# **Global Burden of Cardiovascular Disease**

# **Cardiovascular Diseases in India** Current Epidemiology and Future Directions

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Abstract-Cardiovascular diseases (CVDs) have now become the leading cause of mortality in India. A quarter of all mortality is attributable to CVD. Ischemic heart disease and stroke are the predominant causes and are responsible for >80% of CVD deaths. The Global Burden of Disease study estimate of age-standardized CVD death rate of 272 per 100000 population in India is higher than the global average of 235 per 100000 population. Some aspects of the CVD epidemic in India are particular causes of concern, including its accelerated buildup, the early age of disease onset in the population, and the high case fatality rate. In India, the epidemiological transition from predominantly infectious disease conditions to noncommunicable diseases has occurred over a rather brief period of time. Premature mortality in terms of years of life lost because of CVD in India increased by 59%, from 23.2 million (1990) to 37 million (2010). Despite wide heterogeneity in the prevalence of cardiovascular risk factors across different regions, CVD has emerged as the leading cause of death in all parts of India, including poorer states and rural areas. The progression of the epidemic is characterized by the reversal of socioeconomic gradients; tobacco use and low fruit and vegetable intake have become more prevalent among those from lower socioeconomic backgrounds. In addition, individuals from lower socioeconomic backgrounds frequently do not receive optimal therapy, leading to poorer outcomes. Countering the epidemic requires the development of strategies such as the formulation and effective implementation of evidencebased policy, reinforcement of health systems, and emphasis on prevention, early detection, and treatment with the use of both conventional and innovative techniques. Several ongoing community-based studies are testing these strategies. (Circulation. 2016;133:1605–1620. DOI: 10.1161/CIRCULATIONAHA.114.008729.)

Key Words: cardiovascular diseases ■ coronary disease ■ epidemiology ■ India ■ prevention & control ■ risk

With the turn of the century, cardiovascular diseases (CVDs) have become the leading cause of mortality in India.<sup>1</sup> In comparison with the people of European ancestry, CVD affects Indians at least a decade earlier and in their most productive midlife years.<sup>2,3</sup> For example, in Western populations only 23% of CVD deaths occur before the age of 70 years; in India, this number is 52%.<sup>4</sup> In addition, case fatality attributable to CVD in low-income countries, including India, appears to be much higher than in middle- and high-income countries.5,6 The World Health Organization (WHO) has estimated that, with the current burden of CVD, India would lose \$237 billion from the loss of productivity and spending on health care over a 10-year period (2005-2015).7 Reasons for the high propensity to develop CVD, the high case fatality, and the high premature mortality include biological mechanisms, social determinants, and their interactions. Addressing this significant burden requires an understanding of both the biological and social determinants, and the complex dynamics underlying their interaction, as well. In this review, we summarize the CVD burden in India, the reasons for the high

burden, prevention and treatment strategies for CVD, and future policy strategies to pursue.

The epidemiological transition in India in the past 2 decades has been dramatic; in a short timeframe, the predominant epidemiological characteristics have transitioned from infectious diseases, diseases of undernutrition, and maternal and childhood diseases to noncommunicable diseases (NCDs).8 The disease burden attributable to maternal disorders, measles, protein-energy malnutrition, and diarrheal diseases decreased >50% in the past 2 decades, whereas life expectancy at birth increased from 58.3 to 65.2 years, resulting in the ageing of the population during the same period.<sup>8</sup> Consequently, the NCD burden increased rapidly in India, with a proportional rise in burden attributable to CVD.8 Nearly two-thirds of the burden of NCD mortality in India is currently contributed by CVD-related conditions.9 Despite wide heterogeneity in the prevalence of risk factors across different regions (explained below), CVD is the leading cause of death in all parts of India, including the poorer states and rural areas.<sup>10</sup> The disease transition in India in the past 2 decades resembles the accelerated

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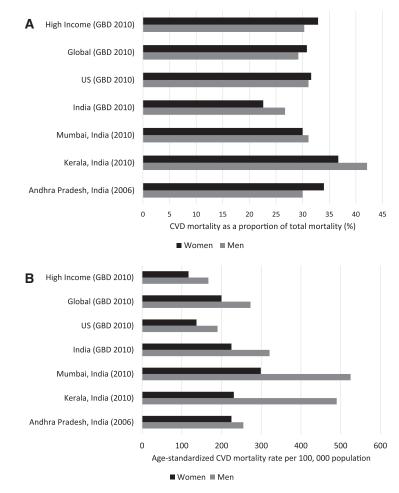
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epidemiological transition model with a rapid shift to the age of delayed chronic diseases.

## Burden of Cardiovascular Diseases in India

According to the Global Burden of Disease study age-standardized estimates (2010), nearly a quarter (24.8%) of all deaths in India are attributable to CVD (Figure 1A).<sup>11</sup> The agestandardized CVD death rate of 272 per 100000 population in India is higher than the global average of 235 per 100000 population (Table 1).<sup>11</sup> However, there is a major gap in knowledge, especially regarding the causes of death in rural India; Global Burden of Disease estimates are based on smaller communitybased studies.<sup>12</sup> Although verbal autopsy data from India were collected after 2004, they have not been analyzed or released for public access, and they were not included in the burden estimation.<sup>12</sup> Currently, there are no nationally representative surveillance data on the prevalence of CVD and the secular trends of CVD mortality in India. However, recent reports of 3 large prospective studies from India suggest a higher proportion of mortality attributable to CVD (30%-42%) and an age-standardized CVD mortality rate (255-525 per 100000 population in men and 225-299 per 100000 population in women) in comparison with the Global Burden of Disease study (2010; Figure 1A and 1B).<sup>13-15</sup> Ischemic heart disease (IHD) and stroke constitute the majority of CVD mortality in India (83%), with IHD being predominant (Figure 2).<sup>11</sup> The ratio of IHD to stroke mortality in India is significantly higher than the global average, and is comparable to that of Western industrialized countries (Figure 2). Together, IHD and stroke are responsible for more than one-fifth (21.1%) of all deaths and one-tenth of the years of life lost in India (years of life lost is a measure that quantifies premature mortality by weighting younger deaths more than older deaths).<sup>8</sup> The years of life lost attributable to CVD in India increased by 59% from 1990 to 2010 (23.2 million to 37 million).<sup>8</sup>

Although systematic studies on IHD prevalence using countrywide representative samples are not available, several small cross-sectional studies performed in different parts of the country suggest rapid increases in IHD burden over the past few decades (Figure 3A and 3B).16-38 Although the prevalence rates in adults from different cross-sectional surveys conducted at different time points cannot be directly compared, the overall trends are informative. The prevalence of IHD in 1960 in urban India was 2%, and increased 7-fold to  $\approx 14\%$  by 2013.<sup>16–28,37,38</sup> Similarly, it more than quadrupled in rural areas, from 1.7% to 7.4% between 1970 and 2013.<sup>29-36,38</sup> These prevalence estimates are probably an underestimate of the burden, because the methods of estimation are based on insensitive tools. In addition, the higher case fatality among Indians following acute coronary syndrome (ACS) could also result in the underestimation of prevalence.<sup>6</sup> The Macroeconomic Commission for Health estimated that the absolute number of IHD patients in India will increase from 36 million in 2005 to 62 million in 2015 (a  $\approx$ 70% increase).<sup>39</sup>



**Figure 1. A**, Proportion of cardiovascular disease mortality in India based on data from available prospective studies and Global Burden of Disease estimates.<sup>11</sup> The prospective studies included in the figure are Pednekar et al<sup>13</sup> (Mumbai, Urban), Soman et al<sup>14</sup> (Kerala, Urban and Rural), and Joshi et al<sup>15</sup> (Andhra Pradesh, Rural). **B**, Age-standardized rate of cardiovascular disease mortality in India based on Global Burden of Disease estimates and data from available prospective studies.<sup>11</sup> CVD indicates cardiovascular disease; and GBD, Global Burden of Disease.

