What existing epidemiological data could serve to better understand the relationship of energy intake and expenditure to obesity and the obesity epidemic?

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Understanding the relationship between energy balance and obesity is a challenge, particularly in low- and middle-income countries (LMICs), where data are limited. Most of the studies have been conducted in high-income countries, and the results may not be generalizable to other settings because of differences in population characteristics.

This chapter provides an overview of studies focusing on determinants of obesity (adiposity) relating to dietary intake (energy intake) and physical activity (energy expenditure) and proposes study designs that could be implemented in LMICs to improve the understanding of the main drivers of obesity in these countries.

Determinants of obesity

Obesity is defined as a state of excess adiposity that presents a risk to health, for example increased risk of chronic diseases [1], and is the consequence of sustained positive energy balance over time.

Factors that influence energy balance can be considered as relating to the host (i.e. people), the environment (i.e. the set of external factors to which people are exposed), and the vector (i.e. foods and drinks). These factors interact in a complex way to influence eating and drinking patterns as well as activity behaviours. Although these factors are experienced at the individual level as the acceptability, availability, and affordability of foods, drinks, and activity behaviours, their roots lie in policies and actions that determine the environment, which may be local, national, or international [2].

Apart from non-modifiable factors, other characteristics may influence energy balance – in particular, the amount of energy expended in physical activity. Increasing energy expenditure might be expected not to influence energy balance, because of appetite control mechanisms that feed back and tend to maintain balance. However, there is evidence that at the low levels of activity characteristic of many high-income countries and increasingly of LMICs, this feedback operates imperfectly and does not suppress appetite to the low levels necessary to maintain energy balance [3]. Many factors relating to the foods and drinks consumed have been shown to influence the amount consumed or energy balance over the short to medium term, such as energy density and portion size [4, 5].

Measurement of adiposity

Several measures for overweight and obesity have been used in epidemiological studies. However, it is important to be aware that such measures are imperfect markers of the internal physiological processes
that are the actual drivers of cancer development.

Body mass index (BMI) is defined as the quotient between weight in kilograms and height in metres squared (kg/m²); overweight and obesity are conventionally defined in relation to cut-offs of 25 kg/m² and 30 kg/m², respectively [6]. BMI is the most commonly used marker of body composition in epidemiological studies, because of the simplicity of assessment and the high precision and accuracy. However, it does not differentiate between lean and adipose tissue or take into account fat distribution, which varies across individuals, among ethnicities, and throughout the lifespan. Nevertheless, BMI at a population level is a useful marker of the body composition in epidemiological studies tends to be as reference methods [4].

Understanding nutritional determinants of obesity

Experimental data

Prevention of weight gain and/or maintenance of weight loss

Short- to medium-term experimental data in humans can illuminate the possible physiological and other mechanisms underpinning how foods, drinks, and nutrients might promote energy overconsumption and positive energy balance.

In such studies, factors relating to the host include genetic variants that are associated with higher risk of obesity; these variants tend to be related to appetite regulation rather than to energy metabolism at a whole-body or cellular level [15]. Such studies may also include the impact of early-life events, so that child growth trajectories can predict later risk of obesity. Thus, children tend to maintain their BMI ranking within their population throughout childhood, particularly after the age of 11 years [16]. Also, the timing of the rebound in BMI in childhood (the so-called adiposity rebound) predicts later obesity, with an earlier rebound indicating a higher risk of obesity [17]. However, such factors are not modifiable in later life, although the effects might be mitigated.

There is evidence that people who are more physically active, and those who spend less time sedentary, are less likely to gain excess weight in adulthood. Results from intervention trials have been inconsistent, but based on observational studies conducted among Caucasian adults, an increase in energy expenditure through physical activity of approximately 6300–8400 kJ/week (1500–2000 kcal/week) was associated with improved weight maintenance [18].

These host factors may also interact with other factors related to the vector (foods and drinks). For example, in studies of young men eating ad libitum diets of different energy density for up to 3 weeks, Stubbs et al. found that the higher the level of activity, the more likely people were to avoid positive energy balance [19]. At high levels of energy density (60% of energy as fat), only the most active people remained in energy balance, whereas the least active were able to maintain energy balance only at low levels of energy density (20% of energy as fat). However, this trial was conducted among a small number of participants and for a short duration (2 weeks).

