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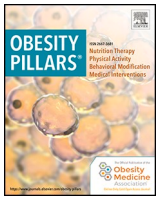

Special considerations for the child with obesity: An Obesity Medicine Association (OMA) clinical practice statement (CPS) 2024

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ABSTRACT

Background: This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) details assessment and management of the child with overweight or obesity. The term "child" is defined as the child between 2 and 12 years of age. Because children are in a continual state of development during this age range, we will specify when our discussion applies to subsets within this age range. For the purposes of this CPS, we will use the following definitions: overweight in the child is a body mass index (BMI) ≥ 85th and <95th percentile, obesity in the child is a BMI ≥95th percentile, and severe obesity is a BMI ≥120% of the 95th percentile.

Methods: The information and clinical guidance in this OMA Clinical Practice Statement are based on scientific evidence, supported by medical literature, and derived from the clinical perspectives of the authors.

Results: This OMA Clinical Practice Statement provides an overview of prevalence of disease in this population, reviews precocious puberty in the child with obesity, discusses the current and evolving landscape of the use of anti-obesity medications in children in this age range, discusses the child with obesity and special health care needs, and reviews hypothalamic obesity in the child.

Conclusions: This OMA Clinical Practice Statement on the child with obesity is an evidence based review of the literature and an overview of current recommendations. This CPS is intended to provide a roadmap to the improvement of the health of children with obesity, especially those with metabolic, physiological, psychological complications and/or special healthcare needs. This CPS addresses treatment recommendations and is designed to help the clinician with clinical decision making.

1. Introduction

The purpose of this clinical practice statement (CPS) regarding children with overweight or obesity is to provide clinicians with tools to clinically assess and manage children living with obesity and its complications. The Obesity Medicine Association (OMA) is an organization of clinicians in the field of obesity medicine dedicated to the comprehensive care of patients with obesity. OMA members are physicians, nurse practitioners, physician assistants, and other healthcare clinicians who take a comprehensive, evidence-based approach to treating obesity. This approach is comprised of four pillars: nutrition therapy, physical activity, behavior modification, and medical interventions. While it is hoped many clinicians may find the recommendations in this CPS helpful, the final decision regarding the optimal care of the patient with overweight or obesity depends on the clinical presentation of the individual and the judgment of the treating clinician. Clinicians are encouraged to construct a treatment plan through shared decision making with the patient, keeping the patient's best interest at the forefront of all decisions. For the purposes of this publication, the term "child" is defined as the child between 2 and 12 years of age; overweight in the child is a body mass index (BMI) > 85th and < than the 95th percentile, and severe obesity is a BMI > than 120% of the 95th percentile.

2. The child with obesity

Obesity prevalence in the United States (Centers for Disease Control statistics for years 2017–2020) was 12.7 % among 2-5-year-olds and 20.7 % among 6-11-year-olds [1]. Prevalence of obesity in children ages 2–5 years disproportionately affects Black and Hispanic children, with rates of 12.1 % and 21.1 % respectively (2017–2020 data); the prevalence for non-Hispanic White 2–5 year olds in this study was 10.8 % [2]. There is increasing evidence that adiposity related conditions manifest in children [3]. An Italian study of pre-school children with obesity found that 39 % had at least 1 metabolic comorbidity, including insulin resistance, metabolic dysfunction-associated steatotic liver disease (MASLD), hypertension, and dyslipidemia [4]. In other studies, researchers found that over 88 % of pre-school children with severe obesity had at least 1 abnormal laboratory value related to increased adiposity [5,6].

Children with the disease of obesity are at high risk of becoming adults with obesity. A 2020 study of 12,142 participants in the International Childhood Cardiovascular Cohort Consortium found that adult obesity developed in 56 % of children with obesity; and 80 % of children

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with severe obesity [7]. Among adolescents with obesity, retrospective studies report that the largest annual abnormal increments of BMI occurred between the ages of 2–6 years [8]. Development of obesity before age 6 years is associated with increased risk of metabolic syndrome as an adult [9].

It is well established that obesity is associated with an increased risk of cardiometabolic disease, including diabetes, hypertension, and dyslipidemia in adulthood [8,10,11]. The Bogalusa heart study demonstrated the presence of fatty streaks in the aorta and carotid arteries in 50 % of the 2–15 year old population, which was strongly associated with BMI [12]. A study by Le et al. (2008) examined the carotid intima-media thickness (IMT) in 70 children (average age 13 years; 57 % with obesity) and found that 75 % of the cohort had advanced vascular age typical of adults 45 years of age [13].

Regarding glucose metabolism, prediabetes occurs in 22–36 % of children and adolescents with severe obesity [10]. Type 2 diabetes mellitus (T2DM) has been documented in children with obesity as young as 5 years old [14]. Data from specialized obesity clinics suggest that, like adult onset T2DM, many cases of pediatric onset T2DM may go undiagnosed [15] and these children are at risk for earlier T2DM complications [10].

Health complications of childhood obesity are associated with a high economic burden [10,16–18]. A meta-analysis by Ling and colleagues estimated the increased annual total medical costs attributed to childhood overweight and obesity at $237.55 per capita [18]. By 2050, researchers project that the annual direct and indirect costs will reach $13.62 billion and $49.02 billion, respectively [18].

Risk factors for development of childhood obesity can be described as modifiable and unmodifiable risk factors. Modifiable risk factors are categorized into societal factors (food insecurity, socioeconomic status, household parental education, school food environments, the built environment, poverty) and household behavioral risk factors (screen time, sleep duration, physical activity, and dietary patterns) [3,8,10,19,20]. Once a child is born, maternal gestational weight gain, epigenetic changes, and genetic mutations are unmodifiable. Excepting surgical procedures, structural pituitary abnormalities are difficult to modify [3,21,22].

Societal risk factors often impact household behaviors that contribute to childhood obesity. In an Australian study, infants with the greatest degree of food insecurity (the lowest quartile) were associated with a 1.35 times risk of obesity at age 4.5 years compared to those without food insecurity [8]. The authors examined the association with screen time, sleep duration, and fast food/soda consumption and report that the risk of obesity increased with exposure to each additional risk factor [8]. In a review by Vargas et al., interaction between social factors and behavioral choices include the increased cost of healthful foods and decreased access of healthful foods in low-income neighborhoods [20]. Notably, a link existed between elementary school children with elevated BMIs and residing in areas with a higher fruit and vegetable price index (as opposed to areas with a lower price index) after adjustment for family characteristic and cost of living [20].

Not all social environmental factors contribute negatively to childhood obesity. Social cohesion may be a protective factor in the development of childhood obesity [20,23,24]. A study of Los Angeles County (California, US) evaluated the effect of acculturation, language, and culture on adiposity in children, finding that residing in communities with the highest level of cohesion, as measured by language, was protective against increased BMI in children ages 2–5 years [23]. Proposed mechanisms for this association include impact of traditional ethnic foods that are often more healthful than processed foods, improved use/access of community resources, and retention of traditional dietary and physical activity behaviors [23].

Gestational weight gain and maternal prenatal factors including obesity, gestational diabetes, and maternal smoking during pregnancy, have well-established links to risk of childhood obesity [3,21,22,25]. Proposed etiologies suggest that excess gestational weight gain can affect epigenetic change and metabolic imprinting, affecting key organs for metabolism and appetite control, including the hypothalamus, adipose tissue, and pancreatic islet cells [3,21]. Excess weight gain during pregnancy, as measured by the Institute of Medicine's pregnancy weight gain recommendations [26] was associated with a relative risk of 1.91 for childhood obesity [22].

Genetic mutations, including congenital leptin deficiency and mutations in leptin signaling and the melanocortin pathway, can lead to early onset childhood obesity characteristically associated with hyperphagia [3]. Additionally, single and polygenic mutations may be associated with childhood obesity, as well as rapid onset hypothalamic dysfunction/hypoventilation and autonomic dysregulation syndrome (ROHHAD) [3]. Additional medical risk factors for childhood obesity include structural pituitary abnormalities, steroid use, and exposure to broad spectrum antibiotics [3].

Many barriers impede the treatment of childhood obesity including family and structural levels [27,28]. At the family level, parental support and peer relationships play a key role in support of recommended behavioral modifications [27,29]. Currently, treatment efforts focusing on behavior modification of nutrition and physical activity may not address social risk factors that contribute to the development of childhood obesity [27]. Intensive health behavior and lifestyle treatment (IHBLT), as reviewed by the American Academy of Pediatrics (AAP), remains the foundational approach for obesity treatment in this age group [30]. IHBLT should be initiated at as early an age as possible to increase the chance for better results and be supported by advanced therapies as indicated [31,32]. However, implementation and access to IHBLT programs are limited due to challenges of financial sustainability, poor insurance reimbursement for essential ancillary staff, lack of availability in rural communities, and continued insurance and employer exclusion of obesity treatment [28].

Treatment of the child with obesity should result in the slowing or stabilization of rate of increase in BMI percentile. A higher level of care may be indicated to manage the child's condition [30]. Early identification of the child with Class 2 or 3 severe obesity or obesity not responding to IHBLT is critical [30]. These children require advanced diagnostic investigation for underlying causes and evaluation for advanced intervention [32].

Therapeutic use of medications, medical devices, and metabolic and bariatric surgery (MBS) in this population remains limited [30,32]. Currently, there is only 1 Food and Drug Administration (FDA) approved medication for treatment of obesity in children under 12 years of age (Table 1). The AAP off-label policy statement reaffirms the off-label use of prescription medications in the pediatric population with chronic disease [33]. Poor insurance coverage and reimbursement for obesity care, lack of childhood obesity training programs, and wide-spread weight bias that obesity is not a chronic disease all limit prescription practices of FDA off-label use of anti-obesity medications in this age group [28,34].

The complex social and genetic factors contributing to childhood obesity often lead to children and their families struggling to access care [27]. Further research is needed to increase knowledge and improve care of this critically important group.

Table 1
Anti-obesity medications FDA approved for indication of obesity under 12 years.

Medication	FDA Approval Age	Indication	Comment
Setmelanotide [57,58]	≥6 years	Obesity	Used in treatment of genetic disease:POMC deficiency, PCSK1 deficiency, LEPRdef, BBS

Abbreviation: Bardet-Biedl syndrome = BBS; leptin receptor deficiency = LEPRdef; pro-opiomelanocortin = POMC; proprotein convertase subtilisin/kexin type 1 = PCSK1.

3. The child with precocious puberty & obesity

Excess adiposity impacts metabolic health in children with the disease of obesity and frequently influences pubertal development. Normal onset of puberty in females occurs at age 10 years on average but ranges from 8 to 13 years of age. Breast development is the first sign of puberty in females with an average of 2–2.5 years from onset of breast development to the first menstrual cycle [35]. In males, normal onset of puberty starts at 11 years of age on average and ranges from 9 to 14 years with enlargement of testicular size as the first sign of puberty. The onset of puberty is under the control of the hypothalamus, which secretes gonadotropin releasing hormone, sending a signal to the pituitary gland to release gonadotropins [35]. These gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH), then signal the ovaries to make estrogen in females or the testes to make testosterone in males.

Precocious puberty is defined as breast development in females younger than 8 years of age [35] or enlarged testicular size in males younger than 9 years of age, with an incidence of 1 in 5000–10,000 children [36]. Studies show that excess adiposity and obesity can affect the start of puberty differently for males and females. There are studies that report a delay in the onset of puberty in males with obesity, while other research suggests obesity may be related to increased risk of early puberty in females and males [37–39]. The average age of first menstrual cycle has remained 12.5–13 years over the past several decades, but newer studies find the average age of pubertal onset in females decreasing to 8 years and even to 7 years in some ethnic backgrounds [39].

A strong association is reported in females between increased body weight at prepubertal ages and the early onset of puberty. What affects this relationship is not certain, but one consideration suggests the role of hormones released from adipose cells. Leptin is produced by adipose cells and plays a role in appetite regulation, body weight and food intake, in addition to a vital role in puberty regulation, particularly in females, with a certain level needed to initiate puberty. Children with obesity are found to have higher levels of leptin than children without obesity, which may have a role in earlier puberty onset [40,41].

There is a link between nutritional status and puberty. Females with underweight have been found to have a later onset of puberty in comparison to earlier onset in those with excessive weight gain [42]. Early rapid weight gain in infancy is a risk factor for obesity in childhood and adulthood and has also been linked to earlier pubertal maturation in girls [43]. Additionally, there is concern about the possible role of endocrine-disrupting chemicals, such as pesticides, in the environment, with studies ongoing [44]. Certain races and ethnicities have higher rates of obesity, including Black, Hispanic, and American Indian/-Alaskan Native children. Black and Hispanic girls start puberty on average 1 year earlier as contrasted with non-Hispanic White females [35].

The adrenal glands produce hormones stimulating the growth of axillary hair and pubic hair, defined as adrenarche. Premature adrenarche is associated with obesity [45,46]. In premature adrenarche, which occurs in females prior to age 8 years, androgen levels produced from the adrenal glands are elevated for actual age but within the range expected for stage of pubic hair. Androgens can be converted by adipose tissue to estrogen, leading to early estrogen effects in females. This process may be related to elevated insulin and leptin levels.

There are concerns regarding the impact on emotional and social development, in addition to decreased final adult height with advanced bone age, in children with early puberty. As obesity is a risk factor for early puberty [47], several risk factors for childhood obesity should be addressed as soon as at-risk patients are identified. It is important to prevent childhood obesity from extending into adulthood by addressing lifestyle factors such as nutrition and exercise early in life and incorporating these changes for the entire family and referring for multidisciplinary care when not responding to these interventions.

The clinician assessing the child for early puberty should astutely examine the child. Early puberty can be misdiagnosed in girls with obesity with adipose tissue being mistaken for breast development. Physical examination and review of linear growth using growth charts are key in the assessment of patients presenting with obesity. Prepubertal growth on average is two inches per year, whereas accelerated linear growth is often seen in precocious puberty with crossing of percentiles on growth charts. Further evaluation includes hormone measurements such as serum morning LH, estradiol in females or total testosterone in males, thyroid-stimulating hormone and free thyroxine in the case of early breast development, and 17-hydroxyprogesterone and dehydroepiandrosterone sulfate in the case of early pubarche. In addition, bone age x-ray or pelvic ultrasound may be indicated, as well as endocrinology consultation, in order that appropriate treatment can be initiated [48].

Treatment of precocious puberty is based on its origin. A study from China suggests that 25.98 % of precocious puberty in girls and 38.58 % in boys was associated with obesity or central obesity [49]. Treatment can be considered when there is concern about the psychosocial impact of early pubertal maturation or impaired final height and involves gonadotropin receptor agonist therapy in the form of subcutaneous or intramuscular injections or a subcutaneous implant [35,39].

