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Understanding the rise of cardiometabolic diseases in low- and middle-income countries

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Increases in the prevalence of noncommunicable diseases (NCDs), particularly cardiometabolic diseases such as cardiovascular disease, stroke and diabetes, and their major risk factors have not been uniform across settings: for example, cardiovascular disease mortality has declined over recent decades in high-income countries but increased in low- and middle-income countries (LMICs). The factors contributing to this rise are varied and are influenced by environmental, social, political and commercial determinants of health, among other factors. This Review focuses on understanding the rise of cardiometabolic diseases in LMICs, with particular emphasis on obesity and its drivers, together with broader environmental and macro determinants of health, as well as LMIC-based responses to counteract cardiometabolic diseases.

In the academic and political community, noncommunicable diseases (NCDs) have been framed as a global emergency[1,2]. The economic burden that NCDs impose on low- and middle-income countries (LMICs) has contributed to the visibility of these conditions within the broader global health policy environment[3], and the projected economic losses worldwide by 2030 associated with NCDs have been calculated to be $47 trillion[4,5]. Furthermore, health is one of the key Sustainable Development Goals (SDGs) proposed by the United Nations (Box 1).

NCDs comprise a variety of conditions including cardiovascular and pulmonary disease, diabetes and cancer; our focus here is on those considered cardiometabolic NCDs—cardiovascular disease, stroke and diabetes. In high-income countries (HICs), such NCDs are heavily clustered among people of low socioeconomic status, and NCDs are an important cause of medical impoverishment[6–9]. However, the highest chances of dying from NCDs are observed in LMICs[6,10], where, although NCDs remain most common among wealthier groups, the fastest rates of increase are again among poorer socioeconomic groups[11].

Changes in the prevalence of cardiometabolic diseases and their major risk factors have not been uniform across settings. Over recent decades, cardiovascular disease mortality has declined in HICs[12–16] and increased in LMICs[12,13], and diabetes prevalence has increased worldwide but at a faster rate in LMICs[17,18]. Moreover, NCD mortality occurs on average at earlier ages in LMICs, and the increasing number of years spent living with such conditions, their complications and multimorbidities, have major consequences at the individual, community, societal and country levels.

Cardiometabolic diseases are linked to several risk factors, in particular obesity, hypertension, diet, tobacco, air pollution and physical inactivity[19,20]. Hypertension and low education are key contributors to cardiovascular events and mortality worldwide, yet the contribution of other risks, such as household air pollution and poor diet, vary with a country's economic level[21]. Even though the overall risk-factor burden appears to be lower in LMICs than in HICs[22], rates of major cardiovascular events, such as death from cardiovascular causes, myocardial infarction, stroke, or heart failure, are lower in HICs than in LMICs, an observation that could reflect poor management and weak health systems infrastructure[22]. Many of the achievements in NCD control in HICs are closely related to better healthcare delivery and management of risk factors[12].

The epidemiology and management of NCDs in LMICs have received detailed attention[10,11,23], and roadmaps to address specific diseases have been devised[24]. Hence, rather than focusing on the epidemiology and treatment of these diseases and their risk factors, in this Review we aim to provide a broader and more nuanced understanding of why the epidemic of cardiometabolic NCDs has exploded in LMIC settings. We address this by focusing on the complex exposures faced by individuals raised in LMICs, in particular as their environments become more toxic and obesogenic. We also explore the commercial determinants of health, particularly in urban populations, together with population-wide responses arising from LMIC settings. As an overarching conceptual approach, we draw on the 'capacity-load' model of NCDs (Fig. 1)[25,26]. Below, we consider how the epidemiology of NCDs in LMICs is shaped by the particular exposure of individuals in these countries to factors affecting both metabolic capacity and load.

Social and environmental determinants of cardiometabolic disease in LMICs

Nutrition. The rise of cardiometabolic diseases has been strongly linked to rises in obesity. For example, a study found that in Africa between 1980 and 2014, the age-standardized mean body mass index (BMI) increased from 21.9 to 24.9 in women and from 21 to 23 in men, and a positive association was observed between diabetes prevalence and BMI[27]. Globally, much of the increase in BMI has recently been linked to a predominant rise of BMI in rural areas[28]. Between 1975 and 2016, the global prevalence of obesity increased from 3% to 11% among men and from 6% to 15% among women[29], with different patterns of change across different world regions. The rise in obesity varies between countries in association with socioeconomic status and gender[30,31]. It is notable that the increase

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Box 1 | The Sustainable Development Goals

The Sustainable Development Goals (SDGs) were proposed by the United Nations as the blueprint to achieving a better and more sustainable future for all by 2030[102]. There are 17 SGDs and 169 SDG targets. Although all SDGs are interconnected, SDG 3 is specifically devoted to ensuring healthy lives and promoting well-being for all at all ages, and its target 3.4 commits countries to reducing premature mortality from NCDs by one-third[210].

Because health is an integral part of human capital and a precondition, driver and outcome of sustainable development, SDG 3 is linked to around 50 health-related targets across the SDGs and the pledge to leave no one behind[211].

in obesity was not just focused in adults, but also occurred in children and adolescents worldwide, from below 1% in 1975 to 6–8% in 2016[29]. Results from a Norwegian longitudinal study with an average follow-up of 45 years showed that obesogenic environments are major contributors to the epidemic of obesity and NCDs, and contribute more than genetic predisposition[32]. This suggests that the environment is the primary determinant of the metabolic load (Fig. 1) that humans accommodate to in their daily lives, particularly in terms of food and physical activity.

