but black-eyed rats when crossed with each other" (Wright 1920, 37). (If each strain had been bred in the same, **uniform laboratory conditions**, this would seem to be a case of different kinds of genetic factors producing light-eyes for the two strains in those conditions.)

- The protective effect with respect to heart disease and stroke of taking a daily low dose of aspirin differs on average for men and women. This means the human population can be treated as a mix of female and male types with respect to the protective effects of aspirin. However, **9% of the patients** in one study appeared "resistant," i.e., their samples didn't show the typical blood-thinning effects of aspirin, meaning that the male and female types are heterogeneous with respect to resistance. In practice, these sub-types are costly to identify and this is rarely done (Eikelboom 2003). Note: It is also possible that the heterogeneous factors underlying the sub-types overlap, that is, the male and female types (which were based on differences on average) can eventually be resolved into a number of types not unique to males or females.
- Evaluations of Closed Circuit television (CCTV) as described by Tilley (2000) might be subject to a meta-analysis. However, such an analysis would **mix together** studies of situations in which **different mechanisms** (or a mix of mechanisms) and **different contexts** apply (as Tilley's list indicate). What meaningful recommendation could emerge from the meta-analysis, even if all results were in the same direction?
- In genetics, homogeneity may be on the surface only, e.g., when it is discovered that **different genetic conditions are expressed as the "same" clinical entity**. Conversely, the clinical expression of mutations at a single genetic locus can vary significantly from one person to the next (Kaplan 2000, 18). This may be because the mutations are at different points within the locus or because the same genetic condition develops in different genetic and environmental contexts, i.e., the other genetic and environmental factors vary among the people.
- In medical sociology Brown and Harris (1989) often find common meaning among subjects' different types of experience. In other words, Brown and Harris code sameness despite surface **heterogeneity**.

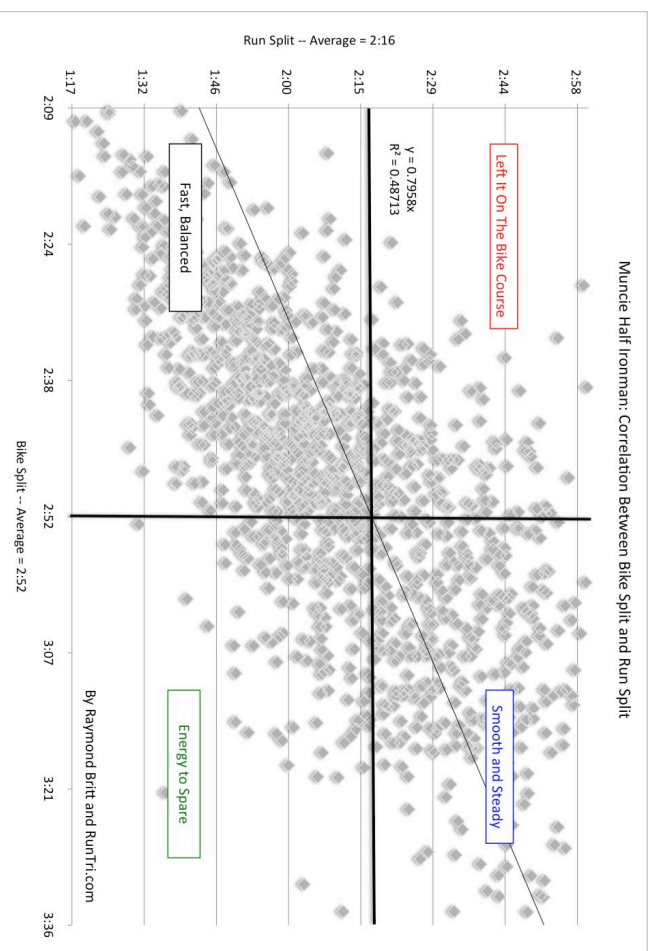
Heterogeneity #4, Deviation from the type

Case: Athletics

There is noise or error, but that is deviation from the type or essential trajectory



