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NEW INSIGHTS INTO THE CAUSES, CONSEQUENCES, AND CONTROL OF CARDIOVASCULAR DISEASES IN INDIA

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Introduction

Of all the non-communicable diseases, cardiovascular diseases (CVD) account for the largest fraction of deaths and remain the foremost public health challenge in the twenty-first century[1]. Data suggest that annually, approximately 60 million people suffer from some form of CVD (***Table 1***) and CVDs account for more than 17.9 million deaths worldwide[2,3]. According to the 2019 Global Disease Burden (GBD) study, the collective impact of CVD on global health was estimated at 22.5 million disability-adjusted life years (DALY), with the largest contribution from the South Asian region[4].

In the past thirty years, India has experienced a significant epidemiological shift from communicable to non-communicable diseases. According to state level data from the GBD 2016 study, all states in India now have a higher prevalence of non-communicable diseases compared to communicable diseases, while this was the case only in the southern state of Kerala and a few union territories in 1990[5]. As of the year 2017, CVD was responsible for 26.6% of total deaths and 13.6% of total DALY in India, compared with 15.2% and 6.9% respectively, in 1990. Data indicate a greater than two-fold increase in the prevalence of CVD, from 25.7 million in 1990 to 54.5 million in 2016 including ischemic heart disease (IHD) and stroke[6,7]. The WHO estimated that India would lose $237 billion from loss of productivity and spending on healthcare over 10 years from 2005 to 2015[8] Experts have projected that between 2012 and 2030 India would incur economic losses of up to $2.2 trillion due to CVD, and have highlighted its socio-economic consequences[9].

Although the CVD epidemic in India largely mirrors that of other regions of the world, it does exhibit some distinctive characteristics. In this review, we delve into the unique differences in CVD in Indians, the risks and biological mechanisms, unique challenges faced by the population, the latest advancements, and a way forward to tackle this burgeoning CVD epidemic in the context of India.

CVD in Indians - how is it different?

India has a significantly higher burden of CVD than the global average. In India, the age-standardized death rates from CVD and the associated DALY are 1.2 and 1.3 times higher than the global averages, respectively[9,10]. In 2016, India accounted for 23.1% of global DALYs due to IHD, 14% of global DALYs due to stroke, and more than 33% of global DALYs due to rheumatic heart disease[10]. Data suggest that 62% of all CVD-related deaths in the Indian population occur prematurely as compared to other countries. South Asians have a lower mean age of first myocardial infarction[11]. Studies involving Indian migrants around the world consistently show that Indians have a greater likelihood of developing coronary artery disease and related mortality at a younger age when compared to other ethnic groups or local populations[12]. The Prospective Urban Rural Epidemiology (PURE) study involving 156,424 individuals found that, despite having a comparatively lower burden of CV risk factors, people from the lower income countries (83% Indians) had significantly worse cardiovascular outcomes compared with individuals from high-income backgrounds[13]. Studies suggest that the diagnosis, treatment, and control of traditional CV risk factors such as diabetes and hypertension in the Indian population remain dismal[14,15].

Although traditional CV risk factors account for a large proportion of the risk, an emerging body of evidence indicates that socio-economic factors, such as poverty, educational attainment, stress, and life experiences exert a significant influence on the onset and progression of CVD, and are particularly relevant in the context of a country like India[9]. These risk factors are affected by foetal programming, early life influences as well as epigenetic and environmental changes that may accumulate across one's lifespan[16,17]. In a nutshell, the inherent biological risk among Indians is further potentiated by population-level changes[18]. Traditional CVD risk factors can be classified as modifiable and non-modifiable risk factors (***Table 2***). Modifiable risk factors may be behavioural (such as tobacco use, diet, and physical activity) or

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Table 1. Common disorders comprising cardiovascular diseases and associated morbidity and mortality	
Disorder	**Prevalence and Mortality**
Ischemic heart disease. [Unstable and stable angina, myocardial infarction]	• Estimated 200 million people living with the disease. • Highest global mortality in 2019 • 1 in 6 deaths globally
Peripheral arterial disease	• Estimated 236-262 million >25 years living with the disease.
Cerebrovascular disease [ischemic stroke, haemorrhagic stroke, transient ischemic attacks]	• Estimated 100 million stroke survivors. • 6.6 million deaths in 2019. • 1 in 9 deaths globally.
Arrhythmias [Atrial fibrillation and flutter, ventricular tachycardia, ventricular fibrillation]	• Difficult to predict prevalence, but affects an estimated 1.5-5% of the population.
Deep vein thrombosis [pulmonary embolism]	• Estimated 0.38/1000 person-year incidence • Third highest CVD-related mortality, with many deaths • 30% of people with previous episodes are at risk for another
Rheumatic heart disease	• Estimated 2% of global CVD-related deaths, or > 300,000 deaths • Most common heart disease worldwide
Heart failure [congestive heart failure, with reduced or preserved ejection fraction]	• Estimated >64 million worldwide living with the disease • 1/3 of patients do not live beyond one year of diagnosis

biological (such as hypertension, diabetes, and dyslipidemia). Non-modifiable risk factors include age, gender, family history, genetics, and ethnicity. In this review, we will discuss unique biological differences relating to the conventional CV risk factors, the influence of early life experiences, and how population-level factors like epidemiological transition, demographic shift, lifestyle choices, environment, and sociocultural and economic conditions impact the CVD risk among Indians.

