# Interethnic Differences in Serum Lipids

## Implications for Cardiometabolic Disease Risk in African Ancestry Populations

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### ABSTRACT

African Americans generally have a healthier lipid profile (lower triglycerides and higher high-density lipoprotein cholesterol concentration) compared with those of other ethnicities. Paradoxically, African Americans do not experience a decreased risk of the cardiometabolic diseases that serum lipids are expected to predict. This review explores this mismatch between biomarker and disease among African ancestry individuals by investigating the presence of interethnic differences in the biological relationships underlying the serum lipids—disease association. This review also discusses the physiologic and genomic factors underlying these interethnic differences. Additionally, because of the importance of serum lipids in assessing disease risk, interethnic differences in serum lipids have implications for identifying African ancestry individuals at risk of cardiometabolic disease. Where possible, data from Africa is included, to further elucidate these ancestral differences in the context of a different environmental background.

African Americans (AA) are generally found to have a healthier lipid profile (lower triglycerides [TG] and higher high-density lipoprotein cholesterol concentration [HDLC]) with a less atherogenic distribution of lipoprotein particles [1-3] compared with those of other ethnicities. Based on the more favorable lipid profile among African ancestry individuals and the established role of serum lipids as a biomarker predictive of cardiometabolic disease, one could reasonably anticipate a reduced burden of these diseases among AA. Epidemiological data, however, do not support this expectation (Table 1) [4]. In fact, AA have a markedly higher prevalence of cardiovascular disease than European ancestry (EA) individuals, driven primarily by a higher prevalence of hypertension. The prevalence of type 2 diabetes (T2D) in AA is more than twice the prevalence in EA individuals. This mismatch between biomarker and disease among AA suggests that ancestry may add further complexity to the underlying relationships that serum lipids are expected to capture. We will try to answer why a favorable lipid profile does not translate into reduced cardiometabolic risk for African ancestry individuals. To address this key question, we will investigate the assumptions necessary to go from biomarker to disease and assess how interethnic differences could affect these assumptions. Moreover, we will discuss the physiologic and genomic factors underlying these interethnic differences. Finally, we will investigate the impact that this mismatch may have on identifying African ancestry individuals at risk of cardiometabolic disease. Much of the evidence relevant to this "metabolic paradox" involves comparisons of AA and EA, yet observations in West Africans may also be of considerable importance. Whereas admixed AA have a large proportion of shared ancestry with West Africans (~80%), the environmental context is dramatically different across populations, which may prove to be very informative for understanding the relative contributions of inherited and environmental influences on these complex traits. West African individuals are generally leaner and more physically active than their AA counterparts, yet with increasing urbanization and Westernization, they are also experiencing dramatic increases in cardiometabolic disease. In fact, it is anticipated that Africa will experience some of the most dramatic increases in T2D worldwide [5]. Complex disease research in Africa is experiencing notable advances, spurred, in part, by efforts such as the Human Health and Heredity in Africa initiative (H3Africa [6,7]), more data from Africa is available, with much more anticipated in the short term as major research projects release results. Thus, in this review, we will address these questions, drawing in data from Africa where available.

### INTERETHNIC DIFFERENCES IN SERUM LIPIDS

Ethnic differences in serum lipids have been widely reported. The most consistently observed difference in the concentration of serum lipids is lower TG among African ancestry individuals. This difference can be seen among ethnicities in the United States in the NHANES (National Health and Nutrition Examination Survey) dataset, which was designed to be representative of the US population: mean TG was 113, 143, and 158 mg/dl in AA, European Americans, and Mexican Americans, respectively [8]. Differences in TG are also observed in children; for example, TG was 15.7 mg/dl lower among AA compared with

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**TABLE 1.** U.S. prevalence of cardiometabolic diseases and predictors of risk

| | African American | | European American | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Cardiovascular disease | 44.8 | 47.3 | 37.4 | 33.8 |
| Coronary heart disease | 7.9 | 7.6 | 8.5 | 5.8 |
| Myocardial infarction | 4.3 | 2.2 | 4.3 | 2.1 |
| Stroke | 4.5 | 4.4 | 2.4 | 3.3 |
| Hypertension | 43.0 | 45.7 | 33.9 | 31.3 |
| Diagnosed diabetes mellitus | 14.3 | 14.7 | 6.8 | 6.5 |
| Undiagnosed diabetes mellitus | 4.8 | 4.0 | 3.9 | 1.9 |
| Heart failure | 4.5 | 3.8 | 2.7 | 1.8 |
| Metabolic syndrome | 25.3 | 38.8 | 37.2 | 31.5 |
| Low HDL | 16.6 | 6.6 | 29.5 | 10.1 |
| Overweight and obesity | 70.8 | 77.7 | 72.3 | 59.3 |

Non-Hispanic white and black individuals ≥20 years. Data from AHA Report on Heart Disease and Stroke Statistics [4]. All data given as percentages.
HDL, high-density lipoprotein.

non-AA children (predominantly EA) [9]. The prevalence of high TG (>150 mg/dl) among NHANES AA children and adolescents was less than one-half that of EA [10]. Data from West Africa agree with these findings, with mean TG values that are generally even lower than what is observed among admixed AA. For illustration, mean TG values from population-based studies of adults without lipid-altering diseases are presented by ethnicity (Figure 1) [8,11-28].