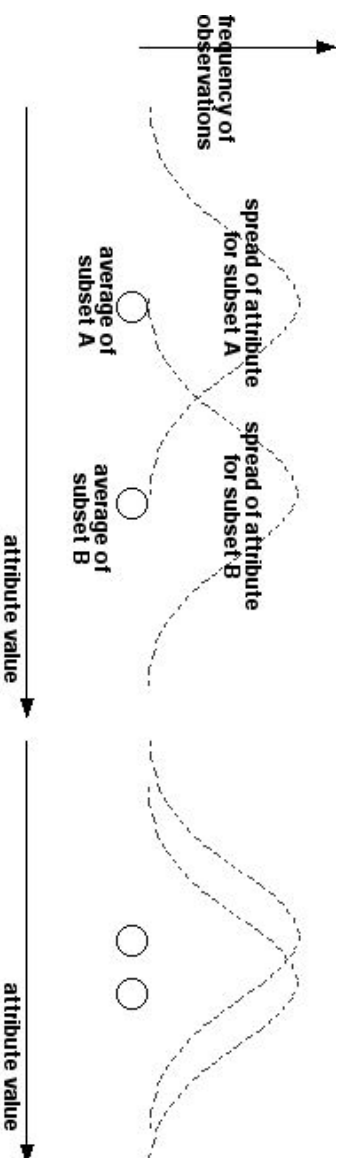
difference in means explained by efs (environmental factors) and gfs (genetic factors)



source:
<http://www.runtri.com/2011/07/muncie-half-ironman-703-results.html>

Heterogeneity #4, Deviation from the type

Statistical analysis rests on a simple kind of heterogeneity, namely, **variation around a mean.**



- Statistical comparison => you are more likely to doubt that subsets A and B are from the same population in the left hand situation than in the right hand one.
- If you doubt that the subsets are from the same population, investigate further, drawing on other knowledge about the subsets. You hope to expose the causes involved and then take action informed by that knowledge about the cause.
- Variation around a mean is not a strong sense of heterogeneity. The emphasis above is on the means (the circles) more than the variation (the dashed curves). Statistical analysis distinguishes types (or decides they are not distinguishable) more than it explores the variation (or error, i.e., deviation from type).

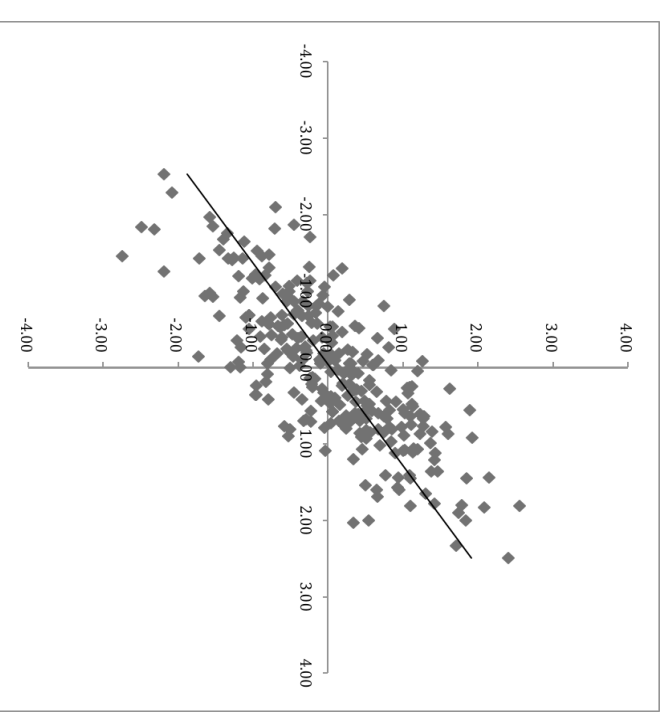
Heterogeneity #4

Deviation from the type or essential trajectory

Cases: Correlation, regression

Here the emphasis lies more on **prediction** than **variation**, as if, as a generalization of the emphasis in t-tests on types, the line or curve of prediction captured the *essential trajectory* of the data (McLaughlin 1989). (Everyone knows that correlation is not causation, but most of us interpret regressions in a causal spirit.) An alternative view of correlation and regression keeps our attention on the variation: Correlation is not only the slope of the regression line when the two measurements are scaled to have equal spread. It also measures how tightly the cloud of points is packed around the line of slope 1 (or slope -1 for a -ve correlation). When both measurements are scaled to have a standard deviation of 1, the average of the squared perpendicular distance from the points to the line of slope 1 (or -1) is equal to 1 minus the absolute value of the correlation (Weldon 2000). The larger the correlation, the tighter the packing. This tightness-of-packing view of correlation affords no priority to one measurement over the other and that reminds us that additional knowledge always has to be brought

in if the patterns in data are used to support causal claims or hypotheses.



