HHS Public Access

Author manuscript

Curr Diab Rep. Author manuscript; available in PMC 2023 March 01.

Published in final edited form as:

Curr Diab Rep. 2022 March ; 22(3): 129–136. doi:10.1007/s11892-022-01451-6.

Racial Disparities and Cardiometabolic Risk: New Horizons of Intervention and Prevention

Eftitan Y. Akam[1,2,3], **Akua A. Nuako**[1,3], **Afkera K. Daniel**[1,2,3], **Fatima Cody Stanford**[3,4]

[1]Massachusetts General Hospital Department of Medicine, 55 Fruit Street, Boston, MA 02114, USA

[2]Massachusetts General Hospital Department of Pediatrics, 55 Fruit Street, Boston, MA 02114, USA

[3]Harvard Medical School, Boston, MA 02115, USA

[4]Massachusetts General Hospital, MGH Weight Center, Department of Medicine-Division of Endocrinology-Neuroendocrine, Department of Pediatrics-Division of Endocrinology, Nutrition Obesity Research Center at Harvard (NORCH), 50 Staniford Street, Boston, MA 02114, USA

Abstract

Purpose of Review—Cardiometabolic diseases are a leading cause of morbidity and mortality in the USA and disproportionately impact racial and ethnic minorities. Multiple factors contribute to this disparity including genetic and socioeconomic factors, the latter of which contributes to disparities both through systemic barriers such as healthcare access and by directly impacting metabolism through epigenetics and environment-related alterations in the gut microbiome. This review will discuss advances in medicine that can be used to identify, prognosticate, and treat cardiometabolic diseases, and how these may be used to address existing disparities.

Recent Findings—There is growing research aimed at identifying novel cardiometabolic disease targets and expanding the use of existing pharmacotherapies based on comorbidities. Advances in metabolomics and genomics can give insight into an individual's unique biochemical profile, providing the means for earlier identification of disease and specific treatment targets. Moreover, developments in telehealth and related medical device technologies can expand access to underserved minority populations and improve control of chronic conditions such as diabetes and hypertension.

Summary—Precision medicine may be integral to bridging the racial gap in cardiometabolic disease outcomes. Developments in genomics, metabolomics, wearable medical devices, and telehealth can result in personalized treatments for patients that account for the socioeconomic and genetic factors that contribute to poor health outcomes in minorities. As research in this field rapidly progresses, special efforts must be made to ensure inclusion of racial and ethnic minority populations in clinical research and equal access to all treatment modalities.

✉Eftitan Y. Akam, eyakam@partners.org.

Declarations

Competing Interests The authors declare no competing interests.

This article is part of the Topical Collection on *Macrovascular Complications in Diabetes*

Keywords

Disparities; Cardiometabolic health; Obesity; Diabetes; Genomics; Metabolomics

Introduction

Cardiovascular disease (inclusive of coronary heart disease, heart failure, and stroke) is the leading cause of death in the USA [1], killing approximately 1 in 4 individuals annually [2•]. It impacts 9.3% of the population (26.1 million individuals in 2018) [1], and despite overall improvement in mortality due to evolving care management, racial and ethnic minority patients experience a disproportionately higher level of morbidity and mortality than non-Hispanic White patients [3•, 4–6]. These disparities are reflected in the prevalence of cardiometabolic risk factors such as hypertension, diabetes mellitus, obesity, and non-alcoholic fatty liver disease (NAFLD).

The most common cardiovascular disease in the USA is hypertension, impacting 47.3% of adults ≥ 20 years old in the USA (121.5 million in 2019). Non-Hispanic Black (NHB) adults have the highest prevalence (57.1%), followed by Hispanic (43.7%) and non-Hispanic White (NHW) (43.6%) adults [2•]. Obesity is a common major risk factor for cardiovascular disease and the leading cause of years lived with disability in the USA [2•]. The prevalence of overweight and obesity has been rising steadily across all racial/ethnic groups. In 2018, 71.3% of Americans were classified with overweight or obesity (defined as body mass index [BMI] ≥ 25 kg/m^2 and ≥ 30 kg/m^2 in adults, respectively). Minority groups have been shown to be disproportionately affected by overweight and obesity at all ages [7], with the highest prevalence of obesity in NHB (49.6%), followed by Hispanic (44.8%), NHW (42.1%), and Asian (17.4%) adults [2•, 8].

Diabetes follows a similar trend to obesity. Diabetes mellitus refers to a group of conditions caused by dysregulation of glucose control, of which 90–95% is the result of type 2 diabetes. It is another major risk factor for cardiovascular disease [9], and its prevalence is on the rise in both the pediatric and adult population. Among American adults ≥ 20 years old, 9.8% (26 million in 2016) carry a diagnosis of diabetes, and a further 37.6% (91.8 million) carry a diagnosis of prediabetes. Estimates for total diabetes prevalence (both diagnosed and undiagnosed) reveal higher rates for ethnic/racial minorities: 16.4% in NHB, 14.9% in Asian, 14.7% in Hispanic, and 11.9% in NHW adults [10].

