Primer

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Child and adolescent obesity

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Abstract

The prevalence of child and adolescent obesity has plateaued at high levels in most high-income countries and is increasing in many low-income and middle-income countries. Obesity arises when a mix of genetic and epigenetic factors, behavioural risk patterns and broader environmental and sociocultural influences affect the two body weight regulation systems: energy homeostasis, including leptin and gastrointestinal tract signals, operating predominantly at an unconscious level, and cognitive–emotional control that is regulated by higher brain centres, operating at a conscious level. Health-related quality of life is reduced in those with obesity. Comorbidities of obesity, including type 2 diabetes mellitus, fatty liver disease and depression, are more likely in adolescents and in those with severe obesity. Treatment incorporates a respectful, stigma-free and family-based approach involving multiple components, and addresses dietary, physical activity, sedentary and sleep behaviours. In adolescents in particular, adjunctive therapies can be valuable, such as more intensive dietary therapies, pharmacotherapy and bariatric surgery. Prevention of obesity requires a whole-system approach and joined-up policy initiatives across government departments. Development and implementation of interventions to prevent paediatric obesity in children should focus on interventions that are feasible, effective and likely to reduce gaps in health inequalities.

Sections

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Introduction

The prevalence of child and adolescent obesity remains high and continues to rise in low-income and middle-income countries (LMICs) at a time when these regions are also contending with under-nutrition in its various forms[1,2]. In addition, during the COVID-19 pandemic, children and adolescents with obesity have been more likely to have severe COVID-19 requiring hospitalization and mechanical ventilation[3]. At the same time, the pandemic was associated with rising levels of childhood obesity in many countries. These developments are concerning, considering that recognition is also growing that paediatric obesity is associated with a range of immediate and long-term negative health outcomes, a decreased quality of life[4,5], an increased presentation to health services[6] and increased economic costs to individuals and society[7].

Body weight is regulated by a range of energy homeostatic and cognitive–emotional processes and a multifactorial interplay of complex regulatory circuits[8]. Paediatric obesity arises when multiple environmental factors − covering preconception and prenatal exposures, as well as broader changes in the food and physical activity environments − disturb these regulatory processes; these influences are now widespread in most countries[9].

The treatment of obesity includes management of obesity-associated complications, a developmentally sensitive approach, family engagement, and support for long-term behaviour changes in diet, physical activity, sedentary behaviours and sleep[10]. New evidence highlights the role, in adolescents with more severe obesity, of bariatric surgery[11] and pharmacotherapy, particularly the potential for glucagon-like peptide 1 (GLP1) receptor agonists[12].

Obesity prevention requires a whole-system approach, with policies across all government and community sectors systematically taking health into account, avoiding harmful health impacts and decreasing inequity. Programmatic prevention interventions operating 'downstream' at the level of the child and family, as well as 'upstream' interventions at the level of the community and broader society, are required if a step change in tackling childhood obesity is to be realized[13,14].

In this Primer, we provide an overview of the epidemiology, causes, pathophysiology and consequences of child and adolescent obesity. We discuss diagnostic considerations, as well as approaches to its prevention and management. Furthermore, we summarize effects of paediatric obesity on quality of life, and open research questions.

Epidemiology

Definition and prevalence

The World Health Organization (WHO) defines obesity as "abnormal or excessive fat accumulation that presents a risk to health"[15]. Paediatric obesity is defined epidemiologically using BMI, which is adjusted for age and sex because of the physiological changes in BMI during growth[16]. Global prevalence of paediatric obesity has risen markedly over the past four decades, initially in high-income countries (HICs), but now also in many LMICs[1].

Despite attempts to standardize the epidemiological classification, several definitions of paediatric obesity are in use; hence, care is needed when comparing prevalence rates. The 2006 WHO Child Growth Standard, for children aged 0 to 5 years, is based on longitudinal observations of multiethnic populations of children with optimal infant feeding and child-rearing conditions[17]. The 2007 WHO Growth Reference is used for the age group 5–19 years[18], and the 2000 US Centers for Disease Control and Prevention (CDC) Growth Charts for the age group 2–20 years[19]. The WHO and CDC definitions based on BMI-for-age charts are widely used, including in clinical practice. By contrast, the International Obesity Task Force (IOTF) definition, developed from nationally representative BMI data for the age group 2–18 years from six countries, is used exclusively for epidemiological studies[20].

For the age group 5–19 years, between 1975 and 2016, the global prevalence of obesity (BMI >2 standard deviations (SD) above the median of the WHO growth reference) increased around eightfold to 5.6% in girls and 7.8% in boys[1]. Rates have plateaued at high levels in many HICs but have accelerated in other regions, particularly in parts of Asia. For the age group 2–4 years, between 1980 and 2015, obesity prevalence (IOTF definition, equivalent to an adult BMI of ≥30 kg/m^2) increased from 3.9% to 7.2% in boys and from 3.7% to 6.4% in girls[21]. Obesity prevalence is highest in Polynesia and Micronesia, the Middle East and North Africa, the Caribbean and the USA (Fig. 1). Variations in prevalence probably reflect different background levels of obesogenic environments, or the sum total of the physical, economic, policy, social and cultural factors that promote obesity[22]. Obesogenic environments include those with decreased active transport options, a ubiquity of food marketing directed towards children, and reduced costs and increased availability of nutrient-poor, energy-dense foods. Particularly in LMICs, the growth of urbanization, new forms of technology and global trade have led to reduced physical activity at work and leisure, a shift towards Western diets, and the expansion of transnational food and beverage companies to shape local food systems[23].
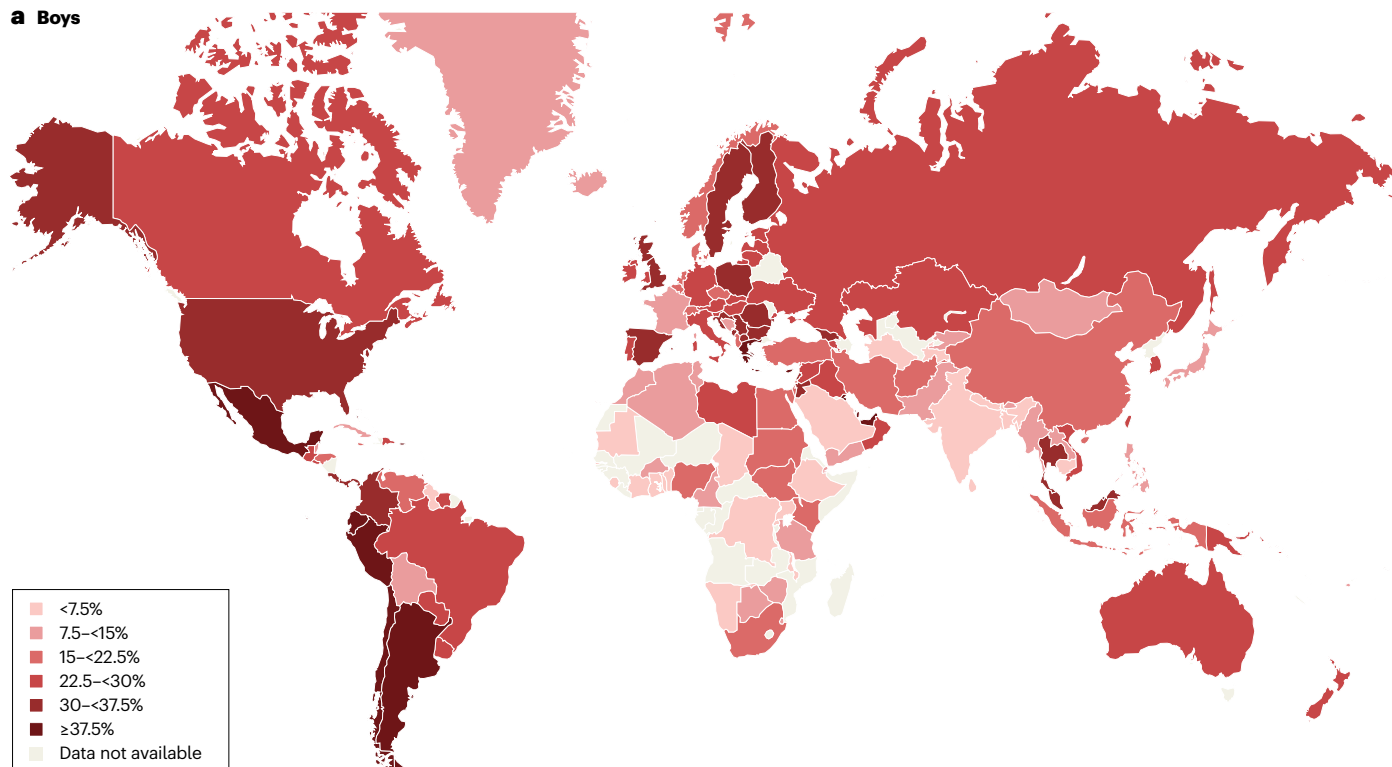
The reasons for varying sex differences in prevalence in different countries are unclear but may relate to cultural variations in parental feeding practices for boys and girls and societal ideals of body size[24]. In 2016, obesity in the age group 5–19 years was more prevalent in girls than in boys in sub-Saharan Africa, Oceania and some middle-income countries in other regions, whereas it was more prevalent in boys than in girls in all HICs, and in East and South-East Asia[21]. Ethnic and racial differences in obesity prevalence within countries are often assumed to mirror variations in social deprivation and other social determinants of obesity. However, an independent effect of ethnicity even after adjustment for socioeconomic status has been documented in the UK, with Black and Asian boys in primary school having higher prevalence of obesity than white boys[25].

Among individuals with obesity, very high BMI values have become more common in the past 15 years. The prevalence of severe obesity (BMI ≥120% of the 95th percentile (CDC definition), or ≥35 kg/m^2 at any age[26,27]) has increased in many HICs, accounting for one-quarter to one-third of those with obesity[28,29]. Future health risks of paediatric obesity in adulthood are well documented. For example, in a data linkage prospective study in Israel with 2.3 million participants who had BMI measured at age 17 years, those with obesity (≥95th percentile BMI for age) had a much higher risk of death from coronary heart disease (HR 4.9, 95% CI 3.9–6.1), stroke (HR 2.6, 95% CI 1.7–4.1) and sudden death (HR 2.1, 95% CI 1.5–2.9) compared with those whose BMI fell between the 5th and 24th percentiles[30].