As children at $\geq$ 95th percentile have a greater chance of maintaining obesity into adulthood [7], it is vital to provide appropriate counseling regarding lifestyle changes to families to prevent the known complications of excess adiposity during childhood and adolescence, including early pubertal maturation. Together with healthful nutrition and physical activity, prompt treatment for excess adiposity and obesity can lessen or prevent adiposity related conditions, which include changes in puberty. Fig. 1 summarizes key points about the young child with precocious puberty and obesity.

4. Anti-obesity medication use in the child with obesity

In 2013, the American Medical Association recognized obesity as a chronic disease which occurs across the lifespan [50]. In the past 2 decades, treatment for children with the disease of obesity has evolved. Lifestyle intervention has been the cornerstone of treatment; however, many studies demonstrate that the outcome of lifestyle intervention is a small change in weight status (1–3%) [30,51] and the intensity needed to achieve this small gain is difficult to provide clinically [52].

Published research regarding the use of anti-obesity medications (AOM) in children and adolescents has increased in the past 10 years with 1 FDA approved medication in children $\geq$6 years, 4 additional FDA approved medications for children $\geq$12 years, and 1 additional FDA approved medication >16 years of age [53,54]. Research data remains limited for children younger than 12 years of age [51,55,56], therefore children <12 with obesity have only 1 medication FDA approved medication, Setmelanotide, for the indication of obesity [57], use of which is limited to specific rare genetic forms of obesity [53,57,58]. As outlined in Srivastava et al. (2019), more data are needed to define the lower age limit for using obesity pharmacotherapy in the pediatric population [59].

In this section, we discuss the recommendations from organizations representing children regarding obesity treatment [30,32,55,56,59–61]. Table 1 lists the anti-obesity medication FDA approved for the indication of obesity under age 12 and Table 2 lists medications affecting weight which are FDA approved for other indications under 12 years. Table 3 summarizes research on the effect on adiposity of medications used for non adiposity diagnoses, and includes outcomes regarding BMI or weight change when reported, along with safety in children under the age of 12 years. Table 4 summarizes research on medications affecting weight used in the treatment of adiposity related diagnoses. Finally, Table 5 reviews planned and ongoing research trials of AOMs that include children less than 12 years of age.

The AAP Clinical Practice Guideline (CPG) (2023) includes a

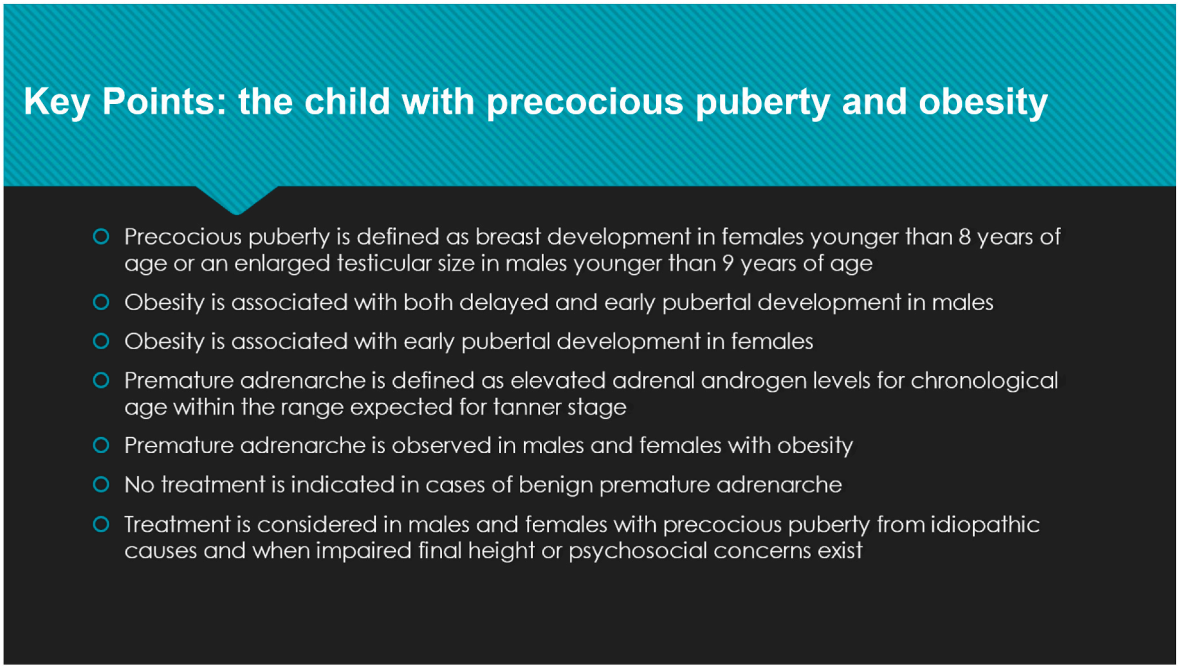

Fig. 1. Summary of key points about the child with precocious puberty and obesity.

Table 2
Medications with weight reducing effects and FDA approved for clinical indications other than obesity in children <12 years.

Medication	FDA Approval Age	Indication
Metformin [62]	≥10 years	T2DM
Liraglutide [63]	≥10 years	T2DM
Dulaglutide [64]	≥10 years	T2DM
Empagliflozin [65]	≥10 years	T2DM
Topiramate [66]	≥2 years	Seizures
Lisdexamfetamine [67]	≥6 years	ADHD

Abbreviation: Attention deficit hyperactivity disorder = ADHD; FDA = Food and Drug Administration; Type 2 diabetes mellitus = T2DM.

consensus recommendation identifying specific conditions for the consideration of anti-obesity medications (AOM) in younger children: "The CPG authors recommend pediatricians and other pediatric healthcare providers may offer children ages 8 through 11 years of age obesity weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an adjunct to health behavior and lifestyle treatment; new evidence may lead to additional options for children younger than 12 years in the future" [30]. Additionally, the European Medicines Agency (EMA) states that the use of pharmacotherapy may be considered for children with severe obesity as young as 6 years of age [56].

Many children under the age of 12 years are presenting at younger ages with obesity, in particular severe obesity, and as a result, have longer exposure to this chronic disease. A meta-analysis by the Cochrane group [70] evaluated the effectiveness of lifestyle interventions in children with excess body weight, finding that the greatest reduction in BMI standard deviation scores (SDS) occurred in the youngest children (ages 2–5 years). Geserick (2018) reports that intervention is recommended in early childhood when risk is highest for acceleration of BMI and sustained risk of obesity [71]. Utilization of medications earlier and without delay upon the diagnosis of obesity may further improve treatment outcomes for our younger patients [30,68]. The AAP off-label policy statement outlines the process to manage many conditions in the pediatric population [33]. The AAP supports the off-label use of pharmacotherapy when the clinician determines that the efficacy and safety of a drug is anticipated to result in a net benefit to the child, based upon the best available evidence. Cuda et al. (2022) describe the importance of providing the best therapy based on the current disease state versus a predefined timeline, initiation of treatment not by a specific age, rather informed by the age at which this chronic disease presents [32]. Discussions with families using shared decision making includes outcome data of delayed care with resultant progression of both obesity and adiposity-driven complications compared to early and comprehensive intervention of the disease of obesity [72–79].

Anti-obesity medications are a tool for the management of childhood obesity, as IHBLT alone results in modest improvement for a small subset of patients with obesity [80]. Additional data from behavioral intervention research illustrate similar results (small to no improvement in obesity metrics.) The AAP CPG notes that typical IHBLT studies resulted in a 1–3% decline in BMI [30]. Wilde et al. (2021) found in a five-year follow up of a family-based intervention, BMI standard deviation score (SDS) reduction was not maintained at 12 months [81]. Similarly, Allender et al. (2021) found in a four-year behavioral program, no significant difference on BMI z score (zBMI) was observed between intervention and control groups either 2 years after treatment (2015–2017) or 4 years after treatment (2015–2019) [82]. In a 12-year evaluation of an obesity multidisciplinary specialist treatment service, Wyse et al. (2022) found a −0.17 BMI SDS change across the whole cohort and that younger age at intervention initiation and longer duration of the intervention resulted in a greater BMI-SDS; there was no significant association with this change and any other parameter studied [83]. The AAP CPG states "Although providing patient-centered and non-stigmatizing nutrition and activity counseling is important for children of all weight classifications, there is no evidence to support either watchful waiting or unnecessary delay of appropriate treatment of children who have already developed obesity. Many children are only referred to treatment programs when their obesity has become more severe. A delay in care ultimately reduces the likelihood of treatment success for the child" [30].

The use of AOM in adults and adolescents is well established [30,32,51,53,84,85]. Clinicians caring for children <12 years are faced with the clinical question of waiting until the child reaches age 12 or using AOM off label for age. Using a shared decision process with the family, the obesity clinician can address the use of medications that have FDA

Table 3
Research on medications affecting weight used in the treatment of other non-adiposity related diagnoses.

Study	Medication	Ages studied	Clinical Indication	Inclusion Criteria	Adverse Events	Impact of BMI/Weight
Grosso et al., 2005 [95]	Topiramate	1–16 years	Epilepsy	1) age 1–16 years; 2) seizures refractory to at least two first-line antiepileptic drugs; 3) at least four seizures a month during the 3 months before topiramate was administered; 4) at least 24 months of follow-up.	Adverse events observed in 161 patients (58 %); primarily weight loss, hyperthermia, sedation, and nervousness; most resolved after slowing titration or reducing the dosage of the drug.	84 patients with weight loss, anorexia, loss of appetite. 11 patients topiramate discontinued due to severe weight loss or anorexia
Reiter et al., 2004 [96]	Topiramate	7.26 ± 5.21 years (range 0.5–17 years)	Epilepsy	1) Children and adolescents ≤18 years; 2) treated with topiramate at least 12 consecutive months	Not reported	Weight change at 12, 24, 36 months: 0.10, −0.18, −0.11kg BMI change at 12, 24, 36 months: −0.13, −0.03, −0.13
Glauser et al., 2007 [66]	Topiramate	6–15 years	Epilepsy	1) children ≥25 kg and adults; 2) epilepsy diagnosed within 3 months of the screening visit on the basis of 2 or more unprovoked lifetime seizures; 3) relapse of epilepsy when not receiving an antiepileptic; 4) patients with generalized epilepsy eligible if seizures generalized-onset tonic-clonic type; 5) only 1 or 2 partial onset or generalized-onset tonic-clonic seizures in the 3-month retrospective baseline; 6) females of childbearing potential practicing adequate birth control methods and negative pregnancy test	Most common adverse events: headache, appetite decrease, weight loss, somnolence, dizziness, concentration/attention difficulty, and paresthesia.	% of patients with potential weight loss 31 % with decrease body weight from baseline on 50 mg/day; 43 % with decrease on 400 mg/day
Gilliam et al., 2003 [97]	Topiramate	>3 years; (11.5 % < 16 years)	Epilepsy	1) ≥ 3 years of age; 2) weight 25–110 kg; 3) diagnosed with localization-related epilepsy (partial-onset seizures with or without secondary generalization) within the previous 3 years; 4) history of 1–6 partial-onset seizures during the 3-month retrospective baseline; 5) untreated with AED or no more than one AED, unless a second agent used for self-limiting conditions (e.g., febrile seizures) or used <1 month; 6) subjects with childbearing potential using an acceptable method of birth control and negative pregnancy test at baseline.	Dose-related adverse events included paresthesia, weight loss, diarrhea, and hypoesthesia.	% of patients with potential weight loss: 3 % in children with weight loss versus 12 % in adults (amount weight loss not reported)
Childress et al., 2022 [100]	Lisdexamfetamine	4–5 years old	ADHD	1) children 4–5 years [inclusive] at time of consent); 2) met DSM-IV-TR criteria for a primary ADHD diagnosis; 3) undergone course of non-pharmacologic treatment; 4) symptoms severe enough to warrant enrollment without prior non-pharmacologic treatment; 5) have a screening Peabody Picture Vocabulary Test standard score ≥70; 6) lived with the same parent/guardian for ≥6 months; 7: subject/guardian able to comply with protocol.	Mild to moderate severity. Most frequent decreased appetite and irritability, both reported by >5 % of participants across all LDX doses. Increases in pulse, systolic blood pressure and diastolic blood pressure as well as mean decreases in BMI percentile relative to baseline were numerically greater with 10, 20, and 30 mg LDX than with placebo	Most frequent TEAE was decreased appetite (13.7 % vs 8.9 %, respectively) Weight loss in 10mg dose: 0.1kg, 20mg dose: 0.3kg, 30mg dose: 0.3kg BMI % change: in placebo: 1.6, In 5mg dose: 0.9, 10mg dose: 5.1, 20mg dose: 6.7, in 30mg dose: 7.4 %
Sugaya et al., 2023 [101]	Lisdexamfetamine	≤7 years	ADHD	Studies that included: 1) double-blinded RCTs that enrolled preschool children (age ≤7 years) with a primary diagnosis of ADHD; 2) administered stimulants against placebo; 3) assessed change in ADHD symptom severity as an outcome; 4) any stimulant, either methylphenidate or amphetamines, irrespective of formulation and dosages; 5) no restrictions on language or publication year	Decreased appetite, irritability, and insomnia frequent adverse events.	Systematic review. Decrease in bodyweight/BMI was reported by 4 RCTs
Fast et al., 2021 [102]	Stimulants	6–17 years	ADHD	1) age 6–17 years at start of treatment 2) diagnosis of ADHD 3) stimulant-naïve; 4) complete growth	Common side effects of stimulants include appetite suppression, increased blood pressure, tachycardia, headache,	Mean (SD) body mass index (BMI) in standard deviation score (SDS) decreased significantly: −0.72 (0.66) compared with 0.17

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Table 3 (*continued*)

Study	Medication	Ages studied	Clinical Indication	Inclusion Criteria	Adverse Events	Impact of BMI/Weight
				data and continuous treatment with stimulants during the studied period.	stomachache, sleeping problems and dysphoria.	(0.43) during the year before treatment ($p < .01$). After 1 year with treatment, 43 % of those with overweight or obesity had reached normal weight

Abbreviations: anti-epileptic drug = AED; body mass index = BMI; body mass index z score = zBMI; Confidence interval = CI; Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision = DSM-IV-TR; gastrointestinal = GI; Exenatide every week = ExQW; kilogram = kg; Lisdexamfetamine = LDX; randomized controlled trial = RCT; standard deviation = SD; standard deviation scores = SDS; total body weight = TBW; treatment emergent adverse event = TEAE.

approval for another age or indication to help inform safety concerns and required appropriate monitoring [32,86].

4.1. FDA on label and off label designation

As in many other areas of medicine, the use of medications off-label for indication and/or population can be life-saving and necessary to improve disease status [86]. Collectively, the AAP Clinical Practice Guideline [30], the Obesity Medicine Association Clinical Practice Statement for advanced therapies [32], and the AAP Pediatric Off-Label Policy Statement [33] guide off-label medication use in children with obesity [30,32] and other conditions [33]. All FDA "approved" medications have been studied for safety and efficacy for a specific population and indication. FDA off-label status indicates that the medication is being used for another population or indication. The term "off-label" does not equate to improper or illegal usage [87].

