

Socioeconomic Status and Cardiovascular Disease: an Update

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Abstract

Purpose of Review The aim of this paper is to summarize the recent and relevant evidence linking socioeconomic status (SES) to cardiovascular disease (CVD) and cardiovascular risk factors (CVRFs).

Recent Findings In high-income countries (HICs), the evidence continues to expand, with meta-analyses of large longitudinal cohort studies consistently confirming the inverse association between SES and several CVD and CVRFs. The evidence remains limited in low-income and middle-income countries (LMICs), where most of the evidence originates from cross-sectional studies of varying quality and external validity; the available evidence indicates that the association between SES and CVD and CVRFs depends on the socioeconomic development context and the stage in the demographic, epidemiological, and nutrition transition of the population.

Summary The recent evidence confirms that SES is strongly inversely associated with CVD and CVRFs in HICs. However, there remains a need for more research to better understand the way socioeconomic circumstances become embodied in early life and throughout the life course to affect cardiovascular risk in adult and later life. In LMICs, the evidence remains scarce; thus, there is an urgent need for large longitudinal studies to disaggregate CVD and CVRFs by

socioeconomic indicators, particularly as these countries already suffer the greatest burden of CVD.

Keywords Cardiovascular disease · Cardiovascular risk factors · Socioeconomic status · High-income countries · Low- and middle-income countries

Introduction

In 2013, over 17 million deaths worldwide were due to cardiovascular disease (CVD) [1], 80 % of which occurred in low- and middle-income countries (LMICs) [1]. In high-income countries (HICs), socioeconomic status (SES) is a major determinant of CVD risk; extensive literature over several decades has confirmed that people of lower SES tend to have higher prevalence of cardiovascular risk factors (CVRFs), and to suffer more and die sooner from CVD than do people of higher SES [2–4, 5•, 6]. However, the direction of the association between SES and CVD and CVRFs has changed over time; in the earlier 20th century, the CVD burden was greater among people of higher SES, partly because of higher prevalence of CVRFs such as smoking, unhealthy diets, and sedentary lifestyles among the privileged groups. Along with the progression of the demographic, epidemiological, and nutrition transitions, and as CVD prevention and treatment improved dramatically, the CVD burden shifted to disproportionately impact people of lower SES [7]. In LMICs, a progressive shift of the burden of CVD and CVRFs from the higher to the lower SES groups is thought to be ongoing [8, 9], at different paces depending on the level of socioeconomic development and the stage in the demographic, epidemiological, and nutrition transitions. In most middle-income countries (MICs), CVD and CVRFs seem to be now more prevalent among the lower SES groups [9–12]. However, in most

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low-income countries (LICs), CVD probably continues to be more prevalent among the most advantaged SES groups, although very few high-quality and representative studies exist in these settings [13••, 14, 15]. Importantly, the association between SES and CVD and CVRFs may differ even within countries, as India illustrates [16, 17]; in rural areas, CVD and CVRFs are more prevalent among higher SES groups [18, 19], whereas in urban areas, CVD and CVRFs are more prevalent among lower SES groups [20, 21]. Recently, Anjana et al. showed that diabetes prevalence was higher among people of higher SES in the rural, poorer and less developed Indian states, while in the urban, richer, and more developed states, diabetes prevalence was higher among people of lower SES [22•]. It is expected that as LMICs continue to become more urbanized, richer, and socioeconomically developed, the SES-CVD association will increasingly mirror that already established in HIC.

In epidemiologic research of CVD, SES is most often measured in adulthood based on education, income, and occupation; in childhood or early life, it is based on a parent's education or occupation, or household income and conditions; in LMICs, wealth is often used [23]. Measures of education, income, and occupation can also be aggregated to define neighborhood or area-level SES [24]. The impact of SES on CVD risk begins in early life and accumulates across the life course [25]. There are a number of mechanisms by which SES is considered to influence CVD risk: behavioral mechanisms including smoking, physical inactivity, and unhealthy diets that contribute to the development of CVRFs such as overweight/obesity, hypertension, and diabetes; psychosocial mechanisms such as social relationship characteristics, cognitive and emotional processes, and depression and depressive symptoms; biological mechanisms such as in-utero adaptations and allostatic load; and environmental mechanisms such as exposure to pollutants and carcinogens [5••, 26].

