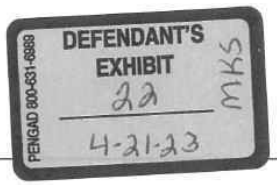
EXHIBIT 51



Pediatric Obesity—Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline

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Objective: To formulate clinical practice guidelines for the assessment, treatment, and prevention of pediatric obesity.

Participants: The participants include an Endocrine Society–appointed Task Force of 6 experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The Task Force commissioned 2 systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: One group meeting, several conference calls, and e-mail communications enabled consensus. Endocrine Society committees and members and co-sponsoring organizations reviewed and commented on preliminary drafts of this guideline.

Conclusion: Pediatric obesity remains an ongoing serious international health concern affecting ~17% of US children and adolescents, threatening their adult health and longevity. Pediatric obesity has its basis in genetic susceptibilities influenced by a permissive environment starting *in utero* and extending through childhood and adolescence. Endocrine etiologies for obesity are rare and usually are accompanied by attenuated growth patterns. Pediatric comorbidities are common and long-term health complications often result; screening for comorbidities of obesity should be applied in a hierarchal, logical manner for early identification before more serious complications result. Genetic screening for rare syndromes is indicated only in the presence of specific historical or physical features. The psychological toll of pediatric obesity on the individual and family necessitates screening for mental health issues and counseling as indicated. The prevention of pediatric obesity by promoting healthful diet, activity, and environment should be a primary goal, as achieving effective, long-lasting results with lifestyle modification once obesity occurs is difficult. Although some behavioral and pharmacotherapy studies report modest success, additional research into accessible and effective methods for preventing and treating pediatric obesity is needed. The use of weight loss medications during childhood and adolescence should be restricted to clinical trials. Increasing evidence

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Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CVD, cardiovascular disease; FDA, Food and Drug Administration; GH, growth hormone; HbA1c, hemoglobin A1c; LAGB, laparoscopic adjustable gastric banding; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; QOL, quality of life; RCT, randomized controlled trial; RYGB, Roux-en-Y gastric bypass; T2DM, type 2 diabetes mellitus; VSG, vertical sleeve gastrectomy; WHO, World Health Organization.

demonstrates the effectiveness of bariatric surgery in the most seriously affected mature teenagers who have failed lifestyle modification, but the use of surgery requires experienced teams with resources for long-term follow-up. Adolescents undergoing lifestyle therapy, medication regimens, or bariatric surgery for obesity will need cohesive planning to help them effectively transition to adult care, with continued necessary monitoring, support, and intervention. Transition programs for obesity are an uncharted area requiring further research for efficacy. Despite a significant increase in research on pediatric obesity since the initial publication of these guidelines 8 years ago, further study is needed of the genetic and biological factors that increase the risk of weight gain and influence the response to therapeutic interventions. Also needed are more studies to better understand the genetic and biological factors that cause an obese individual to manifest one comorbidity vs another or to be free of comorbidities. Furthermore, continued investigation into the most effective methods of preventing and treating obesity and into methods for changing environmental and economic factors that will lead to worldwide cultural changes in diet and activity should be priorities. Particular attention to determining ways to effect systemic changes in food environments and total daily mobility, as well as methods for sustaining healthy body mass index changes, is of importance. (***J Clin Endocrinol Metab*** **102: 709–757, 2017)**

Summary of Recommendations

1.0 Diagnosing overweight and obesity

1.1 We recommend using body mass index (BMI) and the Centers for Disease Control and Prevention (CDC) normative BMI percentiles to diagnose overweight or obesity in children and adolescents ≥2 years of age. (1|⊕⊕⊕○)

1.2 We recommend diagnosing a child or adolescent >2 years of age as overweight if the BMI is ≥85th percentile but <95th percentile for age and sex, as obese if the BMI is ≥95th percentile, and as extremely obese if the BMI is ≥120% of the 95th percentile or ≥35 kg/m^2 (1|⊕⊕○○). We suggest that clinicians take into account that variations in BMI correlate differently to comorbidities according to race/ethnicity and that increased muscle mass increases BMI. (2|⊕○○○)

1.3 We suggest calculating, plotting, and reviewing a child's or adolescent's BMI percentile at least annually during well-child and/or sick-child visits. (Ungraded Good Practice Statement)

1.4 We suggest that a child <2 years of age be diagnosed as obese if the sex-specific weight for recumbent length is ≥97.7th percentile on the World Health Organization (WHO) charts, as US and international pediatric groups accept this method as valid. (2|⊕○○○)

1.5 We recommend against routine laboratory evaluations for endocrine etiologies of pediatric obesity unless the patient's stature and/or height velocity are attenuated (assessed in relationship to genetic/familial potential and pubertal stage). (1|⊕⊕⊕○)

1.6 We recommend that children or adolescents with a BMI of ≥85th percentile be evaluated for potential comorbidities (see Table 2 and Fig. 1). (1|⊕⊕⊕○)

1.7 We recommend against measuring insulin concentrations when evaluating children or adolescents for obesity. (1|⊕⊕⊕○)

2.0 Genetic obesity syndromes

2.1 We suggest genetic testing in patients with extreme early onset obesity (before 5 years of age) and that have clinical features of genetic obesity syndromes (in particular extreme hyperphagia) and/or a family history of extreme obesity. (2|⊕⊕○○)

3.0 Prevention of obesity

3.1 We suggest that clinicians promote and participate in the ongoing healthy dietary and activity education of children and adolescents, parents, and communities, and encourage schools to provide adequate education about healthy eating (1). (2|⊕○○○)

3.2 We recommend that clinicians prescribe and support healthy eating habits such as:

- avoiding the consumption of calorie-dense, nutrient-poor foods (*e.g.*, sugar-sweetened beverages, sports drinks, fruit drinks, most "fast foods" or those with added table sugar, high-fructose corn syrup, high-fat or high-sodium processed foods, and calorie-dense snacks)
- encouraging the consumption of whole fruits rather than fruit juices. (1|⊕⊕○○)

3.3 We recommend that children and adolescents engage in at least 20 minutes, optimally 60 minutes, of vigorous physical activity at least 5 days per week to improve metabolic health and reduce the likelihood of developing obesity. (1|⊕⊕○○)

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3.4 We suggest fostering healthy sleep patterns in children and adolescents to decrease the likelihood of developing obesity due to changes in caloric intake and metabolism related to disordered sleep. (2|⊕⊕○○)

3.5 We recommend balancing unavoidable technology-related screen time in children and adolescents with increased opportunities for physical activity. (1|⊕⊕○○)

3.6 We suggest that a clinician's obesity prevention efforts enlist the entire family rather than only the individual patient. (2|⊕○○○)

3.7 We suggest that clinicians assess family function and make appropriate referrals to address family stressors to decrease the development of obesity. (2|⊕⊕○○)

3.8 We suggest using school-based programs and community engagement in pediatric obesity prevention. (2|⊕⊕○○)

3.9 We recommend using comprehensive behavior-changing interventions to prevent obesity. Such programs would be integrated with school- or community-based programs to reach the widest audience. (1|⊕⊕○○)

3.10 We recommend breast-feeding in infants based on numerous health benefits. However, we can only suggest breast-feeding for the prevention of obesity, as evidence supporting the association between breast-feeding and subsequent obesity is inconsistent. (2|⊕○○○)

4.0 Treating obesity

Lifestyle: general considerations

4.1 We recommend that clinicians prescribe and support intensive, age-appropriate, culturally sensitive, family-centered lifestyle modifications (dietary, physical activity, behavioral) to promote a decrease in BMI. (1|⊕⊕⊕○)

4.2 We recommend that clinicians prescribe and support healthy eating habits in accordance with the following guidelines of the American Academy of Pediatrics and the US Department of Agriculture:

- decreased consumption of fast foods
- decreased consumption of added table sugar and elimination of sugar-sweetened beverages
- decreased consumption of high-fructose corn syrup and improved labeling of foods containing high-fructose corn syrup
- decreased consumption of high-fat, high-sodium, or processed foods
- consumption of whole fruit rather than fruit juices
- portion control education
- reduced saturated dietary fat intake for children and adolescents >2 years of age
- US Department of Agriculture recommended intake of dietary fiber, fruits, and vegetables
- timely, regular meals, and avoiding constant "grazing" during the day, especially after school and after supper
- recognizing eating cues in the child's or adolescent's environment, such as boredom, stress, loneliness, or screen time
- encouraging single portion packaging and improved food labeling for easier use by consumers. (Ungraded Good Practice Statement)

4.3 We recommend that clinicians prescribe and support the reduction of inactivity and also a minimum of 20 minutes of moderate to vigorous physical activity daily, with a goal of 60 minutes, all in the context of a calorie-controlled diet. (1|⊕⊕○○)

4.4 We suggest that clinicians encourage and support patients to limit nonacademic screen time to 1 to 2 hours per day and decrease other sedentary behaviors, such as digital activities. (2|⊕○○○)