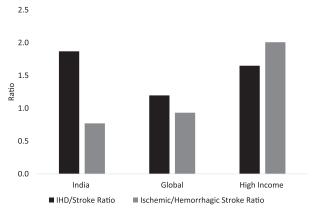
	Death per 100 000 Population		DALYs per 100 000 Population			
Diseases	Male	Female	Total	Male	Female	Total
Ischemic heart disease	178 (128)	112 (85)	144 (106)	3783 (2577)	2053 (1406)	2917 (1972)
Cerebrovascular disease	90 (99)	75 (79)	82 (88)	1605 (1838)	1240 (1295)	1420 (1554)
Rheumatic heart disease	11 (5)	10 (5)	10 (5)	300 (148)	269 (155)	285 (151)
Hypertensive heart disease	18 (14)	15 (13)	17 (13)	343 (252)	270 (215)	306 (233)
Cardiomyopathy and myocarditis	10 (8)	5 (4)	8 (6)	266 (221)	126 (112)	197 (166)
Atrial fibrillation and flutter	1 (2)	1 (2)	1 (2)	49 (65)	36 (46)	42 (55)
Aortic aneurysms	2 (4)	1 (2)	2 (3)	44 (70)	25 (29)	35 (48)
Peripheral vascular disease	<1 (1)	<1 (1)	<1(1)	10 (16)	8 (14)	9 (15)
Endocarditis	1 (1)	1 (1)	1 (1)	18 (27)	18 (19)	18 (23)
Others	10 (12)	5 (9)	7 (10)	229 (272)	196 (239)	210 (254)
Total cardiovascular diseases	321 (273)	225 (200)	272 (235)	6648 (5486)	4241 (3530)	5438 (4471)

Table 1. Age Standardized Death and Disability Rates of CVD in India (Global Burden of Disease 2010 Estimates)

Numbers in parentheses are the global average.

In India, the age-standardized annual stroke incidence rate is 154 per 100000 per year (standardized to the world standard population).<sup>40</sup> Although the stroke incidence and stroke-related case fatality rates in India are higher relative to Western industrialized nations in general, the rates are especially higher among women. Available neuroimaging data suggest that hemorrhagic strokes are more common in India than in the Western population.<sup>40</sup> The ratio of ischemic stroke to hemorrhagic stroke mortality in India is below the global average of close to 1, with hemorrhagic stroke mortality being predominant (Figure 2); this reflects the relatively less advanced stage of the epidemiological transition in India in comparison with Western populations.

Hypertensive heart disease, among other CVDs, is a significant problem in India, with 261694 deaths in 2013; this is an increase of 138% in comparison with the number of deaths in 1990.<sup>12</sup> Rheumatic heart disease also continues to be a problem in several parts of India, with an estimated 88674 deaths (7 per 100000 population) in the year 2010.<sup>8</sup> Reliable national-level data on the rheumatic heart disease burden are not available from India because of the differences



**Figure 2.** Ischemic heart disease to stroke ratio and ischemic to hemorrhagic stroke ratio in India in comparison with global data.<sup>11</sup> IHD indicates ischemic heart disease.

in definitions used in existing studies. However, the available estimates suggest that rheumatic heart disease prevalence is in the range of 1.5 to 2 per 1000 individuals (2–2.5 million cases in absolute numbers).<sup>41</sup>

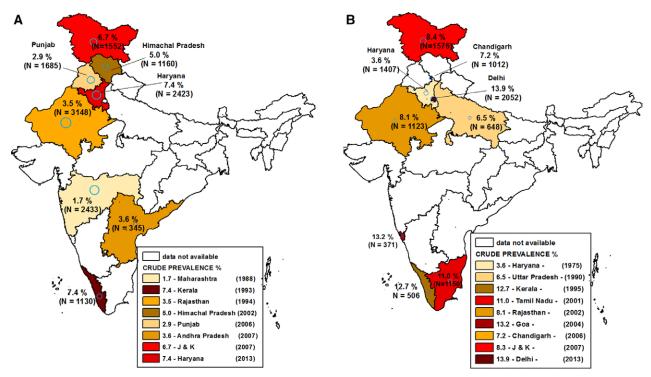
Unlike Western populations, atrial fibrillation appears to be less common in India, with rheumatic heart disease contributing to nearly one-third (31.5%) of the atrial fibrillation burden. These data are based on the Randomized Evaluation of Long Term Anticoagulant Therapy (RE-LY) registry, a registry of 15 400 patients from 46 countries, including 2500 patients from India, presenting to emergency departments.<sup>42</sup> To the best of our knowledge there are no nationwide estimates on the prevalence and incidence of atrial fibrillation, heart failure, and cardiomyopathies in India.

Based on Global Burden of Disease study estimates, the contribution of atrial fibrillation and flutter to the overall CVD burden in India appears to be small.<sup>11</sup> Furthermore, the proportional mortality and morbidity burden attributable to other types of CVD such as aortic aneurysms, peripheral vascular disease, and endocarditis are also relatively small.<sup>11</sup>

### **Burden of CVD Risk Factors**

National-level data for most risk factors (with the exception of tobacco) are not available. However, several large crosssectional surveys have been conducted in India in the past 20 years, and we provide a summary of these studies in the next section. The major recent epidemiological studies are summarized in Table 2.

It is estimated that, currently, 275 million individuals aged  $\geq$ 15 years consume tobacco in India.<sup>50</sup> The mortality burden attributable to tobacco in India is huge, because it is estimated to cause nearly 1 million deaths annually.<sup>51</sup> Overall, more than one-third of adults in India (35%) use tobacco, with prevalence rates varying from 9% in Goa to 67% in the northeastern state of Mizoram.<sup>50</sup> Smokeless tobacco and the smoking of *bidi* (an indigenous form of hand-rolled cigarette with a leaf wrapper) are the most common types of tobacco used in India.<sup>50</sup> Although the overall prevalence of smoking is low



**Figure 3. A**, Ischemic heart disease prevalence rate in rural India. The numbers in the map are the prevalence; the sample sizes are in parentheses. The years of the source data are listed in the figure key in parentheses. Data from a new study in rural Haryana (2013) are included (D. Prabhakaran, unpublished data, 2013). **B**, Ischemic heart disease prevalence rate in urban India. The numbers in the map are the prevalence, with sample sizes in parentheses. The years of the source data are listed are listed in the figure key in parentheses.