In this review, we summarize the recent quantitative evidence of the association between SES and CVD separately for each different SES indicator and for each World Bank country income group.

Review of the Evidence

Education and CVD

Education remains the predominant SES indicator in epidemiologic studies. Systematic reviews and meta-analyses have consistently identified education to be inversely associated with CVD and CVRFs in HICs, confirming that lower educational attainment is associated with higher prevalence of smoking [3, 27–30], hypertension [17, 31, 32], obesity [3, 33–35], sedentary lifestyle [36–38], diabetes [39], depression

[40, 41], and unhealthy diets [42, 43], and with higher CVD incidence and mortality [3, 6, 13••, 25, 44, 45••, 46–48].

In a 2017 meta-analysis of 72 cohort studies from mostly HIC in Europe, North America, and East Asia, Khaing et al. reported pooled risk ratios for low versus high education of 1.36 (95% CI, 1.11 to 1.66) for coronary artery disease; 1.50 (1.17 to 1.92) for cardiovascular events; 1.23 (1.06 to 1.43) for stroke; and 1.39 (1.26 to 1.54) for cardiovascular deaths [13••]. The corresponding risk ratios for medium versus high education were 1.21 (1.06 to 1.40), 1.27 (1.09 to 1.48), 1.17 (1.01 to 1.35), and 1.21 (1.12 to 1.30), respectively [13••]. Such comparison between groups with low and medium education versus high education confirmed the evidence of an educational gradient in CVD risk, including for stroke, which previous systematic reviews failed to include or detect [44, 45••, 47].

In a 2016 meta-analysis of 116 cohort studies from 17 countries with over 22 million individuals, Backholer et al. examined whether the association between SES and CVD varied by sex. The relative risk for CHD for low versus high education was 1.66 (1.46 to 1.88) for women and 1.30 (1.15 to 1.48) for men; for stroke, it was 1.34 (1.07 to 1.69) among women and 1.53 (1.27 to 1.86) among men; for all CVD, it was 1.66 (1.43 to 1.92) among women and 1.42 (1.25 to 1.63) among men [45••]. They also showed that the excess risk of CVD and CHD—but not of stroke—associated with lower education was greater among women; the women-to-men ratio of relative risk was 1.18 (1.03 to 1.36) for all CVD, and 1.34 (1.09 to 1.63) for CHD [45••]. Such disaggregation of CVD outcomes by sex and assessment of interaction between sex and CVD risk remain rare in the literature.

Education has also been consistently related to CVD risk in HICs outside Europe and North America and in MICs [17, 49–53]. A 2014 meta-analysis of 3 cohort studies from Asia reported risk ratios for CVD mortality for lower versus higher education of 1.28 (1.06 to 1.56) among men and 1.37 (1.06 to 1.79) among women in India, 3.13 (1.79 to 5.26) in Thailand, and 4.50 (3.40 to 5.80) in Vietnam [54]. Similarly, in a 2015 meta-analysis of 24 studies with over 216,000 individuals from China, Japan, Taiwan, Thailand, and Singapore, Woodward et al. [55] found higher risk of CVD incidence and mortality for low versus high education with a HR of 2.47 (1.47 to 4.17), and 2.09 (1.34 to 3.26), respectively. In a separate meta-analysis focusing on 10 Chinese cohorts with over 197,000 individuals, the HR for primary versus tertiary education was 1.52 (1.23 to 1.89) [55].

More evidence exists linking education to CVRFs in MICs. A 2016 study of 15,350 individuals from the wealthy Shandong province in China found that lower education was associated with worse CVRFs including smoking, BMI, unhealthy diets, physical activity, blood pressure, and fasting glucose serum, particularly among women [56]. Furthermore, this inverse association appears to already

extend beyond urban and highly developed regions of China; in a 2014 meta-analysis of 11 studies from rural areas in China, Busingye et al. [19] found that lower education was associated with higher hypertension prevalence. The same review yielded opposite findings when meta-analyzing 10 studies from rural India: lower education was associated with lower hypertension prevalence. Similarly, in a 2017 comparative study of 17,708 individuals in China and 1460 individuals in India, education was inversely associated with waist circumference, BMI, and hypertension in China, but positively associated in India [57].

