# Heritability of Common Lab Values and Its Role in Health Disparities Among Diverse Populations

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This paper aims to explore the complex interplay between genetic, existing laboratory values, and health disparities. Existing research suggests a surprising degree of heritability in many common lab test results (some exceeding 30%). This finding raises critical concerns about the moral and practical validity of established reference ranges developed from limited and non-representative populations. The study reveals how genetic variations, such as those in the APOE gene, influence disease susceptibility differently across populations. The primary question of this review is: How do heritable lab values contribute to healthcare disparities, and what strategies can therefore be implemented to create more inclusive reference ranges? In order to answer this, the study conducts an extensive review of up-to-date literature, and examining the impact of genetic diversity on lab results by employing both quantitative and qualitative data. Moving forward, the study proposes strategies for developing more genetically inclusive reference ranges that account for genetic variance within different populations. The research will then analyze how healthcare professionals and researchers can better be equipped to more accurately interpret lab results through a lens that considers a patient's genetic and social background.

## Introduction

Prior to Karl Landesteiner's groundbreaking discovery of blood types in 1901, having a successful blood transfusion was merely a game of luck. Back then, the narrative of blood types discovery and the unravelling of its genetic mysteries were a history filled with endeavor and breakthrough; leading to several well-known scandals consisting of death related to - what then was not known to be - differences in blood groups [1]. Landsteiner's revelation of the ABO blood group system was one of the very first to contribute to precision medicine - shedding light on how understanding genes can influence health - and drastically improving the safety of transfusions. His discovery eventually led to him obtaining a Nobel prize in Medicine and Physiology nearly 30 years later [2].

Currently, the field of genetics is yet experiencing its own rebirth. The bar was set for the understanding of human biology, from the pioneering work of Gregor Mendel in the 19th century in the identification of DNA as the carrier of genetic information to the development of the Sanger sequencing method in 1977 - which has aided researchers in determining mutations and variation in genes. In addition, the Human Genome Project in 2003 was a pivotal moment in offering an extraordinary view of the human genetic blueprint. These advancements in research have concurrently led to the comprehensive mapping of the human genome and have opened doors for advancements in personalized medicine and disease prevention.

To understand the relevance of heritability in lab values and its impact on health disparities, studies have been held to emphasize the complex interactions between genetic factors and disease susceptibility. Genetic markers, like SNPs, are associated to ethnic disparities; SNPs linked with methylation patterns have been shown to impact disease prevalence differently across populations which impacts treatment efficacy [3]. These genetic variants can impact epigenetic factors, phenotypes, and upcoming health outcomes of an individual. However, addressing these disparities requires a strong understanding of gene-environment interactions and how each genetic variant contributes to differences in lab results [3]. Hence, by integrating data on genetic and epigenetic factors, researchers can identify the causal mechanisms that lead to health disparities, paving way for reference ranges that are inclusive and reflect upon population diversity.

For too long, the foundation of healthcare has been built on data predominantly sourced from European males, producing a skewed interpretation of medical norms which result in diagnostics and treatments that may not accurately reflect the health needs of diverse populations. Standard protocol for tests, medical dosages and medical equipment have all been gauged on limited datasets, disregarding the rich diversity in humans. The process of conducting laboratory tests begins with the collection of fluid samples like urine, blood, or saliva. Once collected, these samples are processed in clinical labs where they undergo multiple stages of testing, such as separation of components (like plasma and cells) via centrifugation. Labs then use a range of methods, including polymerase chain reactions (PCR),

immunoassays, and more, to analyse analytes – like levels of cholesterol or glucose – in the samples[4]. However, methods vary across labs, leading to potential inconsistencies in results, particularly when the phases of clinical research were conducted solely on limited populations. This narrow approach is now more than ever being questioned as these medical procedures have become standard in hospitals worldwide, revealing critical malpractices and blind spots in research.

Moreover, addressing these issues present significant challenges as well. The complexity in quantifying these disparities stems from issues like: inaccurate measurement indexes, volunteer biases, and the subjective nature of self-reported health issues present in surveys create significant obstacles for researchers. Influence of structural and social determinants also pose limits to how valid study results are; as these factors can easily be overstated which will shape health outcomes of communities. Thus, focusing solely on individual predispositions without considering broader systemic factors may delay the elimination of health disparities.

