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Enhanced Atherosclerotic Cardiovascular Risk in South Asian Diaspora: A Comprehensive Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The population of South Asians (SA) is growing rapidly, leading to an increase in the global SA diaspora. Foreign-born SAs have been one of the fastest-growing immigrant populations in the United States over the past decade. There is a growing body of evidence suggesting SAs (immigrant and non-immigrant) are at higher risk for developing atherosclerotic cardiovascular disease (ASCVD). While traditional risk factors like diabetes, hypertension, tobacco use, and physical inactivity contribute to ASCVD risk among SAs, the risk remains high even after adjusting

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for these factors, suggesting other etiologies for this heightened risk, including atherogenic dyslipidemia, metabolic syndrome, visceral adiposity, unfavorable adipokine profile, higher lipoprotein (a), acculturation patterns, and unique dietary and psychosocial factors. The existing risk assessment tools for major adverse cardiovascular events have not been well studied in the South Asian population. The cardiovascular assessment strategies should involve using circulating biomarkers like ApoB, subclinical atherosclerosis imaging with coronary calcium scan (or carotid ultrasound), and newer tools like polygenic risk scores. Statins remain the foundation for lipid-lowering in SAs, just as in other populations. There are many knowledge gaps in risk assessment and management, and it is crucial to understand in detail the unique challenges and risk factors faced by the SA diaspora in the US to identify and manage cardiovascular disease in this population effectively.

Keywords: South Asians; Asian Indians; cardiovascular risk; dyslipidemia; ethnic variations; risk management.

ABBREVIATIONS

ASCVD	*Atherosclerotic Cardiovascular Disease*
Apo B	*Apolipoprotein B*
BMI	*Body Mass Index*
CAD	*Coronary Artery Disease*
CAC	*Coronary Artery Calcium*
CCTA	*Coronary Computed Tomography Angiography*
CVD	*Cerebrovascular Disease*
CRP	*C-Reactive Protein*
DM2	*Diabetes Mellitus type 2*
MI	*Myocardial Infarction*
NAFLD	*Non-Alcoholic Fatty Liver Disease*
MASLD	*Metabolic dysfunction-Associated Steatotic liver Disease*
NHW	*Non-Hispanic Whites*
SA	*South Asians*
LP(a)	*Lipoprotein (a)*

1. INTRODUCTION

The population of South Asians (SA), including individuals from India, Pakistan, Bangladesh, Sri Lanka, Maldives, Bhutan, and Nepal, is growing rapidly outside South Asia [1,2]. Over 5.6 million SAs live in the US, and approximately 80% of them are of Asian Indian origin [3]. SAs have an increased risk of adverse coronary heart disease outcomes even after adjustment for traditional risk factors such as diabetes, hypertension, tobacco use, and physical inactivity compared with non-Hispanic White (NHWs) individuals [4,5]. There is now a growing body of evidence that even within SAs, cardiovascular risk profiles vary between migrant and non-migrant communities [6]. In a study comparing non-migrant SAs in India and SAs living in the United Kingdom, British SA Indians had higher mean body mass indices, greater dietary energy intake, fat intake, blood pressure, fasting cholesterol, apolipoprotein B, triglycerides, and C-reactive protein concentrations than SA Indians living in their native country [7]. This suggests that although SAs living in their native countries share genetic and cultural risk factors with SAs living abroad, the two populations have other differences, such as varying socioeconomic status, education, healthcare behaviors, attitudes, access to, and quality of healthcare, and health insurance that contribute to differential cardiovascular risk profiles [8].

The “healthy immigrant effect,” where recent immigrants to a new country have overall better health than the nonimmigrant population in the host country, has been traditionally attributed to Asian Americans generally having lower mortality rates than the White population [9]. However, compared with non-Hispanic White (NHW) individuals, Asian Americans have a higher percentage of deaths from ischemic heart disease or cerebrovascular accidents relative to other causes [10]. Stratifying this further, compared with East Asians (Chinese, Japanese, Koreans, Vietnamese, etc.), SAs have higher mortality due to coronary artery disease and lower incidence of cerebrovascular disease [10]. These data suggest that while overall mortality rates might be lower among Asian Americans compared to NHW, cause-specific mortality rates, particularly for CVD, are not only higher among Asian Americans as a whole but also may be elevated among certain Asian American subpopulations such as South Asians [1]. This underscores the importance of examining unique cardiovascular risk factors prevalent in each of these Asian American subgroups separately [1].

In this review, we focus on the enhanced cardiovascular risk faced by SA in the USA, explore potential pathophysiological mechanisms underlying this enhanced risk, the tools available for measuring cardiovascular risk profiles, and identify the knowledge gaps and areas for additional research in this population. We performed a review of literature in PubMed and Google Scholar up until January 2024 using terms such as “South Asians,” “cardiovascular risk,” “dyslipidemia,” “genetic factors,” and “risk management.”

2. EPIDEMIOLOGY

2.1 South Asian CV Risk

SAs, Asian Indians in particular, have a higher proportion of mortality due to ischemic heart disease compared with other ethnic groups (Fig. 1) [11]. Cardiovascular disease was found to be the most common cause of death (35.5%) among SAs in the PURE (Prospective Urban Rural Epidemiology) study, where SAs from India, Pakistan, and Bangladesh were followed for 11 years [12]. Compared to urban areas, rural areas had a higher mortality rate (10.27 vs. 6.56 per 1000 person-years) and a higher incidence of CVD (5.41 vs. 4.73 per 1000 person-years). Compared with women, men had higher rates of CVD (6.42 vs. 3.91 per 1000 person-years) and death (10.66 vs. 6.85 per 1000 person-years). Bangladesh had the highest incidence of CVD among the SA countries, whereas Pakistan had the highest mortality rate. The largest population-attributable fractions (PAF) for CVD included hypertension (13.1%), high non-high-density lipoprotein (HDL) cholesterol (11.1%), diabetes (8.9%), low education (7.7%), abdominal obesity (6.9%), and household air pollution (6.1%). Low education (18.9%), low physical strength (14.6%), poor diet (6.4%), diabetes (5.8%), tobacco use (5.8%), and hypertension (5.5%) were the main PAFs for death [12]. The economic consequences due to the cost of CVD care in low and middle-income SA countries can be catastrophic [13].

Individuals born in India have a higher incidence of heart disease than US-born Indians. Age-standardized mortality rates (AMR) from all causes rose over time for Asian Indians born in India but fell over time for Asian Indians and NHWs born in the US. [14] These differences in mortality rates and causes of mortality could be due to various factors, including differential access to healthcare and primary prevention and differences in age distribution between the two populations, among other factors [14].