Long-term (> 1 year) experimental data are also available. In the long-term Prevención con Dieta Mediterránea (PREDIMED) study, with a follow-up of 4 years, the impact of a non-calorie-restricted traditional Mediterranean diet enriched with nuts and olive oil (two high-energy foods) was compared with that of a control diet consisting of advice on a low-fat diet. No substantial weight gain was observed in the group eating the enriched Mediterranean diet [19]. In the European Prospective Investigation into Cancer and Nutrition (EPIC), among participants with baseline BMI < 25 kg/m², dietary energy density was weakly associated with weight change, whereas among participants with
BMI > 25 kg/m², greater energy density was inversely associated with weight change [21]. The long-term impact of different macronutrient proportions, of the food sources of those macronutrients, and of energy density on adiposity and the development of obesity remains to be more precisely clarified.

There is also evidence that specific foods, drinks, or food components can have an impact on energy homeostasis. A recent systematic review of randomized controlled trials (RCTs) and prospective cohort data on dietary sugar and body weight concluded that among free-living people eating ad libitum diets, intake of free sugars or sugar-sweetened beverages is a determinant of body weight. The change in body fatness that occurs when intake is modified appears to be mediated via changes in energy intakes, because isoenergetic exchange of sugars with other carbohydrates was not associated with weight change [22]. In addition, in a small experimental study that compared isoenergetic meals with low and high glycaemic index (GI), plasma glucose (2-hour area under the curve) after the high-GI meal was 2.4 times that after the low-GI meal. Thereafter, compared with the low-GI meal, the high-GI meal decreased plasma glucose, increased hunger, and selectively stimulated brain regions associated with reward and craving in the late postprandial period. This suggests that reduced consumption of high-GI carbohydrates (specifically, highly processed grain products, potatoes, and concentrated sugar) may ameliorate overeating and facilitate maintenance of a healthy weight in overweight and obese individuals [23].

Evidence from RCTs conducted in children and adolescents indicates that consumption of sugar-sweetened beverages, compared with non-calorically sweetened beverages, results in greater weight gain and larger increases in BMI; however, the evidence is limited to a small number of studies. The findings of these trials suggest that there is inadequate energy compensation (degree of reduction in intake of other foods and drinks) for energy delivered as sugar [24]. However, a recent RCT showed a similar effect of a low-fat diet and a low-glycaemic-load diet on BMI over 24 months among Hispanic children [25]. There is inconsistent evidence that dietary fibre has an impact on energy balance but some evidence that wholegrain foods may help maintain energy balance [24].

For prevention of weight gain, few reported interventions have continued for more than 12 months; therefore, extrapolation to lifelong effectiveness should be done with caution. A review of diet and nutrition factors in relation to prevention of weight gain found evidence that protective factors against obesity were regular physical activity (convincing), a high intake of dietary non-starch polysaccharides/fibre (convincing), home and school environments that support healthy food choices for children (probable), and breastfeeding (probable). Risk factors for obesity were sedentary lifestyles (convincing), a high intake of energy-dense, micronutrient-poor foods (convincing), heavy marketing of energy-dense foods and fast-food outlets (probable), sugar-sweetened soft drinks and fruit juices (probable), and adverse social and economic conditions (in developed countries, especially for women) (probable) [26].

Understanding weight loss

There is copious evidence relating to various strategies for promoting weight loss through negative energy balance among overweight and obese people, although there is less evidence relating specifically to maintaining energy balance (or preventing weight gain and obesity). In addition, long-term data from RCTs for obesity prevention are more difficult to obtain than those from trials for weight loss. For weight loss, there is widespread but not universal agreement that limiting the proportion of dietary energy from fat (or energy density) helps to reduce ad libitum energy intake [27]. More recently, evidence has accrued for the effects of intermittent partial fasting for 2 days per week [28]. Avoiding calorific beverages, especially sugar-sweetened beverages, aids weight control [29], because consumption of these beverages is not followed by adequate compensation in subsequent intake. Simple calorie counting appears to be relatively ineffective. A recent meta-analysis of RCTs comparing the long-term effect (≥1 year) of dietary interventions on weight loss showed that low-carbohydrate interventions led to significantly greater weight loss than did low-fat interventions (18 studies), and that low-fat interventions did not lead to differences in weight change compared with other, higher-fat interventions (19 studies) [30]. In a 2-year trial, obese subjects were randomly assigned to one of three diets: low-fat, restricted-calorie; Mediterranean, restricted-calorie; or low-carbohydrate, restricted-calorie. For the Mediterranean-diet group and the low-carbohydrate group, weight loss was similar and significantly higher than that for the low-fat group. Among the subjects with diabetes, the Mediterranean diet led to larger changes in plasma glucose and insulin levels compared with the low-fat diet [31].

