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STATE OF THE ART REVIEW
Epidemiology, prevention, and health care policies

Social factors, health policy, and environment: implications for cardiovascular disease across the globe

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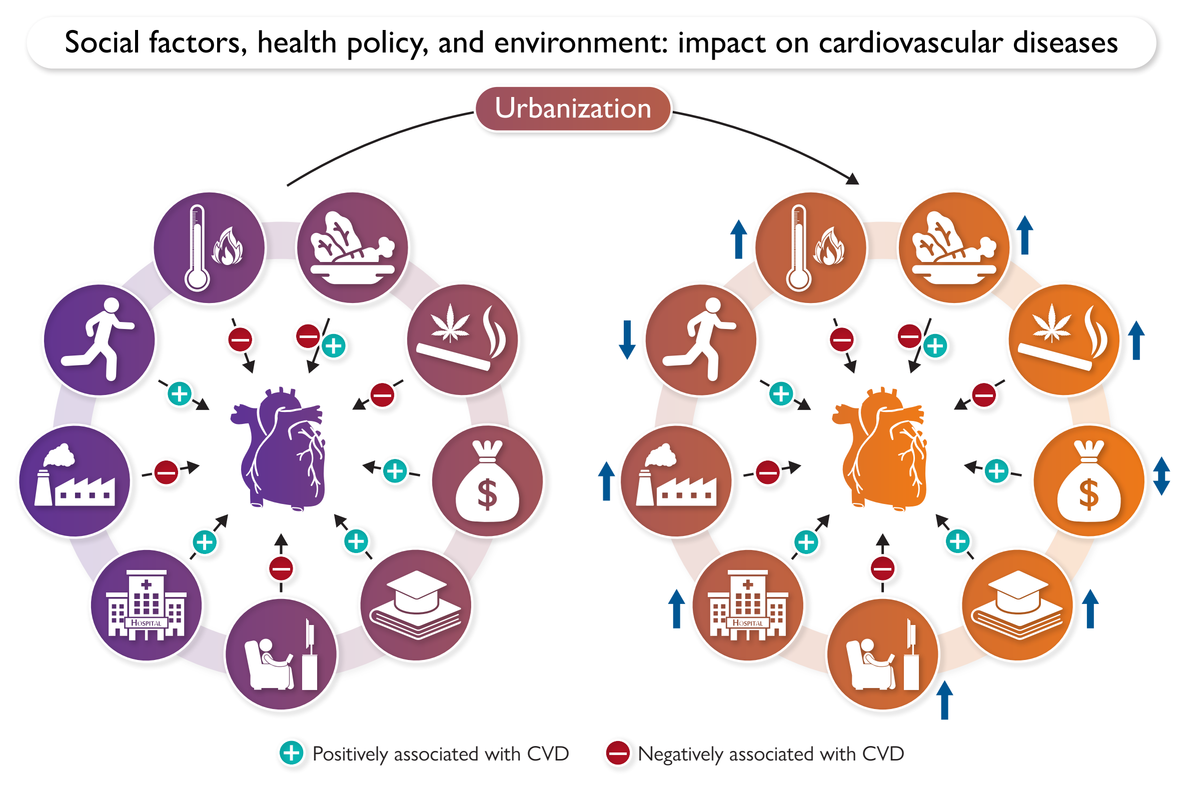
Graphical Abstract



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Abstract

Cardiovascular disease (CVD) is the leading cause of deaths worldwide, with 80% occurring in low- and middle-income countries. These countries are characterized by rapid urbanization, poorly funded health systems, poor access to prevention and treatment strategies, and increasing age and a higher prevalence of chronic disease. Rapid urbanization has contributed to the significant environmental and societal changes affecting daily life habits and cardiovascular health. There is growing awareness that environmental and social exposures and policies can influence CVD directly or through behavioural risk factors. However, much of this knowledge comes from studies in high-income countries and is applied to low- and middle-income countries without evidence to indicate this is appropriate. This state-of-the-art review will present and synthesize key findings from the Prospective Urban Rural Epidemiology study and related studies that have aimed to understand the environmental, social, and policy determinants of cardiovascular health in countries across varying levels of economic development through an urban/rural lens. Emerging from these findings are future policy and research recommendations to accelerate the reduction of the global burden of CVD.

Keywords Social determinants • Environment • Physical activity • Diet • Cardiovascular disease • Pollution • Access to care

Introduction

Cardiovascular disease (CVD) is the leading contributor to the global burden of disease, displacing respiratory infections and maternal and neonatal conditions, which occupied first and second places in 1990.[1] During this time, the absolute number of deaths attributed to CVD has grown by over 50%, driven by increasing numbers in low- and middle-income countries (LIC, MIC) that now account for nearly 80% of global CVD deaths.[2,3] These countries are experiencing rapid urbanization and ageing populations but poorer access, limited funding, and weak health systems, with little prevention of chronic health conditions, so we can expect to see the CVD burden increase further in the coming years.

Traditionally, CVD prevention has focussed on individual risk factors. The INTERHEART[4] and INTERSTROKE[5] case-controlled studies demonstrated how a handful of simple, individual-level risk factors accounted for about 90% of the population-attributable risk for non-fatal myocardial infarction (MI) and strokes worldwide. While their precise contributions varied, these associations were seen regardless of geographic region, ethnicity, and sex.

In recent decades, risk reduction strategies have been complemented by investigating upstream risk factors affecting population risk—essentially the ‘causes of the causes’ of individual risk factors (primordial prevention). This focus has been driven by realization that the growing burden of CVD demands more than reactive interventions targeting individual risk factors or established diseases. It needs to be coupled with evidence of the influence of policies on environmental and social exposures to what have been considered behavioural risk factors (such as tobacco use, poor nutrition, and physical inactivity).

The concept of primordial prevention and the benefits of intervening at the population level are not new. In 1985, Rose[6] questioned how two countries could have remarkably different rates of CVD incidence. He hypothesized that differences may be due to social or environmental factors, so improvement in these areas could lower population risk and thus the rates of CVD. Since then, much research in high-income countries (HIC) has shown how the environment can affect health behaviours and disease risk (*Figure 1*).[7–9] Similarly, policies on tobacco regulation and medication access and prices can substantially influence smoking rates and medication adherence, respectively.[10,11] The environment may also pose a direct risk, independent of traditional risk factors, mediated by factors such as air pollution, inadequate access to nutritious food, and limited opportunities for physical activity (PA). The year 2007 was estimated to be the first year in which more people lived in urban than rural areas.[12] This continued shift from rural to urban living leads to significant changes in environmental and social exposures, which affect living conditions and, thus, cardiovascular health.