Causes and risk factors

Early life is a critical period for childhood obesity development[9,31–33]. According to the Developmental Origins of Health and Disease framework, the early life environment may affect organ structure and function and influence health in later life[34,35]. Meta-analyses have shown that preconception and prenatal environmental exposures, including high maternal pre-pregnancy BMI and, to a lesser extent, gestational weight gain, as well as gestational diabetes and maternal smoking, are

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a Boys

	<7.5%
	7.5–<15%
	15–<22.5%
	22.5–<30%
	30–<37.5%
	≥37.5%
	Data not available

b Girls

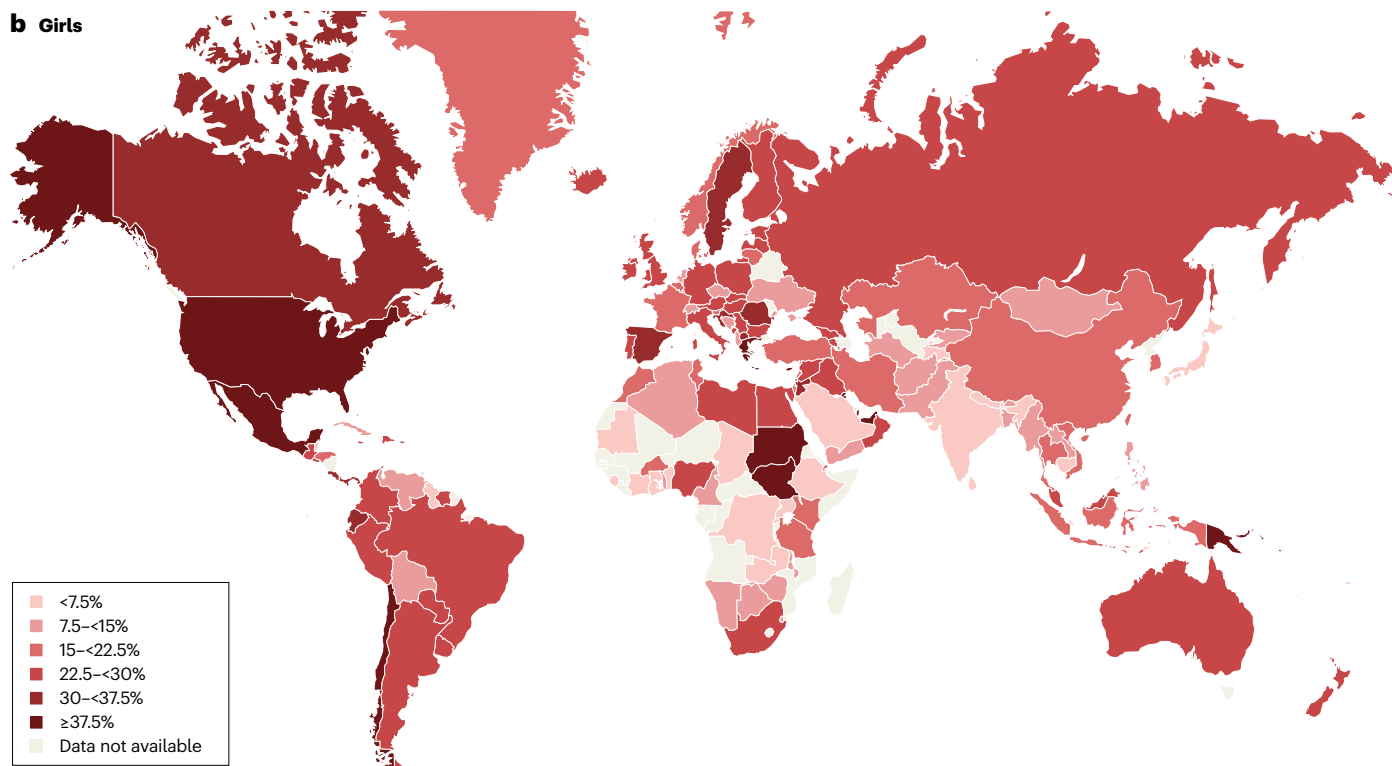|	
	<7.5%
	7.5–<15%
	15–<22.5%
	22.5–<30%
	30–<37.5%
	≥37.5%
	Data not available

Fig. 1 | Prevalence of paediatric overweight or obesity. Maps showing the proportions of children and adolescents living with overweight or obesity (part **a**, boys; part **b**, girls) according to latest available data from the Global Obesity Observatory. Data might not be comparable between countries owing to differences in survey methodology.

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associated with childhood obesity, potentially through effects on the in utero environment[33,36–38]. Paternal obesity is also associated with childhood obesity[33]. Birthweight, reflecting fetal growth, is a proxy for in utero exposures. Both low and high birthweights are associated with later adiposity, with high birthweight linked to increased BMI and low birthweight to central obesity[33,39].

Growth trajectories in early life are important determinants of later adiposity. Rapid weight gain in early childhood is associated with obesity in adolescence[32]. Also, later age and higher BMI at adiposity peak (the usual peak in BMI around 9 months of age), as well as earlier age at adiposity rebound (the lowest BMI reached between 4 and 7 years of age), are associated with increased adolescent and adult BMI[40,41]. Specific early life nutritional factors, including a lower protein content in formula food, are consistently associated with a lower risk of childhood obesity[42,43]. These also include longer breastfeeding duration, which is generally associated with a lower risk of childhood obesity[42]. However, some controversy exists, as these effects are affected by multiple sociodemographic confounding factors and their underlying mechanisms remain uncertain[44]. Some studies comparing higher and lower infant formula protein content have reported that the higher protein group have a greater risk of subsequent obesity, especially in early childhood[41,42]; however, one study with a follow-up period until age 11 years found no significant difference in the risk of obesity, but an increased risk of overweight in the high protein group was still observed[42,43,45]. A high intake of sugar-sweetened beverages is associated with childhood obesity[33,46].

Many other behavioural factors are associated with an increased risk of childhood obesity, including increased screen time, short sleep duration and poor sleep quality[33,47], reductions in physical activity[48] and increased intake of energy-dense micronutrient-poor foods[49]. These have been influenced by multiple changes in the past few decades in the broader social, economic, political and physical environments, including the widespread marketing of food and beverages to children, the loss of walkable green spaces in many urban environments, the rise in motorized transport, rapid changes in the use of technology, and the move away from traditional foods to ultraprocessed foods.

Obesity prevalence is inextricably linked to relative social inequality, with data suggesting a shift in prevalence over time towards those living with socioeconomic disadvantage, and thus contributes to social inequalities. In HICs, being in lower social strata is associated with a higher risk of obesity, even in infants and young children[50], whereas the opposite relationship occurs in middle-income countries[51]. In low-income countries, the relationship is variable, and the obesity burden seems to be across socioeconomic groups[52,53].

Overall, many environmental, lifestyle, behavioural and social factors in early life are associated with childhood obesity. These factors cannot be seen in isolation but are part of a complex interplay of exposures that jointly contribute to increased obesity risk. In addition to multiple prenatal and postnatal environmental factors, genetic variants also have a role in the development of childhood obesity (see section Mechanisms/pathophysiology).

Comorbidities and complications

Childhood obesity is associated with a wide range of short-term comorbidities (Fig. 2). In addition, childhood obesity tracks into adolescence and adulthood and is associated with complications across the life course[32,41,54,55].
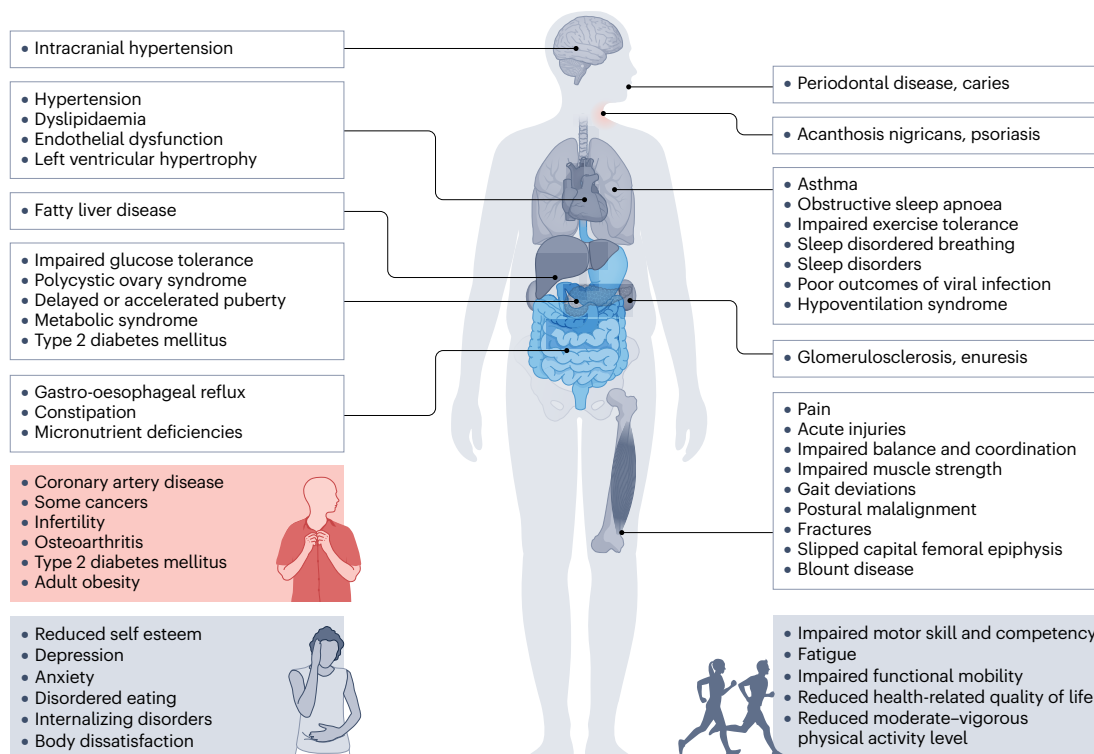