Non-alcoholic fatty liver disease (NAFLD) is becoming recognized as the hepatic manifestation of metabolic syndrome [11]. It is the most common chronic liver disease in the USA and affects an estimated 75–100 million people [12]. Its manifestation ranges from simple steatosis, to non-alcoholic steatohepatitis (NASH), to cirrhosis and end-stage liver disease. The prevalence of NAFLD is disproportionately high in Hispanic populations [13], with rates estimated at 23% for Hispanic, 14% for NHW, and 13% for NHB adults [14]. Dyslipidemia shows a similar trend. Dyslipidemia refers to disorders of lipoprotein metabolism leading to elevated total cholesterol (TC), elevated triglycerides, elevated low-density lipoprotein cholesterol (LDL-C), and low levels of high-density lipoprotein cholesterol (HDL-C). These abnormalities are directly related to the development of

atherosclerosis and cardiovascular disease. A total of 38.1% of Americans (93.9 million in 2018) have elevated total cholesterol ≥ 200 mg/dL. High total cholesterol prevalence is highest in NHW (11.7%), followed by Asian (11.6), Hispanic (10.9%), and NHB (10.0%) adults. Low HDL-C is highest in Hispanic (21.9%), followed by NHW (16.6%), Asian (15.8%), and is lowest in NHB (11.9%) [15].

The causes of disparities in cardiovascular and cardiometabolic disease are not fully understood but likely result from a combination of genetic, metabolic, and socioeconomic factors. Markers of socioeconomic status such as education, income and income inequality, and employment have all been shown to be related to cardiovascular disease risk and outcomes [16]. Other social circumstances like social/familial supports, the built environment in which individuals live, language barriers, and healthcare access are similarly important determinants of cardiovascular health [16]. A number of these factors can directly impact gene expression through epigenetic dysregulation [17] and can impact metabolism by altering the gut microbiome [18]. Thus, a precision medicine approach that accounts for individual social, genetic, and lifestyle variability in the prevention, diagnosis, and treatment of cardiometabolic conditions is essential for improving outcomes and may be key in reducing or eliminating disparities in cardiometabolic disease.

This paper will provide a brief overview of current screening and treatment options for cardiometabolic diseases, describe research areas that may inform future treatment, and discuss barriers to how these may be utilized to reduce racial/ethnic disparities in cardiometabolic risk and cardiovascular disease outcomes.

Screening

Early identification of cardiometabolic disorders for prompt intervention is a health priority, and providers routinely screen for diabetes, hypertension, hyperlipidemia or dyslipidemia, and obesity. The American Diabetes Association (ADA) recommends screening for diabetes with hemoglobin A1C, fasting plasma glucose (FPG), or oral glucose tolerance test (OGTT) for all adults aged ≥ 45 years and adults with BMI ≥ 25 kg/m^2 (≥ 23 kg/m^2 in Asian Americans) with additional risk factors for diabetes. The US Preventive Services Task Force (USPSTF) suggests annual screening for hypertension in all adults aged ≥ 40 years and for adults at increased risk for hypertension (including Black people, people with overweight or obesity, and people with blood pressure in the high-normal range). Regarding obesity, the USPSTF recommends screening all adults, although there is not enough evidence to suggest an optimal screening interval [19]. The American College of Cardiology (ACC) recommends a lipid profile to initially screen for hyperlipidemia or dyslipidemia in adults aged ≥ 20 years with the subsequent reassessment of traditional risk factors for hyperlipidemia every 4 to 6 years [20]. The consideration of race in screening for diabetes and hypertension is a means of accounting for the known disparities in disease risk in certain racial/ethnic minorities, thereby improving rates of early identification in these groups.

Outside of traditional screening mechanisms, technologies enabling the measurement of the products of metabolism are emerging as potential means of screening and prognostication. This field, called metabolomics, allows for direct understanding of the biochemical activity

in cells and tissue, providing a biochemical “snapshot” of a patient’s health [21, 22], and may prove a cost-effective method for cardiovascular disease screening. Researchers have identified that aberrant levels of some lipid metabolites[23, 24] and other organic biomarkers [25] are predictors for coronary artery disease and increased risk of myocardial infarction (MI) [23]/ These metabolites have been implicated in increased inflammatory signaling, activation of stress pathways, impaired insulin signaling, and alterations in normal cell metabolism, leading to metabolic syndrome [21, 26]. Metabolomic screenings for cardiometabolic disease may allow for earlier identification of disease or future disease risk, thereby improving overall outcomes.

Treatment

Lifestyle Modifications

Lifestyle modifications such as weight loss, healthy diet, reduced consumption of alcohol and sodium, and adequate physical activity are first-line recommendations for treating many cardiometabolic diseases [27]. The growth of virtual resources has increased access to weight management, nutrition, and exercise programs to wider audience, specifically to groups of low socioeconomic status and racial/ethnic minorities. This improvement in access may have a significant beneficial impact for minorities: studies have shown that web-based programming, smartphone technology, social media, text messaging, and wearable activity trackers may improve weight loss and diet, sometimes beyond what can be achieved with conventional programs alone [28–31].