Much of the rise in the burden of cardiometabolic conditions in LMICs is closely linked to the recent epidemiological transition observed in these countries: that is, the change in the pattern of causes of mortality from a predominance of infectious disease to a predominance of NCDs[33–35], a change that is occurring in the context of persisting or recent under-nutrition[25,36]. It is notable, however, that the obesogenic environment might also influence different populations differently with respect to disease development. For example, Asian populations develop diabetes at relatively low BMI[23,37,38]. The capacity-load model (Fig. 1) suggests that exposures in early life, such as a large burden of infections and chronic undernutrition, that were experienced decades ago by today's adults in LMICs still have negative effects on their health[39–42]. Importantly, with respect to the present day, in the 1970s and 1980s, more than 50% of the population in LMICs were stunted[43], thus introducing long-term deficits in metabolic capacity in these populations. Adults in LMICs tend to experience cardiovascular and metabolic conditions much earlier in their adulthood than those born and raised in HICs, which may be due to such different population penalties from hardship earlier in life[44–46].

Although undernutrition has not disappeared in LMICs, over the last four decades we have observed a rise in BMI in children and adolescents worldwide[29]. Within one or two generations, as in the cases of Mexico[47] and Chile[48], this transition has resulted in what is known as the "double burden of malnutrition" at the individual, household and community level[49,50]. Children exposed to the double burden will not develop to reach their full potential when transitioning into adulthood[41,51–53], and it is likely that today's children in LMICs will also have higher exposures, to ever more common obesogenic environments, at higher doses and for longer durations than in the past.

Recent work has attributed much of the world's rise in BMI, and thus increases in obesity, to changes in BMI in rural settings[28], and understanding the contribution of the rural and urban environments to obesity is important. When compared to those exposed to rural or urban environments only, migrants serve as tracers of how exposure to different environments affect cardiometabolic adaptations and responses[54]. For example, in the PERU MIGRANT study, it was observed that among rural-to-urban migrants, people who migrated when aged older than 12 years had higher probability of developing diabetes, impaired fasting glucose and metabolic

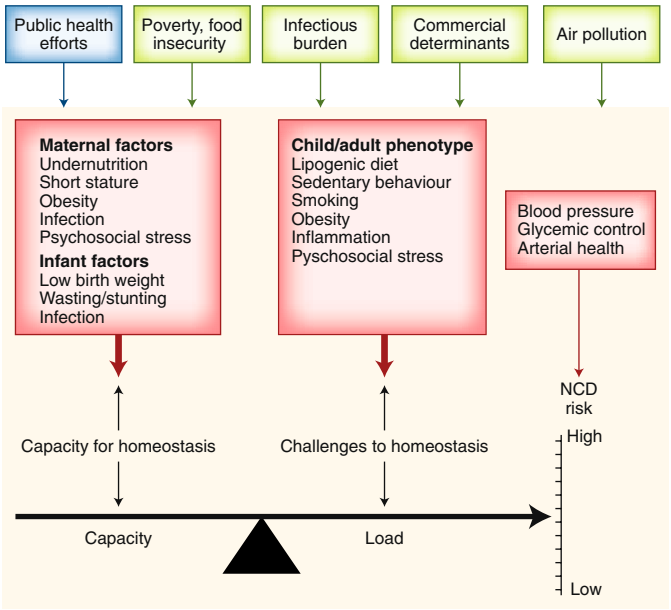

Fig. 1 | The capacity-load model. The capacity-load model considers that NCDs arise through the inability to maintain metabolic homeostasis (healthy blood pressure, glycemic control, arterial health), resulting in the development of pathophysiological traits that eventually lead to overt disease. NCD risk is directly shaped by many components of physiology and behavior (shown in red). A wide range of factors manifesting in the body impose a 'metabolic load' that challenges homeostasis: examples include obesity, sedentary behavior, diets high in sugar or fat, psychosocial stress, smoking and the response to infection. High load elevates NCD risk, whereas low load reduces it. However, the 'metabolic capacity' for homeostasis is also strongly shaped by patterns of growth and development during 'critical windows' in early life, when many physiological traits relevant to homeostasis are determined. High capacity protects against NCDs, whereas insults to metabolic capacity elevate risk. The primary environmental influence on metabolic capacity during early critical windows is maternal phenotype. NCD risk thus emerges through the interaction of metabolic capacity and load. Beyond the body, numerous components of the environment also shape NCD risk. Harsh environmental factors (shown in green) drive elevations in metabolic load and deplete metabolic capacity. Public health efforts (shown in blue) aim to counter these effects by promoting metabolic capacity in early life (promoting maternal and infant health) and reducing metabolic load in children, adolescents and adults (promoting healthy lifestyles). This integrative model serves to clarify how NCD risk is shaped both by developmental experience and by exposure to many aspects of today's unhealthy environments. Simply put, 'the higher the load, and the lower the capacity, the greater the NCD risk'[209].

syndrome than those who migrated at younger ages[55]. These observations indicate different reactions to the exposure to urban environments depending on age, with those migrating at younger ages having greater plasticity to adapt to their new environments.

The nutrition environment. Sustainable food systems are essential to achieve the SDGs[56]. Economic improvement, trade liberalization and increasing urbanization have resulted in important changes in the LMIC food environment, defined as the composition, promotion, availability, accessibility and affordability of foods[57].