Hypertension

Hypertension is one of the leading risk factors for CVD with an estimated 1.28 billion people living with hypertension worldwide, 82% of whom live in low- and middle-income regions[19]. According to a survey between 2012 and 2014, there were approximately 207 million individuals in India living with hypertension at that time[20]. More recently, a study reported that after the implementation of the 2017 American College of Cardiology/American Heart Association guidelines, the prevalence of hypertension in Indians would increase from 29.7% to 63.8%, amounting to 486 million adults[21]. Population-level hypertension control is poor in India. In a study that screened 10,593 adults in India, 28.5% were found to have hypertension, and of these, only 27.9% were aware, 14.5% received treatment, and only 12.6% were controlled[22]. Furthermore, differences exist in the prevalence and control of hypertension in rural and urban Indian populations. For example, blood pressure (BP) control has been noted to be better in southern India compared to other regions; women have better control than men, and increased wealth is associated with improved control[23,24]. Data on the social gradient's relationship with hypertension in Indians is less clear, but a few studies from urban India report a

Table 2. Factors affecting CVD		
Modifiable Risk Factors	**Non-modifiable Risk Factors**	**Socio-economic Factors**
Physical inactivity	Age	Social gradient
Obesity	Sex	Stress
Hypertension	Genetics	Early life
Diabetes	Race & ethnicity	Social exclusion
Dyslipidemia	Chronic kidney disease	Occupation
Diet		Social support
Alcohol and tobacco use		Addiction
		Food access

higher prevalence among people from low socioeconomic and educational status[25,26].

A systematic review and meta-analysis reported that there was upto a two-fold increase in the risk for hypertension among Indians if they smoked orally consumed khaini and tobacco had extra salt intake in their food, had a sedentary lifestyle had central obesity had BMI ≥25 and consumed alcohol[14]. A culturally important factor that might be contributing to the increased prevalence of hypertension in Southeast Asians is the consumption of traditional salted fermented foods and condiments. A study reported that the average daily consumption of salt in Indian adults is approximately 11 grams[27]. Other factors such as climate change, air pollution, high traffic density, lack of green space, poor socioeconomic status, and adverse childhood experiences have been linked with hypertension[28]. A study from India showed a linear increase in blood pressure and incidence of hypertension with increasing particulate matter (PM) in the breathed air, both the short- and long-term [29]. Although genes have been implicated in increased blood pressure at an individual level their role may be minimal. A better understanding of mechanistic processes and pathways involved in the regulation of blood pressure may provide fresh insights and point to novel targets for interventions.

Diabetes

Diabetes is a major global health problem and a significant CVD risk factor. Over 400 million people live with diabetes, and mortality rates continue to rise[30]. The International Diabetes Federation Atlas estimated that, as of 2015, 72.9 million individuals in India were living with diabetes[31,32]. Much like hypertension, the prevalence of diabetes has shown a persistent upward trend, with the most recent figures indicating a count of approximately 101 million cases[33,34]. Data suggest that Indians have a higher prevalence of type 2 diabetes and metabolic syndrome as compared to other ethnic groups[35]. In fact, the prevalence of metabolic syndrome has been noted to be twice as high in the South Asian population as compared to Europeans[36].

The traditional view that diabetes arises from obesity and insulin resistance does not fully explain the prevalence level of diabetes in

Table 3. Most popular dietary patterns recommended for heart health	
Diet	**Components**
Dietary Approaches to Stop Hypertension (DASH)	• High in fruits, vegetables, low-fat dairy products
	• Low in saturated fat and cholesterol
	• Encourages high fibers
	• Limit sodium intake to 1500-2300 mg daily
	• Significantly lowers BP
Mediterranean	• High in whole grains, nuts, seeds, fruits, vegetables, legumes, fish
	• Moderation of low-fat dairy products, eggs, and poultry
	• Eliminates artificial sugar, refined carbs, highly processed snacks, and red meat
	• It is regarded as one of the primary diets that can prolong life and prevent numerous heart disease
Low Carb	• Restricts dietary carbs to 10-40% of total caloric intake
	• Limits bread, sugars, grains, beverages, processed and high-sugar snacks
	• Encourages lean proteins, healthy fats, and high-fiber foods
	• Lowers insulin resistance, improves HDL and triglycerides, reduces BP, and reduces systemic inflammation
Therapeutic Lifestyle Changes (TLC)	• Encourages dietary and lifestyle changes to improve cholesterol and triglyceride levels
	• Encourages 20-30% of calories from healthy fats, limiting saturated fat intake to <7% of total calories, cholesterol intake <200 mg daily, and 20-25% of all calories from fiber
	• Encourages > 30 min physical activity daily
Vegan	• Complete cessation of all animal products
	• Emphasizes whole grains, fruits, vegetables, and proteins from plant sources
	• Decreases BMI, total serum cholesterol, serum glucose, inflammation, and BP
	• Diet is low in LDL, saturated fat, and processed meat while high in fiber and phytonutrients.