(14%), smoking prevalence is higher among men (24%) than among women (3%), and smoking among individuals with less-than-primary education is higher for both sexes (37% and 4% for men and women, respectively).<sup>52</sup> It is alarming that tobacco use is increasing rapidly among young individuals (20–35 years) in India,<sup>53</sup> with a steeper rate of increase among those with lower education.<sup>46</sup> Evidence also suggests that experimentation with tobacco starts relatively early among children in India.<sup>54</sup>

The rate of consumption of fruit and vegetables is low in India; this is contrary to the perception that Indians, being predominantly vegetarians, would consume adequate quantities of fruit and vegetables. The National Family Health Survey-3 (NFHS-3), a large nationally representative cross-sectional survey covering 156316 individuals in India with selfreported data on consumption of fruit and vegetables, reported that half of the population in its survey consumed zero or only 1 serving of fruit in a week.48 The NFHS-3 also reported a social gradient in weekly consumption of fruit, with individuals in the lowest socioeconomic strata consuming a very low quantity of fruit. This is potentially explained by the high cost of fresh fruit and vegetables.55 In addition, the vegetables that are consumed are often overcooked in Indian meals, leading to vital loss of micronutrients.56 Even in the 2 most economically prosperous states, Maharashtra and Tamil Nadu, the WHOrecommended consumption of >5 fruits and vegetables daily is only observed among 24% and 1% of people, respectively.57

Time-series data on nutrient intake captured from the National Sample Survey Organization surveys indicate that, despite no significant change in total calorie consumption from 1972 to 2000, Indians' fat intake increased from 24 to

36 g/d and from 36 to 50 g/d in rural and urban individuals, respectively.<sup>55</sup> Partially hydrogenated vegetable oils with high trans fat content contribute to a significant proportion of total fat intake in Indians, and the consumption of partially hydrogenated vegetable oil is particularly common in urban adult slum dwellers belonging to the lowest socioeconomic status (SES).<sup>58,59</sup> Although the percentage of carbohydrate intake has remained relatively constant, the consumption of refined grain products increased in comparison with the consumption of whole grains.<sup>55</sup>

Data on physical activity in India are sparse. The Indian Council of Medical Research-India Diabetes study (ICMR-INDIAB) is a large cross-sectional survey with data from 3 different states. The ICMR-INDIAB study assessed physical activity using the Global Physical Activity Questionnaire in 14227 individuals aged  $\geq$ 20 years. One of every 2 individuals in the ICMR-INDIAB study was considered physically inactive.<sup>45</sup> In addition, <10% of the studied population engaged in recreational physical activity.45 Physical inactivity was higher in urban areas, for women, and for individuals of higher SES.45 Gupta et al.<sup>60</sup> in their study of 6198 individuals from 11 cities, did not find any difference in physical activity levels between groups based on low versus high education status. However, in a large study conducted in industrial settings, leisure-time physical activity showed an inverse social gradient (ie, higher levels of physical inactivity among lower educational status).<sup>61</sup>

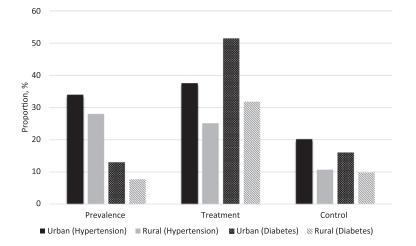
The prevalence of hypertension in adult Indians is estimated to be 30% (34% in urban areas and 28% in rural areas).<sup>62</sup> The number of individuals with hypertension is expected to double from 118 million in 2000 to 213.5 million by 2025.<sup>63</sup> In India, the average blood pressure has increased in the past

Table 2. Major Recent Cardiovascular Disease Epidemiology Studies in India*
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Study Name	Study Design (Year of Study)	Sample Size	Principal Findings	Limitations
PURE study⁵	Cohort study (2014)	24000 from India	The CVD event rate in predominantly Indian population (low- and middle-income region) is 6.43/1000 person-years of follow-up in comparison with 3.99 per 1000 person-years of follow-up in high-income countries.	Underreporting of CVD events resulting from poor access to hospital and diagnostic facilities in India.
The Mumbai cohort study <sup>13</sup>	Cohort study (2011)	148173	Inverse association of CVD mortality and education in men.	Cause of death ascertainment from death registry that does not provide robust data.
PROLIFE <sup>14</sup>	Cohort study (2011)	161 942	40% deaths are attributable to CVD.	Located in a small region in 1 state.
APRHI <sup>15</sup>	Analyses of cause-of death in 1-y period (2006)	180 162	32% mortality from CVD.	Located in a single region.
APCAPS <sup>43</sup> (ongoing)	Intergenerational cohort of children and parents (2014)	10213	Expected to provide data on transgenerational influences of other environmental and genetic factors on chronic diseases in rural India	Located in a single region. High attrition rate.
CARRS surveillance study <sup>44</sup>	Two repeat cross-sectional surveys and follow-up of all participants (2012)	9000	Expected to provide secular trend and risk factor progression of CVD.	Limited to Delhi and Chennai.
Solan surveillance study	Repeat cross-sectional survey (ongoing)	40 000	Expected to provide secular trend in risk factors.	Limited to Solan district in Himachal Pradesh.
ICMR-INDIAB (phase 1) <sup>45</sup>	Cross-sectional survey with multistage cluster sampling design (2014)	16607	Regional variations in prevalence of CVD risk factors.	Data from only 3 states are currently available.
Jaipur Heart watch <sup>46</sup>	5 repeat cross-sectional surveys in an urban city in India (2003)	1992–1994:712 1991–2001: 558 2002–2003: 374 2004–2005: 887 2009–2010: 530	Linear increase in CVD risk factors.	Limited to 1 urban city area. Response rate varied from 55% to 75%.
India Heart Watch (ongoing) <sup>47</sup>	Cross-sectional survey in 15 cities in India (2012)	Plan to recruit 7500 participants.	Identification of regional differences in risk factors.	No follow-up.
ICMR urban rural survey <sup>37</sup>	Repeat cross-sectional surveys in urban and rural areas of the National Capital Region (2013)	≈6000	Prevalence of CHD increased from 10.19% (95% Cl, 9.11–11.27) to 13.91% (95% Cl, 12.41–15.41). Rate of increase in risk factor levels was higher in rural area in comparison with the urban area.	Survey conducted only at 2 time points.
NFHS 348	Cross-sectional representative sample. Multistage cluster sampling in states of India (2013)	156316	Relatively low prevalence of diabetes mellitus.	Self-reported prevalence estimates.
CREATE <sup>3</sup>	ACS registry (2008)	20937	Higher rates of STEMI in Indians (60%) in comparison with Western data.	Only 30 day follow-up is available. Data are essentially from tertiary care centers.
Kerala ACS Registry <sup>49</sup>	ACS registry (2013)	25748	Suboptimal treatment is associated with incidence of major cardiovascular events.	Only in-hospital mortality data were captured.
INSPIRE (ongoing: CTRI/2013/10/004108)	Stroke registry (2015)	11 000	Expected to provide information on etiology, clinical practice patterns of acute care, clinical outcomes, and secondary prevention practices of stroke in India.	Data are essentially from tertiary care centers in urban settings.