Notably, consideration of individual patient characteristics is vital when recommending lifestyle modifications. A “one-size-fits-all” approach fails to account for the social, environmental, and genetic differences that contribute to poor disease outcomes in minority groups. Strelitz et al. found in an observational study that both weight loss and weight gain after diabetes diagnosis were associated with higher mortality, particularly among patients without obesity [32], indicating that a recommendation for weight loss should not be globally applied. Responses to specific diets can also vary widely between individuals, and randomized trials have shown mixed results in the ability of low carbohydrate and high glycemic index diets to control blood glucose [33], which may be due to interpersonal variations in the post-prandial glycemic response to certain foods [34–36] and differences in gut bacteria. Indeed, the gut microbiome is a crucial component of metabolism; there is a growing body of evidence linking gut dysbiosis or negative alterations in the gut microbiome which can result from environmental factors, with cardiometabolic disorders [37–44]. The use of metabolomics to tailor lifestyle and other therapies to individual metabolism can bypass the need to identify and account for the many social/biologic elements that influence racial and ethnic disparities by directly measuring the biochemical impact of these elements and targeting them.

Novel technologies that allow patients to screen for, monitor, and individualize lifestyle interventions for chronic medical conditions show tremendous potential to transform the care of conditions like diabetes and hypertension. For example, continuous glucose monitors (CGMs) have been shown to improve glycemic control and reduce episodes of hyper- and hypoglycemia in patients with type 1 diabetes or type 2 diabetes requiring intensive insulin

[45]. Utilization of other diabetes technology such as insulin delivery devices, mobile health applications, and telemedicine have also been shown to improve disparities in diabetes outcomes [46]. New “cuff-less” blood pressure monitoring devices utilize wearable sensor technologies to estimate blood pressure from electrocardiogram (ECG) signals and skin blood flow estimates from infrared light signals called photoplethysmograms and can be used by patients in a home setting. Blood pressure self-monitoring has been shown to improve blood pressure control and to be a better predictor of end-organ damage than in-clinic measurements when used in conjunction with nursing or pharmacist intervention [45]. When utilized in tandem with smartphone applications and telehealth services, such technologies can allow for more accurate tracking of health status and greater access to healthcare providers, which ultimately leads to better illness control and to reducing gaps in access for medically underserved minority populations.

Pharmacotherapy

Exciting advancements in pharmacotherapy and genomics have led to improvements in the care for patients with cardiometabolic diseases. Several medications developed to address metabolic syndrome have recently risen in prominence due to their benefit in addressing multiple comorbid diseases simultaneously, which helps to optimize pharmacotherapy according to a person’s unique cardiometabolic risks. Applying this approach in pharmacotherapy selection for minority patients can improve overall morbidity and mortality and reduce some of the disparities in disease outcomes. For example, glucagon-like peptide-1 (GLP-1) agonists, sodium-glucose transport protein 2 (SGLT2) inhibitors, and thiazolidinediones are classes of medications originally used primarily to improve glycemic control in patients with type 2 diabetes. Since then, these medications been investigated extensively for their potential additional benefits in fighting cardiometabolic disease.

Liraglutide, a GLP-1 agonist, has been shown to reduce cardiovascular (CV) risks in patients with type 2 diabetes (with lower rates of first occurrence of death from CV causes, non-fatal myocardial infarction, and non-fatal stroke among patients taking liraglutide versus placebo) [47]. The CV benefits of GLP-1 agonists could be mediated by their beneficial effects on blood pressure, vascular inflammation and atherosclerosis progression, and weight loss in patients with obesity [48, 49]. Data show that liraglutide also reduced rates of the development and progression of kidney disease in patients with type 2 diabetes [50]. Another GLP-1 agonist, semaglutide, has been shown in multiple randomized controlled trials to result in significant weight loss in patients with obesity when used in conjunction with lifestyle management compared to lifestyle management and placebo [51, 52]. This was associated with statistically significant improvement in hypertension, lipids, glycemic control [49, 51, 52], and markers of inflammation [49, 51]. SGLT2 inhibitors also have additional benefits for patients with type 2 diabetes; they reduce the risk of major adverse CV events, kidney outcomes, and heart failure [53, 54]. Additionally, patients with heart failure with reduced ejection fraction (HFrEF) (with or without diabetes) taking specific SGLT2 inhibitors (empagliflozin and dapagliflozin) have improved renal and all-cause CV outcomes [55].

Pioglitazone is another anti-diabetes medication that has been investigated in the realm of cardiometabolic disease, namely, non-alcoholic steatohepatitis (NASH). Trials have shown that this medication improves liver histology in patients with NASH (with and without diabetes); however, it also carries an increased risk of weight gain, bone loss, and potentially bladder cancer, limiting its ability to be used safely in all patients. The American Association for the Study of Liver Diseases (AASLD) statement on the management of NAFLD recommends that pioglitazone can be used for patients with biopsyproven NASH but recommends against its use in patients with NAFLD without biopsy-proven NASH [12].

Spironolactone and eplerenone, steroidal mineralocorticoid receptor antagonists (MRAs), are part of guideline-directed medical therapy for patients with symptomatic heart failure with ejection fraction of ≤ 35% [56]. They have been shown to reduce all-cause hospital readmission rates in patients with heart failure and diabetes mellitus or chronic kidney disease (despite greater risk of readmissions for hyperkalemia and acute renal insufficiency in patients taking MRAs) [57]. Recent data has shown that finerenone, a selective non-steroidal mineralocorticoid receptor antagonist, improves CV outcomes among patients with type 2 diabetes and chronic kidney disease and lowers the risk of kidney disease progression in these patients [58, 59]. Finerenone provides cardiometabolic benefit that is similar to spironolactone, but there is a lower risk of hyperkalemia and kidney injury [60].