India, because the prevalence of obesity in India is much lower when compared to other countries[37,38]. A study from the United States showed that among all body mass index (BMI) categories (normal, overweight, and obese), Indian immigrants have the highest prevalence of diabetes as compared to immigrants from other regions[39]. The study also showed that diabetes prevalence among normal-weight Indian immigrants was significantly higher than among obese Europeans and South Americans. A study from India of approximately 10,000 patients with type 2 diabetes found that 66.5% of these patients had low to normal BMI, but were at higher likelihood of experiencing microvascular complications[40]. This phenomenon of diabetes in patients with low to normal BMI has been termed "lean diabetes". This may be attributed to a range of possible factors greater genetic susceptibility, early dysfunction of beta cells, increased glucose production by the liver, and differences in body composition[41,42]. Furthermore, studies show that patients with lean diabetes are more likely to be males who smoke or consume alcohol, suggesting an interplay of genetic, behavioural, and environmental factors as potential causal mechanisms[41].

Recent studies have thrown light on the roles of high output of liver glucose, localized hepatic glucose resistance, and non-alcoholic fatty liver disease (NAFLD) as risk factors for CVD in Indians. NAFLD, an integral part of the metabolic syndrome, is the most common cause of chronic liver disease worldwide and is defined by the accumulation of fat in >5% of hepatocytes, in the absence of significant alcohol intake or any other specific aetiology of liver disease[43]. Although the countrywide prevalence of NAFLD in India is unknown, a study from Kerala reported an urban and rural prevalence of 55.2% and 43.4%, respectively[44,45]. Interestingly, despite robust global evidence of an association between NAFLD and high BMI, Indians have been reported to develop NAFLD even in the absence of obesity[46]. Further research is needed to assess the role of the liver in the increased risk of diabetes.

The mechanism of diabetes in Asian Indians appears to be caused by insulin insufficiency rather than insulin resistance. A study comparing Pima Indians from the Southwestern United States and Asian Indians from India found significant differences in the pathophysiological pathways and natural history of type 2 diabetes between the two groups. The Pima Indians were three times more resistant to insulin than the Asian Indians, whereas the Asian Indians had three times less insulin secretion compared to the Pima Indians, a pattern evident across age, BMI, and glycemic strata. Furthermore, it has been proposed that impaired glucocorticoid action or exposure during foetal development may partly account for diverse patterns and ethnic differences in the prevalence of type 2 diabetes and metabolic syndrome[47,48].

Dyslipidemia and body fat

Lipid metabolism is a crucial player in the pathogenesis of atherosclerotic CVD, and genetic predisposition to dyslipidemias in Indian populations may explain the higher coronary artery disease risk in Indians. In the 2019 GBD study, 44% of IHD and 22% of stroke deaths globally were attributable to high low-density lipoprotein (LDL) levels[49]. In India, hypercholesteremia is estimated between 10-30%, with decreased prevalence in an urban setting[50]. Data from epidemiological studies suggest increasing levels of total cholesterol, LDL cholesterol, non-high-density lipoprotein (non-HDL) cholesterol, and triglycerides[51]. On the other hand, the control of dyslipidemia continues to be low, with studies showing only about 20% of patients have normal lipid parameters[52,53].

Lipid metabolism can be influenced by genetics, diet, smoking, and obesity. South Asians tend to have high ratios of total cholesterol:HDL and triglycerides:HDL, higher levels of ApoB, TG, and Lp(a), and lower levels of ApoA1 and HDL, leading to increased atherogenicity and CVD risk[36,54-56]. A large study from Copenhagen reported that ApoB is a very robust marker of all-cause mortality and myocardial infarction; data from INTERHEART study (a large international case-control study across 52 countries) showed that, among patients with acute myocardial infarction, South Asians had significantly higher ApoB/ApoA1 ratios as compared to patients from other countries[11]. Similarly, a study comparing participants from the United States and India showed that Indians have comparatively higher levels of ApoB and triglycerides but lower levels of HDL-cholesterol[27] This deranged lipid profile, characterized by high triglycerides and low HDL cholesterol occurs not only in Indian adults, but has been reported in Indian school children and adolescents[36,57]. The higher Apo B levels are explained by the higher presence of small dense LDL particles. Every LDL particle,

Table 4 Particulate and gaseous components of air pollution		
Heavy Metals	**Gaseous**	**Particulate Matter**
Cadmium	Sulfur dioxide	Thoracic particles (<10 μm; PM_{10})
Lead	Nitrogen dioxide	Coarse particles (2.5-10 μm; $PM_{2.5-10}$)
Mercury	Nitric oxide	Fine particles (<2.5 μm; $PM_{2.5}$)
Chromium	Carbon monoxide	Ultrafine (<0.1 μm; UFP)
Zinc	Carbon dioxide	
Cobalt	Volatile organic compounds	

irrespective of its size, will have a surface ApoB, leading toa higher mean circulating APoB. This phenomenon, in addition to the lower protective ApoA1 found in HDL cholesterol, translates to an increase in the ApoB/ApoA1 ratio which has been linked to premature IHD in South Asians[36,58,59].

