Childhood obesity

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Worldwide prevalence of childhood obesity has increased greatly during the past three decades. The increasing occurrence in children of disorders such as type 2 diabetes is believed to be a consequence of this obesity epidemic. Much progress has been made in understanding of the genetics and physiology of appetite control and from these advances, elucidation of the causes of some rare obesity syndromes. However, these rare disorders have so far taught us few lessons about prevention or reversal of obesity in most children. Calorie intake and activity recommendations need reassessment and improved quantification at a population level because of sedentary lifestyles of children nowadays. For individual treatment, currently recommended calorie prescriptions might be too conservative in view of evolving insight into the so-called energy gap. Although quality of research into both prevention and treatment has improved, high-quality multicentre trials with long-term follow-up are needed. Meanwhile, prevention and treatment approaches to increase energy expenditure and decrease intake should continue. Recent data suggest that the spiralling increase in childhood obesity prevalence might be abating; increased efforts should be made on all fronts to continue this potentially exciting trend.

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Epidemiology

8 years have passed since the last Seminar on childhood obesity in *The Lancet*.[1] Our goal is to review new information and outline some of the remaining challenges. A review of secular trends in the number of overweight or obese children concluded that prevalence had increased during the past two to three decades in most industrialised countries, apart from Russia and Poland, and in several low-income countries, especially in urban areas.[2] Prevalence doubled or trebled between the early 1970s and late 1990s in Australia, Brazil, Canada, Chile, Finland, France, Germany, Greece, Japan, the UK, and the USA.[2] By 2010, more than 40% of children in the North American and eastern Mediterranean WHO regions, 38% in Europe, 27% in the western Pacific, and 22% in southeast Asia were predicted to be overweight or obese. However, that 2006 review pre-dates recent data, which, although still too soon to be certain, suggest that the increase in childhood obesity in the USA, the UK, and Sweden might be abating.[3–5]

Internationally agreed thresholds of body-mass index (BMI) define underweight, normal weight, overweight, and obesity in adults, but in children, effects of age, sex, puberty, and race or ethnicity on growth make classification difficult. Definition of a standard age-related growth chart and clinically meaningful thresholds for overweight and obesity present challenges. The International Obesity Taskforce (IOTF) international standard growth chart enables global comparison of prevalence.[6] However, many countries continue to use their own country-specific charts, including the USA, where standards are based on a national survey from the early 1960s, before the present epidemic.[7]

Widely used thresholds for being overweight or obese in childhood are: 110% or 120% of ideal weight for height; weight-for-height *Z* scores of higher than 1 or higher than 2, and BMI at the 85th, 90th, 95th, and 97th percentiles (on the basis of international or country-specific reference populations).[2] The IOTF recommend using their international growth charts and limits specific to age and sex that, on average, correspond to adult thresholds. The IOTF classification has high specificity, but low sensitivity.[8]

Determinants and risk factors

A historical convergence of forces, biological and technological, has led to the obesity epidemic. During millennia of frequent food scarcities, natural selection probably favoured people with parsimonious energy metabolism, known as the thrifty gene hypothesis.[9] Although the advent of agriculture about 14 000 years ago ensured more stable food supplies, activities of daily living still needed substantial energy expenditure until about 50 years ago, when radical changes occurred in food availability and energy expenditure. The obesity epidemic is probably the result of evolutionary legacy interacting with our technologically advanced and consumerist society. Population groups in North America who have preserved traditional lifestyles with substantial embedded physical activity have reduced prevalences of obesity.[10] Likewise, in countries with low and middle incomes, the obesity epidemic is largely occurring in urban areas that have easy access to energy-dense cheap foods and low energy requirements in daily life.[2]

Obesity is a complex disorder that is affected by many interacting genetic and non-genetic factors. We focus mainly on prevention and treatment. The table summarises

Search strategy and selection criteria

We identified original research, reviews, and commentaries by searching PubMed using the search terms "paediatric obesity", "childhood obesity", "paediatric overweight", "childhood overweight", and "body mass index in children". All dates and languages were considered. Articles published between 1962 and 2010 were included, but we directed special attention to reports published since 2002. Research developments and published work were also identified by discussions with specialists in paediatric obesity, nutrition, and public health.