The research is grounded in the theoretical framework of precision medicine, which underscores the customization of healthcare based on individual genetic profiles. This framework aligns with the study's approach to analyzing genetic variations and their implications for developing inclusive reference ranges for laboratory values. The study employs a mixed-methods approach, combining qualitative and quantitative data analysis to analyze the heritability of laboratory values and their impact on healthcare outcomes across different racial and ethnic groups, identify genetic variations that influence these lab values, assess the implications of these variations on diagnostic accuracy and treatment efficacy using a case study, and finally, to propose strategies for developing reference ranges while accounting for genetic diversity.

## Results

The relationship between genetic makeup and common laboratory values is a cornerstone in contemporary medicine. This review aims to unravel the extent to which this correlation contributes to health disparities - focusing particularly on the factors of race and gender. An array of secondary data such as medical papers, online articles, and scientific journals from the past decade will set the foundation of the analysis.

### Heritability and Genetics in Lab Values

One of the most critical indicators of health are lab values, which also happen to be significantly affected by genetics. Their role extends from just determining a patient's wellbeing to affecting a doctor's treatment plan for their patients based on test results and lab values. For instance, the APOE gene – involved in making proteins that carry cholesterol in the bloodstream – is a great illustrator of how genetic variations can predispose individuals to higher or lower cholesterol levels. Human APOE apolipoprotein is expressed in three main isoforms (APOE2, APOE3 and APOE4); a study conducted in 2006 indicated that each allele have been found in different distributions globally[5]. Higher frequencies of people carrying the APOE2 allele – which decreases the chances of Alzheimer's – and APOE4 allele – which constitutes the greatest risk factor of Alzheimer's – were both found in the highest frequencies in Oceania and Africa; whereas Indian and Asian populations expressed highest frequencies in the APOE3 allele[5,6]. This effectively shows the greatest coefficient of genetic diversity is in Oceania and Africa. A comprehensive look at the APOE distribution and its implications is one of many examples which highlights the interplay between genetics, geography – and inherently health, which is instrumental in interpreting lab results correctly and tailoring treatments.

Variant uniqueness can be defined as the presence of a specific variant in a polymorphic state only in one of the five considered macro areas[7]. By that standard, the table above shows that the South American macroarea (SAS) has the highest number of unique variants, with 12; none of which have been directly linked with any cardiovascular or neurodegenerative conditions. Compellingly, two of the twelve variants (rs552962455 and rs572713679) have been found in only two individuals in that macroarea and are located in consecutive positions along the second intron of the APP gene and are hence linked[7]. In addition, the African population (AFR) has the second highest number of unique variants: 11. In a different study, it has been proven that in addition to the 11 unique variants, 7 additional ones appeared, three of which (rs61357706, rs115299243, and rs769455) have been tested for linkage with Alzheimer's but are only recognized as a risk factors for hyperlipoproteinemia in Black African populations[8]. Contrarily, the East Asian (EAS) region has only shown nine unique variants. Two of them display no linkage with cardiovascular or neurodegenerative conditions, while the rest do. The American macroarea (AME) is distinguished by 7 variants, none of which have been associated with any of the two diseases. Finally, the European region has the least identified unique variants (only 6). Half of the variants, rs563571689, rs769447, and rs186466504, showed no disease associations, the other half displayed direct coalition with the conditions.

The UK Biobank project stands out as another significant contributor in this domain. The project has collected data from about 500,000 UK residents, varying from the ages of 40 and 69 years. It is so far emerging as a world-leading asset in genetic research, producing a little over 9000 scientific papers[9]. It has amassed diverse phenotypic details including: biological metrics, biomarkers present in blood and urine, and lifestyle information[10]. Groundbreaking discoveries in genetic associations and underpinnings of complex biological

| AFR | AME | EAS | EUR | SAS | Shared |
|---|---|---|---|---|---|
| rs72654467 | rs528229851 | rs373985746 [2] | rs563571689 | rs555840707 | rs565782572 |
| rs1187843706 | rs538246559 | rs192348494 [2] | rs769447 | rs555877419 | rs769450 [2] |
| rs184686013 | rs539807928 | rs150375400 [2] | rs769452 [3] | rs550501196 | rs769449 [2] |
| rs375741166 | rs535397097 | rs373651604 | rs186466504 | rs555914310 | rs440446 [2] |
| rs189660912 | rs1227709957 | rs549553647 | rs121918393 [2] | rs552962455 | rs7412 [4] |
| rs564144591 | rs1313313298 | rs533904656 [3] | rs530010303 [1] | rs572713679 | rs429358 [4] |
| rs148558158 | rs557715042 | rs140808909 [1] | | rs542186645 | |
| rs1368528953 | | rs190853081 [3] | | rs529662056 | |
| rs577618688 | | rs553874843 [1] | | rs563103121 | |
| rs1018669382 [1] | | | | rs555222732 | |
| rs1181840153 | | | | rs774452222 | |
| | | | | rs569017773 | |

[1] Variant involved in CVD. [2] Variant involved in AD. [3] Variant involved in CVD and AD. [4] Variant defining APOE isoforms.

