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Medication-induced weight gain and advanced therapies for the child with overweight and obesity: An Obesity Medicine Association (OMA) Clinical Practice Statement 2022

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ABSTRACT

Background: This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) details medication-induced weight gain and advanced therapies for the child with overweight or obesity.
Methods: The scientific information and clinical guidance in this CPS are based on scientific evidence, supported by the medical literature, and derived from the clinical perspectives of the authors.
Results: This OMA Clinical Practice Statement addresses medication-induced weight gain and advanced therapies for the child with overweight or obesity.
Conclusions: This OMA Clinical Practice Statement on medication induced-weight gain and advanced therapies for the child with overweight or obesity is an overview of current recommendations. These recommendations provide a roadmap to the improvement of the health of children and adolescents with obesity, especially those with metabolic, physiological, and psychological complications. This CPS also addresses treatment recommendations. This section is designed to help the provider with clinical decision making.

1. Introduction

The purpose of this clinical practice statement (CPS) regarding medication-induced weight gain and advanced therapies for the child with overweight or obesity is to provide clinicians with tools to clinically assess and manage children with obesity. The Obesity Medicine Association (OMA) is an organization of providers 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 providers who take a comprehensive, evidence-based approach to treating obesity. This approach is comprised of four pillars: nutrition, physical activity, behavior, and medication. 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 individual clinical presentation and the judgment of the treating clinician. Clinicians should construct a treatment plan through shared decision making with the patient, keeping the patient's best interest at the forefront of all decisions.

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The practice of pediatric healthcare has a long-standing, proud tradition. Clinicians who care for this vulnerable population know that decisions may have long-term implications [1]. Providing the best, timely, evidence-based care for children is simultaneously preventative and interventional. Clinicians in the field of pediatric obesity medicine now have advanced therapies to add to ongoing intensive lifestyle therapy (ILT). Caution in using new therapies should be balanced with reasons for "waiting" to treat. Clinicians should challenge beliefs about age and other restrictions: clinical decision making should consider obesity similarly to other chronic conditions, i.e., cancer, asthma, congenital heart disease, or any chronic condition threatening short- and long-term health. When will longitudinal medical chart documentation of body mass index (BMI) over the 95th percentile (obesity) without intervention or effectual treatment (as based on current pediatric obesity guidelines) be recognized as a delay in diagnosis and treatment? The following sections will discuss advanced therapies available to children with the disease of obesity through the lens of this and other challenging questions [2,3]. Fig. 1 shows the interactions of advanced therapies.

2. Foundational, continuous core treatment for children with obesity

2.1. Intensive lifestyle therapy (ILT)

The bedrock of treatment for obesity in children and adults is intensive lifestyle therapy (ILT). ILT includes baseline and ongoing evaluation and education on a multitude of potential effectors of obesity. Table 1 summarizes the basic components of ILT although other factors found in a thorough history (including psychosocial) and physical examination may be present [4–9].

The effects of trauma, social determinants of health, and other "upstream factors" [10] that may lead to the cascade of chronic stress sequelae are emerging [7,11]. A multitude of psychosocial factors such as weight-based bullying, teasing, and microaggressions can have a profound impact on the individual's ability to manage energy, body composition, and weight [4].The foundational interventions of ILT may be adequate to improve weight status in a subset of individuals with obesity. For many others, these foundational treatments will require the addition of one or more advanced obesity therapies to achieve results [12]. Advanced obesity therapies are never used in isolation of the foundational therapies (ILT). Since obesity is a chronic disease which may plateau or progress over time, adjustments to all modes of available therapy, both foundational and advanced, are considered at every patient encounter.

Table 1
Intensive lifestyle therapy components: Patient evaluation & management.

Components	
Education	Obesity is a chronic disease
Clinical Assessment	Weight-promoting medications
	Obesity-related complications
	Diet
	Activity
	Genetic causes of obesity, early onset of obesity, family history of obesity
	Co-occurring conditions with obesity
	Attention-deficit Hyperactivity Disorder, Behavioral Health disorders
	Mental health conditions
	Loss of Control Eating Disorder/Binge Eating Disorder
	Sleep quality &/or disorders
Psycho-social	Weight-based victimization
	Microaggressions
	Teasing
Environmental	Social Determinants of Health (Adverse Childhood Events, Trauma)
	Chronic stress & sequelae

Examples (not inclusive) of Intensive Lifestyle Therapy components in patient evaluation and management of pediatric obesity.

2.2. Assessment of medication induced weight gain for the child with overweight or obesity

Pharmacotherapy administered for any clinical indication can produce known, or unknown/unintended side effects. Potential effects on weight status are weight promoting, weight neutral, and weight sparing. Ideally, clinicians will prescribe weight neutral medications and monitor for the desired effect to the prescribed condition. Whenever possible,

Fig. 1. Interaction of Advanced Therapies, ILT, and adjustment of weight promoting medications in the treatment of pediatric obesity. Image courtesy of Alyssa Cuda.

clinicians strive to replace a weight promoting medication with another effective medication that does not promote weight gain. When the best therapy requires a medication with the side effect of weight gain, consideration of consultation with an obesity medicine specialist and/or adding a mitigating medication like metformin or topiramate should be considered. Patients who gain excessive weight and/or develop metabolic disease after starting weight promoting medications should be carefully assessed by all care providers for optimal management. In this section, medications and alternatives are discussed for common medical conditions as they pertain to potential weight gain.

2.2.1. Central nervous system (CNS) agents

Many medications that act through the central nervous system (CNS) can be related to changes in weight. Medication classes in this category include atypical anti-psychotics, anti-epileptic drugs (AEDs), mood/depression drugs, attention-deficit/hyperactivity disorder (ADHD) medications, and anti-depressants. Table 2 gives an overview of CNS drugs including medication classes and examples.

2.2.2. Antipsychotic medications

2.2.2.1. Incidence and associations. Antipsychotic prescriptions in children have increased significantly over the past two decades [15]. Second generation antipsychotics such as olanzapine, clozapine, risperidone, and aripiprazole are of particular concern and account for most of the increase in prescribing. Up to 80% of children show significant weight gain when taking antipsychotics [16].

2.2.2.2. Risk factors for weight gain. Adolescents are at greater risk of weight gain from antipsychotic medications than adults [17]. The specific medication with the highest weight gain is olanzapine, followed by clozapine, risperidone, and aripiprazole [18]. There are some differences according to diagnosis; for example, patients with autism who are treated with second-generation antipsychotics (SGAs) tend to have greater weight gain than patients with alternate diagnoses using SGAs [19]. Patients who are older, have a lower baseline BMI z-score, are male, or have a diagnosis of a mood disorder also experience more SGA-induced weight gain [20].

2.2.2.3. Risk factors for diabetes. The atypical antipsychotic medications risperidone and aripiprazole are approved by the Food and Drug Administration (FDA) for use in autism spectrum disorder (ASD) in young children (risperidone age 5 years; aripiprazole age 6 years) [19]. Both of these medications are known to cause weight gain, and greater cumulative exposure is associated with an increased risk for developing type 2 diabetes mellitus (T2DM) [21].

2.2.2.4. Treatment of weight gain complications. Metformin may be minimally effective in decreasing the weight gain associated with atypical antipsychotic use [22]. Prior studies have looked at metformin to mitigate weight gain associated with atypical antipsychotic therapy in children [23]. Although a small study, Anagnostou et al. performed a randomized clinical trial in children and adolescents with ASD aged 6–17 years [22]. Study findings showed metformin reduced BMI *z*-scores from baseline to week 16 significantly more than placebo. In the study, metformin was titrated up to 500 mg twice daily for children aged 6–9 years and 850 mg twice daily for those 10–17 years (dosing for weight gain due to atypical antipsychotics is different than dosing for T2DM) [22].

Table 2
Overview of CNS medications. Shown are CNS medication classes with examples [13,14].

Medication Class	Examples of Weight Promoting Medications (Not inclusive of all available medications)
Atypical Antipsychotics	Olanzapine, Clozapine, Quetiapine, Risperidone, Aripiprazole
Anti-Epileptics (AEDs)	Valproate, Vigabatrin, Pregabalin, Carbamazepine
Mood/Depression	Lithium, Sertindole, Valproate, Trazodone
ADHD	Guanfacine
Anti-Depressants	
SSRIs	Paroxetine, Fluvoxamine, Sertraline, Fluoxetine
Tricyclic Agents	Amitriptyline, Nortriptyline, Imipramine, Doxepin
Migraine & Miscellaneous	Amitriptyline, Divalproex, Flunarizine, Venlafaxine, Mirtazapine

2.2.3. Antiepileptic drugs (AED)

2.2.3.1. Incidence and associations. In the last two decades, more than 11 new antiepileptic drugs (AEDs) have been introduced to the market. Several AEDs are associated with weight gain such as gabapentin, pregabalin, valproic acid (VPA), and vigabatrin, and to some extent carbamazepine (CBZ) [24,25]. Others are weight neutral, such as lamotrigine (LTG), levetiracetam, and phenytoin, or associated with slight weight loss, e.g., felbamate [25]. Topiramate, not a new medication, is another anti-epileptic drug associated with weight loss as discussed below.

2.2.3.2. Risk factors for weight gain. Weight gain occurs in approximately 40% of children taking VPA; of children treated with VPA, 38% gained more than 10% of their body weight compared with 8% treated with lamotrigine [25]. Hyperinsulinemia and hyperleptinemia are also common with VPA and are markedly elevated in children with epilepsy who gained weight [26]. The mechanism of action is likely a rise in insulin and insulin/glucose with VPA treatment, which possibly stimulates appetite. Neither hyperinsulinemia nor hyperleptinemia are seen with CBZ or LTG.

2.2.3.3. Special considerations. Topiramate and zonisamide are the two AEDs associated with weight loss [27]. Topiramate significantly reduces adiposity, reduces leptin/adiponectin ratios, and markedly increases the serum level of adiponectin; it also increases energy metabolism, resulting in weight loss since adiponectin plays a significant role in metabolic regulations [28]. Topiramate has been used, like metformin, to help mitigate weight gain when a weight promoting medication cannot be replaced [29].

2.2.3.4. Treatment of weight gain complications. Weight gain is a common adverse effect of many AEDs. Since AEDs are often required for extended periods of time, clinicians treating children with obesity who also need an AED should carefully select an AED or modify an existing one if the AED contributes to the disease of obesity.

2.2.4. Mood stabilizers

2.2.4.1. Incidence and associations. Mood stabilizers are medications used in the treatment of bipolar disorder in children and adolescents. They can be divided into traditional agents, including lithium, valproate, and carbamazepine, and newer agents, including the anticonvulsants lamotrigine, oxcarbazepine, topiramate, and gabapentin. Mood stabilizers are often used as second-line choices behind atypical antipsychotics (e.g., olanzapine, clozapine, quetiapine, risperidone and aripiprazole) due to lower comparable efficacy.

2.2.4.2. Risk factors for weight gain. Data regarding body composition and fasting metabolic effects of mood stabilizers in pediatric bipolar disorder are sparse. However, combining antipsychotics with mood stabilizers seems to lead to greater weight gain than treatment with mood stabilizers alone [19,30,31].

2.2.4.3. Special considerations. Recently, there has been a resurgence of interest in lithium treatment for bipolar disorder due to its unique anti-suicidal and neuro-protective effects. Lithium may be less effective

than risperidone for treating chronic mixed/manic symptoms in young children but comparable to anticonvulsants [30]. However, in comparison, risperidone was associated with higher weight gain and higher prolactin levels than lithium [29].

2.2.4.4. Treatment of weight gain complications. Some reports indicate that topiramate may be useful as an add-on therapy to induce weight loss in patients who have experienced psychotropic-induced weight gain [29]. In addition, amantadine appears to stabilize weight gain related to psychotropic medications. Amantadine may also help decrease BMI with continued usage, but controlled trials are lacking to date.

Fig. 2 shows a summary of the potential impact of antidepressants and mood stabilizers.