In recent years, LMIC settings have experienced an increased availability of foods produced by large international food corporations, as well as an important expansion of supermarkets and fast-food chains driven in part by the so-called commercial determinants

Box 2 | Air pollution and cardiometabolic disease in India

South Asia has the worst air pollution worldwide, being home to 17 of the top 30 cities with the highest levels[212]. Although a global problem, the manifestation of air pollution in countries such as India has some unique features that exacerbate cardiometabolic disorders. These include the large numbers of two-stroke vehicles, the combustion of lower-quality fuels, the open burning of solid fuel in residential cooking stoves and the poor regulation of industrial processes[213]. One of the most widely investigated markers of air pollution is particulate matter of size ≤2.5 μm (PM2.5). Over the last three decades, PM2.5 concentrations are estimated to have increased by ~25% in the South Asian region, exacerbated by rapid rates of unregulated urbanization and industrialization[212,213], while the high density of urban settlements results in substantial population exposure to this stress. Even in rural areas, indoor air pollution remains substantial. Over 80% of the rural Indian population continues to burn biomass for home cooking and heating[214], though efforts are underway to reduce this practice. Poorer households are least likely to have access to cleaner fuels, and they typically lack a separate kitchen area, resulting in high levels of household air pollution to which women and children are especially exposed[214]. The consequence is that average daily exposure to concentrations of PM2.5 in India consistently and substantially exceeds World Health Organization (WHO) recommendations, primarily through household exposure in rural populations and through outdoor exposure in urban areas[212].

Epidemiological studies identify air pollution exposure as the third most important risk factor for ill health in India[215], with higher levels of particulate matter associated in cross-sectional studies with the risk of hypertension, diabetes and cardiovascular disease, and with biomarkers of inflammation[216]. In the city of Chennai, for example, the prevalence of diabetes was 77.5% higher (34.8% versus 19.6%) in areas of high versus low levels of PM2.5 exposure[217], while in Delhi, higher daily levels of air pollution were associated with a 24% increase in emergency room visits for acute coronary events[218]. Using long-term data from satellite records, premature deaths in India attributable to PM2.5 exposure increased by ~40% between 1999 and 2014. These trends were driven primarily by increases in ischemic heart disease and stroke, which increased by 40% and 48%, respectively[219].

At a mechanistic level, there is increasing evidence that air pollution directly influences cardiometabolic risk markers, such as blood pressure and insulin resistance. In the Andhra Pradesh Children and Parents Study, exposure to PM2.5 was positively correlated with blood pressure and hypertension in women, though the associations were weaker in men[220]. Another study in rural West Bengal found that cooking with biomass exacerbated systemic inflammation, oxidative stress, hypertension and tachycardia[221].

In those who already have cardiometabolic conditions, representing a large proportion of the Indian population, air pollution may worsen the progression of disease. For example, among diabetic patients studied in the city of Pune, exposure to air pollution was associated with poorer glycemic control and systemic inflammation, indicating the exacerbation of diabetes complications[222,223].

Beyond its adverse metabolic impacts in adulthood, air pollution also generates detrimental effects on early growth and development, thus undermining the long-term metabolic capacity for homeostasis. For example, household air pollution has been associated with an increased risk of low birth weight and intrauterine growth delay in India[224,225], which propagates to shorter child height[226].

Trends in air pollution in India are complex and are driven by many different factors associated with economic development. However, the resulting health problems clearly have commercial determinants. The decentralization that is characteristic of Indian cities has increased travel distances and encouraged a shift to motorized transportation, largely through private transport. Between 1981 and 2002, the number of motorized two-wheelers increased 14-fold, and the country currently has the largest sales of such vehicles worldwide[227]. These sales overwhelm urban infrastructure, and persistent traffic congestion substantially elevates emissions.

of health (see below)[58,59]. As a result, people living in urban areas have rapid and cheap access to more packaged, ready-to-eat or ready-to-heat foods manufactured by multinational food corporations, as compared to local foods that could be obtained in traditional open-air markets, such as fruits, vegetables and cereals[60,61]. In the case of children, this scenario is worsened by the presence of street vendors in the surroundings of daycares and schools who now offer snacks and industrialized beverages to children instead of natural foods, as shown in examples from Brazil, Guatemala and Mexico[62–64]. Compounding this, an important proportion of children do not have access to clean water during long periods in the day, and may be offered sugar-sweetened beverages by preference[65]. Similarly, over the past two decades, away-from-home food intake has undergone a large increase, with, for example, fast-food chains now spread all over Latin America[58].

The increased availability of packaged and ready-to-eat foods is worrisome because these tend to be higher in nutrients of concern, such as added sugars, sodium, saturated fat and *trans* fats, than unpackaged foods, while also being deficient in key micronutrients[66–69]. Moreover, recent evidence indicates that the nutrient composition of packaged food products varies substantially around the world, being considerably less healthy in LMICs such as Chile and Mexico[70]. No age group is unexposed to these dietary trends, and even infants are at risk of receiving energy-dense, micronutrient-poor complementary foods[71].

Importantly, food prices have also evolved in recent years in LMICs. Large-scale sells have allowed lower prices for packaged food products, so that it is now relatively cheaper to buy foods high in sugar, fat and sodium, such as sugary sodas or salty snacks, than healthy foods such as fruits, vegetables and dairy products, although this association may vary depending on the income and development level of the country[72]. The result is that these products have become accessible to, and marketed to, the poorer socioeconomic groups. The consumption of ultraprocessed foods has increased, for example throughout the Latin American and Caribbean region, while consumption of healthy foods has remained low[73]. Consumption of ultraprocessed foods is a key factor driving the epidemic of NCDs currently imposing the greatest health and economic burden in LMICs, such as diabetes, cardiovascular disease and some types of cancer[60,74–76].

It is important to note that the penetration of ultraprocessed foods has also reached rural settings, in which women increasingly work more in non-farm occupations, which in turn increases the demand for convenience food[58,77]. Supermarkets initially opened in large cities but have progressively expanded to small towns in rural areas through convenience stores and small supermarkets. Marketing strategies for unhealthy food products have also spread into rural areas. Therefore, not surprisingly, recent reports indicate that is precisely in rural areas that obesity is increasing faster in LMICs[28].

