articulating the causal influence of **race →on health outcomes** in genetic and social epidemiology

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Aetio l o g i c research

Search for **causes** happens in many disciplines

Epidemiological etiologic research looks for genetic and environmental causes for diseases that befall the **demos (gr. municipality)**

Genetic epidemiology

looks for causes at molecular levels –needs a molecular lab, genetics theory

Social epidemiology

looks for causes at levels of social structure

-needs social medical theory and tools

MOSTLY--- Clinical epidemiology – look in clinic

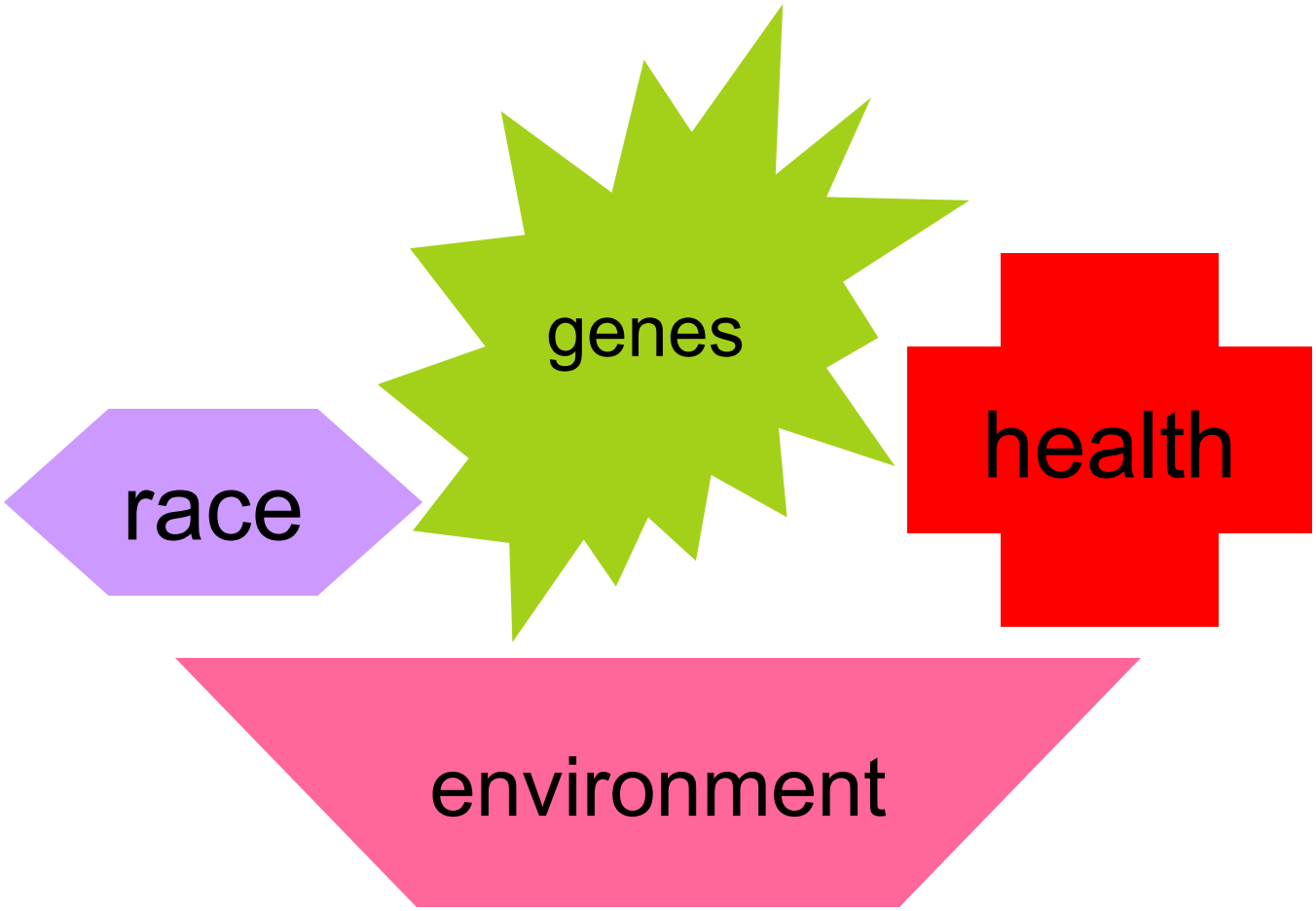
is race bad for you?