2.2.5. Diabetes medications

2.2.5.1. Incidence and associations. The SEARCH for Diabetes in Youth study (2002–2012) found that the rate of newly diagnosed cases of T2DM increased by 4.8% each year [34]. Since T2DM in youth was only recognized in recent years, natural history is limited. Until recently, only metformin and insulin were FDA approved for use under age 18 years. In 2019, the use of the glucagon-like peptide-1 (GLP-1) agonist liraglutide was approved as an add-on therapy to treat T2DM in children 10 years or older who have been receiving metformin with or without basal insulin [35]. The mechanism of action (MOA) of liraglutide is that it mimics the action of the GLP-1 incretin, which stimulates post-prandial insulin secretion, reduces glucagon secretion, delays gastric emptying, and induces weight loss through reduction of hunger and food intake [36–38].

2.2.5.2. Risk factors for weight gain. There is relatively little pediatric data on different insulin regimens, but all seem to have equal efficacy. Insulin and insulin analogs (such as insulin glargine) can cause excessive weight gain in adolescents [39]. Sulfonylureas are not commonly used in pediatric patients and can cause weight gain [40].

2.2.5.3. Special considerations. Metformin has been proven effective in the management of T2DM in adolescents [41]. Metformin decreases hepatic glucose output and enhances primarily hepatic and muscle insulin sensitivity without a direct effect on beta cell function. Metformin has the advantage of weight reduction and a decrease in lipids without the risk of hypoglycemia. See section 3.3.2 for further details about metformin. Among thiazolidinediones (TZD), rosiglitazone and pioglitazone are the only remaining drugs from the TZD family in clinical use; rosiglitazone was used in the TODAY study [42,43].

Although there are only a handful of studies on GLP-1 receptor agonists, such as liraglutide, semaglutide, exenatide, lixisenatide, and dulaglutide, several trials are currently underway with both daily and once weekly agents. To date, results of trials using GLP-1 receptor agonists are showing decreases in HbA1c in patients with T2DM that are as good or better than results from adult studies. In section 3.2.1 we discuss results of a recent trial using Semaglutide in adolescents for weight loss. The TODAY study showed that around 50% of youth with T2DM fail monotherapy with metformin within 11.5 months of treatment initiation; early combination therapy was preferred in pediatric patients with T2DM over waiting for the failure of metformin monotherapy [42–44].

2.2.6. Migraine medications

2.2.6.1. Incidence and associations. There is a positive association between headache and obesity among children [45]. The prevalence of migraines is increased in those with obesity, and risk increases with increasing obesity status [45]. There is overlap between migraine pathophysiology and the central and peripheral pathways regulating feeding; specifically, neurotransmitters like serotonin, peptides such as orexin, and adipocytokines (adiponectin and leptin) may have roles in both feeding and migraine [46].

2.2.6.2. Risk factors for weight gain. Risk of weight gain depends on the type of drug taken for migraines and the drug class. Drug classes and their associations with changes in weight are shown in Table 3.

2.2.6.3. Special considerations. Topiramate is, generally, a well-tolerated migraine therapy in children that tends to result in weight loss [48]. Effective treatment dose range is between 100 and 200 mg/day [49,50]. Side effects of topiramate may include gastroenteritis, paresthesia, concentration difficulty, somnolence, or cognitive impairment [50]. Due to

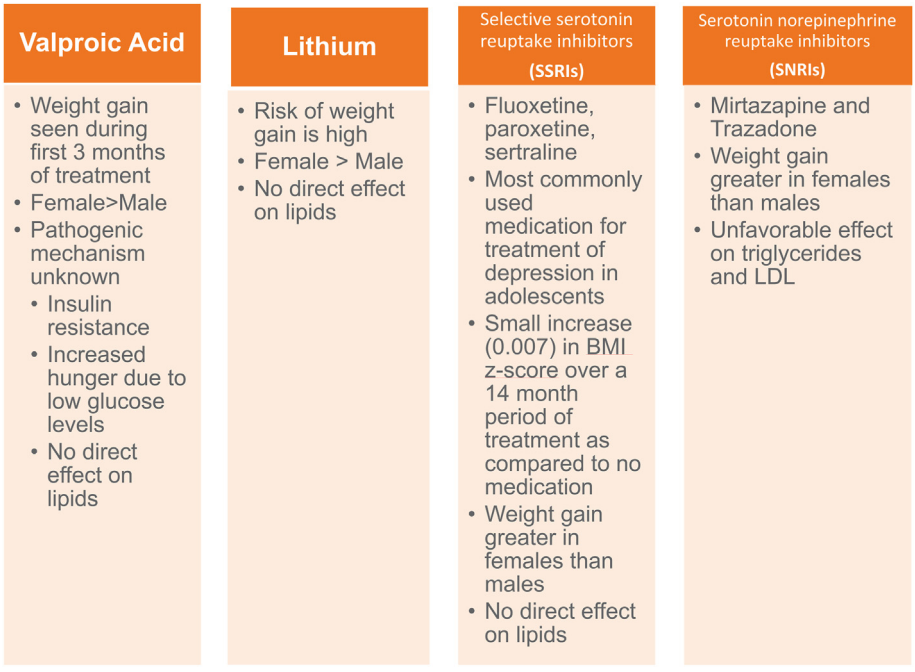

Fig. 2. Antidepressants and Mood Stabilizers: Summary. An overview of the impact of common antidepressants and mood stabilizers [13,30,32,33].

Table 3
Risk Factors for Weight Gain. Migraine medications, their classes, and their potential impacts on weight are shown [13,45,47].

Drug Class	Drug	Impact on Weight
Antidepressants	Amitriptyline	↑↑↑
	Nortriptyline	↑↑
	Protriptyline	↓
	Venlafaxine, Duloxetine	↔↓
Anticonvulsants	Divalproex sodium	↑↑↑
	Lamotrigine	↔
	Gabapentin	↑
	Topiramate	↓↓
Beta blockers	Propranolol	↑
	Nadolol	↔
	Metoprolol	↑
Serotonin antagonists	Cyproheptadine	↑↑↑
Calcium channel blockers	Verapamil	↔
	Flunarizine	↑↑

the low dose required for treatment of migraine, topiramate can be a good choice for the pediatric population due to its efficacy and the low frequency of side effects [48]. Use of Topiramate is limited in adolescent females due to its teratogenic potential. See section 3.4.1 for further details on topiramate.

2.2.6.4. Treatment of weight gain complications. Recognizing and avoiding trigger factors for migraine, in combination with a suitable therapy strategy that is not weight positive, may improve quality of life for a child with migraines. Psychological and physical triggers for migraine often include stress, anxiety, depression, fatigue, fever, illness, poor sleep habits, irregular meals, fasting, hypoglycemia, and dehydration [51,52]. An important part of prophylactic treatment in pediatric migraine is psychological support.

2.3. Endocrine agents

Endocrine agents that may lead to medication-related weight gain include insulin and insulin analogs, glucocorticoids, and hormonal contraceptives; an overview is shown in Table 4 [53–57]. For adult patients with obesity and T2DM requiring insulin, it is recommended to prescribe at least one weight loss-promoting medication, such as metformin, pramlintide, or a GLP-1 agonist, to decrease the weight gain associated with insulin administration [53]. If no alternative medications are available, weight gain can be prevented or decreased by choosing the lowest medication dose to produce clinical efficacy for the shortest duration necessary during treatment [53]. The presumptive clinical advantages of basal analogs compared with shorter acting insulins include reduced injection burden, better efficacy, lower risk of hypoglycemic episodes (especially nocturnal), and mildly reduced weight gain [58]. In incidentally diagnosed or metabolically stable pediatric patients with HbA1c <8.5% and who are asymptomatic, metformin is recommended by the American Diabetes Association (ADA) as the initial pharmacologic treatment of choice in the setting of normal renal function. If glycemic targets are not being met with metformin with or without incorporation of basal insulin, GLP-1 agonist liraglutide should be considered in children ≥10 years of age if there is no medical history or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2 present [59].

Table 4
Overview of Endocrine Medications. Shown are endocrine medication groups with examples.

Medication	Examples of Weight Promoting Medications (Not inclusive of all available medication)
Insulin and analogs	Insulin lispro
	Insulin aspart
	Insulin glulisine
Glucocorticoids	Prednisone
Hormonal Contraceptives	Medroxyprogesterone
	Oral Contraceptives

2.4. Other medication classes

Medication-related weight gain may also occur with medications for hypertension/cardiovascular drugs, antihistamines, sleep aids, and chemotherapy medications [60–63]. Examples are shown in Table 5.

2.5. Summary of medication induced weight gain section

2.5.1. ADHD, anti-seizure, migraine, diabetes, and others

The typical impacts on weight of various medications for ADHD, seizures, migraine, diabetes, and more are shown in Table 6.

2.5.2. Psychiatric medications

Psychiatric medications and their impact on weight are shown in Table 7.

2.5.3. Miscellaneous medications

A review of miscellaneous medications and their impact on weight is shown in Table 8.

2.5.4. Takeaways

The top takeaway messages from the OMA regarding medication-induced weight gain in the child with overweight or obesity are shown in Table 9.

3. Advanced Therapies for Children with Obesity and Severe Obesity

In this section, we discuss advanced therapeutic interventions that can be added either solely with or in combination to ILT efforts. Although there is little literature on timing of implementation of these advanced therapies, ILT continues as an uninterrupted baseline intervention with the addition of any advanced therapy to meet the need of the patient's disease status rather than any specific timeline.

3.1. Pharmacotherapy: FDA approved for indication of obesity in children and adults

3.1.1. Phentermine/topiramate

Phentermine/topiramate is FDA approved for the indication of obesity in patients 12 years and older (Table 10) [79]. The MOA of phentermine/topiramate is appetite suppression. Phentermine stimulates the hypothalamus, leading to the release of norepinephrine while topiramate's actions are multimodal; enhances γ-Aminobutyric acid (GABA) release while inhibiting α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and N-methyl-D-aspartic acid or N-methyl-D-aspartate (NMDA) [63]. A recent randomized, double-blind study of 56-week duration evaluated the efficacy of phentermine/topiramate in adolescents 12–17 years of age. The percent change in BMI at week 56 showed difference from placebo of −10.44% points for the top dose and −8.11% points in those treated with the mid-dose of phentermine/topiramate [80].

Table 5
Overview of Miscellaneous Medications. Miscellaneous medications that may cause weight gain with examples are shown [13].

Medication	Examples of Weight Promoting Medications
Hypertension/Cardiovascular	Beta-Blockers
Antihistamines	Diphenhydramine
Sleep Aids	Zolpedim
Chemotherapy	Tamoxifin, Methotrexate, Corticosteroids

Table 6
Review of Medications. The typical impacts on weight of various medications for ADHD, seizures, migraine, diabetes, and more are shown [27,54,55,63–69].

	Significant Weight Gain		Small Weight Gain to Weight Neutral		Weight Loss (Neutral to Moderate)
ADHD			Guanfacine		Atomoxetine Lisdexamfetamine Amphetamine Methylphenidate
Anti-Seizure	Valproate Vigabatrin	Pregabalin Gabapentin	Carbamazepine Oxcarbazepine	Lamotrigine Levetiracetam Phenytoin	Topiramate Zonisamide Felbamate
Migraine	Amitriptyline Divalproex Flunarizine	Gabapentin Metoprolol Propranolol	Timolol Levetiracetam		Zonisamide Topiramate
Other Medications	Glucocorticoids Imatinib Medroxyprogesterone		Benzodiazepines Statins Antihistamines (Cyproheptadine) Carvedilol Oral Contraceptive Pills		

Table 7
Review of Psychiatric Medications. Shown are various psychiatric medications and their impact on weight in pediatric patients [13,18,30,31,70–78].

	Significant Weight Gain		Small to Neutral Weight Gain	Weight Loss
Antipsychotics	Clozapine Olanzapine Chlorpromazine Quetiapine Risperidone		Aripiprazole Haloperidol Ziprasidone	
Special considerations: "Youth may be particularly sensitive to weight gain, especially with olanzapine, as well as extrapyramidal side effects and metabolic changes." Many of the medications listed here have only been well studied in adults				
Antidepressants	Paroxetine[a] Lithium Amitriptyline Olanzapine Citalopram Nortriptyline Doxepin Mirtazapine	Desipramine Imipramine Duloxetine Escitalopram	Venlafaxine Fluvoxamine Sertraline Trazodone Fluoxetine	Bupropion[a]
Mood Stabilizers	Valproate Lithium Gabapentin			Topiramate
Anxiolytics			Lorazepam Diazepam Oxazepam	

[a] = Black Box Warning.