The tightness of packing view of regression for continuous variables can be extended to multivariate associations through Principal Component Analysis, factor analysis, etc.

Heterogeneity #4, Deviation from the type

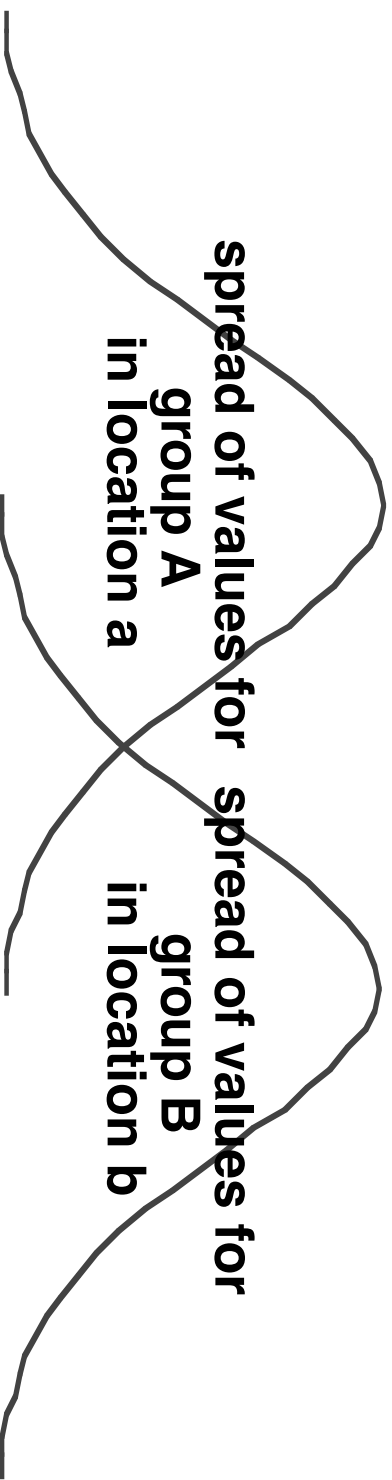
Cases: Dental health, Average Racial IQ test score gap

How do researchers negotiate tension b/w analyses & action based on averages for groups or populations *versus* attention to variation from those averages & heterogeneous pathways of development?

- Imagine dental health of two communities that have the same range of health problems except that the one with naturally high level of fluorides in its water supply has better than average dental health. In each community there will be variation around the average dental health. However, if the variation is small relative to the differences in the two averages, it might seem reasonable to advocate fluoridation of water supplies lacking natural fluoride. In doing so the **variation around the average** (a simple form of heterogeneity) is discounted, as are other deviations from type, such as teeth discoloration that occurs in some individuals. Public health policy-makers discount the variation because the benefits exceed the costs when summed up for the community. The policy-makers are able to do this as long as the infrastructure for water-supply fluoridation remains part of public expenditures covered by taxpayers *and* as long as individuals who bear disproportionate cost (e.g., those who teeth are discolored) do not effectively mobilize resources and allies to resist—in other words, as long as the population is well **controlled**. Opponents of fluoridation who accept the data on benefits and costs (many opponents do not; Colquhoun 1997) could still promote a **participatory alternative**: fluoride tablets to be taken by each individual, which would allow people subject to teeth discoloration to adjust the dosage or to choose to manage their dental health without fluoride. This approach is *not* preferred by most public health policy-makers, who point to lack of "**compliance**" when individuals are responsible for administering their own preventative medicines. **Participation** is seen as unreliable; **control** is more effective. Population health is the guiding idea; **variation** within the communities is not troubling (Rose 2008).