APCAPS indicates Andhra Pradesh children and parents study; APRHI, Andhra Pradesh rural health initiative; CARRS, Cardiometabolic risk reduction survey; CHD, coronary heart disease; CI, confidence interval; CREATE, Treatment and outcomes of acute coronary syndromes in India; CTRI, Clinical Trial Registry of India; CVD, cardiovascular disease; ICMR INDIAB, Indian Council of Medical Research-India, diabetes study; INSPIRE, In Hospital Prospective Stroke Registry; Kerala ACS, Kerala Acute Coronary Syndrome Registry; NFHS, National Health and Family Welfare Survey; PROLIFE, Population registry of lifestyle diseases; PURE, Prospective Urban Rural Epidemiology studies; and STEMI, ST-segment–elevation myocardial infarction.

\*Simple prevalence studies are not included.



**Figure 4.** Prevalence, treatment, and control of hypertension and diabetes mellitus in urban and rural India. Hypertension data are derived from the systematic review and meta-analyses of Anchala et al.<sup>62</sup> Diabetes mellitus data are derived from the ICMR-INDIAB study.<sup>69,70</sup>

2 decades, whereas in most Western nations it has declined.<sup>64</sup> The social gradient for hypertension is unclear. Although a few studies from urban settings report an inverse social gradient, with higher prevalence among individuals from low SES, others report no differences.<sup>61,65–67</sup> Data from low-income countries (83% of the participants being from India) from the Prospective Urban and Rural Epidemiological (PURE) study, also show that low educational status is associated with lower rates of awareness, treatment, and control of hypertension.<sup>68</sup> The prevalence, treatment, and control rates of hypertension and diabetes mellitus are summarized in Figure 4.<sup>62,69,70</sup>

In the urban areas of India, the prevalence of diabetes mellitus has almost doubled in the past 20 years, from 9% to 17%, and in rural areas it has nearly quadrupled, from 2% to 9%.47 In 2013, the International Diabetes Federation estimated that 65.1 million people in India had diabetes mellitus, a high proportion of whom were adults of working age.71 It is estimated that the number of individuals with diabetes mellitus will increase to an alarming 101 million by 2030.71 An estimate based on the ICMR-INDIAB study indicates that the number of individuals in India with prediabetes (impaired fasting glucose or impaired glucose tolerance) is 77 million.<sup>69</sup> In addition, based on epidemiological data and conversion rates among control groups in intervention studies, the conversion rate from prediabetes to diabetes mellitus is high.72-74 Diabetes awareness and control are poor in rural regions in comparison with urban regions (Figure 4).69,70 Diabetes mellitus continues to have a positive social gradient (with a higher burden among the rich and well educated), with the exception of certain settings such as industrial worksites.66,75,76 However, a recently concluded study on risk factors of CVD in urban and rural Delhi suggests that there is no difference in the prevalence of diabetes mellitus across various SES groups (D. Prabhakaran, unpublished data, 2014).

Serial epidemiological studies in India suggest a rapid rise in the mean levels of total cholesterol, low-density lipoprotein cholesterol, non–high-density lipoprotein cholesterol, and triglycerides.<sup>77</sup> In the ICMR-INDIAB study, a large proportion of people had at least 1 lipid abnormality; only 20% had all lipid parameters (total cholesterol, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein cholesterol) within the normal range.<sup>78</sup> The most commonly observed lipid abnormality was low high-density lipoprotein cholesterol; this was observed more often among those with lower levels of education.<sup>78</sup> In a study conducted in Jaipur, low education and SES were associated with low high-density lipoprotein cholesterol and high triglycerides.<sup>79</sup> However, hypercholesterolemia, defined as total cholesterol >5.17 mmol/L, is relatively less common among individuals with low SES than among higher-SES groups.<sup>66</sup> No social gradient was observed in the ICMR-INDIAB study for high low-density lipoprotein cholesterol.<sup>78</sup> Similar to diabetes mellitus and hypertension, control of dyslipidemia was lower in rural populations than in urban populations.<sup>79</sup>

Apart from the risk factors mentioned in the previous sections, long-term material deprivation, unhealthy living conditions, and high levels of stress also appear to contribute to excess CVD risk among socially disadvantaged groups in India.<sup>80,81</sup> Early-life influences, particularly in the first thousand days (the time from conception through the first 2 years), have been putatively implicated to play a significant role in the onset of CVD and its risk factors during adult life.82 Maternal malnutrition, placental insufficiency, and the resulting fetal programming have been hypothesized to be associated with low-muscle-high-fat body composition (thin-fat child), reduction of β-cell mass, and fewer glomeruli in the kidney.<sup>83</sup> In the New Delhi Birth Cohort study, rebound adiposity and weight gain during childhood between the ages of 2 and 12 have been shown to be related to a higher propensity to develop dysglycemia as young adults.<sup>84</sup> Data generated from the ongoing intergenerational cohort study involving children and parents in the South Indian state of Telengana will likely provide reliable scientific evidence on long-term effects of early-life undernutrition on the risk of CVD in adulthood.43 In addition to these biological mechanisms, social factors also appear to play a role.<sup>85</sup> Early-life influences result in impaired cognition, low school performance, and low productivity, all of which are associated with excess cardiovascular risk factors.85

#### **Determinants of CVD in Indians**

Although CVD risk factors are widely prevalent in India, there are significant variations between and within different regions. Diabetes mellitus appears to be more prevalent in the southern states of India, whereas hypertension appears to be higher in the northeastern states.<sup>86</sup> Although this heterogeneity can be attributed to diversity in culture (leading to differences in dietary practices, tobacco use, and physical activity patterns) and variations in economic development between and within different states in India, it is important to understand the social determinants. The studies conducted to understand the relationship between SES and CVD in India are well summarized in recent commentaries.87-91 For example, a recent large cohort study in Mumbai demonstrated that CVD is no longer a disease of the rich; it equally impacts the poor, with a higher CVD mortality among men of lower SES.13 Low SES was associated with a higher odds of having an acute myocardial infarction in case-control studies.92,93 In a cross-sectional study of cardiovascular risk factors in Jaipur, suboptimal social characteristics such as low educational, occupational, and SES status were associated with a clustering of  $\geq$ 3 cardiovascular risk factors and a higher Framingham risk score.94,95

Social determinants appear to play a particularly major role in determining outcomes after a CVD event. In the CREATE registry (a registry of treatment and outcomes of ACSs of 20468 patients from 89 centers in 50 cities), outcomes after ACS were worse in lower-SES individuals.<sup>3</sup> For example, the 30-day mortality rate attributable to ACS was 8.2% for the poor in comparison with 5.5% for the rich.<sup>3</sup> This difference was largely accounted for by variations in in-hospital treatment and discharge medications.

In India, underdiagnosis and underreporting of CVD are more frequent among the poor.96 Economically underprivileged patients with CVD are less likely to receive evidencebased treatments, because medical treatment often involves large out-of-pocket payments.97 Those who are in the lowincome group bear the burden of high out-of-pocket payments, with higher rates of catastrophic health spending and distress financing, in comparison with those who are in the high-income group.97 Consequently, CVD-affected households with lower SES are at an increased risk of distress financing or catastrophic health expenditure.98 Out-of-pocket payments are not only a feature of acute care, but are also evident in chronic care. For example, the low-income group in urban (rural) India spends 34% (27%) of its annual family income for diabetes care.99 The poor and disadvantaged groups are therefore pushed back further into the vicious cycle of poverty and CVD.