4.5 We suggest that the health care team identify maladaptive rearing patterns related to diet and activity and educate families about healthy food and exercise habits. (2|⊕○○○)

4.6 We suggest that the health care team probe for and diagnose unhealthy intrafamily communication patterns and support rearing patterns that seek to enhance the child's or adolescent's self-esteem. (2|⊕○○○)

4.7 We suggest that the health care team evaluate for psychosocial comorbidities and prescribe assessment and counseling when psychosocial problems are suspected. (2|⊕○○○)

4.8 We suggest pharmacotherapy for children or adolescents with obesity only after a formal program of intensive lifestyle modification has failed to limit weight gain or to ameliorate comorbidities (2|⊕○○○). We recommend against using obesity medications in children and adolescents <16 years of age who are overweight but not obese, except in the context of clinical trials. (1|⊕○○○)

4.9 We suggest that Food and Drug Administration (FDA)–approved pharmacotherapy for obesity be administered only with a concomitant lifestyle modification program of the highest intensity available and only by clinicians who are experienced in the use of anti-obesity agents and are

aware of the potential for adverse reactions. (2|⊕○○○)

4.10 We suggest that clinicians should discontinue medication and reevaluate the patient if the patient does not have a >4% BMI/BMI *z* score reduction after taking antiobesity medication for 12 weeks at the medication's full dosage. (2|⊕○○○)

4.11 We suggest bariatric surgery only under the following conditions:

- the patient has attained Tanner 4 or 5 pubertal development and final or near-final adult height, the patient has a BMI of >40 kg/m^2 or has a BMI of >35 kg/m^2 and significant, extreme comorbidities
- extreme obesity and comorbidities persist despite compliance with a formal program of lifestyle modification, with or without pharmacotherapy
- psychological evaluation confirms the stability and competence of the family unit [psychological distress due to impaired quality of live (QOL) from obesity may be present, but the patient does not have an underlying untreated psychiatric illness]
- the patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits
- there is access to an experienced surgeon in a pediatric bariatric surgery center of excellence that provides the necessary infrastructure for patient care, including a team capable of long-term follow-up of the metabolic and psychosocial needs of the patient and family. (2|⊕⊕○○)

4.12 We suggest against bariatric surgery in preadolescent children, pregnant or breast-feeding adolescents (and those planning to become pregnant within 2 years of surgery), and in any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder. (2|⊕○○○)

Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee of the Endocrine Society deemed prevention and treatment of pediatric obesity a priority area in need of practice guidelines and appointed a Task Force to formulate evidence-based recommendations. The Task Force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation group, an international group with expertise in the development and implementation of evidence-based guidelines (2). A detailed description of the grading scheme has been published elsewhere (3). The Task Force used the best available research evidence to develop the recommendations. The Task Force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of a recommendation, strong recommendations use the phrase "we recommend" and the number 1, and weak recommendations ue the phrase "we suggest" and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕○○○ denotes very low quality evidence; ⊕⊕○○, low quality; ⊕⊕⊕○, moderate quality; and ⊕⊕⊕⊕, high quality. The Task Force has confidence that persons who receive care according to the strong recommendations will derive, on average, more good than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the values that the Task Force considered in making the recommendation; in some instances, there are remarks, a section in which the Task Force offers technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the Task Force and their values and preferences; therefore, one should consider these remarks as suggestions.

In this guideline, the Task Force made several statements to emphasize the importance of shared decision making, general preventive care measures, and basic principles of pediatric obesity prevention and treatment. They labeled these as "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised, and thus considered out of the scope of this guideline. The intention of these statements is to draw attention and remind providers of these principles; one should not consider these statements as graded recommendations (4).

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All Task Force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The Clinical Guidelines Subcommittee reviews all conflicts of interest before the Society's Council approves the members to participate on the Task Force and periodically during the development of the guideline. All others participating in the guideline's development must also disclose any conflicts of interest in the matter under study, and most of these participants must be without any conflicts of interest. The Clinical Guidelines Subcommittee and the Task Force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests [*e.g.*, stocks and stock options (excluding diversified mutual funds)]; honoraria and other payments for participation in speakers' bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

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The Endocrine Society provided the funding for this guideline; the Task Force received no funding or remuneration from commercial or other entities.

Commissioned Systematic Review

The Task Force commissioned 2 systematic reviews to support this guideline [Treatments of Pediatric Obesity: An Umbrella Systematic Review (5); The Association of Weight Loss and Cardiometabolic Outcomes in Obese Children: Systematic Review and Meta-Regression (6)]. The first was an umbrella review of randomized controlled trials (RCTs) that had a duration >6 months and evaluated medication, surgery, lifestyle, or community-based interventions in overweight or obese children or adolescents. The purpose of this review was to estimate the effectiveness of these interventions and to rate the quality of supporting evidence. This review summarized data from 133 RCTs enrolling 30,445 patients and provided an evidence profile for each intervention. The second was a study-level meta-regression that identified changes in BMI associated with cardiometabolic changes (lipid panel, liver function tests, systolic blood pressure, diastolic blood pressure, hemoglobin A1c (HbA1c), and fasting blood glucose) in pediatric overweight and obese subjects.

The Problem With Obesity

Pediatric obesity is a persistent, epidemic, international problem, and preventing pediatric obesity and its comorbidities is of paramount importance. Treating children or adolescents is difficult and requires changes in diet, activity, and environment. Intensive lifestyle interventions, contacting both patient and family at least monthly (and weekly if possible) for the first 3 months, and providing dietary and nutritional education, a physical activity prescription, and behavioral therapy are poorly reimbursed, which often impedes these services. Additionally, there is inadequate national and international recognition of the value of addressing global obesity prevention and treatment, and we must work with key policymakers to improve this. Elevated BMI among US children and adolescents 6 to 19 years of age is associated with 1.4 billion dollars of additional health care dollars for outpatient visits and other health care expenditures compared with children and adolescents with normal BMIs (7). The Brookings Institution predicted that if all 12.7 million US children and adolescents with obesity became obese adults, the individual average cost would be >$92,000, and the societal costs during their lifetimes might be >$1.1 trillion (8).

1.0 Diagnosing overweight and obesity

1.1 We recommend using BMI and the CDC normative BMI percentiles to diagnose overweight or obesity in children and adolescents ≥2 years of age. (1|⊕⊕⊕○)

1.2 We recommend diagnosing a child or adolescent >2 years of age as overweight if the BMI is ≥85th percentile but <95th percentile for age and sex, as obese if the BMI is ≥95th percentile, and as extremely obese if the BMI is ≥120% of the 95th percentile or ≥35 kg/m^2 (1|⊕⊕○○). We suggest that clinicians take into account that variations in BMI correlate differently to comorbidities according to race/ethnicity and that increased muscle mass increases BMI. (2|⊕○○○)

1.3 We suggest calculating, plotting, and reviewing a child's or adolescent's BMI percentile at least annually during well-child and/or sick-child visits. (Ungraded Good Practice Statement)

1.4 We suggest that a child <2 years of age be diagnosed as obese if the sex-specific weight for recumbent length is ≥97.7th percentile on the WHO charts, as US and international pediatric groups accept this method as valid. (2|⊕○○○)

Definitions

Children and adolescents ≥2 years of age are diagnosed as overweight if the BMI is ≥85th percentile but <95th percentile and obese if the BMI is ≥95th percentile for age and gender on the revised 2000 CDC charts. A child <2 years of age is obese if the weight for recumbent length is ≥97.7th percentile of WHO growth standards (9). Extreme obesity is defined as a BMI ≥120% of the 95th percentile or ≥35 kg/m^2 (10). A recent proposal suggests redefining this state as class 2 obesity, as it relates to the definition of class 2 obesity in adults; class 3 pediatric obesity is proposed (but not yet fully accepted) to be BMI ≥140% of the 95th percentile or ≥40 kg/m^2, as this is considered to represent an even higher risk group. Class 2 and class 3 obesity are increasing significantly in girls of all ages, most clearly between 6 and 11 years of age, and in boys between 12 and 19 years of age with a nonsignificant trend in boys <12 years of age (11).

Evidence

The CDC BMI charts (12) are the accepted standards for US children and adolescents ≥2 years of age and provide a means for determining changes in pediatric obesity prevalence. The US Preventive Services Task Force found that the BMI of children and adolescents correlates reasonably well to percentile rankings of percent body fat measured by more direct methods (13). However, BMI

cannot differentiate muscle from adipose tissue, and thus cannot differentiate between excess adipose tissue and increased lean muscle mass when classifying a child or adolescent as overweight or obese. Pediatric racial/ethnic differences in the percentage of fat at a specific BMI further complicate BMI measures; for example, non-Hispanic black children and adolescents have a lower percentage body fat than do comparable non-Hispanic whites or Mexican Americans at the same BMI, and they are less likely to have high adiposity (14). Additionally, Singapore Chinese adolescents have a higher percentage fat at the same BMI than do white comparison groups (15). Furthermore, in the 1999–2002 National Health and Nutrition Examination Survey obese male Hispanic adolescents had a higher risk of hepatic steatosis than did girls and other ethnic groups, indicating the limits of BMI alone as a risk factor (16). A systematic review found differences in regional mass and body composition in adults between race/ethnic groups when BMI and height are held constant and further differences within the same gender and race/ethnic group by age (17). Therefore, although we do recommend using BMI in clinical practice, it is not an infallible indicator of overweight or obesity. Clinicians should consult endocrinologists when questions arise.