The Prospective Urban Rural Epidemiology study

The Prospective Urban Rural Epidemiology (PURE) study is a community-based cohort study and one of the few studies designed to assess the impact of environmental (including health systems) and individual-level risk factors on CVD and other non-communicable diseases (*Figure 2*).[13] Beginning in 2002, it now includes 28 countries with 212 299 participants from five continents. These countries are at different levels of economic development, providing an unparalleled heterogeneity of social, economic, environmental, and health systems conditions. Within each country, communities were selected to ensure geographical and economic diversity while maintaining feasibility of recruitment. The PURE study was not designed to be representative of national populations, but an investigation of the original 17 participating countries indicates only modest differences between the PURE cohort and nationally available data.[14]

Approximately 87% of PURE participants live in either LIC or MIC, so the PURE study is uniquely positioned to investigate the effects of the urban transition on individual risk factors. In 2009, the team developed concepts and validated tools [Environmental Profile of a Community’s Health (EPOCH)] to enable the assessment of community-level determinants hypothesized to influence the development of CVD in the diverse settings of PURE.[15,16] The EPOCH tools collated data from local audits, surveys, photos, and secondary data sources, linked by geocoding using Global Positioning Systems across tobacco, food, social, physical, built, and healthcare access domains (see Supplementary data online, *Table S1*).

In this article, we review key data from PURE and related studies to understand the social, environmental, and policy determinants of cardiovascular health through a global and urban/rural lens.

Physical activity environment

Physical inactivity is an independent risk factor for premature mortality, CVD, certain cancers, mental illness, and several other diseases[17,18] and is the fourth leading modifiable risk factor for mortality worldwide.[19] The World Health Organization (WHO) recommends a minimum of

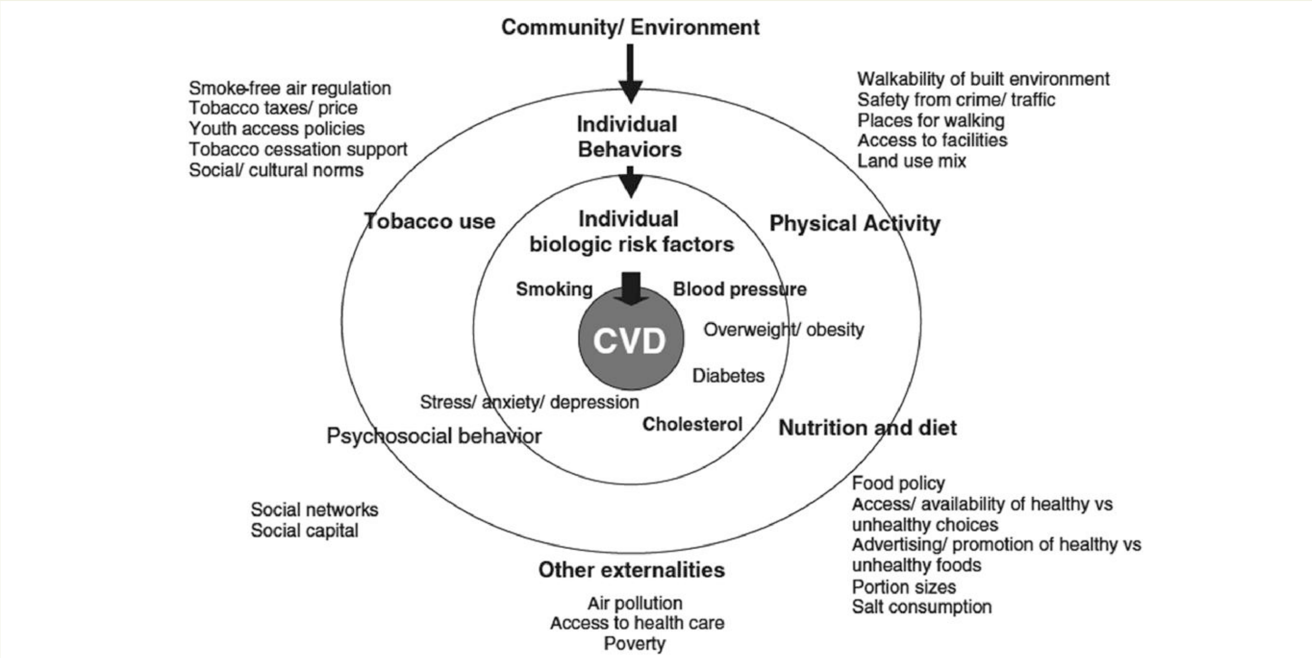

Figure 1 Environmental factors that have been linked to human behaviours and established risk factors that cause cardiovascular diseases. Reprinted with permission from Chow *et al.*[7]

Figure 2 Graphical summary of the Prospective Urban Rural Epidemiology study

150–300 min/week of moderate activity, 75–150 min/week of vigorous activity, or a combination thereof.[20] Worldwide, only 73% of people meet this target,[21] with huge variations among countries.[21,22]

Data from the PURE study support the WHO recommendations. Among PURE participants, achieving 150–750 min/week of PA was associated with a 20% lower risk in premature mortality [hazard ratio (HR) 0.80, 95% confidence interval (CI) 0.74–0.87], while >750 min/week was associated with a 35% reduction [HR 0.65 (0.60–0.71)].[23] Additionally, physical inactivity was the second strongest behavioural determinant of CVD after tobacco use.[24]

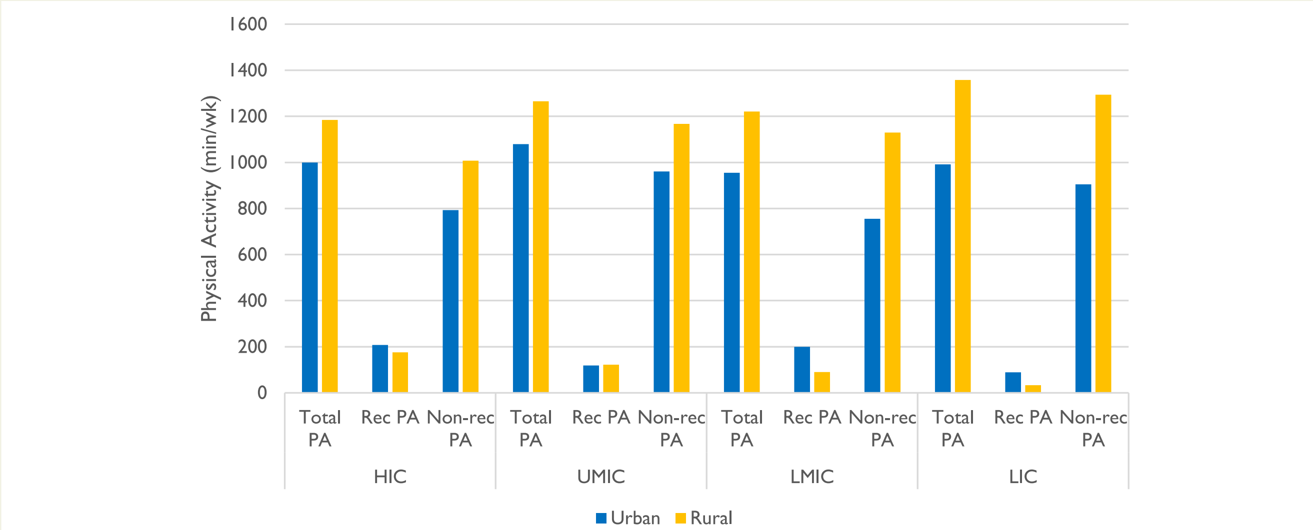

Figure 3 Physical activity patterns by country income level stratified by type of activity and urban/rural area residency. PA, physical activity; Rec, recreational; Non-rec, non-recreational; HIC, high-income country; UMIC, upper middle-income country; LMIC, lower middle-income country; LIC, low-income country

