Obesity in Low- and Middle-Income Countries: Burden, Drivers, and Emerging Challenges

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Annu. Rev. Public Health 2017. 38:145–64

First published online as a Review in Advance on December 23, 2016

The *Annual Review of Public Health* is online at publhealth.annualreviews.org

https://doi.org/10.1146/annurev-publhealth-031816-044604

Keywords

overweight, noncommunicable disease, nutrition transition

Abstract

We have reviewed the distinctive features of excess weight, its causes, and related prevention and management efforts, as well as data gaps and recommendations for future research in low- and middle-income countries (LMICs). Obesity is rising in every region of the world, and no country has been successful at reversing the epidemic once it has begun. In LMICs, overweight is higher in women compared with men, in urban compared with rural settings, and in older compared with younger individuals; however, the urban–rural overweight differential is shrinking in many countries. Overweight occurs alongside persistent burdens of underweight in LMICs, especially in young women. Changes in the global diet and physical activity are among the hypothesized leading contributors to obesity. Emerging risk factors include environmental contaminants, chronic psychosocial stress, neuroendocrine dysregulation, and genetic/epigenetic mechanisms. Data on effective strategies to prevent the onset of obesity in LMICs or elsewhere are limited. Expanding the research in this area is a key priority and has important possibilities for reverse innovation that may also inform interventions in high-income countries.

INTRODUCTION

NCD: noncommunicable disease

DALY: disability-adjusted life year

LMIC: low- and middle-income country (World Bank classification)

BMI: body mass index

By 2013, 2 billion individuals worldwide were overweight or obese, and 62% of the world's obese population resided in developing countries (103). Obesity, in turn, is implicated in the epidemiologic transition from predominantly communicable disease and nutritional deficiency to noncommunicable diseases (NCDs) such as cardiovascular conditions, diabetes, and cancer in the population (98, 106, 113, 116, 164). Currently ranked as the sixth leading cause of disability-adjusted life years (DALYs) globally (75), obesity-related DALYs have been steadily rising in low- and middle-income countries (LMICs) since 1990 (**Figure 1**). In the next 40 years, obesity-related NCDs are expected to double or more than double in LMICs such as Mexico (128). Here, we review the distinctive features of the burden of overweight/obesity in LMICs, including its causes, related prevention and management efforts, data gaps, and recommendations for future research. Although overweight and obesity levels are rising among all age groups in LMICs (107), we focus on adolescents and adults because these populations are currently the most affected by obesity.

DISTRIBUTION AND EPIDEMIOLOGY OF OBESITY IN LMICs

The Global Rise of BMI and Current Prevalence of Overweight and Obesity

In the past three decades, global overweight [body mass index (BMI) $\geq$25 kg/m^2] increased from 28.8% to 36.9% in men and from 29.8% to 38.0% in women (103), while age-standardized obesity (BMI $\geq$30 kg/m^2) increased from 3.2% to 10.8% in men and from 6.4% to 14.9% in women (100). Overweight/obesity is increasing even in countries with historically high levels of undernutrition such as Bangladesh, Nepal, and India, where overweight among women of reproductive age increased from 2.7% to 8.9% in Bangladesh, from 1.6% to 10.1% in Nepal, and from 10.6% to 14.8% in India from 1996 to 2006 (5). Currently, a lower proportion of LMIC

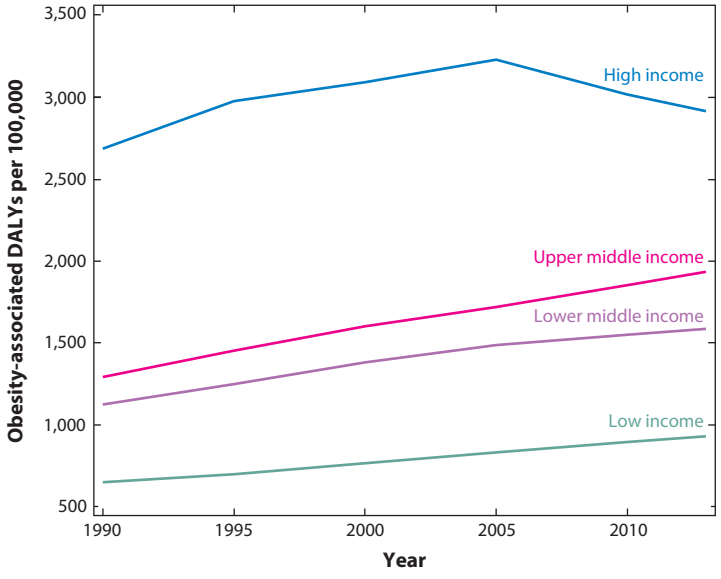

Figure 1

Total obesity-associated disability-adjusted life years (DALYs) per 100,000 population by World Bank Income Category, 1990–2010. Data source: Global Burden of Disease Study (57).