Although the evidence from LICs remains small, an inverse educational gradient appears to already exist for several CVRFs [12, 17, 29, 50, 58••, 59–61]. For instance, in a 2017 systematic review of 75 cross-sectional studies from 39 low and middle-low income countries, Allen et al. reported that lower education was associated with higher smoking prevalence and excessive alcohol consumption [58••]. Another recent meta-analysis including data from 22 LICs found a strong inverse educational gradient in smoking, except in Niger [60]. A 2017 study in Nepal reported an educational gradient in 10-year cardiovascular risk, finding that individuals with no formal education had the greatest risk [62]. In Tanzania, a large nationwide cross-sectional study found a strong inverse association between education and hypertension [63]. However, a large cohort of 63,708 individuals in a rural and less developed area of Bangladesh, no association was found between education and CVD risk [64]. These recent findings highlight the socioeconomic development context dependence of the SES-CVD and CVRFs association in LICs.

Recent large nationwide cohort studies from HICs have added specificity to the education-CVD association. One such study followed all adults aged 35–84 years in Denmark between 1985 and 2009 and found that the educational inequalities in CVD varied by diagnosis; regardless of age and sex, educational differences were large for incident ischemic heart disease, acute myocardial infarction, heart failure, and stroke, while no differences were found for atrial fibrillation and vascular heart disease [65]. Similar findings have been reported in nationwide cohort studies in Norway [66] and the Netherlands [67].

Several studies have also evaluated secular trends in educational inequalities in CVD. In a 2015 study with over two million individuals in Italy, Stringhini et al. showed that absolute inequalities for CVD mortality decreased substantially among men and women between 1971 and 2011 [68]. The aforementioned nationwide study from Norway showed that relative inequalities in acute myocardial infarction mortality remained constant between 2001 and 2009 (RII = 2.10, 2.06 to 2.15), although incidence decreased across all educational levels [66]. Similar findings had been previously reported from cohort studies in Sweden [69], Finland [70], and

Norway [71]. Another study from six European countries (Finland, Norway, England and Wales, France, Italy, and Hungary) showed that in most countries, except Hungary and Norway, absolute educational inequalities in CVD decreased between 1970 and 2010; however, relative inequalities increased in all countries [72]. In the USA, between 1969 and 2011, educational inequalities in all CVD, heart disease and stroke mortality increased over time, due to faster declines in CVD mortality in the higher educational groups [73]. Another study among white women found that educational inequalities, relative and absolute, increased between 1986 and 2006 for heart disease and cerebrovascular disease [74]. Furthermore, several studies have found widening educational inequalities in CVRFs over time, particularly smoking, obesity and diabetes in England [75], Northern Ireland and Ireland [76], Norway [77], and South Korea [78]. Trends in the educational patterning of CVD and CVRFs have yet to be examined in LMICs.

Occupation and CVD

The association between occupation and CVD has been extensively studied in HICs, particularly in Western Europe [2, 4, 26] and the USA [3, 5••]. Longitudinal cohort studies and systematic reviews have found that, in general, the lower the occupational position, the higher the prevalence of CVRFs such as smoking [3, 26, 30], hypertension [31, 32], obesity [3, 33–35], sedentary lifestyle [36, 37], diabetes [39], depression [40, 41], and unhealthy diets [42, 43], and the higher the CVD incidence and mortality [6, 25, 44, 45••, 46, 48].

In a comparative study from the USA and 11 high-income European countries, including over 163,000 individuals, Mackenbach et al. showed that CVD mortality was higher among people with lower occupational position [79]; the association was stronger in Northern and Western European countries, and attenuated or non-existent in Southern European countries [79]. Manrique-Garcia et al., in a 2011 meta-analysis of 30 cohort and case-control studies from HICs, including almost four million participants, reported a pooled RR of 1.41 (1.25 to 1.70) for acute myocardial infarction for the lowest versus highest occupational position [48]. In their 2016 meta-analysis of 15 cohort studies, Backholer et al. reported a relative risk for manual versus non-manual occupational position among women and men, respectively, of 1.59 (1.28 to 1.97) and 1.50 (1.25 to 1.80) for CHD; 1.81 (0.91 to 3.62) and 1.50 (0.96 to 2.36) for stroke; 1.80 (1.51 to 2.40) and 1.74 (1.38 to 2.20) for all CVD [45••].