	Association potentially modifiable	Type of evidence*
Genetic variation		
Rare single gene defects in which obesity is the specific abnormality—eg, those related to the leptin signalling pathway (figure 1)	No, apart from leptin replacement in the few leptin-deficient individuals	Basic science studies, case series, family linkage, and genetic association studies[11]
Obesity is a manifestation of several genetic syndromes (figure 2); Prader-Willi syndrome is associated with hyperghrelinaemia, but the mechanism of hyperphagia remains unclear;[12,13] animal models of ciliopathies (Bardet-Biedl and Alström syndromes) have defects in leptin pathway signalling;[14,15] haploinsufficiency of BDNF, a downstream mediator of leptin action, is associated with hyperphagia and obesity in children with WAGR syndrome[16]	No	Genetic association studies[11]
Genome-wide association studies have identified several common genetic variants associated with high adiposity and obesity, each with weak effects	No	Genome-wide association studies[17]
Epigenetics		
The mechanism whereby in-utero factors can produce heritable changes in adiposity has been suggested to be due to DNA methylation or histone modification of DNA in gene regulatory regions; however, evidence in man is scarce	Possibly; in animals, maternal consumption of folate, methionine, and vitamin B12 during pregnancy can affect DNA methylation in offspring	Non-systematic review of evidence (largely from basic science and animal studies)[18]
Endocrine disease		
Classically, hypothyroidism, growth hormone deficiency or resistance, and cortisol excess; PCOS is a consequence of but also possible contributor to obesity; obesity associated with pseudohypoparathyroidism (caused by Gαs inactivating mutation) might be due to defective signalling at G-protein coupled receptors, including the melanocortin receptor of the leptin pathway[19]	Some—eg, thyroxine and growth-hormone replacement, surgical treatment of Cushing syndrome; for PCOS, oral contraceptives, anti-androgens, and insulin sensitisers have been used, but long-term large RCTs in adolescents are scarce[20]	Non-systematic review of evidence (basic science, epidemiology, clinical)[21]
CNS pathology		
Congenital or acquired hypothalamic abnormalities have been associated with a severe form of obesity in children and adolescents	Possibly, but still under investigation; hyperinsulinaemia due to increased vagal tone has been postulated as a contributing factor, prompting studies using octreotide, which prevented further weight gain in a small RCT, but long-term large RCTs are needed[22]	Non-systematic review of evidence (basic science, epidemiology, clinical)[23]
Intrauterine exposure to gestational diabetes		
In populations at high risk of obesity and diabetes (eg, Pima Indians), exposure to gestational diabetes is associated with increased risk of childhood and early adult obesity in offspring; evidence for similar associations in other populations is poor	Yes	Review of observational studies in Pima Indians;[24] prospective cohorts in other populations[25] (and other studies cited in this reference)
Intrauterine exposure to high maternal adiposity		
Investigators comparing obesity in children whose mothers had undergone bariatric surgery for extreme morbid obesity showed that siblings born before surgery (when mother was very obese) were more obese than were siblings born after weight loss in response to surgery; evidence that less extreme variation in maternal adiposity affects offspring obesity is scarce	Yes	Within sibling comparisons,[26] prospective cohort studies,[24,27] and mendelian randomisation study[27]
Birthweight		
High birthweight is associated with increased offspring fat and lean mass; small-for-gestational age babies who show catch-up growth might be at risk of childhood obesity, but this finding could simply show increased growth resulting in larger size	Safe means of modification of birthweight to improve health are unknown	Prospective cohort studies[28,29]
BMI rebound		
Early age at BMI rebound is associated with greater risk of obesity, but this finding could be a statistical artifact	No, since can only be established retrospectively in individuals	Non-systematic review of largely prospective cohort studies[30]

(Continues on next page)

determinants or risk factors that are associated with childhood obesity or variation in adiposity, and figure 1 shows a simplified model of leptin signalling, which is the key biological pathway controlling energy balance.[2,4,11–45] Since the discovery of leptin, understanding of the mechanisms controlling energy balance has rapidly advanced. Apart from leptin replacement therapy in a few leptin-deficient individuals, interventions that effectively prevent or treat obesity in the general population are yet to emerge. Both insulin and leptin are secreted in proportion to body fat and serve as adiposity signals, acting on the same neurons of the hypothalamic arcuate nucleus to regulate energy homoeostasis. Ghrelin, which is secreted by the stomach and duodenum, serves as a hunger signal at the hypothalamus and brainstem, whereas other peptides secreted by the gastrointestinal tract, including peptide YY, act as satiation signals. The ligands leptin,[46] pro-opiomelanocortin,[47,48] cocaine-amphetamine related transcript,[49] and brain-derived neurotrophic factor (BDNF),[16,50] the receptors for leptin,[51,52] melanocortins,[53–56] and BDNF,[57] and the enzyme prohormone convertase 1[58,59] have function-changing mutations that are associated with obesity in children. Mutations in the ligands and receptors for neuropeptide Y,[60] agouti-related protein,[61]

	Association potentially modifiable	Type of evidence*
(Continued from previous page)		
Diet		
Breastfeeding is unlikely to be causally protective against childhood obesity	Yes	Systematic review of prospective cohort studies,[31] RCT[32]
High-quality prospective evidence is sparse; available evidence suggests that high energy intake in early infancy and high consumption of sweetened drinks in childhood are prospectively associated with raised childhood obesity risk; absence of evidence for other dietary characteristics could be attributable to poor study design and difficulties of accurate assessment of diet in children	Yes	Non-systematic review of observational studies[33]
Energy expenditure		
Low levels of physical activity are associated with high childhood obesity risk	Yes	Systematic review of observational studies[34]
Television viewing		
Large number of hours spent viewing are associated with raised childhood obesity risk	Yes	Systematic review of observational and experimental studies[35]
Sleep		
Short sleep duration in infancy and childhood is associated with raised childhood obesity risk	Possibly	Prospective cohort study[36]
Microbial infection		
Potential role of microbial infection (eg, adenovirus Ad-36) and composition of gut flora (eg, ratio of *Firmicutes* to *Bacteroidetes* spp) in the pathogenesis of obesity; however, epidemiological evidence in the non-selected general population is scarce	Yes	Cross-sectional studies[37,38]
Iatrogenic		
Cranial irradiation or surgery causing hypothalamic damage; psychotropic drugs (eg, olanzapine and risperidone), chemotherapeutics (eg, treatment of acute lymphocytic leukaemia even without cranial irradiation), and hormonal contraception (eg, depot medroxyprogesterone acetate) have been associated with increased weight gain in children and adolescents	Depends on disease or treatment and risk-benefit considerations	Non-systematic review of evidence (basic science, epidemiology, clinical)[23] and prospective cohort studies[39-41]
Ethnic origin		
Some ethnic groups—eg, Hispanic and south Asian—seem to be more likely to become obese; at a specific BMI, children and infants of south Asian origin have higher adiposity than do their counterparts	No	Cross-sectional studies[42,43]
Country of birth		
Children from countries with low and middle incomes tend to be stunted and underweight, but with sufficient nutrition gain healthy weight, and with overnutrition are prone to obesity	No	Cross-sectional and ecological studies[44]
Urban versus rural residence		
Children in urban areas are more likely to be obese than are those in rural areas in many countries, including those with high and low-middle incomes	Unlikely to be able to change where families live, but might be able to modify underlying reasons for association	Cross-sectional studies[2]
Socioeconomic position		
In high-income countries, generations born before the 1950s and 1960s did not show socioeconomic differentials in adiposity or obesity in childhood (though do as adults); some evidence exists that in contemporary populations, children in lowest socioeconomic groups in high-income countries have raised obesity rates	Yes, with major political and cultural changes; might be able to modify underlying reasons for association	Prospective two-generational cohort study[45]

