FACING FUTURE

Reflections on the Use of Population Descriptors in Genomic Research

Stephanie Malia Fullerton, *DPhil*
Bioethics & Humanities

UNIVERSITY *of* WASHINGTON

I stand on traditional Coast Salish land, inhabited by the Duwamish, Muckleshoot, Tulalip, and Suquamish tribes, past and present. I honor with gratitude the land itself and the first peoples of Seattle.

https://www.realrentduwamish.org

MY ‘TAKE HOMES’

- Clinical translation will likely complicate (stymie?) any genetic approach to population description
- Slippages and contradictory categories abound
- “Moving beyond” requires something more than a scientific (genes-first or only) taxonomy

INFORMING MY THINKING

cser

Clinical Sequencing Evidence-Generating Research

https://cser-consortium.org/

NHLBI

TOPMed

https://topmed.nhlbi.nih.gov/

PRIMED consortium

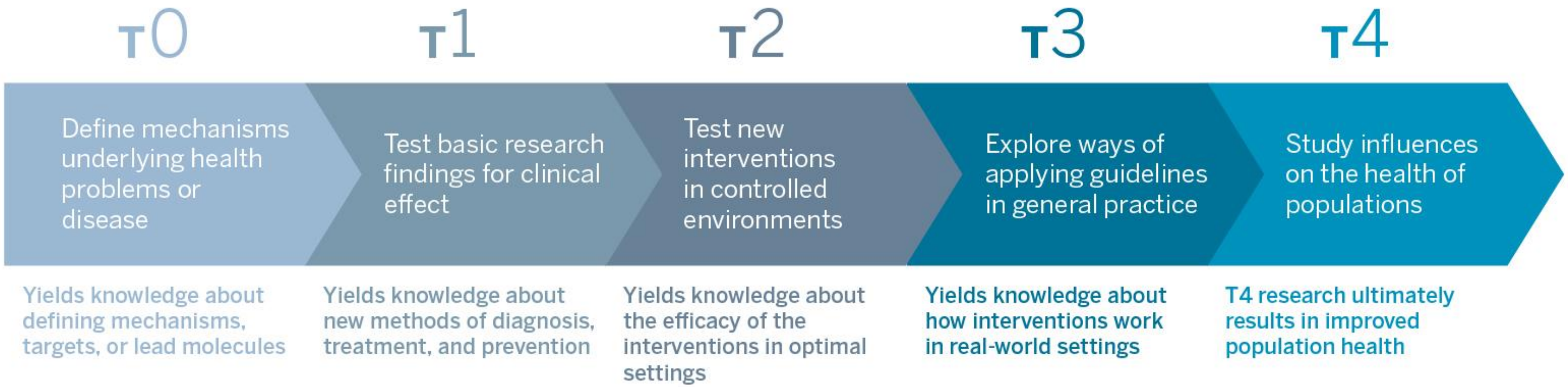
emerge network

ELECTRONIC MEDICAL RECORDS AND GENOMICS