The evidence remains scarce in LMICs, partly because a large proportion of their populations work in the informal sector [23]. A 2014 cohort study with 3246 individuals from the Seychelles found that those with a low versus high occupational position had a HR of 1.95 (1.04, 3.65) for CVD mortality [80]. A 2015 study from Bosnia and Herzegovina

including 3601 individuals found that being economically active versus unemployed or non-economically active was associated with better cardiovascular health [12]. A 2016 study from China following 12,246 patients with ischemic stroke found that the manual laborers, with and without education, were more likely to die after one-year follow-up compared with non-manual laborers (OR = 1.40 (1.02 to 1.90) and 1.49 (1.13 to 1.97), respectively) [81]. A 2015 study including 16,288 individuals from India and Pakistan found that higher occupational position (white-collar versus low skilled) was associated with higher overweight and obesity prevalence, hypercholesterolemia, and hypertriglyceridemia; however, an inverse association was seen with smoking [29].

In a 2014 meta-analysis of rural populations in LMICs, Busingye et al. found that farmers and manual-laborers, compared with other occupations, were at lower risk of hypertension [19]. Importantly, this review found too few studies in Latin America to properly assess the evidence in this continent. In their 2015 meta-analysis of 12 studies, Leng et al. reported a pooled OR for hypertension of 1.31 (1.04 to 1.64) for lowest versus highest occupational position [31]; the corresponding OR from 5 studies in HICs was 1.63 (1.17 to 2.09) but it was 1.08 (0.81 to 1.44) from 6 studies in LMICs.

In a 2016 study, Mackenbach et al. assessed changes in mortality inequalities in 12 European countries between 1990 and 2010; they found absolute occupational inequalities in mortality narrowed by 35% in most countries, driven mostly by decreasing ischemic heart disease and smoking-related causes [82]. A 2014 trends analysis from a cohort study in Sweden found that occupational inequalities in MI and ischemic stroke (manual versus non-manual) persisted between 1987 and 2010 among both men and women [83]. A 2011 study of 7735 British men found that between 1978 and 2000, those in manual positions were less likely to show improvement in CVRFs compared with those in non-manual positions [84]. No evidence on trends in occupational inequalities is available from LMICs.

Income and CVD

Income is less commonly used as an SES indicator in epidemiologic studies, partly because it is sensitive information [23]. However, the association between income and CVD and CVRFs parallels that seen with education [3, 5•, 6, 13•, 26, 47]. In HICs, the lower the income, the higher the prevalence of CVRFs such as smoking [85, 86], hypertension [31, 32], obesity [33, 35], sedentary lifestyle [37, 38], diabetes [39], depression [40], and unhealthy diets [42, 43], and the higher the CVD incidence and mortality [3, 5•, 26].

In their recent meta-analysis including 4 cohorts from Asia, 28 from Europe, and 4 from the USA, Khaing et al. reported pooled risk ratios for low versus high-income groups of 1.49 (1.16 to 1.91) for coronary artery disease, 1.17 (0.96 to 1.44)

for cardiovascular events, 1.30 (0.99 to 1.72) for stroke, and 1.76 (1.45 to 2.14) for cardiovascular deaths [13•]. The corresponding risk ratios for medium versus high income were 1.27 (1.10 to 1.47), 1.05 (0.98 to 1.13), 1.24 (1.00 to 1.53), and 1.34 (1.17 to 1.54), respectively [13•]. In their meta-analysis of 8 cohort studies, Backholer et al. reported a pooled relative risk of lower versus higher-income groups for CHD among men and women, respectively, of 2.01 (1.74 to 2.74) and 2.48 (1.53 to 4.0); for stroke, RR = 1.73 (1.33 to 2.24) and 1.64 (1.36 to 1.96); for all CVD, RR = 1.36 (1.34 to 1.39) and 1.46 (1.43 to 1.50), and showed no evidence of a differential effect of income by sex [45•].