# Early Onset of CVD and High Fatality

The early occurrence of CVD in Indians and the high case fatality attributable to CVD is ominous and merits special attention. Danaraj et al,<sup>100</sup> in their seminal article in 1959, reported higher age-standardized mortality among Indians living in Singapore (even among individuals between 30 and 49 years of age) in comparison with other populations. Although the early age at mortality was observed in several studies of migrant Indians in the 1980s, it was the INTERHEART study (a large international case-control study across 52 countries) that confirmed the early age of onset of incident myocardial infarction among patients from South Asia.<sup>2</sup> In this study, the median age of myocardial infarction in South Asians was 52 years in comparison with 62 years in the European origin

cohort. The study reported that usual cardiovascular risk factors important in older subjects are equally important in the young South Asians; however, these risk factors occurred at a younger age in South Asians, leading to an early age of onset of myocardial infarction. In Gupta et al,<sup>101</sup> a study of age-specific trends in cardiovascular risk factors among the adolescent and young reveals that cardiovascular risk factors increase exponentially with age once Indians reach the 30- to 39-year age group. An additional cause of concern in Indians and South Asians is that they tend to have more severe manifestations of CVD and higher fatality rates.5 In the PURE study, despite having a lower conventional CVD risk factor burden, the incidence of major cardiovascular events and mortality among individuals of low-income countries (96% from South Asia, of whom 83% were from India) was higher than in middle- and high-income countries.<sup>5</sup> The case fatality rates for cardiovascular events in low-income countries, represented largely by India, was 17%; this is much higher than in higherincome countries, which had a case fatality rate of 6.5%.5

# **CVD** Prevention and Treatment Strategies

The emergence of the CVD epidemic in India poses a great challenge to its health systems. However, implementation of knowledge on CVD reduction strategies from Western countries provides an opportunity to combat the epidemic in India. The decline in cardiovascular mortality in these countries was driven by population-level changes in common risk factors and medical therapies, with more than half of the reduction in mortality attributed to improvements in population-level risk factors like tobacco use, cholesterol, and blood pressure.<sup>102–105</sup>

To the best of our knowledge, there are no data evaluating macroeconomic policy changes and nonpersonal interventions on CVD in India. However, modeling studies suggest that substantial benefits could be gained by imposing taxes on tobacco, palm oil, and sugar-sweetened beverages in India. It is estimated that a 20% tax on sugar-sweetened beverages would reduce overweight and obesity prevalence by 3% and the incidence of type 2 diabetes mellitus by 2%.<sup>106</sup> Similarly, a 20% tax on palm oil purchases is expected to avert ≈363 000 deaths (a 1.3% absolute reduction in CVD deaths) from myocardial infarctions (MIs) and strokes over a period of 10 years.<sup>107</sup> Nearly 400000 CVD events (MIs and stroke) and 81000 deaths (a 5% reduction) can be averted by moderate reduction in salt intake (reducing intake by 3 g/d, over a 30-year period) among middle-aged Indians.108 Finally, smoke-free legislation and tobacco taxation together may avert 25% of MIs and strokes in India.<sup>109</sup> In this regard, the policy decisions by the Government of India to raise the excise duty of tobacco products in 2014 up to 72% and to levy a new 5% tax on sugar-sweetened beverages are encouraging (Union budget 2014-2015: http://www.indiabudget.nic.in/). The excise duty for tobacco products has been increased from 11% to 72% for cigarettes, 12% to 16% on pan masala (flavored tobacco), 50% to 55% on unmanufactured tobacco, and 60% to 70% on chewing tobacco. However, *bidis*, which are commonly used by Indians, are not adequately taxed because their manufacture is defined as a small-scale industry. Following the landmark United Nations high-level meeting on NCDs and the endorsement of a global action plan<sup>110</sup> for the prevention

and control of NCDs at the World Health Assembly, India has developed a national monitoring framework to achieve all targets set out by the WHO (Ministry of Health and Family Welfare, Government of India: http://mohfw.nic.in/showfile. php?lid=2622). The key targets include a 30% relative reduction in both salt and tobacco consumption by 2025.

Effective policy-level changes need community acceptance through communication of behavioral changes and health promotion. A recent industrial worksite-based intervention program implemented in India with a combination of population-wide and high-risk approaches was effective in bringing down several cardiovascular risk factors.<sup>111,112</sup> In this demonstration project, conducted in 6 intervention sites and 1 control site, diastolic blood pressure, fasting plasma glucose, and total cholesterol each decreased by >5% in the intervention sites, whereas they increased by 5%, 13%, and 4%, respectively, at the control site. In contrast, a recently concluded community-based cluster randomized trial did not show any improvements in the primary outcome of awareness about 6 lifestyle factors affecting CVD after a shorter period (18 months) of health promotion intervention by trained community health workers.<sup>113</sup> This may be because of a shorter period of intervention and the lack of an environment enabling the participants to change behavior. Therefore, innovative and context-specific primary prevention strategies need to be developed and tested in multiple settings.

The Union Government of India has only recently conferred increasing attention on CVD, with the initiation of the National Program for the Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke. The public health system of India has been engaged and inundated with the communicable disease burden since its formative years; little attention was paid to CVD, stemming from the longstanding perception among policy makers that CVD primarily afflicted the rich urban class and not the poor. Support for the CVD burden by various state and central government agencies, if any, has been limited to the financing of expensive tertiary care interventions for poor patients, with hardly any investment in primary or primordial prevention. The National Program for the Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke was launched as a pilot project in 10 districts of 10 states of India (January 2008) and focuses on screening for risk factors, health promotion, and health education advocacy at various settings. Recently, it has been expanded to 120 districts in India. This initial investment will be scaled up substantially in the near future to meet the enormous public health burden posed by these diseases. However, a careful and detailed evaluation of the program is needed to make necessary modifications to ensure the continuation of the program during the subsequent phases.

The benefits of treating cardiovascular risk factors like high blood pressure and cholesterol are well known. Gaziano et al, in their cost-effectiveness model, demonstrate that incremental cost-effectiveness ratios (dollars/quality-adjusted life year) of a multidrug regimen for secondary prevention and high-risk primary prevention would be \$306 and \$746 in South Asians, respectively.<sup>114,115</sup> Given that 3 times the gross national income of India based on the World Bank estimates for the year 2004 was \$1893, the incremental cost-effectiveness ratio for the use of multidrug regimen will fall within the cost-effective range. These 2 strategies were estimated to increase yearly healthcare expenditure at the population level per head by 1.8% (\$0.47) and 5.4% (\$1.41), respectively, and lead to reduction in corresponding cardiovascular death rates by 13% and 26%. Despite overwhelming evidence, however, a large majority of eligible patients do not receive appropriate care for cardiovascular risk factors.116 In tertiary hospitals, the combination of 4 evidence-based medicines (aspirin, \beta-blocker, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins) was prescribed only to 54% of eligible patients with coronary heart disease, whereas the rates were despairingly low in secondary (28%) and primary care (7%) clinics.117 The PURE study, which involved 5650 self-reported IHD and 2292 stroke participants, observed noticeable underuse of proven therapies for IHD in low-income countries (83% of the low-income country participants in the study were from India). As many as 80% of the participants with CVD were not on any of the 4 evidence-based secondary prevention drugs (aspirin,  $\beta$ -blocker, angiotensin-converting enzyme inhibitors, and statins) in the low-income countries, in comparison with 11% of participants in high-income countries.<sup>118</sup>