Fig. 2 | **Childhood obesity comorbidities.** Obesity in children and adolescents can be accompanied by various other pathologies. In addition, childhood obesity is associated with complications and disorders that manifest in adulthood (red box).
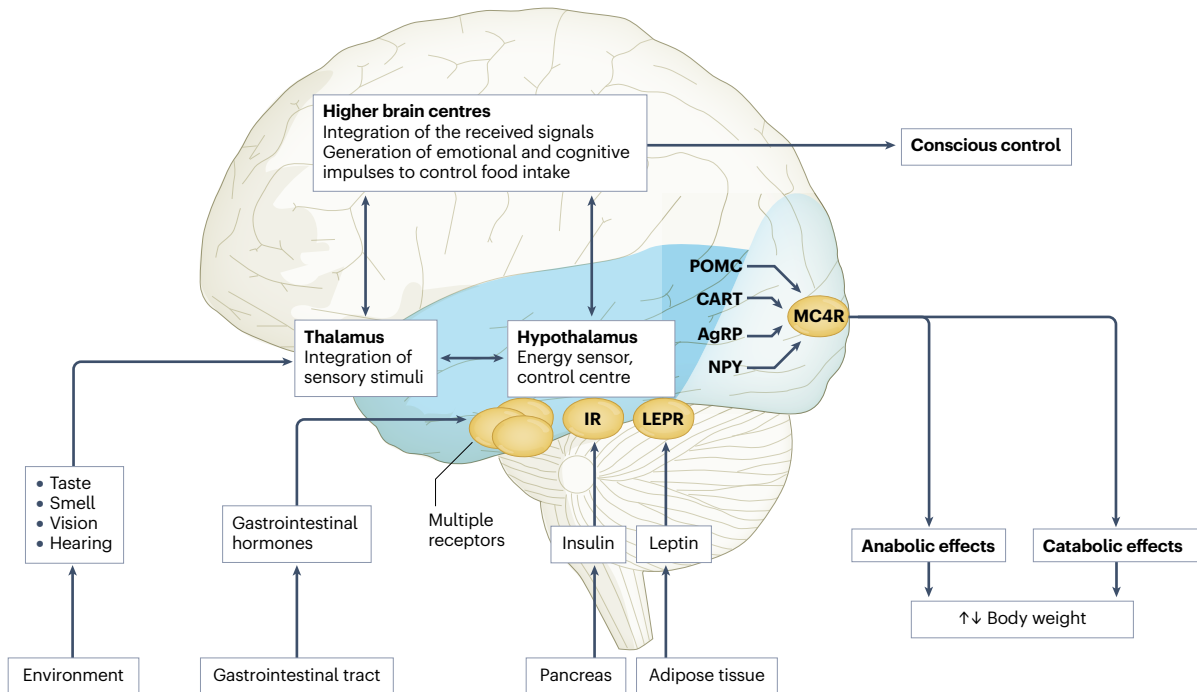
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Fig. 3 | Control circuits of weight regulation. Body weight is predominantly regulated by two systems: energy homeostasis and cognitive–emotional control. Both homeostatic and non-homeostatic signals are processed in the brain, involving multiple hormone and receptor cascades[217–219]. This overview depicts the best-known regulatory pathways. The homeostatic system, which is mainly regulated by brain centres in the hypothalamus and brainstem, operates on an unconscious level. Both long-term signals from the energy store in adipose tissue (for example, leptin) and short-term hunger and satiety signals from the gastrointestinal tract signal the current nutrient status. During gastric distension or after the release of gastrointestinal hormones (multiple receptors are involved) and insulin, a temporary feeling of fullness is induced. The non-homeostatic or hedonic system is regulated by higher-level brain centres and operates at the conscious level. After integration in the thalamus, homeostatic signals are combined with stimuli from the environment, experiences and emotions; emotional and cognitive impulses are then induced to control food intake. Regulation of energy homeostasis in the hypothalamus involves two neuron types of the arcuate nucleus: neurons producing neuropeptide Y (NPY) and agouti-related peptide (AgRP) and neurons producing pro-opiomelanocortin (POMC). Leptin stimulates these neurons via specific leptin receptors (LEPR) inducing anabolic effects in case of decreasing leptin levels and catabolic effects in case of increasing leptin levels. Leptin inhibits the production of NPY and AgRP, whereas low leptin levels stimulate AgRP and NPY production resulting in the feeling of hunger. Leptin directly stimulates POMC production in POMC neurons. POMC is cleaved into different hormone polypeptides including α-melanocyte-stimulating hormone which in turn activates melanocortin 4 receptors (MC4R) of cells in the nucleus paraventricularis of the hypothalamus, leading to the feeling of satiety. CART, cocaine and amphetamine responsive transcript; IR, insulin receptor.

Increased BMI, especially in adolescence, is linked to a higher risk of many health outcomes, including metabolic disorders, such as raised fasting glucose, impaired glucose tolerance, type 2 diabetes mellitus (T2DM), metabolic syndrome and fatty liver disease[56–59]. Other well-recognized obesity-associated complications include coronary heart disease, asthma, obstructive sleep apnoea syndrome (itself associated with metabolic dysfunction and inflammation)[60], orthopaedic complications and a range of mental health outcomes including depression and low self-esteem[27,55,57,61–63].

A 2019 systematic review showed that children and adolescents with obesity are 1.4 times more likely to have prediabetes, 1.7 times more likely to have asthma, 4.4 times more likely to have high blood pressure and 26.1 times more likely to have fatty liver disease than those with a healthy weight[64]. In 2016, it was estimated that, at a global level by 2025, childhood obesity would lead to 12 million children aged 5–17 years with glucose intolerance, 4 million with T2DM, 27 million with hypertension and 38 million with fatty liver disease[65]. These high prevalence rates have implications for both paediatric and adult health services.

Mechanisms/pathophysiology
Body weight regulation
Body weight is regulated within narrow limits by homeostatic and cognitive–emotional processes and a multifactorial interplay of hormones and messenger substances in complex regulatory circuits (Fig. 3). When these regulatory circuits are disturbed, an imbalance between energy intake and expenditure leads to obesity or to poor weight gain. As weight loss is much harder to achieve than weight gain in the long term due to the regulation circuits discussed below, the development of obesity is encouraged by modern living conditions, which enable underlying predispositions for obesity to become manifest[8,66].

In principle, there are two main systems in the brain which regulate body weight[8,66] (Fig. 3): energy homeostasis and cognitive–emotional control. Energy homeostasis is predominantly regulated by brain centres in the hypothalamus and brainstem and operates at an unconscious level. Both long-term signals from the adipose tissue energy stores and short-term hunger and satiety signals from the gastrointestinal tract signal the current nutrient status[8,66].

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Table 1 | Disturbances in the regulatory circuits of energy homeostasis leading to obesity

Disease	Specification	Cause	Phenotype
Monogenic obesity (autosomal recessive inheritance)	Leptin gene (*LEP*)	Biallelic variants in *LEP* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity and hyperphagia as early as the first year of life, extreme food-seeking behaviour, hypogonadotropic hypogonadism
	Leptin receptor gene (*LEPR*)	Biallelic variants in *LEPR* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity and hyperphagia as early as the first year of life, extreme food-seeking behaviour, pituitary hormone disturbances
	Prohormone convertase gene (*PCSK1*)	Biallelic variants in *PCSK1* affecting the leptin–melanocortin signalling pathway	Neonatal diarrhoea and dystrophy in the first year of life, afterwards hyperphagia and severe weight gain, hypoglycaemia, possible secondary adrenocortical insufficiency, hypothyroidism, diabetes insipidus
	Pro-opiomelanocortin gene (*POMC*)	Biallelic variants in *POMC* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity and hyperphagia as early as the first year of life, secondary adrenocortical insufficiency, red hair, pale skin
	Carboxypeptidase E gene (*CPE*)	Biallelic variants in *CPE* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity before the age of 5 years, intellectual disability, hypogonadotropic hypogonadism
	Single-minded homologue 1 gene (*SIM1*)	Biallelic variants in *SIM1* affecting the leptin–melanocortin signalling pathway	Neonatal feeding difficulties and muscular hypotonia in the first year of life, afterwards severe early onset obesity and hyperphagia (Prader–Willi-like syndrome), intellectual disability, behavioural anomalies
Monogenic obesity (autosomal dominant inheritance)	Melanocortin 4 receptor gene (*MC4R*)	Biallelic or monoallelic variants in *MC4R* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity before the age of 5 years, hyperphagia, increased linear growth, hyperinsulinaemia
	Melanocortin 2 receptor accessory protein 2 gene (*MRAP2*)	Monoallelic variants in *MRAP2* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity before the age of 5 years, hyperphagia, hyperglycaemia, hypertension
	SH2B adaptor protein 1 gene (*SH2B1*)	Monoallelic variants in *SH2B1* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity before the age of 5 years, increased food intake, insulin resistance, spectrum of behavioural abnormalities
	Steroid receptor coactivator 1 gene (*SRC1*)	Monoallelic variants in *SRC1* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity before the age of 5 years, hyperphagia, multiple fractures, persistent diarrhoea, partial thyroid hormone resistance, adipose tissue fibrosis and hepatic fibrosis in young patients
	Guanine nucleotide-binding protein, α-stimulating activity polypeptide 1 gene (*GNAS*)	Monoallelic variants in *GNAS* affecting the leptin–melanocortin signalling pathway	Severe early onset obesity before the age of 5 years, brachydactyly, hypothyroidism, intellectual disability, growth hormone deficiency
Syndromic obesity	Prader–Willi syndrome	Deletion or inactivation of the paternal chromosome 15q11-13	Neonatal feeding difficulties and muscular hypotonia in the first year of life, afterwards severe early onset obesity and hyperphagia, behavioural anomalies, intellectual disability, pituitary hormone disturbances
	Bardet–Biedl syndrome or Laurence–Moon syndrome	Biallelic pathogenic variants in different genes on different chromosomes leading to the subtypes BBS1 to BBS22	Severe early onset obesity, polydactyly, retinal dystrophy, genitourinary and kidney anomalies, intellectual disability, hypogonadism, behavioural anomalies, wide spectrum of other minor manifestations
Hypothalamic obesity	Hypothalamic syndrome	Injury to the hypothalamus, such as tumours (craniopharyngioma) and their therapy, accidents and others	Severe obesity, often in combination with hormonal deficiencies of the pituitary gland, abnormal behaviour and intellectual disability

For example, negative energy balance leading to reduced fat mass results in reduced leptin levels, a permanently reduced urge to exercise and an increased feeling of hunger. During gastric distension or after the release of gastrointestinal hormones and insulin, a temporary feeling of fullness is induced[8,66]. Cognitive–emotional control is regulated by higher brain centres and operates at a conscious level. Here, the homeostatic signals are combined with stimuli from the environment (sight, smell and taste of food), experiences and emotions[8,66]. Disorders at the level of cognitive–emotional control mechanisms include emotional eating as well as eating disorders. For example, the reward areas in the brain of people with overweight are more strongly activated by high-calorie foods than those in the brain of people with normal weight[67]. Both systems interact with each other, and the cognitive–emotional system is strongly influenced by the homeostatic control circuits.

Disturbances in the regulatory circuits of energy homeostasis can be genetically determined, can result from disease or injury to the regulatory centres involved, or can be caused by prenatal programming[8,66]. If the target value of body weight has been shifted, the organism tries by all means (hunger, drive) to reach the desired higher weight. These disturbed signals of the homeostatic system can have an imperative, irresistible character, so that a conscious influence on food intake is no longer effectively possible[8,66]. The most important disturbances of energy homeostasis are listed in Table 1.