In a recent study of almost 45,000 individuals in Sweden followed over two decades, Mosquera et al. found that income inequalities in CVD increased gradually from mid-life to older age, while educational and occupational inequalities decreased [87]. No study has assessed secular trends in income inequalities in CVD, but some studies have done so for CVRFs. In a nationwide study in South Korea, trends in income inequalities in CVRFs between 2001 and 2014 varied by sex. Income inequalities increased between 2001 and 2014 among women for smoking, obesity, diabetes, hypertension, but not hypercholesterolemia; inequalities remained stable among men but decreased for hypertension [78]. In the USA, between 1965 and 2008, income inequalities decreased for serum cholesterol, remained stable for high blood pressure, and increased for BMI and waist circumference [88].

The evidence from LMICs remains scarce [15]. A small cohort study from India found that the relative risk for CVD events was 1.15 (1.14 to 1.16) for lower versus higher-income groups [89]. While finding strong association between education and CVD deaths, a study of 1056 deaths in Vietnam found no association between income and CVD deaths (RR = 1.25, 0.83 to 1.67) [90]. More evidence from LMIC exists regarding the association between income and CVRFs. Two recent meta-analyses, one that included 29 studies in Latin America [91], and another that included 93 studies across the world [86], have confirmed the inverse association between income and smoking in all regions of the world except in the Middle East and North Africa. A 2014 systematic review found a positive association between hypertension and income in South Asia, but no association was found in East Asia or Africa [19]. A 2015 systematic review of 15 studies focusing on Iran found that diabetes prevalence was inversely associated with income [92]. In a representative sample of Peruvian adults, income was positively associated with obesity prevalence, but no association was found with diabetes [50].

Wealth and CVD

There is also a dearth of evidence regarding the association between wealth and CVD, and the findings have been inconsistent both in HICs and LMICs. However, one recent cohort

study in the USA found that wealth remained significantly associated with CVD events among women even after adjustment for other SES measures, with a HR of 1.73 (1.36 to 2.66) for low versus high wealth [93]. Another cohort study of almost 20,000 individuals in the USA found that both wealth and income were independently associated with higher stroke risk, but only within the 50–64 age groups [94]. Another cohort study in England found that wealth was inversely associated with CVD mortality, with the HR for the intermediate and lowest versus highest wealth tertile being 2.54 (1.27 to 5.09) and 3.73 (1.86 to 7.45), respectively [95]. In a 2012 study including 41 LMICs, Hosseinpoor et al. found that wealth was inversely associated with angina, depression, and comorbidities, but positively associated with diabetes [49]. A recent study in South Africa with 1100 urban-living individuals found that wealth was positively associated with diabetes, hypercholesterolemia, obesity and fat intake, but inversely associated with smoking, alcohol abuse, and psychosocial stress [96]. In their analysis of large cross-sectional population-based surveys from China, Ghana, India, Mexico, Russia, and South Africa, including 42,236 individuals, Arokiasamy et al. found that the lower the household wealth, the higher the prevalence of multimorbidity (including angina, diabetes, hypertension, and stroke) [97]. Finally, the aforementioned study from India and Pakistan found that the lowest wealth group was significantly more likely to smoke and eat less fruits and vegetables; however, it also found that the higher wealth groups were more likely to be overweight and obese, and to have a higher waist-to-height ratio [29].

Early-Life SES and CVD

Socioeconomic inequalities in CVD and CVRFs originate early in life [5•, 26], through at least three potential mechanisms: (1) latent effect of early-life SES on adult cardiovascular health; (2) cumulative effect of exposures to adverse socioeconomic circumstances throughout the life course, impacting cardiovascular health in a dose-response manner; and (3) pathways effects of early-life socioeconomic circumstances on individual trajectories to SES in adulthood, which in turn affect cardiovascular health [98]. A 2006 systematic review and its 2008 update found a strong inverse association between childhood SES and CVD and CVRFs [44, 99]. A 2015 systematic review focusing exclusively on seven studies of ethnic minorities found support for the inverse childhood SES-CVD association [100]. Additionally, a 2017 systematic review of 43 studies found that the higher the childhood adversity, as measured partly by household income, poverty, and parental education, the greater the CVD risk [101]. Finally, another 2017 meta-analysis of 9 studies found that lower childhood SES—measured mostly by paternal occupation—was associated with greater risk of stroke in adulthood; the HR was 1.31

(1.03 to 1.68) among three studies, and the OR was 1.28 (1.12 to 1.46) among 6 studies [46].