This table has been modified and updated from reference 4. *We cite the most recent systematic review of the highest level of evidence for most risk factors, rather than providing a comprehensive list of all papers for every risk factor, which would be beyond the scope of this Seminar. BDNF=brain-derived neurotrophic factor. WAGR=Wilms tumour, aniridia, genitourinary anomalies, mental retardation. PCOS=polycystic ovary syndrome. RCT=randomised controlled trial. BMI=body-mass index.

Table: **Determinants or risk factors for development of childhood obesity or increased adiposity**

carboxypeptidase E,[62,63] and melanin-concentrating hormone[64] change energy balance in rodents, but have not been convincingly associated with human obesity. For several risk factors, evidence is weak and, although important advances have been made, how to incorporate the information effectively and cost-effectively into prevention programmes for children is unclear.

Differential diagnosis and complications

Endocrine diseases, congenital and acquired hypothalamic defects, genetic syndromes, and use of drugs affecting appetite should be considered during assessment of paediatric patients with obesity (figure 2). Clinical history and examination should guide differential diagnosis. Onset of obesity during early infancy raises suspicion of function-changing genetic mutations affecting the leptin signalling pathway, but these disorders are very rare, with the most common, melanocortin-4-receptor defects, affecting less than 5% of children with early-onset obesity.[56] During assessment of new-onset excessive weight gain, potential side-effects from a recently initiated drug should be