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The leptin pathway

The peptide hormone leptin is primarily produced by fat cells. Its production depends on the amount of adipose tissue and the energy balance. A negative energy balance during fasting results in a reduction of circulating leptin levels by 50% after 24 h (ref. 68). In a state of weight loss, leptin production is reduced[69]. In the brain, leptin stimulates two neuron types of the arcuate nucleus in the hypothalamus via specific leptin receptors: neurons producing neuropeptide Y (NPY) and agouti-related peptide (AgRP) and neurons producing pro-opiomelanocortin (POMC). High leptin levels inhibit the production of NPY and AgRP, whereas low leptin levels stimulate AgRP and NPY production. By contrast, leptin directly stimulates POMC production in POMC neurons (Fig. 3). POMC is a hormone precursor that is cleaved into different hormone polypeptides by specific enzymes, such as prohormone convertase 1 (PCSK1). This releases α-melanocyte-stimulating hormone (α-MSH) which in turn activates melanocortin 4 receptors (MC4R) of cells in the nucleus paraventricularis of the hypothalamus, leading to the feeling of satiety. Rare, functionally relevant mutations in the genes for leptin and leptin receptor, *POMC*, *PCSK1/3* or *MC4R* lead to extreme obesity in early childhood. These forms of obesity are potential indications for specific pharmacological treatments, for example setmelanotide[70,71]. *MC4R* mutations are the most common cause of monogenic obesity, as heterozygous mutations can be symptomatic depending on the functional impairment and with variable penetrance and expression. Other genes have been identified, in which rare heterozygous pathological variants are also associated with early onset obesity (Table 1).

Pathological changes in adipose tissue

Adipose tissue can be classified into two types, white and brown adipose tissue. White adipose tissue comprises unilocular fat cells and brown adipose tissue contains multilocular fat cells, which are rich in mitochondria[72]. A third type of adipocyte, beige adipocytes, within the white adipose tissue are induced by prolonged exposure to cold or adrenergic signalling, and show a brown adipocyte-like morphology[72]. White adipose tissue has a large potential to change its volume to store energy and meet the metabolic demands of the body. The storage capacity and metabolic function of adipose tissue depend on the anatomical location of the adipose tissue depot. Predominant enlargement of white adipose tissue in the visceral, intra-abdominal area (central obesity) is associated with insulin resistance and an increased risk of metabolic disease development before puberty. Accumulation of adipose tissue in the hips and flanks has no adverse effect and may be protective against metabolic syndrome. In those with obesity, adipose tissue is characterized by an increased number of adipocytes (hyperplasia), which originate from tissue-resident mesenchymal stem cells, and by enlarged adipocytes (hypertrophy)[73]. Adipocytes with a very large diameter reach the limit of the maximal oxygen diffusion distance, resulting in hypoxia, the development of an inflammatory expression profile (characterized by, for example, leptin, TNF and IL-6) and adipocyte necrosis, triggering the recruitment of leukocytes. Resident macrophages switch from the anti-inflammatory M2 phenotype to a pro-inflammatory M1 phenotype, which is associated with insulin resistance, further promoting local sterile inflammation and the development of fibrotic adipose tissue. This process limits the expandability of the adipose tissue for further storage of triglycerides. In the patient, the increase in fat mass in obesity is associated with insulin resistance and systemic low-grade inflammation characterized by elevated serum levels of C-reactive protein and pro-inflammatory cytokines. The limitation of adipose tissue expandability results in storage of triglycerides in other organs, such as the liver, muscle and pancreas[74].

Genetics and epigenetics in the general population

Twin studies have found heritability estimates for BMI of up to 70%[75,76]. In contrast to rare monogenic forms of obesity, which are often caused by a single genetic defect with a large effect, the genetic background of childhood obesity in the general population is shaped by the joint effects of many common genetic variants, each of which individually makes a small contribution to the phenotype. For adult BMI, genome-wide association studies, which examine associations of millions of such variants across the genome at the same time, have identified around 1,000 genetic loci[77]. The largest genome-wide association studies in children, which include much smaller sample sizes of up to 60,000 children, have identified 25 genetic loci for childhood BMI and 18 for childhood obesity, the majority of which overlap[78,79]. There is also a clear overlap with genetic loci identified in adults, for example for *FTO*, *MC4R* and *TMEM18*, but this overlap is not complete, some loci are specific to early life BMI, or have a relatively larger contribution in childhood[78–80]. These findings suggest that biological mechanisms underlying obesity in childhood are mostly similar to those in adulthood, but the relative influence of these mechanisms may differ at different phases of life.

The role of epigenetic processes in childhood and adolescent obesity has gained increasing attention. In children, several studies found associations between DNA methylation and BMI[81–84], but a meta-analysis including data from >4,000 children identified only minimal associations[85]. Most studies support the hypothesis that DNA methylation changes are predominantly a consequence rather than a cause of obesity, which may explain the lower number of identified (up to 12) associations in children, in whom duration of exposure to a higher BMI is shorter than in adults, in whom associations with DNA methylation at hundreds of sites have been identified[85–87]. In addition to DNA methylation, some specific circulating microRNAs have been found to be associated with obesity in childhood[84].

The field of epigenetic studies in childhood obesity is relatively young and evolving quickly. Future studies will need to focus on defining robust associations in blood as well as other tissues and on identifying cause-and-effect relationships. In addition, other omics, such as metabolomics and proteomics, are promising areas that may contribute to an improved aetiological understanding or may provide biological signatures that can be used as predictive or prognostic markers of childhood obesity and its comorbidities.

Parental obesity and childhood obesity

There is an established link between increased parental BMI and increased childhood BMI[88,89]. This link may be due to shared genetics, shared environment, a direct intrauterine effect of maternal BMI or a combination of these factors. In the case of shared genetics, the child inherits BMI-increasing genetic variants from one or both parents. Shared environmental factors, such as diet or lifestyle, may also contribute to an increased BMI in both parents and child. In addition, maternal obesity might create an intrauterine environment that programmes metabolic processes in the fetus, which increases the risk of childhood obesity. Some studies show larger effects of maternal than paternal BMI, indicating a potential causal intrauterine mechanism of maternal obesity, but evidence showing similar maternal and paternal effects is increasing. The data may indicate that there is only a limited direct intrauterine effect of maternal obesity on childhood obesity; rather, genetic effects inherited from the mother or father, or both,

and/or shared environmental factors may contribute to childhood obesity risk[90–95].

Diagnosis, screening and prevention

Diagnostic work-up

The extent of overweight in clinical practice is estimated using BMI based on national charts[96–100]. Of note, the clinical classification of overweight or obesity differ depending on the BMI charts used and national recommendations; hence, local guidelines should be referred to. For example, the US CDC Growth Charts and several others use the 85th and 95th centile cut-points to denote overweight and obesity, respectively[19]. The WHO Growth Reference for children aged 5–19 years defines cut-points for overweight and obesity as a BMI-for-age greater than +1 and +2 SDs for BMI for age, respectively[18]. For children <5 years of age, overweight and obesity are defined as weight-for-height greater than +2 and +3 SDs, respectively, above the WHO Child Growth Standards median[17]. The IOTF and many countries in Europe use cut-points of 85th, 90th and 97th to define overweight, obesity and extreme obesity[26].

BMI as an indirect measurement of body fat has some limitations; for example, pronounced muscle tissue leads to an increase in BMI, and BMI is not independent of height. In addition, people of different ethnicities may have different cut-points for obesity risk; for example, cardiometabolic risk occurs at lower BMI values in individuals with south Asian than in those with European ancestry[101]. Thus, BMI is best seen as a convenient screening tool that is supplemented by clinical assessment and investigations.

Other measures of body fat may help differentiate between fat mass and other tissues. Some of these tools are prone to low reliability, such as body impedance analyses (high day-to-day variation and dependent on level of fluid consumption) or skinfold thickness (high inter-observer variation), or are more expensive or invasive, such as MRI, CT or dual-energy X-ray absorptiometry, than simpler measures of body composition or BMI assessment.

Primary diseases rarely cause obesity in children and adolescents (<2%)[102]. However, treatable diseases should be excluded in those with obesity. A suggested diagnostic work-up is summarized in Fig. 4. Routine measurement of thyroid-stimulating hormone (TSH) is not recommended[96]. Moderately elevated TSH levels (usually <10 IU/l) are frequently observed in obesity and are a consequence, and not a cause, of obesity[103]. In a growing child with normal height velocity, a normal BMI at the age of 2 years and normal cognitive development, no further diagnostic steps are necessary to exclude primary diseases[96,104].

Clinical findings which need no further examination include pseudogynaecomastia (adipose tissue mimicking breast development; differentiated from breast tissue by ultrasonography), striae (caused by rapid weight increase) and a hidden penis in suprapubic adipose tissue (differentiated from micropenis by measurement of stretched penis length while pressing down on the suprapubic adipose tissue)[96,105]. Girls with obesity tend to have an earlier puberty onset (usually at around 8–9 years of age) and boys with severe obesity may have a delayed puberty onset (usually at around 13–14 years of age)[106]. Thus, if pubertal onset is slightly premature in girls or slightly delayed in boys, no further endocrine assessment is necessary.