Table 8
Review of Miscellaneous Medications. Shown are miscellaneous medications and their typical impact on weight in pediatric patients [13,60–63].

Medication	Significant Weight Gain	Small to Neutral Weight Gain	Weight Loss
Hypertension/ Cardiovascular	Beta blockers	Angiotensin-converting enzyme (ACE) inhibitors, Calcium channel blockers, Angiotensin-2 receptor antagonist	
Antihistamine Sleep Aids	Diphenhydramine Zolpidem, Trazadone (±)	Loratadine, Cetirizine Melatonin	Melatonin

Phentermine/topiramate is contraindicated for patients who are pregnant, who have taken monoamine oxidase inhibitors within 14 days, who have glaucoma or hyperthyroidism, or who have hypersensitivity or idiosyncrasy to sympathomimetic amines [79]. Notably, phentermine/topiramate has a black-box warning for worsening of depression in patients who are 18–24 years old. Adverse reactions may include paresthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth, suicidal ideation, and possible seizures if the medication is discontinued abruptly [79]. Patients should avoid alcohol while using phentermine/topiramate [79]. Topiramate also has a teratogenic effect requiring a discussion to ensure protection against an unplanned pregnancy.

Table 9
Top takeaways. Medication Induced Weight Gain in the Child with Overweight or Obesity Shown are the top takeaways from the medication induced weight gain in the child with overweight or obesity.

1. Many medications have the potential to cause weight gain in pediatric patients; monitoring and assessment of these effects is important for patient health.
2. CNS medications that may cause weight gain include atypical antipsychotics, antiepileptics, mood stabilizers and antidepressants. These classes, in particular, have the potential to cause significant weight gain in pediatric patients.
3. Endocrine medications that may cause weight gain include insulin and insulin analogs, glucocorticoids, and hormonal contraceptives.
4. Miscellaneous medications that may cause weight gain include hypertension/ cardiovascular drugs, antihistamines, sleep aids, and chemotherapy drugs.

3.1.2. *Phentermine*

Phentermine is FDA approved in children greater than 16 years for weight loss (Table 10) [81]. Duration of therapy varies based on state statutes. The MOA of phentermine is appetite suppression via stimulation of the hypothalamus to release norepinephrine. Weight loss with phentermine tends to be small or moderate (i.e., weight loss in excess of placebo is between 5 and 7.8%) [63]. Phentermine may cause anxiety, tremors, and a mild increase in blood pressure (BP); patients should be routinely monitored for pulse, BP, and side effects every 6–8 weeks (more frequent monitoring may be needed during titration) [81]. Phentermine should not be used in combination with fenfluramine or dexfenfluramine and is contraindicated in patients with serious regurgitant cardiac valvular disease [81]. Use phentermine cautiously in patients with hypertension (monitor closely for an increase in BP) and those with severe renal impairment. If the patient's glomerular filtration rate (GFR) is less than 30 mL/min, limit the dose of phentermine to 15 mg daily. Avoid phentermine use if the GFR is less than 15 mL/min. Phentermine is listed as a FDA Pregnancy Category X medication (medication contraindicated during pregnancy). No animal studies have been conducted, and no studies have been done in nursing mothers. While FDA-approval is for use up to 12 weeks, adult studies support longer-term use (>12 months), with risk of negative cardiovascular disease outcomes and/or death being rare (0.3%) [82].

3.1.3. *Liraglutide*

Liraglutide is FDA approved for management of obesity in adolescents ages 12–17 years and adults (Table 10) [83]. Liraglutide is also FDA approved for T2DM in children 10 years and older (as a separate formulation) [35]. Liraglutide is a GLP-1 receptor agonist given via daily injection. Liraglutide's MOA mimics the action of the GLP-1 incretin,

which stimulates post-prandial insulin secretion, reduces glucagon secretion, delays gastric emptying, and induces weight loss through reduction of hunger and food intake while increasing satiety. Average weight loss over placebo is 7% [84]. Common side effects of liraglutide include gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhea) and hypoglycemia [83]. Liraglutide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2 (MEN2) [83].

3.1.4. Orlistat

Orlistat is FDA approved in children ages 12 years and older (Table 10) [85]. Orlistat is a reversible inhibitor of gastric and pancreatic lipases, thus inhibiting absorption of dietary fats by 30% (MOA). Weight loss with orlistat is usually small (2.9–3.4%) [86]. Side effects preclude usage in most patients; side effects include oily rectal leakage, abdominal pain, flatulence with discharge, bowel urgency, and steatorrhea [85]. Orlistat is contraindicated in patients who are pregnant, breastfeeding, have chronic malabsorption syndrome or cholestasis [85].

3.1.5. Setmelanotide

Setmelanotide is FDA approved for children over 6 years of age and adults (≥18 years) for the following rare genetic causes of obesity: proopiomelanocortin (POMC) deficiency, proprotein convertase 1(PCSK1) deficiency, and leptin receptor (LEPR) deficiency (Table 10) [87,88]. In June 2022, the indication for setmelanotide was extended by the FDA to include patients with Bardet-Biedl Syndrome (BBS). Setmelanotide can also be utilized for patients with variants in POMC, PCSK1, LEPR, or BBS genes considered pathogenic, likely pathogenic, or of uncertain significance (compound heterozygous) [89]. Clinical trials are ongoing for other rare genetic disorders associated with obesity, including POMC epigenetic disorders and other melanocortin 4 receptor (MC4R) pathway heterozygous deficiency-related obesity [90,91].

Setmelanotide is a melanocortin 4 (MC4R) receptor agonist. By reestablishing the MC4R activity, setmelanotide allows for reduced hunger. The medication is given as a once daily injection. Reduction in weight from baseline ranges from 9.7% (patients with LEPR) to 23.1% (patients with POMC or PCSK1) at one year [91]. Side effects include the potential for hyperpigmentation, gastrointestinal symptoms (e.g.: abdominal pain, constipation, diarrhea, nausea, vomiting), changes in the central nervous system (e.g.: depression, dizziness, fatigue, headache, insomnia, vertigo) and prolonged penile erections [87,91].

Table 10
Pharmacotherapy Summary. Shown are indications, medications, and minimum patient ages [35,50,79,83,85,87,92,96,100,102,108,109,114,115].

Pharmacotherapy Summary	Medication	Minimum Age (years)
FDA Approved for Pediatric & Adult Obesity Indication	Orlistat	12
	Liraglutide (3.0 mg daily dose) * *Also has separate formulation that is FDA approved for T2DM for ages 10 and older	12
	Phentermine/Topiramate	12
	Phentermine	>16
	Setmelanotide	6
FDA Approved for Adult (18 years and older) Obesity Indication	Semaglutide (2.4 mg weekly dose) * *Also has separate formulation that is FDA approved for T2DM for 18 years and older	18
	Naltrexone/Bupropion	18
FDA Approved for T2DM Indication	Metformin	10
	Exenatide	10
	Dulaglutide	18
	Tirzepatide	18
	Liraglutide (1.2 or 1.8 mg daily dose) * *Also has a separate formulation that is FDA approved for pediatric and adult obesity for ages 12 years and older	10
	Semaglutide (0.5, 1, or 2 mg weekly dose) * *Also has separate formulation that is FDA approved for adult obesity for 18 years and older	18
FDA Approved for Alternate Indication(s)	Topiramate (Indication: Seizures)* *Also indicated for migraine for 12 and older	2
	Lisdexamfetamine (Indication: ADHD) * *Also, FDA approved for binge-eating disorder for 18 and older	6
	Bupropion (Indication: Depression/Smoking Cessation)	18

Table 11
Top takeaways. Advanced Therapies for Children with obesity and severe obesity Shown are the top takeaways from advanced therapies for children with obesity and severe obesity.

1.	Obesity is a chronic disease requiring a combination of ongoing multimodal therapies and treatment, including MBS
2.	Advanced therapies exist for pediatric population
3.	Despite the potential to offer safer, less invasive, reversable treatment options, there is little data and lack of FDA approval for emerging bariatric technologies
4.	MBS is considered for youth of any age, pubertal status, cognitive or intellectual disability who has severe obesity: BMI ≥120% of the 95th percentile.
5.	Pharmacologic and MBS therapies have significant safety and efficacy data in children and adolescents
6.	Advanced therapies need to be included in a comprehensive pediatric weight management program
7.	Ongoing data on all advanced therapies in pediatric population are needed
8.	Improved access, including payor coverage, of advanced therapies is needed

3.2. Pharmacotherapy: FDA approved for indication of obesity in patients 18 years of age or older.

3.2.1. Semaglutide

Semaglutide, a GLP-1 agonist, is FDA approved for obesity in patients ≥18 years of age with a BMI greater than 30 and or a BMI greater than 27 with at least one obesity-driven disease (Table 10) [92]. Semaglutide is also FDA approved for T2DM in a separate formulation. Semaglutide is **not** currently FDA approved for children, but the STEP 4 Trial for Teens closed in March 2022 and the study results were published in November 2022. In this study, with semaglutide alone, the mean change in BMI from baseline to week 68 was −16.1%. Sixty two percent (62%) of the participants in the semaglutide group achieved a loss of body weight of at least 10%; in addition, 37% of subjects using semaglutide achieved weight loss of at least 20% [44]. Of note, this trial showed a better treatment effect in adolescents than seen in trials with adults.

Semaglutide is given as a once weekly injection. The MOA of semaglutide acts by multiple mechanisms including increased insulin secretion, inhibition of glucagon release and gluconeogenesis, delayed gastric emptying, and reduced appetite and energy intake. The STEP trial in adults showed that the weight loss above placebo was 12.4% (confidence interval 11.5–13.4%) [93–95]. Side effects of semaglutide include nausea, vomiting, diarrhea (particularly with dose titration), headache, and fatigue [92]. Contraindications include a personal or family history of medullary thyroid carcinoma (MTC) and patients with multiple endocrine neoplasia syndrome type 2 (MEN2) [92].

3.2.2. Naltrexone/bupropion

Naltrexone/bupropion is FDA approved for weight loss in patients ≥18 years of age with a BMI greater than 30 or with a BMI greater than 27 with at least one obesity driven disease (Table 10) [96]. It is **not** approved for pediatric use. The MOA of naltrexone/bupropion's is as a reuptake inhibitor of norepinephrine and dopamine (bupropion) and opioid antagonist (naltrexone). Weight loss over placebo for naltrexone/bupropion ranges from 4.8 to 6.0% [97,98]. The advantages of

naltrexone/bupropion over other medications are its use in treating food addiction and data over several years. Common side effects of naltrexone/bupropion include nausea, constipation, headache, vomiting, and dizziness; concerns associated with naltrexone/bupropion are a potential worsening of depression and/or suicidal ideation in youth; the medication carries a black box warning [96]. Contraindications include uncontrolled hypertension, seizure disorders, anorexia, bulimia, drug or alcohol withdrawal, and monoamine oxidase inhibitor (MAOI) usage [96].

3.3. Pharmacotherapy: FDA approved for type 2 diabetes mellitus

3.3.1. Tirzepatide

Tirzepatide is FDA approved for T2DM for patients 18 years and older (Table 10) [99]. Tirzepatide was evaluated for management of obesity in the 2022 SURMOUNT-1 trial, but is not yet FDA approved for obesity in adults or children [100]. In the SURMOUNT-1 trial, mean weight loss above placebo ranged from 11.9% (low dose, 5-mg) to 17.8% (high dose, 15-mg) [100]. Tirzepatide is given via a once weekly injection. The MOA is dual agonism at glucose-dependent insulinotropic peptide (GIP) and GLP-1 receptors, which contribute to the glycemic and weight control effects of this medication [101]. GIP regulates energy balance through cell-surface signaling in the brain and adipose tissue. This activation works synergistically with GLP-1 receptor activation to allow for greater weight reduction. Tirzepatide enhances first- and second-phase insulin secretion, reduces glucagon levels (both in glucose dependent manner) and slows gastric emptying, which reduces appetite. The most common side effects are gastrointestinal (GI) issues including nausea, vomiting, and diarrhea that occur primarily during dose escalation. Other side effects include cholelithiasis, injection site reaction, and fatigue. Tirzepatide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma, MEN2, pancreatitis, or a known hypersensitivity to Tirzepatide [100].