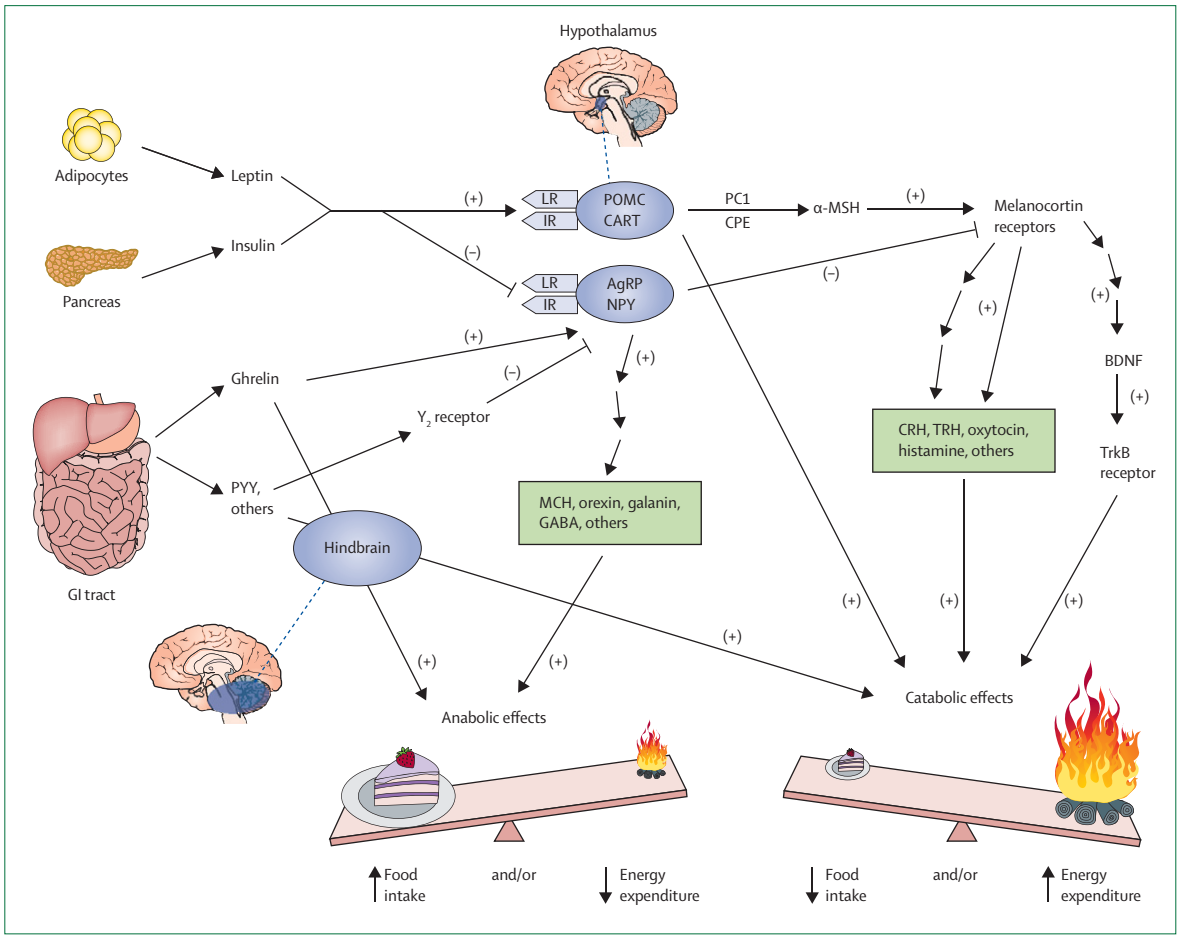

Figure 1: **A simplified model of the leptin signalling pathway**
Lines with arrowheads show stimulatory action. Lines with perpendicular endblocks show inhibitory action. AgRP=agouti-related protein. BDNF=brain-derived neurotrophic factor. CART=cocaine-amphetamine related transcript. CPE=carboxypeptidase E. CRH=corticotropin-releasing hormone. GABA=gamma amino butyric acid. GI=gastrointestinal. IR=insulin receptor. LR=leptin receptor. MCH=melanin-concentrating hormone. MSH=melanocyte-stimulating hormone. NPY=neuropeptide Y. PC1=prohormone convertase 1. POMC=pro-opiomelanocortin. PYY=peptide YY. TRH=thyrotropin-releasing hormone. TrkB=tropomyosin receptor kinase B.

taken into consideration, because weight gain can be associated with administration of insulin or insulin secretagogues, glucocorticoids, hormonal contraceptives (eg, depot medroxyprogesterone acetate), psychotropic drugs (including atypical antipsychotics [eg, clozapine, olanzapine, risperidone], mood stabilisers [eg, lithium], tricyclic antidepressants [eg, amitriptyline, imipramine, and nortriptyline], and anticonvulsants [eg, valproic acid, gabapentin, and carbamazepine]), antihypertensive drugs (eg, propranolol and clonidine), and anti-histamines.[65] In patients with decreased growth velocity despite continued weight gain, an endocrinopathy should be considered; measurement of thyroid-stimulating hormone and free thyroxine and referral to a paediatric endocrinologist are recommended.

Almost all patients, however, do not have any of these identifiable disorders. All patients, irrespective of cause of obesity, should be assessed for modifiable lifestyle factors, including physical activity and diet, and screened for complications of obesity, including measurement of lipid and glucose concentrations after overnight fasting, and alanine aminotransferase. If fasting glucose concentration is 5·6–6·9 mmol/L, an oral glucose tolerance test is recommended. Screening for vitamin D and iron deficiency should also be considered.

Childhood obesity can adversely affect almost every organ system (figure 3) and often has serious consequences, including hypertension, dyslipidaemia, insulin resistance or diabetes, fatty liver disease, and psychosocial complications.[66] Results of one study showed that being overweight or obese between ages 14 and 19 years was associated with increased adult mortality (from age 30 years) from various systemic diseases.[67] The atherosclerotic process[68] seems to be accelerated in obese children and almost half of children with BMI higher than the 97th percentile have one or more of the disorders that make up the metabolic syndrome.[69] High childhood and adolescent BMI is associated with increased risk of cardiovascular disease in adulthood.[70] Pulmonary disorders, including

obstructive sleep apnoea and reactive airway disease,[71] are reported more frequently in obese children than in their normal-weight counterparts. Asthma severity, however, does not seem to be affected by obesity;[72] weight-related but non-asthmatic airflow limitations are perhaps being misdiagnosed as asthma in some obese children.[73]

Specific nutritional deficiencies often accompany childhood obesity. High BMI and adiposity have been associated with low vitamin D concentrations in children.[74] The mechanism underlying low vitamin D concentrations in obesity is unclear, but increased storage of vitamin D in adipose tissue has been proposed.[75] Overweight or obese children are also at least twice as likely to be iron-deficient than children of normal weight.[76] Obesity leads to increased production of proinflammatory cytokines that in turn promote release of hepcidin, which is a peptide hormone produced by the liver and adipocytes that decreases iron absorption from the gut.[77]

Complications of childhood obesity include acceleration in timing of thelarche and menarche in girls,[78,79] pubertal advancement in boys[80] and adverse effects on maturation[81] and alignment[82] of developing bones in both sexes. Advanced skeletal maturation has been attributed to increased adipose tissue aromatisation of weak androgens into more potent oestrogens. Obesity might also affect pubertal timing through nutrition-related signals (eg, insulin and leptin) on the reproductive axis.[83] Orthopaedic complaints, including fractures, musculoskeletal discomfort, impaired mobility, and lower-limb malalignment seem to be more common in obese children than in those who are not overweight.[82] Serious orthopaedic complications of childhood obesity are tibia vara (Blount's disease or adolescent bowing of the legs)[84] and slipped capital femoral epiphyses.[85] By contrast, however, obesity might have some beneficial effect on bone mineral density. Results of a recent study, using variation in the *FTO* gene as an instrumental variable, suggested that high fat mass in children was causally associated with increased total, spinal, and limb bone mineral content.[86]

Prevention

Prevention, especially in young people, is universally viewed as the best approach to reverse the rising global prevalence of obesity. However, evidence about the most effective means of prevention of obesity development in children is scarce. Many prevention trials have had sample sizes too small for expected effect size or insufficient length of follow-up. Some trials have also been criticised for not being based on sound theories of behavioural change and for having inadequate feasibility and pilot work.[87]

Trials of prevention interventions might also have failed to show notable effects because they did not adequately address the energy gap[88] separating children who remain lean from those who gain weight throughout childhood.[89] Butte and Ellis[90] calculated that an energy deficit of more than 250 kcal per day is needed to prevent

