



# Polygenic Risk Methods in Diverse Populations (PRIMED) Consortium



PRIMED at ASHG

## Motivation

Due to the historical oversampling of populations with European ancestry in genetic research, polygenic risk scores (PRS) currently perform less well in other, understudied populations, leading to concerns that clinical use in their current forms could widen health care disparities.

**The PRIMED Consortium is developing and evaluating methods to improve PRS performance and overall risk prediction in diverse ancestry populations.**

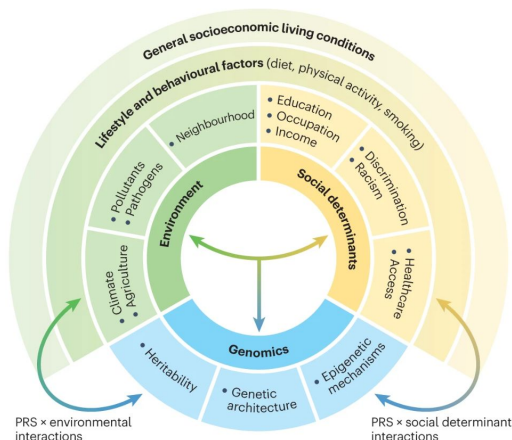


Figure 3a from Kachuri et al. (2023), showing the complex interrelationship among different genomic, environmental, and social risk factors. PMID:37620596

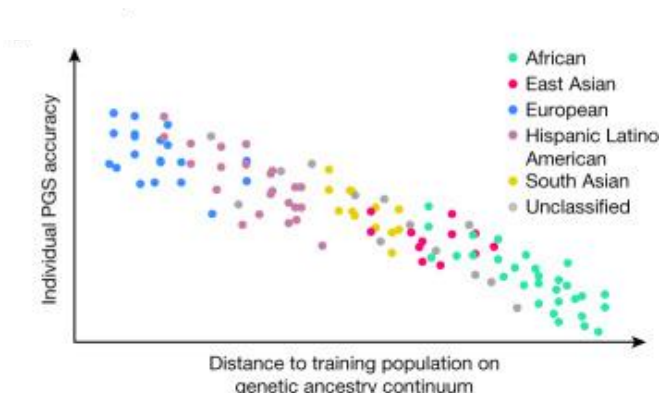


Figure 1d from Ding et al. (2023), illustrating how individual PRS accuracy decreases with increased genetic distance from the training population. PMID:37198491

## Goals

### Gather Diverse Datasets

Bring together large datasets with genomic and health measures from diverse ancestry populations

### Develop New Methods

Develop new methods to improve genetic risk prediction across diverse populations for a broad range of health and disease outcomes

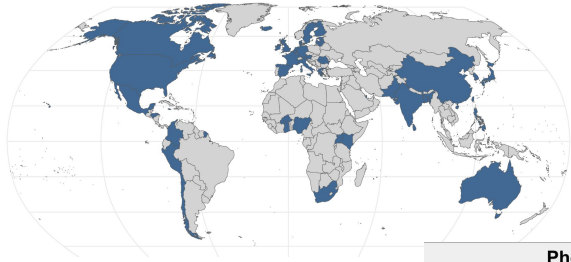
### Enable Collaboration

Enable collaborative analysis by sharing PRS-related data, software, and other resources with the scientific community

### Improve Health

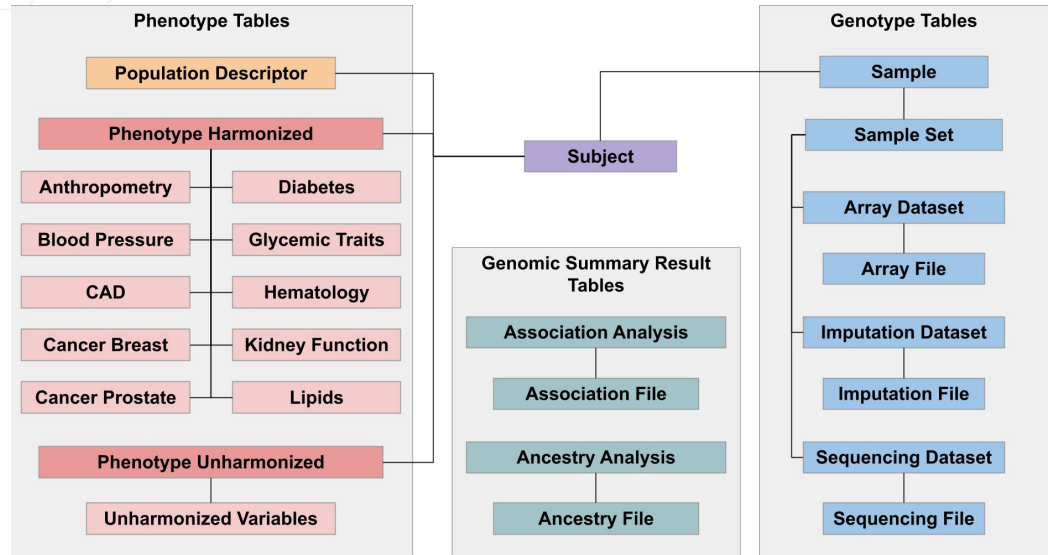
Leverage existing precision medicine partner programs to develop and test PRS in diverse populations to improve health outcomes