Box 3 | Slum conditions and cardiometabolic diseases in Africa

Khayelitsha is the largest informal township in Cape Town, South Africa, and is home to almost half a million predominantly black residents. The history of the establishment of Khayelitsha, which means "our new home" in isiXhosa language, dates back to the apartheid policies of racial segregation in South Africa.

Following the first racially segregated settlements established in the early 1900s, Khayelitsha was established in the mid-1980s as the legal residence for black Africans in Cape Town[97]. Located on low-lying sand dunes beyond Cape Town's urban boundaries, the settlement was planned to be isolated from the rest of the city. Although these segregation laws have since been abolished with the transition to democracy in the 1990s, the spatial marginalization of Khayelitsha means that although there has been a growth of commercial formal and informal activity, the settlement remains characterized by high levels of unemployment and poverty and by health outcomes significantly poorer than the national and city average. Of note, mortality from stroke, hypertensive disease and diabetes is higher than the average for Cape Town[228].

These diseases are influenced by dietary and physical activity habits, which are in turn enabled or impeded by the food and activity environments. In Khayelitsha, the food environment is characterized by food insecurity and poor dietary diversity with insufficient access to healthy food[229]. Geographical inaccessibility, with many households having to travel long distances for food shopping[230], is exacerbated by inadequate access to electricity and consequent inability to store perishable fresh foods such as fruits and vegetables, even where market or non-market sources of these foods exist, as well as by an environment unconducive to urban agriculture. These challenges mean that even when residents are aware of the health impact of high-salt, high-fat processed foods, their agency to make health food choices is significantly diminished. A study exploring food insecurity in patients with hypertension or diabetes residing in Masiphumelele, another low-income informal township in Cape Town, showed that patients with cardiometabolic disease had a good understanding of the importance of a healthy diet, in particular fruit and vegetables[231]. In this study, patients describe receiving nutritional advice from the clinic as part of their diabetes or hypertension clinical management that implied a level of choice that did not exist in reality, and a lack of acknowledgment on the part of clinicians of the lack of food choices in patients' contexts. Barriers to accessing these foods expressed by the study participants included the cost, short shelf-life and poor quality of available fresh foods in their neighborhoods.

Similar barriers to physical activity are experienced in these informal settlements. In other words, although residents recognize the value of taking walks and exercise, the perceived and experienced threat of violence, lack of access to well-maintained open public spaces and playgrounds, and lack of opportunity for active travel due to the remoteness of the location[230] conspire to result in insufficient levels of physical activity to reduce the risk of cardiometabolic disease.

These examples highlight the influence of the built environment, particularly in the context of informal settlements, on cardiometabolic risk. As the proportion of urban residents residing in conditions of informality continues to increase in Africa's rapidly growing cities, a recognition by clinicians of the importance of this urban exposure and a willingness to engage with the urban design and planning sectors, which play a critical role, is vital to reduce these population health inequities.

Air pollution. Another key source of metabolic load in LMICs is air pollution. This contributes to adult morbidity and mortality through chronic obstructive pulmonary disease (COPD), stroke and ischemic heart disease, but also affects young children through acute lower respiratory infections[78], thus undermining metabolic capacity in early life (Fig. 1). Already, air pollution is suggested to account for 19% of all cardiovascular deaths and 21% of all stroke deaths globally[79], and 87% of this burden occurs in LMICs, concentrated in particular in sub-Saharan Africa and South and East Asia[80] (Box 2).

Burning biomass for household fuel has long been a key source of air pollution in LMICs[81,82], and more recently there have been rapid increases in the volume of vehicle traffic in many cities, which pose an additional burden on human health in urban areas where road vehicle emissions are further concentrated[83–86]. As reported by the International Energy Agency, transport accounted for one-quarter of total global CO_2 emissions in 2016, a level 71% higher than in 1990[87]. The highest absolute increase was in road transport, and although the Americas have historically had the highest transport emission levels of all regions, and this trend has continued over recent years, Asia is quickly closing the gap, with annual growth rates in emissions five times larger than that of the Americas[87]. Importantly, urban planning in LMICs has lagged behind the rapidly rising traffic volumes[88,89], and the typical vehicles in LMICs are more polluting than those in HICs[78,90].

There is increasing recognition that air pollution damages almost every organ in the body, and is for example linked with heart disease, dementia and diabetes morbidity and mortality[79]. Air pollution shows a dose-response association with ill health, but beyond that, those already affected by NCDs are also more susceptible to the harmful effects of air pollution[91,92]. Clearly, exposure to air pollution lies largely outside individual control and represents a generic toxic environment (Box 2).

Urbanization. Urbanization has been one of the most important demographic shifts worldwide during the past century. Today, more than half of the world's population resides in urban areas, representing more people than the world's total population in 1960[93]. Between 2015 and 2030, the world will add 1.1 billion new city dwellers, increasing the global urban population by 28 percent, from 4.0 billion to 5.1 billion[94,95]. Furthermore, the majority of projected urban population growth will be in Africa and Asia, followed by the Latin America and the Caribbean region[94,95].

Within cities in LMICs, the majority of individuals simultaneously experience political, economic, housing and ecological vulnerability[96]. Given the large number of individuals residing in urban areas, these vulnerabilities translate into the exposure of the majority of the population to an environment that directly impacts their risk of cardiometabolic disease. Furthermore, within this environment there is inequitable access to opportunities for healthy eating, active living and unpolluted environments—an inequity that exists both within countries and compared to the same context within HICs.