Immune Modulators

For much of the twentieth century, atherosclerosis was regarded as simply a disease of lipid storage. In recent decades, there has been an increasing recognition of the integral role of inflammation in mediating cardiometabolic diseases [61, 62]. Several autoantigens (i.e., oxidized low-density lipoprotein, β2 glycoprotein I, heat shock proteins) and related autoantibodies (i.e., anti-ox-LDL, anti-β2-GPI, and anticardiolipin antibodies) have been implicated in the pathogenesis of atherosclerosis. These antigens and antibodies are thought to form complexes and release cytokines that trigger the inflammatory processes which contribute to vascular damage and plaque progression and rupture [63]. Inflammation increases the risk of developing multiple cardiometabolic diseases, as people with higher levels of serum inflammatory markers secondary to various autoimmune diseases have been found to have higher risks of developing adverse CV outcomes and type 2 diabetes [64]. There is a growing field of research exploring the use of immunotherapies to target various points along these pathways [65], with mixed results.

The phospholipase A2 (PLA2) enzyme superfamily is associated with lipoprotein metabolism and is important in the attraction and maintenance of pro-inflammatory cells in vascular walls [66]. Varespladib, a non-selective inhibitor of secretory PLA2, has been shown in animal studies to significantly decrease the size of atherosclerotic lesions [66] however was associated with increased risk of MI in a double-blind randomized study [67]. Darapladib, a selective inhibitor of lipoprotein-associated phospholipase A2 (Lp-PLA2), has been shown to effectively decrease circulating Lp-PLA2 and interleukin-6 (IL-6) [68], but did not significantly reduce CV events in a double-blind trial [69]. Similarly, a randomized double-blind trial utilizing methotrexate, a commonly used purine and pyrimidine synthesis inhibiting immunosuppressant, did not find a reduction in inflammatory biomarker levels

or, more importantly, CV outcomes [70]. Multiple trials studying the effect of tumor necrosis factor (TNF) antagonists did not find improved CV outcomes when treating with etancercept [50] or with infliximab [71]. Further studies with infliximab also failed to show an improvement in glucose homeostasis [72, 73].

Other treatment options have shown more success; a randomized prospective trial examining the effects of the antioxidant succinobucol resulted in fewer major adverse cardiovascular events (MACEs) and strokes in the treatment group, as well as decreased incidence of new-onset diabetes when compared with placebo [74]. A large randomized double-blind trial of canakinumab, a monoclonal antibody targeting interleukin −1β, showed that treatment with canakinumab led to a significantly lower rate of CV events compared to placebo [75]. Despite the discordant findings in the studies above, this is a promising field that may revolutionize the treatment of cardiometabolic conditions by coupling metabolomic markers with individualized and targeted therapies.

Pharmacogenomics

Genomics is an increasingly important field of study in the treatment of cardiovascular disease and its risk factors. Pharmacogenomics, or the ways in which a person's genetics influences their metabolism of drugs, can allow for a more personalized approach to disease treatment, thereby improving the drug effect and disease outcome. The use of pharmacogenomics in cardiometabolic disease is not new; following percutaneous coronary interventions (PCI), dual antiplatelet therapy (DAPT) which includes a $P2Y_{12}$ inhibitor (clopidogrel, prasugrel, or ticagrelor) and aspirin, is recommended to prevent MACEs [76]. Although clopidogrel is commonly prescribed, it is associated with an increased risk of MACEs in patients with loss-of-function *CYP2C19* alleles, who could represent up to 30% of American adults [77]. Using genetic testing to guide antiplatelet therapy reduces risk of MACEs post-PCI [78] and has become a part of routine care in some institutions.

Newer therapies have been developed that target genetic mutations leading to disease; familial hypercholesterolemia (FH) is an autosomal dominant genetic disorder characterized by elevated serum low-density lipoprotein cholesterol (LDL-C) and which carries an increased risk of premature coronary artery disease (CAD). Though clinical diagnosis of FH and early initiation of statins have been shown to reduce cardiometabolic risk, studies suggest that tailoring medication choices according to specific mutations can lead to better medication responses and clinical outcomes. Tada and colleagues demonstrated in a number of studies that that carriers of certain FH mutations (and related dyslipidemias) may respond well to ezetimibe, in some cases with better results than statins (such as in patients with sitosterolemia) [79–81]. Anti-proprotein convertase subtilisin/kexin type 9 (PCSK9) antibodies lower cholesterol by targeting the protein that degrades LDL and have shown promise in significantly lowering LDL levels in people with FH for whom previous therapies were ineffective [82].

In the field of obesity, setmelanotide recently gained FDA approval for chronic weight management in adults and children ≥ 6 years of age with genetic deficiency of proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) [83]. These deficiencies are only present in a small percentage of

the population affected by obesity, and several other genes like GPR75 are currently under investigation as potential pharmaceutical targets [84]. Other pharmacogenomic opportunities exist for patients with genetic heart conditions such as hypertrophic cardiac myopathy (HCM). Hodatsu and colleagues found that in patients with multiple mutations in myosin binding, protein C has less favorable phenotypes, including early disease onset or end-stage HCM [85]. In addition to the more-specific and rare genetic variations noted in the studies above, studies are also emerging that examine polygenic inheritance of CVD risk involving multiple common genetic variants [86, 87].