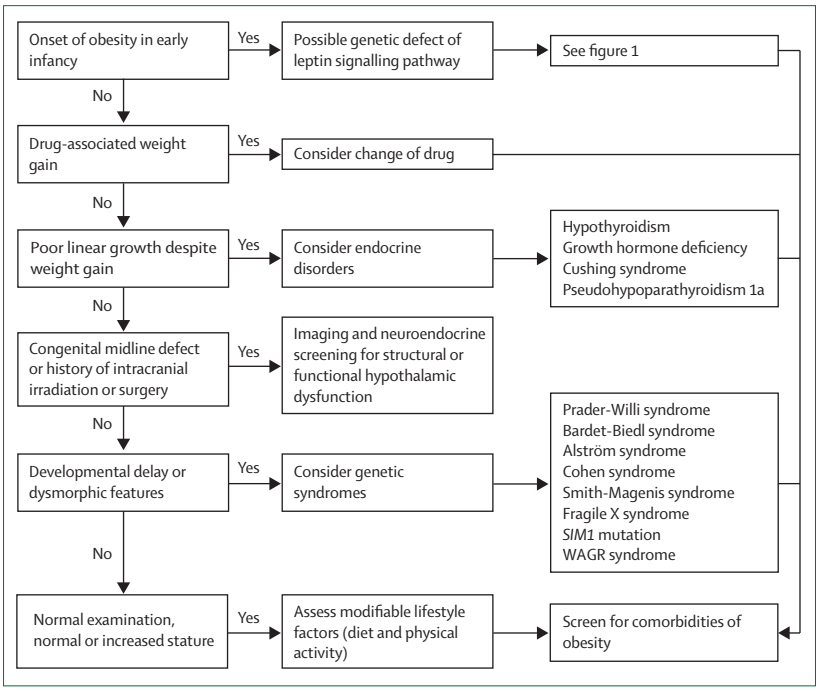

Figure 2: **Recommended assessment of childhood-onset obesity**
Y=yes. N=no. WAGR=Wilms tumour, aniridia, genitourinary anomalies, mental retardation.

further weight gain in 90% of overweight children; this deficit is equivalent to a child walking an additional 1–2 h per day at 1·9 km/h, or consuming roughly a fifth fewer calories than usual per day.

Prevention measures can be instituted at individual, household, institutional, community, and health-care levels. At the individual level, carers should be targeted rather than young children themselves, and focus on mothers seems reasonable. First, developmental or fetal overnutrition as a result of gestational diabetes or maternal obesity might have contributed to the obesity epidemic (table).[1] So far, no intervention studies have examined the long-term effect of reduction of gestational diabetes or maternal adiposity on future obesity risk in offspring. Second, breastfeeding might prevent childhood obesity. However, results of systematic reviews suggest that observational associations could be accounted for largely by residual confounding or publication bias, and in a large randomised trial of a breastfeeding promotion intervention, no causal effect of breastfeeding on obesity risk was reported.[91] Third, mothers might influence diets of offspring more than do fathers;[92] however, no intervention trials of maternal-only interventions to prevent childhood obesity have been done.

At a household or family level, encouragement of parents to offer appropriate food portions, foster physical activity, increase activities of daily living, and keep sedentary behaviours to a minimum are viewed as basic measures of prevention.[93] Most government guidelines have traditionally focused on ensuring that nutritional intake is adequate.[94]

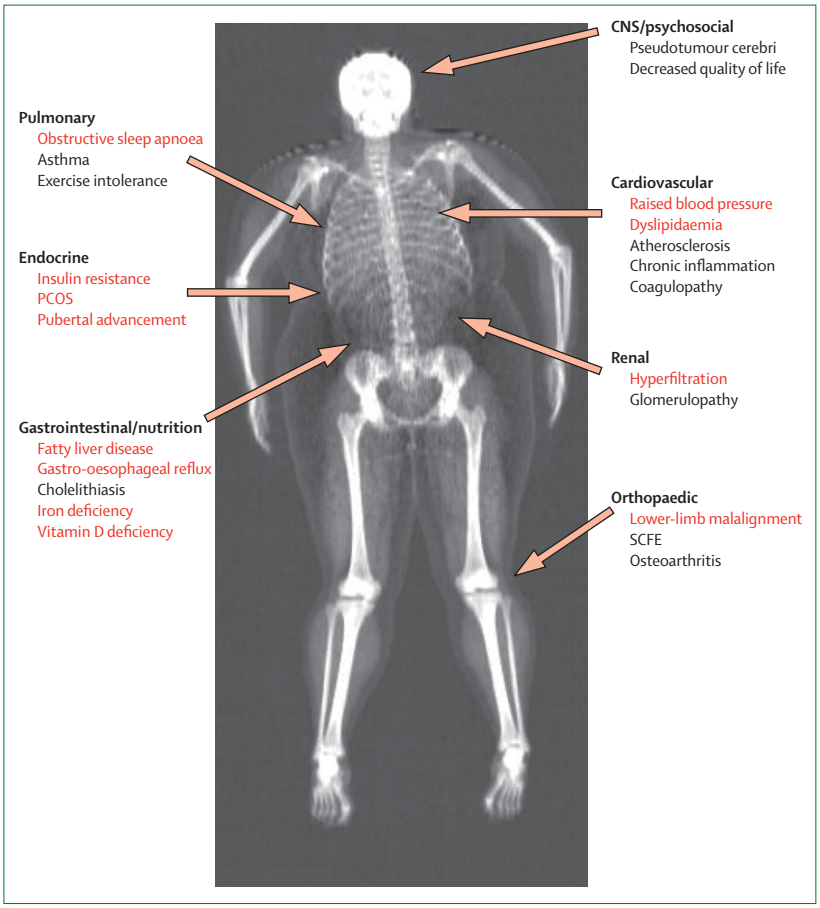

Figure 3: **Complications associated with childhood obesity**
Image obtained by dual energy x-ray absorptiometry from a teenage girl with BMI 38 kg/m^2. Disorders that are of high prevalence and are well established in their association with childhood obesity are shown in red. PCOS=polycystic ovary syndrome. SCFE=slipped capital femoral epiphysis.