Figure 1. List of unique and shared variants across macroareas, with disease involvement.

traits have since been made, paved by the wide range of genotypic data gathered from each participant, the genotype data that was gathered from each participant.This study helped confirm the known connections between these genes and various diseases. Thus, providing invaluable data for comprehending the heritability and genetic factors influencing lab values.

While identifying unique variants is crucial, understanding how these variations affect and manifest in different populations is equally as important. The UKB Health Disparities Browser plays a crucial role in this context. Developed by the UK Biobank (UKB) which has built a database that includes genetic and health information from over half a million people in the UK across different backgrounds, the UKB Health Disparities Browser is a tool that allows researchers to explore health disparities using data directly from the UKB. These disparities can stem from factors such as age, ethnicity, socioeconomic status, and sex all affect an individual's ability to seek proper medication for their health conditions. The study's aim is to scrutinise the patterns and magnitude of health disparities and to pinpoint areas where interventions could yield a reduction in mortality rates, improved accessibility to care, and enhance overall health outcomes.

The study compared numerous diseases and their prevalence across different demographic and racial groups in the UK. According to the table on the left, the country of residence, ethnic groups were the least proportional throughout the study (88.7% from England and 94.2% white), whereas sex was most proportional with approximately half being males and half being females.

The results of the analysis revealed that ethnicity poses the most considerable disparity impact, which underscores the necessity for targeted public health strategies. Self-identifying Pakistanis, Bangladeshis, and Indians had the highest prevalence of many diseases, whereas the Chinese ethnic group had the lowest[11]. This goes to show the diverse variance in the Asian population altogether. Another aspect of importance is that socioeconomic deprivation (SED) was also associated with a higher likelihood of disease. The study employed a metric called the Townsend deprivation index which incorporated several factors – such as unemployment rates, car ownership status, and housing conditions – to measure SED, has helped researchers to shed light on the nature of socioeconomic disadvantage on health outcomes[11].

In summary, the work of the UKB Health Disparities Browser features the potential for combining large-scale genetic datasets with demographic health records to uncover nuanced patterns in the healthcare sector.

| Characteristics | Number (%) |
|---|---|
| Complete cohort | 501 117 |
| Age | |
| 35–44 | 51 559 (10.3) |
| 45–54 | 141 971 (28.3) |
| 55–64 | 211 796 (42.3) |
| 65–74 | 95 791 (19.1) |
| Country of residence | |
| England | 444 618 (88.7) |
| Scotland | 35 739 (7.1) |
| Wales | 20 760 (4.1) |
| Ethnic group | |
| Asian | 9866 (2.0) |
| Black | 8046 (1.6) |
| Chinese | 1569 (0.3) |
| Mixed | 2957 (0.6) |
| Other | 6422 (1.3) |
| White | 472 257 (94.2) |
| Sex | |
| Female | 272 683 (54.4) |
| Male | 228 434 (45.6) |

Table 1. UKB cohort table The numbers and percentages of UKB participants for each population (sub)group analyzed here are shown.

### Existing Health Disparities in Different Populations

Health disparities are defined as the unequal health outcomes evident across different population groups, and are an ongoing

challenge worldwide. These disparities exist in various forms and often not stagnant, they arise from a web of interconnected factors, the most common being: socioeconomics status, geographic barriers, and cultural differences – however, this project would like to specifically focus on the systematic issues existent within health care systems. Ethnic minorities, for instance, face a disproportionate burden of some diseases, which has more than often been an influence of genetic predispositions and external social determinants. Nowadays, these disparities evolve with changing demographics, policies, and healthcare practices, and spotting the disparities is important for devising effective interventions directed at achieving health equity. The exploration of health disparities among different populations seeks to uncover its multifaceted origins and highlight the need for efforts to bridge the gap in this divide.