Assessment of obesity-associated comorbidities

A waist to height ratio of >0.5 is a simple tool to identify central obesity[107,108]. Screening for cardiometabolic risk factors and fatty liver disease is recommended, especially in adolescents, and in those with more severe obesity or central adiposity, a strong family history of T2DM or premature heart disease, or relevant clinical symptoms, such as high blood pressure or acanthosis nigricans[96–99,109]. Investigations
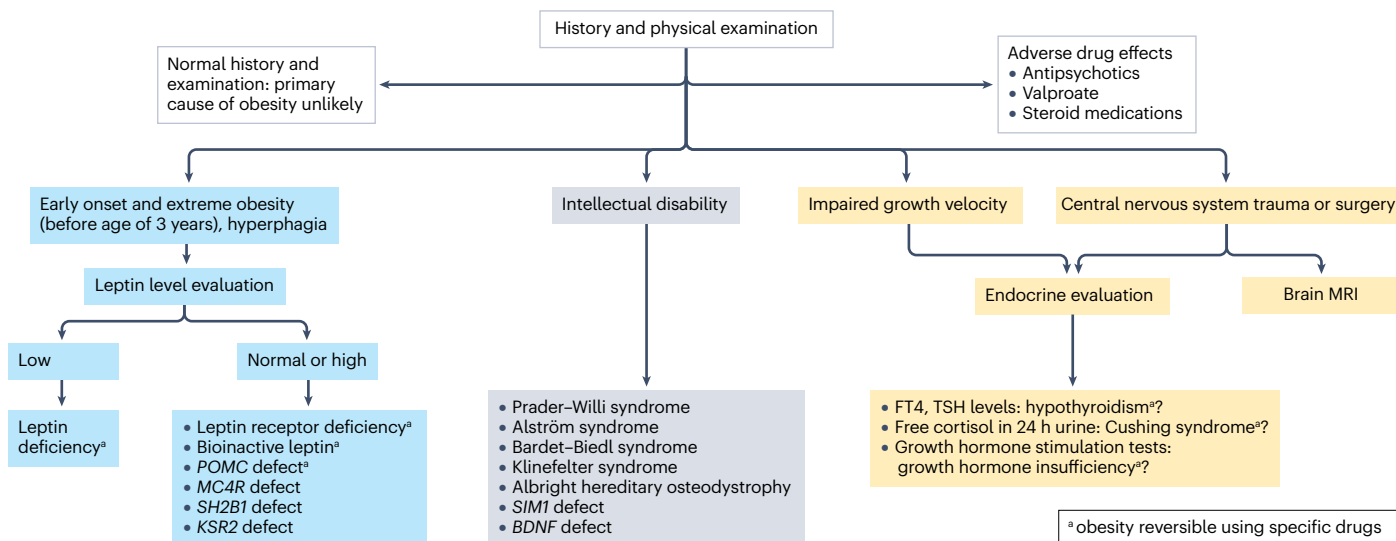

Fig. 4 | Suggested diagnostic work-up in children or adolescents with obesity. Concerning findings from a detailed medical history and physical examination will lead to further examinations. In individuals with early onset, extreme obesity (before age 3 years) and signs of hyperphagia, serum leptin level should be measured to rule out the extremely rare condition of congenital leptin deficiency. In individuals with normal or high leptin levels, genetic testing is indicated to search for monogenetic obesity. In individuals with intellectual disability, a syndromic disease may be present. Signs of impaired growth velocity or the history of central nervous system trauma or surgery will result in deeper endocrine evaluation and/or brain MRI. *BDNF*, brain-derived neurotropic factor; FT4, free thyroxin; *KSR2*, kinase suppressor of ras 2; *MC4R*, melanocortin 4 receptor; *POMC*, pro-opiomelanocortin; *SH2B1*, Src-homology 2 (SH2) B adapter protein 1; *SIM1*, single-minded homologue 1; TSH, thyroid-stimulating hormone.

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generally include fasting glucose levels, lipid profile, liver function and glycated haemoglobin, and might include an oral glucose tolerance test, polysomnography, and additional endocrine tests for polycystic ovary syndrome[96–99].

T2DM in children and adolescents often occurs in the presence of a strong family history and may not be related to obesity severity[110]. T2DM onset usually occurs during puberty, a physiological state associated with increased insulin resistance[111] and, therefore, screening for T2DM should be considered in children and adolescents with obesity and at least one risk factor (family history of T2DM or features of metabolic syndrome) starting at pubertal onset[112]. As maturity-onset diabetes of the young (MODY) type II and type III are more frequent than T2DM in children and adolescents in many ethnicities, genetic screening for MODY may be appropriate[112]. Furthermore, type 1 diabetes mellitus (T1DM) should be excluded by measurement of autoantibodies in any individual with suspected diabetes with obesity. The differentiation of T2DM from MODY and T1DM is important as the diabetes treatment approaches differ[112].

Several comorbidities of obesity should be considered if specific symptoms occur[96,109]. For polycystic ovary syndrome in hirsute adolescent girls with oligomenorrhoea or amenorrhoea, moderately increased testosterone levels and decreased sex hormone binding globulin levels are typical laboratory findings[113]. Obstructive sleep apnoea can occur in those with more severe obesity and who snore, have daytime somnolence or witnessed apnoeas. Diagnosis is made by polysomnography[114]. Minor orthopaedic disorders, such as flat feet and genu valgum, are frequent in children and adolescents with obesity and may cause pain. Major orthopaedic complications include slipped capital femoral epiphyses (acute and chronic), which manifest with hip and knee pain in young adolescents and are characterized by reduced range of hip rotation and waddling gait; and Blount disease (tibia vara), typically occurring in children aged 2–5 years[105,115]. In addition, children and adolescents with extreme obesity frequently have increased dyspnoea and decreased exercise capacity. A heightened demand for ventilation, elevated work of breathing, respiratory muscle inefficiency and diminished respiratory compliance are caused by increased truncal fat mass. This may result in a decreased functional residual capacity and expiratory reserve volume, ventilation to perfusion ratio abnormalities and hypoxaemia, especially when supine. However, conventional respiratory function tests are only mildly affected by obesity except in extreme cases[116]. Furthermore, gallstones should be suspected in the context of abdominal pain after rapid weight loss, which can be readily diagnosed via abdominal ultrasonography[105]. Finally, pseudotumor cerebri may present with chronic headache, and depression may present with flat affect, chronic fatigue and sleep problems[105].

Obesity in adolescents can also be associated with disordered eating, eating disorders and other psychological disorders[117,118]. If suspected, assessment by a mental health professional is recommended.

Prevention

A comprehensive approach.
The 2016 report of the WHO Commission on Ending Childhood Obesity stated that progress in tackling childhood obesity has been slow and inconsistent, with obesity prevention requiring a whole-of-government approach in which policies across all sectors systematically take health into account, avoiding harmful health impacts and, therefore, improving population health and health equity[13,119]. The focus in developing and implementing interventions to prevent obesity in children should be on interventions that are feasible, effective and likely to reduce health inequalities[14]. Importantly, the voices of children and adolescents living with social disadvantage and those from minority groups must be heard if such interventions are to be effective and reduce inequalities[120].

Figure 5 presents a system for the prevention of childhood obesity within different domains of the socioecological model[121] and highlights opportunities for interventions. These domains can be described on a continuum, from (most downstream) individual and interpersonal (including parents, peers and wider family) through to organizational (including health care and schools), community (including food, activity and environment), society (including media and finally cultural norms) and (most upstream) public policy (from local to national level). Interventions to prevent childhood obesity can be classified on the Nuffield intervention ladder[122]. This framework was proposed by the Nuffield Council on Bioethics in 2007 (ref. 122) and distributes interventions on the ladder steps depending on the degree of agency required by the individual to make the behavioural changes that are the aim of the intervention. The bottom step of the ladder includes interventions that provide information, which requires the highest agency and relies on a child, adolescent and/or family choosing (and their ability to choose) to act on that information and change behaviour. The next steps of the ladder are interventions that enable choice, guide choice through changing the default policy, guide choice through incentives, guide choice through disincentives, or restrict choice. On the top-most step of the ladder (lowest agency required) are interventions that eliminate choice.

Downstream and high-agency interventions (on the bottom steps of the Nuffield ladder) are more likely to result in intervention-generated inequalities[123]. This has been elegantly described and evidenced, with examples from the obesity prevention literature[124,125]. A particularly strong example is a systematic review of 38 interventions to promote healthy eating that showed that food price (an upstream and low-agency intervention) seemed to decrease inequalities, all interventions that combined taxes and subsidies consistently decreased inequalities, and downstream high-agency interventions, especially dietary counselling, seemed to increase inequalities[126].

Effectiveness of prevention interventions.
A 2019 Cochrane review of interventions to prevent obesity in children[127] included 153 randomized controlled trials (RCTs), mainly in HICs (12% were from middle-income countries). Of these RCTs, 56% tested interventions in children aged 6–12 years, 24% in children aged 0–5 years, and 20% in adolescents aged 13–18 years. The review showed that diet-only interventions to prevent obesity in children were generally ineffective across all ages. Interventions combining diet and physical activity resulted in modest benefits in children aged 0–12 years but not in adolescents. However, physical activity-only interventions to prevent obesity were effective in school-age children (aged 5–18 years). Whether the interventions were likely to work equitably in all children was investigated in 13 RCTs. These RCTs did not indicate that the strategies increased inequalities, although most of the 13 RCTs included relatively homogeneous groups of children from disadvantaged backgrounds.

The potential for negative unintended consequences of obesity prevention interventions has received much attention[128]. The Cochrane review[127] investigated whether children were harmed by any of the strategies; for example, by having injuries, losing too much weight or developing damaging views about themselves and their weight. Of the few RCTs that did monitor these outcomes, none found any harms in participants.
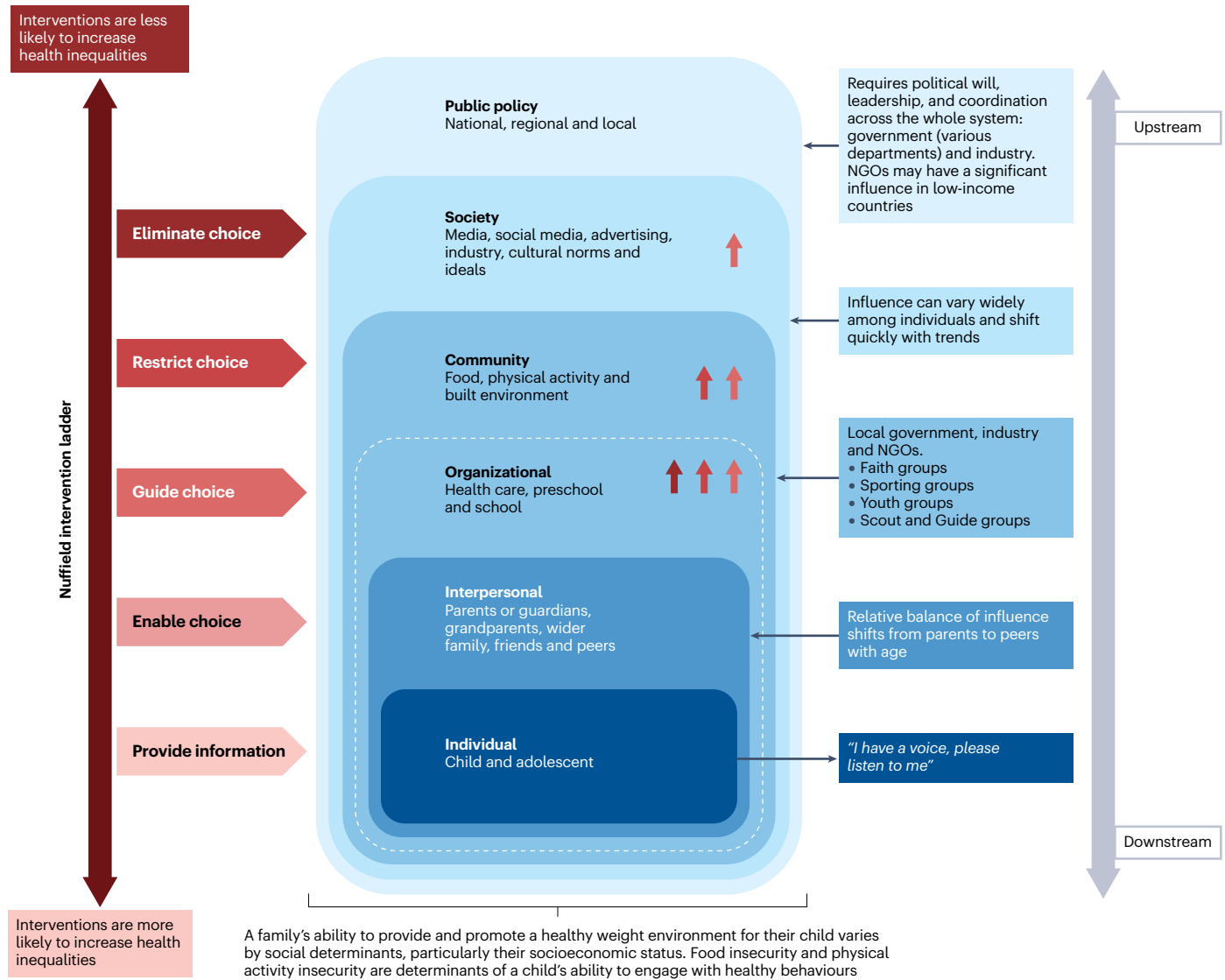
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Fig. 5 | Prevention of childhood obesity within a socioecological model. This schematic integrates interventions that were included in a Cochrane review[127] of 153 randomized controlled trials of interventions to prevent obesity in children and are high on the Nuffield intervention ladder[122]. The Nuffield intervention ladder distributes interventions depending on the degree of agency required for the behavioural changes that are the aim of the intervention. The socioecological model[121] comprises different domains (or levels) from the individual up to public policy. Interventions targeting the individual and interpersonal domains can be described as downstream interventions, and interventions within public policy can be described as the highest level of upstream interventions. Within each of these domains, arrow symbols with colours corresponding to the Nuffield intervention ladder category are used to show interventions that were both included in the Cochrane review[127] and that guide, restrict or eliminate choice as defined by the Nuffield intervention ladder[122]. Upstream interventions, and interventions on the top steps of the Nuffield ladder, are more likely to reduce inequalities. NGO, non-governmental organization.