https://emerge-network.org/

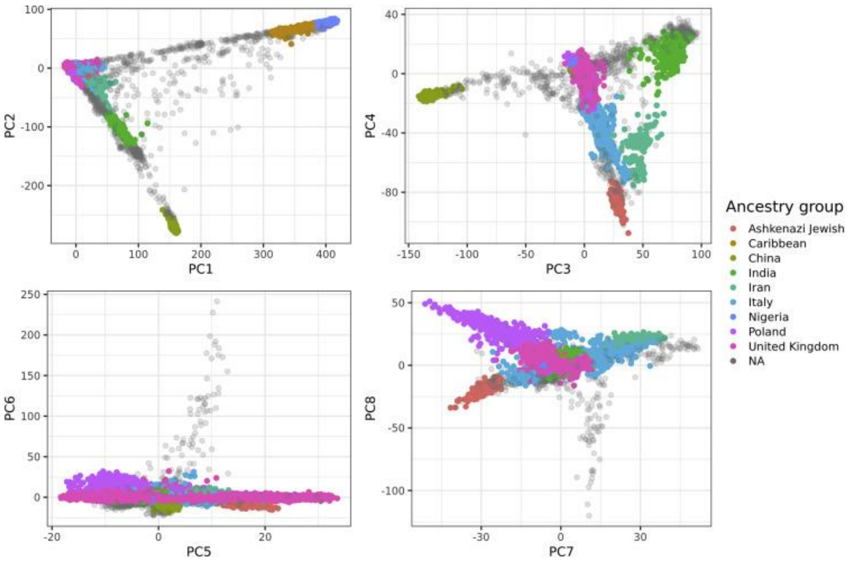
https://primedconsortium.org/

Clinical Translational Research *Pathway*



T0	T1	T2	T3	T4
Define mechanisms underlying health problems or disease	Test basic research findings for clinical effect	Test new interventions in controlled environments	Explore ways of applying guidelines in general practice	Study influences on the health of populations
Yields knowledge about defining mechanisms, targets, or lead molecules	Yields knowledge about new methods of diagnosis, treatment, and prevention	Yields knowledge about the efficacy of the interventions in optimal settings	Yields knowledge about how interventions work in real-world settings	T4 research ultimately results in improved population health

https://med.nyu.edu/departments-institutes/clinical-translational-science/about-us



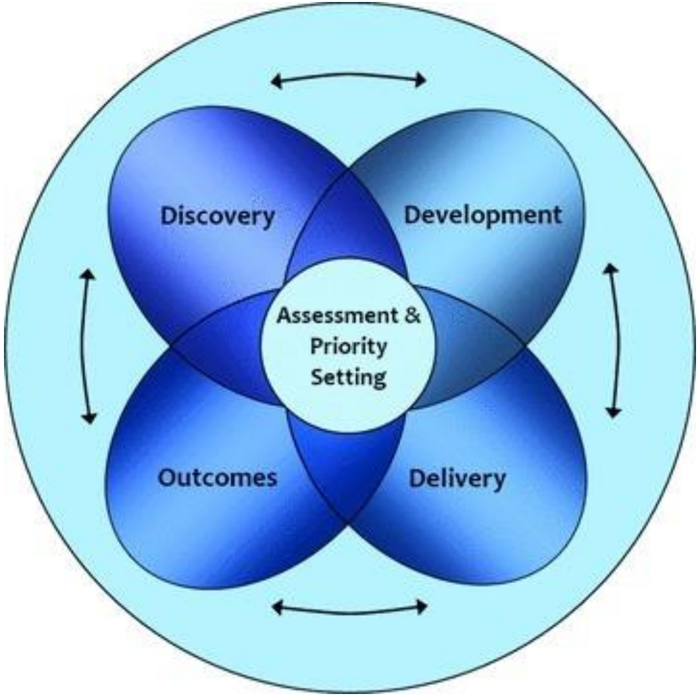
Privé et al. (2022) *AJHG*

"Our tests show you're half white..."