3.3.2. Metformin

Metformin is FDA approved in adults and children 10 years and older for T2DM (Table 10) [102]. Metformin provides a very modest reduction in weight (about 2.5% over placebo) when combined with lifestyle interventions over short time periods [103,104]. Metformin is often used to mitigate weight gain side effects of other medications, such as atypical antipsychotics [105] and may have a role in aiding patients with prediabetes and/or a strong family history of T2DM as well as patients with polycystic ovary syndrome (PCOS). The MOA for weight loss with metformin is increased sensitivity to insulin and leptin, which decreases hunger. Metformin may also increase secretion of the GLP-1 hormone [102]. The dose in adolescents, if tolerated, should be the maximum recommended dose of 1000 mg twice a day (BID) to take advantage of the effect of decreasing appetite. Side effects may include GI upset, especially in the first few weeks, which can be managed with dose titration and extended-release formulations. Long-term use has been associated with Vitamin B12 deficiency and monitoring is recommended. Lactic acidosis, while rare, is also possible (increased risk in patients with renal dysfunction). Contraindications include severe renal dysfunction (estimated GFR less than 30 mL/minute/1.73 m^2) and acute or chronic metabolic acidosis [102].

3.3.3. Exenatide

Exenatide is FDA approved for T2DM in children 10–17 years of age and in adults (Table 10) [106]. Its MOA is the slowing of gastric motility, which suppresses appetite. In a small randomized controlled trial of 10 mcg BID, exenatide produced a reduction of BMI (4%) and body weight in adolescents with severe obesity [107]. There was a slight rebound of BMI after down titration of dose followed by recovery when dose increased again. Preliminary evidence suggests that higher doses for prolonged periods of time may be necessary for weight loss. Side effects include GI symptoms: (abdominal pain or nausea, vomiting, diarrhea), decreased appetite, dyspepsia, fatigue, and hypoglycemia. Contraindications include MEN2, serious hypersensitivity reactions, pancreatitis, or a family history of medullary thyroid carcinoma [108].

3.3.4. Dulaglutide

Dulaglutide is FDA approved for T2DM in patients 18 years and older (Table 10) [109]. However, it is not approved for weight loss in adults or children [110]. Dulaglutide is a GLP-1 receptor agonist. With regards to degree of weight loss, data from the AWARD-11 trial demonstrate that half of patients on the higher dose of dulaglutide (4.5mg) experienced $\geq$5% weight reduction [111]. Common side effects include GI disorders (abdominal pain, nausea, vomiting, diarrhea), decreased appetite, dyspepsia, fatigue, and hypoglycemia. Contraindications include MEN2, serious hypersensitivity reactions, pancreatitis, or a family history of medullary thyroid carcinoma [109].

3.4. Pharmacotherapy: other indications

3.4.1. Topiramate

Topiramate is not FDA indicated in children for weight loss alone (it was FDA approved in 2022 as a combination with phentermine for use in patients aged 12–17 years; Table 10) [79]. Topiramate is FDA approved for seizure control in children ages 2 years and older and migraine prophylaxis in children 12 year and older. The MOA for weight loss may be its effects on appetite suppression and satiety enhancement, which could be based on a combination of potential mechanisms: block of neuronal voltage-dependent sodium channels, enhancement of gamma-aminobutyric acid type A (GABAA) activity, antagonizing α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)/kainite glutamate receptors, and weak inhibition of carbonic anhydrase. Topiramate may also control food cravings [28,66,112]. Studies in adolescents show a mean change in BMI between 2 and 4.9% [66]. Contraindications include hyperthyroidism, glaucoma, and use during or within 14 days following MAOI therapy [50].

Topiramate should not be used in combination with a ketogenic diet. It is also contraindicated in pregnancy (associated with cleft lip and/or palate) [113]. As such, patients should be counseled, referred for contraceptive management when appropriate, and routine urine human chorionic gonadotropin (HCG) monitoring should be performed. Side effects include paresthesia of extremities, cognitive disruption (confusion, difficulty concentrating), and worsening depression; monitor patients for suicidal ideation [50].

3.4.2. Lisdexamfetamine

Lisdexamfetamine (LDX) was FDA approved for ADHD in children in 2007, but it is not approved for the indication of weight loss (Table 10) [114]. LDX was also FDA approved for binge-eating disorder (BED) in adults in 2015 (50–75 mg/day) [114]. The MOA of LDX is that it hydrolyzes to release the active drug, D-amphetamine, which inhibits reuptake of dopamine (DA) and/or norepinephrine (NE) and enhances release of DA, NE, and serotonin. LDX may decrease pathological overeating and therefore treat BED. There are no adult or pediatric weight loss trials for lisdexamfetamine. Side effects may include decreased appetite, insomnia, headache, GI upset, and irritability. Patients are monitored for cardiovascular changes such as increased BP or pulse. Contraindications include MAOI use. LDX is a Scheduled II controlled drug; prescribing rules apply as with other stimulants [114].

3.4.3. Bupropion

Bupropion is FDA approved for depression, seasonal affective disorder, and smoking cessation in adults, but it is not an FDA approved indication for the treatment of weight loss or obesity (Table 10) [115].

Bupropion belongs to the aminoketone class of antidepressants, which are unrelated to SSRIs. Bupropion moderates the levels and activity of the neuro-transmitters norepinephrine and dopamine; however, its exact MOA for treating depression is uncertain. Net weight losses (compared with placebo) were 2.2% and 5.1% for bupropion SR 300mg and 400 mg, respectively (double-blind study, 48 months) [116]. Bupropion has a black box warning for the worsening of depression in patients 18–24 years of age. It may increase risk of seizures, particularly in patients with epilepsy or eating disorders such as bulimia or anorexia nervosa [115].

3.5. Pharmacotherapy summary

Table 10 shows a summary of pharmacotherapies including indications, medications, and minimum patient ages.

3.6. Emerging bariatric technologies (EBT)

Emerging technologies are classified as devices or endoscopic procedures. Clinical researchers continue to devise and evaluate emerging bariatric techniques in the hopes of adding therapeutic options that are increasingly safer, cost-effective, and more accessible to a wider group of patients [117,118].

3.6.1. EBT: devices

Devices target a variety of physiologic mechanisms implicated in energy dysregulation. These mechanisms include change of pressures in the stomach, change of gastric emptying rates, neuromodulation, and bypassing duodenal absorption of nutrients. Devices typically are swallowed or placed endoscopically or laparoscopically. Fig. 3 lists many of the device categories [119–124]. Note: Adjustable gastric band is sometimes listed with metabolic and bariatric surgery options. It is listed here as a device as it is removable and adjustable.

Advantages to using a device include: they are adjustable, removable, temporary, and easy to combine with pharmacotherapy and ILT. Because they are temporary, devices can potentially be a bridge to more invasive therapies if the patient is unable to tolerate an advanced therapy (such as MBS) due to present weight and existing obesity driven diseases. Devices can be placed synchronously (two balloons for example) or sequentially expanding the therapeutic possibilities.

Devices are not without their challenges. While being used and studied globally in adults, there is limited data on use, safety and efficacy in adolescents and children. Thus, no devices are FDA approved for adolescents and children in the US. Insurance coverage is rare. Because of plasticity in children's developmental programming, the minimally invasive and reversible nature of devices may make their use in youth potentially safer and more effective compared to other advanced therapies [125]. Despite these attractive aspects, there has been significant delay in studying these unique therapeutic options in children. Figs. 4–7 show individual devices for weight management.

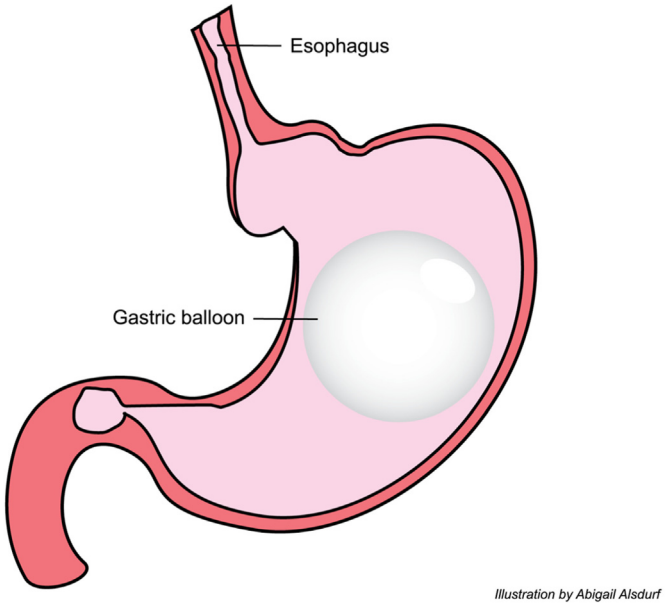

Fig. 4. Device: Intragastric Balloon. Image courtesy of Abigail Alsdurf.

3.6.2. EBT: endoscopic procedures

The second category of EBT are endoscopic procedures. The two most prominent are the endoscopic gastroplasty (ESG) and duodenal mucosal resurfacing (DMR). ESG is similar to laparoscopic sleeve gastrectomy (suturing of stomach into a tube along its long axis) but without gastric resection, and DMR involves thermal ablation of duodenal mucosa affecting duodenal absorption, specifically improvement in glycemia in adults with T2DM [126,127]. Endoscopic procedures are considered less invasive than metabolic and bariatric surgery. However, challenges

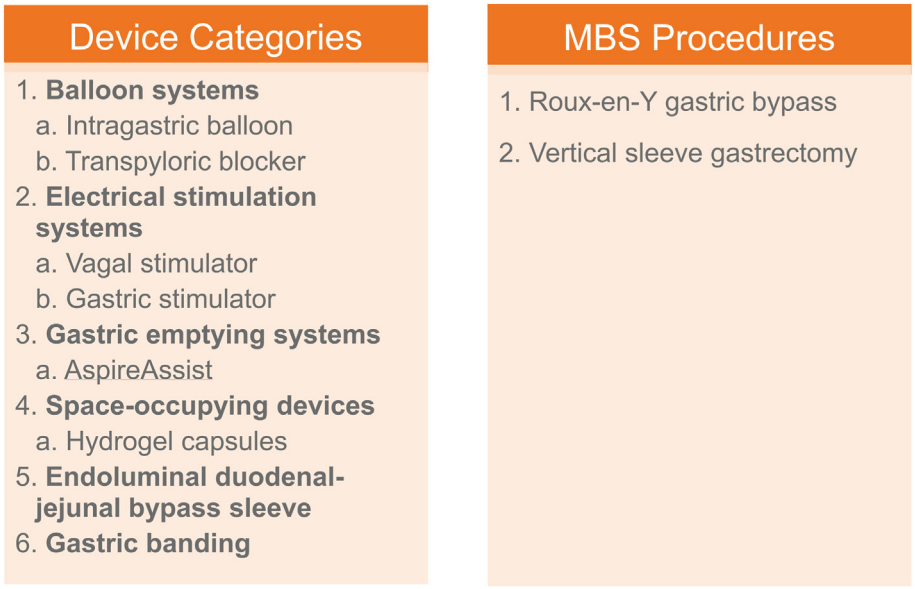

Fig. 3. Categories of devices used in weight management.

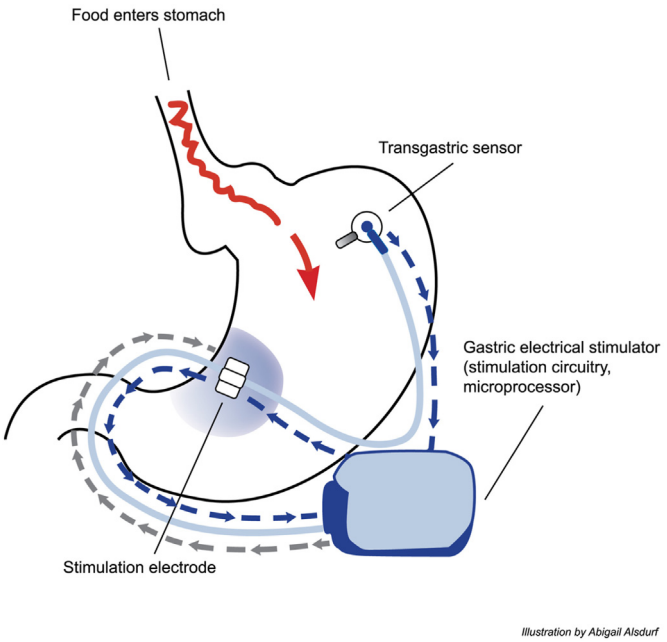

Fig. 5. Device: Gastric Stimulator. Image courtesy of Abigail Alsdurf.