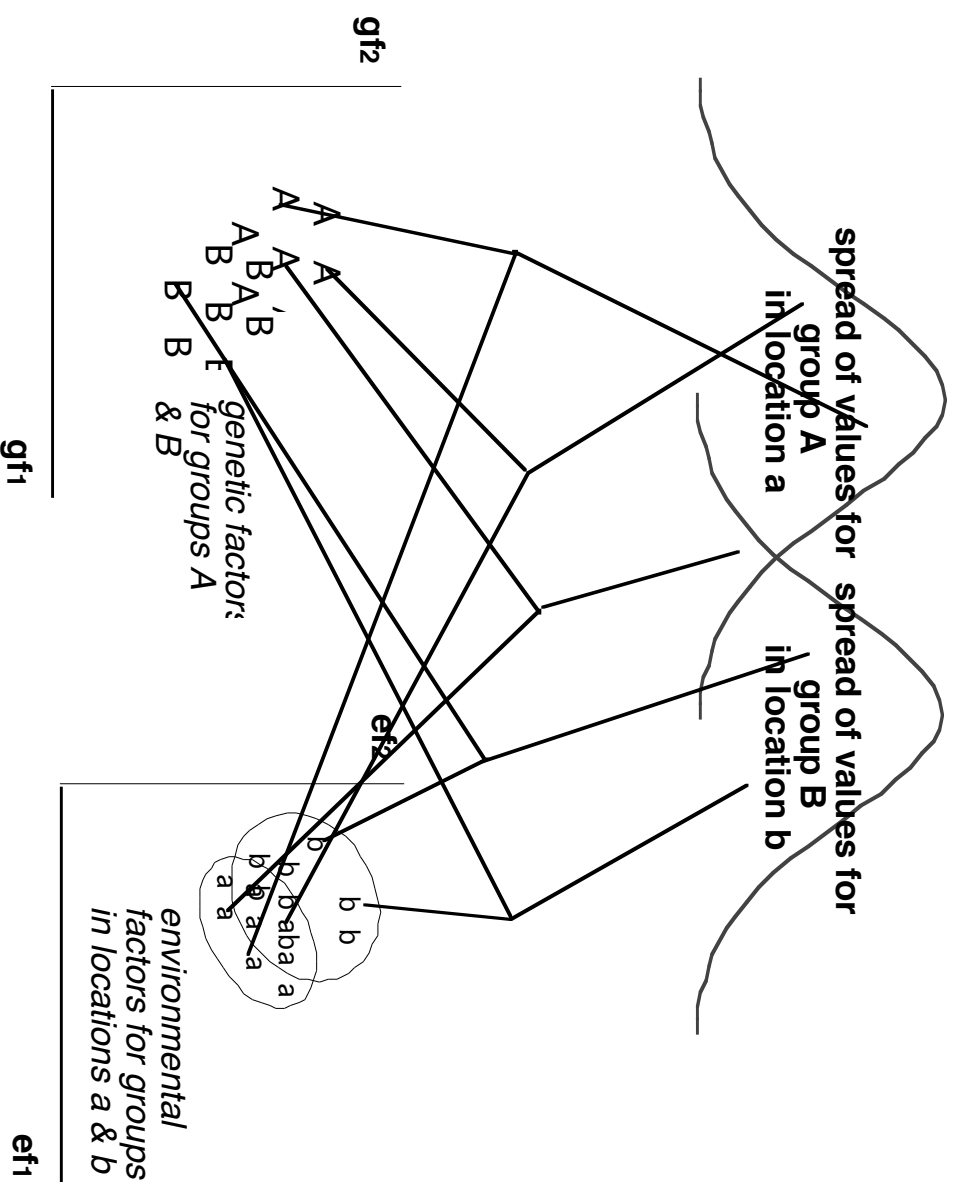
- Suppose two "racial" groups show persistent differences on average in some achievement tests ("racial" groups defined, say, by the U.S. census). By analogy with the fluoride case, we should ascribe the difference to race, i.e., to some social or biological variable(s) that differ from one race to the other. Identifying those variables not as simple as noting the presence or absence of fluoride, *but should researchers even try to find them?* What if they were to succeed?—If the variable were unalterable (say, a matter of genes), would we resign ourselves to the difference? If the variables were biologically or socially alterable, would we administer the same "antidote" to all in the lower-achieving group? What kind of social infrastructure would be involved in that? (Think here of *No Child Left Behind* measures mandated in the name of decreasing racial disparities in K-12 test results.)
 - Imagine researchers or policy-makers, unhappy with explanations and policies based on group membership, who want to shift the focus to the **heterogeneous** pathways of development of, in this case, achievement. Given the social context for such a move, these researchers/ policy-makers face troubling conundrums—How can attention be given to diversity of pathways without bolstering the fiction that racial group membership in the U.S. no longer brings social benefits and costs? *And* without providing support for initiatives trying to prohibit collection and use of racially classified information (e.g., the failed 2003 Prop. 54 in California)? At the same time, racial categories used in censuses and other surveys continue to change—as does people's identification with those categories (Hirschman et al. 2000)—yet longitudinal analysis depends on data collected under the same categories for extended time periods. In short, researchers and policy-makers concerned about **heterogeneity** within and across racial groups have to use data collected under racial categories, and, despite the shifting nature of those categories, get drawn into defending the continued collection of such data lest there be no information and thus no pattern (such as the average IQ test score differences) to push away from (Taylor 2009).