The use of off-label medications of all types is common in pediatric practice, with over 30 % of all medications prescribed to children and adolescents categorized as off-label for indication, population, or both [30,32,86,88]. Although the use of medication off-label for indication or population is common in pediatric practice, off-label medication use does not indicate "off-evidence" [88]. Hoon et al. (2019) studied off-label medication usage in US ambulatory settings and found that off-label usage was supported by high-quality evidence [89]. Risk/benefit analysis along with shared decision-making are a critical part of any decision-making process whether the medication is "on" or "off" label.

4.2. Medication research in children

When research is limited related to population and indication usage, guidance encourages clinical decisions "based on sound scientific evidence, expert medical judgment, or published literature whenever possible" [33]. Medications used in obesity care for children that are off-label for population or indication of obesity have been studied for safety and efficacy for other clinical indications (Table 2). A summation of research on medications affecting weight used in the treatment of other non-adiposity related diagnoses in children under the age of 12 years is found in Table 3.

Yanovski and colleagues (2011) conducted a randomized trial with metformin versus placebo in 100 children with severe obesity which included children 6–12 years of age with insulin resistance [90]. Results indicated that metformin had modest but favorable effects on body weight, body composition, and glucose homeostasis, specifically BMI (difference −1.09 kg/m^2), body weight (difference −3.38 kg.), and zBMI (difference between metformin and placebo groups −0.07) [68]. Additionally, Bassols et al. (2019) [91] included children ages 6–13 years finding a 25 % reduction in BMI-SDS and Pastor-Villaescusa et al. (2017) noted a −0.8 zBMI, which included children ages 7–14 years of age [92].

Topiramate is FDA approved for use in children ≥2 years for seizure disorders and is FDA approved in children 12–17 years of age as a combined medication with phentermine for the treatment of obesity. Weight effects of topiramate when used in the child <12 years for non-obesity conditions show modest but significant improvement (Table 3) [105,106]. Reiter et al., 2004 studied the effect of topiramate on body mass index (BMI) in children with epilepsy with mean age of 7.26 years; findings showed BMI change at 12, 24, and 36 months of −0.13, −0.03, and −0.13 respectively [96]. Glauser et al. (2007) studied children 6–15 years of age and found that 31 % of patients had a decrease in body weight on topiramate dosing of 50 mg/day and 43 % of patients had a decrease using 400 mg/day compared to baseline [66]. Gilliam et al. (2003) studied use of topiramate as monotherapy for seizures in subjects ≥3 years into adulthood; data indicated that 3 % of subjects 3 < 16 years had weight loss (versus 12% of subjects >16 years) although weight loss amounts not reported [97]. As monotherapy, topiramate is used to help with food cravings and compulsive eating patterns [107]. As an anti-epileptic medication, topiramate is used in pediatric patients with FDA approval at age 2 years and older [97]. As a treatment for migraine headaches, topiramate is FDA approved ≥12 years [105,106]. When considering weight effects of topiramate in studies for conditions other than obesity, these changes are impressive given that the study population was not receiving any specific dietary or behavioral lifestyle intervention.

Phentermine, a medication approved for adolescents >16 years of age since 1959, has also been studied in children as young as 3 years of age [99]. Lorber et al. (1966) included children ages 3–15 years of age in their study, finding a −1.3 kg decrease in body weight [99]. Research by Ryder et al. (2017) included adolescents ≥16 years and reported a −4.1 % BMI change at 6 months, followed by the more recent FDA approval of the combination medication phentermine/topiramate for children 12 years and older which found % change in BMI difference from placebo of -10.44% for top dose and -8.11% for mid doses [108]. Lisdexamfetamine has FDA approval for the indication of binge eating disorder (BED) for patients >18 years of age and for attention-deficit/hyperactivity disorder (ADHD) for children ≥6 years, yet not for binge eating disorder for those <18 years [67,107,108]. Lisdexamfetamine has been studied in children as young as 4 years of age (Table 3).

Czepiel et al. (2020) reviewed a clinical data registry of 6.5 million patients ascertaining current prescribing practices of medications with weight modifying effects among its pediatric/young adult population, assessing the effect of these medications on weight status [94]. Results found 1720 patients (83 5–12 year olds; 492 adolescents, 1145 young adults [19–25 years]) with 2210 prescribing instances. The most frequently prescribed medications for 5–12 year olds were metformin (off-label for indication and population) with final percent total body weight loss (%TBWL) mean of −0.06 and topiramate (off-label for indication) with final weight loss %TBWL mean of −0.07. Limitations outlined include no control group, which may underrepresent or overrepresent the benefit of these medications, given results are based on the mean, inability to assess the possible synergistic impact of combination treatments, as well as lack of dosing information.

Currently, both liraglutide 3.0 mg and semaglutide 2.4 mg are FDA approved for the indication of obesity in children ages ≥12 years [110,111]. Liraglutide is FDA approved for indication of T2DM for children ages ≥10 years at the maximum dose of 1.8 mg with a noted weight decrease at week 52 of −1.91 kg versus. 0.87 with placebo [62,109,110]. Exenatide, FDA approved for indication of T2DM ≥ 10 years, has been studied twice in children 9–10 years of age with obesity [103,104];

Table 4
Research on medications affecting weight used in the treatment of adiposity related diagnoses.

Study	Medication	Ages studied	Clinical Indication	Inclusion Criteria	Adverse Events	Impact of BMI/Weight
Yanovski et al., 2011 [90]	Metformin	6–12 years	Obesity and Insulin resistance	1) 6–12 years; 2) BMI ≥95th percentile; 3) prepubertal or early pubertal (defined as breast Tanner stage I–III for girls; testes <8 mL for boys); 4) fasting hyperinsulinemia (fasting insulin ≥15 mU/mL)	No serious or life threatening adverse events reported. Gastrointestinal symptoms significantly more prevalent in metformin-treated children, which limited maximal tolerated dosage in 17 %	Children prescribed metformin had significantly greater decreases in BMI (difference −1.09 kg/m^2), body weight (difference −3.38 kg,), zBMI (difference between metformin and placebo groups −0.07) and fat mass (difference −1.40 kg).
Bassols et al., 2019 [91]	Metformin	6–13 years	Obesity and Insulin resistance	1) age 6–13 years; 2) Tanner stage I-II; 3) BMI between 2 SD (97th centile) to 4 SD, for age and sex; 4) fasting insulin levels >6 mIU/L; 5) visceral-to-subcutaneous fat ratio (MRI) >90th centile, based on a reference of healthy children without obesity; and 6) birth weight above −1.5 SD and below +1.5 SD for gestational age	Metformin and placebo well tolerated; no side effects reported	25 % decrease in BMI-SDS and a 20 % decrease in weight-SDS compared with placebo-treated children over 12 months; maintained after 24 months.
Pastor Villaescusa et al., 2017 [92]	Metformin	7–14 years	Obesity	1) BMI greater than the 95th percentile. 2) age 7–14 years. 3) no underlying disease or a history of pathology; 4) No medical treatment regarding weight control in the previous 12 months; 5) no participation in a previous trial	No serious adverse effects reported.	Patients with BMI ≥95th percentile decreased the zBMI versus placebo in the prepubertal group (−0.8 and −0.6, respectively; difference, 0.2; p = .04).
Matsuura et al., 2018 [93]	Metformin	6–7 years	T2DM and obesity	1) HbA1c level ≥7.0 and < 12.1 %; 2) obesity compared to the school health statistics Japan 2000)	Adverse effects (nausea, diarrhea) observed in 35 of 37 subjects; drug-related adverse events were observed in 19 patients; adverse events were not serious and did not increase with long-term treatment.	Degree of obesity (%) −2.2 ± 5.94 at 52 weeks from baseline degree of obesity (41.55)
Czepiel et al., 2020 [94]	Bupropion, **Bupropion/naltrexone, canagliflozin, exenatide, **liraglutide, lorcaserin, metformin, naltrexone, orlistat, **phentermine, **phentermine/topiramate, pramlintide, topiramate, and zonisamide	5–12 years: Metformin Topiramate Bupropion	Obesity	1) ages 5–25 years old; 2) diagnosis of overweight or obesity; search between 2009 and 2018; taking at least one of following medications (bupropion/naltrexone, canagliflozin, exenatide, liraglutide, lorcaserin, metformin, naltrexone, orlistat, phentermine, phentermine/topiramate, pramlintide, topiramate, and zonisamide.)	1 % GI symptoms	Final weight loss %TBW mean: Metformin: 0.6 Topiramate: 0.01 Bupropion: 0.7
Lorber et al., 1966 [99]	**Phentermine	3–15 years old	Obesity	1) children ages 3–15 years; 2) over 95th percentile	Insomnia	Average weight loss: 1.3kg
Roth et al., 2021 [103]	Exenatide	10–25 years	Obesity, Hypothalamic injury	1) age- and sex-adjusted BMI ≥95 percentile or BMI ≥32 kg/m^2 if ≥ 18 years; 2) evidence of hypothalamic injury by MRI confirmed by one central neuroradiologist; 3) ≥ 6 months postsurgical or radiation treatment; 4) weight stable or increasing over 3 months; 5) stable hormone replacement for ≥3 months.	Vomiting (4/23) and diarrhea (7/23)	Change in BMI (estimated effect of treatment: ExQW: 0.6 ± 0.3 kg/m^2, 95 % CI 0.1–1.1 kg/m^2, P = 0.03; Placebo: 1.4 ± 0.3 kg/m^2, 95 % CI 0.8–2.0 kg/m^2; P < 0.001) - total body fat mass was reduced (estimated treatment difference −3.1 ± 1.4 kg, 95 % CI −5.7 to −0.4 kg, P = 0.02).
Kelly et al., 2012 [104]	Exenatide	9–16 years	Obesity	1) age 8–19 years old; 2) extreme obesity (BMI ≥1.2 times the 95th percentile or BMI ≥35 kg/m^2).	Mild nausea (36 %)	BMI reduction of −1.7 compared to control and −3.9kg body weight compared to control

(*continued on next page*)

Table 4 (*continued*)

Study	Medication	Ages studied	Clinical Indication	Inclusion Criteria	Adverse Events	Impact of BMI/Weight
Tamborlane et al., 2019 [63]	**Liraglutide	10 to <17 years	T2DM, Overweight Obesity	1) 10 < 17 years of age at the time of randomization; 2) had type 2 diabetes; 3) had glycated hemoglobin levels between 7.0 and 11.0 % being treated with diet and exercise alone or between 6.5 and 11.0 % treated with metformin (with or without insulin); 4) body-mass index (BMI) ≥ 85th percentile	Nausea most frequently reported adverse event; majority of all adverse events were mild in severity, resolved, and considered by the investigators unrelated to liraglutide or placebo.	Mean body weight decreased in both groups at week 26 (−2.3 kg with liraglutide and −0.99 kg with placebo) but was maintained only with liraglutide at week 52 (−1.91 kg with liraglutide versus 0.87 kg with placebo).

Abbreviations: body mass index = BMI; body mass index z score = zBMI; confidence interval = CI; exenatide every week = ExQW; glycated hemoglobin = HbA1c; kilogram = kg; magnetic resonance imaging = MRI; milli units per liter = mIU/L; standard deviation scores = SDS; total body weight = TBW; type 2 diabetes mellitus = T2DM.

findings show BMI reduction of −1.7 compared to control and −3.9 kg body weight compared to control in the first study and no significant difference in BMI change between groups in the second study, although Roth et al. [103] reported that in the exenatide group, 2 subjects experienced a BMI decrease >5 %, 4 with a decrease of 2.5 % or more at 36 weeks compared to placebo where no subject experienced >5 % BMI decrease (Table 4). Many studies in Tables 3 and 4 outline, without specifically reported lifestyle interventions, improvement in weight and BMI that exceeds most IHBLT studies in children that provide targeted dietary and physical interventions. The QUEST study (in process, Table 5) is comparing intensive behavioral therapy of 52 contact hours to semaglutide plus behavioral therapy involving 12 hours of contact for patients 12–17 years of age. Results of this study may help guide future recommendations for more effective obesity care.

Several additional obesity clinical trials are currently in process or in the planning phase which include subjects ≤12 years [Table 5]. Both liraglutide (SCALE Kids) and semaglutide (STEP Young) trials will include ages 6–12 years and 6 to < 18 years respectively [Table 5]. A clinical trial of tirzepatide will include 10–18 year olds for indication of T2DM and 12–17 years of age for indication of obesity and overweight with adiposity related comorbidities. As these research data become available, the landscape of FDA approved pharmacotherapy may expand the treatment options available for children (Table 5) [55].

Multiple factors ranging from efficacy, possible on-label alternatives, dosing, safety, monitoring, and risk-benefit ratio should be assessed as standard prescribing practice [33,112]. Patients and clinicians should be empowered to consider treatment plans that incorporate the assessment of each patient's disease status, research data to inform care, and utilize the medications in all available formulations at the best medically tolerated dose that results in improvement in outcomes, not restricted to the costliest formulations. This will vary from one patient to the next, highlighting heterogeneity of this disease, and the importance of clinical expertise in obesity management as well as the need for a longitudinal monitoring approach.

For all patients and families that require medical care for a chronic progressive disease, available research data and best evidence guides therapy. This practice requires assessing the impact of delayed care based on age versus providing treatment based on disease burden. Progression of the disease of obesity and its known complications is more difficult to treat the longer left untreated, with increased poor quality of life leaving lasting negative impacts into adulthood [113]. Providing non-stigmatizing family-centered care, like any chronic disease, is the standard of practice for all patients with obesity, including our youngest patients. With only 5 FDA approved AOMs for use in children <17, clinicians frequently follow the common practice of off-label prescribing. San Giovanni et al. (2021) highlight weight bias resulting in hesitancy in treating obesity which they define as, the "quintessential double standard [34]. Fox et al. (2024) note that providing treatments without long-term safety data is not obesity-specific and is used frequently for the management of many chronic diagnoses in childhood [51]. Off-label for population/indication pharmacotherapy practice mandates a shared decision-making process intended to inform and guide families, based on outcome data for IHBLT versus IHBLT with AOMs. Using the best therapeutic tools for the disease presentation provides optimal treatment and may prevent and/or decrease adiposity-driven diseases like T2DM, hypertension, MASLD, obstructive sleep apnea, polycystic ovary syndrome, cardiometabolic disease, and multiple mental health conditions [30,32,114].

As health care clinicians, we make clinical decisions with the health of the child as our primary concern. Early discussion with families that obesity requires long-term care can create a supportive partnership with improved health for children [30,32,115]. Growing literature supports the need to address even our youngest patients with obesity with early, intensive, and effective comprehensive care [115–117]. Severe obesity in the child is unlikely to remit [68,86]. Lack of intervention is more likely to lead to progression than to resolution of disease.