- Differences in 'race/ethnicity' (regularly) associate with **striking** differences in health outcomes [a *prima facie cause*]
- Controlling for confounds -like **SES, education**- associated with race/ethnicity and accepted as risk factors (regularly) leaves **significant** residual effects of 'race/ethnicity' on the outcomes measured [maybe a *real cause*]

Is something *about race* responsible for the differences measured?

Need a causally capable cast to act the causal story

the current actors



…race to the analytic clinic

biomedical discourse:

reasoning in text, pictures, math

...my etiologic research

symptoms (empirical):
use of 'race' as a variable in biomedicine

diagnosis (theoretical):
'race' cannot track causes of health outcomes [may be useful for understanding other phenomena]

treatment (normative):
biorace and socialrace can track causes

-use of ‘race’ in biomedicine- past history…*loaded…*

-----*I think one should look at this Polish question without emotion,* purely biologically*. We must exterminate them, otherwise they will exterminate us.* ----

Nazi racial hygiene

----*So far, we are keeping the known positive patients from getting treatment*.---

"Tuskegee Study of Untreated Syphilis in the Negro Male”

Most philosophers ask the **normative**

-Should we use 'race' in medicine?

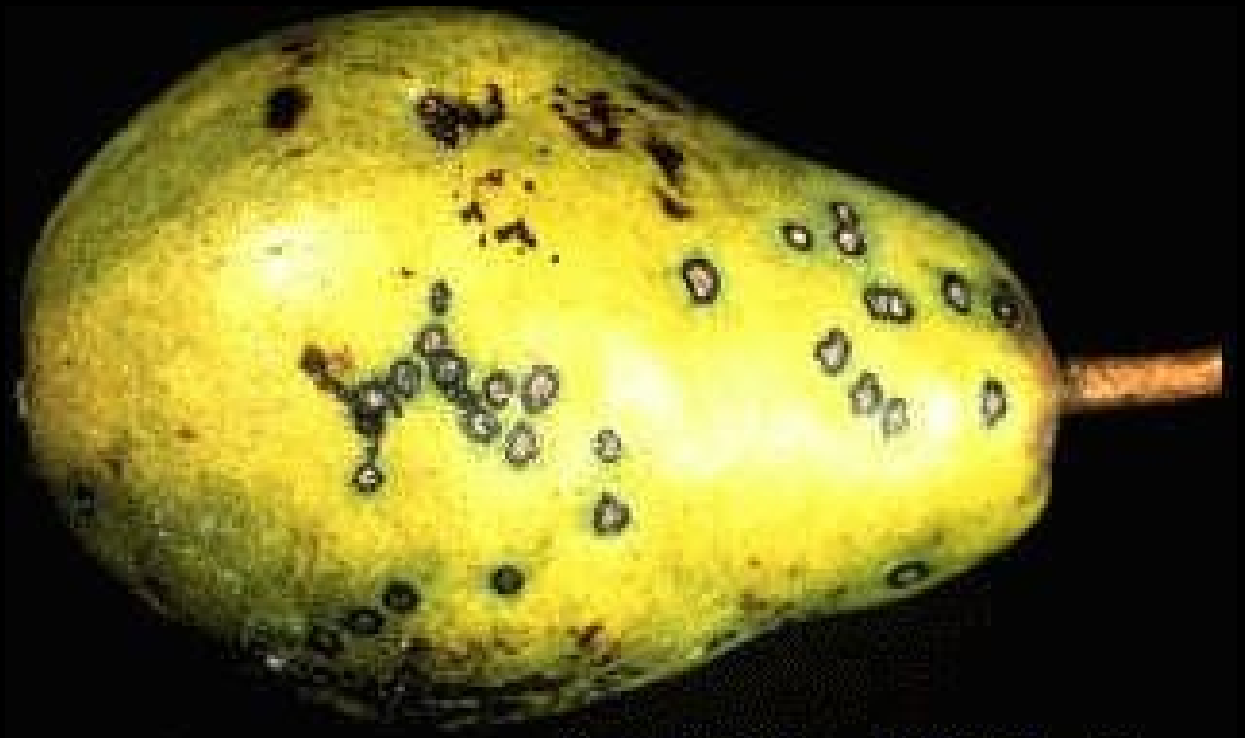
(Michael Root, Peter Singer)

We are using 'race'.