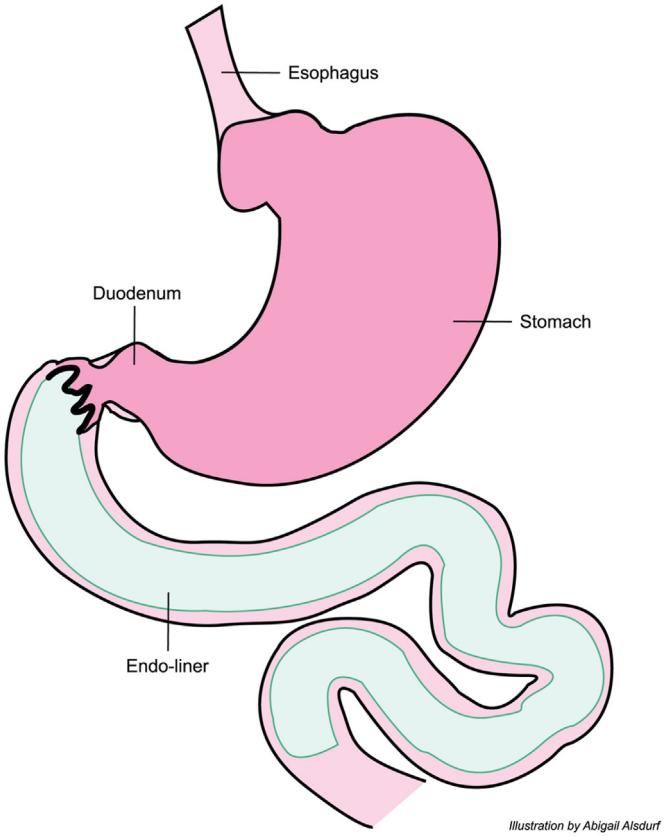

Fig. 6. Device: Endoluminal Duodenal-Jejunal Bypass Sleeve. Image courtesy of Abigail Alsdurf.

include lack of FDA approval in pediatrics, delays in study of safety and efficacy in children, and limited data in the pediatric population [127].

3.7. *Metabolic & bariatric surgery (MBS)*

Metabolic and bariatric surgery (MBS) is considered an advanced

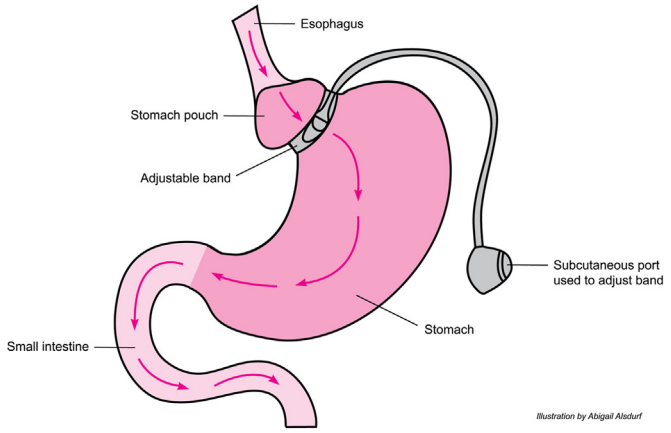

Fig. 7. Device: Gastric Band. Image courtesy of Abigail Alsdurf.

treatment of severe obesity and resulting obesity-related complications [128]. MBS with the foundation of ILT may be used alone or in combination with anti-obesity pharmacotherapy [129]. The safety and efficacy of MBS in adolescents have been established in single and multi-institutional studies managed by multidisciplinary groups utilizing ILT support throughout preoperative and postoperative care [130]. Outcomes of MBS in both adult and adolescent studies show similar results including improvement and resolution of obesity driven diseases [131]. A recent report analyzed trends in adolescent metabolic and bariatric procedures over 15 years finding a significant increase in use of MBS in adolescents although concluding that MBS remains underutilized [132]. MBS guidelines in the pediatric population provide clinical direction for this treatment modality [128,133].

3.7.1. *Indications for MBS in the pediatric population*

Overview of patient selection for MBS in the pediatric population [128,133]:

- A BMI ≥120% of the 95th percentile with an obesity driven disease or BMI ≥140% of the 95th percentile regardless of comorbidity are used when using weight as guide.
- Tanner stage and linear growth should not be used to determine readiness for adolescent MBS.
- Adolescents are defined by the World Health Organization's definition of 10- to 19-years old, but younger children who meet the other criteria including physiologic & psychologic obesity driven diseases should be considered when benefit outweighs risk
- MBS is considered for youth of any age, pubertal status, cognitive or intellectual disability with severe obesity and significant obesity driven disease.

3.7.2. *Outcomes of MBS in pediatric population*

Published US and international data of the safety and efficacy of MBS outcomes are now approaching 20-year follow-up. Research includes 2 multi-institutional consortiums. See Fig. 8 for highlighted results of these studies.

3.7.3. *Recommendations for MBS in pediatric population*

Best practice guidelines recommend the following principles and understanding when utilizing MBS in the pediatric population [128,133]:

- Obesity is a chronic disease requiring a combination of ongoing multimodal therapies and treatment by a team led by a pediatric obesity medicine specialist.
- Obesity increases the risk of T2DM, liver disease, dyslipidemia, sleep disorders, orthopedic conditions, and mental health conditions such as anxiety and depression.

Metabolic & Bariatric Surgery: Pediatric Outcomes

Teen LABS (NEJM, 2019)	Alqahtani et al. (J Am Coll Surg, 2021)	AMOS Study (Lancet, 2017)	De la Cruz-Munoz (J Am Coll Surg, 2022)
• 5-year published follow-up data • Age range at surgery: 13–19 years old • Mean percent weight loss: 26% • 96% patient follow-up at 5 years • 68% normalized blood pressure • 81% normalized triglycerides • 86% with T2DM in remission • 48% low ferritin levels	• 7–10 year published follow-up data • Age range at surgery: 5–21 years old • Mean excess weight loss: 71% • 71.1% ± 26.9% patient follow-up in 7–10-year group • Excellent remission/ improvement of complications of obesity • No change in growth velocity	• 5-year published follow-up data • Mean age at surgery: 16.5 years • Mean weight loss: 36.8 kg • Excellent remission/ improvement of complications of obesity	• 10–18 years of published follow-up data • Age range at surgery: 15–18 years old • Mean total body weight loss: 31% • 74% patient follow-up • Excellent complication remission/ improvement • 91% of subjects satisfied with choice to undergo MBS

Fig. 8. Peer-reviewed published long-term outcomes of MBS in the pediatric population [130,131,134,135].

- Pediatric patients undergoing MBS need to be followed by their pediatric obesity medicine team pre- and postoperatively and transitioned when appropriate to adult obesity medicine specialists.
- Pediatric patients should be counseled as developmentally appropriate on risks and benefits of MBS along with their family/ caretakers.
- Vertical sleeve gastrectomy is currently the most common MBS operation for adolescents; both Roux-en-Y Gastric Bypass and vertical sleeve gastrectomy have similar risks and benefits in the pediatric population. See Figs. 9 and 10 below for details.
- Follow-up is ongoing after MBS:
  - o for potential adverse effects from surgery
  - o obesity is a chronic disease and ongoing supportive care needs to be provided.
- Counsel female patients about increased fertility after MBS.

3.8. Combination therapies

Inadequate weight loss and weight regain are not uncommon in patients who undergo MBS. The chronic nature of the disease of obesity requires a range of therapeutic options to treat patients long-term. This range of multimodal therapies includes nutritional, activity, behavioral, pharmacologic, and surgical interventions, often in combination. Multiple studies demonstrate use of pharmacotherapy after surgical weight loss can result in over 50% of patients seeing an additional 5–15% post-surgical weight loss [136,137]. ILT and pharmacologic therapies used as adjuncts to surgical therapies may provide improved outcomes long term in the pediatric population and will require further study [138] (Table 11).

4. Transition from pediatric to adult clinical healthcare

Obesity is a chronic disease characterized by relapsing episodes of

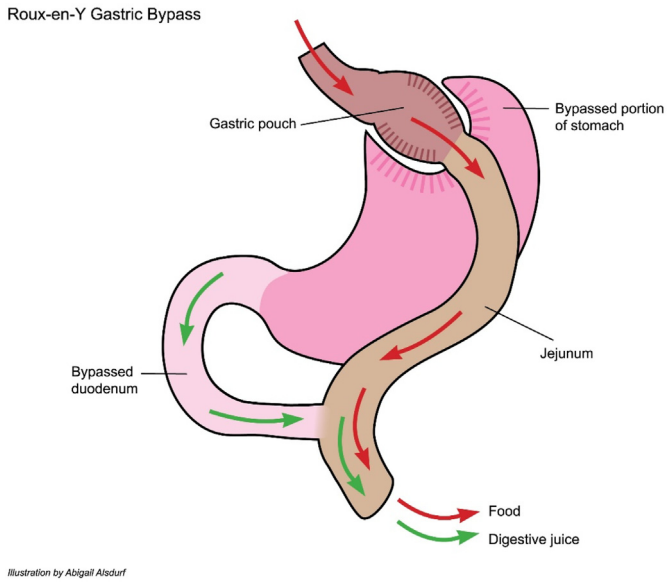

Fig. 9. Roux-en-Y gastric bypass. Image courtesy of Abigail Alsdurf.

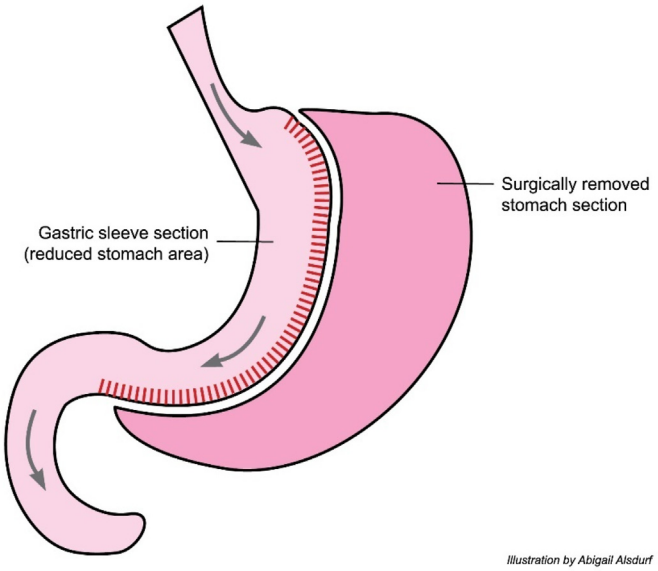

Fig. 10. Vertical sleeve gastrectomy. Image courtesy of Abigail Alsdurf.

weight gain as the body struggles to return to its former set point of body composition. As with other chronic diseases of childhood, a plan of transition to adult obesity medicine specialists should be part of every pediatric obesity medicine care plan. Using principles from the chronic care model [139,140], plans for transition to adult care should begin early in pediatric obesity medicine management and be revised as needed as the child matures. Discussion of long-term health care is embedded in all treatment regimens as the clinical expectation is that intervention and follow-up will be needed long-term. Current literature guides the transition to adult obesity care, incorporating the following principles [141–143]:

- Importance of youth/young adult centered strength-based focus
- Emphasis on self-determination, self-management, and family/caregiver engagement
- Acknowledgement of individual differences and complexities
- Recognition of need for a distinct population health approach for youth/young adults
- Need for early and ongoing preparation and integration into adult models of care
- Importance of shared accountability, effective communication, and care coordination between pediatric and adult clinicians and systems of care
- Recognition of the influences of cultural beliefs and attitudes as well as socio-economic status
- Emphasis on achieving health equity and elimination of disparities
- Need for parents and caregivers to support youth and young adults in building knowledge regarding their own health and skills in making health decisions and using health care

5. Considerations of pediatric obesity care in clinical practice

5.1. Goals

As in any clinical encounter, particularly with patients with a known chronic disease, goals for the patient, family and the clinical management plan guide care specifically (the current encounter) and broadly (encounters over time). Short term or episodic goals will vary during treatment but many core goals will guide practice, particularly during the ebb and flow of chronic care management and with the unique pediatric aspect of growth and developmental stages. Family and clinical goals listed in Fig. 11 are intended to be a guide rather than an exhaustive list.