populations is obese relative to high-income country (HIC) populations (103). The prevalence of overweight and obesity in LMICs ranged from a low of 3.2% in Timor-Leste to a high of 83.5% in Tonga among adult men (>20 years) and from a low of 4.7% in the Democratic Republic of Korea to a high of 88.3% in Tonga among adult women (103). In Tonga, Samoa, and Kiribati, the three LMICs with the highest prevalence of overweight/obesity, more than 75% of men and women were overweight or obese (103). The number of obese and overweight individuals, however, is important for health care resource planning. More than half of the world's 671 million obese people live in 10 countries, 8 of which are LMICs: Brazil, China, Egypt, India, Indonesia, Mexico, Pakistan, and Russia (103). China and India account for 15% of the world's obese individuals despite their relatively low obesity prevalence (103).

HIC: high-income country (World Bank classification)

A regional shift in obesity has occurred over time. In 1980, women in Central and Eastern Europe and southern Africa had the highest mean BMI (25.8–26.6 kg/m^2) among LMICs. By 2008, women in North Africa, the Middle East, and southern Africa had the highest mean BMI ($\geq$28.0 kg/m^2 for all) (36). Currently, the Pacific Islands, Latin America and the Caribbean, and the Middle East have the highest burden of overweight and obesity. More than 20% of women are obese in 14 Latin American countries (103), and more than 30% of women in several countries in the Middle East and in North and southern Africa are obese (100). Rates of overweight and obesity in adolescent girls (15–19 years) follow the same regional patterning as is seen in adult women (103). Among adolescent girls in Latin America and the Caribbean—the most overweight and obese adolescents—obesity prevalence is projected to increase by 5% in the next decade (59).

Features of the Obesity Burden in LMICs

Trends in obesity over time. Some researchers have suggested that obesity may be increasing more rapidly in LMICs than in HICs (142) following marked change in dietary structure in as little as a decade in some LMICs; similar dietary changes occurred over the course of the first half of the twentieth century in the United States and Europe (118). However, with the exception of Honduras and Egypt for women, the Global Burden of Disease study reported that the largest increases in the rate of obesity from 1980 to 2013 were in HICs such as the United States, Australia, the United Kingdom, and Saudi Arabia (103). Furthermore, increases in obesity during the 33-year study period were not smaller among countries that already had high prevalence of obesity (103). Overall, there is a lack of reliable, national-level time-trend data to assess the rate of change in obesity in many LMICs.

The World Health Organization (WHO) introduced a voluntary target to stop the increase in obesity prevalence by 2025 (157). According to NCD Risk Factor Collaboration, there is virtually zero probability of achieving this target at the global level (100). To date, no country has reversed its rising obesity trend (127), and current trends suggest that global adult obesity prevalence will reach 18% in men and 21% in women by 2025 (100). Evidence from some HICs suggests a plateauing in obesity prevalence since the mid-2000s (36, 103, 105). Of the countries with Demographic and Health Survey data, Benin shows a slight decrease in obesity in rural areas and a stabilization in urban areas, and data from Mexico show a slowing in the annual increase in prevalence of overweight among women of reproductive age (60). Furthermore, periods of obesity rate stabilization have historically been followed by later periods of increase, suggesting that current leveling-off trends, where they exist, may be short-lived. For instance, urban areas of Rwanda, Zambia, and Brazil saw large increases in annual change in overweight among women of reproductive age after previously having stable or decreasing rates of overweight (60). Adolescents in LMICs are also experiencing an increase in obesity prevalence; a 2009 study from

SES: socioeconomic status

seven LMICs—Bahrain, China, Democratic Republic of the Congo, Egypt, Mexico, Nigeria, and Vietnam—reported an increasing prevalence of overweight among adolescents across all countries (120). Some researchers suggest that without interventions obesity will continue to increase, albeit at a slower rate than seen in previous decades. It remains unclear whether all LMICs are on a trajectory to reach obesity levels as high as some Pacific Island nations, where more than 50% of men and 75% of women are obese (103).

Dual burden of under- and overnutrition. The increase in overweight and obesity prevalence has occurred alongside large burdens of underweight in many LMICs (29, 67, 70). Although the prevalence of overweight exceeded that of underweight among adult women in most LMICs by 2000, levels of underweight are much higher than what is observed in HICs (90). Only rural areas in East Asia, the Pacific, South Asia, and sub-Saharan Africa have higher levels of underweight than overweight (12); additionally, in select areas of rural East Asia, South Asia, and the Pacific, overweight prevalence is approaching underweight prevalence (60). Among adolescent girls, 18% of LMICs have simultaneous increases in underweight and overweight in urban areas (59). To our knowledge, no country has experienced a meaningful reduction in underweight without experiencing higher overweight and obesity.