The addition of a physical activity component improves the efficacy of a dietary intervention, but physical activity alone has not been shown to lead to weight loss (possibly because in obese people it is difficult to achieve a sufficient volume of activity). Physical activity is helpful for prevention of weight gain, but there is limited evidence for its role in weight loss [32].
in weight maintenance after weight loss [18].

A review of workplace and community interventions found some evidence for the effectiveness of these interventions in changing diet and physical activity behaviours but limited evidence for their effectiveness in changing BMI [32]. However, many interventions are of relatively short duration, whereas changes in BMI are more distal outcomes.

Most of these studies were conducted in high-income countries. This emphasizes the importance of conducting studies in LMICs, in particular long-term dietary intervention trials focusing on alternative dietary patterns with foods readily available in these countries to propose viable changes in nutritional behaviours.

**Epidemiological data**

Population surveys, etiological and population intervention studies, and implementation research are all important to develop the evidence base to tackle the rise in the prevalence of obesity associated with changing dietary and physical activity patterns.

Population surveys in representative samples combining the evaluation of diet, physical activity, and anthropometry and chronic outcomes enable the capture of baseline information and provide an indicator of the health status of the population [33]. Repeated surveys would enable the evaluation of trends and changes over time at the population level. Although cross-sectional analysis of these data limits interpretations on causality, it can provide good indications of the major determinants of obesity in that population. For example, Aburto et al. compared overweight and obese children with non-overweight children and observed a strong association between dietary energy density and body mass status [34]. An analysis of data from the National Health and Nutrition Examination Survey (NHANES) showed that among children and adolescents, replacement of sugar-sweetened beverages with water was associated with reductions in total energy intake for all groups studied, a reduction not negated by compensatory increases in intake of other foods or beverages [35]. Other analyses using population surveys can also be implemented, for example to determine the adequacy of the diet with respect to national recommendations.

The scientific value of prospective epidemiological cohorts has been solidly established for evaluating exogenous and endogenous exposures in relation to change in weight and obesity. Their primary advantage is the ability to measure exposures before the onset of obesity. Cohorts are also instrumental in spurring mechanistic and translational research. One example is the investigation by Mozaffarian et al. of the relationship between changes in lifestyle factors and weight change at 4-year intervals over a 20-year period in a large cohort of men and women in the USA. The study identified food items and lifestyle factors that were highly associated with weight change within each 4-year period; 4-year weight gain was most strongly associated with the intake of potato chips, potatoes, sugar-sweetened beverages, unprocessed red meats, and processed meats, and was inversely associated with the intake of vegetables, whole grains, fruits, nuts, and yogurt. Physical activity was independently associated with weight loss, whereas alcohol consumption, sleep duration (> 8 hours), and television watching were associated with weight gain [36]. A further analysis of the relationship between change of diet quality indexes and concurrent weight change showed that improvement of diet quality was associated with less weight gain [37].

Several cohort studies in high-income countries have shown an impact of healthy dietary patterns on obesity [38] (see Chapter 14). In a 4-year follow-up to an RCT for weight loss, subjects assigned to the Mediterranean diet during the RCT were more likely to maintain weight loss (during the 2-year trial) compared with subjects assigned to the low-fat diet or the low-carbohydrate diet. This finding suggests that compliance with the Mediterranean diet may be easier in the long term [39]. A recent analysis of the EPIC study using biomarkers of highly processed foods, which are increasingly consumed worldwide, reported that increasing blood levels of industrial trans-fatty acids were associated with an increased risk of weight gain and a decreased likelihood of weight loss, particularly among women; this might be particularly relevant in the context of LMICs [40].

Cohort studies conducted in LMICs would be valuable resources for understanding the impact of the nutrition and lifestyle transition on obesity. Some longitudinal studies have already been initiated in LMICs, for instance those included in the Consortium of Health-Oriented Research in Transitioning Societies (COHORTS) [41] and the Mexican Teachers’ Cohort (MTC) [42]. Building on these continuing initiatives may prove informative and cost-efficient. Data from the MTC showed that women with a dietary pattern characterized by high intakes of carbohydrates, sweet drinks, and refined foods had a higher risk of having a larger body shape silhouette and higher BMI, whereas women with a dietary pattern characterized by high intakes of fruits, vegetables, grains, and nuts had a lower risk [43]. This finding emphasizes the need for public health interventions that improve access to...
healthy diets, healthy food choices in the workplace, and ways of limiting consumption of beverages with a high sugar content and of highly processed foods, particularly those rich in refined starches.