Heterogeneity #6, There is variation, not types



Heterogeneity #7, Possibility of "underlying heterogeneity"

When similar responses of different individual (e.g., genetic) types are observed, it is not necessarily the case that similar conjunctions of risk or protective factors have been involved in producing those responses. The challenge is to expose the factors and the ways they contribute to the response in question, *if that is possible*.

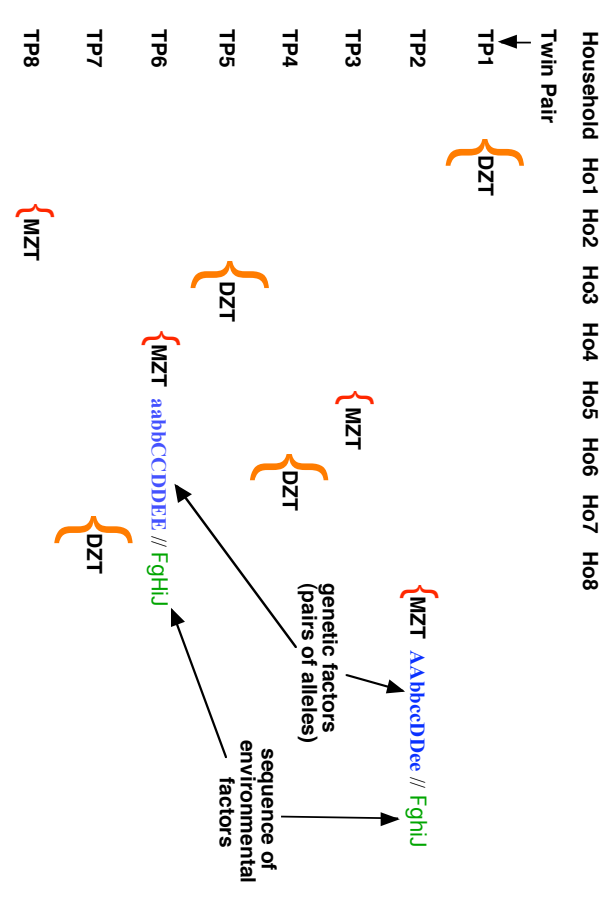


Heterogeneity #7, Possibility of "underlying heterogeneity"

Cases: Heritability, Quantitative genetics

- Studies of heritability of human traits associate similarity among mono- or di-zygotic twins etc. with similarity of (yet-to-be-identified) genes or genetic factors. The data analysis cannot rule out the possibility of factors **underlying** the development of the trait being **heterogeneous** = relatives may be similar for a given trait because they share more genes or environmental conditions than less-related individuals, but the genes and environmental conditions underlying the development of the trait *need not be the same from one set of relatives to another*. Pairs of genetic variants at a number of positions on the genome, say, AabbccDDee, subject to a sequence of environmental factors, say, Fghij, could be associated, all other things being equal,