Pharmacogenomics presents an intriguing opportunity to reduce racial and ethnic disparities in cardiometabolic disease. By investigating and addressing the genetic foundations of metabolic syndrome and response to treatment in racial and ethnic minorities, the gap in cardiovascular disease outcomes can be narrowed.

Surgical Interventions

Metabolic and bariatric surgery (MBS) has great efficacy in the treatment of obesity and associated cardiometabolic diseases such as diabetes, hypertension, dyslipidemia, and obstructive sleep apnea (OSA), among others. Surgical intervention also has effects on satiety hormones and energy metabolism that contribute to the reduction of cardiometabolic risk in patients. Unfortunately, MBS is another area where racial and ethnic minority patients lag behind white patients in access [88]. The American Society for Metabolic and Bariatric Surgery (ASMBS) endorses several options for MBS. These include laparoscopic sleeve gastrectomy (LSG), which removes ~ 80% of the stomach; Roux-en-Y gastric bypass (RYGB), often called the “gastric bypass,” in which the stomach is divided to form a small pouch that is connected directly to a portion of the small intestine, leading food to bypass the rest of the stomach and the proximal small intestine; the adjustable gastric band (AGB), a device that loops around the top of the stomach in order to limit food consumption; biliopancreatic diversion with duodenal switch (BPD-DS), in which a tube-shaped stomach pouch is created similar to the sleeve gastrectomy, and the first portion of the small intestine is separated from the stomach, and a separate portion of small intestine is connected to the sleeved stomach in a manner that facilitates reduction calorie consumption and absorption; and finally single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S), which is identical to BPD-DS except that it involves only one surgical bowel connection instead of multiple [89].

Several endoscopic procedures have been developed in recent years to offer options for weight loss and cardiometabolic risk benefit in patients who are not candidates for MBS or who do not desire surgical interventions. FDA-approved endoscopic therapies include several different intragastric balloon (IGB) devices; the Aspire Assist, an aspiration tube that allows drainage of gastric contents after meal consumption, and two devices for performing stomach tissue apposition termed endoscopic sleeve gastroplasty. There are additional non-FDA approved gastric balloons, gastric plication devices, and small bowel targeted devices. Many of these interventions have been shown to contribute to weight loss as well as improvements in measures of cardiometabolic risk such as Hemoglobin A1c [90]. Thus,

strategies that improve access to these surgeries and procedures for minority patients could greatly reduce disparities in cardiometabolic disease outcomes.

Conclusion

Advances in telehealth, mobile health applications, wearable medical devices, surgical techniques, and metabolomics and pharmacogenomics will likely reshape the identification, prognostication, and treatment of cardiometabolic diseases. The medical community must proactively ensure that racial and ethnic minority patients are represented in this research and have adequate access to resulting treatments.

It is well documented that racial and ethnic minority groups are largely excluded from clinical trials [91] and genetic studies [92]. Barriers to minority involvement in research include lack of diversity within the scientific community, geographic and financial constraints, lack of resources for research in minority-rich areas, limited participant engagement (i.e., mistrust, personal and sociocultural beliefs, limited health literacy), investigator bias, and scarcity of research supports in minority-dense areas [93, 94, 95•]. Many possible strategies for improving diversity in clinical research have been proposed [91, 93, 95•], with a recurrent theme of greater community involvement in the research process. Given the widespread prevalence of cardiometabolic disease, racial and ethnic disparity in outcomes is an economic, public health, and ethics/justice issue. The innovations discussed in this paper can reduce or eliminate these disparities; however, this can only be accomplished with adequate diversity and inclusion of marginalized patient populations in all aspects of clinical research.

Funding

National Institutes of Health NIDDK P30 DK040561 (FCS) and L30 DK118710 (FCS).

References

Papers of particular interest, published recently, have been highlighted as: • Of importance

1. National Center for Health, S., Health, United States, in Health, United States, 2018. 2019, National Center for Health Statistics (US): Hyattsville (MD).

2•. Virani SS, et al. , Heart Disease and Stroke Statistics—2021 Update. Circulation, 2021. 143(8): p. e254–e743. [PubMed: 33501848] This is a very comprehensive review of cardiovascular disease statistics, including cardiometabolic and lifestyle risk factors.

3•. Singh GK, et al. , Widening Socioeconomic and Racial Disparities in Cardiovascular Disease Mortality in the United States, 1969–2013. Int J MCH AIDS, 2015. 3(2): p. 106–18. [PubMed: 27621991] In this paper, researchers used population data to estimate cardiovascular disease disparities over time and found significantly increasing disparities, caused in part by improvements in mortality for high socioecnomic and majority populations.