Income gradients in obesity. The role of socioeconomic status (SES) in the rise of obesity in developing countries is debated. Although overweight has traditionally been considered a disease of affluence in LMICs (136), it is no longer confined to the wealthy (131). Evidence increasingly shows that the burden of obesity shifts to lower-SES groups as countries develop (97). Monteiro et al. (96) found that when GDP per capita per annum is <$2,500, poverty is inversely associated with overweight; above this threshold, the burden of overweight shifts from the wealthy to the poor. In addition to influencing the prevalence of overweight, SES may influence the rate of increase in overweight prevalence and/or the type of obesity. A study of women of reproductive age in 37 LMICs found larger increases in overweight prevalence over time among low-income women relative to high-income women (65).

Furthermore, country-level income inequality also influences obesity. Wilkinson & Pickett (159) found that high income inequality was associated with higher levels of obesity, independent of national wealth, whereas Jones-Smith et al. (64) found that income inequality modifies the association between economic development and the SES gradient for obesity. Among LMICs in the highest GDP tertile and lower country-level income inequality (including Armenia, Egypt, Indonesia, Kazakhstan, and Turkey), there was a faster increase in overweight in women among lower-SES groups relative to higher-SES groups. Among LMICs in the highest GDP tertile and higher country-level income inequality (including Colombia, Guatemala, and Namibia), the opposite was true: There was slower growth in overweight prevalence among the lower-SES groups relative to the higher-SES groups.

The specific drivers of the disproportionate increase in overweight among lower-income groups in LMICs are unclear. People with lower income may be increasingly exposed to classic risk factors for obesity, such as high-calorie diets and low energy expenditures associated with the shift away from subsistence agriculture to industrial and service-oriented economies. Conversely, people with low incomes may have different responses to the same environment; for example, socioeconomically disadvantaged groups may exhibit different coping strategies during food crises relative to those with greater income (64). This notion may explain the finding that economic shocks are associated with a decreased likelihood of obesity among women in low-income countries but are associated with an increased likelihood of obesity in middle-income countries (44).

Gender differences in obesity. Women in LMICs bear a disproportionate burden of obesity (82, 83, 121). In 119 of 130 LMICs examined in a review, women had a higher overweight/obesity prevalence relative to men; the difference in prevalence percentage points ranged from 0.2 in Vietnam to 28.7 in Dominica (103). Nine of 11 countries where men had a higher prevalence of overweight/obesity than did women were in Africa (103). Given that overweight/obesity among girl children is lower or on par with boys in LMICs, it appears that the higher obesity prevalence among females emerges during adolescence or adulthood (103, 109). Data from Tunisia show that compared with childhood, obesity prevalence in adolescence is higher among girls and lower in boys (94). A study of obesity among South African adolescents found that the obesity incidence among girls was highest in adolescence, whereas obesity among boys did not increase (78).

In contrast, large gender differences in overweight/obesity are apparent only in some race/ethnic groups in HICs (38). Higher obesity among women compared with men in LMICs could be driven by several factors, including sex differences in physiological responses to early-life nutrition, pregnancy-associated weight gain combined with higher parity (40), hormonal signaling related to energy expenditure (16), physical activity levels (144), alcohol consumption (137), depression (79), past and present economic circumstances (19), and sociocultural factors such as the perception of ideal body size and beliefs surrounding acceptability of physical activity in some contexts (68, 94). Because maternal obesity is a risk factor for childhood obesity, the increasing obesity prevalence among women of reproductive age could have important intergenerational effects in LMICs (20).

Urbanization and economic development. As of 2014, 33%, 39%, and 63% of people in low-, lower-middle-, and upper-middle-income countries lived in urban areas, respectively (150). Obesity is generally higher in urban compared with rural settings across LMICs. However, as LMICs further urbanize and as the prevalence of overweight/obesity rises globally, the urban–rural obesity differential appears to be shrinking, largely owing to increases in overweight among rural populations. While overweight prevalence is increasing in both rural and urban areas, the rate of increase is higher in many rural populations. In a study of women of reproductive age, Jaacks et al. (60) found that overweight was increasing at a greater rate in rural areas relative to urban areas in nearly half of LMICs. A study of adolescent girls found a trend toward higher overweight over time in rural areas but not in urban areas (59). With the exception of sub-Saharan Africa, Popkin & Slining (119) found greater annual increases in obesity in rural areas relative to urban areas in all regions of the world; however, the burden of overweight is similar in both rural and urban areas in LMICs except in South Asia and sub-Saharan Africa.