To help guide treatment decisions, the clinician can review resources and recommendations from organizations representing children regarding obesity treatment, including AAP Clinical Practice Guideline [30], OMA Pediatric Clinical Practice Statements on advanced obesity therapies and adiposity related complications [32,118,119], OMA pediatric obesity pharmacotherapy review [84], the FDA [33] as well as the European Medicines Agency [55,120]. Watching a young child with deteriorating weight status should prompt a discussion of intervention with the family [30,32]. The need is great for more effective preventive and treatment strategies for obesity care access across the lifespan, and for care for high-risk children. The goal is to impact epigenetic factors and transgenerational risks that contribute to increased prevalence in this age group. This requires supportive, longitudinal, and empathetic discussions as early as possible with families to ensure best health outcomes for all children with the disease of obesity [32,84,116].

5. The child with special healthcare needs and obesity

5.1. Introduction

Patients who present for weight management at young ages tend to present with much more severe levels of obesity than at older ages, and this trend is similar in the case of children who have obesity and special healthcare needs (SHCN) [121]. This section will focus on children under 6 years of age with obesity and SHCN, though many of the recommendations will apply to slightly older children as well. Children with SHCN are broadly defined for this clinical practice statement to include those with intellectual/developmental disability, autism, Down syndrome, other genetic disorders associated with obesity, physical disabilities, and global developmental delay [122].

A careful, initial assessment of the patient with obesity and SHCN is critical, starting with a history of birth and early development [122]. Of

Table 5
Clinical trials in process in childhood obesity.

Medication	Clinical Trial	Age range included	Study Start date	Study Completion	Notes
Liraglutide: SCALE KIDS	Effect and Safety of Liraglutide 3.0 mg on Weight Management in Children with Obesity Aged 6 to Below 12 Years: 56-week, Double-blind, Randomized, Placebo-controlled Trial.	6 < 12 years	03-04-2021	01-15-2027	https://classic.clinicaltrials.gov/ct2/show/NCT04775082
Tirzepatide	A Study of Tirzepatide (LY3298176) in Pediatric Participants with Obesity; Phase 1	6–11 years	2-7-2023	11-13-2024	https://clinicaltrials.gov/study/NCT05696847?cond=obesity&intr=tirzepatide&distance=50&aggFilters=ages:child&rank=1
Tirzepatide	A Study of Tirzepatide (LY3298176) Once Weekly in Adolescent Participants Who Have Obesity or Overweight with Weight-Related Comorbidities	12–17 years	10-16-2023	01-01-2026	https://classic.clinicaltrials.gov/ct2/show/NCT06075667
Tirzepatide	10–18 year olds with T2DM	10–18 years	4-13-2022	February 2025	https://classic.clinicaltrials.gov/ct2/show/NCT05260021
Exenatide BASIC2 [55]	Brain Activation and Satiety in Children 2 (BASIC2)	10–12 years	1-28-2012	11-30-2023	https://clinicaltrials.gov/study/NCT04520490
Semaglutide STEP Young	Long-term Safety and Efficacy of semaglutide subcutaneous once-weekly on weight management in children and adolescents (Aged 6 to <18 years) with obesity or overweight	6-< 18 years	7-07-2023	1-15-2027	https://classic.clinicaltrials.gov/ct2/show/NCT05726227
Semaglutide QUEST [55]	Semaglutide + behavioral therapy (12 contact hours) to control of Intensive behavioral therapy (52 contact hours)	12–17 years (Note: included as comparing 52 hours intensive behavioral therapy which is current therapy for children <12 years of age	3-15-2022	1-1-2024	https://classic.clinicaltrials.gov/ct2/show/NCT04873245?term=04873245&draw=2&rank=1
Setmelanotide	Phase 3 trial evaluating setmelanotide in pediatric patients ages 2 < 6 year old (N = 12) over 52 weeks achieved primary endpoint	2 < 6 years	2-16-2022	9-19-2023	https://classic.clinicaltrials.gov/ct2/show/NCT04966741 Farooqi S, Mohamed Iqbal A, Fennoy I et al. VENTURE: Design of a Phase 3 Multicenter, 1-Year, Open-Label Trial of Setmelanotide in Pediatric Patients Aged 2 to <6 Years with Rare Genetic Diseases of Obesity. Poster presented at European Society for Pediatric Endocrinology. September 15–17, 2022; Rome, Italy. Poster P1-472.
Setmelanotide	Phase 3 Trial: In this trial, patients with acquired hypothalamic obesity aged 4 years or older will be randomized 2:1 to setmelanotide therapy or placebo for a total of 60 weeks, including up to eight weeks for dose titration. The Company expects to obtain top-line study results in H1 2025.	≥6 years	4-26-2023	4-16-2025	https://clinicaltrials.gov/study/NCT05774756 Roth C, Shoemaker A, Gottschalk M et al. Trial Design of a Double-Blind, Randomized, Placebo-Controlled, Phase 3 Study of Setmelanotide in Patients with Hypothalamic Obesity. Poster presented at ENDO (Endocrinology Society National Conference) June 15–18, 2023, Chicago, IL. Poster FRI-065.
Orforglipron [51]	A Study of Orforglipron (oral GLP-1) (LY3502970) in Adult Participants with Obesity or Overweight With Weight-Related Comorbidities (ATTAIN-1)	Phase 3 Adult trial ongoing **Pediatric trial being discussed**	Adult: 6-5-2023 **Pediatric: TBD**	Adult: 9-24-2027 **Pediatric: TBD**	https://classic.clinicaltrials.gov/ct2/show/NCT05869903
Retatrutide [51]	A Study of Retatrutide (LY3437943) in Participants Who Have Obesity or Overweight (TRIUMPH-1)	Phase 3 Adult trial ongoing. **Pediatric trial being discussed**	Adult: 7-10-2023 **Pediatric: TBD**	Adult: 5-13-2026 **Pediatric: TBD**	https://classic.clinicaltrials.gov/ct2/show/NCT05929066

Abbreviations: glucagon-like peptide 1 = GLP-1; milligram = mg; type 2 diabetes mellitus = T2DM.

primary importance is screening for a history of failure to thrive, particularly in the first year of life, or perception by the parent of poor feeding. The child with feeding difficulties may have been managed on high calorie supplemental nutrition to augment insufficient oral food intake [123]. Determining whether parents have used or are still using these types of drink is also important. The child may not be willing to eat food if able to get most of their daily caloric needs from supplemental drinks. Signs of speech delay, motor delay, or other developmental problems after birth are indicators for additional testing or support. A multidisciplinary team trained in obesity medicine, including physician or nurse practitioner, psychologist, dietitian as well as speech or occupational therapist is recommended; a developmental pediatrician can also be beneficial (Fig. 2) [124]. Referral for additional testing is needed for any abnormalities noted.

5.2. Children <2 years of age with obesity and SHCN

There is minimal evidence for specific interventions for children over the 95th percentile and <2 years of age. Exploratory research has found early onset food focus and less interest in other typical enjoyable activities for children, including bubbles, music or reading, can be a risk factor for early onset obesity [125]. Research indicates that children with obesity and SHCN do not have increased food focus and enjoyment with food; rather, they have less enjoyment of other typically enjoyable activities. In clinical practice, this often manifests in families reporting that their child is 100 % focused on food and it seems to be the only thing giving them enjoyment. Families report difficulties in limiting food as it makes their child happy and motivated to perform other tasks. Interventions being assessed in randomized controlled trials include a

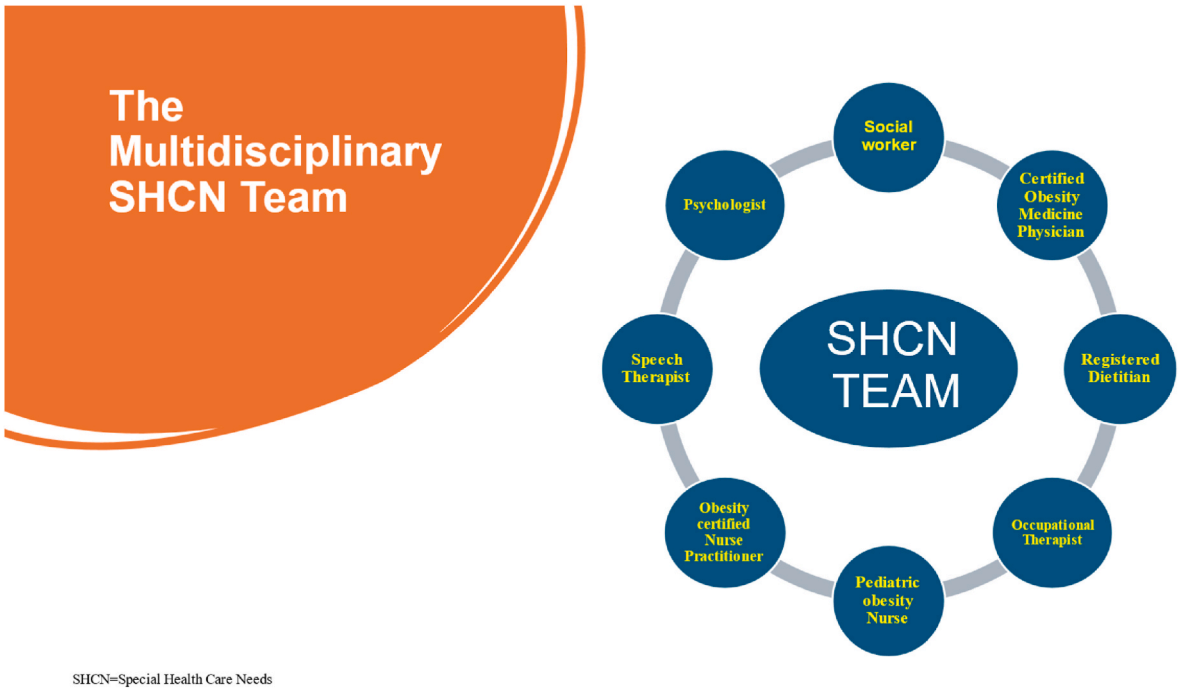

Fig. 2. The multidisciplinary team for the child with SHCN and obesity. (Original Figure).

music intervention to accentuate and develop interest in other areas in infants identified at risk [125].

A typical intervention used in children in this group includes food logging to carefully understand macronutrient quality of the diet, including protein, carbohydrates, and fat content [126]. Children in this group typically need to limit the intake of formula or milk, as daily volume is often higher than needed for development. Typical needs include, for milk or formula, 18–24 ounces total daily. Once children are closer to 24 months, the fat content in the milk can be decreased to reduce caloric intake. Exploring further with families how the introduction of fruits, vegetables, and proteins is progressing is helpful.

Typically, children in this group have significant food selectivity. They have been slow to accept the progression of food variety and typically have a limited diet despite increased hunger and food seeking [127]. Limiting processed foods and added sugar in the diet can assist with decreasing hunger and food seeking, however, introducing variety is often challenging with the limited number of foods in the repertoire. Not offering juice and sugar sweetened beverages is recommended, but a strong preference for flavored beverages can result in difficulty in meeting the child's fluid needs. A gradual transition to zero calorie fluids is assisted by strategies such as diluting juice with water and/or changing to a zero-calorie flavored substitute.

5.3. Children 2–6 years of age with obesity and SHCN

In the 2 to 6-year-old age group of children with obesity, SHCN, and continued rapid weight gain despite initial interventions, a genetic evaluation can be helpful. This evaluation is in addition to a developmental evaluation for speech delays, motor delays and behavioral concerns [122]. An evaluation with pediatric pulmonology/sleep specialist to assess sleep quality and routine is recommended.

5.3.1. Food and behavioral techniques

The pediatric obesity medicine team will suggest specific nutritional recommendations based on the food log. Evaluation for comorbid behavioral, psychological, and developmental challenges facilitates implementation of appropriate therapies [128]. Children with motor and/or speech delays often will have difficulty eating foods that are harder to chew and difficult to swallow; food selectivity with narrow food repertoire is common. Rapid eating and overstuffing of the mouth are frequently seen, sometimes leading to choking. For oral sensory concerns, involvement of an occupational therapist can be helpful in addition to speech therapy. For children who overstuff their mouth and tend to choke or gag, techniques to "wake up the mouth" such as vibration, massage, chewy tubes as well as strong tastes (zero calorie flavored drink powders, crystalized lemon or lime) on a rubber mouth brush or on the inner cheeks are beneficial [129]. These techniques used prior to eating teach awareness of the size of the mouth and can slow down eating as well as prevent overstuffing. Smaller silverware, cutting foods into small bites and using small plates with small portions can assist with a slower eating process. Speech and feeding evaluations are often helpful.

For food selectivity, or picky eaters, the team works with families on processes for adding more lean proteins, fruits, or vegetables. While food selectivity or food neophobia can be very normal between 2 and 6 years of age, children with SHCN such as autism spectrum disorder (ASD) have significantly higher rates [130]. Typically, developing children need to be presented with a new food 10 to 20 times before most are willing to try the food; children with SHCN and increased neophobia will frequently need even more presentations. Parents can model the desired behavior by eating the new foods in front of their children as well as smiling and expressing enjoyment. Online guidance such as "steps to eating" is available to support families and professionals in identifying feeding behaviors and implementing interventions [131].

Feeding therapy with speech, occupational and physical therapy teams may also be helpful. General recommendations for parents often include continuing to offer only 1 new food at meals in addition to other already accepted foods [126]. Children can have a separate plate next to their regular plate to where they can move the nonpreferred food; the goal is interaction with the non-preferred food that does not touch their preferred food. The portion of a new or nonpreferred food should be quite small (e.g., 1 broccoli floret, two baby carrots). Even for those children with limited food acceptance, it is desirable that children have some variety within the rotation of their limited preferred foods. Children often have few different foods that they eat. The process of adopting new foods can take time. Typically, it takes an average of six

months for each new food added [122]. Therefore, the first step is optimizing diet based on foods the child is currently eating.

5.3.2. Meal/snack schedules

A frequent recommendation by the obesity clinic for SHCN patients is to formulate a daily routine for meals, snacks, and activities, particularly for children who seem to want food all the time [122]. For preschool age and normally maturing developmental ability, visual daily schedules help visualize the meal and snack schedule as well as activities between meals. Three meals and 1–2 snacks with only water in between are recommended. If this eating pattern is too great a change from baseline, slower steps are taken with a shared goal between parents and clinicians. Following a plate model, which provides examples of appropriate size plates, assists in portion control. Meal plans in this group recommend meals with 3–4 different food groups and a snack with 1–2 food groups. Both meals and snacks should include fruit, vegetables, and protein. Grain portions are limited to the three meals and not as snacks. Physiologically, some children with obesity have increased hunger but the etiology of their SHCN may indicate a decreased caloric need. A strategy to limit portion is to start with a half portion of the meal and if still hungry, serve the second-half portion about 15 minutes later.