4. Mazimba S and Peterson PN, JAHA spotlight on racial and ethnic disparities in cardiovascular disease. J Am Heart Assoc, 2021. 10(17): p. e023650. [PubMed: 34431360]

5. Mody P, et al. Most important articles on cardiovascular disease among racial and ethnic minorities. Circ Cardiovasc Qual Outcomes. 2012;5(4):e33–41. [PubMed: 22811508]

6. Graham G Disparities in cardiovascular disease risk in the United States. Curr Cardiol Rev. 2015;11(3):238–45. [PubMed: 25418513]

7. Wang Y, Beydoun MA. The obesity epidemic in the United States–gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. Epidemiol Rev. 2007;29:6–28. [PubMed: 17510091]
8. Hales CM, et al., Prevalence of obesity and severe obesity among adults: United States, 2017–2018., in NCHS Data Brief. 2020, National Center for Health Statistics: Hyattsville, MD.
9. Sarwar N, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375(9733):2215–22. [PubMed: 20609967]
10. Prevention Cf.D.C.a., National Diabetes Statistics report, 2020. 2020, Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services: Atlanta, GA.
11. Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. Hippokratia. 2009;13(1):9–19. [PubMed: 19240815]
12. Chalasani N, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328–57. [PubMed: 28714183]
13. Rich NE, et al. Racial and ethnic disparities in nonalcoholic fatty liver disease prevalence, severity, and outcomes in the United States: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2018;16(2):198–210.e2. [PubMed: 28970148]
14. Bonacini M, et al., Racial differences in prevalence and severity of non-alcoholic fatty liver disease. http://www.wjgnet.com/, 2021.
15. Carroll MD and Fryar CD, Total and high-density lipoprotein cholesterol in adults: United States, 2015–2018., N.C.f.H. Statistics, Editor. 2020, NCHS Data Brief: Hyattsville, MD.
16. Havranek EP, et al. Social determinants of risk and outcomes for cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2015;132(9):873–98. [PubMed: 26240271]
17. Soler-Botija C, Gálvez-Montón C, Bayés-Genís A. Epigenetic biomarkers in cardiovascular diseases. Front Genet. 2019;10:950. [PubMed: 31649728]
18. Phillips ML, Gut reaction: environmental effects on the human microbiota, in Environ Health Perspect. 2009. p. A198–205. [PubMed: 19478986]
19. Moyer VA, Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med, 2012. 157(5): p. 373–8. [PubMed: 22733087]
20. Grundy SM, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139(25):e1082–143. [PubMed: 30586774]
21. Ussher JR, et al. The emerging role of metabolomics in the diagnosis and prognosis of cardiovascular disease. J Am Coll Cardiol. 2016;68(25):2850–70. [PubMed: 28007146]
22. Sonnenburg JL, Bäckhed F. Diet-microbiota interactions as moderators of human metabolism. Nature. 2016;535(7610):56–64. [PubMed: 27383980]
23. Ganna A, et al. , Large-scale metabolomic profiling identifies novel biomarkers for incident coronary heart disease. PLoS Genet, 2014. 10(12): p. e1004801. [PubMed: 25502724]
24. Park JY, et al. , Alteration in metabolic signature and lipid metabolism in patients with angina pectoris and myocardial infarction. PLoS One, 2015. 10(8): p. e0135228. [PubMed: 26258408]
25. Tang WH, Hazen SL. The contributory role of gut microbiota in cardiovascular disease. J Clin Invest. 2014;124(10):4204–11. [PubMed: 25271725]
26. Muoio DM, Newgard CB. Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. Nat Rev Mol Cell Biol. 2008;9(3):193–205. [PubMed: 18200017]
27. Whelton PK, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;71(19):e127–248. [PubMed: 29146535]

28. Cheatham SW, et al. The efficacy of wearable activity tracking technology as part of a weight loss program: a systematic review. J Sports Med Phys Fitness. 2018;58(4):534–48. [PubMed: 28488834]
29. Lachausse RG. My student body: effects of an internet-based prevention program to decrease obesity among college students. J Am Coll Health. 2012;60(4):324–30. [PubMed: 22559092]
30. Sorgente A, et al. , Web-based interventions for weight loss or weight loss maintenance in overweight and obese people: a systematic review of systematic reviews. J Med Internet Res, 2017. 19(6): p. e229. [PubMed: 28652225]
31. Napolitano MA, et al. Using Facebook and text messaging to deliver a weight loss program to college students. Obesity (Silver Spring). 2013;21(1):25–31. [PubMed: 23505165]
32. Strelitz J, et al. Association of weight loss and weight loss maintenance following diabetes diagnosis by screening and incidence of cardiovascular disease and all-cause mortality: an observational analysis of the ADDITION-Europe trial. Diabetes Obes Metab. 2021;23(3):730–41. [PubMed: 33269535]
33. Sheard NF, et al. Dietary carbohydrate (amount and type) in the prevention and management of diabetes: a statement by the american diabetes association. Diabetes Care. 2004;27(9):2266–71. [PubMed: 15333500]
34. Vega-López S, et al. Interindividual variability and intra-individual reproducibility of glycemic index values for commercial white bread. Diabetes Care. 2007;30(6):1412–7. [PubMed: 17384339]
35. Vrolix R, Mensink RP. Variability of the glycemic response to single food products in healthy subjects. Contemp Clin Trials. 2010;31(1):5–11. [PubMed: 19737630]
36. Zeevi D, et al. Personalized nutrition by prediction of glycemic responses. Cell. 2015;163(5):1079–94. [PubMed: 26590418]
37. Qin J, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature. 2012;490(7418):55–60. [PubMed: 23023125]
38. Boursier J, et al. The severity of nonalcoholic fatty liver disease is associated with gut dysbiosis and shift in the metabolic function of the gut microbiota. Hepatology. 2016;63(3):764–75. [PubMed: 26600078]
39. Zhu L, et al. Characterization of gut microbiomes in nonalcoholic steatohepatitis (NASH) patients: a connection between endogenous alcohol and NASH. Hepatology. 2013;57(2):601–9. [PubMed: 23055155]
40. Koeth RA, et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. Nat Med. 2013;19(5):576–85. [PubMed: 23563705]
41. Rooks MG, Garrett WS. Gut microbiota, metabolites and host immunity. Nat Rev Immunol. 2016;16(6):341–52. [PubMed: 27231050]
42. Gilbert JA, et al. Microbiome-wide association studies link dynamic microbial consortia to disease. Nature. 2016;535(7610):94–103. [PubMed: 27383984]
43. Zhu W, et al. Gut microbial metabolite TMAO enhances platelet hyperreactivity and thrombosis risk. Cell. 2016;165(1):111–24. [PubMed: 26972052]
44. Tilg H, et al. The intestinal microbiota fuelling metabolic inflammation. Nat Rev Immunol. 2020;20(1):40–54. [PubMed: 31388093]
45. Rodbard D Continuous glucose monitoring: a review of recent studies demonstrating improved glycemic outcomes. Diabetes Technol Ther. 2017;19(S3):S25–s37. [PubMed: 28585879]
46. Eiland L, Thangavelu T, Drincic A. Has technology improved diabetes management in relation to age, gender, and ethnicity? Curr Diab Rep. 2019;19(11):111. [PubMed: 31686221]
47. Honigberg MC, et al. Use of glucagon-like peptide-1 receptor agonists in patients with type 2 diabetes and cardiovascular disease: a review. JAMA Cardiology. 2020;5(10):1182–90. [PubMed: 32584928]
48. Del Olmo-Garcia MI, Merino-Torres JF. GLP-1 receptor agonists and cardiovascular disease in patients with type 2 diabetes. J Diabetes Res. 2018;2018:4020492–4020492. [PubMed: 29805980]
49. Wilding JPH, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989–1002. [PubMed: 33567185]