However, these guidelines might not be useful to ensure energy intakes that are appropriate for contemporary sedentary lifestyles. We are unaware of any randomised controlled trials focusing solely on household or family-based interventions to prevent childhood obesity.

Most randomised prevention trials have taken place in schools since they are viewed as a universal catchment setting for children. The core features of most prevention programmes are to change the caloric content of school meals and encourage physical activity. One policy that is debated in the USA is removal of vending machines from schools to curb availability of energy-dense snack foods. However, a US national survey showed that snack foods from vending machines contributed only 1·3% of total daily calories from snacks, whereas snacks at or from home contributed 69·1%.[95] At least nine systematic reviews have examined randomised controlled trials of school-based childhood obesity prevention programmes[87,96] (see also citations of other systematic reviews within these reports). Early reviews noted scarce evidence of effectiveness and poor quality of studies, whereas more recent reviews suggested that school-based interventions might be effective. Gonzalez-Suarez and colleagues[96] identified 19 high-quality trials of school-based interventions and reported reduced odds of overweight or obesity in intervention compared with control groups (pooled odds ratio 0·74 [95% CI 0·60–0·92]). The key effective characteristics of such programmes remain to be established, and, since most studies were done in the USA, whether they are effective elsewhere. Although initiatives have also been aimed at children in kindergarten or nurseries,[97] the few controlled trials in this setting have not yet been systematically reviewed. One area to be addressed is the built environment of schools or nurseries. Architectural designs of school buildings and their environment can be re-examined for opportunities to impose increased energy expenditure. A multi-storey building with purposefully designed class schedules could lead to substantial stair (or ramp) climbing during the school day.

Prevention in the community includes public policies and mass-media campaigns.[98,99] For the past decade, pressure has been increasing for labelling of caloric contents on menus, especially at fast-food restaurants. However, data for the effects of such labelling on prevention of childhood obesity are scarce.[100] In 2002, the US Centers for Disease Control and Prevention launched a 2-year marketing campaign via media advertisements to promote physical activity in children aged 9–13 years.[101] Children's physical activity (assessed by self-report) increased,[98,99] but effects on BMI were not assessed. In several countries, governments are being urged to address the toxic environment by levying taxes on sugared beverages and fast foods, though the effectiveness of such measures is unknown.[102]

Popular media in several countries have given much attention to the topic of obesity, but no objective information is available about the effect of these messages on the public. Public health surveillance and screening for childhood obesity have been implemented in some communities. In 2003, Arkansas was the first US state to pass legislation for mandatory BMI assessments of children in public schools, with yearly reporting to parents. This approach has since been followed in 13 other states.[103,104] In 2005, a National Child Measurement Programme was introduced in the UK for yearly surveillance of two school year groups. In 2007, the British Government introduced legislation to give parents the results of their child's measurements. Existing evidence is unclear as to whether surveillance or screening of childhood obesity will be valuable for prevention.

Infants and young children are seen frequently in medical settings for well-child and acute care. These visits present an opportunity to detect upward deviations in a child's growth rate, thus placing the primary-care provider at the strategic first line of defence before BMI exceeds recommended values. However, data for the effectiveness of such counselling for obesity prevention

are scarce. Some crucial periods during childhood present both challenges and windows of opportunity for obesity prevention because they are associated with notable changes in adiposity accrual or obesity-related behaviour. These periods are the first year of life,[28] during adiposity rebound (age 3–7 years), and menarche.[105] The transition from childhood to adolescence is a time of striking behavioural changes, including an abrupt reduction in physical activity.[106] Although whether preventive measures instituted during these times will prevent excessive growth is unclear, these opportunities should be investigated further.

Common sense supports a key role for decreased energy intake and increased energy expenditure in human beings, who have adapted through evolutionary processes to parsimonious energy metabolism. Thus, prevention programmes should decrease energy intake, increase activity, and reduce sedentary behaviour. To balance the need for more definitive research into which interventions best achieve changes in these behaviours against the pressure to act now to halt and reverse the obesity epidemic, we need to continue with both prevention activities and research to better understand the means of induction of behavioural changes and their effect on childhood obesity.

For prevention, one might recall the words of Rudolph Virchow, a 19th century German pathologist, who wrote that ‘‘epidemics appear, and often disappear without traces, when a new culture period has started” and that mass diseases are “due to…disturbances of human culture”.[107] Geoffrey Rose promulgated the notion further that whole populations can be sick (such as the case of obesity), and that political action might be needed to improve population health.[108] Thus, we should continue to seek opportunities for prevention at all levels of society, including having responsible public policies to modify our manner of living, since there remain many untapped resources and untried venues.

Non-pharmacological treatment

We recommend that children with BMI higher than the 95th percentile, or higher than the 85th percentile when accompanied by comorbidities, such as hypertension, hyperlipidaemia, or impaired glucose tolerance, be considered for treatment. Non-pharmacological approaches should be the foundation of all obesity treatments, especially in children, and should always be considered as first-line therapy. In a systematic review[109] of randomised controlled trials of treatments for childhood obesity, investigators identified 64 trials, 54 of which assessed non-pharmacological lifestyle interventions. These trials were generally of small sample size (16 to 218 participants), with 70% including fewer than 30 participants. Most trials had substantial methodological limitations and short-term follow-up. Despite these limitations, the investigators concluded that “…this review shows that family-based, lifestyle interventions with a behavioural program aimed at changing diet and physical activity and thinking patterns provide significant and clinically meaningful decreases in overweight in both children and adolescents…in the short- and the long-term”. These findings are encouraging and provide useful guidance for treatment of obese children, but they also emphasise the need for additional large randomised controlled trials with long-term follow-up.