# Data Overview



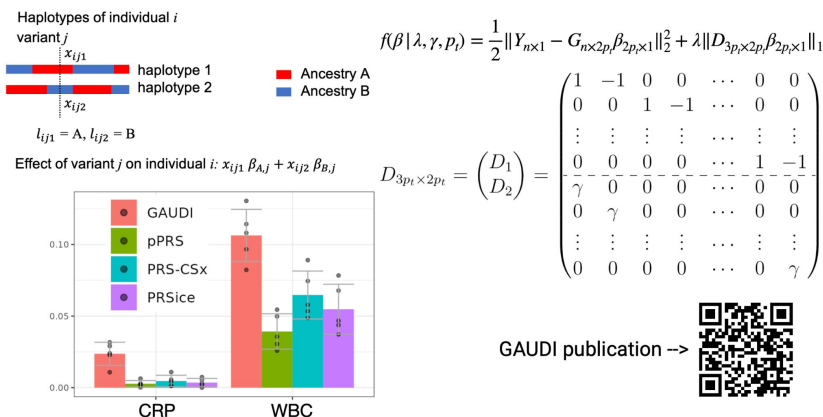
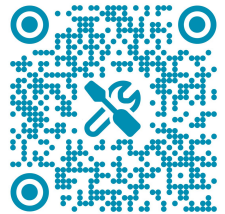
Over **40 countries** are represented among study participants whose data are used by the PRIMED Consortium to improve PRS development and use in diverse genetic ancestry populations.

PRIMED developed a common **data model** to enable aggregation and harmonization of genotype and phenotype data with structured metadata that supports cross-study analysis across many phenotypes. Data is shared and analyzed on the **NHGRI AnVIL cloud platform**.



## Methods

PRIMED researchers are **developing methods** that improve PRS performance across diverse ancestry populations (two examples below). Analysis tools and workflows are made available in the **PRIMED Dockstore Organization**.



$$f(\beta | \lambda, \gamma, p_i) = \frac{1}{2} \|Y_{n \times 1} - G_{n \times 2p_i} \beta_{2p_i \times 1}\|_2^2 + \lambda \|D_{3p_i \times 2p_i} \beta_{2p_i \times 1}\|_1$$

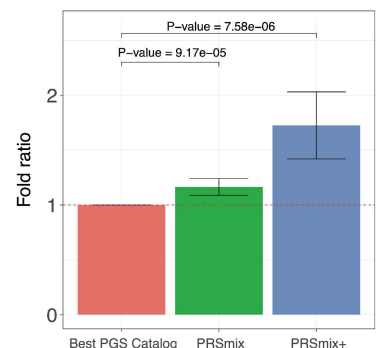
$$D_{3p_i \times 2p_i} = \begin{pmatrix} D_1 \\ D_2 \end{pmatrix} = \begin{pmatrix} 1 & -1 & 0 & 0 & \dots & 0 & 0 \\ 0 & 0 & 1 & -1 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \dots & 1 & -1 \\ \gamma & -\gamma & 0 & 0 & \dots & 0 & 0 \\ 0 & \gamma & 0 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \dots & 0 & \gamma \end{pmatrix}$$

**GAUDI** explicitly models ancestry-specific effect sizes while encouraging them to be similar. It achieves higher accuracy by detecting variants with large ancestry-differential effects (Sun et al. 2024, PMID: 38310129)

**PRSmix** integrates PRSs from secondary traits with a penalized regression to improve PRS accuracy (Truong et al. 2024, PMID:38642556)



Image by Ricardo Job-Reese, Broad Communications

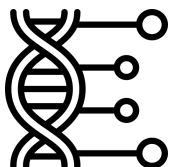


# Research Highlights



Perspectives on the field of PRS methods and development

PRS methods and software to improve prediction across diverse and admixed populations