However, studies assessing the association between early-life SES and CVD independently of adult SES remain few. A 2013 study in the Netherlands with over 11,000 individuals found that lower childhood SES (father's occupational position) was associated with higher adult CVD death [102], but the association was explained by adult socioeconomic position and health behaviors. Similarly, a 2014 cohort study from Finland with almost 100,000 individuals found that more privileged childhood SES (higher parental occupation and education, and better housing conditions) were associated with lower CVD mortality in adulthood, even after adjusting for adult education and occupation [103]. However, a 2017 study from Finland including 94,501 individuals found that childhood SES—measured via parental education, occupation, and household crowding—was not associated with MI incidence and survival once adult education and income were taken into account [104]. Finally, a 2017 study from the USA including 30,623 individuals found that those with low childhood SES and adult SES were at greater risk of CHD compared with those with high childhood SES and adult SES (OR = 2.34, 2.18 to 2.64); similarly, those with low childhood SES and high adult SES were also at greater risk (OR = 1.94, 1.77 to 2.14) [105].

Neighborhood SES and CVD

The evidence is growing regarding an association between place of residence and CVD, mostly from the USA and a few other HICs. In 2001, Diez Roux et al. reported that living in a disadvantaged neighborhood in the USA was associated with increased risk of CHD, even after adjusting for individual education, occupation, and income (HR = 3.1, 2.1 to 4.8) [106]. Similarly, a 2013 study from the USA found that living in a disadvantaged neighborhood was associated with higher mortality at 1 year following an incident stroke (HR = 1.77, 1.17 to 2.68) [107]. Two other studies, one conducted among white US citizens [108] and one in Japan found that neighborhood SES/deprivation was associated with higher risk of incident stroke risk (HR = 1.32, 1.01 to 1.73, and HR = 1.19, 1.02 to 1.41), [109], after adjusting for individual SES, the latter also finding a clear gradient in stroke risk [109]. A similar 2016 US nationwide study found no association between neighborhood SES and stroke risk after adjusting for individual SES and risk factors [110]. Another study, from the UK, found that the risk of CVD mortality also showed a graded relationship with neighborhood deprivation; the multivariable-adjusted OR for CVD mortality was 1.44 (1.09 to 1.89) for the most deprived versus least deprived neighborhood [111]. One study of 59,000 African American women followed from 1995 to 2011 found that neighborhood SES was associated with CVD mortality among less-educated

women, with the multivariable-adjusted HR = 1.40 (1.10 to 1.78) [112]. In a recent cohort study of over one million individuals in Sweden, the HR for low versus middle neighborhood SES was 1.29 (1.17 to 1.41) among men, and 1.27 (1.08 to 1.49) among women, for MI risk before the age of 50 years. For CHD risk, the HR were 1.27 (1.18 to 1.37) and 1.34 (1.19 to 1.51), respectively [113]. The same analysis focusing on stroke risk found similar results, with an HR for both men and women of 1.12 (1.02 to 1.23) [114]. In a large cohort study of 1.9 million men and women in England, the HR for all CVDs except abdominal aortic aneurysm increased linearly with higher socioeconomic deprivation, while in men no associations were found for several CVDs [115]. Finally, a 2016 systematic review of 12 studies from North America, Europe, and Australia and New Zealand found a reduction of the risk of CVD mortality in areas with higher residential greenness—another measure of neighborhood SES [116].

The evidence in LMICs remains scarce. In Brazil, between 1996 and 98 and 2008–10, although CVD mortality decreased across all levels of neighborhood SES, relative inequalities increased between the least and most deprived neighborhoods of Sao Paulo [117]. Another study showed that stroke mortality decreased across all levels of neighborhood SES, based on income, but greater declines were observed in the more privileged neighborhoods of Sao Paulo. Consequently, relative inequalities increased [118].