5.2. Early vs delayed intervention

The age of the patient should not be the determining factor in the initiation of effective treatment. All medical treatments require full consideration of the risk/benefit ratio for any disease process with a respect for possible known or unknown side-effects. Armed with current evidence and clinical expertise, the clinician and patient/family discuss the use of any therapeutic in the context of the patient's evaluation and circumstances [6–9]. Through shared decision making, a treatment plan is devised and implemented. Once initiated, ongoing monitoring, evaluation, and redirection are key elements of all clinical care plans. Fig. 12 shows the expected pathway of early and delayed intervention with the disease of obesity demonstrating that the earlier the successful intervention, the less the risk of developing health consequences [144–147].

5.3. Decision making: when to use advanced therapy of anti-obesity medications (AOM)

The use of AOMs in children and adolescents is a shared clinical decision made between the health care provider, team, and the family/child. Decisions are based on current (and updated) clinical and psychosocial parameters assessed during initial and ongoing chronic care visits for obesity medicine care. Evidence does not support delays in pharmacotherapy while incorporating ILT interventions into therapeutic treatment plans [12]. A prospective study collecting data from 31 pediatric weight management programs across the US showed that early BMI reduction in the first month of treatment was found to be significantly associated with greater long-term reduction of BMI at 6 and 12 months (defined as a >5% BMI reduction from baseline) in adolescents with obesity [145]. To meet the goal of improvement of the child's health, at least a 5% reduction in BMI percent of the 95th percentile is recommended [90]. Published literature finds that this percentage reduction is rarely achieved with lifestyle therapy alone [12,149,150]. If the

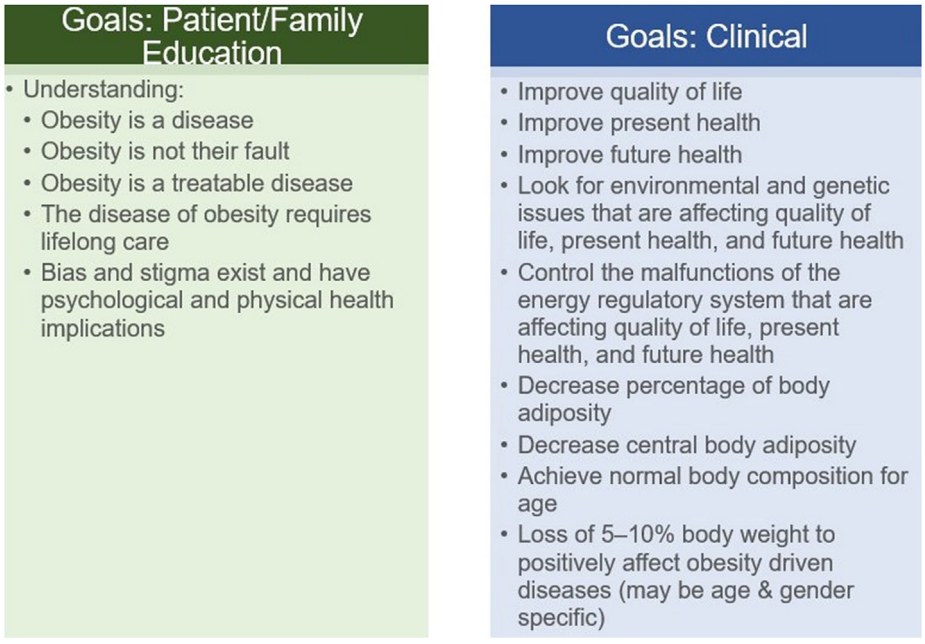

Fig. 11. Family and clinical goals of pediatric obesity care.

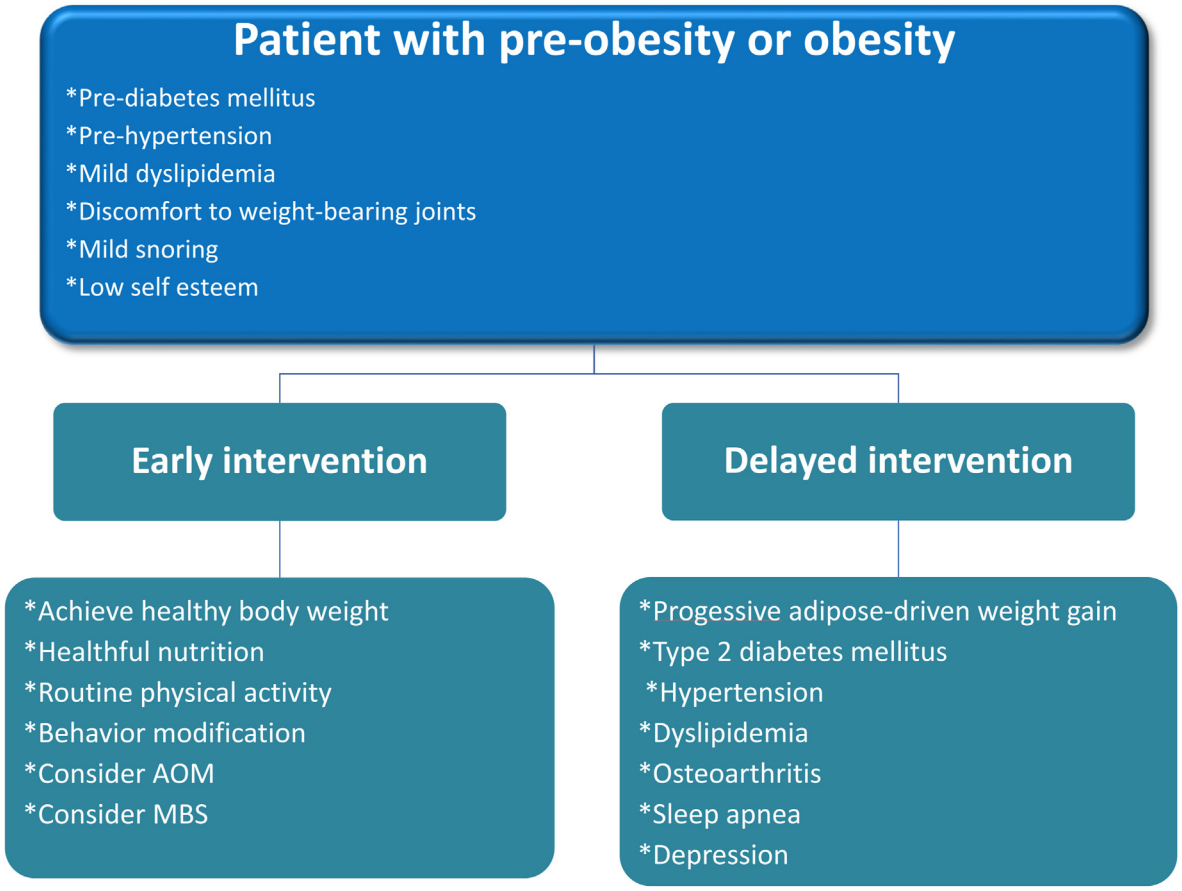

Fig. 12. Early versus delayed intervention in treatment of pre-obesity or obesity [148].

child/adolescent's metabolic profile is in normal range despite their BMI percentile being over the 95th percentile, a family/clinician discussion should discuss the use and timing (if considered) of anti-obesity medication. Any obesity driven psychosocial consequences that the child is experiencing should be considered in all clinical decisions.

Given the complex pathophysiology of the disease of obesity, as well as the many co-occurring disorders involved in obesity management, multiple mechanisms of action are likely required to improve outcomes. This frequently requires the use of multiple AOMs. The additive effectiveness of new combination medications (phentermine/topiramate, naltrexone/bupropion, and most recently tirzepatide) for many patients highlight the synergist effects and safety of combination therapy. When AOMs are used in combination, more significant improvements are achievable. This can be done using the newer combinations when accessible to the patient, or simultaneously prescribed as individual medications when newer formulations are not possible, along with combining with medications for the many obesity driven diseases, such as adding metformin when a patient also has pre-DM or PCOS [80]. If we consider the chronic disease of asthma as an example, for many children this chronic disease requires multiple medications with different mechanisms of action to appropriately manage symptoms.

As outlined in the decision tree, key components of the history and physical and laboratory screening will help guide AOM utilization based on presenting symptoms and co-occurring diseases (see Figs. 13–15). To help prioritize these options, evaluation of weight-promoting medications and review of weight-losing or weight neutral alternatives should be discussed with the patient and specialist managing the medication. As obesity medicine specialists, we frequently co-manage patients with multiple conditions and mental health diagnoses where medications with weight gain side effects are utilized. Working collaboratively, via consultation or referral, with our colleagues to reduce the significant weight gain associated with these therapies is vital. Understanding the detrimental impact of worsening obesity on our pediatric population requires ongoing education of obesity as a disease. Understanding which medications have the greatest risk of weight gain, including lower risk medications as first-line options, and monitoring closely for weight gain when the patient does require the higher risk medication should be considered standard of care. As clinicians, the medications we use undoubtedly have side effects. We should discuss the risks and benefits of the side effects and the potential to improve the disease state. This requires patient-specific shared-decision making and ongoing care of our patients. Patients with obesity should be screened for obesity-related co-occurring diseases; when positive, treatment should be initiated. Many AOMs can reduce obesity and resolve many of these complications (i.e., T2DM).

The expanding understanding of monogenic and polygenic obesity when early onset obesity is present provides an additional opportunity to provide patient specific interventions. In addition to these screening steps, we strive to elicit details to guide treatment options that best address the patient's phenotype [151]. Taken collectively, this process allows the clinician to fully assess disease status and formulate a comprehensive treatment strategy which may require combinations of existing AOMs.

5.4. *Duration of treatment*

Obesity is a chronic disease; the patient and family should be counseled that lifelong treatment is likely necessary. The goal in obesity medicine management is the stabilization of the disease process and improvement in health status (including mental health), not a specific