Intervention levels. Most interventions (58%) of RCTs in the Cochrane review aimed to change individual lifestyle factors via education-based approaches (that is, simply provide information)[129]. In relation to the socioecological model, only 11 RCTs were set in the food and physical activity environment domain, and child care, preschools and schools were the most common targets for interventions. Of note, no RCTs were conducted in a faith-based setting[130]. Table 2 highlights examples of upstream interventions that involve more than simply providing information and their classification on the Nuffield intervention ladder.

Different settings for interventions to prevent childhood obesity, including preschools and schools, primary health care, community settings and national policy, offer different opportunities for reach and effectiveness, and a reduction in inequalities.

Preschools and schools are key settings for public policy interventions for childhood obesity prevention, and mandatory and voluntary food standards and guidance on physical education are in place in many countries. Individual schools are tasked with translating and implementing these standards and guidance for their local context. Successful implementation of a whole-school approach, such as that

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used in the WHO Nutrition-Friendly Schools Initiative[131], is a key factor in the effectiveness of interventions. Careful consideration should be given to how school culture can, and needs to, be shifted by working with schools to tailor the approach and manage possible staff capacity issues, and by building relationships within and outside the school gates to enhance sustainability[132,133].

Primary health care offers opportunities for guidance for obesity prevention, especially from early childhood to puberty. Parent-targeted interventions conducted by clinicians in health-care or community settings have the strongest level of evidence for their effectiveness in reducing BMI z-score at age 2 years[134]. These interventions include group programmes, clinic nurse consultations, mobile phone text support or nurse home visiting, and focusing on healthy infant feeding, healthy childhood feeding behaviours and screen time.

A prospective individual participant data meta-analysis of four RCTs involving 2,196 mother–baby dyads, and involving nurse home visiting or group programmes, resulted in a small but significant reduction in BMI in infants in the intervention groups compared with control infants at age 18–24 months[134]. Improvements were also seen in television viewing time, breastfeeding duration and feeding practices. Interventions were more effective in settings with limited provision of maternal and child health services in the community. However,

effectiveness diminished by age 5 years without further intervention, highlighting the need for ongoing interventions at each life stage[135]. Evidence exists that short-duration interventions targeting sleep in very early childhood may be more effective than nutrition-targeted interventions in influencing child BMI at age 5 years[136].

Primary care clinicians can provide anticipatory guidance, as a form of primary prevention, to older children, adolescents and their families, aiming to support healthy weight and weight-related behaviours. Clinical guidelines recommend that clinicians monitor growth regularly, and provide guidance on healthy eating patterns, physical activity, sedentary behaviours and sleep patterns[97,100]. Very few paediatric trials have investigated whether this opportunistic screening and advice is effective in obesity prevention[100]. A 2021 review of registered RCTs for the prevention of obesity in infancy found 29 trials[137], of which most were delivered, or were planned to be delivered, in community health-care settings, such as nurse-led clinics. At the time of publication, 11 trials had reported child weight-related outcomes, two of which showed a small but significant beneficial effect on BMI at age 2 years, and one found significant improvements in the prevalence of obesity but not BMI. Many of the trials showed improvements in practices, such as breastfeeding and screen time.

At the community level, local public policy should be mindful of the geography of the area (such as urban or rural) and population

Table 2 | Potential obesity prevention interventions in different settings

Settings	Interventions	Nuffield intervention ladder classification[83]
Preschool and school settings	Monitor the content of packed lunches	Eliminate/restrict choice
	Limit vending machine contents in schools	Eliminate choice
	Eliminate choice of sugar-sweetened beverages and replace with water	Eliminate choice
	Limit chips or French fries to once a week	Restrict choice
	Offer free fruit at break and snack times	Guide/enable choice
	Include bursts of physical activity during classroom time	Guide/enable choice
	Introduce after-school dance or sport sessions	Guide/enable choice
	Provide safe cycling and walking routes to school, particularly when supported by trusted adults	Guide/enable choice
Clinical settings	Encourage breastfeeding and provide developmentally appropriate guidance on child nutrition for parents	Guide/enable choice
	Support parents to recognize sleep cues and encourage adequate sleep	Guide/enable choice
	Monitor weight, ensuring children avoid rapid or excessive weight gain and growth velocity	Guide/enable choice
	Encourage parents to establish habits of daily physical activity and play for young children	Guide/enable choice
Community-level settings	Town planning policies on mobile food and beverage vans close to schools	Restrict choice
	Local government planning restrictions on the number and locations of takeaway food outlets on walking journeys undertaken by children	Restrict choice
	Local faith-led groups run by religious leaders that promote physical activity	Enable/guide choice
	Local youth groups run by non-governmental organizations targeted in disadvantaged areas that promote physical activity	Enable/guide choice
Public policy	Ban on the advertising of foods high in fats, sugar and salt and of sugary beverages during prime-time children's television	Enable/guide choice
	Introduce supermarket policy to remove all high-fat, high-sugar and high-salt snack foods from payment counter areas (to limit 'pester power')	Enable/guide choice
	Provide industry financial support for sporting and physical activities and events for children	Enable/guide choice
	Provide positive messages about healthy lifestyles and healthy weight from role models via social media	Enable/guide choice

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demographics. Adolescents usually have more freedom in food and beverage choices made outside the home than younger children. In addition, physical activity levels usually decline and sedentary behaviours rise during adolescence, particularly in girls[138,139]. These behavioural changes offer both opportunities and barriers for those developing community interventions. On a national societal level, public policies for interventions to prevent obesity in children include the control of advertising of foods and beverages high in fat, sugar and/or salt in some countries. Industry and the media, including social media, can have a considerable influence on the food and physical activity behaviours of children[13,119].

Public policy may target interventions at all domains from the individual to the societal level. The main focus of interventions in most national public policies relies on the ability of individuals to make the behavioural changes that are the aim of the intervention (high-agency interventions) at the individual level (downstream interventions).

Box 1

Strategies for minimizing weight stigma in health care[220–222]

Minimizing weight bias in the education of health-care professionals

- Improved education of health professionals:
  - pay attention to the implicit and explicit communication of social norms
  - include coverage of the broader determinants of obesity
  - include discussion of harms caused by social and cultural norms and messages concerning body weight
  - provide opportunities to practise non-stigmatizing care throughout education
- Provide causal information focusing on the genetic and/or socioenvironmental determinants of weight.
- Provide empathy-invoking interventions, emphasizing size acceptance, respect and human dignity.
- Provide a weight-inclusive approach, by emphasizing that all individuals, regardless of size, have the right to equal health care.

Addressing health facility infrastructure and processes

- Provide appropriately sized chairs, blood pressure cuffs, weight scales, beds, toilets, showers and gowns.
- Use non-stigmatizing language in signage, descriptions of clinical services and other documentation.

Providing clinical leadership and using appropriate language within health-care settings

- Senior clinicians and managers should role-model supportive and non-biased behaviours towards people with obesity and indicate that they do not tolerate weight-based discrimination in any form.
- Staff should identify the language that individuals prefer in referring to obesity.
- Use person-first language, for example a 'person with obesity' rather than 'an obese person'.

An equal focus on low-agency and upstream interventions is required if a step change in tackling childhood obesity is to be realized[140,141].

COVID-19 and obesity

Early indications in several countries show rising levels of childhood obesity, and an increase in inequalities in childhood obesity during the COVID-19 pandemic[142]. The substantial disruptions in nutrition and lifestyle habits of children during and since the pandemic include social isolation and addiction to screens[143]. Under-nutrition is expected to worsen in poor countries, but obesity rates could increase in middle-income countries and HICs, especially among vulnerable groups, widening the gap in health and social inequalities[143]. Public health approaches at national, regional and local levels should include strategies that not only prevent obesity and under-nutrition, but also reduce health inequalities.

In summary, although most trials of obesity prevention have occurred at the level of the individual, the immediate family, school or community, effective prevention of obesity will require greater investment in upstream, low-agency interventions.

Management
Treatment goals

Treatment should be centred on the individual and stigma-free (Box 1) and may aim for a reduction in overweight and improvement in associated comorbidities and health behaviours. Clinical considerations when determining a treatment approach should include age, severity of overweight and the presence of associated complications[144,145].