So comes the **empirical:**

-How are we using 'race' in medicine?

Symptoms: the case of the U.S.



The term 'race/ethnicity' is used in different biomedical domains

research

- **Epidemiologists, clinical researchers** measuring health outcomes stratified according to '*race/ethnicity*'.
- **Geneticists** exploring medically significant genetic variation between '*self-identified race/ethnicity*' groups.

practice

- Department of **Health and Human Services** catering to the health needs of *minority* populations.
- **Drug companies** creating *markets* catering to the pharmaceutical needs of particular racial populations.
- **Doctors** prescribing different treatment according to *observed* or self-identified race.
- **Patients** *identifying themselves* by race when seeking treatment.

U.S. Office of Management and Budget:

"Race and Ethnicity **Standards for Federal Statistics** and Administrative Reporting" stats policy directive 15

1. **American Indian or Alaska Native**
   A person having ***origins*** in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or ***community*** attachment.
2. **Asian or Pacific Islander**
   A person having ***origins*** in: a) any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam or b) a person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
3. **Black or African American**
   A person having ***origins*** in any of the **black** racial groups of Africa.
4. **Hispanic or Latino**
   A person of Cuban, Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish ***culture*** *or* ***origin,*** ***regardless of race***.
5. **White**
   A person having ***origins*** in any of the original peoples of Europe, the Middle East, or North Africa.

OMB (1997):

"The categories that were developed *represent a* ***political-social construct*** designed to be used in the collection of data on the race and ethnicity of major broad population groups in this country, and are *not anthropologically or scientifically based*."

next sentence:

"The standards ***are used*** not only in the decennial census (which provides the "denominator" for many measures), but also in household surveys, on administrative forms (e.g., school registration and mortgage lending applications), and ***in medical and other research***."

Epidemiologists (use standards) measure disparities

- Blacks in the U.S. are more likely than whites to suffer **heart failure**, develop more rapidly deteriorating symptoms of **heart disease**, at a younger age than whites
- **Diabetes** mellitus is over **50% more common** in African American adults than in their white counterparts, contributing to alarming rates of end-stage renal dysfunction and lower-extremity amputation among blacks
- Blacks' risk of dying of **tuberculosis** is **7 times** that of whites'
- **48%** of all new cases of **AIDS/HIV** reported in 2004 in the U.S. are blacks though **12%** of the population are blacks
- The U.S. death rate for black **infants** is more than **twice** that for white - difference almost **fourfold** for Arizona

Public health efforts (use standards) target communities

- Language
- Aesthetic values
- Community-specific health behaviours: diet, contraception

--but the causal chain leading to racially disparate health outcomes is thought to *also* include **biological difference** **--- why and how???**

Diabetes mellitus, race, and socioeconomic status; A population-based study (1996)

Age-race subgroup compared with renin profile as predictors of **blood pressure** response to antihypertensive therapy (1998)

Racial differences in the outcome of left ventricular dysfunction (1999)

Lesser response to angiotensin-converting enzyme inhibitor therapy in black as compared to white patients with **left ventricular dysfunction** (2001)

Survival variability by race and ethnicity in childhood **acute lymphoblastic leukemia** (2003)

--do not control for SES, education;

difference possibly due to environmental confounds

--try to control for SES, education;

residual effects of race sometimes put down to **genetic difference**

Could there be medically interesting genetic variation between ‘race/ethnicity’ groups?

Michael Root (2003): no

NO: Ordinary races are not "biological races":

Human populations have not been geographically OR reproductively isolated for long enough for any distinctive heritable characteristic to appear

1. There is **no cluster of genes** possessed by all and only individuals customarily sorted as members of the same race.

2. The populations are **differentiated "only by average frequencies** of a few polymorphic genes"

The biological differences between customary categories are "**at best statistical"**

SO… **they are *bad proxies* for medically relevant genetic variation**

Root (2003) positive

- **INSTEAD of race**

  use self-identified geographical ancestry to *better* (no data) **approximate genetic traits**
- Using **race** as a proxy for **social status** can make it a **useful category** for medicine.