Research has consistently shown that certain ethnic and racial groups are disproportionately affected by various health conditions. For instance, Southwest American Indians have a much higher dependency on alcohol than other ethnic groups such as Asians. Studies have demonstrated that alcoholism often appears to be hereditary, due to genotypic variations in how alcohol is metabolised; this has been linked to differences in the enzymes responsible for alcohol metabolism: alcohol dehydrogenase and aldehyde dehydrogenase and the genetic predispositions for alcoholism being predominantly controlled by the genes, ADH1B, ADH1C,ALDH2[12]. It has been highlighted that the absence of the protective alleles ADH1B and ALDH2 were typically found in Asian populations. These alleles are responsible for adverse reactions such as facial flushing, nausea, and increased heart rates which occur subsequent to alcohol consumption[13]. Contrarily, those alleles were absent in Southwest American Indians; instead variations in the ADH1C gene were more prominently exhibited in this group.

When discussing the effects of genetic predispositions on health disparities, it's important to explore the broader context. The National Health and Nutrition Examination Survey (NHANES) by the National Institutes of Health (NIH) which is amongst the largest biomedical research agencies in the world, conducts diverse studies which offer comprehensive views of these health disparities, underscoring them, showing how genetic factors contribute to higher disease prevalence in specific ethnic groups.

## The Relationship Between Laboratory Values and Health Disparities

Genetics, race, and disease all play a part in exploring how laboratory values affect health disparities. This connection is elucidated through my correspondence with Dr. Nancy Cox, a 2023 ASHG Leadership award recipient and Vanderbily genetics researcher, and further justified by findings in scientific research articles which will be covered later on in this section.

Dr Cox highlighted the complexity of interpreting lab values across different ethnicities, emphasising the significance of considering genetic variability in healthcare; "Most physicians don't think much about the heritability (or lack thereof) of lab values, because they use them largely because of the dynamic way that lab values alert them to changes in health," Dr. Cox noted. It is particularly relevant to study genetic differences underlying health disparities, especially when such disparities persist even after factors like access to healthcare and socioeconomic status are accounted for. Failing to consider genetics might not only prevent the resolution of these disparities but also harm the populations that critics of a biological definition of race aim to protect[14]. This is based on the idea that genetic factors are contributors to health disparities, hence acknowledging these factors are essential to ceasing these gaps effectively.

Dr. Cox then emphasised the multifaceted nature of health disparities, challenging the notion that genetic factors are the primary cause. She argued that while genetics is scientifically the predominant cause of these disparities, they actually stem from socioeconomics inequalities – particularly income – which influences healthcare access, especially in the contexts like the United States where healthcare is not universally guaranteed. Hence, the divide in healthcare outcomes is not merely due to biological factors but because of the economic barrier which limits the potential genetic testing holds for enhancing healthcare. "Because it (genetic testing) is a new technology, it's still relatively expensive… only those who have good insurance, or who can afford to pay for genetic testing directly will be able to access it." she states, which leads us to the nuanced issue: the institutionalization of health disparities within healthcare systems as a result of lack of awareness about the variance of human populations integrated into laboratory measures. Reference ranges for contemporary medicine worldwide – specifically in developing nations – have been derived from men with European ancestries for years[15]

## Laboratory Tests and Their Significance

### Complete Blood Cell Count (CBC)

One of the most ordered clinical tests is the CBC which provides a snapshot of overall health by measuring red blood cell count (RBCs), white blood cell count (WBCs), and platelets. WBC count indicates infections or immune diseases, while RBC count helps diagnose conditions like anemia. Genetic variations significantly influence CBC values, as seen with individuals with the Nuffy-null phenotypes, which results in lower WBC counts (This will be further discussed in section 1.5).

### Basic Metabolic Panel (BMP)

The BMP assesses levels of minerals such as glucose, calcium, potassium, chlorides, and creatine to provide insight

on kidney and metabolic function, blood sugar levels, and electrolyte balance [16]. Variation in the SLC12A3 gene linked to sodium transport for example, impacts a person's susceptibility to electrolyte imbalance. If left untreated, electrolyte imbalance can negatively affect vital body systems, resulting in potential seizures, cardiovascular conditions, or even comas. These genetic influences make it essential to consider variations when interpreting BMP results to avoid misdiagnosis in metabolic disorders.

**Lipid Panel**

The lipid panel measures total cholesterol, including high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels, which are key indicators of cardiovascular disease risk and Alzheimer's. High levels of HDLs are generally considered protective, while high levels of LDLs are associated with increased prevalence of heart diseases. The APOE gene discussed earlier has alleles that influence metabolism differently. The APOE4 allele more commonly found in Oceanian and African populations have an increased risk of Alzheimer's. Reference ranges for lipid levels that account for genetic differences could improve cardiovascular risk assessment, ensuring individuals receive adequate treatment from their practitioners.