Another very important risk factor for CVD in South Asians is Lp(a), which has been reported to be elevated in about 25% of Indians living in the United States[60]. Indian newborns have notably higher Lp(a) levels as compared to Chinese newborns, potentially explaining the significant differences in IHD between the two populations[60]. Lp(a) not only increases CVD risk itself but also acts as a risk enhancer in the presence of type 2 diabetes and high total cholesterol:HDL ratio[36]. The conventional lipid panel results are complex and sometimes confusing; replacing it with routine ApoB and Lp(a) testing could perhaps lead to earlier identification of high-risk patients and improved outcomes. However, their use in regular clinical practice in India remains a challenge due to high costs, lack of quality control between various assays, and the absence of long-term data in Indians.

Dietary patterns

Dietary risk factors contribute to just under half of all CVD deaths and related disabilities[61]. These include excessive intake of dietary components associated with an elevated CV risk and insufficient intake of components linked to reduced risk. The concept of diet quality is employed to assess the overall healthiness of a dietary pattern based on its constituents[62]. Human dietary patterns are typically a composite of various food groups and nutrients with synergistic interactions. Consequently, to comprehend the association between diet and CVD risk, it is imperative to consider all nutrients, food groups, dietary patterns, and their interrelationships[63]. Many scientifically backed dietary patterns claim to prevent heart diseases and they could be adopted to improve heart health (***Table 3***). Due to the established connection between blood cholesterol levels and CVD risk, studies have mostly focused on dietary fats and their impact on CVD. It is well known that consumption of a diet rich in trans-fats, and refined carbohydrates increases CVD risk. In contrast, a diet rich in fiber and unsaturated fats like omega-3 and omega-6 can reduce the risk of CVD by reducing cholesterol absorption, lowering LDL levels, and anti-inflammatory effects.

Recent data suggests that dietary patterns in Indians are changing: there is trend towards decreased consumption of healthy foods like whole grains, legumes, fruits, and vegetables, with a corresponding increase in the consumption of meat, processed foods, and high-salt foods[64]. A large national survey involving 156316 Indians found that half of the population ate either no fruit or just one serving of fruit per week[65]. Furthermore, the vegetables that people consume are often overcooked, causing a significant loss of essential nutrients[66]. In the states of Maharashtra and Tamil Nadu, only 24% and 1% of the population, respectively, met the WHO's recommended daily intake of more than five servings of fruits and vegetables[67]. The possible reasons for these observations include limited awareness of healthy eating habits, limited access to and affordability of healthier foods, and the increased availability and affordability of energy-dense processed foods[68]. A majority of Indians consume a predominantly vegetarian diet; however, this does not seem to confer protection against CVD[68]. This is probably because the Indian diet is usually rich in saturated fats and carbohydrates, and poor in protein quality, regardless of whether it is vegetarian or non-vegetarian[69]. A study comparing dietary patterns and their association with cardiometabolic risk factors among participants from the United States and South Asia showed that vegetarians in the United States tend to consistently eat healthier foods as compared to South Asian vegetarians[70]. The South Asian vegetarian diet was more or less similar to its non-vegetarian counterpart in terms of food choices and contained fewer healthy foods as compared to the diet of U.S. vegetarians. A diet high in animal protein has been positively associated with high homocysteine concentrations, which in turn are associated with a higher risk of IHD[71]. Plant-protein diets, on the other hand, have been inversely linked with homocysteine concentrations. Therefore, increasing the intake of folic acid (found in fruits and vegetables) and B vitamins might help to lower homocysteine levels[72].

Lastly, despite India's economic progress over the past two decades, problems of food insecurity and malnutrition persist. Data from the National Sample Survey suggest that the rate of food insecurity in India has decreased over time but at a very slow pace[73]. A recent study of 9,000 adults in both northern and southern India found that 10% of the participants faced food insecurity to some extent between October 2018 and February 2019[74]. The study also revealed that dietary diversity was quite low (50% of the participants consumed ≤3 food groups per day) and prevalence of poor-quality diets was high, particularly among women[74].

Other lifestyle factors

Lifestyle is one of the most ubiquitous factors affecting the risk of CVD. Making healthier lifestyle choices is an active process requiring deliberate change and proactive maintenance. Components of a healthy lifestyle include a healthy diet (as discussed above), adequate exercise, preventing obesity, and avoiding tobacco use. Exercise has several benefits, not only in reducing the risk of CVD but other health risks as well. It has been shown to be beneficial as regards insulin resistance, cholesterol levels, body weight, sleep patterns, and overall mental health[75-77].

Studies show that, even when started later in life, maintaining the recommended activity levels even in middle age reduces CVD risk[78].