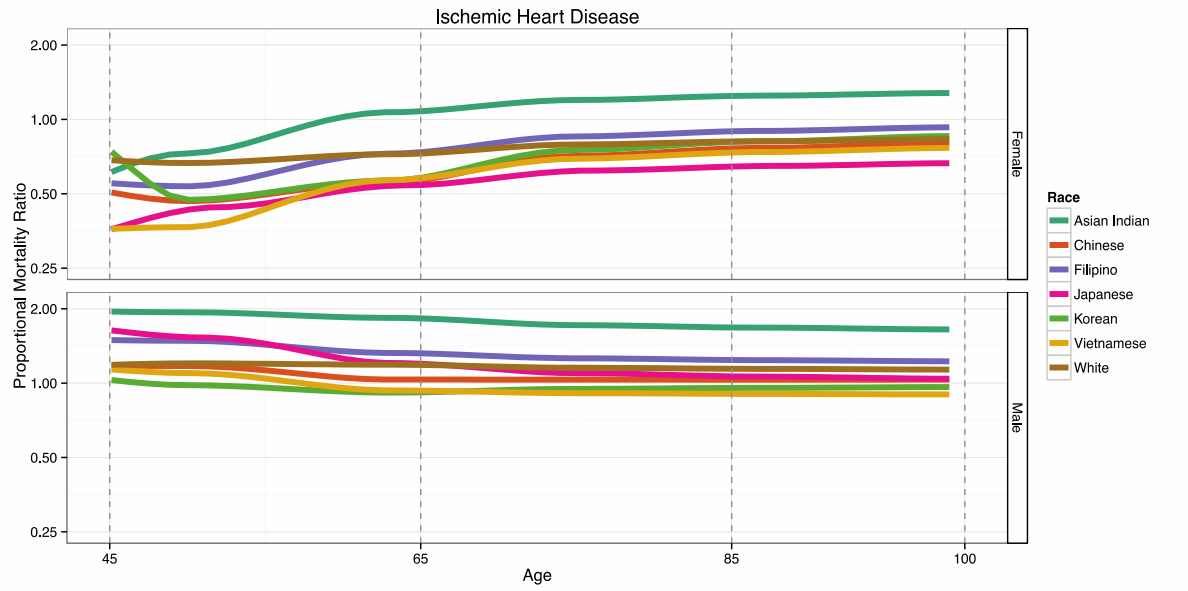

Fig. 1. Increased proportional mortality from ischemic heart disease in Asian Indians
The figure highlights the high proportional mortality ratio for Asian Indians in all age groups between 2003-2010 (*Fig. 1. Reprinted from Jose PO, Frank AT, Kapphahn KI, et al. Cardiovascular disease mortality in Asian Americans. Am Coll Cardiol. 2014;64(23):2486-2494. Copyright (2014) by Elsevier)*

2.2 South Asian Diaspora Cardiovascular Risk

Hastings et al. (2015) compared the top causes of death for the six main Asian subgroups (Asian Indian, Chinese, Filipino, Japanese, Korean, and Vietnamese) and NHWs from 2003 to 2011 based on US national mortality records [15]. Compared with all other Asian subgroups, Asian Indian females had the highest risk of heart disease (111.8 per 100,000 people). Both Asian Indian females (28.9 per 100,000) and males (28.1 per 100,000) had the lowest stroke mortality. For Asian Indian men, deaths from heart disease were nearly twice as common as those from cancer (31% vs. 18%) [15].

SAs living in the US also have a high incidence rate of diabetes compared to other ethnic groups [16]. In a prospective cohort study that followed over 2 million Americans, the incidence of diabetes was highest in Pacific Islanders (19.9 cases per 1,000 person-years; RR 3.08), followed by SAs (17.2 per 1000 person-years; RR 2.31), compared to 6.3 cases per 1,000 person-years in white individuals [16].

2.3 Pathophysiologic Basis for the increased ASCVD Risk in SAs

Traditional risk factors such as smoking, elevated Apo B/Apo A1 ratio, hypertension, diabetes, obesity, low levels of physical activity, and unhealthy diet all contribute to high cardiovascular mortality in SAs, just as in any other population [17]. However, SAs have a higher prevalence of additional contributing factors, including atherogenic dyslipidemia, metabolic syndrome/visceral adiposity/insulin resistance, unfavorable adipokine profile, higher lipoprotein (a), and unique dietary and psychosocial factors (Fig. 2).

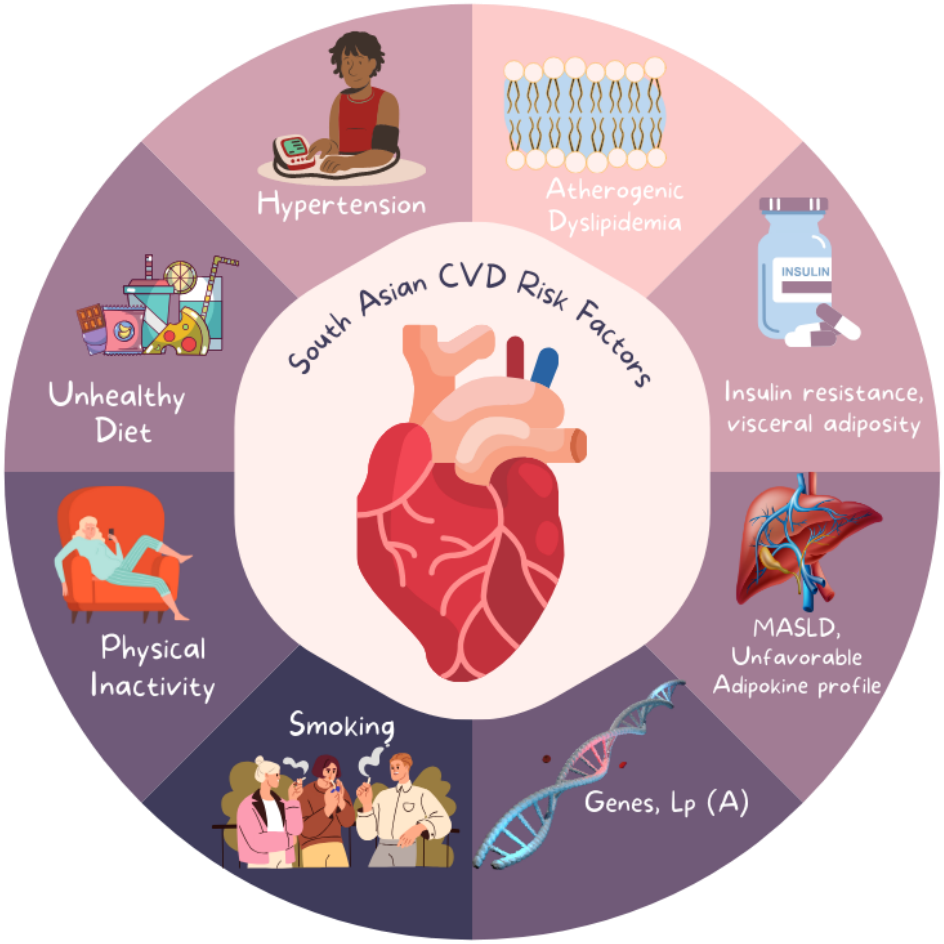

Fig. 2. Central illustration. Factors contributing to enhanced cardiovascular risk in South Asians

2.4 Atherogenic Dyslipidemia

Compared to NHWs, SAs have higher triglycerides, lower HDL-C, and higher apolipoprotein B (ApoB) levels [18]. SAs also have a lower LDL-C/ ApoB ratio and non-HDL-C/ApoB ratio [18]. In a matched case-control sub-analysis of the INTERHEART study of acute myocardial infarction among Asians, ApoA1 levels were lowest in SAs, and ApoA1 predicted cardiovascular risk better than HDL-C [19]. The ratio of ApoB to ApoA1 positively correlated with a high risk of acute myocardial infarction in SAs [19]. The increased risk for coronary artery disease is potentially due to the increased prevalence of smaller and denser LDL particles seen in Asian Indians [20]. This increased prevalence of small-density LDL is also significantly associated with insulin resistance in SAs [20].