PRS models for key traits to reduce health inequities

PRS models to improve biomarker accuracy



Environmental and social determinants to refine risk estimation

Innovative approaches to representing and using diversity in PRS

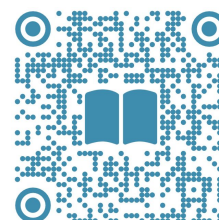


Social and ethical considerations to responsibly develop and implement PRS

Cloud-based approach to collaboratively share and analyze data on the AnVIL platform

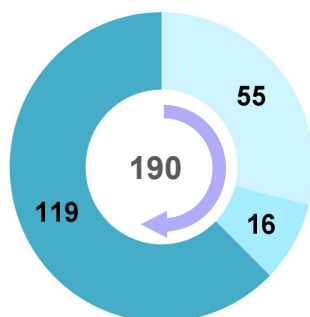


Research Highlights with select publications

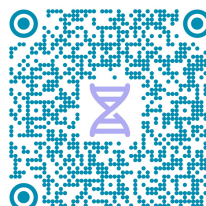


## Publications

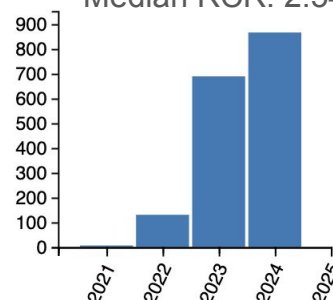
- Proposals in Progress
- Pre-prints
- Publications



PRIMED Publications in PGS Catalog



Citations by year cited (1,692 total)  
Median RCR: 2.54

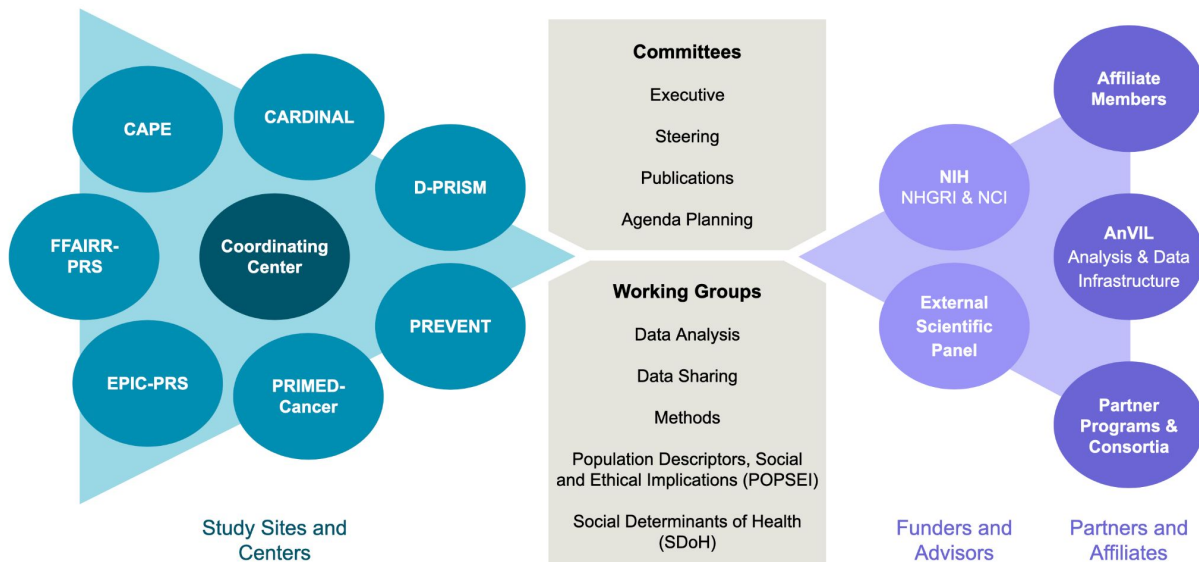


Icons from Flaticon



# Who We Are

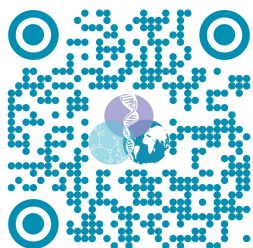
The Consortium has seven Study Sites, a Coordinating Center, NIH program staff, and Affiliate Members. Investigators and collaborators span dozens of institutions and countries.



NHGRI and NCI funding: U01HG011697, U01HG011717, U01CA261339, U01HG011719, U01HG011720, U01HG011723, U01HG011715, U01HG011710

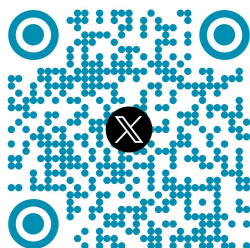
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