We also examined the effects of differing PA patterns, with those living in HIC engaged in more recreational activity, with non-recreational (occupational, transportation, and domestic) PA dominant in LIC.[23] Self-reported total PA was highest in HIC, yet people in LIC tended to sit less. Only 4.4% of LIC participants reported sitting more than 8 h/day compared with 22.2% of HIC participants.[25] Recreational PA was also lower in rural residents across country income levels, while non-recreation PA was higher (*Figure 3*). This may be due in part to fewer labour-saving devices in rural areas, such as car, computer, and TV.[26]

Research, predominantly from HIC, has shown how various environmental features, such as multi-purpose land use, grid-like street patterns, green space, public transit systems, and sidewalks, are associated with increased PA.[27,28] Analyses from PURE were consistent with this; land-use mix diversity [odds ratio (OR) 1.08 (1.01–1.17)], land-use mix access [OR 1.22 (1.11–1.33)], safety from traffic [OR 1.07 (1.01–1.13)], and safety from crime [OR 1.07 (1.01–1.14)] were all associated with higher odds of recreational walking, while land-use mix diversity [OR 1.08 (1.01–1.15)] and access [OR 1.27 (1.17–1.37)] and street connectivity [OR 1.14 (1.07–1.21)] were associated with higher odds of transportational walking.[29] Population density and area of impervious surfaces (two measures of urbanization) were also associated with increased recreational and transportational PA, but only in HIC and MIC.[30] Indeed, these associations may be reversed in LIC and MIC compared with HIC. For example, in Indonesia, urban density was associated with less vigorous PA.[31] A plausible explanation is that urban density in LICs and MICs is associated with narrow roads, high traffic density, and reduced pedestrian safety. A more walkable environment, as assessed from photos of PURE communities, was associated with more walking [427.55 MET*min/week (250.30–604.81)] and less obesity [relative risk (RR) 0.58, 95% CI 0.35–0.93].[32] These associations were stronger in urban than rural communities.

Food environment

Pricing, availability, and consumption of nutrient-dense foods vary widely across countries,[33,34] with implications for diet quality. Health-promoting foods often cost more than low-nutrient, calorie-dense options,[35] so poorer people and those who are socially and economically disadvantaged typically have less healthy diets.[36,37] In the PURE study, mean daily consumption of fruits and vegetables ranged from 2.14 servings per day in LIC to 5.42 in HIC (*Figure 4*).[38] At all country income levels, availability of fruits and vegetables was higher in urban than rural residents. Also, stores in HIC had a greater variety of fruits and vegetables than in MIC, which in turn had a greater variety than in LIC. While the absolute cost of fruits and vegetables was lowest in LIC, the cost relative to income was 50 times greater for fruits and 19 times greater for vegetables than in HIC. Indeed, the proportion of household incomes spent on food was highest in LIC (61.8%) and lowest in HIC (13.3%).[38] The relative costs were also higher for rural compared with urban residents across all country income levels. These higher costs may force families to purchase the least expensive foods, thereby restricting their choices of healthier, but more expensive, food items.

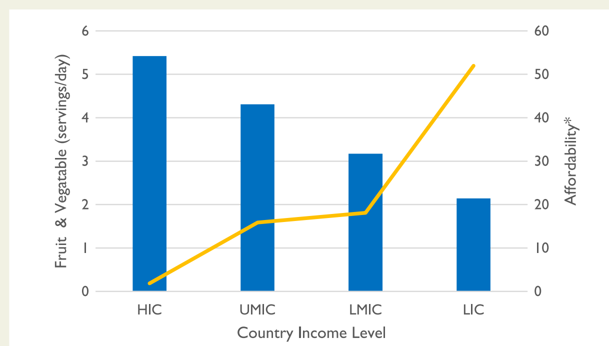

Figure 4 Fruit and vegetable servings per day (bars) and affordability (line) by country income level. *Affordability is the percentage of household income spent to purchase two servings of fruit and three servings of vegetables per day. HIC, high-income country; UMIC, upper middle-income country; LMIC, lower middle-income country; LIC, low-income country. Modified from Miller *et al.*[38]

Using a healthy diet score from the PURE study population, we found overall diet quality also differs; HIC had the highest healthy diet score (indicative of a diet containing fruit, vegetables, legumes, nuts, fish, and dairy), followed by LIC and MIC.[39] The most notable regional differences were in diet composition, with fruit and vegetable intake higher in North and South American countries in PURE and lowest in African and Asian countries.[40] While consumption of whole grains and white rice was highest in African and Asian countries, intake of dairy products was lowest in these regions.

Studies in HIC have underscored the contribution of the food environment to CVD risk. In particular, higher prevalences of fast food restaurants in the neighbourhood and unavailability of healthy food options were associated with greater CVD risk.[41–45] In the PURE study, ratios of fast food to full-service restaurants and bars/pubs to liquor stores were positively associated with obesity [OR 1.09 (1.06–1.14) and OR 1.10 (1.07–1.15), respectively], while there was a negative association with food markets [OR 0.97 (0.95–0.99)].[46] Regardless of country income, the availability and affordability of fruits and vegetables were greater in urban areas, corresponding with higher daily intake.[38] A systematic review of mostly MIC concluded that the food environment is associated with food intake and some health outcomes, such as obesity.[47]

The tobacco environment

Current and past smoking are associated with an increased relative risk of CVD and premature mortality.[48,49] With more than one billion active tobacco users worldwide, mostly in LIC and MIC, tobacco is a leading preventable cause of CVD.[50] The increased risk varies with intensity and duration of exposure, but data from the PURE study, along with INTERHEART and INTERSTROKE, have shown these associations differ among countries at different levels of development, possibly reflecting differences in the products used.[51–53] For example, the adjusted HR for the composite of premature mortality, CVD, cancer, and respiratory disease in current smokers (vs never smokers) was higher in HICs [1.87 (1.65–2.12)] than in MICs [1.41 (1.34–1.49)] and LICs [1.35 (1.25–1.46)].[51] Regardless of country, the increased risk for major CVD associated with smoking is typically 50%–150% greater.[51]

The most effective tobacco policies, such as price increases, restricting availability, and prohibiting smoking and marketing,[54] have been implemented mostly in HICs. However, LICs and MICs are beginning to adopt these policies, especially with increased monitoring of compliance with the Framework Convention on Tobacco Control using the MPOWER instrument.[55] In addition, despite strenuous attempts by the tobacco industry to conceal the evidence,[56] some evidence points to a risk of CVD from exposure to second hand smoke, so policies that reduce smoking will have benefits beyond those who smoke.[57]

The PURE EPOCH tool was used to study how the environment in which people live influences smoking initiation and quitting in 545 communities across 17 countries.[58] We noted that while non-smoking signs were visible in 38% of all communities, this ranged from 15% in LIC and MIC to 73% in HIC. This coincided with lower social acceptability of smoking in HIC and greater knowledge of the health consequences of smoking in HIC. Intolerance to smoking indoors was also highest in HIC, as was disapproval of youth smoking [92.2% compared with 75.0% in upper MIC, 85.8% in lower MIC, and 63.7% in LIC ($P < .0001$)], suggesting tobacco control measures and social acceptability of smoking go hand in hand.