Despite its proven benefits, few people in India and other low-income countries engage in regular physical activity to maintain their health. Very few studies on the true prevalence of exercise in India exist. In a study from an Indian city, over 90% of participants failed to meet WHO recommendations for at least 150 minutes of moderate-intensity aerobic physical activity per week[70]. A multicenter pan-India study showed that 57% of the study population was physically inactive or only mildly active, thereby not meeting the WHO recommendations[80]. A large survey conducted in three Indian states investigated physical activity in 14227 individuals aged ≥20 years and found that half of the participants were physically inactive and <10% of them engaged in discretionary physical activity[81]. The low prevalence of discretionary exercise contributes to the rising rate of obesity in India. More than 13% of the global population was obese in 2016, and it is expected that more than half of the global population will be obese by 2030[82]. In India, the prevalence of over-nutrition is estimated to be around 40.3%; the prevalence of over-nutrition is higher in urban, educated women[83,84]. BMI and waist circumference cutoffs for Asians are lower than those for their Western counterparts[85]. While a BMI >23 but <25 is considered normal elsewhere, it is considered over-nourished for Asians. Abdominal obesity has been linked with non-communicable chronic diseases, independent of BMI. This can partly be explained by the "Thin Fat Indian" phenotype, or "normal weight obesity," defined as a disproportionately high body fat percentage in an individual with a normal BMI[86]. This phenotype is very common in Indians and is associated with a high cardiometabolic risk and mortality, similar to that in individuals with overt obesity[87].

Tobacco use and secondhand smoke are associated with a high risk of CVD. Over 1.3 billion people worldwide use tobacco, resulting in an estimated 7 million deaths annually, predominantly due to CVD[88]. India accounts for 12% of the global prevalence of CVD and 1 million deaths[89]. Tobacco use is strongly rooted in Indian culture, often in the form of *bidi* (an indigenous form of hand-rolled cigarette with a leaf wrapper) or smokeless tobacco (chewed tobacco) mixed with betel leaf and lime (known variously as paan, gutka, khaini, or zarda)[90]. There are no specific geographic patterns of use, but it tends to be more common among younger men with lower levels of education and socioeconomic status[89,91]. What is more alarming is that experimentation with tobacco starts relatively early among children in India[92]. It has been estimated that tobacco control interventions could avert up to 25% of all predicted CVD deaths, equivalent to over 9 million averted deaths over 10 years[93]. Fortunately, many countries, including India, have been able to decrease the prevalence of smoking over the last 20 years, suggesting that tobacco control measures have been applied with some success[94].

Socioeconomic status

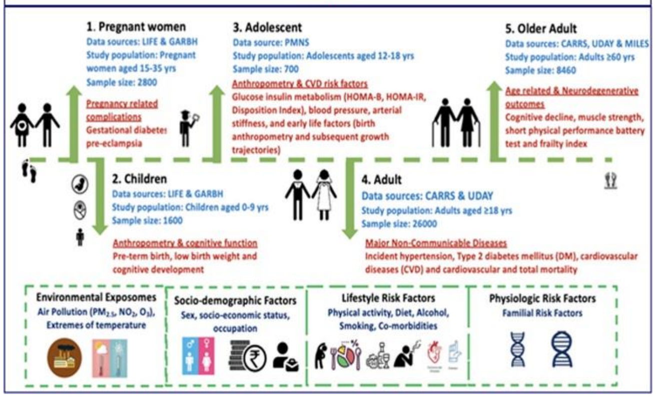
In addition to the risk factors mentioned in previous sections, factors like long-term material deprivation and poor living conditions also add to the CVD risk among socially disadvantaged groups in India[95]. Differences in socioeconomic status (SES) are linked with healthcare disparities, CVD risk, and overall life expectancy[96]. SES depends on geographic location, education status, occupation and wealth, and even early life factors. In India, there is a significant socioeconomic gap between the lowest and highest strata; eg, in the year 2022, the top 10% of the population was responsible for 57% of the total national wealth[97]. Despite the introduction of universal health coverage in 2018, 12% of all Indians still had unmet healthcare needs, and 16.5% of the population experienced poverty due to healthcare expenses in the previous one year[98]. Although CVD was once considered a problem of wealthy people, recent studies demonstrate increasing CVD-related mortality and morbidity among people with lower SES as well[28,99]. In a large registry of patients who experienced myocardial infarction selected from across 50 Indian cities, lower-SES individuals were at a 1.5-fold higher risk for worse outcomes as compared to those in a higher SES[100]. In a cross-sectional study in Jaipur, social indicators like lower educational, occupational, and SES status were associated with higher CVD risk [101]. This is likely due to poor access to quality healthcare, further exacerbated by insufficient financial resources to access acute and chronic CVD care, given that medical treatment in India often involves large out-of-pocket expenses[16,102]. Furthermore, SES impacts literacy and education levels. Studies have shown that low educational status is associated with lower rates of awareness, treatment, and control of CVD risk factors, thereby increasing the prevalence of the disease and the risk for mortality[26,28,103]. On the other hand, a recent study from India did not find any association between higher education levels and better CV health[104]. It showed, on the contrary, that people in rural areas with fewer resources had better CV health markers than those in cities with more resources.