‘Race/ethnicity’ can be a good proxy for how social status affects health outcomes

TABLE. Ten leading causes of death among non-Hispanic blacks and non-Hispanic whites — National Vital Statistics System, United States, 2002

	Black, non-Hispanic			White, non-Hispanic		
Rank	Cause of death	No.	(%)	Cause of death	No.	(%)
1.	Heart disease	76,694	(26.8)	Heart disease	577,761	(29.2)
2.	Cancer	61,996	(21.6)	Cancer	458,754	(23.1)
3.	Stroke	18,691	(6.5)	Stroke	133,118	(6.7)
4.	Diabetes	12,583	(4.4)	Chronic lower respiratory disease	112,128	(5.7)
5.	Unintentional injury	12,285	(4.3)	Unintentional injury	80,605	(4.1)
6.	Homicide	8,147	(2.8)	Influenza and pneumonia	55,419	(2.8)
7.	Chronic lower respiratory disease	7,730	(2.7)	Alzheimer’s disease	53,486	(2.7)
8.	Human immunodeficiency virus	7,714	(2.7)	Diabetes	52,463	(2.6)
9.	Nephritis	7,410	(2.6)	Nephritis	30,669	(1.5)
10.	Septicemia	6,074	(2.1)	Suicide	26,691	(1.3)
	All others	67,249	(23.5)	All others	400,879	(20.2)
Total		286,573	(100.0)	Total	1,981,973	(100.0)

Leading causes of death: **common** for Non-Hispanic Blacks and Whites (Heart Disease, Cancer, Stroke)

Three causes of death are **particular** to each group**:**

Homicide, HIV, septicemia: blacks

Alzheimer’s, suicide, influenza & pneumonia: whites

- A concept of **race** as a proxy for **social status** explains the increased prevalence of **homicide** among Non-Hispanic Blacks.
- Thinking of **race** as a proxy for **genetic variability** doesn't explain it.

…Still it is argued that **race** can well approximate medically interesting **genetic** variation…

Abdallah Daar & Peter Singer (2005): YES

- **Race** is a **good proxy** for *medically interesting* genetic variation: there is documented **genetic variation** between these human populations – (cite *Rosenberg*)
- **"selling points"** for *Nat. Rev. Genetics* readers:

  a.Race-specific pharmacogenomics contrasted to *"boutique 'personalized' medicine"*- **ethics** claim (no argument)

  b.Race-specific pharmacogenomics is **profitable**:

  1. There is a **big market** 2. Race is a **cheaper proxy** than **individual** genetic tests

Singer and Daar CITE:

"**Genetic structure of human populations**" Rosenberg et al. (2002)

- Used 377 markers in the DNA of 1056 individuals, from 52 populations across the world to track variability in allele frequencies

Reported: program "Structure" picked out **six *main* genetic clusters**, of which five correspond to major geographic regions: **America, East Asia, Pacific Islands Africa and Eurasia**.

-----"*self-reported ancestry can facilitate assessments of epidemiological risks*"

****links **self-reported ancestry** to **health***

genetic variation interesting qua racial?

- Why talk of "**six** *main* genetic clusters"?

  'structure' picks K genetic clusters, *where K is a number chosen in advance*. Rosenberg et al stop at and report K=6

"At K=5, clusters corresponded largely to major geographic regions. ***However***, the next cluster at K=6 ***did not match a major region*** but consisted largely of ***individuals*** of the isolated Kalash group, who speak an Indo-European language and live in northwest Pakistan"

- Did they report K=6 because of geography or **race**? If geography, then why not K=2, or K=3?

  K=2 Africa and America

  K=3 Africa, Eurasia-East Asia and America

- If we cared about genetic structure we'd study the **Kalash**

but we seem to care about 'race'…

Explicit test that **race approximates genetic structure**
"Genetic structure, Self-Identified Race/Ethnicity, and *confounding* in case-control association studies"
Tang et al (2005)

- Individuals self-identified as belonging to four major '**racial/ethnic'** groups: white, African American, East Asian, ***and Hispanic***. 326 microsatellite markers taken; 15 different locales within the US and Taiwan.
- Of 3,636 subjects of varying race/ ethnicity, only 5 (0.14%) belonged to a genetic cluster different from their self-identified race/ethnicity [SIRE]
- Link suggested between an ***explicitly non-racial*** category --a ***very "bad"* proxy** candidate by Root's standards--- and genetic variation [objections to study design exist, to interpretation of findings persist]

Tang et al. conclude:

" **ancient geographic ancestry,** which ***is highly correlated*** *with* **self-identified race/ethnicity** —as opposed to current residence— is the *major determinant of* **genetic structure** in the U.S. population."