The prevalence of pediatric overweight and obesity in all racial and ethnic groups increased between the 1960s and 1970s until about 2000 when it leveled off in most groups (Table 1). As of 2014, the prevalence of obesity in subjects 2 to 19 years old is 17%. The reason 17% of the population is above the 95th percentile for age is that the CDC only uses weight data prior to 1980 (using NHANES II data) for ages >6 years (before the obesity epidemic developed) and uses height data up to the end of 1994 (the end of NHANES III data collection) for the stature charts. Some recent data suggest a decrease in the prevalence of overweight and obesity in children <5 years of age, but the durability of this potential decline remains unknown. This trend may be explained by the oversampling of Asian preschoolers in that particular dataset; these children had a lower overall BMI.

Different racial and ethnic populations demonstrate differences in the prevalence of obesity and overweight and in the trajectory of change during the last decades (Table 1). Thus, using these BMI definitions may underestimate risk to the health of pediatric Asian patients. Furthermore, a recent meta-analysis including 53,521 patients between a mean age of 4 to 18 years demonstrated that using these BMI cutoffs led to a specificity of 0.93 but a sensitivity of only 0.73 when compared with reference standard methods for measuring body adiposity, such as dual energy X-ray absorptiometry, hydrostatic weighing, air-displacement plethysmography, isotope dilution, bioelectrical impedance analysis, and skin-fold thickness measurements. This suggests that most children and adolescents diagnosed as obese by BMI do indeed have excess fat, but that a normal BMI is compatible with excess body fat in ~25% of subjects (22). Clinical judgment must augment the definitions of obesity based on BMI alone to determine which children or adolescents are actually overfat.

The odds ratio of adult obesity increases for obese adolescents as they approach 18 years of age. The odds ratio of adult obesity rises progressively with the number of parents who are obese, but the greatest predictive effect of parent obesity is found in infancy regardless of the infant's weight (23). Determining overweight or obesity in young children may also help identify which individuals are most likely to become overweight or obese in adulthood. There is an increase in BMI in the first year followed by a fall and then a second rise in BMI at about 6 years of age (termed the adiposity rebound); an early BMI rebound before 5 years of age carries a higher risk for adult obesity. Recent analysis suggests that BMI (or possibly just height) at 7 years of age may provide equally robust predictive ability (24). Longitudinal data from 7738 participants from the National Center for Educational Statistics, Early Childhood Longitudinal Study, Kindergarten Class of 1998–1999 demonstrated the greatest incidence (new onset) of obesity and overweight between the first to third grades; furthermore, there was a fourfold higher risk for obesity at age 14 years in the subjects overweight in kindergarten. These data support a focus on prevention before 9 years of age (25). However, a longitudinal study of 4884 subjects from the National Longitudinal Survey of Youth, the Population Study of Income Dynamics, and the National Health and Nutrition Evaluation Surveys demonstrated that screening for obesity at 5 years of age would miss 50% of those who became obese by 18 years of age, whereas screening at 15 years of age would miss only 9%; the authors recommend using universal prevention methods instituted at a young age and continuing through childhood and adolescence, rather than focusing only on overweight young children (26). These contrasting study conclusions demonstrate a continued need for research into childhood prediction of obesity.

Values and preferences

The Task Force placed a high value on the ease of calculating BMI and familiarity with this measure among providers and patients over other limitations of using BMI. BMI currently is the most reasonable measure for evaluating overweight and obesity, guiding proper

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Table 1. Prevalence of Pediatric Overweight and Obesity in the United States

	Obesity				Combined Overweight and Obesity		
Age	1963–1970	1999–2000	2004	2011–2014	1999–2000	2003–2004	2011–2012
0–23 mo	7.20%	11.60%		8.10%			
2–5 y	5	10.50%	13.90%	8.90%	22.0%	26.50%	22.80%
6–11 y	4.20%	15.30%	18.80%	17.50%	29.8%	37.20%	34.20%
12–19 y	4.60%	15.50%	17.40%	20.50%	30.0%	34.30%	34.50%
2–19 y		13.9%	17.1%	17.0%	28.2%	33.60%	31.80%
12–19 y by race			Hispanic	21.90%	43.3	34.3%	38.1
			Boys	22.4	43.6	37.3%	39.6%
			Girls	221.4	42.9	31.1%	36.5%
			African American	19.50%	39.5	36.5%	39.8%
			Boys	18.40%	35.6	31.4%	37.3%
			Girls	20.70%	43.7	42.1%	42.5%
			White	14.70%	26.2	34.7%	31.2%
			Boys	14.30%	27.4	38.70%	31.5%
			Girls	15.10%	24.8	30.4%	31.0%
			Asian	8.60%	—	—	24.6%
			Boys	11.80%	—	—	33.9%
			Girls	5.30%	—	—	15.0%
			All	16.90%	30.0	34.30%	34.5%
			Boys	16.90%	30.0	36.8%	35.1%
			Girls	17.10%	30.0	31.70%	33.8%

Years of study for all ethnicities are noted under the column headings "Obesity" and "Combined Overweight and Obesity." [Derived from Ogden *et al.*, 2015 (18), Hedley *et al.*, 2004 (19), Ogden *et al.*, 2014 (20), and Ogden *et al.*, 2002 (21).]

management, and determining the need for specialist referral (when values rise toward the extreme). The utility of predicting adult obesity and comorbidities from childhood and adolescent BMI calculations may be somewhat limited, supporting a universal prevention approach to obesity that begins in early childhood.

1.5 We recommend against routine laboratory evaluations for endocrine etiologies of pediatric obesity unless the patient's stature and/or height velocity are attenuated (assessed in relationship to genetic/familial potential and pubertal stage). (1|⊕⊕⊕◯)

Evidence

Endocrine and syndromic disorders as a cause of overweight/obesity are rare in children and adolescents and are associated with additional symptoms (26). The distinguishing feature of endocrine causes of obesity, such as growth hormone (GH) deficiency, hypothyroidism, or Cushing syndrome, is that stature and height velocity are decreased, whereas a normal or increased growth rate generally excludes endocrine causes. However, Albright hereditary osteodystrophy/pseudohypoparathyroidism, although associated with short stature in adolescence, may be associated with increased growth velocity in the first 2 to 3 years of life. Pediatric overweight/obesity is also associated with earlier breast development, pubarche, and menarche in girls, and advanced skeletal development in boys that will lead to increased growth rate (27–30). The evidence is stronger in girls than boys because a subgroup of boys with obesity exhibit delayed testicular development (31). Thus, clinicians should not test for endocrine causes of obesity unless the patient is short relative to genetic potential and has decreased growth velocity against the backdrop of continued weight gain (26, 32).

This rule is not inviolable, however, as acquired hypothalamic obesity is a syndrome of intractable weight gain caused by hypothalamic damage from a tumor or its treatment with surgery or radiotherapy (33). Such patients may have adequate growth velocity even when GH deficient but have tumor-related signs and symptoms or have already undergone tumor treatment.

Values and preferences

The Task Force placed a high value on limiting endocrine assessments for the etiology of pediatric overweight or obesity to those rare patients who are obese and short or with decreased height velocity and placed a low value on the unnecessary diagnostic endocrine laboratory screening of children and adolescents who are obese without other signs or symptoms or contributory neurosurgical history.

Remarks

Clinicians can determine a deceleration in height velocity (as needed to account for the stage of puberty) either by using a height velocity (34) curve normalized for age and/or

stage of puberty or by observing that the patient is crossing height percentile curves downward on the standardized height attainment charts (12) for average-maturing, early-maturing, and late-maturing children (35). Clinicians should refer maturing children who are obese with short stature and decreased growth velocity despite continued weight gain to a pediatric endocrinologist, as these patients may have an endocrinopathy.