Further research within PURE confirmed how the industry has shifted its focus from HIC to LIC and MIC.[59] For example, the density of tobacco retail outlets was greatest in LIC and lower MIC, less in upper MIC, and lowest in HIC and in urban than rural areas (*Figure 5*). Visible marketing was also more common in LIC, with tobacco advertisements 81 times more likely to be found there than in HIC. Of the 11 842 participants interviewed, 30% reported seeing TV tobacco advertisements in the past 6 months, followed by posters (20%), print media (16%), signage (16%), radio (12%), and cinema marketing (5%). Again, the likelihood of being exposed to tobacco marketing was much higher (10 times) in LIC than in HIC and likely reflects bans on tobacco marketing in most HIC. Cigarette packet labelling was also weaker in LMIC, reflecting the uptake of policies also needs to be monitored for implementation.[60] These tobacco control measures are also associated with reduced initiation and increased quitting.[58]

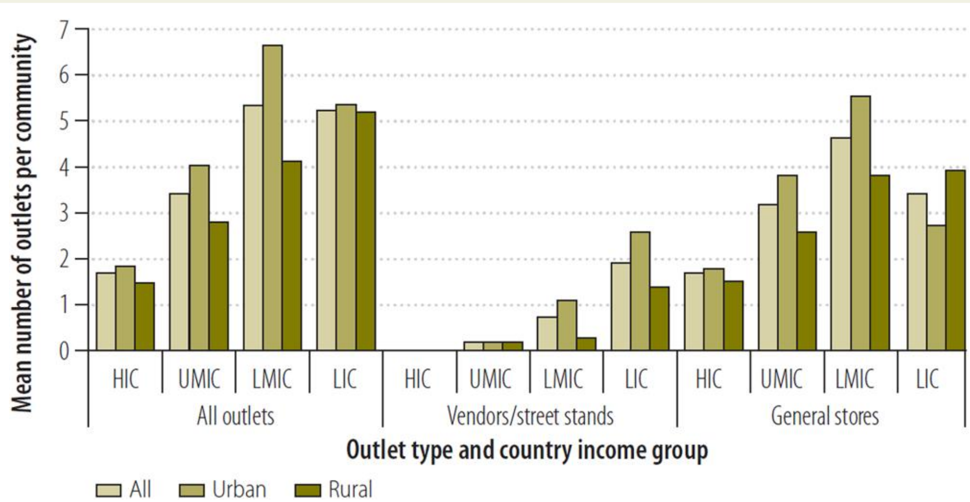

Figure 5 Tobacco-selling outlets in urban or rural study community, 16 countries, 2009–12. HIC, high-income country; UMIC, upper middle-income country; LMIC, lower middle-income country; LIC, low-income country. Reprinted with permission from Savell *et al.*[59]

Education and economic factors

In HIC, the risk of CVD is greatest among those who are socially and economically disadvantaged.[61] This is typically measured by low education, limited financial resources, or an occupation predominantly involving manual labour. This association is likely mediated through several ways, including a greater likelihood of having modifiable risk factors, such as obesity, type 2 diabetes, smoking, and physical inactivity[62] as well as less access to proven healthcare measures.

Analyses from the PURE study confirmed the social gradient of risk factors in HIC, with the INTERHEART risk score inversely associated with education (*Figure 6*).[63] However, in LIC, education was positively associated with INTERHEART risk score, with those who had no more than primary education having the lowest score. Despite this, low education was associated with higher premature mortality, with the effect strongest in LIC. For instance, the HR for mortality among those with no more than primary education was 2.76 (2.29–3.31) in LIC compared with some post-secondary education, while in HIC, it was only 1.50 (1.14–1.98). In addition, education was a stronger predictor of premature mortality and CVD incidence than wealth. One explanation is that educational attainment is generally established early in life and may serve as, making it a better marker of socio-economic position over the life course. Subsequent analysis also revealed that, among the traditional risk factors, low education had the highest population-attributable fraction (12.5%) for premature mortality.[24]

There are many mechanisms by which education influences health. In the PURE study, this included greater ability to access to secondary prevention treatment.[63,64] Another is less knowledge of CVD risk and risk factors making it more difficult to implement prevention and/or initiate steps for treatment. Conversely, education likely improves the ability to gather information, thereby boosting agency. For example, those in PURE with greater education were more likely to have quit smoking in all countries.[58]

Social isolation and cohesion

The association between increased risk for premature mortality and social isolation, characterized as the absence of social relationships that arise from social contacts, social resources, and participation in social or religious activities, has been known for over 40 years. In one of the earliest studies, men with the fewest social contacts were 2.3 times more likely to die, with the figure 2.8 for women.[65] Other research has shown that men who are divorced are at increased risk of premature mortality than their married counterparts.[66] While many of these studies were in HIC, similar associations were seen in Bangladesh.[67] More recently, a large, pooled analysis of cohorts from Asia provided strong evidence of a positive association between being unmarried or single and total and cause-specific mortality, with a 20% higher multi-adjusted risk of CVD mortality.[68] Social ties and contacts tend to shrink as populations age, birth rates fall, and urbanization leaves more people living isolated lives and lacking social support. The association between social isolation and premature mortality and with CVD and stroke incidence has also been shown in meta-analyses.[69,70] However, there is little known about the scale and nature of these in LIC and MIC.

We developed a social isolation scale in PURE incorporating five items from the Social Network Index, a construct initially developed by Berkman and Syme.[65] We found social isolation was greater in MIC and HIC than in LIC and higher in urban residents (where people are more likely to live alone in smaller places), and among older people, women and those with less education and who were unemployed (*Figure 7*).[71] Regardless of country, social isolation was associated with a greater risk of premature mortality [HR 1.26 (1.17–1.36)], incident stroke [HR 1.23 (1.07–1.40)], and CVD [HR: 1.15 (1.05–1.25)], contributing to a population-attributable fraction of 2.4%. These associations were stronger among men than women and younger than older individuals. Mediation analysis attributed 18% of the association of social isolation with premature mortality to current smoking, physical inactivity, and diet, with another 3% due to comorbidities such as presence of depression, hypertension, cancer, stroke, and CVD. In a separate analysis in PURE, there was an increased risk of incident CVD among those with four or more depressive symptoms at baseline [HR: 1.14 (1.05–1.24)], which was apparent in urban and rural settings in countries at all levels of development.[72] Thus, while we cannot exclude other unobserved factors, and the pathways remain unclear, social isolation seems important everywhere.