A catabolic state of stored energy is needed to induce weight loss. Guidelines from the American Academy of Pediatrics recommend that weight-reducing diets contain “less energy than that required to maintain weight but not less than 1200 kilocalories a day.”[110] Equivalent UK guidance emphasises energy balance between intake and expenditure, but does not specify amounts of intake.[111] Another recommended approach is to construct a diet that is 300–400 kcal per day lower than weight-maintenance requirements as assessed by dietary history or as calculated on the basis of a formula relating anthropometry to energy expenditure, such as the Harris-Benedict equation. In view of the magnitude of the energy gap, a sizeable energy deficit would be needed to induce appreciable weight reduction in an obese child, and many weight-loss diets might be energy neutral in young children or even lead to weight gain in sedentary female adolescents.[88,90]

Some guidelines (eg, in the UK) and commentators emphasise behavioural strategies that do not specify actual caloric intake. Results of a randomised trial of behavioural treatment without specified calorie limits showed no effect on BMI.[112,113] A protein-sparing modified fast has a very low calorie regimen (600–800 kcal per day) and seems to be promising, but this notion has not progressed since it was first reported.[114] Transient growth deceleration was recorded, but growth returned to normal by 14 months.[115] However, this trial was not randomised and had few follow-up data.

Promotion of increased energy expenditure for weight reduction has not received the same attention as have dietary prescriptions. We found only one randomised controlled trial of 6–11-year-old obese children that compared hypocaloric diet, 90 min of moderate exercise 3 days per week, or both. Weight loss was greater in the diet or diet-plus-exercise group (being similar in these two) than in the exercise-only group, but there was no control group and follow-up lasted only 9 months.[116] Interventions to decrease sedentary activity, such as restriction of television viewing, have been examined and are promising.[117]

The macronutrient composition of diets has been examined for differential weight-loss benefits. Several popular diets, including Atkin’s, have emphasised increasing protein intake, but not changing energy content. Although some results show increased weight loss with this diet in adults,[118–120] data from long-term studies generally show no difference in weight loss between diets of varying macronutrient contents that do not change total energy intake.[121,122] Demol and

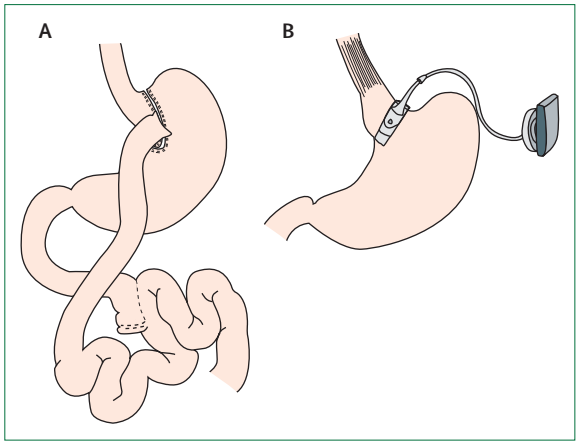

Figure 4: **Operations undertaken for weight loss**
(A) Roux-en-Y gastric bypass. (B) Adjustable gastric band. Reproduced from reference 138, by permission of Elsevier Ltd.

colleagues[121] reported no differences in BMI decrease in obese adolescents on different macronutrient diets. Dietary glycaemic index has also been implicated in weight reduction.[123] Two small, short-term studies of obese adolescents reported increased weight loss on a diet with reduced glycaemic load, but the numbers were small and long-term effects are unknown.[124,125]

Strategies to change dietary habits to a more calorie-reduced intake are based on behavioural principles, of which Bandura's social cognitive model[126] is the most widely used. The model is based on the notion that lifestyle changes succeed through cognitively driven, intentional behaviours such as self-monitoring, goal setting, and rewarding of successful change. A widely adopted approach in children uses the traffic light system, which was developed by Epstein and colleagues.[127] Motivational interviewing has been advocated as an especially useful technique for patients who might not feel ready for change.[128] It is a so-called empathetic way of being, including reflective listening, shared decision making, and agenda setting.[129] American Heart Association guidelines recommend motivational interviewing for paediatric weight management.[130] However, the effectiveness of this approach versus other behavioural approaches is not known.

Most weight reduction programmes are provided by outpatient clinics. In one study, investigators examined an inpatient intervention and showed some evidence of effectiveness.[131,132] Although the school setting has not been regarded as a site for treatment of childhood obesity (as opposed to prevention), promising results from a randomised trial of classroom-based weight reduction in obese Mexican-American children suggest that this venue needs further examination.[133] Residential summer camps for obese adolescents have short-term effectiveness,[134] but long-term effects remain unknown. Internet intervention for obese adolescents has been examined, without promising results.[135]

Better research into non-pharmacological treatment is urgently needed, especially into extent of caloric restriction and effectiveness of increasing energy expenditure. Consensus guidelines for age-appropriate safety monitoring of weight-reducing regimens are also needed to ensure appropriate height growth and biological and social development. Since randomised clinical trials are costly, multicentre collaborative research with common protocols might be the most cost-effective and generalisable approach. In view of ageing populations worldwide and increasing use of technology-intensive medical treatments, allocation of increasingly scarce medical resources will demand more evidence-based information for treatment of childhood obesity. Questions such as how often an obese child should have dietary counselling will not be readily answered unless improved evidence is made available.