1.6 We recommend that children or adolescents with a BMI ≥85th percentile be evaluated for potential comorbidities (see Table 2 and Fig. 1). (1|⊕⊕⊕○)

1.7 We recommend against measuring insulin concentrations when evaluating children or adolescents for obesity. (1|⊕⊕⊕○)

Evidence

Pediatric overweight and obesity is associated with substantial comorbidities, including prediabetes/type 2 diabetes mellitus (T2DM); dyslipidemia; prehypertension/hypertension; sleep apnea; nonalcoholic fatty liver disease (NAFLD); proteinuria and focal segmental glomerulosclerosis; early subclinical atherosclerosis; hyperandrogenemia/polycystic ovary syndrome (PCOS); slipped capital femoral epiphysis and pseudotumor cerebri (36–42); and cardiovascular disease (CVD) morbidity, and premature mortality in adulthood (43–47). The greater the severity of obesity, the higher the risks of cardiometabolic risk factors, particularly among boys (11). Importantly, the risks of CVD outcomes among children and adolescents who were obese and became nonobese by adulthood appear similar to those who were never obese (46). Thus, clinicians should carefully examine medical and family histories and laboratory assessments of children and adolescents who are overweight or obese to identify comorbidities early and initiate appropriate management.

Values and preferences

The Task Force placed a high value on identifying adiposity-related complications and screening for comorbidities because of their high prevalence and their association with morbidity and mortality. The Task Force also placed a high value on reducing unnecessary testing and evaluation, such as the routine measurements of fasting insulin, because of lack of scientific evidence for its usefulness in clinical practice by general providers.

Remarks

A thorough medical and family history is crucial for assessing obese youths, because obesity and associated comorbidities may be asymptomatic/subclinical but have familial tendencies. The family history should encompass obesity; bariatric surgery (typically not revealed by families unless specifically asked); T2DM; gestational diabetes; dyslipidemia; hypertension; NAFLD; cirrhosis; sleep apnea and use of continuous positive airway pressure; premature CVD events/deaths (such as heart attacks or strokes); and (in women) infertility, PCOS, or hyperandrogenism-associated signs and symptoms. Clinicians should assess the presence of polyuria/polydipsia, blurry vision, fungal vaginitis/discharge in girls, and unexplained weight loss, all of which could be indicative of hyperglycemia. Clinicians should also look for the presence of frequent unexplained headaches, which raise the possibility of hypertension or sleep apnea; habitual snoring, restless sleep, morning headaches, generalized tiredness, and/or excessive daytime sleepiness, as well as hyperactive inattentive behavior in young children as manifestations of sleep apnea (48); gastrointestinal discomfort as a manifestation of NAFLD (39); musculoskeletal symptoms (49); and (in pubertal girls) acne, hirsutism (including the recent use of hair removal techniques that would mask the degree of hirsutism at the time of the examination), and onset and pattern of menses to screen for the possibility of PCOS. Clinicians should obtain a careful history for psychiatric disorders, because children and adolescents who are overweight or obese are more likely to suffer from mental health disorders than their normal weight counterparts (50, 51). Furthermore, clinicians should obtain a history of second-generation antipsychotics use, such as clozapine, risperidone, olanzapine, and quetiapine, because of their association with weight gain (52, 53). Although the various techniques assessing dietary intake are unreliable and subject to error (9, 54), it is still important to estimate the type and quantity of beverage intake, the frequency of dining out and where, and the frequency and type of snacks (among other dietary issues). Clinicians should also obtain a history of sedentary behaviors, such as hours spent on screen activities, and physical activity (*e.g.*, duration, frequency, in school and at home, sports participation, walking to school and stores).

Clinicians should evaluate the following:

- weight, height, and BMI calculation [Even though the International Diabetes Federation includes waist circumference (an indicator of insulin resistance measured at the level of the iliac crest ≥ 90th percentile) as a defining factor for metabolic syndrome in children and adolescents 10 to 16 years of age and as a finding of concern in children 6 to 10 years old (55, 56), given the intermeasurement variability of waist circumference measurements in a clinical setting performed by different support staff, this research tool does not add significantly to what we learn from BMI (57).]

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Table 2. Screening for Comorbidities of Pediatric Overweight or Obesity

Comorbidity	Tests and Interpretation	Source
Prediabetes HbA1c	5.7% to <6.5% (39 to <48 mmol/mol) (note the unpredictability of this test in pediatrics in the text)[a]	American Diabetes Association (59)
IFG (verify fasting status)	Fasting plasma glucose of ≥100 but <126 mg/dL (≥5.6 but <7.0 mmol/L)	
IGT (if OGTT is used)	Two-hour glucose of ≥140 but <200 mg/dL (≥7.8 but <11.1 mmol/L)	
Diabetes mellitus	HbA1c ≥ 6.5% (≥48 mmol/mol)[a,b] Fasting plasma glucose of ≥126 mg/dL (≥7.0 mmol/L) (fasting is defined as no caloric intake for 8 h)[b] Two-hour plasma glucose of ≥200 mg/dL (≥11.1 mmol/L) during an OGTT[b] In a patient with classic symptoms of hyperglycemia, a random plasma glucose of ≥200 mg/dL	American Diabetes Association (59)
Dyslipidemia	Fasting lipids Triglycerides (mg/dL) (multiply by 0.0113 to convert to mmol/L): 0–9 y < 75 (acceptable), 75–99 (borderline high), ≥100 (high); 10–19 y < 90 (acceptable), 90–129 (borderline high), ≥130 (high) LDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <110 (acceptable), 110–129 (borderline high), ≥130 (high) Total cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <170 (acceptable), 170–199 (borderline high), ≥200 (high) HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <40 (low), 40–45 (borderline low), >45 (acceptable) Non–HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L) (can be nonfasting) <120 (acceptable), 120–144 (borderline high), ≥145 (high)	Expert Panel Summary Report (58)
Prehypertension and hypertension	3–11 y: (standardized according to sex, age, and height percentile) BP > 90th percentile to <95th percentile = prehypertension BP ≥ 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP ≥ 99th percentile + 5 mm Hg = stage 2 HTN 12–17 y: (standardized according to sex, age, and height percentile) BP of >90th percentile to <95th percentile or >120/80 = prehypertension BP ≥ 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP ≥ 99th percentile + 5 mm Hg = stage 2 HTN 18 to 21 y: BP ≥ 120/80 to 139/89 mm Hg = prehypertension BP ≥ 140/90 to 159/99 mm Hg = stage 1 HTN BP ≥ 160/100 to 179/109 mm Hg = stage 2 HTN BP > 180/110 mm Hg = stage 3 HTN	Expert Panel Summary Report (58); Mancia *et al.*, 2013 (61)
NAFLD	ALT > 25 U/L (boys) and >22 U/L (girls)	Schwimmer *et al.*, 2010 (62)
PCOS	Free and total testosterone and SHBG, per Endocrine Society PCOS guidelines[c]	Legro *et al.*, 2013 (63)
Obstructive sleep apnea	If positive history, refer to pulmonary for nocturnal polysomnography and if not available overnight oximetry	Wise *et al.*, 2011 (48)
Psychiatric	If positive history, refer to mental health specialist	Zamethkin *et al.*, 2004 (51)

To convert mg/dL to mmol/L, multiply by 0.0555 for glucose, 0.0259 for cholesterol, and 0.0113 for triglycerides.

Abbreviations: BP, blood pressure; HDL, high-density lipoprotein; HTN, hypertension; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LDL, low-density lipoprotein; NAFLD, non-alcoholic fatty liver disease; OGTT, oral glucose tolerance test (1.75 g/kg, maximum 75 g); PCOS, polycystic ovary syndrome.

[a]The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

[b]In the absence of unequivocal hyperglycemia, should be confirmed by repeat testing.

[c]Given variability in testosterone levels and the poor standardization of assays, it is difficult to define an absolute level that is diagnostic of PCOS or other causes of hyperandrogenism (familiarity with local assays recommended) (63). The preferred assay is HPLC tandem mass spectroscopy (64). [Derived from (a) ADA, 2014 (60); (b) Expert Panel 2011 (58); (c) Schwimmer *et al.*, 2010 (62); (d) Legro *et al.*, 2013 (63); (e) Wise *et al.*, 2011 (48); (f) Zametkin *et al.*, 2004 (51)].

- blood pressure [using height/age/sex percentile normalized blood pressure tables to interpret the findings (58)]
- acanthosis nigricans and skin tags
- extreme acne and hirsutism in pubertal girls
- fundoscopic examination for pseudotumor cerebri
- tenderness and range of motion of the knee, leg, or foot
- peripheral edema, thyroid examination for goiter
- physical findings associated with syndromic obesity, particularly if there is a neurodevelopmental abnormality (see section 3).

We list suggested screening tests in Table 2.