Social capital, which is related to social isolation, may partly explain some of these associations. Social capital is characterized by trust, reciprocity, and cooperation and has been positively associated with

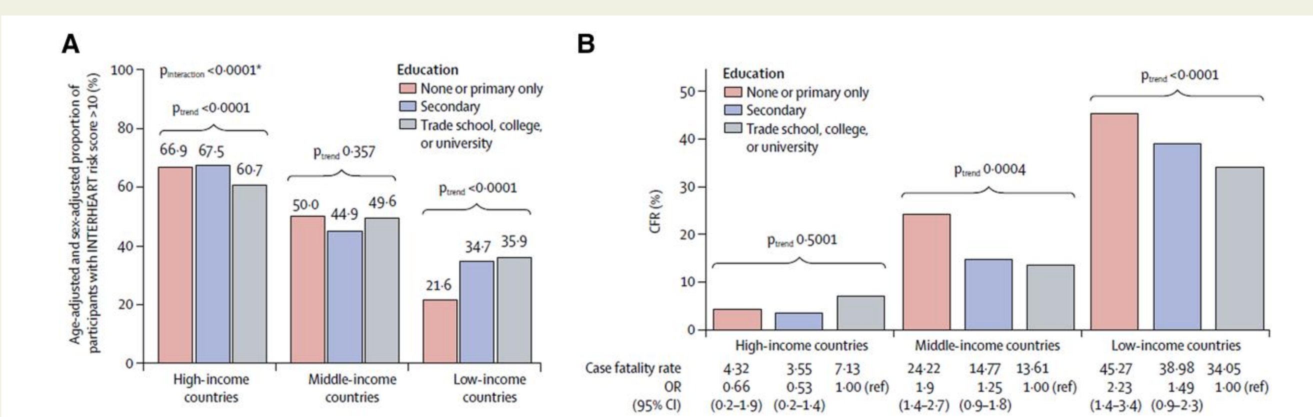

Figure 6 Age-standardized and sex-standardized proportion of PURE participants with INTERHEART risk score > 10 in high-income, middle-income, and low-income countries by education (*A*) and 28-day case fatality rate after a first cardiovascular event and odds ratio by country income and level of education among participants without previous cardiovascular disease (*B*). Data are adjusted for age and gender. CFR, case fatality rate; OR, odds ratio. Reprinted with permission from Rosengren *et al.*[63]

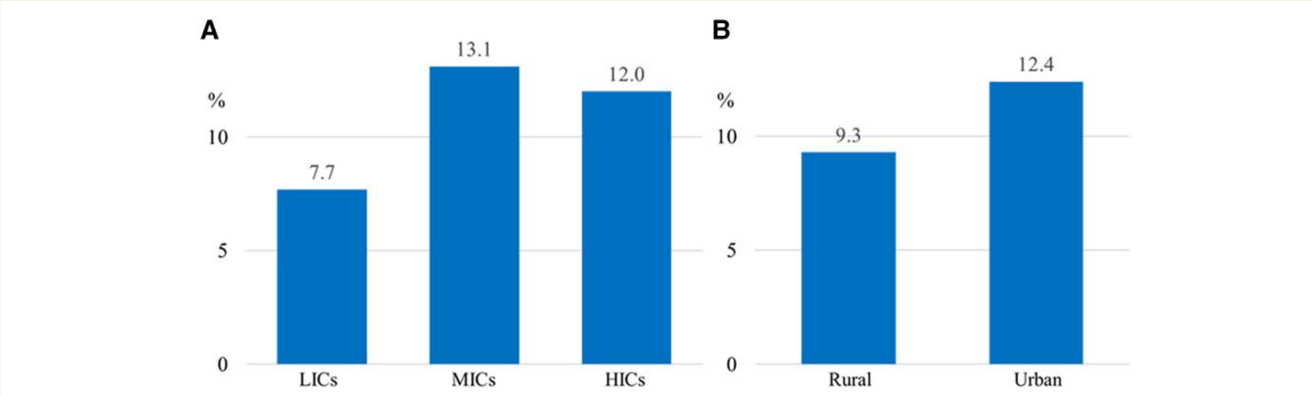

Figure 7 Age-sex adjusted prevalence of social isolation (%) by country income levels (*A*) and by residence areas (*B*). The prevalence of social isolation is the lowest in the low-income countries (*A*). The prevalence of social isolation is higher in the urban areas (*B*). LIC, low-income country; MIC, middle-income countries; HIC, high-income countries. Reprinted with permission from Naito *et al.*[71]

numerous health outcomes.[73] We showed greater social capital was associated with improved hypertension control in LIC and MIC but not HIC.[74] These networks may be critical in LIC and MIC, where access to healthcare is lacking and may be vital in attenuating the association between social isolation and CVD.

Access to medications and treatment and healthcare systems

In many HIC, CVD mortality rates have been declining over recent decades,[2] due, in part, to advances in prevention and treatment through medications such as anti-hypertensives and statins.[75] Access to medications is essential for the prevention and treatment of CVD. However, while the overall risk factor burden for CVD is lower in LIC and MIC than in HIC, higher mortality rates for CVD in LIC, a CVD risk factor paradox, could be due to prevention and treatment gaps.[76]

Data from the PURE study revealed a worryingly low usage of medications for secondary prevention of CVD globally.[77] Medications such as aspirin, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins are proven treatments available in low-cost generic formulations. These medications were available in 95% of urban and 90% of rural communities in HICs, but availability bottomed out at 25% and 3% in LICs, respectively (*Figure 8*).[78] Out of 21 countries studied, the proportion of people with CVD taking at least three of these medications ranged from 0% (South Africa, Tanzania and Zimbabwe) to 49% in Canada.[79] The proportion of patients receiving at least one of these medications ranged from 2.0% in Tanzania to 91.4% in Sweden. The countries with the lowest use also displayed the largest inequality, with much higher use among the rich. This low use of proven drugs remained essentially unchanged over 12 years in all groups of countries, indicating that current efforts to improve their use appear to have, at best, a modest impact (unpublished data).