Improving adherence to prescribed therapies also requires the use of newer strategies; one example is the use of a polypill (a combination pill of multiple drugs), as seen in the recent Use of a Multidrug Pill In Reducing Cardiovascular Events (UMPIRE) trial, which is especially useful for secondary prevention.<sup>119</sup> This was a multinational study conducted in India and Europe that demonstrated 33% better adherence with the polypill in comparison with the standard treatment.<sup>119</sup> Similarly, for primary prevention, the polypill was equally effective in reducing cardiovascular risk factors as the equivalent administration of individual drugs.120,121 Another polypill study (The International Polycap Study 3 [TIPS-3]) is currently ongoing; it evaluates the role of the Polycap (a polypill), low-dose aspirin, and vitamin D supplementation in the prevention of major adverse cardiovascular events (ClinicalTrials.gov Identifier NCT01646437).

There are significant areas that need improvement in the processes and therapy in the management of CVD in India. In the CREATE registry, patients arrived at hospitals very late (mean time of symptom to hospital presentation was 360 minutes), leading to poorer outcomes and higher case fatality.<sup>3</sup> Only 58.5% and 8% of patients with ST-segment-elevation MI presenting to hospitals received thrombolysis and percutaneous coronary interventions, respectively. At discharge, only 52% received statins. Importantly, poor patients with ACS more frequently missed out on evidence-based treatments like thrombolysis,  $\beta$ -blockers, statins, and revascularization. It should be noted that the CREATE registry included modern hospitals in primarily urban areas of India and thus may not be truly reflective of medical care in rural and distant urban centers, where the care provided may be even worse.<sup>3</sup> A recent large ACS registry from Kerala (a state with comparatively better health indicators) demonstrated several inadequacies.<sup>49</sup> In this registry of 25748 patients, >40% of patients with ST-segment elevation MI reached the healthcare facility after 6 hours of symptom onset. Furthermore, only 41% and 13% received thrombolytic treatment and percutaneous coronary interventions, respectively.

Surprisingly, 19% of patients with non–ST-segment–elevation MI received unindicated thrombolytic therapy. The registry also demonstrated that optimal in-hospital and discharge medical care were delivered in only 40% and 46% of admissions, respectively, and this was worse in rural areas than in urban areas. Importantly, patients receiving optimal in-hospital medical therapy reported a 21% lower chance of in-hospital major adverse cardiovascular event rates.<sup>122</sup>

The implementation of quality improvement programs in India may improve adherence to evidence-based in-hospital and discharge care in ACS.<sup>123</sup> In this regard, 2 large studies funded by National Heart, Lung, and Blood Institute are evaluating the role of quality improvement programs in ACS. The Secondary Prevention of Coronary Events After Discharge From Hospital (SPREAD) study, which recently completed recruitment, is a randomized, open-label trial comparing postdischarge interventions by using community health workers to improve adherence to medications and lifestyle advice for secondary prevention of ACS (ClinicalTrials.gov Identifier NCT01207700) with usual care. The Acute Coronary Syndrome-Quality Improvement (ACS-QUICK) program being conducted in Kerala is a large (15750 participants, 63 hospitals) stepped-wedge randomized, controlled trial assessing the implementation and effect of a locally developed quality improvement toolkit for patients with ACS in Kerala, India (ClinicalTrials.gov Identifier NCT02256657). INSPIRE, a large registry of acute stroke patients (similar to the CREATE registry for ACS) completed recruitment of 11000 patients from 61 sites across India (Clinical Trial Registry of India [CTRI]/2013/10/004108). This study, with 6 months followup of all registered patients, will provide important information on etiology, clinical practice patterns of acute care, clinical outcomes, and secondary prevention and rehabilitation practices of stroke care in India.

Cardiac rehabilitation is almost nonexistent in India. Lowcost methods and traditional approaches like yoga (a disciplined method of controlling body and mind) have the potential to address this issue. However, data on the efficacy of traditional methods as a means of secondary prevention are sparse. One such study is the Yoga-Care Trial (CTRI/2012/02/002408), a randomized, controlled trial evaluating the efficacy of a yoga-based cardiac rehabilitation program on the incidence of major cardiovascular events and mortality. This study is being performed in 16 different centers in India, with a plan to recruit >4000 patients after ST-segment-elevation MI. The results of this study will provide evidence on the effectiveness of a yoga-based cardiac rehabilitation program. Such contextspecific and resource-sensitive traditional approaches that are acceptable to the general community should be researched to see if they will enhance CVD prevention and management. Major intervention studies in the area of CVD in India are summarized in Table 3.

# Gaps in Knowledge, Future Directions, and Innovations

The gaps in available knowledge on the CVD burden, prevention, and control strategies from India and the research and policy needs are summarized in Table 4 and discussed below.

### Establishing a Robust Surveillance System

India needs better surveillance and reporting systems given the rapidly changing disease burden, because surveillance data have the potential to make major contributions to shaping health policies and designing interventions. Although the level of detail in developing a surveillance model is debatable, there is a need to evaluate and develop a model surveillance system. The National Heart, Lung, and Blood Institute recently supported a project aimed to develop such a model for South Asia.44 This model is designed to generate information on both the secular trends in CVD risk factors in the population (repeat cross-sectional surveys) and the trajectories of these risk factors (a cohort model) in a representative sample population. Another large CVD surveillance study involving 40 000 individuals is ongoing in a rural area, ie, the Solan district in the Indian state of Himachal Pradesh (D. Prabhakaran, unpublished data, 2014). In addition, 1 possible opportunity to obtain representative surveillance data at the national level would be to expand the scope of the routinely conducted NFHS to include blood tests to detect glucose and cholesterol levels along with blood pressure measurements. In addition, it would be useful to embed cohort studies within the framework of surveillance projects to understand disease epidemiology, investigate the contribution of risk factors, and develop algorithms for absolute risk of individuals in the population.

# **Improving Efficiency of Care**

Although cost-effective interventions are available for the prevention and control of CVD risk factors, there are major barriers to their widespread use in India, including low detection rates, inadequate awareness, poor use of evidence-based interventions, and low adherence rates. Innovative methods need to be developed and tested in Indian settings to overcome these challenges. Some approaches that could potentially improve the efficiency of care include incorporating information communication technology tools, and task-shifting and tasksharing strategies, as well (discussed below). Several such initiatives are currently being tested in India; one example is the evaluation of a complex intervention strategy using innovative mobile health (mHealth) software applications (mPOWER study: CTRI/2013/02/003412). This mHealth platform can collect a patient's health profile, provide decision support for clinical care, and act as a monitoring and feedback tool for use in primary care settings. A cluster randomized trial evaluating the use of a point-of-care electronic decision support tool for management of hypertension has been completed in Andhra Pradesh, India, in 16 primary healthcare centers.<sup>128</sup> This study concluded that electronic clinical decision support systems are both effective and cost-effective in the management of hypertension in resource-constrained primary care settings.<sup>129</sup> In addition, a multifaceted strategy using mobile technology to assist rural primary healthcare doctors and frontline health workers in CVD risk management has been developed and was implemented in 18 primary health centers and 54 villages in rural Andhra Pradesh involving ≈15000 adults aged ≥40 years at high CVD event risk.<sup>127</sup> The results of these studies have the potential to inform policy on scalable strategies to improve the efficiency of the health system in managing CVD.