There is also evidence that HDL is more dysfunctional in SAs. The oxidative and anti-inflammatory capacity of HDL is lower in SA males compared to White males [21]. Cholesterol Ester Transfer Protein (CETP) activity is 30% higher in SAs compared to Caucasians, and this correlates with elevated triglycerides, high LDL particle number, and low HDL-C [22]. These findings, as a whole, prompted the National Lipid Association to revise the optimal primary prevention targets for lipid profiles in SAs, namely changing LDL-C cut-offs to <70, <50, and <30 mg/dL for high, very high, and extreme lipid risk profile respectively [23].

2.5 Insulin Resistance and Visceral Adiposity

SAs have very high rates of insulin resistance and diabetes [16]. Aside from insulin resistance, SAs are suspected of having early pancreatic beta-cell dysfunction [24]. Compared with healthy, young, lean men of other ethnicities, the prevalence of insulin resistance is 3- to 4-fold higher among healthy, young, Asian-Indian men [25]. This is associated with doubling hepatic triglyceride content and plasma IL-6 concentrations compared with Caucasian men [25]. Individuals of Asian descent can thus develop non-alcoholic fatty liver disease (NAFLD) even at “lean” BMI [26]. These differences prompted the World Health Organization to amend BMI cut-offs to 23.0 for Overweight, 27.5 for Obesity Class 1, 32.5 for Obesity class 2, and 37.5 for Obesity Class 3 for South Asians [27].

SAs have a high incidence of visceral adiposity, which is characterized by a high waist-to-body mass index (BMI) ratio. This is often referred to as ‘hypertriglyceridemic waist” [18]. In addition to the atherogenic metabolic triad of hyperinsulinemia, increased apolipoprotein B, and small dense LDL particles, hypertriglyceridemic waist is well documented to be associated with atherosclerosis [28]. Compared with Caucasian men, for a given BMI, SA men have a higher percentage of total fat [29]. SA men preferentially accumulate this fat in truncal adipose tissue, which consists of abnormally large dysfunctional adipocytes and is associated with high levels of non-esterified fatty acids and leptin, but low adiponectin levels [29]. SA women, on the other hand, have increased amounts of total and subcutaneous fat and less visceral and hepatic fat than SA men [30]. However, many SA men and women both have the thin-fat metabolic phenotype, characterized by elevated fasting glucose, low HDL-C, and lower lean mass.

2.6 Inflammatory Markers and Adipokines

Elevated plasma high-sensitivity C-reactive protein (hsCRP), a systemic measure of inflammation, has been linked to atherothrombotic events in clinical and epidemiological investigations [31]. In a prospective study in the UK, among healthy males from the general population, the CRP concentrations were significantly higher in Indian Asians than in European whites, resulting in an approximately 14% increase in coronary heart disease risk in Asian Indians [31]. Adipocytes secrete two adipokines, adiponectin and leptin, which influence metabolism and insulin resistance. Visceral adipose tissue secretes adiponectin, which increases tissue fat oxidation and insulin sensitivity, thereby reducing circulating fatty acid levels [32]. The hormone leptin circulates in proportion to body fat mass and communicates with brain regions that control eating habits, hunger, and energy expenditure regarding nutritional status and subcutaneous fat mass [32]. For the same level of adiposity as Europeans, SAs have reduced adiponectin and increased leptin levels, thus an unfavorable adipokine profile [32].

2.7 Genetic Factors

Genetic factors likely contribute to the increased risk of ASCVD in SAs. A family history of coronary artery disease in a first-degree relative

at any age was associated with a high coronary artery calcium score of >300 in SAs living in the United States [33]. Multiple SNPs have been identified in the 9p21 locus that predisposes SAs (and other ethnicities) to coronary artery disease (CAD) and premature CAD [34]. More research is needed to identify unique loci predicting coronary artery disease, specifically in SAs. Multiple novel loci (GRB14, ST6GAL1, VPS26A, HMG20A, AP3S2, and HNF4A) have been identified in SAs, which increases their predisposition for type 2 diabetes [35]. SAs tend to have higher rates of heterozygous mutations in the Niemann-Pick type C1 (NPC1) gene linked to highly-penetrant obesity [36]. Alterations in the FTO locus in SA adults have been linked to the development of T2DM at much lower BMIs than in white Europeans [37]. Similarly, variants in TCF7L2 are strongly associated with T2DM in SAs [38].

2.8 High Lipoprotein(a)

Lipoprotein(a) is an LDL-like particle and is a causal risk factor for cardiovascular disease [39]. Like LDL particles, lipoprotein(a) has a cholesterol ester-rich core, but the apolipoprotein B-100 is linked to apolipoprotein(a) by a disulfide bond. The Apo(a) moiety consists of a single copy of Kringle KIV types 1 and 3 to 10, multiple copies of Kringle IV, type 2, and a protease domain analogous to plasminogen [39]. Lp(a) levels are highly genetically determined. In the Mediators of Atherosclerosis in SAs Living in America (MASALA [40]) longitudinal prospective cohort study, SAs had a higher median lipoprotein (a) level than Whites, Hispanics, and Chinese Americans [41]. SAs were confirmed to have a very high population-attributable risk for myocardial infarction resulting from this disparity, as demonstrated in the INTERHEART study [42]. Additionally, this study showed that Asian Indians had the highest total cholesterol/HDL-C and Apo-B/Apo-A1 ratios compared to other subgroups. Some studies posit that the generally accepted cut point for CHD risk of > 30 mg/dl Lp(a) may underestimate the risk, and a lower cut point may be appropriate for Asian Indians [43].

2.9 Dietary Factors

SA diet has been increasingly loaded with refined sugars and highly processed foods. In the typical modern Asian Indian diet, white rice, white flour, and refined sugar account for over 70% of all the calories consumed [44]. At this level of consumption, the mean daily intake of carbohydrates and added sugar can easily reach 330 g/day, a level at which the incidence of diabetes increases [44]. High-heat cooking, commonly seen in SA cuisine, has been hypothesized to release high amounts of trans-fatty acids and advanced glycation end products, possibly predisposing individuals to coronary artery disease [45]. Long periods of fasting for religious events and seasonal festivals followed by large meal consumption may also outpace basal insulin secretion and lead to development of insulin resistance.