The urban–rural obesity differential is hypothesized to occur because of changes in infrastructure, transportation, employment, income, food access, and physical activity, which accelerate obesity in urbanized and economically developed areas (139). The urban food environment is characterized by a high availability of calorie-dense, cheap foods (138). Urbanization also facilitates reduced physical activity through changes in infrastructure, transportation, and occupational activities (17, 115). Additionally, a higher obesity prevalence in urban areas may be due to higher individual- and community-level SES in urban centers (102). In more developed LMICs, such as India and Brazil, the prevalence of overweight/obesity is even increasing in urban slums despite persistent poverty (93, 111). As countries continue to develop economically and urban centers expand, the distinction between urban and rural residence has become less pronounced. For example, elements of economic development that were historically concentrated in urban environments, such as packaged and ultraprocessed foods, have spread to rural areas, aided by media and marketing (49). Thus, rural areas may not continue to enjoy an obesity advantage as they have in the past.

Regional/ethnic differences in defining obesity. International BMI thresholds for overweight and obesity are defined on the basis of risks to cardiovascular health in European populations (122, 155). However, the relationship between anthropometry and adiposity tends to differ by ethnic background. For example, young African American men are more likely to be classified as obese on the basis of BMI, despite lacking excess directly measured adipose tissue (53). Conversely, adiposity in South Asians may be underestimated by BMI classifications of obesity (25, 154). In addition, the association between BMI and health risks appears to vary by ethnic background; evidence from multiethnic studies suggests that several non-European groups experience the same levels of glucose and lipids at roughly 6 kg/m^2 lower BMI than do Europeans (124). Most studies assessing the need for alternative ethnic-specific cutpoints focus on Asians and suggest that they are more likely to have diabetes and other cardiovascular disease outcomes than are non-Asians at any given BMI (26, 123, 135, 152). The WHO has recommended alternative lower cutpoints for action for Asians, defining excess risk at a BMI of >22.5 kg/m^2 (157). Some authors have concluded that data in other non-Caucasian groups are too limited to make a determination about alternative cutpoints (74).

General versus central obesity. BMI has long been recommended as a measure by which to assess adult overweight/obesity (155) and is the most commonly reported metric of obesity in the literature (119). However, measures of central adiposity (waist-based measures such as waist circumference, waist–height ratio, and waist–hip ratio) are also associated with excess risk of cardiometabolic disease and may more accurately assess NCD risk relative to BMI in some populations. In the 52-country INTERHEART study, each standard deviation in waist–hip ratio was associated with 37% higher adjusted odds of myocardial infarction, whereas each standard deviation in BMI was associated with 10% higher adjusted odds. However, one recent study found comparable effect sizes associated with waist circumference and BMI in models of prevalent hypertension in South Asians, South Africans, and South Americans and higher (though statistically indistinguishable) effect sizes for waist circumference than for BMI in relation to diabetes in South Africans and South Asians (108). Given that the location of fat may be responsible for specific health effects (101), waist circumference could provide information complementary to that provided from BMI (156).

DRIVERS OF OBESITY IN LMICs

Traditional Drivers of Obesity: Diet and Physical Activity

Obesity has conventionally been thought to be a consequence of prolonged caloric intake in excess of energy requirements (63). However, emerging data challenge the notion that a simple sum of energy input through diet and energy output through physical activity explain obesity and instead suggest that factors contributing to dysregulation of neuroendocrine mechanisms may be involved in the complex process that leads to obesity (86). The following section outlines changes in global diets, the global food system, and physical activity as well as emerging risk factors of interest. Emerging risk factors are not unique to LMICs; however, they likely represent a different proportion of the risk burden relative to HICs and might help inform obesity prevention or management strategies in developing countries.

Nutrition transition. The nutrition transition refers to the shift from traditional diets composed of whole foods, such as pulses and whole grains, and that are low in animal-source foods, salt, and refined oils, sugars, and flours (95), to an energy-dense and nutrient-poor diet composed of refined

carbohydrates, high fat intake, and processed foods (12, 32, 125). Relative to traditional diets, both total caloric intake and energy density tend to be higher in modern diets owing to increased consumption of processed foods and fats (114) facilitated by increased income, urbanization, and shifts in food availability and pricing (112). Relevant to excess caloric consumption, ultraprocessed foods—typically high in fat, salt, and sugar—are designed to be highly palatable and can overcome homeostatic eating signals; for example, high salt content can override fat-mediated satiety cues and promote overconsumption (11).

Traditional diets are not necessarily healthy, however, and some aspects of dietary change associated with the nutrition transition are desirable. Staple food-based diets typically lack dietary diversity and have been associated with micronutrient deficiencies (56). Furthermore, diets high in carbohydrates and low in fat are associated with increased plasma triglycerides and decreased high-density lipoprotein cholesterol (HDL-c), both of which are associated with cardiometabolic disease (37, 39). In a US cohort of Puerto Rican adults, adherence to the traditional rice and beans dietary pattern was associated with higher risk of metabolic syndrome [odds ratio (OR) = 1.7, 95% confidence interval (CI) = (1.04, 2.70)] and lower HDL-c (104). A positive effect of the nutrition transition includes improved dietary diversity through greater inclusion of fruits and vegetables, eggs, cheese, milk, meat, and fish in some settings; however, processed foods are often included along with the new fresh, whole foods (32) and are typically energy dense, nutrient poor, and low in fiber (95). Adherence to balanced diets that are high in whole grains, fruits and vegetables, and healthy fats, such as the Mediterranean diet, have been associated with reduced obesity incidence (91) and NCDs, including diabetes (130).