And recall: Rosenberg (2002) and Root (2003) suggest that **ancestry** could capture epidemiological risk…

self-identified 'race/ethnicity'
is highly correlated with
ancient geographical ancestry
that approximates
genetic variation

Root: 2 → 3

1 ↛ 3

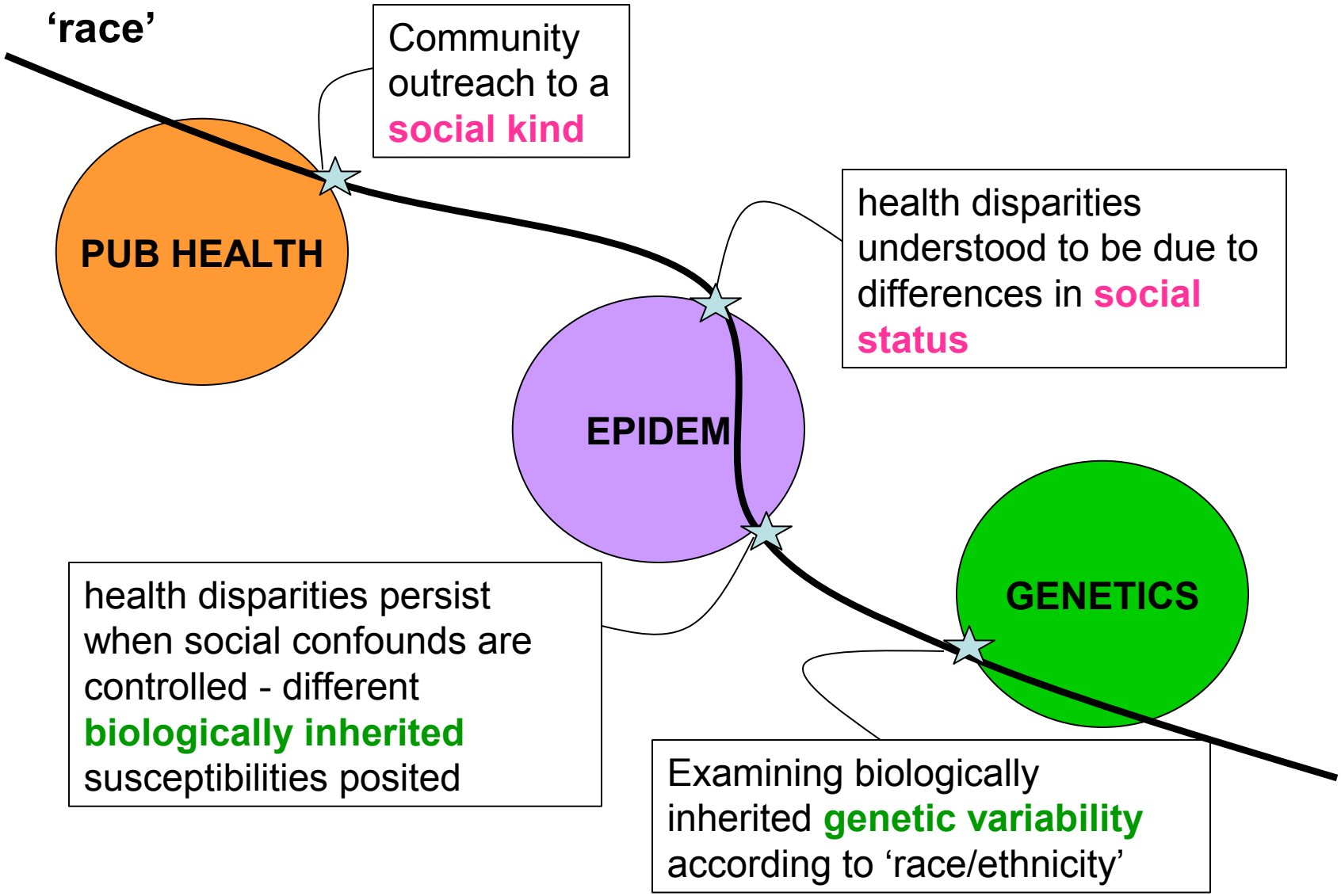
Tang: 1 → 2 → 3

Race

what Race?