Treatment guidelines

Clinical guidelines advise that first-line management incorporates a family-based multicomponent approach that addresses dietary, physical activity, sedentary and sleep behaviours[97,99,109,146]. This approach is foundational, with adjunctive therapies, especially pharmacotherapy and bariatric surgery, indicated under specific circumstances, usually in adolescents with more severe obesity[144,145]. Guideline recommendations vary greatly among countries and are influenced by current evidence, and functionality and resourcing of local health systems. Hence, availability and feasibility of therapies differs internationally. In usual clinical practice, interventions may have poorer outcomes than is observed in original studies or anticipated in evidence-based guidelines[147] because implementation of guidelines is more challenging in resource-constrained environments[148]. In addition, clinical trials are less likely to include patients with specialized needs, such as children from culturally diverse populations, those living with social disadvantage, children with complex health problems, and those with severe obesity[149,150].

Behavioural interventions

There are marked differences in individual responses to behavioural interventions, and overall weight change outcomes are often modest. In children aged 6–11 years, a 2017 Cochrane review[150] found that mean BMI z-scores were reduced in those involved in behaviour-changing interventions compared with those receiving usual care or no treatment by only 0.06 units (37 trials; 4,019 participants; low-quality evidence) at the latest follow-up (median 10 months after the end of active intervention). In adolescents aged 12–17 years, another 2017 Cochrane review[149] found that multicomponent behavioural interventions resulted in a mean reduction in weight of 3.67 kg (20 trials; 1,993 participants) and reduction in BMI of 1.18 kg/m² (28 trials; 2,774 participants). These effects were maintained at the 24-month follow-up. A 2012 systematic

review found significant improvements in LDL cholesterol triglycerides and blood pressure up to 1 year from baseline following lifestyle interventions in children and adolescents[151].

Family-based behavioural interventions are recommended in national level clinical practice guidelines[97,100,146,152]. They are an important element of intensive health behaviour and lifestyle treatments (IHBLTs)[109]. Family-based approaches use behavioural techniques, such as goal setting, parental monitoring or modelling, taught in family sessions or in individual sessions separately to children and care givers, depending on the child's developmental level. The priority is to encourage the whole family to engage in healthier behaviours that result in dietary improvement, greater physical activity, and less sedentariness. This includes making changes to the family food environment and requires parental monitoring.

Family-based interventions differ in philosophy and implementation from those based on family systems theory and therapy[153]. All are intensive interventions that require multiple contact hours (26 or more) with trained specialists delivered over an extended period of time (6–12 months)[10]. Changing family lifestyle habits is challenging and expensive, and the therapeutic expertise is not widely available. Moving interventions to primary care settings, delivered by trained health coaches, and supplemented by remote contact (for example by phone), will improve access and equity[154].

Very few interventions use single psychological approaches. Most effective IHBLTs are multicomponent and intensive (many sessions), and include face-to-face contact. There has been interest in motivational interviewing as an approach to delivery[155]. As client-centred counselling, this places the young person at the centre of their behaviour change. Fundamental to motivational interviewing is the practitioner partnership that helps the young person and/or parents to explore ambivalence to change, consolidate commitment to change, and develop a plan based on their own insights and expertise. Evidence reviews generally support the view that motivational interviewing reduces BMI. Longer interventions (>4 months), those that assess and report on intervention fidelity, and those that target both diet and physical activity are most effective[155,156].

More intensive dietary interventions

Some individuals benefit from more intensive interventions[98,144,157,158], which include very low-energy diets, very low-carbohydrate diets and intermittent energy restriction[159]. These interventions usually aim for weight loss and are only recommended for adolescents who have reached their final height. These diets are not recommended for long periods of time due to challenges in achieving nutritional adequacy[158,160], and lack of long-term safety data[158,161]. However, intensive dietary interventions may be considered when conventional treatment is unsuccessful, or when adolescents with comorbidities or severe obesity require rapid or substantial weight loss[98]. A 2019 systematic review of very low-energy diets in children and adolescents found a mean reduction in body weight of −5.3 kg (seven studies) at the latest follow-up, ranging from 5 to 14.5 months from baseline[161].

Pharmacological treatment

Until the early 2020s the only drug approved in many jurisdictions for the treatment of obesity in adolescents was orlistat, a gastrointestinal lipase inhibitor resulting in reduced uptake of lipids and, thereby, a reduced total energy intake[162]. However, the modest effect on weight in combination with gastrointestinal adverse effects limit its usefulness overall[163].

A new generation of drugs has been developed for the treatment of both T2DM and obesity. These drugs are based on gastrointestinal peptides with effects both locally and in the central nervous system. GLP1 is an incretin that reduces appetite and slows gastric motility. The GLP1 receptor agonist liraglutide is approved for the treatment of obesity in those aged 12 years and older both in the USA and Europe[164,165]. Liraglutide, delivered subcutaneously daily at a higher dose than used for T2DM resulted in a 5% better BMI reduction than placebo after 12 months[166]. A 2022 trial of semaglutide, another GLP1 receptor agonist, delivered subcutaneously weekly in adolescents demonstrated 16% weight loss after 68 weeks of treatment, with modest adverse events and a low drop-out rate[12]. Tirzepatide, an agonist of both GLP1 and glucose-dependent insulinotropic polypeptide (GIP), is approved by the FDA for the treatment of T2DM in adults[167]. Subcutaneous tirzepatide weekly in adults with obesity resulted in ~20% weight loss over 72 weeks[168]. Of note, GIP alone increases appetite, but the complex receptor–agonist interaction results in downregulation of the GIP receptors[169], illustrating why slightly modified agonists exert different effects. A study of the use of tirzepatide in adolescents with T2DM has been initiated but results are not expected before 2027 (ref. 170). No trials of tirzepatide are currently underway in adolescents with obesity but without T2DM.

Hypothalamic obesity is difficult to treat. Setmelanotide is a MC4R agonist that reduces weight and improves quality of life in most people with *LEPR* and *POMC* mutations[71]. In trials of setmelanotide, 8 of 10 participants with *POMC* deficiency and 5 of 11 with *LEPR* deficiency had weight loss of at least 10% at ~1 year. The mean percentage change in most hunger score from baseline was −27.1% and −43.7% in those with POMC deficiency and leptin receptor deficiency, respectively[71].

In the near future, effective new drugs with, hopefully, an acceptable safety profile will be available that will change the way we treat and set goals for paediatric obesity treatment[171].

Bariatric surgery

Bariatric surgery is the most potent treatment for obesity in adolescents with severe obesity. The types of surgery most frequently used are sleeve gastrectomy and gastric bypass, both of which reduce appetite[172]. Mechanisms of action are complex, involving changes in gastrointestinal hormones, neural signalling, bile acid metabolism and gut microbiota[173]. Sleeve gastrectomy is a more straightforward procedure and the need for vitamin supplementation is lower than with gastric bypass. However, long-term weight loss may be greater after gastric bypass surgery[174].

Prospective long-term studies demonstrate beneficial effects of both sleeve gastrectomy and gastric bypass on weight loss and comorbidities in adolescents with severe obesity[175,176]. In a 5-year follow-up period, in 161 participants in the US TEEN-LABS study who underwent gastric bypass, mean BMI declined from 50 to 37 kg/m² (ref. 11). In a Swedish prospective study in 81 adolescents who underwent gastric bypass, the mean decrease in BMI at 5 years was 13.1 kg/m² (baseline BMI 45.5 kg/m²) compared with a BMI increase of 3.1 kg/m² in the control group[176]. Both studies showed marked inter-individual variations. Negative adverse effects, including gastrointestinal problems, vitamin deficits and reduction in lean body mass, are similar in adults and adolescents. Most surgical complications following bariatric surgery in the paediatric population are minor, occurring in the early postoperative time frame, but 8% of patients may have major perioperative complications[177]. Up to one-quarter of patients may require subsequent related procedures within 5 years[109]. However, many adolescents with severe

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obesity also have social and psychological problems, highlighting the need for routine and long-term monitoring[109,178].

Recommendations for bariatric surgery in adolescents differ considerably among countries, with information on long-term outcomes emerging rapidly. In many countries, bariatric surgery is recommended only from Tanner pubertal stage 3–4 and beyond, and only in children with severe obesity and cardiometabolic comorbidities[177]. The 2023 American Academy of Pediatrics clinical practice guidelines recommend that bariatric surgery be considered in adolescents ≥13 years of age with a BMI of ≥35 kg/m² or 120% of the 95th percentile for age and sex, whichever is lower, as well as clinically significant disease, such as T2DM, non-alcoholic fatty liver disease, major orthopaedic complications, obstructive sleep apnoea, the presence of cardiometabolic risk, or depressed quality of life[109]. For those with a BMI of ≥40 kg/m² or 140% of the 95th percentile for age and sex, bariatric surgery is indicated regardless of the presence of comorbidities. Potential contraindications to surgery include correctable causes of obesity, pregnancy and ongoing substance use disorder. The guidelines comment that further evaluation, undertaken by multidisciplinary centres that offer bariatric surgery for adolescents, should determine the capacity of the patient and family to understand the risks and benefits of surgery and to adhere to the required lifestyle changes before and after surgery.

Long-term weight outcomes

Few paediatric studies have investigated long-term weight maintenance after the initial, more intensive, weight loss phase. A 2018 systematic review of 11 studies in children and adolescents showed that a diverse range of maintenance interventions, including support via face-to-face psychobehavioural therapies, individual physician consultations, or adjunctive therapeutic contact via newsletters, mobile phone text or e-mail, led to stabilization of BMI z-score compared with control participants, who had increases in BMI z-score[179]. Interventions that are web-based or use mobile devices may be particularly useful in young people[180].

One concern is weight regain which occurs after bariatric surgery in general[181] but may be more prevalent in adolescents[176]. For example, in a Swedish prospective study, after 5 years, 25–30% of participants fulfilled the definitions of low surgical treatment effectiveness, which was associated with poorer metabolic outcomes[176]. As with adults, prevention of weight regain for most at-risk individuals might be possible with the combination of lifestyle support and pharmacological treatment[182]. Further weight maintenance strategies and long-term outcomes are discussed in the 2023 American Academy of Pediatrics clinical practice guidelines[109]. The appropriate role and timing of other therapies for long-term weight loss maintenance, such as anti-obesity medications, more intensive dietary interventions and bariatric surgery, are areas for future research.

In summary, management of obesity in childhood and adolescence requires intensive interventions. Emerging pharmacological therapies demonstrate greater short-term effectiveness than behavioural interventions; however, long-term outcomes at ≥2 years remain an important area for future research.

Quality of life

Weight bias describes the negative attitudes to, beliefs about and behaviour towards people with obesity[183]. It can lead to stigma causing exclusion, and discrimination in work, school and health care, and contributes to the inequities common in people with obesity[184]. Weight bias also affects social engagement and psychological well-being of children.