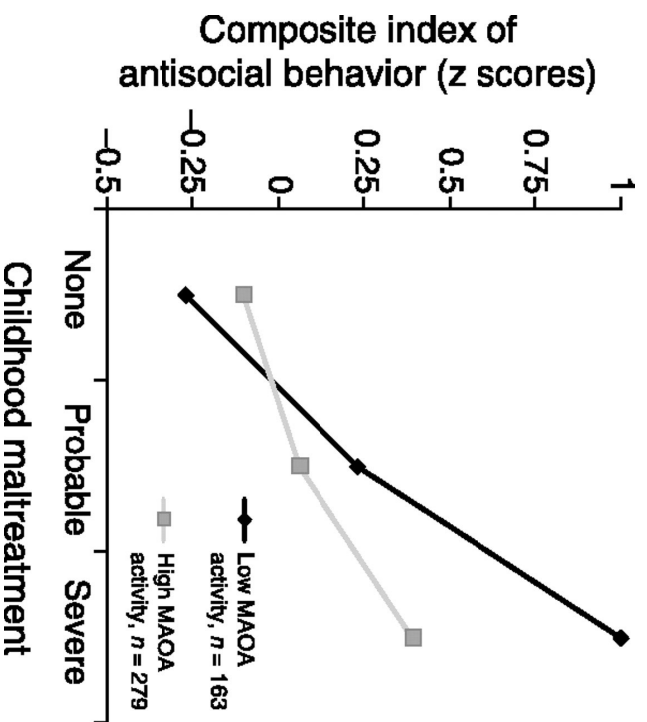
with the same outcome for the trait as are variants aabbCCDDEE subject to a sequence of environmental factors Fghij.



- Implication: The common use of heritability as a basis for judging a trait to be a good candidate for molecular research (e.g., Nuffield Council on Bioethics 2002) is not so helpful if underlying factors can be **heterogeneous** (Taylor 2010).

Heterogeneity #8, Variation produces qualitative changes in results from standard theory based on populations

Cases: MAOA, gene-environment interaction, personalized medicine



Mean adult composite anti-social behavior score in relation to levels of MonoAmineOxidaseA and Level of Childhood Maltreatment for a sample from Dunedin, New Zealand (Caspi et al. 2002, 852).

Notice that this figure presents the means; around any mean there will be variation. Other figures in

the study indicate that some of the high-MAOA individuals end up with higher anti-social behavior scores than some of the low-MAOA individuals. Depending on the threshold, a substantial fraction of the low-MAOA plus severe-maltreatment category does not end up as anti-social adults. Yet, in practice, once the **resources were invested to screen children** for MAOA levels, the attention of parents, teachers, social workers, and so on would be **focused on all low-MAOA children**. Indeed, *how could*

treatment on the basis of group membership be avoided if such adults do not know from a childhood MAOA assessment whether any particular individual is one who would go on, after childhood maltreatment, to become an antisocial adult?

Now, some of the parents of low-MAOA children might resist their children being treated according to the mean of the MAOA group. They might also balk at years of **prophylactic drug treatment or of maltreatment monitoring** by social workers.

These parents—together with others concerned about the same

issues—could push for additional research to identify other **characteristics that differentiate** among low-MAOA children (and perhaps also help predict who among the high-MAOA children are vulnerable). Even if no systematic characteristics were found, it would have been understandable that researchers had sought a more refined account of risk factors than given by the population-level approaches.

If an analogy to the MAOA case holds, the path to personalized medicine would often involve a phase in which large numbers of people are **treated according to their group membership**. The kinds of medical conditions that would receive the necessary investment in pharmaceutical and sociological research, screening, and preventative treatment or monitoring to address the conjunction of genetic and environmental factors involved would be conditions with a large value for the *average benefit* of ameliorating the effect of the genetic difference multiplied by *number of people* considered vulnerable.

For high-average-benefit conditions, *if the effect of the genetic difference depends on identified social or environmental factors, and if variability within the groups that have on-average high and low vulnerability produces a problem of misclassification, then pressure would arise for researchers to differentiate among individuals within the groups*. However, until distinguishing characteristics were found, parents, teachers, doctors, social workers, insurance companies, policy makers, friends, and individuals themselves could make no better use of genetic information than to treat individuals according to which genetic group they belonged to. Moreover, *if additional research were not conducted or not successful, or if the cost of differentiating among individuals were too high, we might never get beyond treating individuals according to their genetic-group membership => Irony: An underacknowledged issue in pursuing personalized medicine lies in genetic information being used to treat people according to the mean of their genetic group (Taylor 2014).*

Heterogeneity #9a, Heterogeneity in pathways of development

Case: Genomic medicine, PKU

"Imagine a world where families leave the hospital with their newborns and take their baby's complete genetic profile with them on a CD-ROM," Venter told his audience. "And imagine a world where your physician has as part of your medical record your genetic code, which can be used to determine, for example, your risk profile for side effects from drugs or other medical treatments.