In 2009 an International Expert Committee recommended using HbA1c to diagnose diabetes and prediabetes (65). It recommended classifying asymptomatic individuals as having diabetes if they had HbA1c ≥ 6.5% (≥48 mmol/mol) on 2 separate occasions and classifying asymptomatic individuals with prediabetes if they had HbA1c ≥ 6.0% (≥42 mmol/mol) (65), or HbA1c of 5.7% to <6.5% (39 to <48 mmol/mol) (66). Although they based these recommendations on studies in adults with no validation in pediatrics (65), the committee recommended that the same criteria be applied in adolescents. However, several studies have demonstrated poor performance of HbA1c in diagnosing prediabetes or diabetes in pediatrics, underestimating the prevalence of both (67–69). Another pitfall in using the HbA1c is the unresolved issue of racial/ethnic disparities in the correlation between HbA1c and ambient blood glucose (70). Given such drawbacks, HbA1c screening (alone) in overweight or obese children and adolescents is a poor diagnostic tool for prediabetes and T2DM. Additional definitive testing (fasting or random glucose or oral glucose tolerance test) may be necessary in high-risk youths based on medical history, familial risk, race/ethnicity, and/or the presence of additional risk factors for diabetes (71). In a cost effectiveness analysis of various screening strategies for identifying pediatric diabetes and dysglycemia, the preferred strategy for dysglycemia was the 2-hour oral glucose tolerance test with 100% effectiveness (proportion of cases identified) and efficiency (cost per case identified) at $390 per case, and the least effective and efficient was HbA1c (ranges, 7% to 32% and $938 to $3370 per case) (72).

NAFLD is usually asymptomatic and thus requires screening for detection. Presently, no screening guidelines exist outside of recognizing those at risk by weight categorization (BMI ≥ 85% for age and sex) (39). Recently new normative standards were proposed for alanine aminotransferase (ALT) concentrations (≤25 U/L for boys and ≤ 22U/L for girls) (62), because pediatric liver biopsy specimens from patients with normal or mildly elevated ALT (≥26 to 50 U/L for boys and ≥23 to 44 U/L for girls) had significant histologic abnormalities, including advanced fibrosis (73). Using highly sensitive research methods of magnetic resonance spectroscopy or magnetic resonance imaging, fatty liver is likely present in most pediatric obesity whether the liver enzymes are high or not. High ALT levels would suggest a more advanced stage of NAFLD, hepatitis, or fibrotic changes. Thus, even though ALT elevation underestimates liver injury in NAFLD, it is still an easily available screen for clinicians to use when assessing children and adolescents who are overweight or obese.

Many clinicians measure insulin values thinking it adds to the diagnosis of comorbidities. In fact it does not, and such measurements are not recommended. Although obesity is associated with insulin resistance/hyperinsulinemia, attempts to diagnose insulin resistance by measuring plasma insulin concentration or any other surrogate (74) in the clinical setting has no merit because it has no diagnostic value. Fasting insulin concentrations show considerable overlap between insulin-resistant and insulin-sensitive youths (74). Therefore, there is no well-defined cut point differentiating normal from abnormal and no universally accepted, clinically useful, numeric expression that defines insulin resistance (75), unlike the case for glucose or lipids. A major requirement for any screening program is the availability of an accurate, reliable, reproducible, standardized, and easily applicable method of measurement. Adult studies have shown that measures of fasting insulin explain no more than 5% to 50% of the variability in insulin sensitivity in nondiabetic subjects (76). Different studies have proposed different cutoffs for so called "insulin resistance values" varying by 2.5-fold (76). In pediatrics, the transient puberty-related insulin resistance that occurs with the completion of puberty further complicates this (77, 78). Moreover, measuring insulin is hampered by the lack of standardized insulin assays, and poor reproducibility of even the same assay (79). Further limitations include race/ethnicity-related differences in insulin concentrations due to differences in the metabolic clearance rate of insulin (80) and the cross-reactivity between insulin and proinsulin. In youths with T2DM, despite severe deficiency in insulin secretion, fasting insulin concentrations are higher than in youths without diabetes (81). Importantly, fasting insulin concentrations are similar in youths who are obese with normal glucose tolerance vs impaired glucose tolerance (82), allowing for the possible danger of missing a diagnosis of impaired glucose tolerance if one uses fasting insulin concentrations as a screening tool. Because of these limitations, measuring plasma insulin concentrations remains a research tool with no clinical value for evaluation of obesity. Measuring fasting

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insulin concentrations to try to diagnose insulin resistance within general practice should be abandoned.

2.0 Genetic obesity syndromes

2.1 We suggest genetic testing in patients with extreme early onset obesity (before 5 years of age) and that have clinical features of genetic obesity syndromes (in particular extreme hyperphagia) and/or a family history of extreme obesity. (2|⊕⊕○○)

Evidence

In addition to the obvious environmental drivers, multiple common and rare genetic variants contribute to substantial heritability for BMI and waist circumference (83, 84). Approximately 7% of patients with extreme pediatric obesity may have rare chromosomal abnormalities and/or highly penetrant genetic mutations that drive their obesity (85). This percentage is likely to increase with newer methods for genetic testing.

Values and preferences

When assessing children and adolescents with extreme obesity, clinicians should consider potentially treatable causes and genetic conditions (Fig. 1). The diagnosis of a genetic obesity syndrome can provide information that helps the family and health care providers appropriately manage the child's or adolescent's health and possibly lessen the social stigma. Additionally, clinicians can provide genetic counseling. A genetic diagnosis can inform management, including the possibility of bariatric surgery (many such patients are relatively resistant to weight loss through changes in diet and exercise).

Remarks

It is currently useful to categorize genetic obesity syndromes as those with developmental delay and/or dysmorphism and those without these features, although the clinical spectrum can be quite variable (Table 3). Clinicians should obtain a careful family history to identify potential consanguineous relationships, a family history of severe obesity/bariatric surgery, the ethnic and geographical origin of the child or adolescent, and family members to guide the appropriate use of diagnostic tests (Fig. 1).

Obesity syndromes with developmental delay

Dominant disorders

Prader-Willi syndrome is a methylation disorder caused by the deletion of a critical segment on the paternally inherited chromosome 15q11.2-q12, loss of the entire paternal chromosome 15 with the presence of 2 maternal copies (uniparental maternal disomy), or an imprinting defect that can be sporadic or due to a mutation of the paternally derived imprinting control site of the 15q13 region (88). Plasma ghrelin levels are markedly elevated in children, adolescents, and adults with Prader-Willi syndrome, although the physiological relevance of this finding is unknown (89). GH treatments decrease body fat and increase linear growth, muscle mass, and energy expenditure (90).

Maternal transmission of heterozygous mutations in GNAS1 leads to classical Albright hereditary osteodystrophy and resistance to several hormones that activate heterotrimeric G proteins in their target tissues, whereas paternal transmission leads only to Albright hereditary osteodystrophy (91).

Chromosomal rearrangements and heterozygous mutations involving single-minded 1 brain-derived neurotrophic factor (92, 93), or its receptor, TrkB, lead to hyperphagia and developmental and behavioral abnormalities (94, 95). Clinicians should consider *de novo* mutations if both parents are of normal weight and intelligence quotient.

Recessive disorders

Homozygous mutations that disrupt 1/some of the 16 Bardet-Biedl syndrome genes lead to Bardet-Biedl syndrome (96). Other recessive disorders affecting proteins localized to the basal body of the monocilium, such as Alström syndrome and TUB gene mutations (97), are also associated with obesity.

Obesity syndromes without developmental delay

Rare copy number variants (deletions/duplications) that disrupt multiple genes can cause extreme pediatric obesity without learning difficulties (98). Mutations in specific genes, mostly involving the leptin–melanocortin pathway, cause extreme obesity characterized by hyperphagia (increased drive to eat) and impaired satiety (reduced sensation of fullness after a meal) (Table 3). Clinicians should take a careful history to identify food-seeking behavior, searching for/stealing food, waking at night to find food, and eating food others leave behind, which should prompt genetic investigation (neurologic causes should be excluded in patients with a new history of these behaviors). These behaviors typically occur as a result of the disruption of hypothalamic pathways involved in the regulation of energy balance. Pica syndrome is evident in only a small subset of children and adolescents with hyperphagia.