50. Mann JFE, et al. Liraglutide and renal outcomes in type 2 diabetes. N Engl J Med. 2017;377(9):839–48. [PubMed: 28854085]
51. Wadden TA, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 Randomized Clinical Trial. JAMA. 2021;325(14):1403–13. [PubMed: 33625476]
52. Rubino D, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 Randomized Clinical Trial. JAMA. 2021;325(14):1414–25. [PubMed: 33755728]
53. McGuire DK, et al. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. JAMA Cardiology. 2021;6(2):148–58. [PubMed: 33031522]
54. Perkovic V, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380(24):2295–306. [PubMed: 30990260]
55. Zannad F, et al. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. Lancet. 2020;396(10254):819–29. [PubMed: 32877652]
56. Yancy CW, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136(6):e137–61. [PubMed: 28455343]
57. Cooper LB, et al. , Use of mineralocorticoid receptor antagonists in patients with heart failure and comorbid diabetes mellitus or chronic kidney disease. Journal of the American Heart Association, 2017. 6(12): p. e006540. [PubMed: 29275368]
58. Bakris GL, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. N Engl J Med. 2020;383(23):2219–29. [PubMed: 33264825]
59. Pitt B, et al. , Cardiovascular events with finerenone in kidney disease and type 2 diabetes. N Engl J Med, 2021.
60. Pitt B, et al. Safety and tolerability of the novel non-steroidal mineralocorticoid receptor antagonist BAY 94–8862 in patients with chronic heart failure and mild or moderate chronic kidney disease: a randomized, double-blind trial. Eur Heart J. 2013;34(31):2453–63. [PubMed: 23713082]
61. Libby P, Hansson GK. From focal lipid storage to systemic inflammation: JACC review topic of the week. J Am Coll Cardiol. 2019;74(12):1594–607. [PubMed: 31537270]
62. Ross R Atherosclerosis–an inflammatory disease. N Engl J Med. 1999;340(2):115–26. [PubMed: 9887164]
63. Cinoku II, Mavragani CP, and Moutsopoulos HM, Atherosclerosis: beyond the lipid storage hypothesis. The role of autoimmunity. Eur J Clin Invest, 2020. 50(2): p. e13195. [PubMed: 31868918]
64. Dregan A, et al. Chronic inflammatory disorders and risk of type 2 diabetes mellitus, coronary heart disease, and stroke: a population-based cohort study. Circulation. 2014;130(10):837–44. [PubMed: 24970784]
65. Murphy AJ, Febbraio MA. Immune-based therapies in cardiovascular and metabolic diseases: past, present and future. Nat Rev Immunol. 2021;21(10):669–79. [PubMed: 34285393]
66. Shaposhnik Z, et al. The synergistic inhibition of atherogenesis in apoE−/− mice between pravastatin and the sPLA2 inhibitor varespladib (A-002). J Lipid Res. 2009;50(4):623–9. [PubMed: 19029066]
67. Nicholls SJ, et al. Varespladib and cardiovascular events in patients with an acute coronary syndrome: the VISTA-16 Randomized Clinical Trial. JAMA. 2014;311(3):252–62. [PubMed: 24247616]
68. Wilensky RL, et al. Inhibition of lipoprotein-associated phospholipase A2 reduces complex coronary atherosclerotic plaque development. Nat Med. 2008;14(10):1059–66. [PubMed: 18806801]
69. White HD, et al. Darapladib for preventing ischemic events in stable coronary heart disease. N Engl J Med. 2014;370(18):1702–11. [PubMed: 24678955]