Clinical Translational Research *Cycle*

GENETIC ANCESTRY ESTIMATION

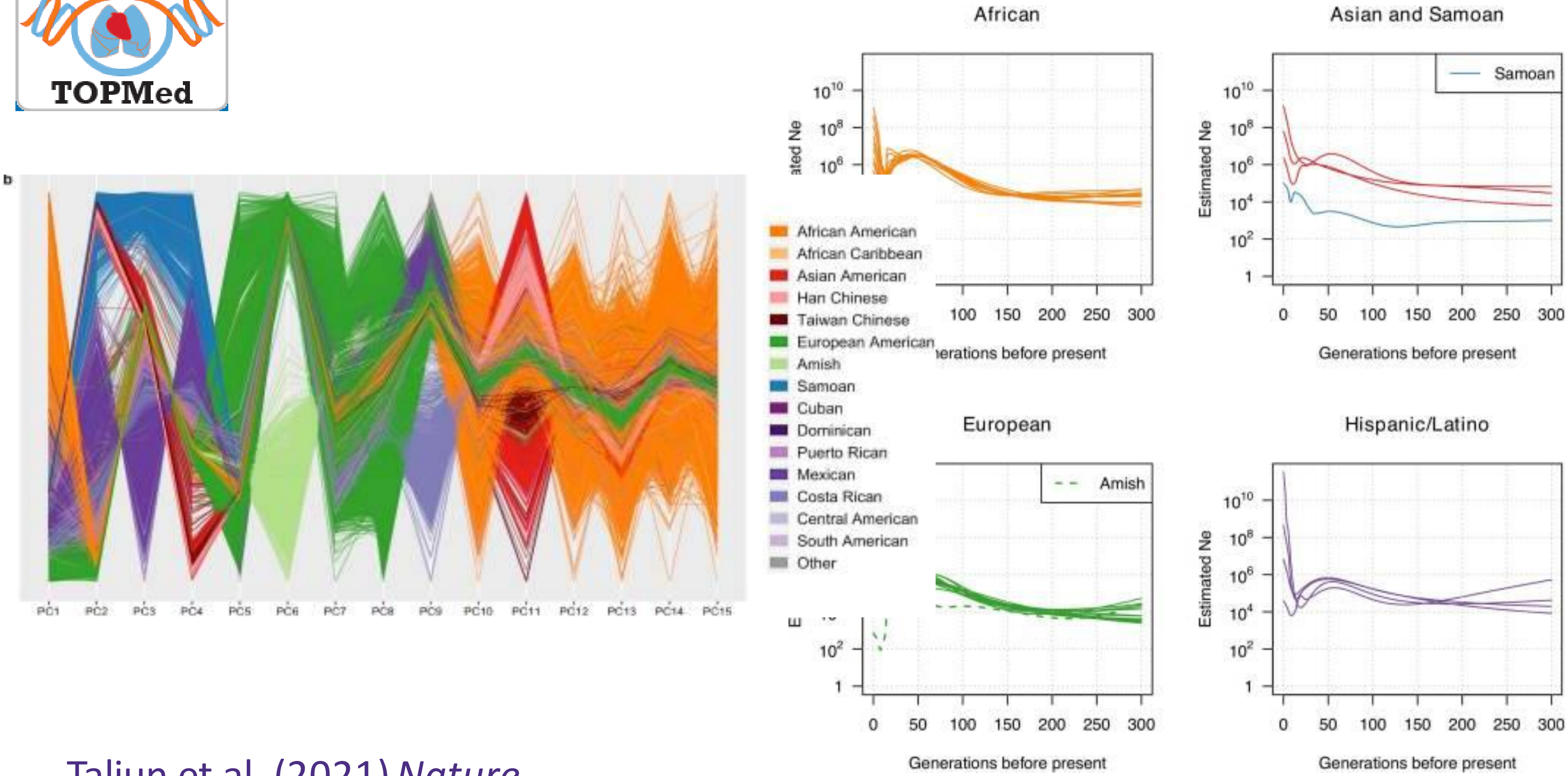
RECRUITMENT (Demographic Characteristics)