A shift away from traditional foods has led to a sweetening of the global diet. Added sugars are a dietary driver of obesity worldwide, especially when consumed in beverages such as soft drinks, sweetened coffee and tea, juices, and alcoholic beverages (54). In most LMICs, sugar-sweetened beverage (SSB) sales are increasing (in daily calories per person) (117) and represent an important source of caloric intake in many parts of the developing world—the consequences of which have been well documented in Mexico (61, 126). Liquid calories influence weight gain by contributing to excess caloric consumption because, relative to solid foods, liquids are less satiating (28, 84). Consequently, people do not compensate for energy consumed from beverages, contributing to excess caloric intake (85). A meta-analysis of SSBs and health outcomes commissioned by the WHO found a positive association between SSB intake, total caloric intake, and body weight (53).

Global trade and the food environment. Globalization and trade liberalization play a role in the nutrition transition in LMICs through their influence on the food system, particularly the availability and price of food (51). Broadly, trade liberalization encourages greater imports of food, facilitates foreign direct investment in food production and processing, and stimulates growth of transnational food companies (51). Treaties such as the Central American Free Trade Agreement (CAFTA) and the proposed Trans-Pacific Partnership (TPP) reduce or eliminate tariffs on animal feed and meat, processed foods, and ingredients for processed foods. Notably, trade liberalization has led to increased availability of edible oil; global availability of plant oils tripled from 1961 to 1990 (32). Increased importation and production of vegetable-source fats lead to increased availability and affordability (32). These changes in food availability and pricing in turn lead to new food consumption patterns such as snacking and consumption of processed or fast foods (58) and, subsequently, increased caloric intake. For example, each snacking occasion was associated with 102–289 kcal higher mean daily energy intake among Mexican schoolchildren (143). More research is needed on the factors that influence food choice in LMICs to better target obesity prevention efforts.

Declining physical activity. Decreases in physical activity have been cited as a primary driver of the rise in obesity levels (69). A study of 122 countries representing 88.9% of the world's population found that 31.1% of adults ages ≥15 years are physically inactive (47). Shifts from manual labor to more sedentary jobs have resulted in a significant loss of physical activity (138) and are an important dimension of low energy expenditure. Moreover, modern technology such as refrigeration and other conveniences has decreased the energy expenditure needed for domestic activities (114). Mechanization of domestic work such as washing clothes and cleaning dishes was associated with a 111 kcal/day mean savings in energy expenditure relative to manually performing these tasks (73). Active transportation (i.e., commuter walking and cycling) has also decreased. Data on active transport in LMICs is scarce; however, only 64.1% of adults in 120 countries worldwide reported walking for at least 10 minutes consecutively on ≥5 days per week (47). China has witnessed a substantial increase in motorized transportation since 1990 with strong associations between vehicle ownership and obesity (7). There is little indication that people in LMICs are compensating for reductions in occupational physical activity and active transport with increased leisure time physical activity (47). In fact, leisure time may be more sedentary than in the past owing to technologies such as TVs, and sedentary activities are often associated with obesogenic behaviors such as snacking (114).

The diet-versus-physical-activity debate. Diet and physical activity are two competing and complementary drivers of obesity. Findings from a systematic review of sedentary behavior and obesity risk were equivocal owing to limited evidence from high-quality studies (80). Swinburn et al. (142) argue that excessively caloric diets due to changing food systems, rather than declining physical activity, are the predominant driver of obesity. Their arguments rest on two primary ecological observations. First, the increase in population-level BMI in the United States more closely corresponds to the time period of surplus caloric availability rather than the time period of energy expenditure decline. Second, temporal changes and regional variation in the built environment are not sufficient to account for global obesity patterns. Similarly, at the individual level, modifying caloric consumption rather than physical activity has been cited as an optimal strategy to achieve energy balance (77). High energy consumption would require substantial increases in energy expenditure (via vigorous intensity and/or long-duration physical activity) to prevent weight gain (89). A small but persistent positive energy balance of only 30 kJ per day could explain observed increases in overweight (46). For this reason, obesity reduction policy efforts, such as the soda tax implemented in Mexico, aim to address obesity through the caloric consumption side of the energy balance equation (15). Because many of the health risks associated with physical inactivity are independent of its influence on body weight (71), promoting active lifestyles would be beneficial for overall health regardless of its impact on obesity or weight loss.