The historical contexts around which cities in LMICs have developed have influenced vulnerabilities that persist and continue to influence the nature of urbanization, and hence the risk of cardiometabolic disease development, in LMICs (Box 3). First, the urban centers of many cities in Africa, Asia and Latin America are rooted in colonial legacies of sociopolitical exclusion that evince today as spatial inequalities that manifest in terms of proximity to aspects of the city that are meant to confer an urban advantage, such as infrastructure and amenities, and are consequently closely linked to

health inequities[97]. Second, unplanned and unmanaged growth in rapidly growing LMIC cities creates opportunities to live exceeding the opportunities for employment, along with high rates of poverty, resulting in an urban form overwhelmingly characterized by conditions of informality: in Africa, for example, 62% of urban dwellers live in slum conditions[98]. Last, the population pyramids of LMICs highlight a distortion in urban versus rural populations, with an increasing proportion of adolescents and young people residing in cities, exposed to environments that are not conducive to health-promoting behavior[99].

Despite being largely unplanned and illegal, informal settlements are persistent features of the urban landscape of LMIC cities, and a growing proportion of the population lives in such settlements[100]. In response to this, the New Urban Agenda[101] adopted by the United Nations Conference on Housing and Sustainable Urban Development and endorsed by the UN General Assembly and the SDGs[102] (Box 1) advocates for a shift away from eradication to upgrading of informal settlements for inclusive human settlements (SDG 11) and health and well-being (SDG 3). Such 'Healthy Cities' interventions have primarily focused on improving access to water and sanitation[103], with little or no attention to primary NCD prevention through improving active living and healthy eating environments or reducing air pollution. One example of a city in Africa taking the initiative to address unhealthy environments associated with NCD risk is the collaboration between the city government of Accra, Ghana, and the World Health Organization (WHO) on an air pollution campaign[104]. The poor urban environment particularly affects the urban poor.

The WHO's Health-in-All-Policies approach[105] aims to increase access to healthy, affordable foods and opportunities for human interaction and for physical activity[106], all of which are driven by sectors outside of health or healthcare. These obesogenic elements of the urban built environment that influence obesity and NCDs—high prevalence of energy-dense foods, marketing of unhealthy foods, lack of or limited footpaths and cycle infrastructure and safe places to play, exposure to air pollution—are multiple, entangled and interconnected, and people living in informality are particularly vulnerable to them because they are least equipped to compensate for the inextricable obesogenic conditions that epidemiological, nutritional and urban transitions generate. Informal built environments add complexity to the process of addressing the causes and complications of cardiometabolic disease as, for example, it may not be possible to implement interventions to address obesity through formal regulated structures[99].

Nonetheless, cities can play a vital role in addressing health and social inequity[99,103,107], and greater coordination across sectors could help improve health outcomes. This would require making connections between relevant health indicators and urban infrastructure initiatives, such as monitoring changes in the urban food environment and their long-term impact on healthy eating behavior and cardiometabolic disease outcomes. For example, case studies have demonstrated how integrated urban planning can support the development of equitable access to healthy food systems and prevent food deserts, where fresh food is unavailable and only unhealthy, heavily processed foods high in sugar, fat and carbohydrates are readily available and affordable[108].

Commercial determinants of health

The etiology of cardiometabolic diseases is complex and influenced by different individual, social, environmental and private sector determinants[109]. The recent increased risks of developing many of the major cardiometabolic diseases are associated with the production, marketing and consumption of commercially produced products, food and drinks—such as those containing sugar, salt and *trans* fats, alcohol and tobacco[110]. For example, the global adult per-capita consumption of alcohol per year increased from 5.9 to 6.5 liters between 1990 and 2017 and is projected to reach 7.6 liters by 2030[111]; this includes a 104% increase in the South-East Asian and a 54% increase in the Western Pacific regions as defined by the WHO. This increase in alcohol use is especially high in upper-middle-income countries such as China, India and Vietnam, where levels of alcohol consumption are now higher than in some European countries (Box 4). The growth in the intake of snacks, soft drinks and processed foods in LMICs is also faster than that in HICs, and is projected at 20% in the next 5 years, whereas little or no growth is expected in HICs[112].

Commercial determinants of health are "strategies and approaches used by the private sector to promote products and choices that are detrimental to health"[113]. This single concept includes consumer and health behavior, individual choice at the micro level, global risks to society, the global consumer society and the global economy at the macro level. In fact, reaching any set target to reduce cardiometabolic disease will be challenging as long as strategies and policies are not designed to govern the commercial drivers contributing to the rising burden of cardiometabolic disease worldwide. As internationalization of trade, capital and information in the food, beverage, and tobacco industries have substantially increased, progress toward preventing and controlling cardiometabolic diseases will require the public health community to address industry responsibility in relation to the burden of cardiometabolic diseases[112,114–116].

The rise in the consumption of unhealthy commodities reflects the fact that multinational companies are increasingly targeting LMICs not only for their huge collective population size, but also because governmental legislation protecting LMIC populations from unhealthy commodities remains much weaker than in HICs, where the impacts on health are already well recognized and supported by a strong scientific evidence base[26]. The role of commercial interests in negative health effects is highlighted by the promotion of private vehicle ownership, which simultaneously increases air pollution and undermines physical activity patterns[117,118].

Commercial influences may have both direct and indirect influences on cardiometabolic diseases and on contributory factors such as smoking, inactivity and obesity, and these influences often operate through long and complex causal pathways. The commercial influences can also interact with one another, their contexts and society, which has implications for interventions at different levels[109]. For example, researchers have identified practices from industry-funded charities, such as the International Life Science Institute (ILSI)—an institute with the purported mission "to provide science that improves human health and wellbeing"[119] founded and funded by Coca Cola and supported by McDonalds, Nestle and other corporate entities—that act against their purported objectives. Studies found instances of ILSI seeking to influence research, conferences, public messages and policy, including instances of punishments for related bodies failing to promote industry-favorable messaging[120].