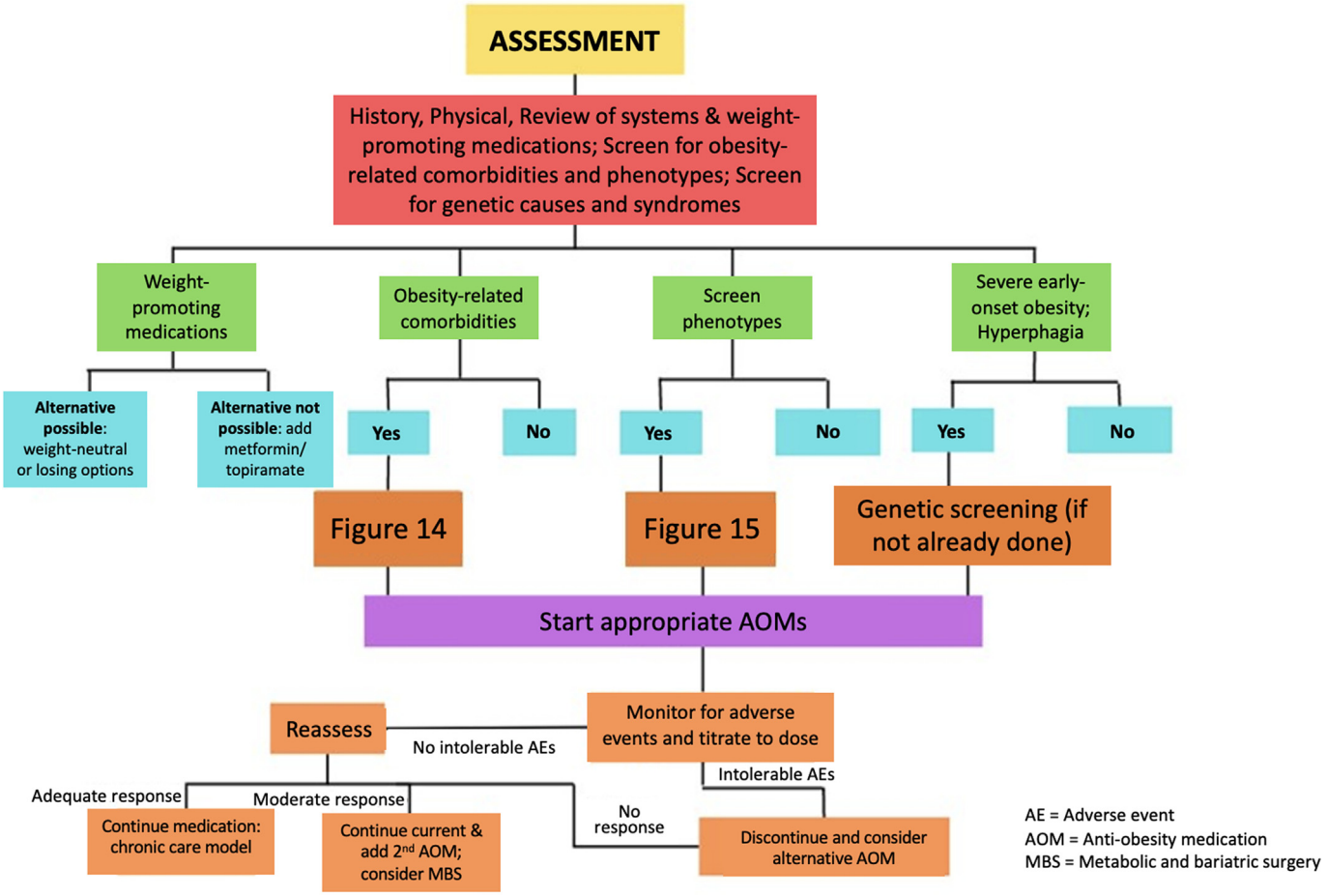

Fig. 13. Decision tree: Guide to assessment and treatment Implementation
Graphic: Alyssa Cuda.

weight goal [12]. Successful changes in the treatment of obesity are seen through the lens of successful management, not cure of the disease. Patients and families should understand that cessation of a treatment modality comes with a high risk of return of increased adiposity storage and subsequent weight regain.

5.5. *Off label usage in pediatrics*

Off-label is a common concept in pediatric care with implications for pediatric obesity treatment options. Off-label should not be equated with illegal; rather, the term off-label indicates there is not sufficient (or any) evidence from double-blinded, randomized trials to demonstrate the efficacy of a treatment for a particular indication. Therapies for pediatric conditions, including obesity treatment, are guided by clinical practice statements and guidelines along with clinical best practice. Pediatric clinicians are guided by the American Academy of Pediatrics statement on off-label medication use in children which emphasizes that "the term "off-label" refers to use [indication] of a drug that is not included in the package insert (FDA approved labeling) [and] does not imply improper, illegal, contraindicated, or investigational use" [152]. The AAP statement further states "The administration of an approved drug for a use [indication] that is not approved by the FDA is not considered research and does not warrant special consent or review if it is deemed to be in the individual patient's best interest" [152]. Over 30% of all medications prescribed to children and adolescents are "off label" and the rate of off label prescriptions decrease with age (50% at one year of age, <30% by 18 years of age) [153]. The AAP statement includes specific recommendations to clinicians related to patient education and documentation when using medications (this would include AOM) that are administered for off-label indications [152].

5.6. *Treatment approach 2022 and beyond*

Through the dedicated work of pediatric obesity medicine clinicians, both individually and in concert with professional organizations and adult obesity medicine colleagues, progress has been made in the care and treatment of children with the disease of obesity.

Even as we acknowledge the progress made in treatment and management of pediatric obesity, numerous challenges remain. Solving these challenges will require collaboration between many groups: particularly patients/families with obesity, clinicians and healthcare administrators, policy makers, payors of care, government agencies, researchers, and educators of all healthcare clinicians. Upstream challenges that cause toxic stress from poor social determinants of health should be addressed especially as they impact energy dysregulation. Table 12 lists further challenges to be addressed and potential solutions as we move forward in providing optimal obesity care for children.

5.7. *Advanced treatment for pediatric obesity: summary statements*

The management of children with obesity is in an exciting period of transition. Many interventions used in adults are as effective, or more effective in children. Advanced therapies including anti-obesity medications, devices, and metabolic and bariatric surgery provide powerful tools to treat the disease of obesity when added to ILS. Data from increased usage of AOMs, both off label and FDA approved for obesity

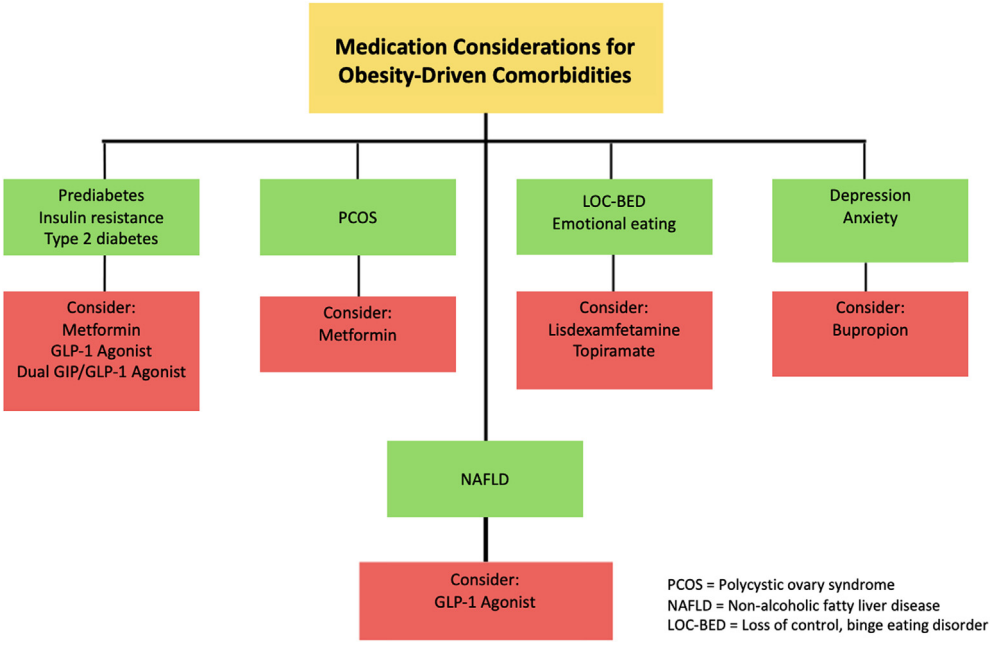

Fig. 14. Decision Tree: Medication considerations for obesity-driven comorbidities
Graphic: Alyssa Cuda.

treatment in children, along with the increasing use of MBS show that children with obesity can be treated safely and effectively. A strong argument can be made that using age as the reason for waiting to treat a child with obesity is harmful to the child, both medically and psychologically.

We need clinical trial data to guide treatment but like many other therapies used in children, we currently rely on best practice and clinical expertise to guide us. Additional therapies are in development and in trials now, but many are limited to adults. Children should be included in trials concurrently with adults. Treatment is available in the adult population for years before trials are started in the pediatric population, spawning off-label use. Advocacy for these trials and for payor coverage is imperative.

Despite our challenges, we are seeing widespread recognition that the disease of obesity should be treated in children at the time of disease diagnosis and that children can benefit from advanced therapies. The complex, chronic disease of obesity can be overwhelming to both families and clinicians. We need a robust system to manage patients at the primary care and the specialty care system level. Obesity medicine specialists are uniquely prepared to handle this specialized care. We need a shift from a system of limited tertiary care pediatric obesity medicine clinics involving extensive patient contact hours to the development of multiple models of care that meet the unique needs of each community. Increased education at all levels (medical and nursing school, residency, postgraduate) is needed for a disease that affects 30% of our children. Rapid progress is possible in the next few years!

In summary:

1 Pediatric obesity is a disease characterized by complex pathophysiology of the energy regulatory system, chronicity requiring lifelong management using multiple treatment modalities, and disease heterogeneity that currently has few known treatment predictors. Pediatric obesity medicine specialists are in a position to evaluate and lead patient management using the entire spectrum of therapeutic options

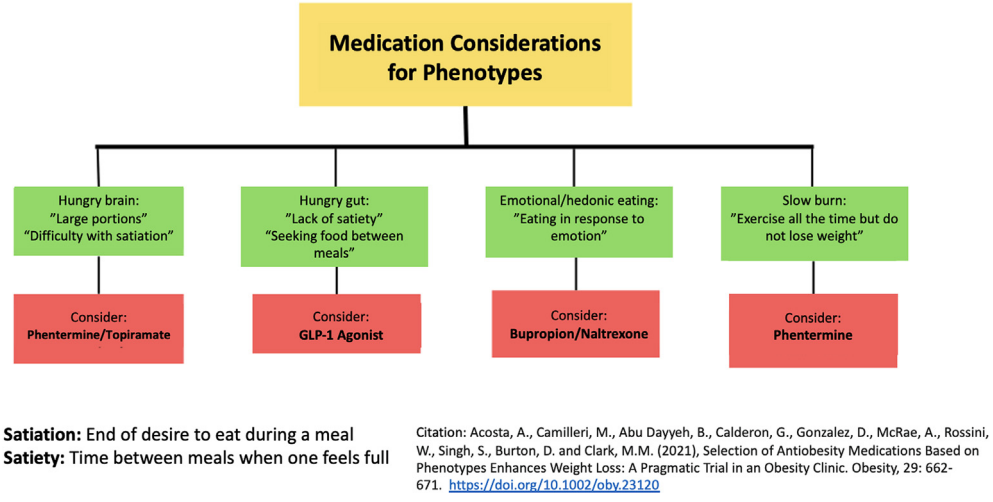

Fig. 15. Decision tree: Medication considerations for phenotypes
Graphic: Alyssa Cuda.

Table 12
Lists further challenges to be addressed and potential solutions.

Challenge	Proposed Solution
FDA approval of AOMs; lack of coverage for medications when FDA approved	Use adult studies, existing studies in children, and clinical judgement. Use processes for other therapies used in children that are not FDA approved for the prescribed indication after shared decision making
Access to MBS advanced therapy	More MBS programs collaborating with children's weight management programs
Educate payers about the disease of obesity.	Educate payers that treating the disease of obesity at diagnosis is both medically appropriate and financially prudent. Waiting until the child is 18 years old insures a poorer response to therapy, and high risk to develop expensive and harmful complications [154]
Educate policy makers about the disease of obesity.	Advocacy is needed with policy makers to support patients with obesity.
Support obesity research	Support funding of pediatric obesity research to develop effective prevention and treatment strategies.
Training of all healthcare disciplines about obesity as a disease.	All clinicians need to be comfortable diagnosing obesity and providing prompt, effective treatment. Education about obesity as a disease will reduce the bias and stigma that exists now in healthcare.
Educate patients and their families that obesity is a disease	Empowers patients and families to seek and receive treatment. Educates patients and families that obesity is not their fault.

Abbreviations: AOM = Anti-obesity medication; FDA=Food and Drug Administration; MBS = metabolic and bariatric surgery; WMP = weight management program.

(ILT, addressing weight promoting medications, pharmacotherapy, devices, and MBS), develop a shared treatment plan with the patient and family, and use collegial (particularly primary care) and community resources to implement the plan.

2 Frequency/Intensity of care: Few studies exist that inform the frequency or intensity of comprehensive management that achieve sustained, successful clinical outcomes for children with obesity [154, 155]. CPS5 recommends treatment for pediatric obesity at the highest level of pediatric obesity medicine care with the greatest number of provider visits over the longest period of time possible (includes ongoing monitoring). Optimally, treatment of pediatric obesity is provided by clinician(s) in a pediatric obesity medicine clinic. If a pediatric obesity medicine clinic is not accessible, primary care providers can start by increasing their knowledge base in obesity medicine, screen for obesity and obesity driven diseases, and consult with obesity medicine specialists to determine treatment options. Referral or consultation with obesity medicine specialists will result in better outcomes with the challenge of creating more platforms to extend clinical reach [145,156].