Diagnosis:
pernicious conceptual conflation

race meets biomedicine



Race concepts *for/in medical use*

Socialrace= [M.Hardimon]

a human social group that is *taken to be a 'race'* within a particular society

- **second order** race concept: presupposes the existence of a first order race concept that groups are taken to be.

  The first order race concept is **racialist race**
- **social** concept (picks out social kinds)
- concept useful for exploring social/environmental factors that influence health outcomes differentially for each socialrace. Medical discourse acknowledges their existence as confounds rather than causes.
- Is not *itself* racialist or essentialist

Biorace concept(s)—

biologically respectable but none is agreed upon as biologically significant…

- Biorace notions defined operationally by their attempt to re-translate the *logical core* of the (Hardimon 2003) *ordinary race concept*:

(2) common ancestry

(3) distinctive geographic origin

(4) visible physical features

…into scientifically respectable terms

- aim to track biologically interesting difference
- used to **ask** whether there is genetic variation which is stratified according to race/ethnicity and medically significant
- Not nec. typological or essentialist: population concepts

Some biorace concepts

biological concept of race (Hardimon)

(1) biological lineage
(2) founding populations initially isolated
(3) phenotypic characters genetically transmitted

cladistic race concept (Andreasen 2000) **phylogenetic:**

races as lineages –emphasis on 1, 2 above

----- *Leaves out visible difference*

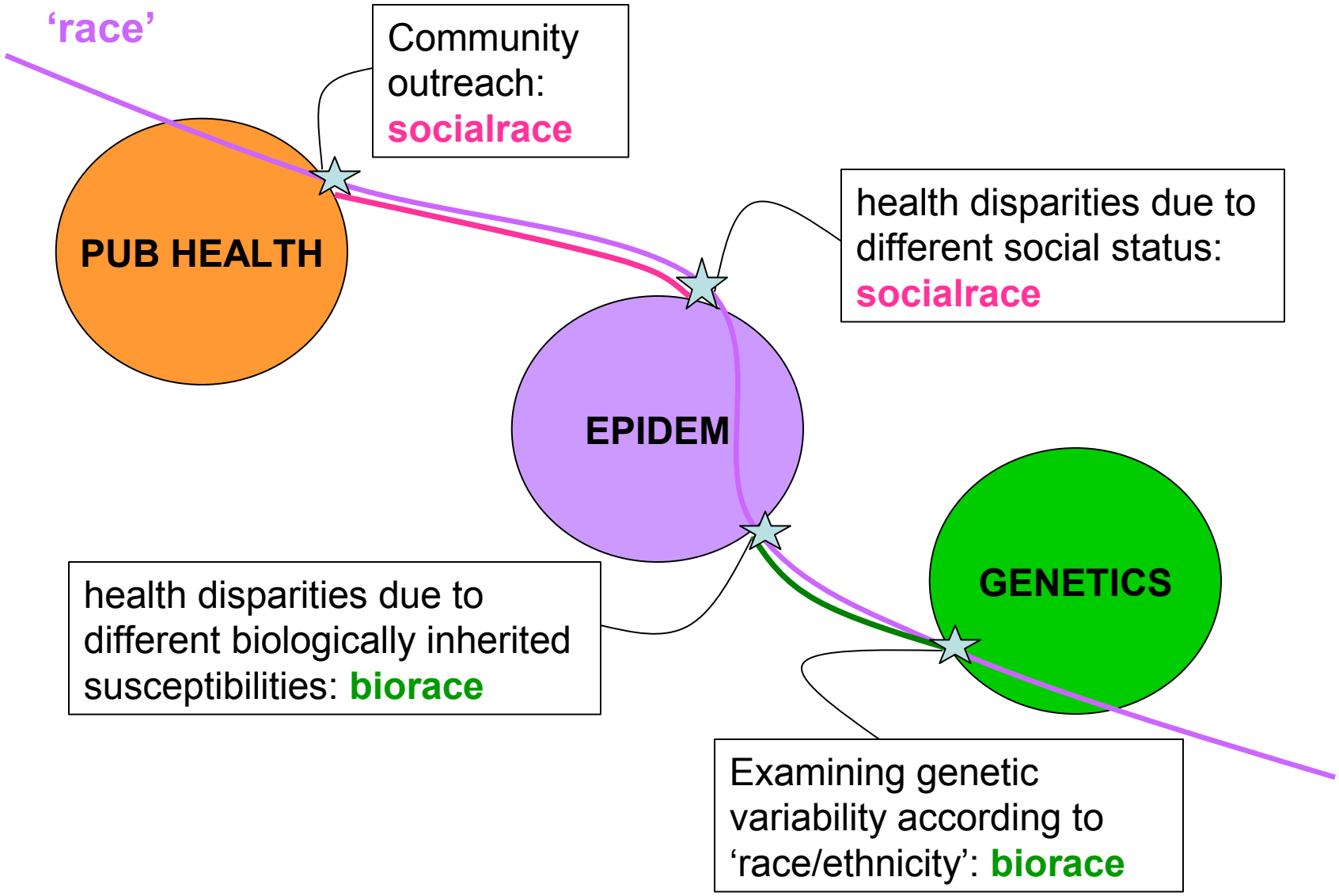
-----*Asians* do not form a monophyletic group, so not a cladistic race