Dominant disorders

Heterozygous mutations in the melanocortin 4 receptor are found in 2% to 5% of subjects with extreme pediatric obesity, making this the most common genetic form of obesity (99, 100) (Table 3). Homozygous mutations in

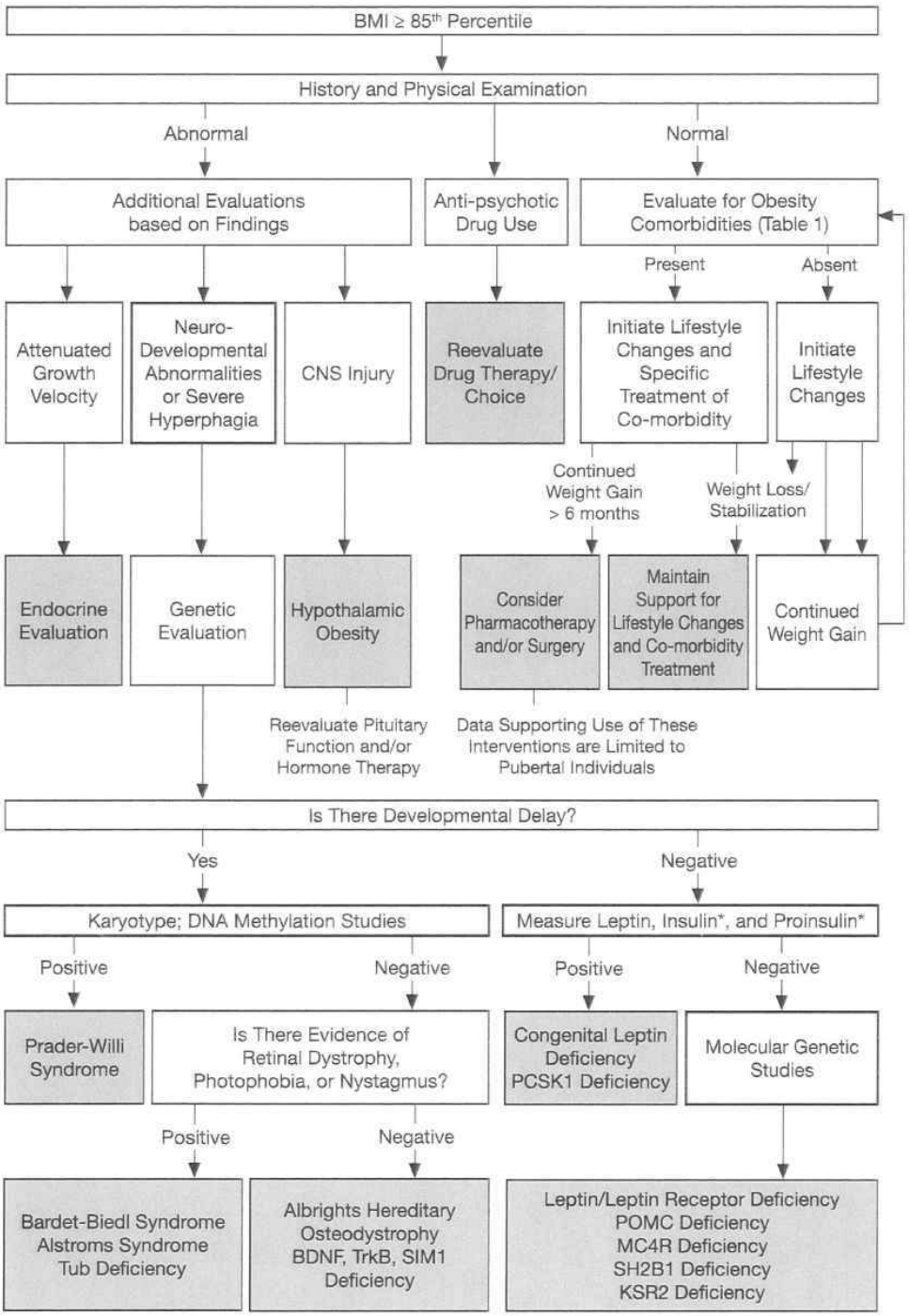

Figure 1. Diagnosis and management flowchart. *Measure insulin and proinsulin in patients with clinical features of PCSK1 deficiency. [Adapted from August GP *et al.* (86) with permission, © Endocrine Society.] [Republished with permission of Springer Science and Bus Media BV from Farooqi S and O'Rahilly S (87); permission conveyed through Copyright Clearance Center, Inc.]

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Table 3. Genetic Obesity Syndromes With and Without Developmental Delay

Genetic Obesity Syndrome	Clinical Features
Obesity with developmental delay	
Dominant	
Prader-Willi syndrome	Hypotonia, failure to thrive in infancy followed by weight gain, short stature (due to GH deficiency), hyperphagia, hypogonadotropic hypogonadism, sleep disturbance, obsessive behaviors
Albright hereditary osteodystrophy	Short stature in some but not all patients, skeletal defects, impaired olfaction, and hormone resistance (*e.g.*, parathyroid hormone) if a mutation is maternally inherited
SIM1 deficiency	Hyperphagia with autonomic dysfunction (characterized by low systolic blood pressure), speech and language delay, neurobehavioral abnormalities, including autistic type behaviors
BDNF/TrkB deficiency	Hyperactivity, impaired concentration, limited attention span, impaired short-term memory and pain sensation
Recessive	
Bardet-Biedl syndrome	Dysmorphic extremities (syndactyly/brachydactyly/polydactyly), retinal dystrophy or pigmentary retinopathy, hypogonadism, renal abnormalities/impairment
TUB deficiency	Retinal dystrophy, deafness
Obesity without developmental delay	
Dominant	
Alström syndrome	Retinal dystrophy; extreme insulin resistance; deafness; dilated cardiomyopathy; progressive pulmonary, hepatic, and renal dysfunction
MC4R deficiency	Hyperphagia, accelerated linear growth, disproportionate hyperinsulinemia, low/normal blood pressure
SH2B1 deficiency	Hyperphagia, disproportionate hyperinsulinemia, early speech and language delay that often resolves, behavioral problems including aggression
KSR2 deficiency	Mild hyperphagia and reduced basal metabolic rate, insulin resistance often with acanthosis nigricans, irregular menses, early development of T2DM
Recessive	
Leptin deficiency	Extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, mild hypothyroidism
Leptin receptor deficiency	Extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, mild hypothyroidism
POMC deficiency	Hyperphagia, cholestatic jaundice or adrenal crisis due to ACTH deficiency, pale skin, and red hair in whites
PCSK1 deficiency	Small bowel enteropathy, hypoglycemia, hypothyroidism, ACTH deficiency, diabetes insipidus

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Abbreviations: ACTH, adrenocorticotropic hormone; BDNF, brain-derived neurotrophic factor; GH, growth hormone; POMC, proopiomelanocortin; T2DM, type 2 diabetes mellitus.

melanocortin 4 receptor have also been identified in offspring from consanguineous families (101). Heterozygous missense mutations affecting proopiomelanocortin-derived peptides and rare variants in melanocortin 2 receptor accessory protein 2 may also contribute to extreme obesity by modulating melanocortin signaling (102, 103). In the near future, selective melanocortin receptor agonists may be feasible therapies for patients with mutations in the melanocortin pathway. Several studies have shown that adolescents and adults with heterozygous melanocortin 4 receptor mutations lose weight following Roux-en-Y gastric bypass (RYGB) surgery (104).

Recessive disorders

Homozygous mutations that reduce the production, secretion, or biological activity of leptin are associated with extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, and mild hypothyroidism; these features can be fully treated with subcutaneous injections of recombinant human leptin (105–107). Recombinant human leptin is currently available on a named patient basis through selected centers.

Serum leptin is a useful test in patients with severe obesity, as undetectable serum leptin is highly suggestive of congenital leptin deficiency. Mutations that result in detectable but bioinactive leptin are rare (107). Serum leptin concentrations are usually appropriate for the degree of obesity in most patients with homozygous mutations in the leptin receptor gene that have comparable clinical features (108) (Table 3).

Children and adolescents who are homozygous or compound heterozygous for mutations in the proopiomelanocortin

gene require long-term corticosteroid replacement, as proopiomelanocortin is a precursor of adrenocorticotropic hormone in the pituitary gland (102). Compound heterozygous or homozygous mutations in the PCSK1 gene, which encodes the processing enzyme (prohormone convertase 1/3), may present in infancy with persistent diarrhea requiring parenteral feeding. An abnormally high level of plasma proinsulin (compared with mature insulin) indicates this possible diagnosis (109).

3.0 Prevention of obesity

The prime objective in addressing the obesity epidemic should be prevention to avoid the comorbidities of obesity. Although beyond the scope of this statement, which addresses postnatal prevention, preconception and prenatal interventions are also of major importance, and the Task Force supports the recommendations of the WHO to address this area of prevention (110).

3.1 We suggest that clinicians promote and participate in the ongoing healthy dietary and activity education of children and adolescents, parents, and communities, and encourage schools to provide adequate education about healthy eating (1). (2|⊕◯◯◯)

Evidence

The authors of the Endocrine Society's previous guideline on pediatric obesity commissioned a meta-analysis (111) which summarized evidence from RCTs that measured the impact of lifestyle interventions to prevent pediatric obesity. The study found modest effects of these interventions; there was decreased sedentary behavior in long-term trials ($P = 0.05$) with a significantly greater effect when directed toward children in contrast to adolescents ($P = 0.02$), reduced unhealthy dietary habits ($P = 0.02$), but only a trend towards increased physical activity ($P = 0.06$–0.07). These beneficial effects did not translate into important changes in BMI (111), but the Task Force recognized that weight maintenance in a growing child or adolescent is as effective as weight loss in an adult. The present committee updated and expanded upon these findings as listed below and in Table 4.