70. Ridker PM, et al. Low-dose methotrexate for the prevention of atherosclerotic events. N Engl J Med. 2019;380(8):752–62. [PubMed: 30415610]
71. Chung ES, et al. Randomized, double-blind, placebo-controlled, pilot trial of infliximab, a chimeric monoclonal antibody to tumor necrosis factor-alpha, in patients with moderate-to-severe heart failure: results of the anti-TNF Therapy Against Congestive Heart Failure (ATTACH) trial. Circulation. 2003;107(25):3133–40. [PubMed: 12796126]
72. Esser N, Paquot N, Scheen AJ. Anti-inflammatory agents to treat or prevent type 2 diabetes, metabolic syndrome and cardiovascular disease. Expert Opin Investig Drugs. 2015;24(3):283–307.
73. Bernstein LE, et al. Effects of etanercept in patients with the metabolic syndrome. Arch Intern Med. 2006;166(8):902–8. [PubMed: 16636217]
74. Tardif JC, et al. Effects of succinobucol (AGI-1067) after an acute coronary syndrome: a randomised, double-blind, placebo-controlled trial. Lancet. 2008;371(9626):1761–8. [PubMed: 18502300]
75. Ridker PM, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med. 2017;377(12):1119–31. [PubMed: 28845751]
76. Levine GN, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016;68(10):1082–115. [PubMed: 27036918]
77. Mega JL, et al. Reduced-function CYP2C19 genotype and risk of adverse clinical outcomes among patients treated with clopidogrel predominantly for PCI: a meta-analysis. JAMA. 2010;304(16):1821–30. [PubMed: 20978260]
78. Klein MD, et al. Clinical utility of CYP2C19 genotyping to guide antiplatelet therapy in patients with an acute coronary syndrome or undergoing percutaneous coronary intervention. Arterioscler Thromb Vasc Biol. 2019;39(4):647–52. [PubMed: 30760018]
79. Tada H, et al. Rare and deleterious mutations in ABCG5/ABCG8 genes contribute to mimicking and worsening of familial hypercholesterolemia phenotype. Circ J. 2019;83(9):1917–24. [PubMed: 31327807]
80. Tada H, et al. Sitosterolemia, hypercholesterolemia, and coronary artery disease. J Atheroscler Thromb. 2018;25(9):783–9. [PubMed: 30033951]
81. Tada H, et al. Beneficial effect of ezetimibe-atorvastatin combination therapy in patients with a mutation in ABCG5 or ABCG8 gene. Lipids Health Dis. 2020;19(1):3. [PubMed: 31901240]
82. Ogura M PCSK9 inhibition in the management of familial hypercholesterolemia. J Cardiol. 2018;71(1):1–7. [PubMed: 28784313]
83. FDA approves first treatment for weight management for people with certain rare genetic conditions. 2020.
84. Akbari P, et al. , Sequencing of 640,000 exomes identifies GPR75 variants associated with protection from obesity. Science, 2021. 373(6550): p. eabf8683. [PubMed: 34210852]
85. Hodatsu A, et al. Compound heterozygosity deteriorates phenotypes of hypertrophic cardiomyopathy with founder MYBPC3 mutation: evidence from patients and zebrafish models. Am J Physiol Heart Circ Physiol. 2014;307(11):H1594–604. [PubMed: 25281569]
86. Khera AV, et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. Nat Genet. 2018;50(9):1219–24. [PubMed: 30104762]
87. Tada H, Kawashiri MA, Yamagishi M. Comprehensive genotyping in dyslipidemia: mendelian dyslipidemias caused by rare variants and Mendelian randomization studies using common variants. J Hum Genet. 2017;62(4):453–8. [PubMed: 28055004]
88. Byrd AS, Toth AT, Stanford FC. Racial disparities in obesity treatment. Curr Obes Rep. 2018;7(2):130–8. [PubMed: 29616469]
89. Committee PE Bariatric surgery procedures. 2021 [cited 2021 November 21].
90. McCarty TR, Thompson CC. The current state of bariatric endoscopy. Dig Endosc. 2021;33(3):321–34. [PubMed: 32301158]
91. Coakley M, et al. Dialogues on diversifying clinical trials: successful strategies for engaging women and minorities in clinical trials. J Womens Health (Larchmt). 2012;21(7):713–6. [PubMed: 22747427]

92. Sirugo G, Williams SM, Tishkoff SA. The Missing Diversity in Human Genetic Studies. Cell. 2019;177(1):26–31. [PubMed: 30901543]

93. Bentley AR, Callier S, Rotimi CN. Diversity and inclusion in genomic research: why the uneven progress? J Community Genet. 2017;8(4):255–66. [PubMed: 28770442]

94. Kahn JM, et al. , Strategies to improve diversity, equity, and inclusion in clinical trials. Cancer, 2021.

95•. Clark LT, et al. , Increasing Diversity in Clinical Trials: Overcoming Critical Barriers. Current Problems in Cardiology, 2019. 44(5): p. 148–172. [PubMed: 30545650] In this paper, the authors investigated barriers to participation in clinical trials in minority communities both through literatire review and direct interviews with stakeholers. They identified critical themes in barriers and proposed solutions for how to increase minority participation in clinical research.