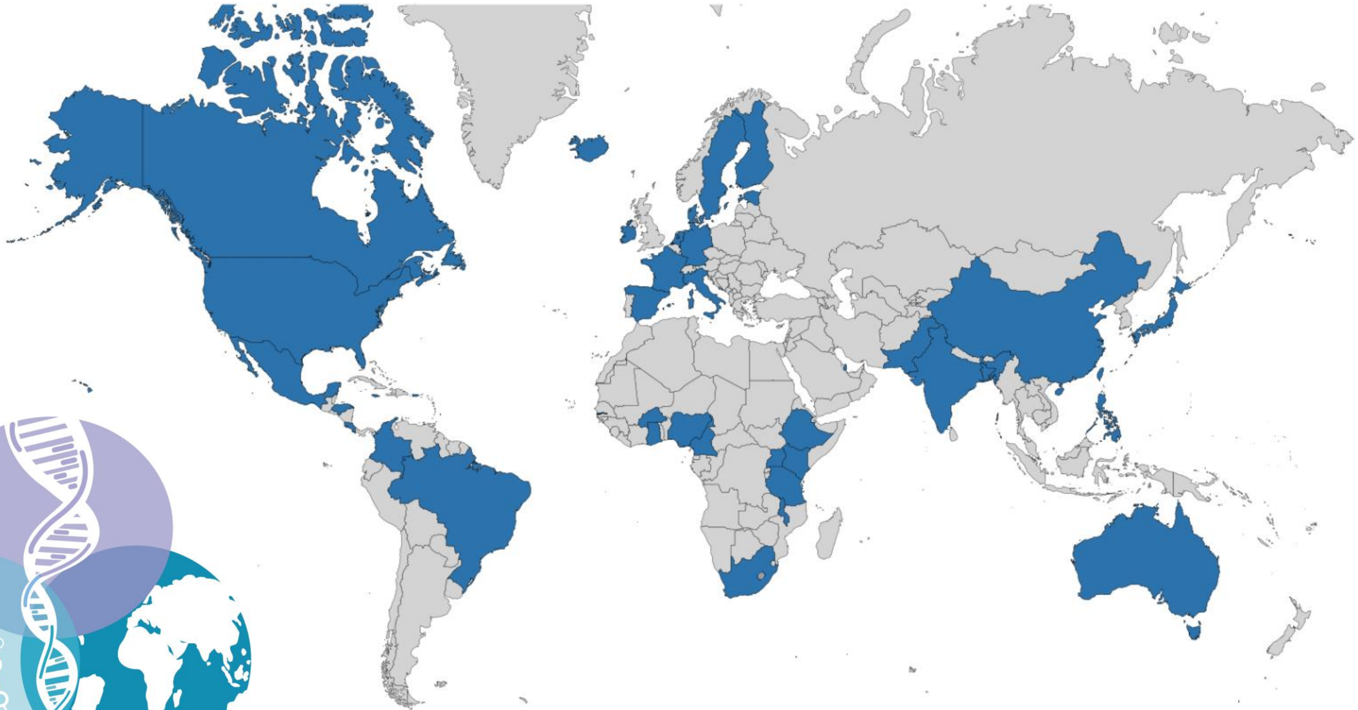
RACE/ETHNICITY

Kelley et al. (2012) *Clin Transl Sci*

NHLBI
TOPMed



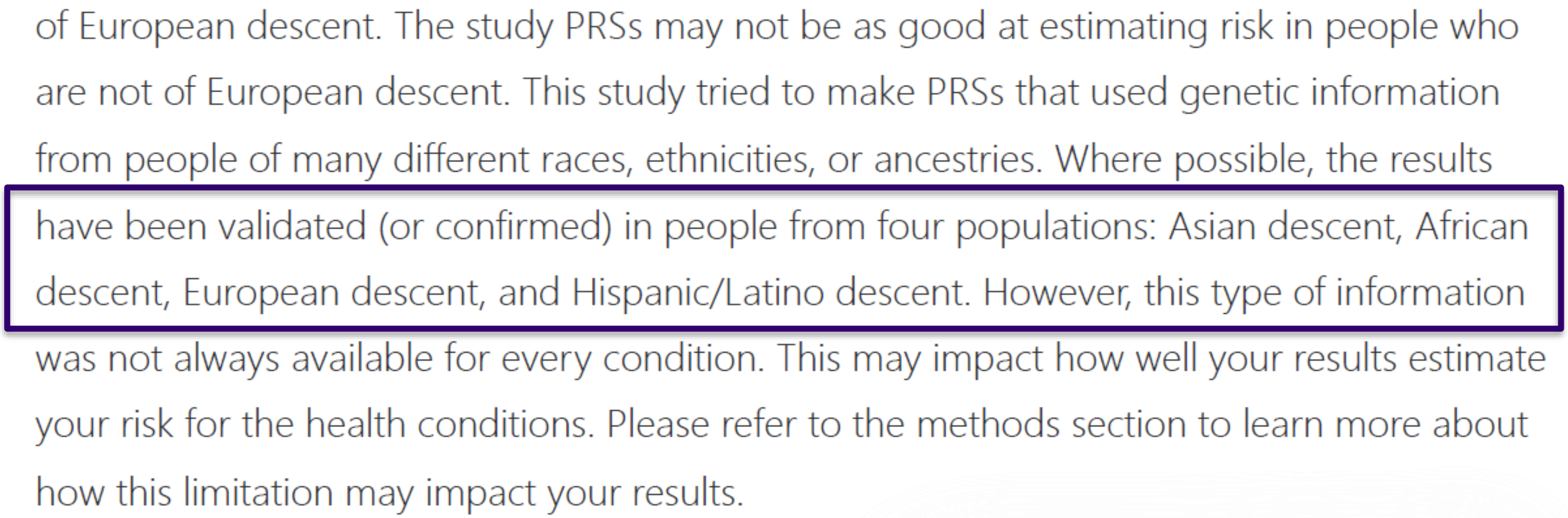
Taliun et al. (2021) *Nature*



Countries

USA
Australia
Bangladesh
Barbados
Brazil
Burkina Faso
Cameroon
Canada
China
Colombia
Costa Rica
Denmark
England
Estonia
Ethiopia
Finland
France
Gambia
Germany
Ghana
Honduras
Iceland
India
Ireland
Italy
Jamaica
Japan
Kenya
Korea
Malawi
Mexico
Netherlands
Nigeria
Pakistan
Philippines
Puerto Rico
Qatar
Scotland
Singapore
South Africa
Spain
Sweden
Taiwan
Tanzania
Uganda
Wales