Decreasing caloric intake by consuming more fruits and vegetables and reducing dietary fat and refined carbohydrate intake can decrease the risk of developing obesity and T2DM (152). Many children and adolescents eat fewer than 3 servings of fruits and vegetables a day rather than meeting the US Department of Agriculture dietary recommendation of 5 to 7 fruit and vegetable servings per day. Inadequate consumption of dietary fiber may contribute to excessive weight gain, highlighting the need to continue to address vegetable and whole fruit intake (153). Whole fruit intake increased and fruit juice intake decreased from 2003–2004 to 2009–2010 (154).

Children and adolescents in the public school system in the United States consume up to 40% of their calories at school, so attention to the composition of foods and drinks available to them during the school day is critical (155). New US federal guidelines are encouraging, in that they eliminate trans fat, limit saturated fat, and decrease total sugar content of foods served in schools (156).

Values

The committee places a high value on increasing vegetable and fruit intake to decrease the risk of developing obesity. Calorie-dense, nutrient-poor foods should not be available in the school and school sports environments, where their presence increases their consumption and implies adult assent.

3.2 We recommend that clinicians prescribe and support healthy eating habits such as:

- avoiding the consumption of calorie-dense, nutrient-poor foods (*e.g.*, sugar-sweetened beverages, sports drinks, fruit drinks, most "fast foods" or those with added table sugar, high-fructose corn syrup, high-fat or high-sodium processed foods, and calorie-dense snacks)
- encouraging the consumption of whole fruits rather than fruit juices. (1|⊕⊕◯◯)

Evidence

Drinking sugar and sugar-sweetened beverages is associated with developing obesity (157, 158). Table sugar consists of 50% glucose and 50% fructose; sugar-sweetened beverages often have a higher percentage of fructose, sometimes up to 65%; and high-fructose corn syrup is found in many foods besides liquid beverages. Metabolic responses differ significantly between fructose and glucose.

Consuming nutrient-poor, calorie-dense, high-fat foods and sugar-sweetened beverages is a risk factor for obesity (156). Reducing sugared-beverage consumption (*e.g.*, soda, fruit drinks, sports drinks, and excessive consumption of fruit juices) is an effective way to reduce ingested calories (159). However, children and adolescents currently consume, on average, 30% to 40% of calories from nutrient-poor, energy-dense foods and drinks (160). Although sugar-sweetened beverage intake is decreasing in younger children, it has actually increased since 2007 in adolescents (161). Fruit juice provides a more concentrated dose of carbohydrates than does whole fruit and may not lead to the feeling of satiety experienced after ingesting whole fruits. Thus, healthy children should limit fruit juice ingestion and children with dental caries or excessive weight should ingest less than the maximal

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recommended volumes. Therefore, fruit juice has no role in the diet of infants under 6 months of age. After 6 months of age, fruit juice must be limited to 4 to 6 ounces per day until children reach 6 years of age, after which 8 to 12 ounces is an acceptable serving, according to the American Academy of Pediatrics policy. In view of the fact that it is easy for children to exceed such limits, the Early Childhood Longitudinal Study—Birth Cohort of >4000 children demonstrated that daily ingestion of fruit juice at 2 years of age resulted in an increase in BMI at 4 years compared with children who had no or infrequent fruit juice. The study also demonstrated that whole fruit provides increased nutritional benefit over juice. This committee encourages the consumption of whole fruits rather than fruit juices (162, 163).

Since 1965, teens have doubled their consumption of sugar-sweetened and fruit-flavored beverages (156, 164). School-based interventions can reduce soda consumption and reduce weight in students at the highest BMI percentiles (152, 165). Although there has reportedly been a 95% decrease in the amount of regular sodas shipped to schools, other sweetened beverages (such as sports drinks) have become more available in schools (166).

However, as of 2014–2015, federal guidelines now restrict the use of such "competitive foods" in the school environment. Obese or normal weight children and adolescents who substituted noncaloric beverages in lieu of sugar-sweetened beverages had less of an increase in BMI at 1 year (115, 116). Because there was no difference in satiety between those who drank sugar-sweetened beverages and those who did not, it appears that a child or adolescent will not compensate for the decreased caloric intake of nonsweetened drinks by increasing his or her caloric intake via other foods or drinks. This lack of compensation may partly explain the reduced weight gain associated with nonsweetened drinks (115, 167).

Although there are reports that reducing glycemic load may have a beneficial effect in the prevention or treatment of obesity, a systematic review of epidemiologic, prospective, and intervention studies did not demonstrate consistent results (168).

Water is frequently recommended as a beneficial replacement for sugar-sweetened beverages. Whereas a systematic review found only a weak association between water consumption and weight control in longitudinal studies, the introduction of water jets to New York City elementary school students led to a 0.022 to 0.025 decrease in BMI and a 0.6% to 0.9% decrease in risk for overweight; this is possibly related to a 12.3% decrease in milk purchases (169). Water remains the most reasonable "drinking" choice for quenching thirst and changing behavior from high-sugar drinking habits (170).

Values

The Task Force placed a high value on decreasing access to sugar-sweetened beverages by children and adolescents as a means of obesity prevention and treatment and a high value on strengthening the message to families that these beverages contribute to pediatric obesity.

Remarks

The costs of comorbidities related to pediatric and adult obesity are spiraling, and we must explore measures to limit nonnutritive excess calories as one means of preventing obesity. No nation can afford the social and financial ramifications of increased obesity incidence left unchecked. The individual practitioner cannot prevent obesity alone; a multidisciplinary health care team including dieticians, mental health practitioners, and nurses provides the optimal setting.

However, the committee agrees with the WHO that such changes must reach beyond the clinical setting and require policy changes at the highest level, as well as the cooperation of commercial entities. The committee supports the suggestion by the WHO for worldwide tax leverage on calorie-dense, nutrient-poor foods (110, 171).

3.3 We recommend that children and adolescents engage in at least 20 minutes, optimally 60 minutes, of vigorous physical activity at least 5 days per week to improve metabolic health and reduce the likelihood of developing obesity. (1⊕⊕○○)

Evidence

A common goal for preventing obesity is to increase physical activity and decrease sedentary time in addition to reducing energy intake. A meta-analysis showed a positive association between sedentary time and the risk for obesity, although the effects were small (172). The 2008 Physical Activity Guidelines for Americans (173) and other sources suggest 1 hour of activity per day for children and adolescents at a minimum; although this is a reasonable aspirational goal, the minimal achievable activity level that produces beneficial effects may be less. Shorter bursts of activity, such as 20 minutes a day 3 to 5 days per week, can improve metabolic measurements in obese children and adolescents in a 3 to 6 month period, and these lower activity levels may also prevent obesity (124). The beneficial effects of exercise are most consistent in the heaviest children and adolescents who previously had not engaged in activity. See Table 4 and section 5 on treatment for more information on how activity and sedentary time affect obesity.

Lack of activity may lead to obesity and overweight, but obesity also decreases the coordination and exercise capacity of affected and adolescents, as well as the

likelihood of being chosen for team sports, resulting in an overall decreased desire for physical activity (174–177).

Values

The Task Force placed a high value on interventions with a low potential for adverse effects and burdens such as increasing physical activity and decreasing sedentary time. The benefits on metabolic fitness are regularly demonstrated, although changes in weight or BMI are less consistent.

3.4 We suggest fostering healthy sleep patterns in children and adolescents to decrease the likelihood of developing obesity due to changes in caloric intake and metabolism related to disordered sleep. (2|⊕⊕◯◯)

Evidence

Disordered sleep length and quality in adults, children, and adolescents affects appetite and decreases insulin sensitivity (150). Table 4 lists 8 studies that show how different sleep durations or changes in sleep duration affect dietary intake in children and adolescents. These results suggest that sleep duration affects obesity development, although 2 other studies challenge these findings, weakening the strength of the evidence (130, 131).

Values

The committee puts a high value on ensuring adequate sleep time for all children and adolescents, although the effect on dietary intake and weight gain is not definitive. The National Sleep Foundation recommends 8 to 11 hours of sleep for school age children and adolescents (178).

3.5 We recommend balancing unavoidable technology-related screen time in children and adolescents with increased opportunities for physical activity. (1|⊕⊕◯◯)

Evidence

A systemic analysis of 24 papers reviewing 15 studies demonstrated strong evidence for decreasing screen time and increasing physical activity to prevent obesity (135); another study reported that decreasing screen time decreases sedentary time (136). A 2-generation study associated increased BMI with >2 hours of screen time per day for both parents and offspring (134). Data from >11,000 preschool children 4 to 6 years of age linked increased caloric intake from snacks and sugar-sweetened beverages to increased screen time (135, 179, 180).

Values

There are frequent requirements for video screen use for schoolwork; as technology becomes more prevalent, such requirements will not decrease. However, the committee put a high value on adhering to the American Academy of Pediatrics guidelines limiting discretionary screen time for children (85, 181).