High homocysteine concentrations have been reported in patients with coronary artery disease [46]. Asian Indians may have reduced intake of vitamin B12 and folate, which is one of the determinants of plasma levels of homocysteine [46]. In a study of Indians living in the UK, plasma homocysteine levels were higher than their Caucasian counterparts, which was linked to a slightly higher risk of coronary artery disease [46].

2.10 Other Contributory Factors

Anatomic differences may partly explain the enhanced risk for coronary artery disease in SAs. In a single-center observational study, compared with Caucasians undergoing cardiac catheterization, SAs had more severe coronary artery disease, as shown by smaller proximal LAD luminal diameters, higher mean percent stenosis per vessel, and more patients with multivessel disease [47]. However, a recent study showed that LAD cross-sectional area in SA men and women, measured with CCTA, after adjusting for traditional risk factors including BMI did not show a difference when compared to Caucasian men and women [48].

Aside from biological factors, socioeconomic status and access to healthcare also influence cardiovascular mortality among SAs. According to the PURE study, patients with diabetes in low-income countries had significantly higher CVD, all-cause mortality, and CV mortality rates than those in middle- and high-income nations [49]. This enhanced mortality risk remained unchanged after adjusting for risk factors and treatments [49].

3. RISK ASSESSMENT TOOLS

Proper risk assessment of CVD risk helps to plan risk mitigation strategies. Although several population-specific risk assessment tools exist to

calculate the risk of major adverse cardiovascular events based on risk factor profiles, none of the currently available models have been well-studied in the US SA population [50]. The traditional tools that are commonly employed in risk assessment include the Framingham risk score, AHA/ACC pooled cohort equation, and QRISK (based on the UK population) [8]. However, multiple studies have demonstrated that these tools underestimate cardiovascular risk among SAs. In addition, the clinical methods used to identify high risk patients will need to be modified. For example, the threshold for defining abdominal obesity as a part of the definition of metabolic syndrome should be different for SAs as compared to Caucasians [51]. An increased cardiovascular risk occurs at a waist circumference of >90 cm for SA men and > 80 cm for SA women as compared to >102 cm in Caucasian men and >88 cm in Caucasian women [51]. Thus, lower waist circumference cutoffs should be used for SA individuals compared to Caucasians when determining cardiovascular risk on this metric.

3.1 Risk Calculators

Historically, multi-variable risk assessment models based on data from North American and European populations have been used for risk assessment in SA populations. Patel et al. (2021) analyzed a prospective cohort from the UK biobank. Despite the doubling of atherosclerotic cardiovascular disease risk among SAs compared with European individuals in the cohort, the AHA/ACC Pooled Cohort and the QRISK-3 equations did not capture this risk [52]. Findlay et al. (2020) conducted a retrospective cohort study of 80 UK-based patients of SA origin admitted with first presentation myocardial infarction and calculated a 10-year CV risk for each patient using four cardiovascular risk models: Framingham Risk Score ($Risk_{FRS}$), World Health Organization ($Risk_{WHO}$), American College of Cardiology/American Heart Association (ACC/AHA) ($Risk_{ACC/AHA}$), and 3rd Joint British Societies'($Risk_{JBS}$) [53]. Most SA migrants were classified as "high risk" by $Risk_{JBS}$, with 65% of the participants having an estimated 10-year CV risk of >20%. The SA migrant cohort's 10-year CV risk estimations from $Risk_{WHO}$ were the lowest, with 21.25% of the cohort being at >20% risk of a major CV event. The CV risk estimations by the Risk ACC/AHA calculator for a 10-year risk > 20% in this cohort was 28.9%. A comparative analysis with the South Asian cohort showed that the $Risk_{JBS}$ was found to be the best predictor [53].

3.2 Subclinical Atherosclerosis Imaging

Coronary artery calcium (CAC), measured by rapid CT, is strongly associated with CAD events in all ethnic populations [54]. CAC is a reliable way to assess the risk of major cardiovascular outcomes, especially in asymptomatic individuals, and helps plan initiating or deferring lipid-lowering and other preventive therapies [54]. Data from MASALA and MESA studies have shown that SA men had comparable CAC scores to white men, but had higher CAC scores compared to African Americans, Latinos and Chinese Americans [55]. South Asian women have had similar scores when compared to all women in MESA cohort [55].

There may be some nuances with CAC score interpretation in South Asians [56]. SAs have higher odds of a zero CAC score than Non-Hispanic Whites in the low and intermediate-risk groups defined by the ACC/AHA pooled cohort equations; however, the high-risk groups had a similar distribution of CAC scores compared with Non-Hispanic Whites [56]. Thus, a substantial fraction of SA patients has a calcium score of zero despite being predicted to be intermediate risk based on standard pooled cohort equation, raising the possibility that there may higher amount of non-calcified plaque seen in South Asians [57]. This is a topic that warrants further study. Coronary computed tomography angiography (CCTA) is a more sensitive technique than CAC to assess noncalcified plaque burden; however, to date, there is a paucity of CCTA data in SAs.

Carotid intima-media thickness (cIMT), measured by ultrasound, is strongly associated with ASCVD events but has not consistently enhanced risk prediction [58]. In an analysis of the MASALA cohort, cIMT was associated with lifetime risk of ASCVD in SAs but was inferior to CAC [59]. cIMT appears to better predict CV events in SA women than in SA men [59].

3.3 Circulating Biomarkers

Biomarkers such as ApoB, Lp(a), and CRP have been shown to be predictive of ASCVD risk in SAs. In SAs, CRP remained independently associated with CVD after adjustment for the traditional risk factors (age, sex, blood pressure, LDL cholesterol, HDL cholesterol, smoking

status, and diabetes), atherosclerosis measured by carotid ultrasound, anthropometric parameters, (waist circumference and BMI), triglycerides, and ethnicity [60]. The differential levels of these markers in SAs compared with other ethnicities could be leveraged to assess CVD risk profiles in this particular population.

3.4 Polygenic Risk Scores

Genome-wide polygenic risk scores (PRS) are a newer method for estimating hereditary risk for common complex diseases including CAD (REFs). PRS are based on large amounts of GWAS data for specific diseases such as CAD, and as such, are heavily weighted toward European ancestry individuals. Wang et al. (2020) developed a PRS for CAD that is specific to individuals of SA ancestry. In 491 participants of a case-control study in Bangladesh and 7,244 SA participants of the UK Biobank, the GPS_{CAD} was strongly associated with CAD [61]. There was a three-fold increase in risk of CAD when comparing the highest to lowest quintiles of GPS_{CAD}, and this risk was independent of traditional CAD risk factors [61]. CAD-PRS could be an additional approach to risk stratify SAs.