Environmental pollution

Air pollution has recently been recognized as an important contributor to CVD risk: 12% of all deaths in 2019 were related to household and air pollution[105]. India has one of the highest rates of pollution in the world, and 17.8% of all deaths in India in 2019 were attributed to air pollution[102]. The worsening air quality in many parts of India, along with continued exposure to indoor air pollution, has been identified as important factors contributing to the rising health problems in the country. Air pollution comprises a complex mixture of gases and particulate matter (PM), characterized by aerodynamic diameter (***Table 4***). PM2.5 is suspected to be the principal component posing the greatest threat, and is believed to have caused 4.2 million deaths[107]. PM 2.5 is released into the air from road traffic, fuel combustion, and natural dust, and is affected by meteorological conditions. The primary mechanisms underlying the pathophysiology include 1) endothelial dysfunction, 2) systemic inflammation, 3) prothrombotic milieu, 4) autonomic imbalance with increased sympathetic tone, 5) central nervous system effects on the metabolism and hypothalamic-pituitary-adrenal axis activation, and 6) epigenomic changes. These pathways have considerable overlap as PM2.5 crosses the blood-alveolar barrier easily.

Several studies have linked air pollution - particularly PM 2.5 - to CVD. It has been associated with the development of atherosclerosis and traditional CVD risk factors such as hypertension and diabetes[108-112]. Additionally, it has been shown to increase the risk of mortality in patients with IHD, stroke, arrhythmias, and heart failure[113,114]. Pre-conception PM exposure has also been shown to be associated with cardiac dysfunction later in life, highlighting PM's potential long-term impact on cardiovascular health[115]. A systematic review involving 224829 individuals, living or working in environments with high exposure to noise showed that noise pollution was associated with increased risk of hypertension, and a linear dose-response relationship was

Fig 1 Program linking environmental pollution to health outcomes across the lifespan



noted, with a risk ratio of hypertension of 1.13 per 10-decibel higher ambient noise[116]. With increasing industrialization, urbanization, and climate change, these findings have become particularly relevant in the context of India and other low- and middle-income countries. Over 60% of India's labour force are farmers, and face the risk of exposure to pesticides, which in turn is associated with adverse health outcomes[117,118]. Organophosphate pesticides increase the risk of developing diabetes, hypertension, asthma, and obesity[119-122]. Systematic studies should be carried out to explore the linkages between exposure to various pesticides and CVD risk and mortality.

Population-level Factors

Over the past four decades there have been technological advancements and improved access to affordable healthcare in India. As a result, there has been a progressive and sustained increase in longevity. Indian census data show that 8% of the total population in 2011 was above the age of 60 years and this proportion is expected to rise to 19% by the year 2050[9,123]. The aging population adds to the overall burden of CVD in India. Rapid industrialization, urbanization, and globalization in India over the past few decades have directly or indirectly impacted the burden of CVD in Indians. Increasing reliance on machines and technology has led to a rise in sedentary lifestyles and CVD risk factors such as hypertension, obesity, diabetes, dyslipidemia, substance abuse, and air pollution[124]. Rural-to-urban migration is common in India; in contrast to their siblings who stayed in rural areas migrants who moved from rural to urban areas had a risk factor profile similar to the urban population within a decade of migration[125].

Life-course perspective

While conventional risk factors and population level changes can explain a significant portion of the CVD risk in Indians, there are unique aspects that need attention. For instance, one study found a stronger link between diabetes and stroke in South Asians as compared to Europeans[126]. This might imply that the levels at which traditional risk factors become problematic might be lower in South Asians than in other ethnic groups. It would be advisable to adopt a life course perspective while assessing CVD risk.

The life course theory relies on a multidisciplinary approach to determine how early- and later-life biological, behavioural, social, and psychological exposures affect an individual's health[127]. Early-life experiences, especially during the first two years, significantly impact the risk factors for CVD to develop in adult life[128]. Issues like maternal malnutrition and placental problems can lead to a phenomenon called foetal programming, which can result in alteration in body composition (low muscle and high fat: thin-fat child), reduced β-cell mass, and fewer kidney glomeruli[129]. Studies show that maternal malnutrition, smoking, gestational diabetes, elevated maternal blood pressure, and increased gestational weight gain are all associated with an unfavourable cardiometabolic risk profile in the offspring[130-134]. Severe maternal pre-eclampsia has been shown to be associated with hypertension in the offspring six to seven decades after birth[135]. Environmental factors like exposure to air pollution during pregnancy can have trans-generational impact on CVD risk factors. Maternal exposure to PM 2.5 concentration ≥13μg/m^3 and black carbon during the third trimester has been associated with elevated blood pressure in neonates and in offspring aged 3 to 9 years, even after accounting for potential confounders and postnatal PM 2.5 exposure[136,137]. It is important to explore potential mechanisms for these associations such as inflammation, oxidative stress, sympathetic activation, and transforming growth factor-β1 signalling[138].

