The Benefits of Population Representation in Genetic Research

American Society of Human Genetics

The Problem:

Overall, humans are remarkably similar at the genomic level - two unrelated people share about 99.9 percent of their DNA sequences. However, the small percentage that does differ can hold important genetic clues about our traits and health.

Genome-wide association studies (GWAS) can be a valuable tool for identifying genetic variants associated with diseases and other human traits. Yet, 16 percent of the global population is made up of people of European decent, despite the chart below showing data used in GWAS.

Ancestry catogory distribution of individuals in GWAS catalog

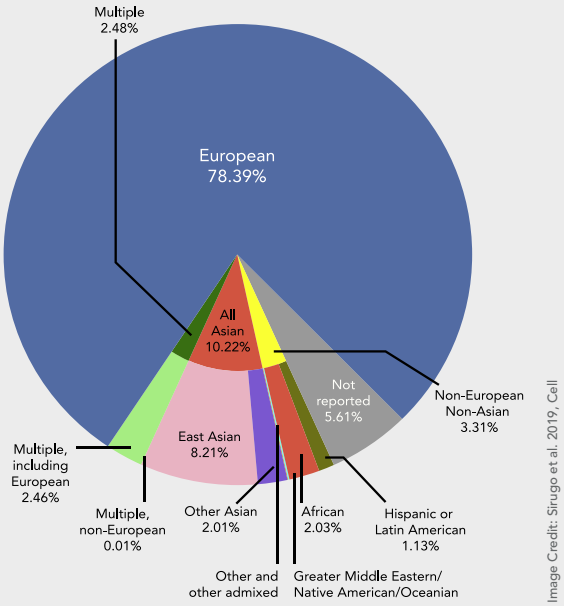

Image Credit: Sirugo et al. 2019, Cell

Broad Benefits:
The failure to include diverse populations in genetic studies also means researchers are likely missing discoveries that can benefit *everyone*.

Some individuals of African descent carry a nonfunctional copy of a gene called *PCSK9* that results in unusually low levels of LDL cholesterol in the blood. This finding led to the development of a new class of cholesterol-lowering drugs.

The Mosuo people of Southwest China possess genetic adaptations to high-altitude living that appear to also lower the risk for hypertension and diabetes-associated anemia. The discovery could lead to research into novel treatments for these chronic diseases.

The Consequences:
If scientists study only one group of people, the results can have limited utility across different populations. The Eurocentric bias in most GWAS translates into poorer disease prediction and treatment for individuals of under-represented ancestries.

A recent study revealed why asthma-related deaths are four to five times higher in people of African, Puerto Rican, and Mexican descent. These groups carry genetic variants making them less sensitive to albuterol, a drug used in inhalers.

Lack of diversity could keep precision medicine, in which doctors use each patient's unique genetic makeup to tailor treatments, from working for everyone. Therapies developed on the basis of biased GWAS will likely work best only in people who share that same ancestry.

At present, Methods used to estimate genetic risk for specific health conditions are more accurate in people of European descent.

Solutions:
Researchers and funding agencies are working to increase inclusivity and build trust with communities that have historically been left out of genomic studies. The National Institutes of Health and Food and Drug Administration have both issued policies and guidance to promote inclusion in research.

The Human Heredity and Health in Africa Initiative (H3Africa) is collecting genetic samples from participants in 27 African countries, as well as funding African investigators working in African institutions.
H3africa.org

In the next phase of the Population Architecture using Genomics and Epidemiology (PAGE) Consortium, researchers will genotype approximately 50,000 individuals from non-European populations.
Pagestudy.org

All of Us Research Program plans to recruit one million American individuals — at least half of whom are of non-European ancestry — to learn more about how differences in lifestyle, environment, and genetics influence health and disease.
Joinallofus.org