Cost is also a factor. While only 0.14% of households in HICs found the four medications for CVD secondary prevention potentially unaffordable, this figure was 60% in LIC households.[78] In communities where all four medications were present, patients were less likely to use them if their household could not afford them. We also found the absolute risk of catastrophic spending (defined as healthcare expenditure equating to or exceeding 40% of post-subsistence household income) was twice as high in households with at least one of CVD, diabetes, kidney disease, cancer, or respiratory disease than those without, particularly in LIC and MIC.[80] The prevalence of catastrophic spending and impoverishment (defined as household income dropping below the poverty line due to healthcare expenditures) was highest in households in LIC and MIC that had at least one occupant with an NCD. Counter-intuitively, catastrophic spending was less frequent in LICs, possibly because those with NCDs in LICs failed to obtain care. A substantial proportion of those in LICs with NCDs, especially women (38.7% compared with 12.6% in men), reported avoiding taking medication due to cost.[80] Availability and affordability of medicines to manage diabetes and blood pressure also influenced control of these risk factors in the PURE study populations.[81,82] In communities where blood pressure-lowering drugs, anti-platelets, and statins were available but not affordable, or all three drugs were unavailable, the risk of CVD was higher than in communities where the drugs were both available and affordable.[83]

Air pollution

Fine particulate matter less than 2.5 microns (PM2.5) contributes to air pollution and is now an accepted modifiable risk factor for CVD.[84–86] Approximately 86% (2.5 billion) of urban residents live in areas that exceed the WHO's guideline of annual average PM2.5 of less than 10 μg/m^3.[87] While the relationship between exposure to outdoor air pollution and CVD is established in HIC, the magnitude of this risk remains uncertain as there are few high-quality prospective cohort studies in LIC and MIC outside of China where air pollution exposures are typically highest.[87–89]

To address this, satellite-derived estimates of long-term exposure to outdoor PM2.5 were applied to PURE community locations and compared with CVD events.[90] The mean 3-year PM2.5 concentration ranged from 6 μg/m^3 in Vancouver, Canada, to 140 μg/m^3 in Jaipur, India. Adjusted for individual, household, and geographical characteristics, a 10 μg/m^3 increase in 3-year mean PM2.5 was associated with a small but significant increased risk for incident MI [HR 1.03 (1.00–1.05)], stroke [HR 1.07 (1.04–1.10)], and CVD mortality [HR 1.03 (1.00–1.05)] (*Figure 9*). While PM2.5 was slightly higher in urban areas, the association was greater in rural areas. Importantly, the association was similar when analyses were restricted to LIC and MIC or communities with very high PM2.5 concentrations (>35 μg/m^3), indicating that air

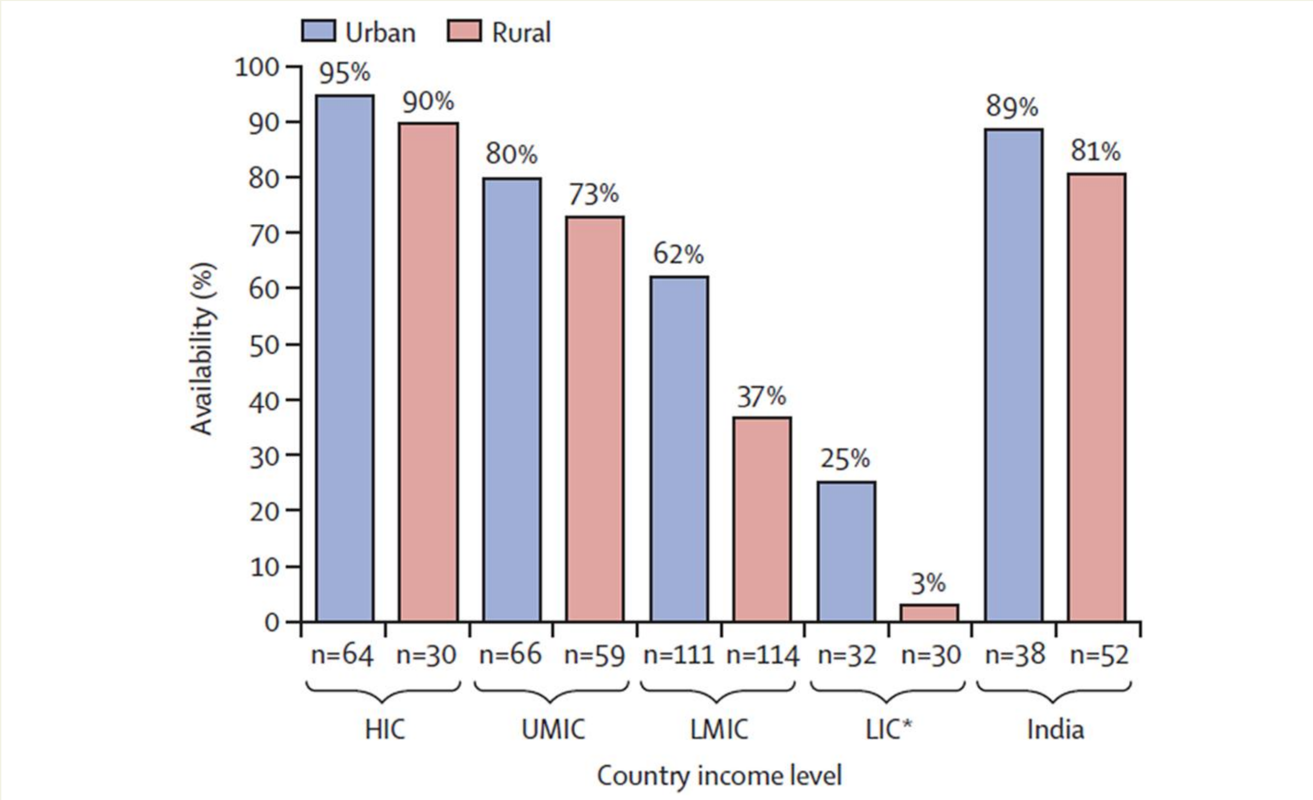

Figure 8 Percentage availability of aspirin, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins. *P* for trend < .0001 across country income levels (excluding India due to large generic pharmaceutical industry) for both urban and rural areas. *n*, total number of communities in each location of each country income group. Reprinted with permission from Khatib *et al.*[78]

pollution epidemiological findings in HICs apply to LMIC settings. The estimated population-attributable fraction for PM2.5 was 8.4% for MI, 19.6% for stroke, and 8.3% for CVD mortality. These values are consistent in magnitude for stroke and CVD mortality but smaller for MI compared with the few cohort studies conducted in non-HIC settings such as China[92–94] and to studies conducted in the cleaner settings of North America and western Europe.[92–94]

In addition to ambient air pollution, household air pollution (HAP) from the dirty fuels used for cooking, heating and lighting presents substantial risk to nearly half of the world's population.[95] In the PURE study, cooking with wood, crop waste, or coal in rural households was nearly nine times more common compared with urban households: 71.7% vs 8.2%, respectively. Using these solid fuels compared with using gas or electricity was associated with increased CVD [HR 1.08 (0.99–1.17)], which was more pronounced for stroke [HR 1.12 (0.99–1.27)] and premature mortality [HR 1.12 (1.04–1.21)] (*Figure 9*).[91] Further, cooking with kerosene was associated with increased risk of premature mortality and cardiorespiratory outcomes compared with clean or solid fuels.[96] There was no consistent association between dirty cooking fuel use and elevated blood pressure, suggesting that hypertension may not mediate the relationship between HAP and CVD risk.