4. RISK MANAGEMENT

Cardiovascular risk can be managed among SAs by following the same principles as that for other populations: lifestyle modification such as increased physical activity, a low-carbohydrate diet, a plant-based Mediterranean diet rich in whole grains and polyunsaturated fat, better control of risk factors such as insulin resistance, hypertension, abstinence from tobacco, etc.

4.1 Therapeutic Lifestyle Modification

SAs taking a calorie-restricted, moderately low-carbohydrate diet had weight loss, reduced insulin resistance, and improved cardiovascular risk factors, like individuals of other ethnicities adopting these lifestyle modifications [62]. In the MASALA cohort, consumption of 4-7 alcoholic drinks per week in SAs was inversely associated with the presence of coronary artery calcium [63]. On the other hand, greater than seven alcoholic drinks per week was associated with higher carotid intima-media thickness [63].

Acculturation patterns influence diet, which in turn influences cardiometabolic risk. SA respondents in the MASALA cohort exhibited variable acculturation strategies such as separation, assimilation, and integration [64]. There were differences in dietary patterns among SAs who had weaker traditional cultural beliefs than those who did not. Those with weaker traditional cultural beliefs had a higher Alternative Healthy Eating Index (AHEI) diet quality score – they consumed higher amounts of animal protein but lower amounts of fried snacks, sweets, and high-fat dairy products [65]. There was no association between traditional cultural beliefs and consuming fruits, vegetables, nuts, and legumes [65]. These variations may affect cardiovascular risk among SAs, and additional studies are needed to explore the impact of diet, immigration, and acculturation strategies on SA cardiovascular health. Overall, a multi-faceted approach to promote earlier screening for diabetes and coronary artery disease in South Asians is crucial to promote better cardiovascular outcomes in this population [66].

4.2 Pharmacotherapy

The risk assessment tools used to determine whether a patient should commence statin treatment for primary prevention have not necessarily been optimized for the SA population and requires further research. However, therapy to reduce LDL-C (and ApoB) are foundational to reducing ASCVD risk in all patients, including SAs. Statins remain the cornerstone of LDL-lowering therapy. In the IRIS study, hypercholesterolemic patients of SA descent tolerated rosuvastatin or atorvastatin well, and the treatment effectively lowered LDL-C levels [67]. It has been shown that SA had a higher proportion of ApoB for the same LDL-C levels, highlighting the importance of targeting ApoB in addition to LDL-C in South Asians [19]. In those patients whose LDL-C levels remain suboptimal despite maximally tolerated statin therapy (+/- ezetimibe), non-statin advanced lipid-lowering therapies should be considered. Sodium-glucose co-transporter 2 inhibitors are effective in SAs with type 2 diabetes in reducing cardiovascular events and slowing the progression of chronic kidney disease [68,69]. The Lipid Association of India recently published guidelines for managing patients with diabetes and dyslipidemia [23]. Patients with diabetes, without ASCVD and no target organ damage or ≤ one ASCVD risk factor, have a high risk of future adverse CV events and are recommended an LDL-C goal <70 mg/dl. Indian patients with diabetes but without ASCVD and target organ damage or ≥ two ASCVD risk factors are recommended an LDL-C goal <50 mg/dl [23]. Those with diabetes and ASCVD with

< 1 other major ASCVD risk factors and no evidence of target organ damage are classified as extreme risk category A and are recommended an LDL-C goal of 50 mg/dl and optionally 30 mg/dl. Indian patients with diabetes and with ≥2 major ASCVD risk factors or with target organ damage are classified as extreme risk category B, with a recommended LDL-C goal <30 mg/dl [23].

5. KNOWLEDGE GAPS

Inequalities in health status and outcomes among Asian American subgroups are masked when Asian Americans are aggregated together as a single group due to the heterogeneity in the burden of mortality from ischemic heart disease, heart failure, and cerebrovascular illness among Asian American subgroups [10]. Currently, less than 2% of the participants in the largest National Heart, Lung, and Blood Institute (NHLBI)-supported cohorts have people of SA ancestry and studies focusing on SAs comprise a tiny fraction of the total NIH budget [70]. Further data is needed to assess SA immigration patterns, generational status, length of residence, and acculturation patterns to better identify factors that influence the health of this population [70]. We also need better tools to accurately estimate risk of cardiovascular disease in SAs living in the US.

A report from the NIH workshop on health and prevention research identified the following areas that need more research in SAs: immigration patterns, acculturation strategies, diet, physical activity, reasons for higher ectopic adiposity, reasons for lower muscle mass and sarcopenia, reasons for higher rates of insulin resistance, reasons for higher rates of lean NAFLD, reasons for higher ASCVD risk but lower stroke risk, the role of subclinical atherosclerosis imaging, etc [70]. Some of the important areas that require further study is summarized in the table below (Table 1). Medication non-adherence, potentiated by language barriers faced by immigrants, could be contributing to high rates of cardiovascular disease in SAs, but this has not been rigorously studied in immigrants in developed countries [71]. Access to care also remains a significant barrier for SAs, particularly for low SES or new immigrants outside of South Asia, without proper insurance and subsequent access to preventive care.

Table 1. Summary of some of the important areas for research in South Asian CV risk

Unique Cardiovascular Risk Factors, Biomarkers, Risk Prediction and Management in SAs	Knowledge Gap/ Areas that require further research
Body composition	Reasons for high visceral fat and low muscle mass with aging in South Asians
Diabetes Mellitus	Reasons for high insulin resistance in South Asians
MASLD (Metabolic dysfunction Associated Steatotic Liver Disease)	What are the mechanisms responsible for high amount of MASLD despite “lean BMI” in South Asians?
Atherogenic dyslipidemia	Reasons for higher atherogenicity as shown by a high prevalence of low LDL-C/Apo B ratio?
Socio-cultural Factors	How do immigration, acculturation, dietary, and behavioral patterns in South Asians influence their cardio-metabolic health?
Subclinical Atherosclerosis Imaging	What is the role of CAC, CCTA, and carotid ultrasound in improving risk discrimination in South Asians?
Cardiovascular Risk Calculators and other Tools	What are the best risk prediction calculators for South Asians? Role of Polygenic Risk Scores in risk prediction?
ASCVD Risk Management	What is the optimal pharmacotherapy to treat insulin resistance, visceral adiposity and MASLD in South Asians? What are the optimal LDL-C targets and pharmacotherapy agents for primary ASCVD risk prevention in South Asians?

Adapted from Kanya et al. Knowledge Gaps, Challenges, and Opportunities in Health and Prevention Research for Asian Americans, Native Hawaiians, and Pacific Islanders: A Report from the 2021 National Institutes of Health Workshop [72]

6. CONCLUSIONS

SAs are a rapidly growing population in the United States. They are highly predisposed to insulin resistance and high cardiovascular mortality due to traditional social, cultural, and biological risk factors. There is a need to develop better cardiovascular risk prediction tools for this group. Diet, physical activity, and standard management of atherosclerotic cardiovascular disease using pharmacotherapy are currently being used. However, further studies are needed to personalize management and treatment strategies for this high-risk population. Given the significant diversity and high proportion of immigrants, the SA population offers chances to distinguish between the roles played by biology, socioeconomic factors, and acculturation pressures in cardiovascular disease etiologies [73].