Research studies have documented a link between prematurity, low and high birth weight, and development of obesity, hypertension, and dyslipidemia in the first decade of life[139,140]. Findings from the Hyderabad nutrition trial showed that improving the nutritional status of pregnant women and young children may result in a more favourable CVD risk factor profile in undernourished population groups[141]. The New Delhi Birth Cohort study showed that children who experience a rebound in adiposity and weight gain between the ages of 2 and 12 are more likely to develop dysglycemia as young adults[142]. Research studies have shown that early-life influences can lead to cognitive impairment, lower school performance, and reduced productivity, all of which are associated with an increased risk of CVD[143].

Challenges, innovations, and way forward

The rising CVD problem in India presents a significant challenge to its healthcare system. The complex interplay of known risk factors and unique biological characteristics renders Indians more susceptible to CVD. By leveraging our current understanding of these mechanisms and with effective implementation of appropriate interventions, the future burden of CVD in India can be substantially limited. India can benefit from adopting successful strategies used in various Western as well as low-to-middle-income countries to reduce CVD mortality through population-level lifestyle changes and treatment of common risk factors. Novel strategies such as polypill (a combination pill of multiple drugs) can be used for primary and secondary prevention of CVD[144,145]. This strategy would not only reduce overall treatment cost and pill burden but would also improve treatment adherence. There is a need to improve acute cardiac care and chronic post-discharge management of CVDs. Data from the CREATE registry showed that patients with myocardial infarction arrived at hospitals very late (6 hours after onset of symptoms) leading to poorer outcomes[100]. Of these, only 58% received lytics and 8% received percutaneous coronary intervention. Of those discharged, only 52% were prescribed a statin. These data highlight the need for performance auditing and quality improvement initiatives in India to ensure that

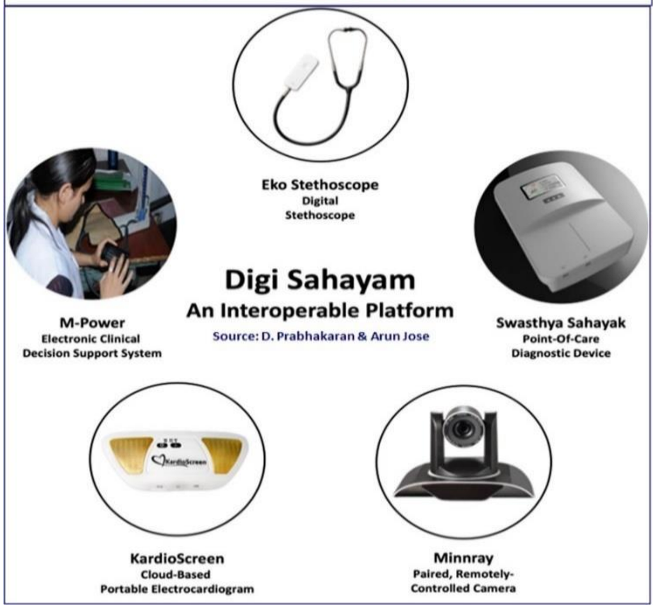


Fig 2 The technologies of DigiSahayam. Paired with a drug delivery system, it is able to provide multiple service delivery models

evidence-based timely care is provided during both the acute and the chronic phases of CVD[146].

It is equally important to: (i) continue to document the knowledge gaps and work with various stakeholders at individual, community, and policy levels; (ii)establish large longitudinal cohorts to understand the epidemiology of CVD in Indians, and (iii) launch robust surveillance systems for CVD factors, events, and mortality. One such project, the GEOHEALTH (Global Environmental and Occupational Health) programme, uses publicly available information to undertake a robust exposure assessment and develop models linking PM 2.5 levels to cardiometabolic disease and outcomes. This program, had documented that long- and short-term exposures to increased PM are associated with increased BP and risk of developing hypertension in urban India. Data suggests that even 25% reduction in PM 2.5 can substantially lower this risk, and that achieving the national air standards set by the Central Pollution Control Board (<60 μm/m^3) could decrease the overall prevalence of hypertension by 15%[147]. CARRS (Centre of Cardiometabolic Risk Reduction in South Asia Surveillance) a is a population-based prospective cohort study that follows study participants via questionnaires, anthropometric measurements and biospecimen collections to understand the drivers of CVD and mortality[148]. Both projects are ongoing and continue to expand, providing data to inform policy changes. They are currently local programmes, but their results will be crucial in leading to health-related policy changes. The next step is to integrate these technologies at national and global levels to enhance cardiac care, as outlined in the World Heart Federation's roadmap for digital health in cardiology[149].