5.3.3. Intensive lifestyle therapy modified for child with SHCN

Behavioral and environmental controls are the treatments of choice for the youngest children with SHCN [132]. Stimulus control is the first-line recommendation for the family. Collaboration with parents through shared decision making in determining strategies that limit foods that trigger their child is the initial conversation. Acceptable environmental control will be different for each family; some may appreciate the "permission" to lock/restrict access to food in pantry or refrigerator as it decreases the need for constant vigilance. Other families may view this intervention as too restrictive, limiting autonomy, choice, and privacy. Reframing for families that locking is an external signal that the "kitchen is closed" between meal and snack times can assist in decreasing the negative connotations or fear.

Food rewards are prevalent in schools. Applied behavior analysis programs for children with SHCN are helpful and close partnerships with these care teams are recommended to determine alternative reinforcers [122]. A simple letter to the educators/clinicians can be successful, as well as periodic, collaborative meetings with the child's school representatives, the child's family, and the health care team. This strategy decreases the imposed responsibility of conveying messages by the family.

Another key advanced behavioral strategy is designing close coordination with all caregivers involved with the child with obesity and SHCN, including before and after school care, teachers, other family members, as well as the community [122]. Children often have multiple caregivers, therefore seamless communication between those caregivers is critical. Children with obesity and SHCN have increased hunger, lack of satiety, and will almost always accept food if offered. A communication notebook recording the desired food related schedule that accompanies the child throughout the day can promote consistency.

5.3.4. Sleep considerations

In children living with obesity and SHCN, reviewing sleep patterns is critical. Many children with SHCN have disrupted sleep schedules, either frequent night wakings or very early waking [133]. Many children, and by default, parents, are sleep deprived. This pattern of sleep deprivation increases hunger and promotes food seeking behavior. During the assessment of sleep, it is important to approach assessment with open-ended questions that allow the parents to respond non-defensively, as it is more common to have co-sleeping and other arrangements due to elopement risk and other sleep disruptions. Support from a sleep psychologist or behavioral sleep medicine clinician may be warranted to address sleep-wake cycle issues, behavioral insomnia, and obstructive sleep apnea. Assisting parents with brief sleep hygiene counseling and bedtime routines for their child as well as an "electronics bedtime" can be beneficial.

5.3.5. Screen time

In young children with obesity and SHCN, limiting screen time can be very helpful. The AAP recommends no media use under age 2 years, a one-hour limit ages 2–5 years and parent monitored media plan in older children with emphasis on quality of screen content [30]. Remote access or timer for the device is recommended so that the device turns itself off, avoiding the potential struggle of physically taking the device from the child.

5.3.6. Pharmacotherapy

There are limited options for use of FDA approved AOM and metabolic & bariatric surgery (MBS) in this age group [134]. Setmelanotide has FDA approval for children $\geq$6 years for children for the indication of specific genetic disorders of obesity including proprotein convertase subtilisin/kexin type 1, pro-opiomelanocortin, and leptin receptor homozygous genetic mutations or Bardet Biedl syndrome [135]. Further evaluation and successful treatment (often with pharmacotherapy) for early onset of ADHD or mood disorders can improve ability to focus on obesity treatment behavioral options [136]. If clinically feasible, obesogenic medications prescribed for asthma, allergies, or other medical conditions should be replaced with weight neutral medication or mitigated with weight modifying medications such as topiramate [137].

5.4. Child with SHCN and obesity conclusion

Comprehensive evaluations of children with obesity and SHCN, informed by the complex interplay of medical, behavioral, nutrition, activity, and family are essential. Treatment recommendations are tailored to the unique needs of the child and may include behavioral strategies to address food selectivity, dietary changes and pharmacotherapy in the case of high hunger drive, management of behavioral or medical comorbidities, and genetic evaluation. Coordination of care across environments and caregivers is of utmost importance. Fig. 3 summarizes the care of the young child with SHCN and obesity.

6. The child with hypothalamic Obesity/ROHHAD

6.1. Hypothalamic obesity

Children with hypothalamic dysregulation are a subset of the larger population of children with obesity. The complex neuronal environment in the hypothalamus, the control center for hunger, requires the coordination of signaling between the orexigenic (appetite stimulating) agouti related neuropeptide Y neuron, the anorexigenic (appetite inhibiting) proopiomelanocortin neuron and the melanocortin 4 expressing neuron. In addition, the hypothalamus also communicates with extra-hypothalamic regions in the brain and the gut. This sophisticated, multi-level coordination allows for regulation of hunger and satiety. Malfunctioning in the hypothalamus is associated with severe obesity and can arise from physical damage or from variants in DNA coding within the hypothalamus, leading to dysfunctional production of proteins for hunger regulation.

The most common cause of hypothalamic obesity in children is as a sequalae of damage to the medial hypothalamic region, including the arcuate nucleus, paraventricular nucleus, the ventromedial nucleus, the dorsomedial nucleus, or the dorsal hypothalamic area. Damage to these areas is most frequently the result of the treatment of craniopharyngioma or other mass brain lesion (i.e., resection and/or radiation). Up to 50 % of children treated for craniopharyngioma develop hypothalamic obesity, with younger children and those with underlying metabolic disease typically having a more severe course [138]. Although the short term survival rate of children treated for craniopharyngioma is

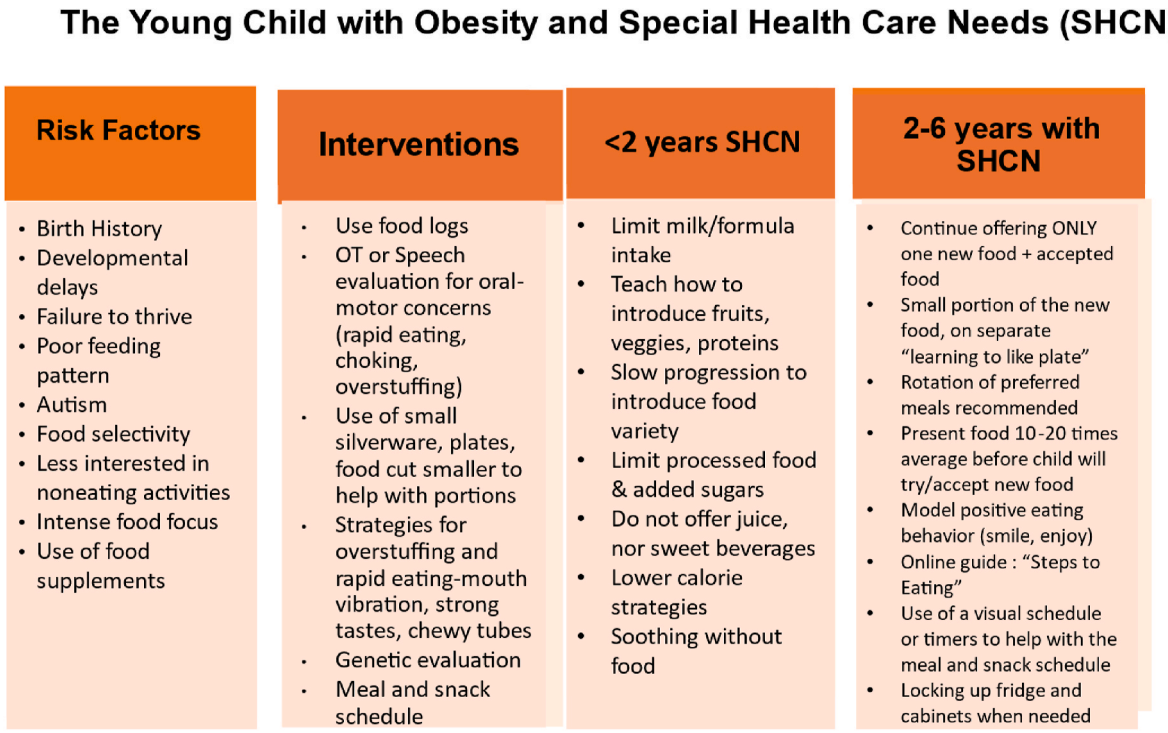

Fig. 3. Summary of the care of the child with SHCN and obesity. (Original Figure).

excellent, the long term morbidity is high due to three times the rate of cardiovascular disease compared to the general population and five times the morbidity rate [139]. Additionally, hypothalamic damage can also result from alternate suprasellar tumors, swelling in the brain, because of trauma, or from radiation over 51 Gy (Gy) to the hypothalamus [138].

The typical clinical scenario that is seen after damage to the hypothalamus is rapid weight gain with concomitant decreased energy expenditure, loss of satiety and thermogenesis, and an increase in vagal tone. The increase in vagal nerve stimulation results in increased lipogenesis and beta cell production of insulin. In patients with normal metabolism, the effect of an increase in beta cell stimulation is a production of insulin, which leads to increased glucose utilization in adipocytes and ultimately production of leptin, which is supposed to provide feedback to the hypothalamus [140]. Unfortunately, those with hypothalamic lesions lack this feedback communication and thus have no satiety. Children with hypothalamic obesity have rapid weight gain and then generally plateau at a higher weight, even with reduced energy intake [141]. The inability to reduce weight is thought to be due to the decrease in metabolic rate and thus energy expenditure [141]. Even if calorie restricted, children with hypothalamic lesions can gain weight and are functionally leptin resistant [142].

Melatonin secretion is also dysregulated with hypothalamic obesity. Disruption of the circadian clock leads to uncoupled secretion of melatonin at nighttime. Sleep disorder and irritability ensue, leading to further hormone dysregulation and weight gain. Sleep disorders can be severe, even progressing to narcolepsy and hypersomnolence. Melatonin administration has had mixed results. Some patients require stimulants in addition to melatonin, particularly those with narcolepsy [140,143,144].

Although different therapeutic options have and continue to be explored, none have yet proven successful in combatting hypothalamic obesity [141]. Attempts at treating hypothalamic obesity have had disappointing results. Most efforts have been aimed at bypassing the damaged hypothalamic circuits. Because children with hypothalamic obesity have hyperinsulinism, carbohydrate restricted diets (50 g per day or less) and increased activity have been utilized, albeit with poor outcomes. Pharmacotherapy approaches include octreotide, which has been used to block the first phase insulin response, with mixed results. Octreotide use is limited by significant adverse effects, including abdominal pain and diarrhea. In a double-blind controlled trial, 2 out of 9 patients developed impaired glucose tolerance and 1 patient developed diabetes [145]. Combined treatment with metformin and diazoxide was also trialed in a nine-patient study with a small decrease in weight [146]. Only seven patients made it through the study, however. Two dropped out due to peripheral edema and emesis with elevated liver enzymes. In another study, the combination of metformin and fenofibrate was not effective in reducing weight in children with hypothalamic obesity [147]. Stimulants have been used in children with hypothalamic obesity, mostly resulting in weight stabilization [148]. GLP1-receptor agonists have resulted in small amounts of weight loss in two small studies of adults with hypothalamic obesity [149]. Methionine aminopeptidase 2 inhibitors did show promising weight loss, but use was prohibited by development of thromboembolic events. A case report using a single dose of intranasal oxytocin combined with naltrexone resulted in sustained weight loss, but no larger study has been done [150]. Currently, a clinical trial in patients' status-post treatment of craniopharyngioma with setmelanotide is in a stage 3 trial [151].

Surgical vagotomy has been used in 1 case report of a 19-year old woman who lost 11 kg and reportedly maintained the weight loss [152]. Roux-en-Y gastric bypass has produced mixed results in adolescents, with most losing at least some weight, although not as much as adolescents with obesity who did not have hypothalamic obesity [153].

6.2. *ROHHAD/ROHHAD-NET syndrome*

Rapid-onset obesity with hypothalamic dysfunction, hypoventilation and autonomic dysregulation (ROHHAD) and ROHHAD-NET (ROHHAD with neural crest tumor syndrome) are forms of hypothalamic obesity that occur without the preliminary treatment of a suprasellar mass or known trauma to the region. Suggested etiologies for ROHHAD/ROHHAD-NET have included genetic variants and autoimmune disease. Although no specific mutations have been found, epigenetic factors

may be responsible. The possibility of autoimmune etiology is supported by some small success with cyclophosphamide treatment. Children with ROHHAD/ROHHAD-NET have a high rate of mortality, with the median age of death being 10 years of age. The diagnosis is based on clinical presentation. There is no specific biomarker currently available.

A key feature of ROHHAD/ROHHAD-NET is rapid weight gain over a six-to 12-month period, generally in the first 10 years of life. Prior to disease onset, growth and development are normal. Central hypoventilation is the life-threatening manifestation of the syndrome. As children get older, they may also develop thermal dysregulation, excessive sweating, temperature instability, cardiac arrhythmias or blood pressure dysregulation, strabismus, abnormal pupillary reaction to light, and gastrointestinal issues. A publication summarizing clinical findings in 43 patients, outcomes were reported in 32 children, six of whom died [154]. The cause of death was cardiorespiratory in two children and unknown in the others. Hypoventilation with hypercapnia and the need for tracheostomy can occur. Hypercapnia can produce aggressiveness, mood disorders and neurocognitive impairment. Neural crest tumors, specifically ganglioneuroma or ganglioneuroblastoma, occur in up to 40 % of patients with ROHHAD-NET. Because of the increased frequency for neural crest tumors, imaging should be performed and repeated periodically if the diagnosis of ROHHAD is made. There is no consensus on how often to re-image the child. Urinary catecholamine screening has not been found to predict tumor development [155].

The differential diagnosis of patients with ROHHAD/ROHHAD-NET includes Prader–Willi syndrome, given the early onset severe obesity, and congenital central hypoventilation syndrome, due to breathing abnormalities and autonomic nervous system dysregulation. Early diagnosis is pertinent to reduce morbidity and mortality, with treatment for ROHHAD/ROHHAD-NET based on clinical features. Treatment regimens include intensive lifestyle optimization, anti-obesity medications, hormone replacement for hypothalamic dysfunction, respiratory support for hypoventilation, medications for autonomic dysregulation, and treatment of neural crest tumors (i.e., chemotherapy, radiation and/or surgery).

7. Limitations and acknowledgements

The authors acknowledge that the treatment of children with obesity, especially those < than the age of 12, faces many limitations. Many children with obesity in this age group are not diagnosed with the disease of obesity at all, and even fewer are referred and/or have access to care. Children with any chronic disease who are in high risk situations due to poverty, ethnicity, cultural norms, etc. have the poorest outcomes. Children also suffer from societal norms discouraging the treatment of obesity in children. In addition, pharmaceutical trials have historically excluded children from studies, along with other vulnerable populations. Clinicians treating the disease of obesity are advocates for more inclusive treatment for children with obesity to include coverage and reimbursement for health care and inclusion of children in trials of new therapeutic options. Thankfully, the growing acknowledgement from both the public at large and the medical community of the lifelong nature of the disease of obesity has produced an increase in options. Children with obesity have had to wait years past when their parents were able to seek care and be treated. Continuing research shows equivalent or better outcome data with treatment in children as compared to adults. Treatment of a child with obesity creates the opportunity to improve health across a lifespan and reduces morbidity. The authors are optimistic about the future.