These might be possible in a genomics-based medical system in the near future." (Massoglia 2003)

"Imagine a world..." If the case of phenylketonuria (PKU) is any guide to our imagination, significant complexities should be expected to arise if neonatal genetic diagnosis and advice about risks and possible protective measures become widespread. Until the 1960s people with two PKU genes always suffered severe mental retardation. But now the brain damage can be averted by a **special diet free of the amino acid phenylalanine** following **detection of those newborns having high phenylalanine levels**. Yet the certainty of severe retardation has been replaced by a chronic disease with a new set of problems (Paul 1988). Screening of newborns became routine quite rapidly during the 1960s and 70s, but there remains an ongoing struggle in the USA to secure health insurance coverage for the special diet and to enlist family and peers to support PKU individuals **staying on that diet** through adolescence and into adulthood. For women who do not maintain the diet well and become pregnant, high phenylalanine levels adversely affect the development of their non-PKU fetuses; such "maternal PKU" is a public health concern that had not previously existed.

In contrast with the picture of environment overcoming genetic determination, PKU individuals are

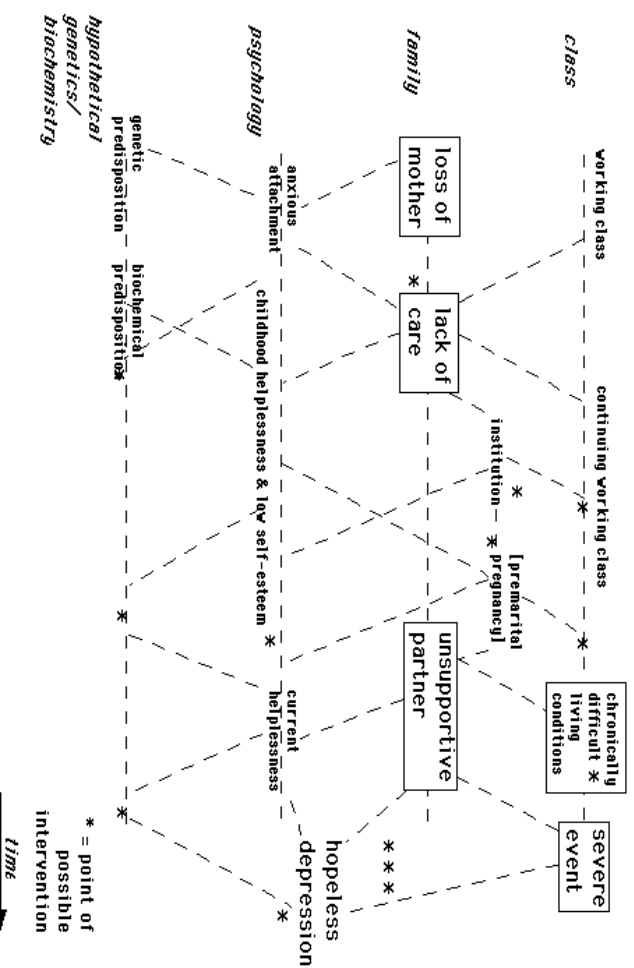
subject to **heterogeneous** influences on their pathways of development over the life course. A person with PKU who **complies** with the special diet may have experienced one or more of the following during their upbringing: health insurance coverage of the diet, a family that went without other amenities so as to afford it without insurance, or parents affluent enough to afford it anyway; a family that bent their cultural or religious dietary norms to accommodate the diet or a family without such norms; parental support for resisting peer pressure to eat other foods and/or a school community that instilled sensitivity to special needs; a sense of responsibility as a female in relation to the adverse effects of high levels of phenylalanine if they become pregnant on the development of their fetuses; summer camps where they meet other teenagers with PKU; and so on.

The multi-stranded life-course development of a person with PKU involves questions about **control** and social infrastructure and opens up **possibilities for participation**. Who is responsible if a baby is diagnosed with PKU, protective measures are not taken or are not sustained, and the child becomes a retarded adult or mother of a child with maternal PKU? Anyone wanting to improve the lives of PKU individuals needs to consider where they are prepared to get involved—Would the best point of engagement be around reduction in false positives or negatives? Diagnosis of variability in effects of exposure? Personal motivation and understanding of people with some mental deficits? Support groups for individuals and families? Insurance coverage for the special diet and for counseling? Paid family leave, or...? The possibilities for participation are diverse, depending on how people who want to help... can build or adjust the relevant social infrastructure.