Similarly, children are important to industry marketers for many reasons: they often have access to their own money to spend, they influence parental selection of products and they will grow up to be life-long consumers[121]. Most families have televisions at home, and simultaneous with the spread of televisions, exposure to food advertisements has increased across all socioeconomic groups[122–125]. With the higher penetration of the Internet, new forms of food promotion are being developed, particularly for children and adolescents[126,127]. There is robust evidence showing that unhealthy food products are more heavily advertised than healthier food options; therefore, higher exposure to food marketing is likely promoting or sustaining unhealthy dietary behaviors in LMICs, especially among children[128]. Moreover, increasing evidence indicates that food marketing has been changing its potential audience, now targeting socioeconomic and ethnic minorities and hence increasing the risk of widening existing health and nutrition disparities[129].

Box 4 | Alcohol, a strong commercial determinant of health

One of the leading risk factors of deaths worldwide is the harmful use of alcohol, which is linked to over 200 different types of diseases and injuries and can have substantial social and economic implications for a country[232,233]. In 2016, almost 5.3% (3 million) of all deaths worldwide were caused by harmful use of alcohol[234]. According to recent statistics, alcohol is consumed by some 2.3 billion people worldwide, and the total per capita consumption has risen from 5.5 liters in 2005 to almost 6.4 liters in 2016[234]. In 2016, an estimated 1.7 million NCD deaths and 65.5 million NCD disability-adjusted life years (DALYs) were caused by alcohol consumption[234]. Additionally, an estimated 0.9 million injury deaths and 52.4 million injury DALYs are attributed to alcohol[234].

The risk from alcohol is associated with the production, marketing and consumption of alcohol products by commercial entities[110]. The alcohol industry, much like the tobacco industry, exerts influence through four main channels: marketing, lobbying, corporate social responsibility strategies and extensive supply chains worldwide[113]. One of the most impactful factors associated with alcohol consumption is alcohol marketing, and the regulation of such marketing has been identified by WHO as a "Best Buy" policy for reducing the harmful use of alcohol[235]. Although limited in number, existing studies show that the alcohol industry uses policy-influencing direct and indirect strategies that include extensive lobbying and attempts to shape public perceptions of alcohol and the scientific content of regulatory debates[236]. For example, 23 grants were given to researchers by the industry in 13 countries over 6 years to influence the generation of evidence against alcohol[237]. For this reason, calls for researchers to sever financial ties with the alcohol industry and warnings about engaging with the alcohol industry altogether have been issued[238,239].

Companies in the alcohol industry also uses corporate social responsibility activities to define themselves as corporate citizens that are part of policy solutions, and organizations such as the International Alliance for Responsible Drinking, previously the International Center for Alcohol Policies, are a major component of this strategy[236,240]. For example, the alcohol industry has been promoting weak interventions to control drunk driving; a 2016 study showed that less than 1% of the industry's actions to reduce drunk driving aligned with evidence-based recommendations[241], and at the same time the industry increased its involvement in policymaking and scientific research[242].

India has in recent years seen a staggering increase in alcohol consumption, in which the average adult per capita alcohol consumption increased by 19% between 2005 and 2010[241]. Diageo, a London-based multinational alcohol corporation, is one of the largest sellers of alcoholic spirits in India and has over $1.1 billion of investment in the country[242]. The company has employed various tactics to speed its growth in emerging markets such as India. However, some of this growth involved controversial activities: for example, in 2011 Diageo was charged with major violations of the Foreign Corrupt Practices Act by the US Securities and Exchange Commission, having paid over $1.7 million to hundreds of Indian government officials. The company also uses strategic marketing to attract new, young consumers: for example, sale of alcohol in small sachets ("tetrapacks") or mini-bottles. Diageo also recognized a trend of growing alcohol consumption by Indian women and launched "a community investment program that aims to empower women through learning"[243]. These programs promote individual-level, voluntary behavior change strategies, diverting investment and attention from effective public health strategies that modify the alcohol environment to reduce its misuse[241].

This generation of social collective harm is only one strategy being used to open new markets in LMICs and promote the consumption of products linked to increased risk of cardiometabolic disease. Industry also engages with and markets to stakeholders—people with influence in the health policy and health investment world, as well as donors, policy influencers, staffers, legislative aides, etc.—and politicians to influence the policy agenda and undermine public health legislation[121]. This has been quite effective for their work to prevent industry regulation at national level (Box 4).

Countering cardiometabolic diseases in LMICs

Population-based efforts. Strategies to address cardiometabolic diseases in the majority of LMICs to date have predominantly focused on the identification of risk factors as well as on screening to detect and treat diseases[130]. Although these approaches are important, there is a need for a greater focus on prevention strategies that act on the upstream determinants. As NCDs have risen up the global agenda, population-wide interventions merit attention[131]. Population-wide preventive strategies focus on intervening to influence the determinants of health in large groups, with the aim of shifting the whole population's distribution of a given risk factor[132–134]. For example, it has been proposed that reducing sodium intake and eliminating the intake of artificial *trans* fatty acids could delay 94 million deaths worldwide within 25 years[135]. This strategy has been recently applied in Peru, where a pragmatic population-based approach using a salt-substitution strategy has produced community-wide reductions in blood pressure levels and incidence of hypertension[136,137].

Until recently, few instances of population-level interventions targeting cardiometabolic risk factors in LMICs were available. As one example, the Framework Convention for Tobacco Control (FCTC) provided a clear and systematic effort to include population-wide interventions as a critical step to change the tide of tobacco consumption. The FCTC proposed structural interventions, such as banning indoor smoking, increasing tobacco prices and restricting marketing channels promoting smoking, along with individual-level interventions such as the provision of smoking cessation programs, to reduce tobacco-related health problems[138]. It is now recognized that these strategies have been key to stabilizing and reducing tobacco consumption globally[139], and in particular in LMICs such as Mexico[140], Brazil[138] and Thailand[141].