Other Emerging Risk Factors

Genetic and epigenetic influences. The heritability of BMI is estimated to be 40%–70% (2), through means including the control of the physiologic response to caloric excess and regulation of appetite via hormones such as leptin (3). There is increasing interest in how interactions among the environment, behavior, and the genome can modify gene expression. The epigenome—or nonsequence-based DNA modifications—includes alterations such as DNA methylation. Dalgaard and colleagues (24) elucidated an epigenetic network, tested in mouse models, that triggers obesity in an ON/OFF manner; however, it is not yet known whether this bimodal system

exists in humans. Human studies have shown that four distinct variably methylated regions, located in or near genes previously implicated in body weight regulation, covary with BMI (35).

Epigenetic mechanisms regulate several obesity-related pathways, including food intake, energy expenditure, and adiposity (161). Diet influences epigenetic states both directly (e.g., vitamin A) and indirectly (e.g., methyl donors such as folate). Studies from The Gambia have shown that maternal diet influences DNA methylation patterns (31). Environmental factors, such as exposure to persistent organic pollutants (POPs), can also perturb epigenetic mechanisms. Furthermore, the availability of certain nutrients can effect toxicant metabolism, suggesting an overlap between dietary and environmental exposures and the development of the epigenetic footprint (30). This point could be especially important for populations with high toxin exposure coupled with nutritional insufficiencies. Because epigenetic changes can be heritable during cell division, future generations can be affected by past nutrition or environmental exposures (133). Advances in understanding of genetic and epigenetic influences on obesity could inform future personalized medicine to prevent or treat obesity on the basis of the genotype and phenotype to the extent that adverse changes are modifiable (42).

Early-life undernutrition and later-life obesity and cardiometabolic disease. The vast majority of undernourished children reside in LMICs (9). With socioeconomic advancement and improved living conditions, these children are increasingly exposed to obesogenic environments outside of the womb. Adult obesity and cardiometabolic disease in LMICs may be influenced by the mismatch between conditions in early and later life. The developmental origins of health and disease hypothesis posits that structural and functional adaptations in response to in utero undernutrition—possibly to preserve brain and vital organ development—combined with a plentiful environment outside of the womb predispose an individual to develop cardiometabolic disease (153). Although the initial hypothesis was developed to address human disease patterns observed in HICs (England and Wales) (45), there has been much supporting evidence from mechanistic studies in animals (13) as well LMIC cohorts where low birth weight (a proxy for fetal undernutrition) and childhood underweight continue to be high (33, 129, 162, 163). Birth size has been associated with adiposity, obesity, type 2 diabetes, lipid profile, and blood pressure (1, 8, 21, 22, 52). Taken together, early-life undernutrition and a rapid shift in diet and physical activity could explain why people in LMICs are experiencing chronic disease, on average, 10–15 years younger than people in HICs (99).

Nutrition supplementation/food assistance programs. Nutrition supplementation programs targeting childhood undernutrition may be inadvertently increasing risk for adult obesity (41, 149). Interventions to promote rapid growth following prenatal and/or infant growth deficits may increase the risk of overweight and adiposity in later childhood (6, 55). A nutrition supplementation program for preschool children in Chile was associated with a 50% increase in the number of overweight children and a threefold increase in the number of obese children during the first year of the program (66, 148). Understanding how nutrition supplementation to promote linear growth in early life is associated with obesity is particularly important in LMICs where food assistance policies are common (148).

Gut microbiome and enteric infections. The gut microbiome is a collection of microbial organisms that reside in the gut. Together with host genotype and lifestyle factors, the gut microbiome may play a role in the pathophysiology of obesity (147) through energy use and storage and by regulating expression of genes associated with fat production and deposition (4). For example,

the "obese microbiome" has a greater capacity to harvest energy from the diet and to promote fat deposition as compared with the "lean microbiome" (147).

Researchers speculate that interaction between dietary changes, such as a shift to a modern diet from a traditional diet or differences in microbial ecology between individuals in LMICs versus those in HICs, and the gut microbiome affect individuals' predisposition to obesity (4). There is a core microbiome, and deviation from this core is associated with obesity and poor child growth (10, 146). Breastfeeding, food, and water security are critical factors in the maturation of healthy gut microbiota (92). Gut microbiome maturation generally occurs by three years of age and is associated with increased microbe diversity; microbiota are vertically transmitted from mother to child via in utero colonization, vaginal delivery, and breastfeeding (92). Microbiota are also shaped by diet throughout life. Administration of a Western diet to nonobese mice altered the composition of the gut microbiota, and subsequently increased the transfer of calories from the diet to the host and affected energy metabolism (146).

Environmental contaminants. POPs are man-made chemicals used as agricultural fertilizers and insecticides for mosquito control, which were largely restricted in HICs beginning in the 1970–1980s. Organochloride insecticides like dichlorodiphenyltrichloroethane (DDT), however, are still heavily used for malaria control in countries such as India and throughout the African continent (151). These chemicals are resistant to natural environmental degradation, biomagnify in the food chain, and bioaccumulate in human tissues. POPs are thought to influence obesity risk by disrupting endocrine function by mimicking hormones, modulating gene transcription factors, or altering endogenous hormone availability, or through epigenetic mechanisms (110).