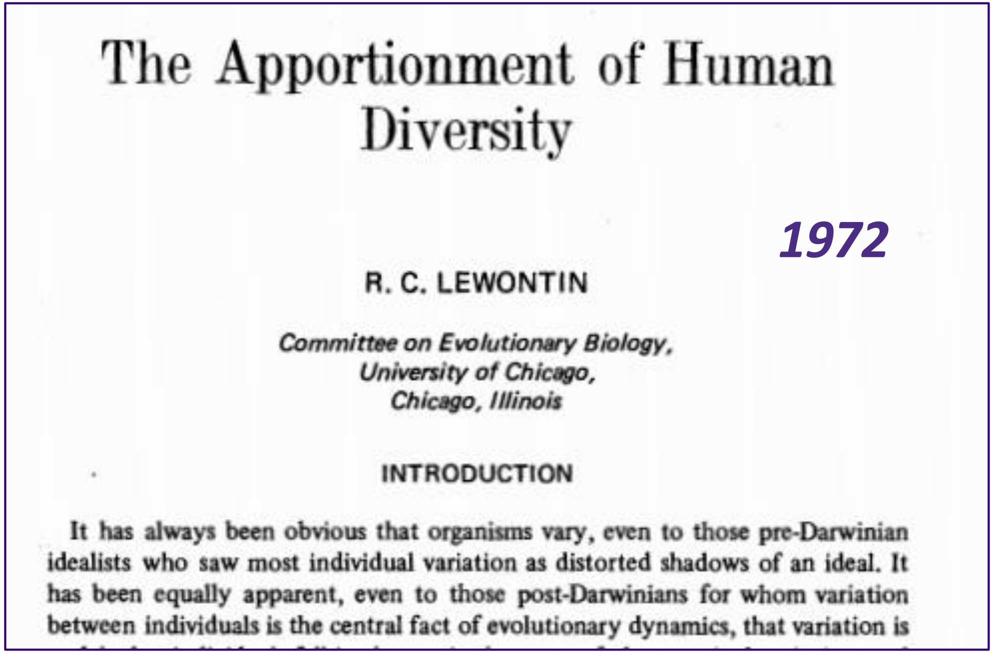
PRIMED
consortium



of European descent. The study PRSs may not be as good at estimating risk in people who are not of European descent. This study tried to make PRSs that used genetic information from people of many different races, ethnicities, or ancestries. Where possible, the results have been validated (or confirmed) in people from four populations: Asian descent, African descent, European descent, and Hispanic/Latino descent. However, this type of information was not always available for every condition. This may impact how well your results estimate your risk for the health conditions. Please refer to the methods section to learn more about how this limitation may impact your results.

National Human Genome Research Institute (NHGRI) Strategic Plan’s “Bold Prediction” #4 for 2030 (Box 5, Green et al. 2020 *Nature*)

> *“Research in human genomics will have moved beyond population descriptors based on historic social constructs such as race.”*



The Apportionment of Human Diversity

R. C. LEWONTIN

Committee on Evolutionary Biology,
University of Chicago,
Chicago, Illinois

INTRODUCTION

It has always been obvious that organisms vary, even to those pre-Darwinian idealists who saw most individual variation as distorted shadows of an ideal. It has been equally apparent, even to those post-Darwinians for whom variation between individuals is the central fact of evolutionary dynamics, that variation is

1972

Richard Lewontin
(March 29, 1929 – July 4, 2021)

“Human racial classification is of no social value and is positively destructive of social and human relations. Since such racial classification is now seen to be of virtually no genetic or taxonomic significance either, no justification can be offered for its continuance.”

Kaplan & Fullerton (forthcoming) *Proc. Roy. Soc. Pt B*

IN CONCLUSION

- Clinical translation of genetic discovery is iterative not linear, genetics can inform but not transcend social understanding
- Slippages in current projects illustrate the problem
- Not clear that we can, or really should, “move beyond” social categories

THANKS TO PAST AND CURRENT COLLABORATORS

- **Clinical Sequencing Evidence-Generating Research (CSER) Consortium** (U24 HG007307)
- **Polygenic RIsk MEthods in Diverse populations (PRIMED) Consortium** (1U01 HG011697)
- **Trans-Omics for Precision Medicine (TOPMed) Program** (U01 HL120393)
- **Electronic Medical Records & Genomics (eMERGE) Network** (U01 HG008657)
- **Ethics of Inclusion Project** (R01 HG010330)
- **UW Center for Genomics & Healthcare Equality** (P50 HG003374)
- **Jonathan Kaplan** – Oregon State University