It is also important to invest in capacity building and task shifting by involving community health workers in primary and secondary care settings. There is an urgent need to adopt innovative technology-based models that are cost effective and scalable, in order to improve access to care in marginalized population groups. Modern wearable devices, such as digital watches and wrist bands can act as biomedical sensors for increased surveillance and screening[150]. Portable diagnostic equipment, such as lab-on-chip devices and portable electrocardiograms, enable more detailed screening. The data generated can be managed with tele-health and digital health systems, even from afar, and used for creating India-specific models of care without the need for intensive resources[151]. Programmes such as mPOWER and DigiSahayam, are already using these concepts to provide CVD care in different regions of India. The mPOWER system is a clinical decision support system that enables engagement and personalization during patient care while reducing demands on physicians[152]. It is a part of the DigiSahayam system, a telemedicine platform with embedded electronic health records, point-of-care diagnostics, and clinical support systems (***Figure 2***). Its utilization has improved the quality of care and has resulted in better control of hypertension and diabetes. However, telemedicine is not the only delivery model of DigiSahayam. It includes on-foot assistance, DigiSahayam on wheels, drug delivery systems, and even designated telemedicine centers. It has benefited >4000 patients with CVD and other chronic diseases and has resulted in an average saving of ₹917 per visit[54].

Although data are lacking about the impact of large-scale economic policy changes on CVD in India, modelling studies indicate that levying higher taxes on tobacco, palm oil, and sugary drinks will potentially reduce the rates of obesity and type 2 diabetes, and avert approximately 25% of the myocardial infarctions and strokes in India[93,153]. After the World Health Assembly approved a global action plan for preventing and controlling non-communicable diseases, India has established a national monitoring system to meet all the goals set by the WHO, including a 30% decrease in the use of both salt and tobacco by 2025[154]. To achieve this goal, a multi-pronged approach involving various stakeholders at individual, community, policy, and government levels is required. There is a need to pursue transdisciplinary research in emerging fields like prenatal, early life, and transgenerational experiences which have the potential to impact risk of CVD in adult life.

A number of ongoing studies in India will help to further strengthen our understanding of the impact of early life influences on CVD disease in adulthood. A few of these are: HeLTI (Healthy Life Trajectories Initiative) study investigating the effects of life course approach-based interventions; IndEcho study evaluating the effects of birth size and growth from infancy through adolescence on CVD risk factors in young adulthood and myocardial structure and function in midlife; and MYNAH (MYsore study of Natal effects on Ageing and Health) study that aims to understand cognitive function, cardio-metabolic disorders and mental disorders in late life[155-157].

Conclusion

Cardiovascular disease is the foremost cause of global mortality and poses a major public health challenge. India alone is responsible for approximately 20% of the world's 17.9 million deaths, which is only expected to increase with the growing population of the elderly and inadequate access to appropriate and timely health interventions. CVD in Indians is characterized by a higher risk compared to other ethnicities, an earlier age of onset, and a higher proportion of premature deaths. In addition to the established cardiovascular risk factors, Indians have an inherently increased biological risk which is further enhanced by various socioeconomic and population-level factors. Further, the threshold at which these risk factors operate is different among Indians as compared with other populations. The proposed hypotheses explaining this excess risk include the role of genetic predisposition, differences in the metabolism of lipids and glucose metabolism, early life and inter-generational influences, dietary patterns, environmental pollution, and socioeconomic factors. Reducing the risks and burden of cardiovascular diseases in India will require innovative methods, population-level studies, and a multidisciplinary approach involving state and national stakeholders to affect policy changes.

The global impact of CVD cannot be overstated, and it continues to remain a matter of concern. If not addressed in a timely manner, the long-term health and economic consequences of CVD can have serious repercussions for a country like India that is going through epidemiological, demographic, socioeconomic, and environmental transitions. Considering the high burden of CVD and limited healthcare resources, improving CVD health in India will require a multi-pronged approach with involvement of various stakeholders, incorporation of technology to improve access to care, strengthening and integration of primary, secondary, and tertiary health systems, and disruptive innovations to affect policy changes and bring about a meaningful change at the national level. Programmes such as GEOHEALTH and DigiSahayam are some of the essential steps in that direction that have already shown favourable effects in thousands and can potentially impact millions more.

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FOUNDATION NEWS

Prof. M.S. Swaminathan, internationally renowned agricultural scientist and head of the MSSRF passed away in Chennai on 28 September, 2023. We at NFI will miss his steadfast support and wise guidance. May his soul rest in peace.

The Fourth Dr C Gopalan Memorial Webinar is scheduled to be held on 03.10.2023 from 10.00 AM to 1.30 PM The theme of the Webinar is “Diabetes in India during the dual nutrition burden era”. Dr Kamala Krishnaswamy will chair the webinar. The three speakers and their topics are:

- Dr R. M. Anjana Epidemiological data on diabetes in India
- Dr. Chittaranjan Yajnik Double burden of malnutrition across life-course and trans-generationally in a rapidly transiting society
- Dr. G.V. Krishnaveni Ongoing nutrition transition in women and its impact on diabetes

Dr Soumya Swaminathan, Chairperson MSSRF, Chennai, will be delivering the C Ramachandran Memorial Lecture in virtual mode on 29.11.2023 from 3.00 PM to 5.00 PM

NUTRITION NEWS

The 55th Annual Conference of Nutrition Society of India is scheduled to be held on 25th and 26th of November 2023 at the National Institute of Nutrition, Hyderabad. The theme of the Conference is “Nutri-cereals for one health”.

Two pre-conference workshops will be organized on 24th Nov. 2023. Workshop 1: Nutrient requirement and adequacy and Workshop 2: Nutrition Survey method