Exposure to chemicals including polychlorinated biphenyls (PCBs), DDT, bisphenol A (BPA), and arsenic is positively associated with obesity (134), and there is concern that exposure during sensitive developmental periods, such as in utero or in infancy through breast milk consumption, could have important implications for the epigenome and the regulation of endocrine function. The highest concentration of DDT in breast milk was observed in Africa with slightly lower concentrations among mothers in Asia, Mexico, and Central America; high levels of PCBs were also reported in breast milk in mothers from Asia (34). More long-term, longitudinal research is needed to elucidate the role of POPs on obesity pathophysiology, particularly in how simultaneous exposures to various environmental contaminants might behave synergistically.

Chronic stress. Chronic stress associated with poverty, unemployment, crime, lack of safety, poor social networks, and other factors in LMICs could be contributing to rising obesity. In the short term, hormonal response to acute stressors (i.e., release of cortisol) helps to reestablish homeostasis; however, repeated hypothalamic-pituitary-adrenal axis activation due to chronic stress can overload the regulatory system (88). Elevated cortisol from a stress response is associated with increased appetite, visceral adiposity, and the propensity for weight gain (88). In addition to the hormonal changes, stress-related coping behaviors such as emotional eating are positively associated with obesity risk (145). Although much of the evidence on chronic stress and obesity are from HICs, data from India showed that chronic stress (measured by an urban stress index) was associated with poor health behaviors, including tobacco use (141).

Sleep deprivation. Sleep deprivation has been associated with poor food choices and an increased risk of obesity. Longitudinal studies have shown a positive association between short sleep duration and obesity risk. A meta-analysis of prospective studies found an increased risk of obesity for short sleep duration ($\leq$5 h) relative to normal sleep duration (7 h) [pooled OR 1.45, 95% CI = (1.25,

1.67)] (160). To our knowledge, there is only one study of sleep duration and obesity risk from a LMIC (i.e., India) (81). The mechanisms through which short sleep duration increase obesity risk are not entirely understood; however, sleep deprivation is thought to increase hunger and preference for high-fat and sweet foods (18). An experimental study in adolescents found that while self-reported hunger was not increased, sleep restriction (<6.5h) was associated with an 11% increase in total energy intake relative to healthy sleep duration (10 h) (132). Another study found that sleep loss in adults increases the hedonic reward for consuming sweet, salty, and fatty snack foods via increased levels of endocannabinoid (48). Finally, stress and sleep deprivation are thought to have a synergistic effect on obesity risk; increased cortisol secretion associated with the acute stress reaction is linked to impaired sleep (54).

CHALLENGES

Obesity Prevention and Management Efforts

Obesity prevention. Intentional weight loss, and subsequent weight management, is challenging. Only one in six US adults who were ever overweight or obese have long-term weight-loss maintenance of at least 10% of initial body weight (72). In LMICs where obesity is still emerging as a major health issue, obesity prevention, as compared with obesity management, is seen as a more effective strategy; obesity management is challenging particularly because health systems developed to attend to infectious disease and maternal and child undernutrition must be entirely redesigned to contend with the dual burden of disease (27). Poverty and other factors affecting access to health care services further limit obesity management in LMICs. Children may be the most effective target group for prevention efforts because evidence suggests that the propensity for overweight and obesity begins as early as six months of age (43, 87), and data from HICs show that overweight tracks from childhood into adulthood (23). Furthermore, diet-related behaviors such as food preference are established early in life (50), motivating obesity prevention programming that targets children. Examples of initiatives to promote healthy diet and weight in children include efforts by public educational institutions to purchase locally produced healthy foods (127) and school-based nutrition education to improve food literacy (50). Although focusing on obesity prevention in children will have little short-term impact on the population prevalence of overweight/obesity, it would support long-term goals of reducing the burden of overweight over time. Approaches intended to promote obesity prevention in the entire population include subsidizing nutritious food (140) or, conversely, taxing unhealthy foods such as SSBs (14).

Obesity management. In consideration of more conventional clinical approaches, the American Heart Association (AHA)'s summary of recommendations for obesity management may be applicable to LMICs. To identify individuals who need to lose weight, the AHA recommends that both BMI and waist circumference be measured and patients be advised according to their classification on the basis of current cutpoints (62). Furthermore, the AHA strongly advises clinicians to counsel overweight/obese patients with cardiovascular disease risk factors regarding the benefits of lifestyle changes, including improved diet. Strong evidence also indicates that bariatric surgery for obesity treatment is advised for individuals with BMI $\geq$40 or BMI $\geq$35 with comorbid conditions that have not responded to other lifestyle changes, but this approach applies to a very narrow fraction of the obese population. Surgical options may also not be feasible in low-resource settings.