8. Conclusion

In this Clinical Practice Statement, we discuss the disease of obesity as it manifests in the child, defined as < than the age of 12. The prevalence of obesity in this age group is growing, with that of severe obesity increasing at an alarming rate. Frequently, these children develop precocious puberty as a sequela of obesity, leading to psychosocial problems associated with advanced physical maturation early in chronological age. Treatment for the disease of obesity in the child has historically been limited to nutrition and activity modification, with no consensus on what those modifications should be. Only one AOM is FDA approved for indication in this age group, yet studies of medications with weight modifying effects show therapeutic efficacy with better outcomes than IHBLT. Off label use of anti-obesity and other anorexigenic medication is growing. The child with SHCN and obesity is ideally managed by a team of family, educators, medical and behavioral health clinicians, speech and occupational therapists. The child with hypothalamic obesity is characterized by extremely rapid weight gain with significant mortality. These children are exceedingly difficult to manage and therapeutic options for treatment remain investigational.

To summarize, children with obesity are a group that is characterized by a lack of clear, consensus-based management. Yet these children can have a significant disease burden that will predictably progress as they age. More studies are needed to help limit the progression of disease but studies we have now show promising results, including safe and efficacious use of AOM. These youngest of our patients with obesity have a great deal to gain from intervention as soon as possible. Preventing the progression of obesity will provide benefits to both their psychosocial and medical health. This is the primary mission for those of us dedicated to the health of our children.

- The prevalence of obesity in children <12 is increasing, particularly in high risk populations.
- Obesity in the child <12 is frequently associated with precocious puberty.
- Use of AOM in the child <12 is growing, with data supporting efficacy and safety.
- The child with obesity and SHCN needs multidisciplinary management and has a right to the same treatment as children with obesity without SHCN.
- Hypothalamic dysregulation is a rare subset of the larger population of children with obesity, but is rapidly progressive, has a high morbidity and is difficult to manage.

Author contributions

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Ethics review

This OMA Clinical Practice Statement manuscript was peer-reviewed and approved by the OMA Board of Trustee members prior to publication. Edits were made in response to reviewer comments and the final revised manuscript was approved by the authors prior to publication. This submission did not involve human test subjects or volunteers. Responsibility for editorial decisions and peer review process for this article was delegated to non-author Editors or non-author Associate Editors.

Evidence

The content of this manuscript is supported by citations, which are listed in the References section.

Conclusions and recommendations

This Clinical Practice Statement is intended to be an educational tool that incorporates the current medical science and the clinical experiences of obesity specialists. The intent is to better facilitate and improve the clinical care and management of patients with pre-obesity (overweight) and obesity. This Clinical Practice Statement should not be interpreted as "rules" and/or directives regarding the medical care of an individual patient. The decision regarding the optimal care of the patient with pre-obesity (overweight) and/or obesity is best reliant upon a patient-centered approach, managed by the clinician tasked with directing an individual treatment plan that is in the best interest of the individual patient.

Updating

It is anticipated that sections of this Clinical Practice Statement may require future updates. The timing of such an update will depend on decisions made by the Obesity Pillars Editorial team, with input from the OMA members and OMA Board of Trustees.

Disclaimer and limitations

In areas regarding inconclusive or insufficient scientific evidence, the authors used their professional judgment. This Clinical Practice Statement is intended to represent the state of obesity medicine at the time of publication. Thus, this Clinical Practice Statement is not a substitute for maintaining awareness of emerging new science. Finally, decisions by practitioners to apply the principles in this Clinical Practice Statement are best made by considering local resources, individual patient circumstances, patient agreement, and knowledge of federal, state, and local laws and guidance.

Transparency

Since 2022, the Obesity Medicine Association Clinical Practice Statements have represented a diverse range of clinicians, allied health professionals, clinical researchers, and academicians. The authors reflect a multidisciplinary and balanced group of experts in obesity science, patient evaluation, and clinical treatment.

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work the authors did not use AI.

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References

[1] Stierman B, Afful J, Carroll M, et al. National health and nutrition examination survey 2017–march 2020. 2021. Natl Health Stat Rep 2020. https://stacks.cdc.gov/view/cdc/106273.
[2] Hu K, Staiano AE. Trends in obesity prevalence among children and adolescents aged 2 to 19 years in the US from 2011 to 2020. JAMA Pediatr 2022;176(10):1037–9. https://doi.org/10.1001/jamapediatrics.2022.2052.
[3] Mirza N, Phan TL, Tester J, Fals A, Fernandez C, Datto G, Estrada E, Eneli I. A narrative review of medical and genetic risk factors among children age 5 and younger with severe obesity. Child Obes 2018 Oct;14(7):443–52. https://doi.org/10.1089/chi.2017.0350.
[4] Shashaj B, Bedogni G, Graziani MP, et al. Origin of cardiovascular risk in overweight preschool children: a cohort study of cardiometabolic risk factors at the onset of obesity. JAMA Pediatr 2014;168(10):917–24. https://doi.org/10.1001/jamapediatrics.2014.900.
[5] Baughcum AE, Gramling K, Eneli I. Severely obese preschoolers in a tertiary care obesity program: characteristics and management. Clin Pediatr 2015;54(4):346–52. https://doi.org/10.1177/0009922814555975.
[6] O'Hara V, Browne N, Fathima S, et al. Obesity cardiometabolic comorbidity prevalence in children in a rural weight-management program. Glob Pediatr Health 2017;4:2333794X17729303. https://doi.org/10.1177/2333794X17729303. Published 2017 Sep. 8.
[7] Woo JG, Zhang N, Fenchel M, et al. Prediction of adult class II/III obesity from childhood BMI: the i3C consortium. Int J Obes 2020;44(5):1164–72. https://doi.org/10.1038/s41366-019-0461-6.
[8] Malihi Z, Portch R, Hashemi L, et al. Modifiable early childhood risk factors for obesity at age four years. Child Obes 2021 Apr;17(3):196–208. https://doi.org/10.1089/chi.2020.0174.
[9] Kim J, Lee I, Lim S. Overweight or obesity in children aged 0 to 6 and the risk of adult metabolic syndrome: a systematic review and meta-analysis. J Clin Nurs 2017 Dec;26(23–24):3869–80. https://doi.org/10.1111/jocn.13802.
[10] Bendor CD, Bardugo A, Pinhas-Hamiel O, Afek A, Twig G. Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity. Cardiovasc Diabetol 2020 Jun 13;19(1):79. https://doi.org/10.1186/s12933-020-01052-1.
[11] Chung ST, Onuzuruike AU, Magge SN. Cardiometabolic risk in obese children. Ann N Y Acad Sci 2018 Jan;1411(1):166–83. https://doi.org/10.1111/nyas.13602.
[12] Berenson GS, Srinivasan SR, Bao W, Newman 3rd WP, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med 1998 Jun 4;338(23):1650–6. https://doi.org/10.1056/NEJM199806043382302. PMID: 9614255.
[13] Le J, Spencer M, McCrary D, et al. Cardiac and vascular dysfunction in children with heart disease. Circulation 2008;118:S1056.
[14] Hutchins J, Barajas RA, Hale D, Escaname E, Lynch J. Type 2 diabetes in a 5-year-old and single center experience of type 2 diabetes in youth under 10. Pediatr Diabetes 2017 Nov;18(7):674–7. https://doi.org/10.1111/pedi.12463. Epub 2016 Nov 3. PMID: 27807935.
[15] Sinha R, Fisch G, Teague B, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. N Engl J Med 2002 Mar 14;346(11):802–10. https://doi.org/10.1056/NEJMoa012578.
[16] Finkelstein EA, Graham WC, Malhotra R. Lifetime direct medical costs of childhood obesity. Pediatrics 2014 May;133(5):854–62. https://doi.org/10.1542/peds.2014-0063. Epub 2014 Apr 7. PMID: 24709935.

[17] Kumar A, Kompaniyets L, Belay B, Pierce SL, Grosse SD, Goodman AB. Body mass index and associated medical expenditures in the US among privately insured individuals aged 2 to 19 years in 2018. JAMA Pediatr 2023 Aug 1;177(8):827–36. https://doi.org/10.1001/jamapediatrics.2023.2012.

[18] Ling J, Chen S, Zahry NR, Kao TA. Economic burden of childhood overweight and obesity: a systematic review and meta-analysis. Obes Rev 2023 Feb;24(2): e13535. https://doi.org/10.1111/obr.13535. Epub 2022 Nov 27. PMID: 36437105; PMCID: PMC10078467.

[19] Tester JM, Phan TT, Tucker JM, et al. Characteristics of children 2 to 5 years of age with severe obesity. Pediatrics 2018 Mar;141(3):e20173228. https://doi.org/10.1542/peds.2017-3228. PMID: 29487163; PMCID: PMC5847086.

[20] Vargas CM, Stines EM, Granado HS. Health-equity issues related to childhood obesity: a scoping review. J Publ Health Dent 2017 Jun;77(Suppl 1):S32–42. https://doi.org/10.1111/jphd.12233. Epub 2017 Jul 14. PMID: 28708245.

[21] Mamun AA, Mannan M, Doi SA. Gestational weight gain in relation to offspring obesity over the life course: a systematic review and bias-adjusted meta-analysis. Obes Rev 2014 Apr;15(4):338–47. https://doi.org/10.1111/obr.12132. Epub 2013 Dec 9. PMID: 24321007.

[22] Diesel JC, Eckhardt CL, Day NL, Brooks MM, Arslanian SA, Bodnar LM. Is gestational weight gain associated with offspring obesity at 36 months? Pediatr Obes 2015 Aug;10(4):305–10. https://doi.org/10.1111/ijpo.262. Epub 2014 Sep 30. PMID: 25267200; PMCID: PMC4379119.

[23] Nobari TZ, Wang MC, Chaparro MP, Crespi CM, Koleilat M, Whaley SE. Immigrant enclaves and obesity in preschool-aged children in Los Angeles County. Soc Sci Med 2013;92:1–8. https://doi.org/10.1016/j.socscimed.2013.05.019.

[24] Kimbro RT, Denney JT. Neighborhood context and racial/ethnic differences in young children's obesity: structural barriers to interventions. Soc Sci Med 2013 Oct;95:97–105. https://doi.org/10.1016/j.socscimed.2012.09.032. Epub 2012 Oct 6. PMID: 23089614.

[25] Centers for Disease Control. Weight control in pregnancy. Updated June 2022, https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-weight-gain.htm#weight. [Accessed 10 April 2024].

[26] Rasmussen KM, Yaktine AL. Institute of medicine (US) and national research Council (US) committee to reexamine IOM pregnancy weight guidelines. Weight gain during pregnancy: reexamining the guidelines. Washington (DC): National Academies Press (US); 2009. https://doi.org/10.17226/12584.

[27] Schaller KE, Stephenson-Somers LJ, Ariza AJ, Quadri M, Binns HJ. Case reports: multifaceted experiences treating youth with severe obesity. Int J Environ Res Publ Health 2019 Mar 14;16(6):927. https://doi.org/10.3390/ijerph16060927. PMID: 30875836; PMCID: PMC6466372.

[28] Srivastava G, Browne N, Kyle TK, et al. Caring for US children: barriers to effective treatment in children with the disease of obesity. Obesity 2021 Jan;29 (1):46–55. https://doi.org/10.1002/oby.22987. PMID: 34494365.

[29] Salvy SJ, Miles JN, Shih RA, Tucker JS, D'Amico EJ. Neighborhood, family and peer-level predictors of obesity-related health behaviors among young adolescents. J Pediatr Psychol 2017 Mar 1;42(2):153–61. https://doi.org/10.1093/jpepsy/jsw035. PMID: 27246867; PMCID: PMC6075537.

[30] Hampl SE, Hassink SG, Skinner AC, et al. Clinical Practice Guideline for the evaluation and treatment of children and adolescents with obesity. Pediatrics 2023 Feb 1;151(2):e2022060640. https://doi.org/10.1542/peds.2022-060640. PMID: 36622115.

[31] Danielsson P, Svensson V, Kowalski J, Nyberg G, Ekblom O, Marcus C. Importance of age for 3-year continuous behavioral obesity treatment success and dropout rate. Obes Facts 2012;5(1):34–44. https://doi.org/10.1159/000336060.

[32] Cuda S, Censani M, Kharofa R, et al. Medication-induced weight gain and advanced therapies for the child with overweight and obesity: an Obesity Medicine Association (OMA) Clinical Practice Statement 2022.4. Obes Pillars 2022;4: 100048. https://doi.org/10.1016/j.obpill.2022.100048. ISSN 2667-3681.

[33] Frattarelli DA, Galinkin JL, Green TP, et al. Off-label use of drugs in children. Pediatrics 2014;133(3):563–7. https://doi.org/10.1542/peds.2013-4060.

[34] San Giovanni CB, Sweeney B, Skelton JA, Kelsey MM, Kelly AS. Aversion to off-label prescribing in clinical pediatric weight management: the quintessential double standard. J Clin Endocrinol Metab 2021 Jun 16;106(7):2103–13. https://doi.org/10.1210/clinem/dgab276. PMID: 33901290; PMCID: PMC8600003.

[35] Wolf RM, Long D. Pubertal development. Pediatr Rev 2016;37(7):292–300. https://doi.org/10.1542/pir.2015-0065.

[36] Carel JC, Lahlou N, Roger M, Chaussain JL. Precocious puberty and statural growth. Hum Reprod Update 2004;10(2):135–47. https://doi.org/10.1093/humupd/dmh012.

[37] Giglione E, Lapolla R, Cianfarani S, et al. Linear growth and puberty in childhood obesity: what is new? Minerva Pediatr 2021;73(6):563–71. https://doi.org/10.23736/S2724-5276.21.06543-5.

[38] Huang A, Roth CL. The link between obesity and puberty: what is new? Curr Opin Pediatr 2021 Aug 1;33(4):449–57. https://doi.org/10.1097/MOP.0000000000001035. PMID: 34173790.

[39] Li W, Liu Q, Deng X, Chen Y, Liu S, Story M. Association between obesity and puberty timing: a systematic review and meta-analysis. Int J Environ Res Publ Health 2017;14(10):1266. https://doi.org/10.3390/ijerph14101266. Published 2017 Oct 24.

[40] Chung S. Growth and puberty in obese children and implications of body composition. J Obes Metab Syndr 2017;26(4):243–50. https://doi.org/10.7570/jomes.2017.26.4.243.

[41] Shi L, Jiang Z, Zhang L. Childhood obesity and central precocious puberty. Front Endocrinol 2022;13:1056871. https://doi.org/10.3389/fendo.2022.1056871. Published 2022 Nov 18.

[42] Itriyeva K. The effects of obesity on the menstrual cycle. Curr Probl Pediatr Adolesc Health Care 2022;52(8):101241. https://doi.org/10.1016/j.cppeds.2022.101241.