The PURE-AIR companion study assessing HAP exposures (PM2.5 and black carbon) is the largest study of its kind conducted to date (2541 households and 998 individuals in 120 communities from Bangladesh, Chile, China, Colombia, India, Pakistan, Tanzania, and Zimbabwe).[97] Individuals using clean fuels (gas and electricity) for cooking and heating had substantially lower PM2.5 concentrations in their kitchens. Importantly, average kitchen and personal PM2.5 measurements for all primary fuel types exceeded WHO's Interim Target-1 (35 μg/m^3 annual average), highlighting the need for comprehensive indoor and outdoor air pollution mitigation strategies. Factors associated with household and personal PM2.5 and with black carbon air pollution exposures included location, cooking fuel type, home and personal characteristics, and behaviours such as second hand smoke and cooking time.[98,99] Community-level factors (e.g. larger population density and urbanization) were the strongest predictors of polluting-to-clean fuel switching in all communities, followed by household-level factors (e.g. larger household size, higher wealth, and higher education level).[100]

Climate change

Climate change poses many risks for CVD, including acute temperature changes (increases and decreases), increased severity and frequency of extreme weather events, and long-term changes in food availability, air quality, water security, healthcare access, and population migration. Global surface temperature has risen faster since 1970 than in any other 50-year period over the last 2000 years, and global average temperature is projected to increase between 1.0 and 5.7°C by the end of this century.[101] Climate change is affecting weather and climate extremes in every region of the world, increasing the frequency of heatwaves, floods, droughts, and storms.[101] Climate hazards have been

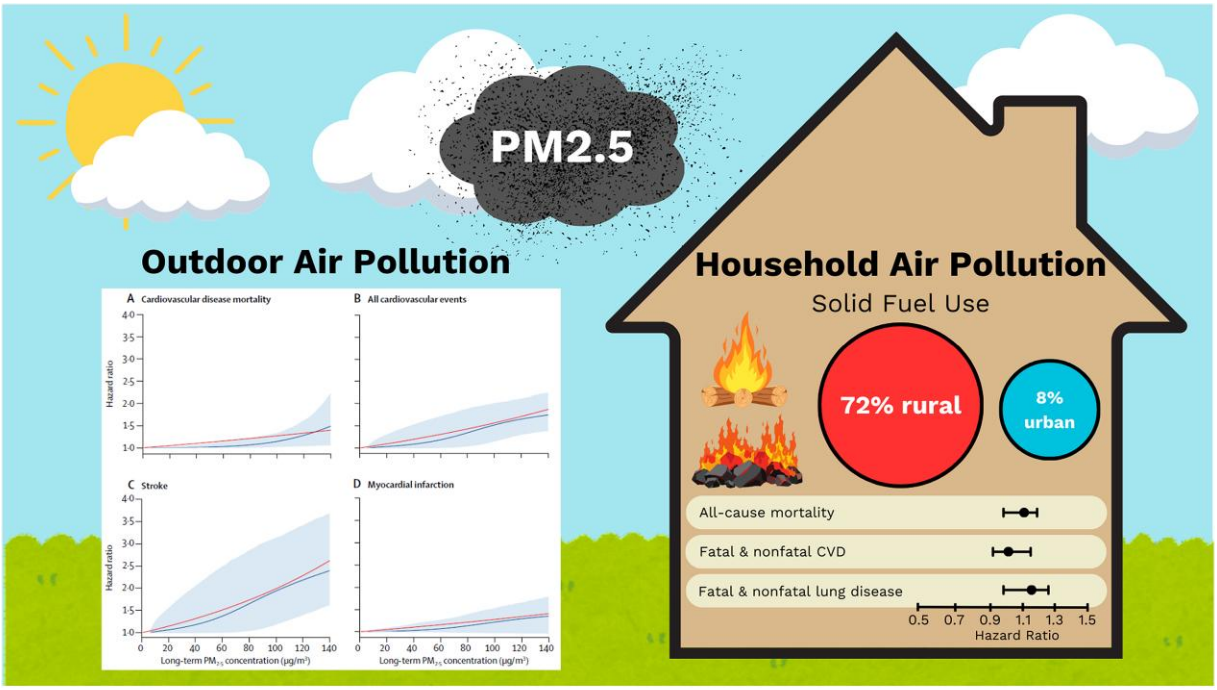

Figure 9 Effects of outdoor air pollution (left) and household air pollution (right). In the left panel, red lines show linear hazard ratios and blue lines show non-linear hazard ratios for cardiovascular disease mortality (*A*), all cardiovascular disease events (*B*), stroke (*C*), and myocardial infarction (*D*). Shaded areas represent 95% confidence intervals for the non-linear models. In the right panel, hazard ratio and 95% confidence interval for living in a household using solid fuels for cooking. Graphs on the left reprinted with permission from Hystad *et al.* (2020)[90] with additional modification from Hystad *et al.* (2019)[91]

linked directly—via temperature—or indirectly via impacts on air pollution, diet, and PA, to CVD.[102] Individuals in LMICs are likely to be most susceptible, but few studies have been conducted on this topic to date.[103,104]

Our preliminary analysis of daily temperature and mortality in the PURE study, using a case-crossover design (unpublished data), found an increased OR of 1.29 (1.24–1.35) for CVD mortality for a one °C increase in daily temperature above the minimum mortality temperature (MMT) derived for each PURE community. For temperatures below the MMT, an increased OR of 1.06 (1.04–1.09) was observed a one °C decrease in daily temperature. When restricted to rural locations in LICs, the OR for hot temperatures increased to 1.48 (1.36–1.60) for a one °C change above the MMT, while estimates remained stable for colder temperatures below the MMT. This provides critical new information on how rural populations in low-income settings are especially susceptible to acute heat impacts on CVD.

In the future, the PURE cohort will provide information on the complex indirect pathways linking climate change to CVD. Several conceptual frameworks have described the pathways linking climate change and health,[105–107] emphasizing the dynamic interplay among environmental, social, economic, and biological factors. This complexity underscores the need for integrative approaches, such as those provided by the PURE cohort, to unravel the pathways and interactions driving climate-related health outcomes. For example, the MMT is an important indicator to assess the temperature–mortality relationship and reflects human adaptation to the local climate. Since minimum mortality estimates are unavailable for most LMICs, we used the most frequent temperature as a surrogate, which agrees well with MMTs observed in PURE.[108] The MMT shows large variation across PURE sites (range: 10–35°C), providing important variation that can be exploited in future analyses that examine acute and chronic exposures related to climate changes and subsequent human adaptation. Given future projections of climate impacts (PURE communities are predicted to see a 1.10°C increase in 2050 and a 2.90°C increase in 2100 based on the NEX-GDDP climate projections; *Figure 10*),[109] assessing the direct and indirect pathways linking climate change to CVD remains an urgent critical gap that PURE can fill.

Opportunities and Challenges with Urbanization

Over the past 50 years, CVD mortality has declined in HIC due to improvements in acute care and risk factor management (behavioural and pharmacological). However, these advances have not been realized in LMIC. Instead, CVD deaths continue to increase in these countries,[3] keeping CVD as the leading cause of death worldwide and threatening the achievement of the United Nation's Sustainable Development Goal 3.[110] For nearly 20 years, the PURE study has investigated the role of the physical, social, and policy environments across countries at diverse levels of economic development to identify potential levers that can be used to reduce the global risk for CVD.