Study Name	Study Design	Sample Size	Principal Findings	Limitations
SSIP <sup>111</sup> (completed)	Evaluation of complex public health intervention in worksites.	19973	Risk factors of CVD are amenable to interventions.	Demonstration project.
RAPCAPS <sup>113</sup> (completed)	Cluster randomized trial in 44 villages comparing a clinical approach (opportunistic screening for CVD risk factors by health workers initially and then by trained physicians) and population-based health promotion	1137 high-risk individuals and 3712 general population.	The trial identified no effect of the health promotion strategy on the primary knowledge outcome.	Not adequately powered to detect clinically significant differences.
UMPIRE <sup>119</sup> (completed)	Randomized controlled trial of fixed-dose combination pill (polypill) versus usual care.	2004 high-risk individuals (1000 from India)	Improved medication adherence and statistically significant but small improvements in systolic blood pressure and LDL cholesterol.	No hard outcomes.
TIPS1 <sup>120</sup> (completed)	Randomized controlled trial of Polycap (polypill of low doses of thiazide, atenolol, Ramipril, simvastatin, and aspirin)	2053 high-risk individuals.	Polycap formulations reduce multiple cardiovascular risk factors.	No hard outcomes.
TIPS2 <sup>121</sup> (Completed)	Randomized controlled trial of single-dose Polycap or 2 capsules of the Polycap plus K+ supplementation.	518 high-risk individuals.	The full-dose Polycap reduces blood pressure and LDL cholesterol to a greater extent than the low dose, with similar tolerability.	No hard outcomes.
TIPS3 (ongoing: NCT01646437)	Randomized controlled trial of Polycap, low-dose aspirin and vitamin D supplementation in prevention of CVD.	2000 high-risk individuals from India.	Expected to provide results on the efficacy of Polycap, aspirin, and vitamin D in reducing hard CVD outcomes.	Only 2000 individuals from India.
SIMCARD <sup>124</sup> (completed, awaiting results)	Cluster randomized trial (task shifting and decision support systems for lifestyle changes in high-risk patients and to improve uptake of evidence-based drugs)	2000	Expected to provide data on rate of increase in uptake of evidence- based medicines in high-risk patients.	No hard CVD outcomes.
CARRS Trial <sup>125</sup> (completed, awaiting results)	Randomized controlled trial (intervention includes electronic health records and involvement of care coordinators in management of diabetes mellitus and compared it with usual care).	1120	Expected to provide evidence on improvements in blood sugar, blood pressure, and lipid parameters in patients with diabetes mellitus.	No hard outcomes.
SPREAD (ongoing)	Randomized controlled trial comparing postdischarge interventions by community health workers with usual care in secondary prevention of ACS.	806 patients with ACS from India.	Expected to demonstrate the feasibility of conducting a secondary prevention trial on adherence to medications and lifestyle advice by using community health workers.	Small sample size
PREPARE <sup>126</sup> (completed recruitment)	Cluster randomized trial (household level).	2438 households	Expected to provide the efficacy of household-based intervention strategy (delivered by community health workers) in improving treatment adherence and risk-factor control.	No hard outcomes.
DISHA (ongoing: CTRI/2013/10/004049)	Cluster randomized trial (intervention includes use of frontline health workers for lifestyle interventions and compares it with usual care)	18 000 (phase 1) + 18 000 (phase 2)	Expected to provide evidence on task shifting for control of blood pressure at the population level.	Intermediate-level physiological outcomes (blood pressure).
mPower Heart (ongoing: CTRI/2013/02/003412)	Pre-post evaluation of mHealth strategy (screening, decision support system, monitoring, and feedback tool)		The study is expected to inform the acceptability of the mHealth tool and its potential effect on health outcomes.	No comparison group.
SMARTHealth (ongoing) <sup>127</sup>	Stepped wedge, cluster randomized controlled trial (mobile devise–based decision support system) in 18 primary health centers and 54 villages in rural Andhra Pradesh.	15 000	Expected to provide data on achieving blood pressure targets.	No hard outcomes.
ACS QUICK (ongoing: NCT02256657)	Quality improvement initiative. A stepped wedge cluster randomized design.	15750	Expected to identify cost-effective strategies for improving outcomes of ACS patients in hospital settings.	It will not improve case detection and symptoms to presentation time.

Table 3.	Major Cardiovascular Dis	ease Intervention Studies in India*
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(Continued)

#### Table 3. Continued

Study Name	Study Design	Sample Size	Principal Findings	Limitations
Yoga CaRe Trial (ongoing: CTRI/2012/02/002408)	Randomized controlled trial of yoga-based cardiac rehabilitation.	4000	Expected to demonstrate the efficacy of traditional yoga-based cardiac rehabilitation program in comparison with usual care in reducing major adverse cardiovascular events.	Only 1-y follow-up.

ACS indicates acute coronary syndrome; ACS QUICK, Acute Coronary Syndrome Quality Improvement Initiative; CTRI, Clinical Trial Registry of India; CVD, cardiovascular disease; DISHA, Diet and lifestyle interventions for hypertension risk reduction through Anganwadi Workers and Accredited Social Health Activists; LDL, low-density lipoprotein; PREPARE, Primary prevention strategies at the community level to promote treatment adherence to prevent cardiovascular disease; RAPCAPS, Rural Andhra Pradesh Cardiovascular Prevention study; SIMCARD Trial, Simplified cardiovascular management trial; SPREAD, Secondary Prevention of Coronary Events After Discharge from hospital; SSIP, Sentinel surveillance in Indian industrial population; TIPS, The Indian Polycap study; and TIPs-3, The International Polycap study.

#### Health System Preparedness and Quality of Care

There is a huge shortage in the availability of trained human resources for health care and health research in India.<sup>130</sup> The shortage of a trained workforce is observed at all levels of health care, including specialists, primary care physicians, and frontline health workers. There is an uneven distribution in numbers and in quality of the healthcare workforce, not only between rural and urban India, but also between and within different regions and states. Improving the human resource capacity for the prevention and control of CVD should be a national priority, and efforts should be made to

ensure equitable distribution of available resources in both rural and urban settings.