Strategies similar to that of the FCTC are being implemented in various countries to reduce obesity and metabolic diseases. Latin America has been at the forefront of the implementation of interventions aimed at reducing the consumption of sugar-sweetened beverages (SSBs) and low-nutrition, high-energy foods (junk food). The SSBs tax in Mexico was one of the first nationwide taxes aimed at reducing the consumption of sugary drinks in the country; two years after its implementation, consumption had decreased on average 8.2%, while that of untaxed beverages, such as water, increased 2.1%[142]. These changes, along with projections of the potential impact of the tax in deaths, health care costs, and obesity and diabetes cases, created momentum for the implementation of similar taxes in other countries and for a consideration of doubling the current 1-peso-per-liter-tax in Mexico[143].

More recently, Chile has set a global example in the implementation of a complete package of structural interventions to curb obesity[144,145]. In 2014, Chile modified its previous tax on sugar-sweetened beverage, increasing the tax rate from 13% to 18% on industrialized beverages with high levels of sugar (>6.25 g sugar/100 ml) and decreasing the rate from 13% to 10% on industrialized

beverages with low or no sugar. By 2016, the country implemented food labels to clearly identify foods and beverages high in sugars, calories, sodium or saturated fats (now called "high-in" products). Simultaneously, the food environment was regulated, banning the sales of these foods in schools and the marketing of products in the media aimed at children under 14 years of age[144–146]. Although the overarching impact of these changes is still under analysis, recent studies have shown that people understand the labeling well and that after its implementation they improved the healthiness of their food and decreased the purchases of "high-in" products of some food categories, such as sweet-sugared beverages and breakfast cereals. Similarly, food-ad exposure on television decreased among preschoolers and adolescents, and exposure to unhealthy food products at school also decreased substantially. Interestingly, it also seems that the food industry is responding to the onset of regulation by decreasing the amount of sugar and sodium in some food categories. Other countries in the Latin American and Caribbean region, such as Uruguay and Peru, have approved similar policies[147,148].

Efforts to regulate the obesogenic environment are closely linked with the urban health agenda in Latin America[149,150], which also includes the redesign of urban spaces and the provision of better infrastructure to increase active transportation, reduce car use, provide green areas and increase public safety so as to incentivize utilitarian and leisure-time physical activity[151]. Combating obesity requires integrated governmental and societal action to protect population health[152,153].

Improving healthcare. LMICs face major challenges in regard to treating cardiometabolic diseases. Usually, health systems, especially the primary healthcare care level, are better prepared to respond to acute conditions, to provide maternal and child care, and to target prevention and control efforts oriented to infectious diseases. The response to chronic conditions is poorer, mainly because, to combat these, people need frequent access to the health care system, good and long-term adherence to pharmacological and non-pharmacological treatment, and good coordination of care across levels of specialized treatment. In this context, different solutions have been proposed to strengthen the current health system, to implement different strategies to promote disease self-management or to identify stakeholders that can support the health system[154]. Here we briefly mention the role of technologies and health (mHealth), integration of care and task shifting, whose application has been highly innovative in LMIC settings.

mHealth has been applied in LMICs by different actors and with diverse purposes. For example, in terms of disease prevention, particularly in weight reduction, patients and caregivers have been offered different types of technological support to promote behavioral change, such as mobile phone apps, Web pages and short messaging services (SMS)[155–158] as reminders to increase adherence to lifestyle changes through improving knowledge and enhance motivation to change behavior[159]. On the other hand, health workers have received training in the diagnosis and management of cardiometabolic diseases through eHealth, whereas in other cases, both in HICs and LMICs, health professionals in remote areas have received support through telemedicine[23,160–163].

Given the limitations and shortcomings of existing healthcare systems and infrastructure in LMICs in terms of budget, services and human resources, compounded with the challenges of chronic conditions and multimorbidity[164], moving away from addressing single diseases toward the integration of care seems to be a suitable response in LMICs[165–171]. Different projects have been working toward improving health systems at all levels (primary care, hospitals, specialized institutes) and working with all stakeholders (health workers, managers, regional health directors) to improve access to care, increase availability and affordability of medicines, improve coordination of care or improve patient satisfaction[172–175].

Given the comorbidity between mental health and cardiometabolic conditions, some projects have promoted the opportunistic screening of mental health disorders in this group of patients and their referral using existing resources[176]. Other ongoing initiatives are using mHealth technologies to treat mild to moderate depressive symptoms among patients with cardiometabolic conditions[177].

It is well known and commonly reported that health workers are overwhelmed by their daily activities, and this is also true in LMICs. To overcome this, some initiatives have targeted the transfer of some work from health workers to other key actors—community health workers, caregivers, and others[178–182]. Also, to address the shortage of physicians, task shifting has moved some tasks to other healthcare professionals, for example, by assigning nurses to manage hypertension[183]. These strategies have usually been accompanied by training and technological support, leveraging mobile technology, and have been used mostly to diagnose or identify patients at risk[154,184,185].

Future directions

Intersectoral strategies. Although both LMICs and HICs have rising trends of obesity and diabetes, cardiovascular disease mortality is decreasing in HICs but not in LMICs. Strategies to reduce the increasing burden of cardiometabolic diseases in LMICS are desperately needed. Recognizing the links between NCDs and the wider development and economic agendas within LMIC policy environments is crucial to countering NCDs. Among the possible approaches, promoting leadership to champion health issues in non-health sectors, such as agriculture, economics or trade, is an urgent task to ensure that a health perspective is included in all policy decisions. Long-term exposure to obesogenic and toxic environments, including fundamental drivers such as the commercial determinants of health, will require comprehensive responses going well beyond the health sector. Industry is wealthy, complex and heterogeneous, so public health organizations will need more than simple facts to confront it. Addressing the role of industry in NCDs raises discomfort for many institutions and policy makers, due to potential conflicts of interest and distrust toward some companies. This does not mean that there is no potential to engage and partner with industry, but rather that such partnerships are complicated and raise potential ethical issues, especially for those who generate evidence or policy around cardiometabolic diseases.