**Blood Clotting Tests (aPPT, PT)**

Blood clotting tests, like Prothrombin Time (PT), and Activated Partial Thromboplastin (aPPT) evaluate coagulation pathways, and help diagnose bleeding disorders and monitor anticoagulation therapy. Additionally, inherited bleeding disorders, such as hemophilia A and B, also caused by mutations in the clotting factor genes, lead to longer clotting times. Factor V, a genetic factor which increases clotting risk, is more prevalent in individuals of european descent – with 1 in 5000 of those affected carrying 2 copies of the mutation in their cells – necessitating tailored diagnostic and therapeutic approaches to suit the differences in clotting genes [17].

**Case Study: Duffy-Null in African American Populations**

Endometrial cancer is the most common gynaecological condition in developed countries, and while treatments are being developed and survival rates have improved, Black women continue to experience a disproportionate burden of the disease [18]. Researchers are actively investigating the biological antecedent on the disparity, and seem to come to a conclusion that the main accomplice stems from a variation in the Duffy antigen receptor.

The Duffy antigen, also known as the Duffy glycoprotein, is a receptor for chemicals that are secreted by blood cells during inflammation [19]. A specific genetic variation, rs2814778, disrupts the Duffy antigen promoter, giving rise to the "Duffy null"phenotype where the protein is absent from red blood cells in individuals homozygous for this variant [20]. Interestingly, the Duffly null phenotypes is quite a rare sighting in Asian and Caucasian population, but is most common in Blacks – occurring in >65% in African Americans [20].

This disparity manifests in a higher occurrence of aggressive tumours, poorer treatment responses, and higher mortality rates to the cancer than white females [21]. Interestingly, the study also revealed a link between the Duffy-null genotype and tumour aggressiveness in Black women. Duffy-null genotype patients were more likely to have more intact mismatch repair mechanisms within their tumours [21]. Furthermore, all endometrial cancer related deaths in the study group were exclusively in the Duffy-null cohort. However, understanding the interplay between Duffy antigen variations and endometrial cancer requires acknowledging the potential limitations of relying merely on laboratory values. This can be problematic when interpreting results from patients with genetic variations like the Duffy-null allele. Unnecessary procedures like bone marrow biopsies or exclusion from clinical trials can be put into effect due to predetermined white blood cell count [22]. This misinterpretation arises from the Duffy-null homozygosity being associated with lower white blood cell count – which inherently leads to misinterpretations of diseases or treatment-induced side effects [22].

In conclusion, integrating genetic knowledge into clinical practice is required to ensure accurate diagnosis, treatment strategies, and improved survival rates – especially in the context of women from African origin who are at risk of disproportionately being affected by endometrial cancer. Research should aim to explore the interplay between genetics, lab values, and specific diseases in necessitating a more comprehensive approach in clinical practices. And by recognizing the potential influence of genetics on lab results and incorporating that knowledge into clinical decision-making, the gap in endometrial cancer disparities can be bridged and ensure equitable access to optimal healthcare for women.

## Discussion

Having explored the different components that make up this paper and how they link up using research findings detailing health disparities and laboratory values in healthcare, attention now turns to the interpretation of these findings and their significance. This chapter examines three main areas: by unpacking the meaning of the results in the previous chapter, considering the ethical viewpoints of the research, investigating current barriers that this research is facing, and finally, proposing policies and future research directions which can improve the current state of health disparities across the board.

## Interpretation of Findings

When exploring the intricate relationship between genetics and health disparities, it's essential to delve into how genetic variants influence laboratory values and disease susceptibility amongst different racial and gender groups; which will be touched upon in this section. Notably, the gene distribution variation in the APOE gene illustrates a genetic distribution to diseases like cardiovascular conditions and Alzheimer's, emphasizing the importance of considering genetic components when assessing health conditions[6].

The APOE gene as previously discussed exists in three isoforms – APOE2, APOE3 and APOE4 – which differ in distribution globally and evolutionary analysis even goes to show that the isoform APOE4's existence dates as far as 300,000 years ago[7].The APOE4 isoform increases the risk of developing Alzheimer's disease by affecting how the brain clears beta-amyloid plaque – a major indicator of the condition[7]. This understanding of the APOE gene has paved the way for preventative strategies which are currently being clinically tested, by targeting the apolipoprotein function in Alzheimer's patients[22]. But while alleles like APOE4 are associated with an increased risk of Alzheimer's disease in certain populations, different populations may exhibit other forms of genetic predispositions that may alter disease risk and treatment efficacy. Understanding and using geographic and ethnic distribution of genetic variants helps researchers develop better-targeted preventative measures that address the specific health risks that prevail in certain demographic groups, fostering health equity internationally.