[43] Huang A, Reinehr T, Roth CL. Connections between obesity and puberty: invited by manuel tena-sempere, Cordoba. Curr Opin Endocr Metab Res. 2020 Oct;14: 160–8. https://doi.org/10.1016/j.coemr.2020.08.004. Epub 2020 Aug 27. PMID: 33043167; PMCID: PMC7543977.

[44] Darbre PD. Endocrine disruptors and obesity. Curr Obes Rep 2017;6(1):18–27. https://doi.org/10.1007/s13679-017-0240-4.

[45] Rosenfield RL. Normal and premature adrenarche. Endocr Rev 2021;42(6): 783–814. https://doi.org/10.1210/endrev/bnab009.

[46] Witchel SF, Pinto B, Burghard AC, Oberfield SE. Update on adrenarche. Curr Opin Pediatr 2020;32(4):574–81. https://doi.org/10.1097/MOP.0000000000000928.

[47] Zhou X, Hu Y, Yang Z, et al. Overweight/obesity in childhood and the risk of early puberty: a systematic review and meta-analysis. Front Pediatr 2022;10:795596. https://doi.org/10.3389/fped.2022.795596.

[48] Cuda SE, Censani M. Assessment, differential diagnosis, and initial clinical evaluation of the pediatric patient with obesity: an Obesity Medical Association (OMA) Clinical Practice Statement 2022. Obes Pillars 2022;1:100010. https://doi.org/10.1016/j.obpill.2022.100010. Published 2022 Jan 13.

[49] Chen C, Zhang Y, Sun W, et al. Investigating the relationship between precocious puberty and obesity: a cross-sectional study in Shanghai. China BMJ Open 2017: 7e014004. https://doi.org/10.1136/bmjopen-2016-014004.

[50] Frellick M. AMA declares obesity a disease. Medscape Medical News June 19, 2013. https://www.medscape.com/viewarticle/806566. [Accessed 6 April 2024].

[51] Fox CK, Kelly AS, Reilly JL, Theis-Mahon N, Raatz SJ. Current and future state of pharmacological management of pediatric obesity. Int J Obes 2024. https://doi.org/10.1038/s41366-024-01465-y. Published online February 6.

[52] Smith HJ, Piotrowski JI, Zaza S. Ethics of implementing US preventive services task force recommendations for childhood obesity. Pediatrics 2021;148(1): e2020048009. https://doi.org/10.1542/peds.2020-048009.

[53] Cuda S, Censani M, O'Hara V, et al. Pediatric obesity algorithm. In: Presented by the obesity medicine association; 2024. www.obesitymedicine.org/childhood-obesity. [Accessed 5 April 2024]. https://obesitymedicine.org/resources/obesity-algorithm/pediatric-obesity-algorithm/.

[54] Borzutzky C, King E, Fox CK, et al. Trends in prescribing anti-obesity pharmacotherapy for paediatric weight management: data from the POWER Work Group. Pediatr Obes 2021;16(1):e12701. https://doi.org/10.1111/ijpo.12701.

[55] Torbahn G, Jones A, Griffiths A, et al. Pharmacological interventions for the management of children and adolescents living with obesity-An update of a Cochrane systematic review with meta-analyses. In: Pediatr obes. Published online march 7; 2024. https://doi.org/10.1111/ijpo.13113.

[56] Karres J, Tomasi P, Saint Raymond A. The development of pharmacological treatment of obesity in children. A European regulatory perspective. Bundesgesundheitsblatt - Gesundheitsforsch - Gesundheitsschutz 2011;54(5):570–6. https://doi.org/10.1007/s00103-011-1271-8.

[57] Haqq AM, Chung WK, Dollfus H, et al. Efficacy and safety of setmelanotide, a melanocortin-4 receptor agonist, in patients with Bardet-Biedl syndrome and Alström syndrome: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial with an open-label period [published correction appears in Lancet Diabetes Endocrinol. 2023 Feb;11(2):e2]. Lancet Diabetes Endocrinol 2022;10 (12):859–68. https://doi.org/10.1016/S2213-8587(22)00277-7.

[58] Trapp CM, Censani M. Setmelanotide: a promising advancement for pediatric patients with rare forms of genetic obesity. Curr Opin Endocrinol Diabetes Obes 2023 Apr 1;30(2):136–40. https://doi.org/10.1097/MED.0000000000000798. Epub 2023 Feb 1. PMID: 36722447; PMCID: PMC9973437.

[59] Srivastava G, Fox CK, Kelly AS, et al. Clinical considerations regarding the use of obesity pharmacotherapy in adolescents with obesity. Obesity 2019;27(2): 190–204. https://doi.org/10.1002/oby.22385.

[60] Mazur A, Zachurzok A, Baran J, et al. Childhood obesity: position statement of polish society of pediatrics. Polish Society for Pediatric Obesity, Polish Society of Pediatric Endocrinology and Diabetes, the College of Family Physicians in Poland and Polish Association for Study on Obesity. Nutrients 2022;14(18):3806. https://doi.org/10.3390/nu14183806. Published 2022 Sep. 15.

[61] Drewa A, Zorena K. Prevention of overweight and obesity in children and adolescents in European countries. Pediatr. Endocrinol. Diabetes Metab 2017;23: 152–8. https://doi.org/10.18544/PEDM-23.03.0087.

[62] Thomas I, Gregg B. Metformin; a review of its history and future: from lilac to longevity. Pediatr Diabetes 2017;18(1):10–6. https://doi.org/10.1111/pedi.12473.

[63] Tamborlane WV, Barrientos-Pérez M, Fainberg U, et al. Liraglutide in children and adolescents with type 2 diabetes. N Engl J Med 2019;381(7):637–46. https://doi.org/10.1056/NEJMoa1903822.

[64] Arslanian SA, Hannon T, Zeitler P, et al. Once-weekly Dulaglutide for the treatment of youths with Type 2 diabetes. N Engl J Med 2022;387(5):433–43. https://doi.org/10.1056/NEJMoa2204601.

[65] Laffel LM, Danne T, Klingensmith GJ, et al. Efficacy and safety of the SGLT2 inhibitor empagliflozin versus placebo and the DPP-4 inhibitor linagliptin versus placebo in young people with type 2 diabetes (DINAMO): a multicentre, randomised, double-blind, parallel group, phase 3 trial. Lancet Diabetes Endocrinol 2023;11(3):169–81. https://doi.org/10.1016/S2213-8587(22)00387-4.

[66] Glauser TA. Topiramate use in pediatric patients. Can J Neurol Sci 1998;25(3): S8–12. https://doi.org/10.1017/s0317167100034843.

[67] Biederman J, Boellner SW, Childress A, Lopez FA, Krishnan S, Zhang Y. Lisdexamfetamine dimesylate and mixed amphetamine salts extended-release in

children with ADHD: a double-blind, placebo-controlled, crossover analog classroom study. Biol Psychiatr 2007;62(9):970–6. https://doi.org/10.1016/j.biopsych.2007.04.015.
[68] Cunningham SA, Hardy ST, Jones R, Ng C, Kramer MR, Narayan KMV. Changes in the incidence of childhood obesity. Pediatrics 2022;150(2):e2021053708. https://doi.org/10.1542/peds.2021-053708.
[70] Mead E, Brown T, Rees K, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. Cochrane Database Syst Rev 2017;6(6):CD012651. https://doi.org/10.1002/14651858.CD012651. Published 2017 Jun 22.
[71] Geserick M, Vogel M, Gausche R, et al. Acceleration of BMI in early childhood and risk of sustained obesity. N Engl J Med 2018;379(14):1303–12. https://doi.org/10.1056/NEJMoa1803527.
[72] Li C, Ford ES, Zhao G, Mokdad AH. Prevalence of pre-diabetes and its association with clustering of cardiometabolic risk factors and hyperinsulinemia among U.S. adolescents: national Health and Nutrition Examination Survey 2005-2006. Diabetes Care 2009;32(2):342–7. https://doi.org/10.2337/dc08-1128.
[73] Verhulst SL, Van Gaal L, De Backer W, Desager K. The prevalence, anatomical correlates and treatment of sleep-disordered breathing in obese children and adolescents. Sleep Med Rev 2008;12(5):339–46. https://doi.org/10.1016/j.smrv.2007.11.002.
[74] Pardee PE, Lavine JE, Schwimmer JB. Diagnosis and treatment of pediatric nonalcoholic steatohepatitis and the implications for bariatric surgery. Semin Pediatr Surg 2009;18(3):144–51. https://doi.org/10.1053/j.sempedsurg.2009.04.004 [89] Schwimmer et al. Pediatrics 2006;118:1388–1393.
[75] Freedman DS, Mei Z, Srinivasan SR, Berenson GS, Dietz WH. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. J Pediatr 2007;150(1):12–17.e2. https://doi.org/10.1016/j.jpeds.2006.08.042.
[76] Small L, Aplasca A. Child obesity and mental health: a complex interaction. Child Adolesc Psychiatr Clin N Am 2016;25(2):269–82. https://doi.org/10.1016/j.chc.2015.11.008.
[77] Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes and consequences. J Fam Med Prim Care 2015;4(2):187–92. https://doi.org/10.4103/2249-4863.154628.
[78] Sawyer MG, Harchak T, Wake M, Lynch J. Four-year prospective study of BMI and mental health problems in young children. Pediatrics 2011;128(4):677–84. https://doi.org/10.1542/peds.2010-3132.
[79] Puhl RM, Himmelstein MS, Pearl RL. Weight stigma as a psychosocial contributor to obesity. Am Psychol 2020;75(2):274–89. https://doi.org/10.1037/amp0000538.
[80] Fox C, O'Hara V. Understanding obesity and setting the stage for comprehensive treatment. In: Fox C, editor. Managing pediatric obesity using advanced therapies practical guide for pediatric health care providers. 25. Springer; 2023. p. 1.
[81] Wild CEK, Wynter LE, Triggs CM, Derraik JGB, Hofman PL, Anderson YC. Five-year follow-up of a family-based multidisciplinary program for children with obesity. Obesity 2021;29(9):1458–68. https://doi.org/10.1002/oby.23225.
[82] Allender S, Orellana L, Crooks N, et al. Four-year behavioral, health-related quality of life, and BMI outcomes from a cluster randomized whole of systems trial of prevention strategies for childhood obesity. Obesity 2021;29(6):1022–35. https://doi.org/10.1002/oby.23130.
[83] Wyse C, Case L, Walsh Ó, et al. Evaluating 12 Years of implementing a multidisciplinary specialist child and adolescent obesity treatment service: patient-level outcomes. Front Nutr 2022;9:895091. https://doi.org/10.3389/fnut.2022.895091. Published 2022 Jun 3.
[84] O'Hara V, Cuda S, Kharofa R, Censani M, Conroy R, Browne NT. Clinical review: guide to pharmacological management in pediatric obesity medicine. Obes Pillars 2023;6:100066. https://doi.org/10.1016/j.obpill.2023.100066. Published 2023 Apr 27.
[85] Tondt J, Freshwater M, Benson-Davies S, et al. Obesity algorithm slides, presented by the obesity medicine association. www.obesityalgorithm.org. [Accessed 6 April 2024]. https://obesitymedicine.org/resourses/obesity-algorithm/.
[86] Braüner JV, Johansen LM, Roesbjerg T, Pagsberg AK. Off-label prescription of psychopharmacological drugs in child and adolescent psychiatry. J Clin Psychopharmacol 2016 Oct;36(5):500–7. https://doi.org/10.1097/JCP.0000000000000559. PMID: 27529772.
[87] Food & Drug Administration. Development & approval process/drugs. https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label; 2023.
[88] Petkova V, Georgieva D, Dimitrov M, Nikolova I. Off-label prescribing in pediatric population-literature review for 2012-2022. Pharmaceutics 2023;15(12):2652. https://doi.org/10.3390/pharmaceutics15122652. Published 2023 Nov 21.
[89] Hoon D, Taylor MT, Kapadia P, Gerhard T, Strom BL, Horton DB. Trends in off-label drug use in ambulatory settings: 2006-2015. Pediatrics 2019;144(4):e20190896. https://doi.org/10.1542/peds.2019-0896.
[90] Yanovski JA, Krakoff J, Salaita CG, et al. Effects of metformin on body weight and body composition in obese insulin-resistant children: a randomized clinical trial. Diabetes 2011;60(2):477–85. https://doi.org/10.2337/db10-1185.
[91] Bassols J, Martínez-Calcerrada JM, Osiniri I, et al. Effects of metformin administration on endocrine-metabolic parameters, visceral adiposity and cardiovascular risk factors in children with obesity and risk markers for metabolic syndrome: a pilot study. PLoS One 2019;14(12):e0226303. https://doi.org/10.1371/journal.pone.0226303. Published 2019 Dec 10.
[92] Pastor-Villaescusa B, Cañete MD, Caballero-Villarraso J, et al. Metformin for obesity in prepubertal and pubertal children: a randomized controlled trial. Pediatrics 2017;140(1):e20164285. https://doi.org/10.1542/peds.2016-4285.
[93] Matsuura N, Amemiya S, Sugihara S, et al. Metformin monotherapy in children and adolescents with type 2 diabetes mellitus in Japan. Diabetol Int 2018;10(1):51–7. https://doi.org/10.1007/s13340-018-0361-3. Published 2018 Jun 27.
[94] Czepiel KS, Perez NP, Campoverde Reyes KJ, Sabharwal S, Stanford FC. Pharmacotherapy for the treatment of overweight and obesity in children, adolescents, and young adults in a large health system in the US. Front Endocrinol 2020;11:290. https://doi.org/10.3389/fendo.2020.00290. Published 2020 May 13.
[95] Grosso S, Franzoni E, Iannetti P, et al. Efficacy and safety of topiramate in refractory epilepsy of childhood: long-term follow-up study. J Child Neurol 2005;20(11):893–7. https://doi.org/10.1177/08830738050200110601.
[96] Reiter E, Feucht M, Hauser E, Freilinger M, Seidl R. Changes in body mass index during long-term topiramate therapy in paediatric epilepsy patients–a retrospective analysis. Seizure 2004 Oct;13(7):491–3. https://doi.org/10.1016/j.seizure.2003.12.001. PMID: 15324828.
[97] Gilliam FG, Veloso F, Bomhof MA, et al. A dose-comparison trial of topiramate as monotherapy in recently diagnosed partial epilepsy. Neurology 2003;60(2):196–202. https://doi.org/10.1212/01.wnl.0000048200.12663.bc.
[99] Lorber J. Obesity in childhood. A controlled trial of anorectic drugs. Arch Dis Child 1966;41(217):309–12. https://doi.org/10.1136/adc.41.217.309.
[100] Childress AC, Lloyd E, Jacobsen L, Gunawardhana L, Johnson Jr SA, Findling RL. Efficacy and safety of lisdexamfetamine in preschool children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2022;61(12):1423–34. https://doi.org/10.1016/j.jaac.2022.03.034.
[101] Sugaya LS, Farhat LC, Califano P, Polanczyk GV. Efficacy of stimulants for preschool attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. JCPP Adv 2023;3(3):e12146. https://doi.org/10.1002/jcv2.12146. Published 2023 Feb 25.
[102] Fast K, Björk A, Strandberg M, Johannesson E, Wentz E, Dahlgren J. Half of the children with overweight or obesity and attention-deficit/hyperactivity disorder reach normal weight with stimulants. Acta Paediatr 2021;110(10):2825–32. https://doi.org/10.1111/apa.15881.
[103] Roth CL, Perez FA, Whitlock KB, et al. A phase 3 randomized clinical trial using a once-weekly glucagon-like peptide-1 receptor agonist in adolescents and young adults with hypothalamic obesity. Diabetes Obes Metab 2021;23(2):363–73. https://doi.org/10.1111/dom.14224.
[104] Kelly AS, Metzig AM, Rudser KD, et al. Exenatide as a weight-loss therapy in extreme pediatric obesity: a randomized, controlled pilot study. Obesity 2012;20(2):364–70. https://doi.org/10.1038/oby.2011.337.
[105] Wu X, Zhang Y, Lu M, et al. The efficacy and safety of topiramate in the prevention of pediatric migraine: an update meta-analysis. Front Pediatr 2020 Feb 27;8:28. https://doi.org/10.3389/fped.2020.00028. PMID: 32175291; PMCID: PMC7056737.
[106] Oskoui M, Pringsheim T, Billinghurst L, et al. Practice guideline update summary: pharmacologic treatment for pediatric migraine prevention: report of the guideline development, dissemination, and implementation subcommittee of the American academy of neurology and the American headache society. Neurology 2019 Sep 10;93(11):500–9. https://doi.org/10.1212/WNL.0000000000008105. Epub 2019 Aug 14.
[107] Brownley KA, Berkman ND, Peat CM, et al. Binge-eating disorder in adults: a systematic review and meta-analysis. Ann Intern Med 2016 Sep 20;165(6):409–20. https://doi.org/10.7326/M15-2455. Epub 2016 Jun 28. PMID: 27367316; PMCID: PMC5637727.
[108] Ryder JR, Kaizer A, Rudser KD, Gross A, Kelly AS, Fox CK. Effect of phentermine on weight reduction in a pediatric weight management clinic. Int J Obes 2017;41(1):90–3. https://doi.org/10.1038/ijo.2016.185.
[109] Lisdexamfetamine dimesylate (Vyvanse). Prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208510lbl.pdf Accessed April 6, 2024.
[110] Kelly AS, Auerbach P, Barrientos-Perez M, et al. A randomized, controlled trial of liraglutide for adolescents with obesity. N Engl J Med 2020;382(22):2117–28. https://doi.org/10.1056/NEJMoa1916038.
[111] Weghuber D, Barrett T, Barrientos-Pérez M, et al. Once-weekly semaglutide in adolescents with obesity. N Engl J Med 2022;387(24):2245–57. https://doi.org/10.1056/NEJMoa2208601.
[112] Van Norman GA. Off-label use vs Off-label marketing of drugs: Part 1: off-Label use-patient harms and prescriber responsibilities. JACC Basic Transl Sci 2023;8(2):224–33. https://doi.org/10.1016/j.jacbts.2022.12.011. Published 2023 Feb 27.
[113] Cardel MI, Atkinson MA, Taveras EM, Holm JC, Kelly AS. Obesity treatment among adolescents: a review of current evidence and future directions. JAMA Pediatr 2020 Jun 1;174(6):609–17. https://doi.org/10.1001/jamapediatrics.2020.0085. PMID: 32202626; PMCID: PMC7483247.
[114] Vajravelu ME, Tas E, Arslanian S. Pediatric obesity: complications and current day management. Life 2023 Jul 20;13(7):1591. https://doi.org/10.3390/life13071591. PMID: 37511966; PMCID: PMC10381624.
[115] Szczyrska J. Pediatric obesity - time to act as early as possible. Pediatr Endocrinol Diabetes Metab 2023;29(4):267–73. https://doi.org/10.5114/pedm.2023.133122. PMID: 38282496; PMCID: PMC10826697.
[116] Armstrong SC, Skinner AC. Severe obesity in toddlers: a canary in the coal mine for the health of future generations. Pediatrics 2024;153(1):e2023063799. https://doi.org/10.1542/peds.2023-063799.
[117] Zhao L, Freedman DS, Blanck HM, Park S. Trends in severe obesity among children aged 2 to 4 years in WIC: 2010 to 2020. Pediatrics 2024;153(1):e2023062461. https://doi.org/10.1542/peds.2023-062461.
[118] Cuda SE, Kharofa R, Williams DR, et al. Metabolic, behavioral health, and disordered eating comorbidities associated with obesity in pediatric patients: an