LMICs have historically suffered the double burden of malnutrition, leaving a long-lasting metabolic mark in their population. Understanding the role in later health outcomes of the biological penalties suffered by LMIC populations in early life may provide additional information to help develop population-wide prevention initiatives that complement existing approaches to managing individuals at high risk. LMICs also host areas of conflict and are politically fragile states, introducing another example of rapid changes that may affect NCD development and control[186–188]. LMIC populations are also those most vulnerable to wider planetary injuries, including climate change[2,189,190]. Efforts to prevent NCDs should not be considered as competing with other health and development agendas, but rather can serve as a unifying force, ultimately driving the common goal of improving people's well-being across the life course.

We think that there is a need for multi-stakeholder dialog platforms—that is, involving public, private and civil society sectors—dialog platforms and mechanisms to support intersectoral policy action plans that bring together sectors that influence NCDs and its risk factors, to ensure that policies are aligned to prevent cardiometabolic diseases. Such spaces are vital to bridging the gap between those working to address knowledge gaps, such as researchers; actors responsible for implementation at scale, such as policymakers and practitioners; and potential beneficiaries and advocates, which involve the wider society.

Improved disease surveillance. In addition to the intersectoral governance mechanism required, there is a need for integrated surveillance of cardiometabolic disease risk that incorporates both individual-level health outcomes and community-level health-determinant exposures. Although surveillance of this nature using traditional survey methodologies is resource intensive, ongoing advances in technologies to capture area-level data on health determinants are noteworthy and should be incorporated into NCD prevention efforts. For example, advances in earth observation data derived from satellite imagery, which are increasingly available at neighborhood scales[191], could be harnessed to monitor relevant changes in the urban environment and the health impact of built-environment interventions on healthy eating behavior and NCD risk.

Prioritizing adolescents and youth. There must also be a focus on reducing the exposure of adolescents and young people to risk factors for cardiometabolic disease. Multifaceted intersectoral efforts that seek to intervene appropriately over a long time period are crucial to reduce NCDs in children and adolescents. This is particularly vital in considering strategies that target young people for cardiometabolic disease prevention. Introducing healthier behaviors and protective factors during childhood and adolescence can significantly change an individual's health trajectory into adulthood[192,193]. However, besides sexual and reproductive health, the majority of adolescents do not perceive a need for NCD prevention, nor do they routinely access health care[194–196]. Therefore, there is a need for strategies to identify ways to improve the health of younger populations that are not purely within the context of either the health sector, the household or educational establishments[194,196]. Such strategies would need to be multisectoral, recognizing the interactions between environmental and economic factors, social norms and personal choice[197].

Improving our understanding of complex systems. Investment in the long-term understanding of NCD-related outcomes produced by LMIC environments will be needed. Scientific research is a fundamental resource for informing policy and decision making. The LMIC scientific community must seek to understand the rise in cardiometabolic diseases in their regions to identify successful interventions to control cardiometabolic diseases. This will require, at minimum, capacity in key and emergent disciplines such as complex systems thinking[198], implementation science[199,200] and decision-based models[201,202].

It is now clear that the key risk factors for cardiometabolic diseases arise in a heavily interrelated physical, biological, social and economic space. Given this complexity, we will need to find creative solutions that generate the benefits we expect, without producing negative reverberations in the rest of the system. Complex systems thinking provides an appropriate conceptual and methodological framework to pose and solve some of these questions; however, its use remains limited, even in HICs[203]. Similarly, research in LMICs remains mainly directed toward simple etiological studies that try to uncover the causes of diseases or their complications. For cardiometabolic diseases, a lot is already known about prevention and treatment, but the implementation of these solutions is painfully slow. Implementation science tries to close the gap between knowledge and practice, by proposing specific frameworks and methods to translate, adapt and facilitate the implementation of proven interventions[204]. As yet, however, there are few implementation science departments in LMICs[205]. Finally, mathematical models are increasingly being used in the public health arena to help overcome data limitations, understand the dynamics of complex problems, simulate different intervention scenarios and provide long-term estimates of potential interventions. Although some examples of these efforts produced in LMICs exist, their use is still rare and is not fully embraced by the academic community[206]. While imperfect, mathematical models can be informative for policy decision making and extremely cost-effective for understanding the potential impacts of decisions at the population level. However, such modeling requires strong interdisciplinary teams, capable of bridging methodological and conceptual differences, that are sorely lacking in LMIC settings.

Funding. LMICs need to drive their research agenda and keep relevant research thriving in order to achieve and secure population gains given the large burden imposed by cardiometabolic diseases. Yet sufficient funding remains a challenge. Health priorities in LMICs are often different from those in HICs. Local funding for the development of structural interventions to solve population health issues remains scarce, and new models of funding will be necessary[207]. Maternal and child health agendas have achieved significant advances, which the NCD agenda has yet to replicate, in terms of the alignment of political will and the development of agendas accompanied by adequate funding[208]. To harness large population gains, given the widespread nature of NCDs, funding will likely not need to target cellular or molecular biology, but rather the complexity of the inter-relationships between humans, private capital, public interest, the role of governments and the ability of the civil society to collectively work toward a more humane, equitable and sustainable world. Increasing the funding for population health interventions is also needed. This funding would be needed to be made available to study the development and evaluation of interventions, acknowledging their complexity, and how best to implement them. Funding for the actual implementation and scaling-up of proven interventions will also be necessary to guarantee advancements in cardiometabolic diseases, and NCDs in general, in LMICs.

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