Complicating the common claims that molecular biology and biotechnology will allow genetic information to reshape human life, in practice many diverse materials, tools, and other people have to be engaged to realize any enduring result (Taylor 2009).

Heterogeneity #9a, Intersecting processes & #10, Participatory restructuring of the dynamics that generated the data

Case: Social origins of depression



Pathways to severe depression in a study of working class women (discussed in Taylor 2009, building on Brown and Harris 1989). The dashed lines indicate that each strand tends to build on what has happened earlier in the different strands.

* indicate possible points of intervention that **different kinds of agents** could pursue to modify the intersecting processes. No intervention is **guaranteed to prevent** the clinical depressions; the interventions need to be **jointly pursued**.

Heterogeneity #11, Participatory restructuring in tension with deployment/withholding of trans-local knowledge & resources

Case: Participatory community planning

This takes seriously the creativity & capacity-building from well-facilitated participation among the **different people** who share a place or livelihood (Stanfield 2002; e.g., LH figure). The challenge is to mitigate adverse **trans-local decisions** (e.g., RH figure), doing so perhaps by **incorporating knowledge-making** of non-local or trans-local researchers—including their analyses of abstracted dynamics of political-economic change (Taylor 2009).

Vision 20/20		WEST NIPISSING VISION		February 1993					
STRONG DIVERSIFIED ECONOMIC BASE	EXCITING ATTRACTIVE COMMUNITY TO LIVE IN	ACTIVELY INVOLVED POPULATION	LIFELONG EDUCATION FACILITIES						
WIDELY PROMOTED TOURISM BASE	EXPANDED BUSINESS DEVELOPMENT	APPROPRIATE NATURAL RESOURCES DEVELOPMENT	WELL-MAINTAINED EXPANDING INFRA-STRUCTURE	COMMUNITY BASED SERVICES	RESPONSIVE ACCOUNTABLE GOVERNMENT	ACTIVE INVOLVED COMMUNITY	IMPROVED RECREATION OPPORTUNITY	ACCESIBLE EXPANDED ADULT EDUCATION	
Board Based Tourism Promotion	Modern Recreiving Facilities	Forestry Development	Transportation Network Locally/Area	First Response Teams	Effective Corporation Between Municipalities	Active Involvement of Citizens in All Community Developments	Youth Activities Promoted and Supported	Accessible Expanded Adult Education	
Improved Four Season Accommodation	Northern Ontario Service Industry Appropriate Natural & Resource Based Industry	Expanded Local Agricultural Market	Well Served Community	Community Based Services For Health & Physically Challenged	Opening Citizen Involvement in Local Government	West Nipissing Transit Corporation	Improved Access to Lake Nipissing	Focused Job Training Programs	
Accessible and Waterfronts	Insipative Programs to Attract Business	Fish Hatcheries	Environmentally Responsible Community	Expanded Local Services	Local Service Boards in Unincorporated Municipalities	Rural Development	Broadened Leisure Activities and Facilities		
Packaged Amenities & Tours	Franchises From Regional Colleges			Coordinated Integrated Services under One Roof	Open Land Use By-Laws	Open Communication	Improved Organized Sports	Enhanced Post Secondary Education	
Expanded Conventional Festivals	Business meet all needs	Clean Lake Nipissing		Senior Citizen Community	Re-evaluate Land Use By-Laws	Nipissing			
	Business meet all needs	Clean Lake Nipissing		Restored Environmental System	Re-evaluate Land Use By-Laws	Youth Involved in Planning All Activities			

Gripped by uncertainty: Sturgeon Falls springs into action. *Koldo...*

<http://www.thefree-library.com/jpan/vfmainarticle.aspx?id=966...>

Gripped by uncertainty: Sturgeon Falls springs into action following the closure of its primary employer.

[Print](#)

Author: Haddock, Scott Hunter

Date: Jan 1, 2003

Words: 942

Publication: Northern Ontario Business ISSN: 0710-2755

Sturgeon Falls is again facing the job loss blitzkrieg that is sweeping across Northern Ontario. Weyerhaeuser closed their containerboard mill in Sturgeon Falls on Dec. 5. The closure affected 140 workers and an entire community.

"It translates into a major financial loss to the municipality," says Gary O'Connor, mayor of Sturgeon Falls.

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