Children and adolescents with obesity score lower overall on health-related quality of life (HRQoL)[4,5]. In measures that assess domains of functioning, most score lower in physical functioning, physical/general health and psychosocial areas, such as appearance, and social acceptance and functioning. HRQoL is lowest in treatment-seeking children and in those with more extreme obesity[185]. Weight loss interventions generally increase HRQoL independent of the extent of weight loss[186], especially in the domains most affected. However, changes in weight and HRQoL are often not strongly correlated. This may reflect a lag in the physical and/or psychosocial benefit from weight change, or the extent of change that is needed to drive change in a child's self-perception.

Similar observations apply to the literature on self-esteem. Global self-worth is reduced in children and adolescents with obesity, as is satisfaction with physical appearance, athletic competence and social acceptance[187]. Data from intensive interventions suggest the psychological benefit of weight loss may be as dependent on some feature of the treatment environment or supportive social network as the weight loss itself[188]. This may include the daily company of others with obesity, making new friendships, and experienced improvements in newly prioritized competences.

There is a bidirectional relationship between HRQoL and obesity[189], something also accepted in the relationship with mood disorder. Obesity increases the risk of depression and vice versa, albeit over a longer period of time and which may only become apparent in adulthood[190]. Obesity also presents an increased risk of anxiety[191].

Structured and professionally delivered weight management interventions ameliorate mood disorder symptoms[192] and improve self-esteem[193]. Regular and extended support are important components beyond losing weight. Such interventions do not increase the risk of eating disorders[194]. This is despite a recognition that binge eating disorder is present in up to 5% of adolescents with overweight or obesity[195]. They are five times more likely to have binge eating symptoms than those with average weight. Importantly, adolescents who do not have access to professionally delivered weight management may be more likely to engage in self-directed dieting, which is implicated in eating disorder development[196].

The literature linking childhood obesity with either attention deficit hyperactivity disorder or autism spectrum disorder is complex and the relationship is uncertain. The association seems to be clearer in adults but the mechanisms and their causal directions remain unclear[109,197]. Young children with obesity, especially boys, are more likely to be parent-rated as having behavioural problems[198]. This may be a response to the behaviour of others rather than reflect clinical diagnoses such as attention deficit hyperactivity disorder or autism spectrum disorder. Conduct and peer relationship problems co-occur in children, regardless of their weight.

Children with obesity experience more social rejection. They receive fewer friendship nominations and more peer rejections, most pronounced in those with severe obesity[199]. This continues through adolescence and beyond. Children with obesity are more likely to report being victimized[200]. Younger children may respond by being perpetrators themselves. While it is assumed that children are victimized because of their weight, very few studies have looked at the nature or reason behind victimization. A substantial proportion of children with obesity fail to identify themselves as being fat-teased[187]. Although the stigma associated with obesity should be anticipated in children, especially in those most overweight, it would be inappropriate to see all as victims. A better understanding of children's resilience is needed.

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Outlook

Many gaps remain in basic, translational and clinical research in child and adolescent obesity. The mechanisms (genetic, epigenetic, environmental and social) behind the overwhelming association between parental obesity and child and adolescent obesity are still unclear given the paradoxically weak association in BMI between adopted children and their parents in combination with the modest effect size of known genetic loci associated with obesity[201].

Early manifestation of extreme obesity in childhood suggests a strong biological basis for disturbances of homeostatic weight regulation. Deep genotyping (including next-generation sequencing) and epigenetic analyses in these patients will reveal new genetic causes and causal pathways as a basis for the development of mechanism-based treatments. Future work aiming to understand the mechanisms underlying the development of childhood obesity should consider the complex biopsychosocial interactions and take a systems approach to understanding causal pathways leading to childhood obesity to contribute to evidence-based prevention and treatment strategies.

Long-term outcome data to better determine the risks of eating disorders are required. Although symptoms improve during obesity treatment in most adolescents, screening and monitoring for disordered eating is recommended in those presenting for treatment[202] and effective tools for use in clinical practice are required. A limited number of tools are validated to identify binge eating disorder in youth with obesity[203] but further research is needed to screen appropriately for the full spectrum of eating disorder diagnoses in obesity treatment seeking youth[203]. Recent reviews provide additional detail regarding eating disorder risk in child and adolescent obesity[117,202,204].

Most studies of paediatric obesity treatment have been undertaken in HICs and predominantly middle-class populations. However, research is needed to determine which strategies are best suited for those in LMICs and low-resource settings, for priority population groups including indigenous peoples, migrant populations and those living with social disadvantage, and for children with neurobehavioural and psychiatric disorders. We currently have a limited understanding of how best to target treatment pathways for different levels of genetic risk, age, developmental level, obesity severity, and cardiometabolic and psychological risk. Current outcomes for behavioural interventions are relatively modest and improved treatment outcomes are needed to address the potentially severe long-term health outcomes of paediatric obesity. Studies also need to include longer follow-up periods after an intervention, record all adverse events, incorporate cost-effectiveness analyses and have improved process evaluation.

Other areas in need of research include the role of new anti-obesity medications especially in adolescents, long-term outcomes following bariatric surgery and implementation of digital support systems to optimize outcomes and reduce costs of behavioural change interventions[205]. We must also better understand and tackle the barriers to implementation of treatment in real-life clinical settings, including the role of training of health professionals. Importantly, treatment studies of all kinds must engage people with lived experience — adolescents, parents and families — to understand what outcomes and elements of treatment are most valued.

Obesity prevention is challenging because it requires a multilevel, multisectoral approach that addresses inequity, involves many stakeholders and addresses both the upstream and the downstream factors influencing obesity risk. Some evidence exists of effectiveness of prevention interventions operating at the level of the child, family and school, but the very poor progress overall in modifying obesity prevalence globally highlights many areas in need of research and evidence implementation. Studies are needed especially in LMICs, particularly in the context of the nutrition transition and the double burden of malnutrition. A focus on intergenerational research, rather than the age-based focus of current work, is also needed. Systems research approaches should be used, addressing the broader food and physical activity environments, and links to climate change[206]. In all studies, strategies are needed that enable co-production with relevant communities, long-term follow-up, process evaluation and cost-effectiveness analyses. In the next few years, research and practice priorities must include a focus on intervention strategies in the earliest phases of life, including during pregnancy. The effects of COVID-19 and cost of living crises in many countries are leading to widening health inequalities[207] and this will further challenge obesity prevention interventions. Available resourcing for prevention interventions may become further constrained, requiring innovative solutions across agendas, with clear identification of co-benefits. For example, public health interventions for other diseases, such as dental caries or depression, or other societal concerns, such as urban congestion or climate change, may also act as obesity prevention strategies. Ultimately, to implement obesity prevention, societal changes are needed in terms of urban planning, social structures and health-care access.

Future high-quality paediatric obesity research can be enabled through strategies that support data sharing, which avoids research waste and bias, and enables new research questions to be addressed. Such approaches require leadership, careful engagement of multiple research teams, and resourcing. Four national or regional level paediatric weight registries exist[208–211], which are all based in North America or Europe. Such registries should be established in other countries, especially in low-resource settings, even if challenging[208]. Another data-sharing approach is through individual participant data meta-analyses of intervention trials, which can include prospectively collected data[212] and are quite distinct from systematic reviews of aggregate data. Two recent examples are the Transforming Obesity Prevention in Childhood (TOPCHILD) Collaboration, which includes early interventions to prevent obesity in the first 2 years of life[213], and the Eating Disorders in Weight-Related Therapy (EDIT) Collaboration, which aims to identify characteristics of individuals or trials that increase or protect against eating disorder risk following obesity treatment[214]. Formal data linkage studies, especially those joining up routine administrative datasets, enable longer-term and broader outcome measures to be assessed than is possible with standard clinical or public health intervention studies.

Collaborative research will also be enhanced through the use of agreed core outcome sets, supporting data harmonization. The Edmonton Obesity Staging System – Paediatric[215] is one option for paediatric obesity treatment. A core outcome set for early intervention trials to prevent obesity in childhood (COS-EPOCH) has been recently established[216]. These efforts incorporate a balance between wanting and needing to share data and adhering to privacy protection regulations. Objective end points are ideal, including directly measured physical activity and body composition.

Collaborative efforts and a systems approach are paramount to understand, prevent and manage child and adolescent obesity. Research funding and health policies should focus on feasible, effective and equitable interventions.

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Author contributions

Introduction (L.A.B., J.F.F. and N.B.L.); Epidemiology (L.A.B. and J.F.F.); Mechanisms/pathophysiology (L.A.B., J.F.F., T.R. and M.W.); Diagnosis, screening and prevention (L.A.B., N.B.L., T.R., C.S. and M.W.); Management (L.A.B., N.B.L., A.J.H., C.M. and T.R.); Quality of life (L.A.B., N.B.L. and A.J.H.); Outlook (L.A.B., N.B.L., J.F.F., A.J.H., C.M., T.R., C.S. and M.W.); Overview of the Primer (L.A.B. and N.B.L.).

Competing interests

A.J.H. reports receiving payment for consultancy advice for Slimming World (UK). L.A.B. reports receiving honoraria for speaking in forums organized by Novo Nordisk in relation to management of adolescent obesity and the ACTION-Teens study, which is sponsored by Novo Nordisk. L.A.B. is the Australian lead of the study. T.R. received funding from the German Federal Ministry of Education and Research (BMBF; 01GI1120A/B) as part of the German Competence Network Obesity (Consortium 'Youth with Extreme Obesity'). T.R. receives payment for consultancy advice related to pharmacological treatment of obesity from Novo Nordisk and Lilly, as well as honoraria for lectures in symposia organized by Novo Nordisk, Novartis and Merck. C.M. receives payments for consultancy advice and advisory board participation from Novo Nordisk, Oriflame Wellness, DeFaire AB and Itrim AB. C.M. also receives honoraria for speaking at meetings organized by Novo Nordisk and Astra Zeneca. C.M. is a shareholder and founder of Evira AB, a company that develops and sells systems for digital support for weight loss, and receives grants from Novo Nordisk for epidemiological studies of the effects of weight loss on future heath. M.W. received funding from the German Federal Ministry of Education and Research (BMBF; 01GI1120A/B) as part of the German Competence Network Obesity (Consortium 'Youth with Extreme Obesity'). M.W. receives payment for consultancy advice related to pharmacological treatment of obesity from Novo Nordisk, Regeneron, Boehringer Ingelheim and LG Chem, as well as honoraria for speaking in symposia organized by Novo Nordisk, Rhythm Pharmaceuticals and Infectopharm. M.W. is principal investigator in phase II and phase III studies of setmelanotide sponsored by Rhythm Pharmaceuticals. N.B.L., J.F.F. and C.S. declare no competing interests.

Additional information

Peer review information *Nature Reviews Disease Primers* thanks C. Maffeis, L. Moreno, R, Weiss and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

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