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hastings KG, Jose PO, Kapphahn KI, et al. Leading causes of death among asian american subgroups (2003-2011). PLoS One. 2015;10(4):e0124341.
   DOI: 10.1371/journal.pone.0124341
2. Kalra D, Vijayaraghavan K, Sikand G, et al. Prevention of atherosclerotic cardiovascular disease in south asians in the US: A clinical perspective from the national lipid association. J Clin Lipidol. 2021;15(3):402–422.
   DOI: S1933-2874(21)00058-1
3. US CB. DEC detailed demographic and housing characteristics file A; Total Population.
   Available:https://data.census.gov/table/DECENNIALDDHCA2020.T01001?t=3781
   Updated 2020.
4. Pursnani S, Merchant M. South asian ethnicity as a risk factor for coronary heart disease. Atherosclerosis. 2020;315:126–130.
   DOI:10.1016/j.atherosclerosis.2020.10.007
5. Brister SJ, Hamdulay Z, Verma S, Maganti M, Buchanan MR. Ethnic diversity: South asian ethnicity is associated with increased coronary artery bypass grafting mortality. J Thorac Cardiovasc Surg. 2007;133(1): 150–154.
   DOI: 10.1016/j.jtcvs.2006.05.068
6. Reddy NK, Kauso V, Kanaya AM, Kandula NR, Gujral UP, Shah NS. Cardiovascular risk factor profiles in north and South Indian and Pakistani Americans: The MASALA study. Am Heart J. 2022;244: 14–18.
   DOI: 10.1016/j.ahj.2021.10.115
7. Patel JV, Vyas A, Cruickshank JK, et al. Impact of migration on coronary heart disease risk factors: Comparison of gujaratis in britain and their contemporaries in villages of origin in india. Atherosclerosis. 2006;185(2):297–306.
   DOI: S0021-9150(05)00378-3
8. Volgman AS, Palaniappan LS, Aggarwal NT, et al. Atherosclerotic cardiovascular disease in south asians in the United States: Epidemiology, risk factors, and treatments: A scientific statement from the american heart association. Circulation. 2018;138(1):e1–e34.
   DOI: 10.1161/CIR.0000000000000580
9. McDonald JT, Kennedy S. Insights into the 'healthy immigrant effect': Health status and health service use of immigrants to canada. Soc Sci Med. 2004;59(8):1613–1627.
   DOI: 10.1016/j.socscimed.2004.02.004
10. Shah NS, Xi K, Kapphahn KI, et al. Cardiovascular and cerebrovascular disease mortality in asian american subgroups. Circ Cardiovasc Qual Outcomes. 2022;15(5):e008651.
    DOI:10.1161/CIRCOUTCOMES.121.008651
11. Jose PO, Frank AT, Kapphahn KI, et al. Cardiovascular disease mortality in asian

americans. J Am Coll Cardiol. 2014;64(23):2486–2494.
DOI: 10.1016/j.jacc.2014.08.048

12. Joseph P, Kutty VR, Mohan V, et al. Cardiovascular disease, mortality, and their associations with modifiable risk factors in a multi-national south asia cohort: A PURE substudy. Eur Heart J. 2022;43(30):2831–2840.
DOI: 10.1093/eurheartj/ehac249
13. Huffman MD, Rao KD, Pichon-Riviere A, et al. A cross-sectional study of the microeconomic impact of cardiovascular disease hospitalization in four low- and middle-income countries. PLoS One. 2011;6(6):e20821.
DOI: 10.1371/journal.pone.0020821
14. Fernandez Perez C, Xi K, Simha A, et al. Leading causes of death in asian indians in the United States (2005-2017). PLoS One. 2022;17(8):e0271375.
DOI: 10.1371/journal.pone.0271375
15. Hastings KG, Jose PO, Kapphahn KI, et al. Leading causes of death among asian american subgroups (2003-2011). PLoS One. 2015;10(4):e0124341.
DOI: 10.1371/journal.pone.0124341
16. Karter AJ, Schillinger D, Adams AS, et al. Elevated rates of diabetes in pacific islanders and asian subgroups: The diabetes study of northern california (DISTANCE). Diabetes Care. 2013;36(3): 574–579.
DOI: 10.2337/dc12-0722
17. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in south asians compared with individuals in other countries. JAMA. 2007;297(3):286–294.
DOI: 297/3/286
18. Singh K, Thanassoulis G, Dufresne L, et al. A comparison of lipids and apoB in asian indians and americans. Global Heart. 2021;16(1).
DOI: 10.5334/gh.882
19. Karthikeyan G, Teo KK, Islam S, et al. Lipid profile, plasma apolipoproteins, and risk of a first myocardial infarction among asians an analysis from the INTERHEART study. J Am Coll Cardiol. 2009;53(3):244–253.
DOI: 10.1016/j.jacc.2008.09.041
20. Kulkarni KR, Markovitz JH, Nanda NC, Segrest JP. Increased prevalence of smaller and denser LDL particles in Asian Indians. Arterioscler Thromb Vasc Biol. 1999;19(11):2749–2755.
DOI: 10.1161/01.atv.19.11.2749
21. Bakker L, Boon MR, Annema W, et al. HDL functionality in south asians as compared to white caucasians. Nutrition Metabolism and Cardiovascular Diseases. 2016;26(8):697–705.
DOI: 10.1016/j.numecd.2016.02.010
22. Rashid S, Sniderman A, Melone M, et al. Elevated cholesteryl ester transfer protein (CETP) activity, a major determinant of the atherogenic dyslipidemia, and atherosclerotic cardiovascular disease in South Asians. Eur J Prev Cardiol. 2015; 22(4):468–477.
DOI: 10.1177/2047487314528461
23. Puri R, Mehta V, Duell PB, et al. Management of diabetic dyslipidemia in indians: Expert consensus statement from the lipid association of India. J Clin Lipidol. 2023;17(2):e1–e14.
DOI: 10.1016/j.jacl.2022.11.002
24. Gujral UP, Mohan V, Pradeepa R, et al. Ethnic variations in diabetes and prediabetes prevalence and the roles of insulin resistance and beta-cell function: The CARRS and NHANES studies. J Clin Transl Endocrinol. 2016;4:19–27.
DOI: 10.1016/j.jcte.2016.02.004
25. Petersen KF, Dufour S, Feng J, et al. Increased prevalence of insulin resistance and nonalcoholic fatty liver disease in Asian-Indian men. Proc Natl Acad Sci U S A. 2006;103(48):18273–18277.
DOI: 0608537103
26. Weinberg EM, Trinh HN, Firpi RJ, et al. Lean americans with nonalcoholic fatty liver disease have lower rates of cirrhosis and comorbid diseases. Clin Gastroenterol Hepatol. 2021;19(5):996–1008.e6.
DOI: S1542-3565(20)30930-7
27. WHO Expert Consultation. Appropriate body-mass index for asian populations and its implications for policy and intervention strategies. Lancet. 2004;363(9403):157–163.
DOI: 10.1016/S0140-6736(03)15268-3
28. Namdarimoghaddam P, Fowokan A, Humphries KH, Mancini GBJ, Lear S. Association of "hypertriglyceridemic waist" with increased 5-year risk of subclinical atherosclerosis in a multi-ethnic population: A prospective cohort study. BMC Cardiovasc Disord. 2021;21(1): 63–1.
DOI: 10.1186/s12872-021-01882-1
29. Chandalia M, Lin P, Seenivasan T, et al. Insulin resistance and body fat distribution