Acknowledging unique genetic profiles allows healthcare professionals to develop more precise diagnostic benchmarks and treatment plans that cater for all racial groups. Like the findings from the Duffy-null case study highlights, population-specific genetic markers influence individuals' response to disease or treatments. And while the Duffy-null variant mostly affects African-American populations, this example underscores the broader relevance: many different populations carry different unique genetic markers. G6PD deficiency in African populations for instance, influences susceptibility to anemia; or thalassemia mutations in Mediterranean and Southeast Asian populations, which affect blood count and oxygen transport[23]. Cases like these further emphasize the need for a shift in developing reference ranges that account for variation to minimize misdiagnosis errors. Therefore, integrating applications of findings for specific cases facilitates a healthcare framework that is truly equitable.

## Ethical Implications

Is it ethically justifiable for a society to allow preventable health problems to flourish based on factors like race or income? It is a known reality that a person living in a low-income neighborhood is likely to experience worse health outcomes compared to someone living in a wealthier area. It has also been scientifically proven and discussed throughout this paper that reference ranges used in healthcare may not be universally applicable to all patient populations. The consequences may result in inequities in diagnosis and treatment. This subchapter argues that addressing health disparities is not only a matter of social justice, but a multifaceted ethical imperative.

Firstly, the three main ethical theories will be compared and contrasted. Contractarian ethics, for example, underscore the vitality of just policies and institutions[24]. This has yet to be pertained in the healthcare sector due to current limitations preventing the resolvement of health disparities on a fast scale (this will be contended in more detail in the next subchapter). The presence of health inequalities suggests that the current system is flawed and disadvantages persons based on race, ethnicity, or socioeconomics status. Hence, violating the Kantian principle which preaches respect for all individuals, as everyone deserves the right to basic goods like healthcare[24]. Finally, utilitarianism, which seeks the greatest number of goods for the biggest population – which is afflicted by disparities – and creates inequalities which represent a missed opportunity to improve the health of everyone in that population (whether majority or minority)[24].

Consequences of failing to address health disparities extend beyond an ethical viewpoint. These gaps can hinder a medical patient's trust in public health institutions, especially amongst disadvantaged communities. Would you revisit a practitioner who has misdiagnosed you before? Or would you redo a blood test at a blood testing centre that had previously consigned you with faulty results? This can lead to a decreased use of preventive services and impede efforts to control infectious diseases. The tenet of beneficence is a well-known clinical principle which compels us – and physicians in particular – to act in the best interest for both ourselves and for others, which clearly conflicts with the existence of populations facing health inequalities. Similarly, nonmaleficence – described as the principle of avoiding harm – is violated by negative health outcomes. So, distributive justice exemplifies an unfair distribution of burdens and benefits presented even by first world countries[24]. Furthermore, disparities can exacerbate existing social injustices, limiting any opportunity for education or economic improvements[24]. In the sense that poor health can significantly impact an individual's performance and productivity in the workforce; It can also increase absenteeism in school, hence limiting educational attainment, resulting in difficulty in securing or maintaining a job. These factors can trap individuals in a cycle of poverty, perpetuating reduction in access to resources and magnifying social and economic disadvantages caused by health inequalities[25].

Another significant issue that pertains whilst discussing the ethical framework for health equity is informed consent. Patients

need a clear understanding of what genetic testing is, and the implications it has for themselves and even family members. For instance, genetic testing can possibly reveal predispositions to certain diseases, which can lead to psychological distress and tension between family members if not handled with sensitivity. Genetic privacy is a concern, as potential misuse of personal genetic information by insurance companies, or employers can lead to fear and mistrust amongst patients when it comes to being genetically tested. Ethical policies must be put in place, with strict regulations concerning the limitations of the amount of patients' data different parties can have access to.

**Limitations of Current Research**

Despite advancements in any field, there will always be limitations, and achieving equitable healthcare remains a persistent challenge. Current research limitations can obstruct progress in trying to effectively address these disparities. Drawing insights from varied sources, this subchapter will analyse the areas where evolution of research methods is necessary for a more impactful approach.