Research suggests that obesity and chronic diseases in adulthood may be traced back to exposures that occurred during fetal development, childhood, and adolescence. Therefore, cohort studies covering the whole life-course, focusing on critical windows of exposure and the time course of exposure to disease (birth cohorts, adolescent cohorts, and young adult cohorts), should be considered. Of particular interest are multicentre cohorts and intergenerational cohorts, which would create resources to enable research on the interplay between genetics, lifestyle, and the environment. For example, in the Avon Longitudinal Study of Parents and Children (ALSPAC), increased intake of energy-dense, nutrient-poor foods during childhood (mainly due to a rise in free [added] sugars) was associated with obesity development, and diets with higher energy density were associated with increased fat mass [44]. Most relevant to LMICs is the observation that children who were stunted in infancy are more likely to be relatively fat at puberty at the same BMI, compared with children who were not stunted in infancy [45]. Poor maternal prenatal dietary intakes of energy, protein, and micronutrients have been shown to be associated with an increased risk of adult obesity in the offspring, and a high-protein diet during the first 2 years of life was also associated with increased obesity later in life, whereas exclusive breastfeeding was associated with a lower risk of later obesity [46]. Results from a cohort study conducted in Mexico showed that children exclusively or predominantly breastfed for 3 months or longer had lower adiposity at age 4 years [47].

**Conclusions**

Obesity is a state of excess adiposity and is a consequence of sustained positive energy balance over time. Measurements of energy intake, expenditure, and balance are difficult. Measurements of anthropometric indices such as BMI or WC, although imperfect, are useful markers of or proxies for adiposity or visceral adiposity. Establishing repeated population-based measurements of such anthropometric measures, together with estimates of the macronutrient composition of diets, food consumption patterns, and estimates of physical activity and time spent sedentary (preferably with objective measures, such as accelerometers, used in subsamples) will help track changes in the population levels of overweight and obesity, and point to the key nutritional drivers.

Most research has tended to focus on Caucasians, but these findings may not be generalizable to other populations because of differences in age structure, genotype, body composition, lifestyle, culture, religion, and socioeconomic status. Detailed analyses that consider differences in genetic and environmental factors and gene–environment interactions between populations, and take account of the whole life-course, are required to elucidate these complex relationships. Importantly, measures of obesity prevention and control in LMICs will benefit if they are evaluated in the context within which they will be implemented.

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**Key points**

- Obesity is a state of excess adiposity and is a consequence of sustained positive energy balance over time.
- Short-term experimental studies show that among men eating ad libitum diets of different energy density, the higher the level of activity, the less likely was positive energy balance, and at any level of activity, higher energy density led to more positive energy balance.
- In long-term experiments, intake of free sugars or sugar-sweetened beverages was a determinant of body weight. The change in body fatness when intake is modified appears to be mediated via changes in energy intakes.
- Studies in children and adolescents show that consumption of sugar-sweetened beverages results in increases in BMI, mainly by inadequate energy compensation (degree of reduction in intake of other foods and drinks).
- In weight-loss trials, low-carbohydrate interventions led to significantly greater weight loss than did low-fat interventions. Little attention has been paid to the effects of different types of carbohydrate.
- Cohort studies with repeated measurements have identified unhealthy dietary patterns and lifestyle factors associated with weight gain over time, and healthy dietary patterns have been shown to decrease the risk of obesity.
- Exposures during fetal life and early childhood may affect the risk of obesity.
Research needs

- Data from LMICs are limited, and further research is needed in these countries.
- Population surveys, etiological and population intervention studies, and implementation research are all important to develop the evidence base to tackle the rise in the prevalence of obesity associated with changing dietary and physical activity patterns.
- Research needs to take account of differences in age structure, genotype, body composition, lifestyle, culture, religion, and socioeconomic status. In this context, measurements of anthropometric indices such as BMI or WC are useful markers of or proxies for adiposity.
- Measures of obesity prevention and control in LMICs will benefit if they are evaluated in the context within which they will be implemented.

References