Obesity Medical Association (OMA) Clinical Practice Statement 2022. Obes Pillars 2022;3:100031. https://doi.org/10.1016/j.obpill.2022.100031. Published 2022 Aug 6.
[119] Cuda S, Censani M, Kharofa R, et al. Social consequences and genetics for the child with overweight and obesity: an obesity medicine association (OMA) clinical practice statement 2022. Obes Pillars 2022;3:100032. https://doi.org/10.1016/j.obpill.2022.100032. Published 2022 Aug 6.
[120] Tully L, Arthurs N, Wyse C, et al. Guidelines for treating child and adolescent obesity: a systematic review. Front Nutr 2022;9:902865. https://doi.org/10.3389/fnut.2022.902865. Published 2022 Oct 12.
[121] Bandini L, Danielson M, Esposito LE, et al. Obesity in children with developmental and/or physical disabilities. Disabil Health J 2015;8(3):309–16. https://doi.org/10.1016/j.dhjo.2015.04.005.
[122] Dreyer Gillette ML, Killian HJ, Fernandez C, Sweeney BR. Treating obesity in children and adolescents with special healthcare needs. Curr Obes Rep 2022;11(4):227–35. https://doi.org/10.1007/s13679-022-00484-y.
[123] Nützenadel W. Failure to thrive in childhood. Dtsch Arztebl Int 2011;108(38):642–9. https://doi.org/10.3238/arztebl.2011.0642.
[124] Pona AA, Dreyer Gillette ML, Odar Stough C, Gerling JK, Sweeney BR. Long-term outcomes of a multidisciplinary weight management intervention for youth with disabilities. Child Obes 2017;13(6):455–61. https://doi.org/10.1089/chi.2016.0334.
[125] Kong KL, Shisler S, Eiden RD, Anzman-Frasca S, Piazza J. Examining the relationship between infant weight status and parent-infant interactions within a food and nonfood context. Child Obes 2022;18(6):422–32. https://doi.org/10.1089/chi.2021.0126.
[126] Centers for Disease Control. Infant and toddler nutrition. 2022. https://www.cdc.gov/nutrition/infantandtoddlernutrition/index.html. [Accessed 6 April 2024].
[127] Chawner LR, Blundell-Birtill P, Hetherington MM. Interventions for increasing acceptance of new foods among children and adults with developmental disorders: a systematic review. J Autism Dev Disord 2019;49(9):3504–25. https://doi.org/10.1007/s10803-019-04075-0.
[128] Ptomey LT, Walpitage DL, Mohseni M, et al. Weight status and associated comorbidities in children and adults with Down syndrome, autism spectrum disorder and intellectual and developmental disabilities. J Intellect Disabil Res 2020 Sep;64(9):725–37. https://doi.org/10.1111/jir.12767. Epub 2020 Jul 27. PMID: 32716138; PMCID: PMC8486319.
[129] Leader G, Tuohy E, Chen JL, Mannion A, Gilroy SP. Feeding problems, gastrointestinal symptoms, challenging behavior and sensory issues in children and adolescents with Autism Spectrum Disorder. J Autism Dev Disord 2020;50(4):1401–10. https://doi.org/10.1007/s10803-019-04357-7.
[130] Bandini LG, Curtin C, Phillips S, Anderson SE, Maslin M, Must A. Changes in food selectivity in children with autism spectrum disorder. J Autism Dev Disord 2017;47(2):439–46. https://doi.org/10.1007/s10803-016-2963-6.
[131] SOS. SOS approach to feeding. https://sosapproachtofeeding.com/. [Accessed 6 April 2024].
[132] Hodges AK, Hathaway KL, McMahon MXH, Volkert VM, Sharp WG. Treatment of feeding concerns in children with Autism Spectrum Disorder: a systematic review of behavioral interventions with caregiver training. Behav Modif 2023;47(4):936–58. https://doi.org/10.1177/01454455221137328.
[133] Blackmer AB, Feinstein JA. Management of sleep disorders in children with neurodevelopmental disorders: a review. Pharmacotherapy 2016;36(1):84–98. https://doi.org/10.1002/phar.1686.
[134] Matheson BE, Colborn D, Bohon C. Bariatric surgery in children and adolescents with cognitive impairment and/or developmental delay: current knowledge and clinical recommendations. Obes Surg 2019;29(12):4114–26. https://doi.org/10.1007/s11695-019-04219-2.
[135] Wabitsch M, Farooqi S, Flück CE, et al. Natural history of obesity due to POMC, PCSK1, and LEPR deficiency and the impact of setmelanotide. J Endocr Soc 2022;6(6):bvac057. https://doi.org/10.1210/jendso/bvac057. Published 2022 Apr 15.
[136] O'Hara VM, Curran JL, Browne NT. The co-occurrence of pediatric obesity and ADHD: an understanding of shared pathophysiology and implications for collaborative management. Curr Obes Rep 2020;9(4):451–61. https://doi.org/10.1007/s13679-020-00410-0.
[137] Sweeney B, Kelly AS, San Giovanni CB, Kelsey MM, Skelton JA. Clinical approaches to minimize iatrogenic weight gain in children and adolescents. Clin Obes 2021;11(1):e12417. https://doi.org/10.1111/cob.12417.
[138] Ahmet A, Blaser S, Stephens D, Guger S, Rutkas JT, Hamilton J. Weight gain in craniopharyngioma–a model for hypothalamic obesity. J Pediatr Endocrinol Metab 2006;19(2):121–7. https://doi.org/10.1515/jpem.2006.19.2.121.
[139] Bülow B, Attewell R, Hagmar L, Malmström P, Nordström CH, Erfurth EM. Postoperative prognosis in craniopharyngioma with respect to cardiovascular mortality, survival, and tumor recurrence. J Clin Endocrinol Metab 1998;83(11):3897–904. https://doi.org/10.1210/jcem.83.11.5240.
[140] Müller HL, Handwerker G, Gebhardt U, et al. Melatonin treatment in obese patients with childhood craniopharyngioma and increased daytime sleepiness. Cancer Causes Control 2006;17(4):583–9. https://doi.org/10.1007/s10552-005-9012-7.
[141] Abuzzahab MJ, Roth CL, Shoemaker AH. Hypothalamic obesity: prologue and promise. Horm Res Paediatr 2019;91(2):128–36. https://doi.org/10.1159/000496564.
[142] Jung UJ, Choi MS. Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. Int J Mol Sci 2014;15(4):6184–223. https://doi.org/10.3390/ijms15046184. Published 2014 Apr 11.
[143] Pickering L, Jennum P, Gammeltoft S, Poulsgaard L, Feldt-Rasmussen U, Klose M. Sleep-wake and melatonin pattern in craniopharyngioma patients. Eur J Endocrinol 2014;170(6):873–84. https://doi.org/10.1530/EJE-13-1025.
[144] Müller HL. Increased daytime sleepiness in patients with childhood craniopharyngioma and hypothalamic tumor involvement: review of the literature and perspectives. Int J Endocrinol 2010;2010:519607. https://doi.org/10.1155/2010/519607.
[145] Lustig RH, Hinds PS, Ringwald-Smith K, et al. Octreotide therapy of pediatric hypothalamic obesity: a double-blind, placebo-controlled trial. J Clin Endocrinol Metab 2003;88(6):2586–92. https://doi.org/10.1210/jc.2002-030003.
[146] Hamilton JK, Conwell LS, Syme C, Ahmet A, Jeffery A, Daneman D. Hypothalamic obesity following craniopharyngioma surgery: results of a pilot trial of combined diazoxide and metformin therapy. Int J Pediatr Endocrinol 2011;2011(1):417949. https://doi.org/10.1155/2011/417949.
[147] Wysocki J, Belowski D, Kalina M, Kochanski L, Okopien B, Kalina Z. Effects of micronized fenofibrate on insulin resistance in patients with metabolic syndrome. Int J Clin Pharmacol Therapeut 2004;42(4):212–7. https://doi.org/10.5414/cpp42212.
[148] Ismail D, O'Connell MA, Zacharin MR. Dexamphetamine use for management of obesity and hypersomnolence following hypothalamic injury. J Pediatr Endocrinol Metab 2006;19(2):129–34. https://doi.org/10.1515/jpem.2006.19.2.129.
[149] Zoicas F, Droste M, Mayr B, Buchfelder M, Schöfl C. GLP-1 analogues as a new treatment option for hypothalamic obesity in adults: report of nine cases. Eur J Endocrinol 2013;168(5):699–706. https://doi.org/10.1530/EJE-12-0997. Published 2013 Apr 15.
[150] McCandless SE, Yanovski JA, Miller J, et al. Effects of MetAP2 inhibition on hyperphagia and body weight in Prader-Willi syndrome: a randomized, double-blind, placebo-controlled trial. Diabetes Obes Metab 2017;19(12):1751–61. https://doi.org/10.1111/dom.13021.
[151] National Library of Medicine. Open label study of setmelanotide in hypothalamic obesity. https://clinicaltrials.gov/study/NCT04725240.
[152] Smith DK, Sarfeh J, Howard L. Truncal vagotomy in hypothalamic obesity. Lancet 1983;1(8337):1330–1. https://doi.org/10.1016/s0140-6736(83)92437-6.
[153] Faucher P, Carette C, Jannot AS, et al. Five-year changes in weight and diabetes status after bariatric surgery for craniopharyngioma-related hypothalamic obesity: a case-control study. Obes Surg 2022;32(7):2321–31. https://doi.org/10.1007/s11695-022-06079-9.
[154] Harvengt J, Gernay C, Mastouri M, et al. ROHHAD(NET) syndrome: systematic review of the clinical timeline and recommendations for diagnosis and prognosis. J Clin Endocrinol Metab 2020;105(7):dgaa247. https://doi.org/10.1210/clinem/dgaa247.
[155] Lee JM, Shin J, Kim S, et al. Rapid-onset obesity with hypoventilation, hypothalamic, autonomic dysregulation, and neuroendocrine tumors (ROHHADNET) syndrome: a systematic review. BioMed Res Int 2018;2018:1250721. https://doi.org/10.1155/2018/1250721. Published 2018 Nov 21.

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