The shift to living in urban environments has accelerated in recent decades. The United Nations expects this to continue, with 68% of the world's population in urban environments by 2050, with 90% of that increase occurring in Asia and Africa.[111] Despite this, most studies are

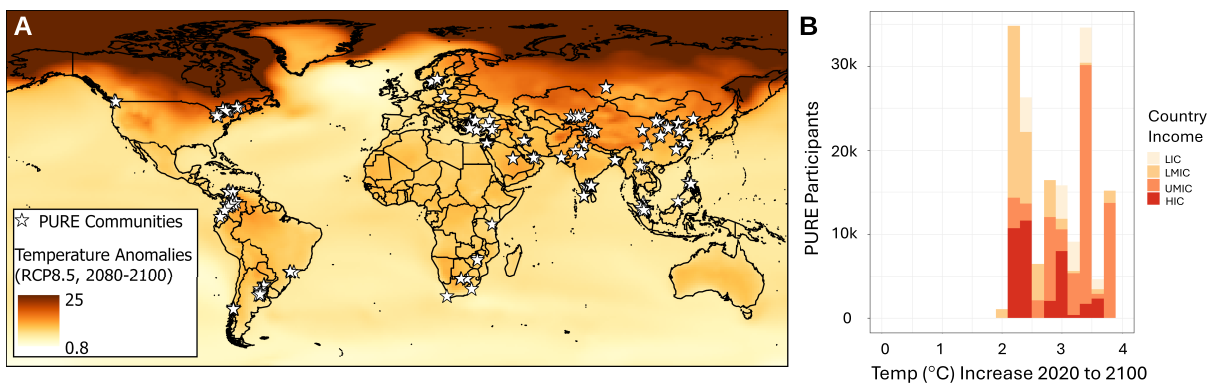

Figure 10 Locations of PURE communities (*A*) and the mean annual temperature anomalies predicted under the RCP 8.5 scenario for the 2020–99 time period (*B*)

conducted in HIC, where over 90% of the population lives in urbanized areas. Thus, one is left to assume that findings and recommendations based on research in HIC apply to LIC and MIC, but as the PURE study shows, this may not always be true.

With urbanization comes challenges and opportunities (*Graphical Abstract*). The nature of urbanization occurring in LIC and MIC will likely differ from that in HIC. For example, LIC will see an increase in the number of people living in slums or other disadvantaged circumstances in which PA is necessary.[112] This may raise concerns about safety and exposure to air pollution, which can attenuate or even counteract PA benefits.[113] These circumstances may partly explain our finding that while built environment measures (such as density, connectivity, and land use diversity) are associated with greater PA in HIC,[114–116] similar measures of urbanization were inversely associated with PA in LIC.[30] Also, urban infrastructure designed to support PA in LIC and MIC is generally more common in higher SES communities,[117] where residents are more likely to have labour-saving devices and be less physically active.[26] These findings emphasize the characteristics of the interactions that exist between environmental exposures, which are complex in nature, involving non-linear associations, feedback loops, and path dependency, so their influences on health-related behaviours and CVD outcomes may vary across different contexts.

Urbanization can, however, create opportunities, such as greater access to education, better medical care and treatments, and a reduced likelihood of HAP exposure. In the PURE study, education was higher among urban residents, and low education had the highest population-attributable risk among common risk factors.[24] The effect of education, along with other socio-economic characteristics, is so pronounced that even within a few blocks in the same city, life expectancy can vary by as much as a year.[118,119] In the PURE study, regardless of country income level, those with the lowest education had the highest mortality.[63] Given that 44% and 54% of people in LIC and MIC, respectively, have primary education or less, education is a potentially key modifiable risk factor. We also found access to CVD medications and healthy food options to be higher in urban areas across all country income levels. The urban/rural difference in medication access was most pronounced in LIC. These medications were eight times more likely to occur in urban than rural areas.[78] Regardless of country income, the availability and affordability of fruits and vegetables were greater in urban areas, which corresponded with higher daily intake.[38] Lastly, urbanization was associated with cleaner indoor fuel sources and less exposure to HAP.[100] This has the potential to substantially improve health outcomes, given that nearly half of pollution-attributable deaths are linked to HAP.[120]

With economic development and social changes in LIC and MIC happening rapidly, now is the time to translate the findings of PURE and similar studies into policy to ensure development is also seen through a health lens. This aligns with the emerging concept of Health for All Policies, in which measures in health and other sectors are mutually reinforcing.[121] For example, healthier populations are more productive and are more likely to participate in the labour force, thereby increasing economic growth, while flourishing communities increase opportunities to make healthier choices.[122]

Recommendations

Based on the collected findings from the PURE study, we propose the following recommendations for future research and public health policy:

- To incorporate global evidence into influential guidance documents like WHO's list of 'best buys',[123] it is crucial to consider studies from all over the world, not just HIC. Contextual factors must be considered to ensure that recommendations are tailored to diverse settings.
- Enhancing collaborations between researchers with diverse backgrounds is essential. The PURE study demonstrates the benefits of linking researchers from different regions and disciplines, breaking down the silos that often characterize research and public policy.[124] Strengthening these collaborations with greater involvement of political, social, and implementation sciences will improve the translation of evidence into policy.
- Increasing the number of multi-country studies with participants from communities in diverse settings. This makes it possible to know whether associations of risk factors with CVD and mortality vary by societal, geographic, and economic factors.
- Awareness of barriers to evidence-based health policies, including commercial determinants of health such as obstruction by vested interests.[125] Research and advocacy to overcome these barriers are essential.
- To reduce CVD risk, urban and regional planning should integrate better PA opportunities, healthy food options, and better air quality. However, the context of the local environment must be considered to understand facilitators and barriers to uptake better.
- Policymakers should prioritize population-level measures to make healthy choices easier. Measures should thus seek to reduce prices and increase the availability of healthy options while doing the

opposite with unhealthy ones and curtailing the marketing that promotes harmful products.
- Educational attainment should be viewed as a social determinant of health, and governmental and non-governmental health organizations should partner with educational organizations to help meet the United Nations' Sustainable Goal 4 (Ensure inclusive and equitable quality education and promote lifelong learning for all).
- Finally, climate change is poised to exert additional pressure on cardiovascular risk factors. Urgent action is needed to implement adaptation strategies that maximize health benefits. Many of these actions will go hand in hand with reducing pollution and can synergistically affect health behaviours.

Conclusions

Over the past two decades, much has been learned from the PURE and related studies on how the built, social, and policy environments affect risk for CVD across populations with varying levels of economic development. This work highlights the challenges and opportunities posed by urbanization and what measures can be taken to prevent the increasing global burden of CVD. Success can only come through engagement of multiple sectors and countries beyond HIC.

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

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