3 All clinicians providing obesity care should have training in obesity medicine practice. Certification by the American Board of Obesity Medicine (https://www.abom.org/) signifies specialized knowledge and competency in the field of obesity medicine. Nurse practitioners (NP) and physician assistants (PA) who complete the Obesity Medicine Association NP/PA Certificate of Advanced Practice (https://obesitymedicine.org/cme/np-pa-certificate-obesity-medicine/) demonstrate extensive knowledge of evidence-based obesity medicine treatment approaches. Ongoing CME education in obesity medicine provided by educators certified or with certificates in obesity medicine is recommended.

4 The entire toolbox of advanced obesity therapies should be available to any child with the disease of obesity and not be limited by age or obesity classification [128,154]. There is no current evidence that certain interventions work better after particular ages, bearing in mind that the field of pediatric obesity medicine has limited robust trial data in children. Off label prescribing of AOM for the indication of obesity is current practice due to paucity of trials in pediatric

Table 13
Resources to support ILT and Advanced Therapies.

Resources	
Food Insecurity	American Academy of Pediatrics (AAP) and the Food Research & Action Center (FRAC). Addressing Food Insecurity: A Toolkit for Pediatricians. http://frac.org/aaptoolkit (accessed January 2018) SNAP: https://www.fns.usda.gov/snap/supplemental-nutrition-assistance-program WIC: www.fns.usda.gov/wic/women-infants-and-children-wic National School Lunch Program: https://www.fns.usda.gov/nslp National School Breakfast Program: https://www.fns.usda.gov/sbp/school-breakfast-program Child & Adult Care Food Program: https://www.fns.usda.gov/cacfp Summer Food Service Program: https://www.fns.usda.gov/sfsp/summer-food-service-program
Sleep Disorders, Binge Eating Disorder, Sleep-related eating disorder	Sleep Disorders: • https://emedicine.medscape.com/article/870192-overview • https://emedicine.medscape.com/article/304381-medication#2 BED Screening Tools: • https://psychology-tools.com/test/binge-eating-scale • bingeeatingdisorder.com/en/binge-eating-disorder-symptoms#binge-eating-disorder-checklist Sleep-related eating disorder: https://sleepfoundation.org/sleep-disorders-problems
Adverse Childhood Experiences (ACE)	Centers for Disease Control and Prevention, Violence Prevention Program, ACEs Study: https://www.cdc.gov/violenceprevention/aces/ Robert Wood Johnson Foundation, The Truth about ACEs: http://www.rwjf.org/en/library/infographics/the-truth-about-aces.html ACEs Connection: http://www.acesconnection.com/blog/aces-101-faqs
Bullying/ Weight Stigma and Victimization	Bullying: • Stop Bullying Now: https://www.stopbullying.gov/ • Centers for Disease Control: www.cdc.gov/ncipc/dvp/electronic_aggression.htm Weight Stigma and Victimization: • Rudd Center for Food Policy & Obesity: www.uconnruddcenter.org (Resources regarding weight stigma, how to incorporate into a practice, media, literature) • AAP Institute for Healthy Childhood Weight - Change Talk: https://go.kognito.com/changetalk • Obesity Action Coalition: www.obesityaction.org
Trauma-informed Care	The Substance Abuse and Mental Health Services Administration (SAMHSA) is the agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation. SAMHSA's mission is to reduce the impact of substance abuse and mental illness on America's communities. SAMHSA website: https://www.samhsa.gov/

pharmacotherapy specific to obesity care and in general practice [152]. Pediatric data that does exist suggest that advanced therapeutic interventions that are successful in adults are successful in children as well with no evidence that intervention affects growth or development [12,134,135]. On the contrary, we have evidence that early intervention prevents or treats obesity driven disease(s) [145].

5 Access to care is a health equity issue. Comprehensive obesity care for children is limited by the inadequate (often no) healthcare insurance coverage for obesity treatment, including ILT services (clinicians, registered dietitians, physical therapists, behavioral health colleagues), FDA approved AOMs, EBT, and MBS. Obesity treatment coverage is scarce for pediatric patients on governmental insurance plans [157]. Insurance products that do offer pediatric obesity treatment coverage frequently reimburse at very low rates which creates a substantial financial burden not compensated by clinic volume or reduction in no-show rates leading to unsustainability of many pediatric obesity treatment clinics [157]. Children with obesity deserve the same access to quality care that is provided to other chronic diseases [129,157]. To provide less is unconscionable [2,158]. We need to use our collective experience at all levels of society to provide comprehensive, equitable coverage for the disease of obesity in children.

6 Every child with overweight or obesity disease should receive counseling to achieve a healthy diet and active lifestyle but we recognize that this basic care is rarely successful in treating the disease of obesity. Therefore, we advocate for a higher level of treatment that uses shared decision-making to address the concerns of the child and family and those of the experienced obesity clinician. There is little evidence that staged management where the child should complete any duration of treatment using any obesity treatment modality to "qualify" for a different treatment achieves faster or better results [129,145,159].

7 Obesity medicine specialists should be involved in the management of children with obesity. The disease of obesity is chronic and requires management of many obesity driven diseases. Management often involves longer and more frequent visits than can be accomplished in a primary care setting. We believe that working collaboratively with our primary care provider colleagues and with other subspecialists is in the best interest of the many children suffering with the disease of obesity as we do with all chronic conditions in pediatrics. This chronic care shared model has stood the test of time as evidenced by chronic care subspecialists partnering with primary care colleagues to provide comprehensive care that utilizes resources efficiently [160].

6. Conclusions

Obesity needs to be treated just like any other disease that threatens children's lives and where treatment is provided based on clinical need and not arbitrary age categories. To address pediatric obesity effectively, policymakers, health professionals and other stakeholders need to create a health system that ensures that every child has early access to high quality care for the management of overweight and obesity. Advocates for ***early*** treatment of children with obesity have published numerous papers for over 30 years and yet minimal, if any, progress in diminishing the prevalence of obesity in children has occurred [144,161–163]. Despite significant progress in evidence-based and effective obesity therapies, these modalities are not reaching affected children and remain woefully underutilized and poorly covered financially. Though there are studies and reviews that propose the nature of these barriers, the moral imperative is to eliminate the barriers and provide treatment with similar urgency as any other disease in children [133,157]. To do less is intolerable, unjust, and unethical.

Currently, in the field of pediatric obesity medicine and as champions for children, we have the opportunity and obligation to improve the lives of children with obesity. Through state-of-art-obesity education for all clinicians [OMA], patient advocacy organizations such as the Obesity Action Coalition [OAC], and growing obesity research that expands obesity treatment tools, the outlook for improving the care of children with obesity is hopeful. While challenges remain, pediatric obesity requires our unwavering commitment to providing the best evidence-based care for all children with obesity.

This Clinical Practice Statement on medication-induced weight gain and advanced therapies for the child with overweight or obesity provides clinicians with recommendations regarding their pediatric patients. The information and interventions presented may lead to improvements in the health and wellbeing of children and adolescents with overweight and obesity, especially those with metabolic, physiological, and psychological complications, and provide patients and families with the clinical tools and resources they need for a healthy future. Table 13 shows resources to support ILT and advanced therapies.

Transparency [164]

This manuscript was largely derived and edited from the 2020–2022 Obesity Medicine Association (OMA) Pediatric Obesity Algorithm. Beginning in 2016, the OMA created and maintained an online Pediatric "Obesity Algorithm" (i.e., educational slides and eBook) that underwent updates approximately every two years by OMA authors and was reviewed and approved annually by the OMA Board of Trustees. Authors of prior years' versions are included in Supplement #1. This manuscript is the first published version of the applicable chapter/s of the 2020–2022 OMA Pediatric Obesity Algorithm.

Group composition

Over the years, the authors of the OMA Pediatric Obesity Algorithm have represented a diverse range of clinicians, allied health professionals, clinical researchers, and academicians. (Supplement #1) The authors reflect a multidisciplinary and balanced group of experts in obesity science, patient evaluation, and clinical treatment.

Author contributions

NTB transcribed the first draft of this CPS from the 2020–2022 OMA Pediatric Obesity Algorithm. SEC, MC, RK, VO, RC, DW, JP, AB, SK wrote specific sections based on 2020–2022 Pediatric Obesity Algorithm. SEC reviewed, edited, and approved the document for pre-peer review submission and post-peer review publication.

Disclosures (declaration of potential competing interest)

Potential dualities or conflicts of interest of the authors are listed in the Individual Disclosure section. Assistance of a medical writer paid by the Obesity Medicine Association is noted in the Acknowledgements section. Neither the prior OMA Pediatric Algorithms nor the publishing of this Clinical Practice Statement received outside funding. The authors of prior OMA Pediatric Obesity Algorithms never received payment for their writing, editing, and publishing work. Authors of this Clinical Practice Statement likewise received no payment for their writing, editing, and publishing work. While listed journal Editors received payment for their roles as Editors, they did not receive payment for their participation as authors.

Individual Disclosures

SEC declares a relationship with Novo Nordisk as a member of an Advisory Board and a relationship with Rhythm Pharmaceuticals as a member of their Gold Panel. NTB reports no disclosures pertaining to this project. MC reports no disclosures pertaining to this project. RK reports a relationship with Rhythm Pharmaceuticals including an ongoing funded study, one clinical trial, and the RGDO Speaker's Bureau. VO reports no disclosures pertaining to this project. RC reports a relationship with

Rhythm Pharmaceuticals through the Speaker's Bureau. DRW reports no disclosures pertaining to this project. JP reports a relationship with Rhythm Pharmaceuticals as a member of the GOLD faculty and the Speaker's Bureau. AFB reports no disclosures pertaining to this project. SK reports an active relationship with Abbott Nutrition through the Speaker's Bureau.

Evidence

The content of the OMA Pediatric Obesity Algorithm and this manuscript is supported by citations, which are listed in the References section.

Ethics review

After approval by the authors, a draft manuscript was peer-reviewed and approved by the OMA Board of Trustees prior to publication. This submission did not involve human test subjects or volunteers.

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 medicine specialists. The intent is to better facilitate and improve the clinical care and management of patients with pre-obesity 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 overweight and 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 Obesity Pillars Editorial team, with input from the OMA members and OMA Board of Trustees.

Disclaimer and limitations

Both the OMA Obesity Algorithms and this Clinical Practice Statement were developed to assist health care professionals in providing care for patients with pre-obesity and obesity based upon the best available evidence. 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.

Supplement #1: historic citation and acknowledgement of authorship of the Obesity Medicine Association Obesity Algorithms

2020–2022 ebook Citation: Cuda S, Censani M, Paisley J, Browne N, O'Hara V. Pediatric Obesity Algorithm eBook, presented by the Obesity Medicine Association. www.obesitymedicine.org/childhood-obesity.

2020–2022 Pediatric Algorithm slides: Cuda S, Censani M, O'Hara V, Browne N, Paisley J. Pediatric Obesity Algorithm, presented by the Obesity Medicine Association. www.obesitymedicine.org/childhood-obesity. 2020–2022. www.obesitymedicine.org/childhood-obesity.

2018–2020 Pediatric Algorithm slides: Cuda S, Censani M, Joseph M, Browne N, O'Hara V. Pediatric Obesity Algorithm, presented by the Obesity Medicine Association. www.obesitymedicine.org/childhood-obesity. 2018–2020. www.obesitymedicine.org/childhood-obesity.

2016–2017: Cuda SE, Censani M, Joseph M, Green R, Scinta W. Pediatric Obesity Algorithm. (2016-17). Available online at: www.Pediatricobesityalgorithm.org.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Suzanne Cuda, Medical Director Alamo City Healthy Kids & Families reports a relationship with Rhythm Pharmaceuticals that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Suzanne Cuda, Medical Director Alamo City Healthy Kids & Families reports a relationship with Novo Nordisk Inc that includes: consulting or advisory and travel reimbursement. Roohi Karofa reports a relationship with Rhythm Pharmaceuticals that includes: funding grants and speaking and lecture fees. Sara Karjoo reports a relationship with Abbott Laboratories that includes: speaking and lecture fees and travel reimbursement. Jennifer Paisley reports a relationship with Rhythm Pharmaceuticals that includes: speaking and lecture fees and travel reimbursement. Rushika Conroy reports a relationship with Rhythm Pharmaceuticals that includes: speaking and lecture fees and travel reimbursement.

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