in south asian men compared to caucasian men. PLoS One. 2007;2(8):e812.
DOI: 10.1371/journal.pone.0000812

30. Shah A, Hernandez A, Mathur D, Budoff MJ, Kanaya AM. Adipokines and body fat composition in south asians: Results of the metabolic syndrome and atherosclerosis in south asians living in america (MASALA) study. Int J Obes (Lond). 2012;36(6):810–816.
DOI: 10.1038/ijo.2011.167
31. Chambers JC, Eda S, Bassett P, et al. C-reactive protein, insulin resistance, central obesity, and coronary heart disease risk in Indian Asians from the United Kingdom compared with european whites. Circulation. 2001;104(2):145–150.
DOI: 10.1161/01.cir.104.2.145
32. Mente A, Razak F, Blankenberg S, et al. Ethnic variation in adiponectin and leptin levels and their association with adiposity and insulin resistance. Diabetes Care. 2010;33(7):1629–1634.
DOI: 10.2337/dc09-1392
33. Patel J, Al Rifai M, Cainzos-Achirica M, et al. Family history of CHD is associated with severe CAC in south asians: Comparing the MASALA and MESA studies. JACC Cardiovasc Imaging. 2017;10(8):958–960.
DOI: S1936-878X(17)30509-0
34. Kalpana B, Murthy DK, Balakrishna N, Aiyengar MT. Genetic variants of chromosome 9p21.3 region associated with coronary artery disease and premature coronary artery disease in an asian indian population. Indian Heart J. 2019;71(3):263–271.
DOI: S0019-4832(18)31122-2
35. Kooner JS, Saleheen D, Sim X, et al. Genome-wide association study in individuals of south asian ancestry identifies six new type 2 diabetes susceptibility loci. Nat Genet. 2011;43(10): 984–989.
DOI: 10.1038/ng.921
36. Chiorean A, Garver WS, Meyre D. Signatures of natural selection and ethnic-specific prevalence of NPC1 pathogenic mutations contributing to obesity and niemann-pick disease type C1. Sci Rep. 2020;10(1):18787–4.
DOI: 10.1038/s41598-020-75919-4
37. Yajnik CS, Janipalli CS, Bhaskar S, et al. FTO gene variants are strongly associated with type 2 diabetes in south Asian Indians. Diabetologia. 2009;52(2):247–252.
DOI: 10.1007/s00125-008-1186-6
38. Chandak GR, Janipalli CS, Bhaskar S, et al. Common variants in the TCF7L2 gene are strongly associated with type 2 diabetes mellitus in the indian population. Diabetologia. 2007;50(1):63–67.
DOI: 10.1007/s00125-006-0502-2
39. Berglund L, Ramakrishnan R. Lipoprotein(a): An elusive cardiovascular risk factor. Arterioscler Thromb Vasc Biol. 2004;24(12):2219–2226.
DOI:10.1161/01.ATV.0000144010.55563.63
40. Kanaya AM, Kandula N, Herrington D, et al. Mediators of atherosclerosis in South Asians living in America (MASALA) study: Objectives, methods, and cohort description. Clin Cardiol. 2013;36(12):713–720.
DOI: 10.1002/clc.22219
41. Makshood M, Joshi PH, Kanaya AM, et al. Lipoprotein (a) and aortic valve calcium in south asians compared to other race/ethnic groups. Atherosclerosis. 2020;313:14–19.
DOI:10.1016/j.atherosclerosis.2020.09.010
42. Pare G, Caku A, McQueen M, et al. Lipoprotein(a) levels and the risk of myocardial infarction among 7 ethnic groups. Circulation. 2019;139(12):1472–1482.
DOI:10.1161/CIRCULATIONAHA.118.034311
43. Hoogeveen RC, Gambhir JK, Gambhir DS, et al. Evaluation of lp[a] and other independent risk factors for CHD in Asian Indians and their USA counterparts. J Lipid Res. 2001;42(4):631–638.
44. O'Keefe EL, DiNicolantonio JJ, Patil H, Helzberg JH, Lavie CJ. Lifestyle choices fuel epidemics of diabetes and cardiovascular disease among Asian Indians. Prog Cardiovasc Dis. 2016;58(5): 505–513.
DOI: 10.1016/j.pcad.2015.08.010
45. Kakde S, Bhopal RS, Bhardwaj S, Misra A. Urbanized South Asians' susceptibility to coronary heart disease: The high-heat food preparation hypothesis. Nutrition. 2017;33: 216–224.
DOI: S0899-9007(16)30126-5
46. Chambers JC, Obeid OA, Refsum H, et al. Plasma homocysteine concentrations and risk of coronary heart disease in UK Indian

Asian and European men. Lancet. 2000;355(9203):523–527.
DOI: S0140-6736(99)93019-2