An obstacle in the fight against health disparities lies in the complexity of quantifying the issue itself. Existing pointers, such as the Gini coefficient (an index that measures socioeconomic inequalities across different regions globally), often fail to capture the multifaceted nature of the problem[26] . Much like the main constraint the UK Biobank faced throughout the study, it was not able to accurately emulate the diversity in disease prevalence across the UK due to a volunteer recruitment bias. These measures thus struggle to reflect the transfer of health benefits between advantaged and disadvantaged groups. In addition, limitations in data collection and the subjective nature of self-reported health status further complicate the measurement process, as many factors need to first be taken into account: Is the individual telling the truth? Are they overestimating/underestimating the extent of their condition? Are they consuming their medications as per their prescriptions? Subsequently, research may struggle to accurately assess the true extent of health disparities and impact the interventions aimed at reducing them.

While individual choices undoubtedly influence health outcomes, an increasing body of data and literature emphasises the crucial role of structural determinants of health. Social, economic and environmental factors, such as poverty, discrimination, and limited access to quality education and healthcare, significantly shape health trajectories. Throughout the course of my exchanges with Dr. Cox, she stated, "Most health disparities have nothing to do with genetics. Income – and income in recent generations – is a huge issue in health care access in places like the US where healthcare is not free or guaranteed," underscoring how important socioeconomic factors are in solving health inequities. For example, if a study aims to focus solely on the genetic predisposition to high cholesterol, as measured by laboratory values, addressing health disparities linked to it might face limited success if access to preventative medications remains unequal across populations.

By adopting an approach where research shifts its focus towards a more holistic approach to address health disparities, by considering the broader social context, research can have a substantial impact on influencing future policies and interventions that lead to a more just and equitable healthcare system for all.

**Policy Recommendations and Future Directions**

By moving beyond a narrow focus on individual behaviours and genetics, research and policy can play a transformative role in creating a more equitable healthcare system. This subchapter proposes key policy recommendations and explores promising future directions aimed at dismantling the structural barriers set by healthcare systems generations before.

In recent years, a new project has been piloted in several first world countries and that is: the whole-genome sequencing (WGS) of newborns. Due to its novelty in the healthcare sector, it has sparked heated debates on its ethical position, but as well the revolutionary stance it holds on evolving personalised medicine. WGS can identify genetic variations linked to diseases, allowing for early intervention and potentially better outcomes; particularly for childhood-onset diseases with existing treatments (eg. Muscular Atrophy)[27]. By identifying these mutations early on, parents can make informed decisions about family planning, which can help reduce the prevalence of certain diseases later in life. Though complete reliance on cloud storage to securely store data of hundreds of millions of newborns to come in the next few years comes with uncertainties. Storing and protecting vast amounts of sensitive and personal genetic data raises concerns about breaches, misuse by insurance companies, or social stigma. Currently, health professionals mainly advocate for targeted genetic screening, focusing on known disease genes with treatable conditions in newborns. WGS remains ethically and practically controversial, with pilot studies underway to assess its viability.

While existing health policies address broader health equities, and newer policies are being tested to assess their feasibility, there is still room for improvements and potential policy recommendations for incorporating genetics into a more holistic approach. The first is by promoting equity in genetic research and data collection. This can be accomplished by ensuring clinical trials consider genetic factors to include diverse populations throughout the trial process. This is vital for developing accurate genetic tests and treatment strategies that are effective across different ethnicities. As well, by standardizing data collection on race, ethnicity, and socioeconomic status alongside genetic information, allowing for a more extensive

interpretation of the individual's lifestyle and identity; so that researchers can identify and address any potential biases in genetic testing.

In order to ensure clinical trials are fair and inclusive of diverse genetic backgrounds, policies should mandate that recruitment efforts target underdispersed populations. Clinical trials that lack diversity only fail to bridge the gap in health disparities and lead to treatments that are less effective – if not harmful – to certain ethnic groups. Diversity in clinical trials can be increased via partnerships with community organizations and incentivising participation among minority groups. By subsidizing or providing insurance coverage for genetic testing, it can be included as part of public health programs; it also ensures that all patients, regardless of income, have access to personalized healthcare insights.

Furthermore, implementing policies to require medical and nursing schools to add genetic testing and personalized medicine into their curricula, and administering continuing education programs for current healthcare professionals. This equips all certified healthcare professionals the knowledge to interpret genetic test and accurately apply genetic insights into clinical decision-making, ensuring genetic information is used effectively in patient care.

As well, much like the UK Biobank, having governments invest in national genetic data registries to centralize and standardize genetic data for research purposes. Developing anonymous data collection standards, and limit access to authorized researchers allows for strict and ethical safeguarding measures to protect individual identities from being misused. This facilitates genetic research across populations while respecting individual privacy. Moreover, it provides researchers with a valuable resource to study genetic factors in diseases across diverse populations, supporting the development of personalized medicine.