Although it is not restricted to obese individuals, the Exercise is Medicine Global Initiative is designed to support health care professionals in prescribing exercise for patients by training

providers to assess patient physical activity levels, imparting behavioral counseling to increase activity using change models, and referring patients to resources to facilitate physical activity (76). This initiative already exists in LMICs, and evaluation of its impact will provide important data on how to adapt and scale up this program to encourage healthy activity levels and weight status.

Data Gaps and Research Agenda

Data gaps and recommendations for research include the following.

1. We lack sufficient surveillance systems to monitor national-level overweight and obesity in both genders and at all ages. We recommend including population subgroups such as men, adolescents, and older adults in existing surveys of weight status and to build routine surveillance of weight status into national health programs.
2. We lack surveillance systems to monitor obesity-related health outcomes. We recommend including routine collection of data on diabetes, cardiovascular disease, and hypertension as well as other obesity-related conditions such as sleep apnea and osteoarthritis in population-based surveys.
3. We lack validated cutpoints to define overweight and obesity, especially in some ethnic groups, children, and adolescents, which makes cross-country and cross-study comparisons difficult. We recommend developing a consensus around internationally accepted cutpoints alongside ethnic- and age-specific cutpoints and encourage reporting overweight and obesity by both internationally accepted and locally accepted classifications. This approach will require access to more population-level data on BMI, waist circumference, and related health outcomes (i.e., addressing gaps 1 and 2 above).
4. Little obesity prevention research has catered to the needs of LMICs. We recommend conducting intervention trials in LMICs to build the evidence base needed to support obesity prevention and treatment in these populations.
5. We lack policy-level data on designing food systems and a built environment that promote healthy weight. We recommend implementation of primordial prevention strategies that encourage children to develop healthy habits early in life and avert the onset of obesity in later life. We also need more evaluation research on food policy, such as improved front-of-package food labeling, taxation on SSBs, or restricted marketing of unhealthy foods to children.

CONCLUSION

Obesity is rising in every region of the world, across even the poorest of LMICs. The food environment has been a primary driver of the rise in obesity worldwide over the past half-century. Other established and emerging contributing factors include a combination of diet, physical activity, the built environment, genetics and epigenetics, environmental pollutants, and stress. Although each driver may have only a small effect on obesity risk, the accumulation of many small effects could explain the substantial increases in overweight/obesity seen in LMICs. Perhaps the most salient distinguishing feature of the obesity epidemic in LMICs is that it is unfolding against the backdrop of a large burden of maternal and child undernutrition and related disorders. The appearance of dual burdens of child undernutrition and adult overnutrition may exacerbate the risk of obesity and associated cardiometabolic disorders through hypothesized fetal programming pathways and is also taxing on underdeveloped health systems. In addition, common cardiometabolic disorders such as hypertension and diabetes exist in large proportion in LMICs even in the absence of widespread obesity; increasing obesity levels are therefore particularly worrisome. Yet, data on

effective strategies to maintain weight as we age and to prevent the onset of obesity in LMICs are scarce. Improving this evidence base is a key priority for future research and has important possibilities for reverse innovations that may inform interventions in HICs as well.

SUMMARY POINTS

1. Although age-standardized obesity is generally lower in LMICs relative to HICs, overweight has increased in all regions of the world.
2. Increasing prevalence of overweight and obesity occurs alongside persistent burdens of underweight in LMICs, especially in young women.
3. Overweight and obesity is higher in women compared with men, in urban compared with rural settings, and in older compared with younger individuals; however, the urban–rural divide is shrinking in many countries.
4. The global diet has become sweeter, higher in fat, and saltier, while physical activity—especially related to occupation—has declined; these are among the hypothesized leading contributors to the rise in obesity.
5. Emerging risk factors for obesity include environmental contaminants, chronic psychosocial stress, and sleep deprivation. The role of genetics, epigenetics, the gut microbiome, and neuroendocrine regulation is also being explored.
6. Obesity prevention theoretically offers a more effective strategy than obesity management for LMICs where obesity is still emerging as a major health issue and where obesity management is challenging.
7. Obesity prevention efforts that target children have the greatest potential to avert obesity into adulthood and should be rigorously evaluated.
8. Surveillance systems to monitor weight status in both genders at all ages and obesity-related chronic diseases are needed in LMICs. Similarly, prevention research and policy-level data to better understand how to design environments that promote healthy weight in LMICs should be a public health priority.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review. Funding for this study was provided by the Laney Graduate School at Emory University. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

ACKNOWLEDGMENTS

All authors conceived the original study idea, formulated the research question, and designed the study. N.D.F. and S.A.P. wrote the initial manuscript draft. All authors interpreted findings, contributed to the intellectual content of the work, and edited subsequent drafts. All authors approve the final version to be published.

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