47. Hasan RK, Ginwala NT, Shah RY, Kumbhani DJ, Wilensky RL, Mehta NN. Quantitative angiography in South Asians reveals differences in vessel size and coronary artery disease severity compared to caucasians. Am J Cardiovasc Dis. 2011;1(1):31–37.
48. Short RT, Lin F, Nair S, et al. Comparing coronary artery cross-sectional area among asymptomatic South Asian, white, and black participants: The MASALA and CARDIA studies. BMC Cardiovasc Disord. 2024;24(1):158–4.
DOI: 10.1186/s12872-024-03811-4
49. Anjana RM, Mohan V, Rangarajan S, et al. Contrasting associations between diabetes and cardiovascular mortality rates in low-, middle-, and high-income countries: Cohort study data from 143,567 individuals in 21 countries in the PURE study. Diabetes Care. 2020;43(12):3094–3101.
DOI: 10.2337/dc20-0886
50. Narayan KM, Aviles-Santa L, Oza-Frank R, et al. Report of a national heart, lung, and blood institute workshop: Heterogeneity in cardiometabolic risk in Asian Americans in the U.S. opportunities for research. J Am Coll Cardiol. 2010;55(10):966–973.
DOI: 10.1016/j.jacc.2009.07.075
51. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: A joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the y of obesity. Circulation. 2009;120(16):1640–1645.
DOI:10.1161/CIRCULATIONAHA.109.192644
52. Patel AP, Wang M, Kartoun U, Ng K, Khera AV. Quantifying and understanding the higher risk of atherosclerotic cardiovascular disease among South Asian individuals: Results from the UK biobank prospective cohort study. Circulation. 2021;144(6):410–422.
DOI: 10.1161/CIRCULATIONAHA.120.052430
53. Findlay SG, Kasliwal RR, Bansal M, Tarique A, Zaman A. A comparison of cardiovascular risk scores in native and migrant South Asian populations. SSM Popul Health. 2020;11:100594.
DOI: 10.1016/j.ssmph.2020.100594
54. Greenland P, Blaha MJ, Budoff MJ, Erbel R, Watson KE. Coronary calcium score and cardiovascular risk. J Am Coll Cardiol. 2018;72(4):434–447.
DOI: 10.1016/j.jacc.2018.05.027
55. Kanaya AM, Kandula NR, Ewing SK, et al. Comparing coronary artery calcium among U.S. South Asians with four racial/ethnic groups: The MASALA and MESA studies. Atherosclerosis. 2014;234(1):102–107.
DOI:10.1016/j.atherosclerosis.2014.02.017
56. Al Rifai M, Cainzos-Achirica M, Kanaya AM, et al. Discordance between 10-year cardiovascular risk estimates using the ACC/AHA 2013 estimator and coronary artery calcium in individuals from 5 racial/ethnic groups: Comparing MASALA and MESA. Atherosclerosis. 2018;279:122–129.
DOI:10.1016/j.atherosclerosis.2018.09.015
57. Haque W, Grandhi GR, Kanaya AM, et al. Implications of the 2019 American college of cardiology/American heart association primary prevention guidelines and potential value of the coronary artery calcium score among South Asians in the US: The mediators of atherosclerosis in South Asians living in America (MASALA) study. Atherosclerosis. 2021;334:48–56.
DOI: S0021-9150(21)01291-0
58. Oygarden H. Carotid intima-media thickness and prediction of cardiovascular disease. J Am Heart Assoc. 2017; 6(1): e005313. DOI:10.1161/JAHA.116.005313.
59. Kandula NR, Kanaya AM, Liu K, et al. Association of 10-year and lifetime predicted cardiovascular disease risk with subclinical atherosclerosis in south asians: Findings from the mediators of atherosclerosis in South Asians living in America (MASALA) study. Journal of the American Heart Association. 2014;3(5).
DOI: 10.1161/JAHA.114.001117
60. Anand SS, Razak F, Yi Q, et al. C-reactive protein as a screening test for cardiovascular risk in a multiethnic population. Arterioscler Thromb Vasc Biol. 2004;24(8):1509–1515.
DOI:10.1161/01.ATV.0000135845.95890.4e
61. Wang M, Menon R, Mishra S, et al. Validation of a genome-wide polygenic score for coronary artery disease in South Asians. J Am Coll Cardiol. 2020;76(6):703–714.

DOI: S0735-1097(20)35644-8
62. Backes AC, Abbasi F, Lamendola C, McLaughlin TL, Reaven G, Palaniappan LP. Clinical experience with a relatively low carbohydrate, calorie-restricted diet improves insulin sensitivity and associated metabolic abnormalities in overweight, insulin resistant South Asian Indian women. Asia Pac J Clin Nutr. 2008;17(4): 669–671.
63. Chevli PA, Aladin AI, Kanaya AM, Kandula NR, Malaver D, Herrington DM. Alcohol consumption and subclinical atherosclerosis among South Asians: Findings from the mediators of atherosclerosis in South Asians living in America (MASALA) study. Nutr Metab Cardiovasc Dis. 2020;30(1):123–131.
DOI: S0939-4753(19)30289-3
64. Needham BL, Mukherjee B, Bagchi P, et al. Acculturation strategies among south asian immigrants: The mediators of atherosclerosis in South Asians living in America (MASALA) study. Journal of Immigrant and Minority Health. 2017; 19(2):373–380.
Available:https://doi.org/10.1007/s10903-016-0372-8
DOI: 10.1007/s10903-016-0372-8
65. Gadgil MD, Kandula NR, Kanaya AM. Acculturation is associated with dietary patterns in South Asians in America. J Immigr Minor Health. 2020;22(6):1135–1140.
DOI: 10.1007/s10903-020-01016-3
66. Misra A, Tandon N, Ebrahim S, et al. Diabetes, cardiovascular disease, and chronic kidney disease in South Asia: Current status and future directions. BMJ. 2017;357:j1420.
DOI: 10.1136/bmj.j1420
67. Deedwania PC, Gupta M, Stein M, Ycas J, Gold A, IRIS SG. Comparison of rosuvastatin versus atorvastatin in South-Asian patients at risk of coronary heart disease (from the IRIS trial). Am J Cardiol. 2007;99(11):1538–1543.
DOI: 10.1016/j.amjcard.2007.01.028
68. Kadowaki T, Nangaku M, Hantel S, et al. Empagliflozin and kidney outcomes in Asian patients with type 2 diabetes and established cardiovascular disease: Results from the EMPA-REG OUTCOME((R)) trial. J Diabetes Investig. 2019;10(3):760–770.
DOI: 10.1111/jdi.12971
69. Lam CSP, Ferreira JP, Pfarr E, et al. Regional and ethnic influences on the response to empagliflozin in patients with heart failure and a reduced ejection fraction: The EMPEROR-reduced trial. Eur Heart J. 2021;42(43):4442–4451.
DOI: 10.1093/eurheartj/ehab360
70. Kanaya AM, Hsing AW, Panapasa SV, et al. Knowledge gaps, challenges, and opportunities in health and prevention research for Asian Americans, native Hawaiians, and pacific islanders: A report from the 2021 national institutes of health workshop. Ann Intern Med. 2022;175(4): 574–589.
DOI: 10.7326/M21-3729
71. Ens TA, Seneviratne CC, Jones C, Green TL, King-Shier KM. South Asians' cardiac medication adherence. European Journal of Cardiovascular Nursing. 2014;13(4): 357–368.
DOI: 10.1177/1474515113498187
72. Kanaya AM, Hsing AW, Panapasa SV, et al. Knowledge gaps, challenges, and opportunities in health and prevention research for Asian Americans, native Hawaiians, and pacific islanders: A report from the 2021 national institutes of health workshop. Ann Intern Med. 2022;175(4): 574–589.
DOI: 10.7326/M21-3729
73. Narayan KM, Aviles-Santa L, Oza-Frank R, et al. Report of a national heart, lung, and blood institute workshop: Heterogeneity in cardiometabolic risk in Asian Americans in the U.S. opportunities for research. J Am Coll Cardiol. 2010; 55(10):966–973.
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