Among US populations, AA are also generally found to have HDLC concentrations about 4 to 5 mg/dl higher than those of other ethnic groups [8], differences that are also apparent in studies of children and adolescents [1,9,10,29,30]. However, this difference in distribution is not what is observed among Africans, where the HDLC concentration is more similar to [31,32] or lower [33,34] than what is observed in EA individuals. It is unclear what leads to this discrepancy between African ancestry individuals in different locations, but it seems reasonable that HDLC is under the influence of an environmental factor that differs between the United States and Africa. Some environmental factors—malnutrition and urbanization—are worth investigating further in order to understand these low HDLC concentrations among Africans. Researchers have found the low HDLC co-occurs with micronutrient deficiencies, as well as with low body weight [35]. Studies of the Capetown, South Africa, in 1990 and in 2008/2009 showed marked increases in the prevalence of low HDLC, from 37.3% to 55.1% among men and 30.0% to 67.7% among women. Peer et al. [36] highlight increasing adiposity and urbanization as likely contributors. In contrast, higher HDLC values were observed among members of the Gbagi tribe in Abuja, Nigeria, who were living in an urban compared with a rural environment, despite higher body mass index (BMI) and waist circumference among the urban dwellers [11]. Further work is necessary to disentangle the components of "urbanization" that are most relevant for cardiometabolic disease risk. An intriguing study of 1,266 diabetic individuals in the Congo suggests a different association between HDLC and cardiometabolic disease in this environment: among individuals with low HDLC, the rate of fatal cardiovascular events was 13.5%, but among those with high HDLC, the rate was 20%. Additionally, the mean change in blood glucose after a meal was similar in the high and low categories (131.2 and 137.0 mg/dl, respectively) and was much lower in those with intermediate HDLC levels (87 mg/dl). Importantly, HDLC also had a U-shaped relationship with risk of atherosclerotic complications [37]. Further investigations into this relationship in other African populations are needed.

## PHYSIOLOGY UNDERLYING INTERETHNIC DIFFERENCES IN SERUM LIPIDS

Serum lipids are strongly correlated with fat distribution, particularly an individual's visceral adipose tissue. Visceral adipose tissue is known to be a uniquely pathogenic fat depot in terms of cardiometabolic risk. Visceral adipose tissue is more strongly associated with development of key perturbations for cardiometabolic risk, including impaired glucose tolerance, blood pressure, and dyslipidemia, than are other anthropometric measures (including BMI, waist circumference, waist-hip ratio, leg fat percentage, trunk fat percentage) [38] or subcutaneous adipose tissue [39,40]. Visceral adipose tissue is known to correlate strongly with serum lipids, with increased visceral adipose tissue contributing to increased liver fat content, which, in turn, leads to greater production of very low-density lipoprotein and higher circulating TG [41]. In fact, in a study of 723 AA and EA men and women, visceral adipose tissue explained over 24% of the variation in fasting TG and 31%

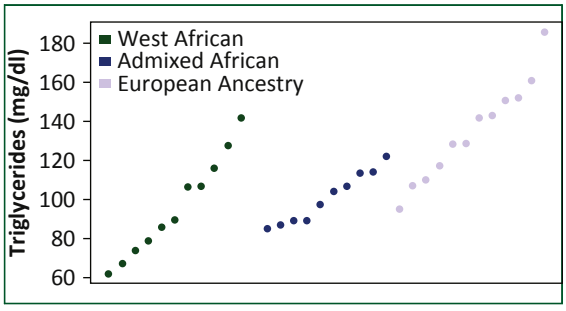


**FIGURE 1. Distribution of triglycerides by ancestry.** Reported triglyceride values in studies of West Africans [11-20], African Americans [8,14,17,21-23,25-28], and those of European ancestry [8,21-25,27]. Limited to those without disease (type 2 diabetes, hypertension, human immunodeficiency virus, or liver disease). Weighted means were used to combine by sex and alcohol drinking status (if reported). Due to amount of available data, European ancestry studies were limited to the United States and the United Kingdom.