Pharmacological and surgical treatment

A Cochrane review[109] identified ten randomised controlled trials of pharmacological treatments for obese children. Most of these trials had small sample sizes (range 24–539 participants, with 60% including fewer than 30 participants), but most were high quality. With one exception, all the pharmacological treatment trials were in older children or adolescents (minimum age 12 years); the exception enrolled individuals aged 9–18 years. Trials meeting criteria for pooled meta-analysis included only two drugs: orlistat (a lipase inhibitor that prevents absorption of dietary fat from the gut) and sibutramine (an inhibitor of serotonin, norepinephrine, and dopamine reuptake). The additional effect of orlistat compared with placebo when given in combination with a lifestyle intervention was a difference in BMI of –0·76 kg/m² (95% CI –1·07 to –0·44) at 6 months. The additional effect of sibutramine compared with placebo when given in combination with a lifestyle intervention was a difference in BMI of –1·66 kg/m² (95% CI –1·89 to –1·43) at 6 months. For long-term outcomes, there has been only one randomised trial of orlistat, which showed a change in BMI of –0·55 kg/m² with orlistat versus 0·31 kg/m² with placebo at 12 months (p=0·001),[136] and only one randomised trial of sibutramine, in which investigators reported a change in BMI of –2·9 kg/m² with sibutramine versus –0·3 kg/m² with placebo at 12 months (p<0·001).[137] Side-effects (reported as prevalence in excess of that reported for placebo) of orlistat were oily stool (42%), abdominal pain (11%), faecal incontinence (9%), and new cholelithiasis (2%).[136] Side-effects of sibutramine were tachycardia (6%), dry mouth (5%), constipation (4%), dizziness (4%), insomnia (3%), and hypertension (2%).[137] Thus, although evidence exists for slight effectiveness of orlistat and sibutramine when combined with lifestyle intervention, treatment with these drugs is associated with more adverse effects than is lifestyle intervention alone.

No randomised controlled trials of bariatric surgery have been done in children or adolescents.[109] In a

systematic review of observational studies reporting outcome data in patients aged 21 years or younger (range 9–21 years, mean 16·8 years) with a minimum follow-up of 12 months, investigators identified four studies of Roux-en-Y gastric bypass (a restrictive and malabsorptive procedure)[138] and six of laparoscopic adjustable gastric banding (LAGB; a purely restrictive procedure) that met inclusion criteria for meta-analysis (figure 4).[139] For gastric bypass, the 95% CI for change in BMI from baseline was –17·8 to –22·3 kg/m² at 1–6·3 years, and for gastric banding, –13·7 to –10·6 kg/m² at 1–3 years.[139] Complications of gastric bypass were pulmonary embolism, shock, intestinal obstruction, postoperative bleeding, staple-line leak, and severe malnutrition;[139] those of gastric banding were band slippage or erosion, micronutrient deficiency, port or tube dysfunction, hiatal hernia, wound infection, and pouch dilatation.[139] Long-term prospective studies are needed to establish safety and efficacy of restrictive and malabsorptive procedures and to establish whether reductions in morbidity and mortality outweigh the risks of serious surgical complications and life-long nutritional deficiencies.

Large trials that are sufficiently powered to examine long-term effects and that allow direct comparisons of non-pharmacological, pharmacological, and surgical treatments are needed. In view of the paucity of data, poor effectiveness, and unknown risks for long-term drug use, we recommend a conservative approach—namely, to use pharmacotherapy only in patients with BMI higher than the 95th percentile who have substantial medical complications of obesity and after a reasonable period of behavioural intervention. The risks of bariatric surgery are substantial, and long-term safety and effectiveness in children remain largely unknown. Therefore, surgery should be reserved for only the most severely obese (BMI ≥50 kg/m², or ≥40 kg/m² with important comorbidities), and even then, considered with extreme caution.

Conclusion

Much progress has been made in understanding of the genetics and physiology of appetite control and, from this, the elucidation of the causes of some very rare obesity syndromes. Much work remains to be done, however, since these rare disorders have so far taught us few lessons about how to prevent or reverse obesity in most children. No evidence-based, clinically meaningful definition of childhood obesity has been established. Calorie intake and activity recommendations need to be reassessed and better quantified at a population level because of the modern sedentary lifestyles of children. For individual treatment, the currently recommended calorie prescriptions might be too conservative in view of evolving insight into the energy gap. Quality of scientific reports needs to improve to allow comparisons between interventions and pooling of studies. Because obesity is a chronic disorder needing continuing management, long-term clinical trials are needed to show safety and efficacy of treatments, not only for a few months, but also during the crucial period of active growth and maturation. In children, safety of treatment needs to be examined as an equal outcome to efficacy.

Despite remaining challenges, glimmers of hope can be seen. Recent statistics suggest that prevalence of childhood obesity might be stabilising in developed countries. All past efforts made towards prevention and treatment of obesity, though not of notable individual effect in trials, might still have contributed collectively to this trend.[108] The increased attention that has been directed to obesity by the media might have helped to raise public awareness of energy balance. Expansion of food-product availability and more informative food labelling by the private sector might have helped the consumer to make better choices. We cannot wait to delineate the complex causal web of the obesity epidemic. Unravelling of even one thread might allow an important degree of prevention.[140] Efforts to prevent obesity should continue at all levels, with the goal of an outcome that is greater than the sum of its parts. These efforts should be made in tandem with an increased commitment to more robust research. We expect that the next 10 years will be a time of new discoveries and collective societal actions that will help to eliminate this scourge of the new millennium.

Contributors

All authors participated in deciding content, reviewing evidence, and writing of this Seminar.

Conflicts of interest

SYSK serves as a member of the Medical Advisory Board of the Aspartame Resource Center, from which she received no support for her research or her effort in this Seminar. JCH and DAL declare that they have no conflicts of interest.

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