In England, between 1982 and 2006, absolute inequalities in CVD mortality decreased between the lowest and highest deprivation quintiles, but only among individuals aged 30–64, while it increased in older individuals; relative inequalities increased across all age-sex groups [119].

Mechanism Linking SES and CVD

The evidence points to several main mechanisms by which SES likely influences CVD risk, and these have been extensively discussed elsewhere [5•, 25, 26]; briefly, (1) behavioral mechanisms include CVRFs that are more prevalent among lower SES groups in HICs, including smoking, physical inactivity, and unhealthy diets which contribute to the development of CVRFs; (2) psychosocial mechanisms such as social network and support, culture and language, ethnic discrimination and racism, effort/reward balance, and work-family conflict; (3) psychological mechanisms such as depression and depressive symptoms; (4) biological mechanisms such as in utero adaptations and allostatic load; and (5) environmental mechanisms such as exposure to pollutants and carcinogens [5•, 25, 26]. By far, most of the evidence in HICs has allowed testing primarily the behavioral and psychosocial mechanisms, although the expanding evidence is allowing to test the other mechanisms as well. In LMICs, where data remain scarce, the available evidence only allows to test for behavioral mechanisms. The above mechanisms driving

socioeconomic inequalities in CVD in turn interact with and are influenced by access to medical care, that is in turn affected by multiple factors such as approachability, acceptability of medical services, availability, and affordability, among others, as discussed in detail elsewhere [5•]. In HICs, access to medical care seems to contribute only modestly to the socioeconomic gradient of CVD [120, 121]; however, in LMICs, widely unequal access to medical care—often only accessible to wealthy groups in urban areas—likely has a stronger role in driving the socioeconomic inequalities in CVD [121–123].

Discussion

As presented in this review, extensive evidence continues to accumulate in HICs, confirming the inverse association between SES and CVD and CVRFs. The existence of large prospective cohort studies in these countries has allowed for detailed assessment of the SES-CVD association, such as to examine whether the SES-CVD association holds across different SES indicators; to assess the association between SES and specific cardiovascular outcomes; to evaluate whether the SES-CVD association varies by sex; to examine the impact of early-life versus adult SES on CVD in later life; and to assess trends in socioeconomic inequalities. Such detailed analyses are important to improve our understanding of the way SES impacts CVD risk, as well as to develop evidence-based clinical and public health recommendations to reduce and eliminate socioeconomic inequalities in cardiovascular health.

However, such detailed analyses remain largely absent in LMICs, where prospective cohort studies are too recent, too small, or more often, inexistent, with most of the evidence originating from cross-sectional studies of varying sample sizes, quality, and external validity. The evidence from LMICs indicates that the direction of association between SES and CVD and CVRFs varies greatly across countries and within countries, depending on the level of socioeconomic development of the sampled population, as well as its stage in the demographic, epidemiological, and nutrition transition. Countries and within-country regions with higher socioeconomic development and at more advanced stages of the demographic, epidemiological, and nutrition transition, such as China, already consistently show an inverse SES-CVD and CVRFs association. Other less developed countries and regions continue to show a positive association. The evidence of the SES-CVD and CVRFs remains scarce from MICs in Central Asia, the Middle East, and Latin America, except regarding smoking and alcohol abuse, both of which are inversely associated with education and income in most MICs. In LICs, the evidence remains even scarcer. The available evidence, however, already shows a strong inverse educational and income gradient in smoking and alcohol abuse. No trends assessment has been conducted in LMICs for SES

inequalities in CVD. In light of this, there is an enormous need for prospective cohort studies or repeated nationwide cross-sectional surveys to take place in LMICs, particularly as these countries are already experiencing the greatest world burden of CVD.