Considering the escalating cost and devastating economic consequences of CVD care, the development of standards of care and the adoption of cost-effective case management for CVD, especially in secondary and tertiary settings, should be considered priority. Quality improvement initiatives need to be encouraged, and priority should be given to continuous quality monitoring and improvement. Regular performance audits need to be performed to identify key issues related to quality of care. Ongoing feedback from these performance

Gaps in Knowledge	Research Needs	Policy Requirements/Innovations
Cohorts and surveillance		
No representative data on prevalence and incidence of cardiovascular disease risk factors and events.	To study prevalence, incidence, and progression of risk factors, and incidence of cardiovascular events and mortality.	Establishment of large cohorts to understand the epidemiology of diseases.
No representative national level data on secular trends in CVD risk factors and events.	To capture population-based change in cardiometabolic risk factors and events.	Establishment of robust surveillance system for cardiovascular risk factors, events, and mortality.
Health system preparedness		
Lack of integration of primordial prevention and management of cardiovascular diseases in primary and secondary care settings.	Health system preparedness to implement primordial and primary prevention strategies and management of CVD in primary and secondary care settings.	Invest in human resource capacity to improve trained workforce.
	Efficiency and effectiveness of task shifting for integrated CVD care.	Encourage task shifting and task sharing for efficient care delivery.
Improving quality and efficiency of care		
Quality of cardiovascular care (detection, treatment, adherence, and control) in India.	Test quality improvement initiatives in management of cardiovascular disease in primary and secondary care settings.	Performance auditing and evaluation of quality improvement initiatives.
Improving access		
Cost-effective interventions in Indian settings.	Test innovative models to address the rise in CVD for efficacy and effectiveness.	Implement scalable technology-based innovations.
		Support research and development of low-cost polypill. Establish central procurement of drugs and electronic drug prescriptions. Implement universal health coverage for management of cardiovascular risk factors and events (essential medicines and therapies).
Effective policy interventions		
Potential policy interventions for control of CVD in Indian settings.	Test the effectiveness of policy interventions on diet, tobacco, and physical activity. To identify the major barriers and challenges in implementing evidence-based policy measures in India.	Implement established policy interventions such as taxation on tobacco, trans fat-rich oils, and sugar-sweetened beverages based on current available evidence.

Table 4. Gaps in Knowledge and Future Directions

CVD indicates cardiovascular disease.

audits and timely corrective action may improve the delivery of overall quality of care.

The capacity for CVD research also needs to be strengthened to generate appropriate contextualized evidence. Several programs are underway in India with support from national and international funding bodies, including the National Heart, Lung, and Blood Institute, Wellcome Trust, Department of Science and Technology, and the Department of Biotechnology. Such efforts will help achieve the goal of increasing the number of trained researchers in India.

#### **Improving Access**

Despite the acknowledgment of CVD as a major public health problem, access to cardiovascular care in India remains relatively poor. This is reflected in the poor detection, treatment, and adherence to evidence-based treatment options among Indians. The primary health system in India has largely been geared toward the management of communicable diseases, maternal and child health care, and immunization. The integration of CVD preventive care in the primary healthcare system in India therefore requires special attention, with a need for innovative models in health promotion.

Several such initiatives are being tested. One example is a task force study titled "Effectiveness of diet and lifestyle intervention through information education communication tools with Angan Wadi workers (frontline health workers) as the center of knowledge dissemination for hypertension risk reduction (DISHA)," which is funded by the Indian Council of Medical Research (CTRI/2013/10/004049). The DISHA project is a cluster randomized, controlled trial testing the effectiveness of health promotion activities delivered by trained frontline health workers on population-level changes in blood pressure.<sup>131</sup> This study is the largest cluster randomized, controlled trial in India, with 120 clusters and nearly 36000 study participants, and it has the power to detect epidemiologically significant changes in blood pressure. The results of another large cluster randomized trial, evaluating the intervention strategy of task shifting to community health workers for the management and follow-up of patients with high CVD risk, along with aid from a decision support system, are also expected; this study took place in in Haryana, India and Tibet, China.<sup>124</sup> Similarly, a translational trial (funded by National Heart, Lung, and Blood Institute) that evaluated an intervention strategy of task shifting to care coordinators for the management of diabetes mellitus (aided by electronic health records and a decision support system at tertiary and secondary care centers) has completed the study follow-up over a median period of 30 months.<sup>125</sup> Last, another multicenter householdlevel cluster randomized trial has completed recruitment; this study involves community health workers in primary prevention strategies at the community level to promote adherence of treatments to prevent CVD (Primary Prevention Parameters Evaluation [PREPARE]).<sup>126</sup>

To provide greater efficiency and equity in the delivery of health services, the Indian government has announced its commitment to advance universal health coverage through its health plans. However, the pathways for achieving universal health coverage are not clearly identified, and debates regarding the role of the private sector and insurance continue. The state of Andhra Pradesh has initiated a joint venture with private insurers (public-private partnerships) to provide health insurance to the general population (Rajiv Aarogyasri Insurance Scheme). However, the impact of such schemes on health outcomes has not been studied.<sup>132</sup> In addition, the focus of the current insurance schemes is on downstream management, and therefore they have limited impact on the prevention of CVD.

#### **Effective Policy Interventions**

India was one of the first countries to ratify the framework convention on tobacco control and MPOWER strategies (measures introduced by the WHO that are intended to assist in the country-level implementation of effective interventions to reduce the demand for tobacco) by enacting the Cigarette and Other Tobacco Product Act; this includes the prohibition of smoking in public places, the prohibition of advertisement, promotion, and sponsorship of all tobacco products, the prohibition of sale of tobacco to minors, requirement of health warnings on tobacco products, and the regulation of contents of tobacco products. However, in the Indian context, implementation of these measures is a challenge. For example, only about half of the states (52%) have mechanisms for monitoring provisions under the act.<sup>133</sup>

Implementing a salt reduction strategy in India for controlling blood pressure is also a challenge, for several reasons. First, salt is used as a vehicle for iodine supplementation to reduce the prevalence of iodine deficiency disorders in India. Unless measures are taken to increase iodine content, in consultation with experts in the field of endocrinology, we may give inconsistent health communications and lead to bewilderment among the target population. Also, salt is often added during cooking, and any policy interventions to reduce salt use would therefore require active community participation and behavior change.

Policies and programs that impact cardiovascular health cover a wide range of areas beyond the healthcare domain, including development, economics, agriculture, urban infrastructure, the environment, and so forth. Therefore, research on the social determinants of cardiovascular health needs to be promoted to positively influence policy decisions, made by nonhealth departments within the governance structure of the central and state governments in India, that have important health implications.

#### Conclusion

CVD is a major public health problem in India, often impacting the most productive years of an individual's life. The epidemiological transition plays out differently in different regions of India because of varied economic development. Disparate relationships between SES and CVD risk factors are evident in regions that are at different stages of epidemiological transition. However, tobacco use and hypertension in urban settings are consistently associated with lower levels of education and income. As the country progresses along the direction of epidemiological transition, other risk factors of CVD may in the future show similar social gradients. Taking control of the CVD epidemic in India needs all the stakeholders, including the policy makers, to acknowledge and address the social determinants that are strongly linked to CVD risk factors and to the related morbidity and mortality. The rising CVD burden and the damaging consequences it has on individuals, families, and populations require urgent attention. Innovative strategies are needed to halt the progression of the CVD epidemic in resource-poor settings in India. To address the socioeconomic differentials in the burden of disease and healthcare needs of Indians, more resources need to be directed toward applying the existing knowledge base to tackle the CVD epidemic in policy, programs, capacity building, and research arenas.

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# Disclosures

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