ecotypic race concept (Pigliucci & Kaplan 2003) **phenetic:**

races are genetic adaptations to environmental conditions

----- *Leaves out genetic lineage*: One ecotype can have many origins

race meets biomedicine



race meets medicine, meets philosophy

Daar and Singer (2005)

- Do not demonstrate that genetic variation between human populations is **medically** interesting
- Do not worry about trans-global **applicability** of 'race' categories
- Do not worry about socio-political **risks** for populations sampled

--- Work with a **biorace** notion of race to the exception of socialrace

race meets medicine, meets philosophy

Root (2003)

- Accepts that race **correlates** well with disease.
- Rejects the ***medical usefulness*** of **associations** between race and genetics because our evolutionary (**causal**) story does not feature 'race'
- Proposes **self-identified geographical ancestry** as a *better proxy* for genetic variation

…but lacks data:

Tang et al find **'race/ethnicity'** well correlated with **ancient geographical ancestry**…

Root's working notion of 'race' as **socialrace** prevents him from examining the significance of biorace notions of 'race'

conceptual confusion can breed medical mistakes

1. **Race/ethnicity standards** stratify biomedical research
2. Epidemiologists describe **racial health disparities** in the course of common disease
3. Genomics studies [Hap-map underway] explore **genetic variation** along race/ethnicity lines
4. Government attempts to address health disparities plaguing **ethnic minorities**

→ Opportunities emerge for ***race-specific drug patents*** (**BiDil**: drug patent obtained in 1999, NDA granted June 2005)

The Case of BiDil

- **First race-specific drug** to be approved by the FDA (June 2005) –to be used in combination with standard heart failure treatment
- **Self-identified African American** patients on BiDil show a **43%** reduction in death and a **39%** decrease in hospitalization for heart failure compared to placebo, and a decrease of their symptoms of heart failure. (**A-HeFT, 2004**)

BiDil: works
but is it race-specific?

The first socialrace specific medication ?

- Prospective trial done on patients of *self-identified African American race* ***ONLY***: Conclusion? Drug works for African-Americans.

  According to this logic, most drugs are race and sex specific: **white-male-specific.** Instead of showing that the drug works [period] the status of African-American bodies as '**other**' was relegated to the status of the drug as other-race-specific.
- **Costs:** Combination of generic drugs hydralazine and isosorbide dinatrate H/I, in a new dosage (A-HeFT, 2004) -- from 0.25$ per pill to 1.80$
- **No causal explanation** for how ***race*** accounts for the difference in response: increased nitric oxide deficiency in black patients reported as a cause, but is **socialrace** or **biorace** a cause of this deficiency?

BiDil

Cohn:

"But my assumption is that everybody will respond to this drug, to varying degrees. Since it's an effective therapy, I think it could be an option for ***every patient who remains symptomatic despite taking whatever other heart failure drugs they have taken***."

Prescription…

- In a time where there is **political interest** in addressing the disparate health needs of the various US **socialraces**, the risk of essentializing socialrace categories, as well as the risk of taking them for **bioraces** is great.
- **To ask the right questions** about how 'race' relates to 'health' we must first distinguish between different understandings of race.

a fact about a hat

the phrygian cap:

hat of **Telesphoros** god of recovery and hat of **Liberty**

---recovery involves *wearing the hats of doctors and politicians* ---

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