The findings presented in this review show that education was the socioeconomic indicator more consistently associated with CVD and CVRFs, irrespective of the country income level; this has historically been the case in countries that have predominantly or exclusively used education as the socioeconomic indicator, such as the USA [3, 5••]. However, in European countries, particularly the UK, socioeconomic stratification has been historically measured using occupation, so more evidence is available linking this indicator with CVD and CVRFs than in countries outside Europe [4, 5••]. In LMICs, it may be that education better captures the socioeconomic stratification that is relevant to CVD and CVRFs compared with income and occupation [23]. At the same time, in LMICs studies have predominantly used education as the indicator of SES, because it is easier to capture and measure than occupation or income [23]. However, education becomes more problematic as an indicator of SES at older ages, as it is acquired relatively early in life. In elderly populations, other indicators such as wealth or income show more consistent associations with CVD and CVRFs [87•, 111].

In HICs, the extensive body of evidence has confirmed a clear inverse SES gradient—measured via education, occupation, or income—not only for all-CVD mortality, but also for CVD events, stroke and CHD. The effect of education appears to be stronger among women for all-CVD and CHD, but it seems to be the same for occupation and income. The educational, occupational and income inequalities in CVD appear to have decreased over time in absolute terms but remained stable or even increased in relative terms in most European countries. In the USA, educational inequalities in CVD appear to have increased over time. Educational and income inequalities in CVRFs have increased in several HICs, particularly with smoking, alcohol abuse, obesity and diabetes. However, given the few number of studies, there is a need for more trends assessment of income and occupational inequalities.

Furthermore, as recommended by the American Heart Association, there remains a need to implement and evaluate interventions that address the socioeconomic determinants of CVD [5••]. This is particularly critical given recent findings from a systematic review of 57 studies that lower SES was associated with lower access to coronary procedures and secondary prevention, which may explain the higher risk of CVD death among disadvantaged groups [124]. Thus, further research needs to evaluate disparities in access to medical care, including approachability, availability and accommodation, affordability, and acceptability, as suggested by Havranek et al. [5••]. Related, a review of results from CVD intervention clinical trials found that only 5% of studies incorporated

measures of SES in their trial assessment [125]. This remains a major limitation in assessing interventions for their potential to reduce socioeconomic inequalities. Future research must incorporate socioeconomic disaggregation of clinical trial intervention results.

Additionally, there remains a need for research to assess the additive and detrimental effect of SES and comorbidities in CVD risk and mortality, in HICs and, especially, in LMICs, where the double burden of disease is the greatest; this issue was highlighted by a recent systematic review of 39 studies that found that the lower the socioeconomic status, the higher the comorbidities [126]. Furthermore, more research is needed to explore the combined effect of SES and CVD risk factors to allow for clearer understanding of the pathways through which these factors affect CVD risk. Future analyses should also explore the mediating role of common CVD risk factors in driving the SES and CVD association, as a few previous studies have attempted [108, 127, 128], to enable potential targeted measures for interventions and policy to reduce CVD inequalities.

In both HICs and LMICs, the recent evidence indicates an inverse association between wealth and CVD and CVRFs. Future studies should further explore the role of wealth on CVD risk, particularly given that large proportions of the populations in LMICs continue to work in the informal sector. Similarly, the role of neighborhood SES should be further studied, in both HICs and LMICs, specifically in the way it may interact with individual SES. This is particularly important to better understand the interplay between individual and structural factors in CVD risk, and to maximize the impact of interventions and policies to reduce CVD inequalities, especially as many countries continue to become more urbanized.

Finally, a growing body of evidence already indicates the presence of an inverse association between early-life SES—measured in various ways—and CVD risk in later life. However, further research is needed to examine whether early-life socioeconomic circumstances are related to CVD risk in later life either directly or indirectly, via adult SES. Thus, longitudinal studies that follow individuals across the life course are needed to properly assess how socioeconomic circumstances become embedded and influence CVD risk.

Conclusion

The recent evidence presented in this review add to the extensive body of evidence in HICs that confirm the inverse association between SES and CVD and CVRFs; the growing body of evidence in LMICs that show the direction of the association continues to be positive in countries and regions with less socioeconomic development and at less advanced stages of the demographic, epidemiological, and nutrition transitions.

However, the evidence remains scarce and mostly from cross-sectional studies in LMICs, where the need is urgent for longitudinal studies to disaggregate CVD and CVRFs by socioeconomic indicators, particularly as these countries already suffer the greatest burden of CVD.

Compliance with Ethical Standards

Conflict of Interest Carlos de Mestral and Silvia Stringhini declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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