In navigating future directions, it is essential to remain vigilant in ensuring that efforts sustained do not inadvertently widen the gap being bridged. The path forward requires a blend of innovation, collaboration, and changes to policies, including the development of inclusive reference ranges and equitable access to genetic testing. By integrating insights from recent research, emerging healthcare trends, and technological advancements, this review aims to highlight interdisciplinary strategies that can contribute to the minimization of health disparities across all groups.

Synthetic data – defined as information that is artificially generated, either by algorithms or artificial intelligence – can be deployed to train machine learning. It serves as a powerful tool in addressing health disparities by mitigating data scarcity and privacy concerts that regular genome sequencing would have. With challenges such as volunteer recruitment biases and limited data collections, methods could be developed to generate synthetic data using a small portion of existing data to accurately reflect unique health profiles of underrepresented populations. This can be investigated by the use of federated learning, a method where data remains siloed but the models are still trained collaboratively, or by exploring the potential of user-guided synthetic data generation, where researchers and stakeholders can provide input so that data reflects the experience of all populations.

Finally, the exploration of how synthetic data can be used to increase genetic datasets can be utilised in conjunction with traditional research methods, such as randomised controlled trials, to enhance research efficiency and overcome limitations in data availability. Synthetic data can also be used to fill in gaps in retrospective studies, enabling researchers to address historical health disparities with greater accuracy[28]. And by pursuing these future directions and focusing the lens on newer technologies, researchers and healthcare professionals can leverage the power of synthetic data to minimize health disparities by helping mitigate biases in health datasets.

## Conclusion

To summarise, relying on the integration of genetics into healthcare is essential, but not sufficient. Broader contexts need to be considered in which these disparities thrive. Moving forward, a more holistic approach, incorporating both into policy and research. Advocacy for equity in research and policy recommendations is crucial in dismantling structural barriers. And synthetic data may serve as a useful asset, overcoming traditional research limitations by reflecting the diverse nature of the human genome sequences. In a future enriched by technology promising personalised medicine, it is crucial to strive for equity in genetic research, data collection, and clinical trials, so that personalised medicine is not a privilege for the few, but rather a standard of care for all.

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## Glossary

ABO blood group system – A classification of human blood based on the presence or absence of antibodies and inherited antigenic substances.

**Allele** – A variant form of a gene at a particular locus on a chromosome.

**Apolipoprotein E (APOE)** – A class of proteins involved in the metabolism of fats in the body.

**Beta-amyloid plaque** – Accumulations of protein fragments that build up in the spaces between nerve cells, associated with Alzheimer's disease.

**Biomarkers** – Biological molecules found in blood, other body fluids, or tissues that are a sign of a normal or abnormal process, or of a condition or disease.

**Blood transfusion** – The process of transferring blood or blood-based products from one person into the circulatory system of another.

**Cardiovascular diseases** – A class of diseases that involve the heart or blood vessels.

**Disparities** – A great difference in level of treatment, which is seen as highly unfair and unjust.

**Duffy antigen receptor** – A protein on red blood cells that is known to act as a receptor for chemicals secreted during inflammation.

**Duffy-null allele** – A genetic variation associated with the absence of the Duffy antigen on red blood cells.

**Genetic predisposition** – An inherited genetic pattern that makes one susceptible to a certain disease.

**Genomic data** – Information about an organism's complete set of DNA, including all of its genes.

**Health equity** – The state in which everyone has a fair and just opportunity to be as healthy as possible.

**Heritability** – The proportion of a trait that can be passed down, typically to the next generation.

**Hyperlipoproteinemia** – A disorder resulting in the inability of the body to breaking down lipids.

**Isoforms** – Different forms of the same protein.

Mutation – The changing of the structure of a gene due to an abnormal alteration in the DNA.

**Phenotypic** – Relating to the observable characteristics of an individual resulting from the interaction of its genotype with the environment.

**Polymorphic state** – The presence of two or more alleles at a locus that produce different phenotypes.

**Precision medicine** – Medical care designed to optimise efficiency or therapeutic benefit for particular groups of patients, especially by using genetic or molecular profiling.

**Preventative strategies** – Approaches aimed at preventing disease or injury.

**Synthetic data** – Artificially generated data produced by algorithms that mimic the properties of real data.

**Variants** – Different forms or versions of genes.

**Volunteer recruitment bias** – The skewness of research results due to the characteristics of volunteers being systematically different from the general population