3.6 We suggest that a clinician's obesity prevention efforts enlist the entire family rather than only the individual patient. (2|⊕◯◯◯)

Evidence

A meta-analysis commissioned by the original Task Force demonstrated a nonsignificant trend associating family involvement with the prevention of obesity, especially if the child is <8 years of age (140, 181).

One recent meta-analysis suggested that family-based therapy is effective for treating obesity (137), and another highlighted the importance of the intensity of parental involvement in the success of family interventions to prevent and treat obesity (138). Furthermore, studies of weight loss in obese children and adolescents demonstrated the importance of including family members in the process; without parental inclusion, the effect on weight loss was not significant (182). However, there is a need for more research into the influence of family participation for the prevention or treatment of pediatric obesity (139, 140, 183). In spite of a general consensus that an authoritative parenting style is optimal and restrictive parenting in terms of food choice is not, there are insufficient data to determine what type of parenting approach is most effective in preventing pediatric obesity (184).

Values

The Task Force placed a high value on involving the entire family in obesity prevention efforts as a practical low-risk approach, while understanding that much of the evidence comes from treatment studies and even those studies are not unanimous on the effects of family intervention.

3.7 We suggest clinicians assess family function and make appropriate referrals to address family stressors to decrease the development of obesity. (2|⊕⊕◯◯)

Evidence

There is evidence for an association between the development of pediatric obesity and family dysfunction as well as exposure to stress (Table 4).

Values

The committee placed a high value on fostering healthy family functioning and minimizing pediatric stress, as

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adverse life events are linked to the development of obesity as well as numerous other complications throughout life.

3.8 We suggest using school-based programs and community engagement in pediatric obesity prevention. (2|⊕⊕○○)

Evidence

A school-based program offers the promise of standardization across multiple sites and also can reach large populations of children and adolescents during the early and teenage years.

Numerous school-based interventions focused on reducing obesity rates. The Cardiovascular Health in Children study improved outcomes by decreasing body fat and cholesterol (185). The Cardiovascular Health in Children II study was effective in reducing body fat and blood pressure in middle school children and adolescents (186).

A school-based intervention can reduce body fat and blood pressure in young adolescents (186). One reason the short-term Cardiovascular Health in Children interventions were successful in affecting physiological variables may be the increased time spent in moderate to vigorous physical activity in school (20 minutes per day in elementary schools, 30 minutes in middle schools). Both school design and adult supervision for physical activity affect the amount of physical activity that sixth to eighth graders engage in during free time (187). Additionally, school-based intervention for >4000 middle school children and adolescents at risk for T2DM in the HEALTHY Study Group demonstrated efficacy in decreasing overweight and obesity in both the intervention and control groups, and decreased BMI *z* score, fasting insulin, prevalence of obesity, and percentage of students with waist circumference > 90th percentile in the intervention group (188). School systems have begun to initiate before- and after-school lifetime fitness programs that appear to be helpful in controlling weight gain (189). As noted, evidence supports prevention efforts in the third grade, which could be carried out in an entire school and preschool environment.

There is moderate evidence that community-based pediatric obesity prevention programs, when combined with a school-based component, can have positive 1-year effects on preventing obesity (145). Community-based participatory research may help enhance school-community involvement, resulting in effective obesity prevention programs (146). A review of multiple settings (early care and education, school, community, health providers, and the home) demonstrated strength for each of these approaches and suggested that a combined approach holds more promise (190).

Values

In making these suggestions, the committee set a high value on the ability of school-based programs to reach a wide population that would benefit from obesity prevention and emphasized the need for additional community-based interventions that used techniques coordinated with a school setting.

3.9 We recommend using comprehensive behavior-changing interventions to prevent obesity. Such programs would be integrated with school- or community-based programs to reach the widest audience. (1|⊕⊕○○)

Evidence

A systematic review of RCTs using behavior change techniques to prevent or treat obesity demonstrated that 6 techniques held promise for preventing obesity during a period of at least 6 months. These techniques were:

- providing individualized information on the consequences of behaviors conducive to the development of obesity
- restructuring the environment to make individualized behavior change more successful
- guiding practices expected to decrease the development of obesity
- guiding the identification of role models or advocates to change behavior
- implementing stress management/emotional control training
- providing general communication skills training.

Values

The committee realized the difficulty in providing widespread exposure to behavior change programs but placed a high value on the pursuit of effective techniques of behavior change.

3.10 We recommend breast-feeding in infants based on numerous health benefits. However, we can only suggest breast-feeding for the prevention of obesity, as evidence supporting the association between breast-feeding and subsequent obesity is inconsistent. (1|⊕○○○)

The previous guidelines supported breast-feeding as an effective method of preventing obesity. However, reports on the effect of breast-feeding on preventing obesity are mixed during the last 10 to 15 years. In particular, sibling analyses point to confounding effects

in interpreting the results of cohort studies (151). Furthermore, a 6.5-year-long longitudinal cluster-randomized study of 13,889 subjects demonstrated no effect of breast-feeding on the development of obesity, even among those with more sustained breast-feeding duration (149).

Likewise, 2 meta-analyses showed no strong evidence for the associating between the time of introducing complementary feeding and the development of pediatric overweight or obesity (191, 192).

Values

The committee places high value on promoting breast-feeding to improve infant health but can only suggest breast-feeding as a method for preventing obesity.

Remarks

For most children and adolescents and their families, lifestyle patterns related to eating and exercise are established early, affecting children and adolescents not only when they are young but also throughout life. Health care providers should follow universal prevention methods to avoid the harmful health consequences of less-than-optimal lifestyle choices, conveying to all patients and families in a culturally sensitive and language-appropriate manner the energy needs and essential nutrient requirements of young children, and the importance of physical activity. This is of particular importance when we consider the increased efficacy of prevention trials when directed toward younger children.

The intestinal microflora may influence the development of obesity. Although it is premature to discuss methods of altering the intestinal flora, evidence suggests that *Bacteroides fragilis* is more frequent in the stool of overweight vs normal weight children, adolescents, and adults (193). The intestinal microflora varies between vaginal and cesarean section birth and also due to the composition of early diets, including breast milk. Upcoming results of clinical trials, which modify the microbiome, may suggest new methods of obesity prevention and treatment.

A recent systematic review that looked at the way urban environments affect health behaviors or outcomes for children and adolescents reported some evidence of potential health benefits from urban environment interventions relating to road safety and active travel. However, evidence for the effectiveness of such interventions was weak due to study designs that were opportunistic and nonrandomized, used subjective outcome measures, and did not incorporate follow-up of study participants (194). Nonetheless, health care providers are encouraged to advocate for common sense changes, including providing safe walking/biking areas in parks, school routes, and neighborhoods and providing programs for active play in free time. Environmental change recommendations require additional research with more robust study designs incorporating objective outcome measures to inform meaningful policy change.

4.0 Treating obesity

Lifestyle: general considerations

4.1 We recommend clinicians prescribe and support intensive, age-appropriate, culturally sensitive, family-centered lifestyle modifications (dietary, physical activity, behavioral) to promote a decrease in BMI. (1⊕⊕⊕◯)

Evidence

The 2015 Endocrine Society Task Force commissioned a systematic review to evaluate the impact of weight change on metabolic outcomes in children and adolescents who are obese (5). The results showed that change in BMI was associated with improvements in triglycerides, high-density lipoprotein, and systolic blood pressure. This analysis is limited by the fact that it used aggregate data. Other studies also showed associations between weight change and other metabolic outcomes (Fig. 2) (195, 196).

Successful weight management, through lifestyle interventions, delays the onset of T2DM in adults (197) and improves cardiovascular fitness (198, 199). Many pediatric weight management programs have found improved body composition and metabolic parameters (13, 200).

A commonly held belief is that lifestyle modification is not sufficiently efficacious. Children and adolescents may not lose weight, or despite initial success, children and adolescents might regain weight after the active phase of the program has ended (201). A factor in weight regain may be lack of continued exercise. The odds for weight regain are twofold greater in those who are sedentary (201). In a 10-year study of adults who participated in the National Weight Control Registry, >87% of participants maintained at least 10% weight loss for 5 to 10 years. A worse outcome was associated with decreased physical activity, decreased dietary restraint, decreased frequency self-weighing, increased energy intake as fat, and increased disinhibition (202).

There is sufficient evidence that intensive lifestyle modification programs can be effective tools for pediatric weight control in the short term (203, 204). Furthermore, implementing a formal maintenance program after the completed treatment phase can be important for

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maintaining achieved weight loss (205). This finding is consistent with the concept of obesity as a chronic disease (206).

A Task Force–commissioned meta-analysis of randomized pediatric trials of combined lifestyle interventions for treating obesity (diet and exercise) showed a modest but significant effect on obesity (equivalent to a decrease in BMI of 1.5 kg/m^2; $P < 0.00001$) when interventions targeted family involvement. When parents were not specifically included, the effect on weight loss was not significant (182). These results suggest involving the family when delivering combined lifestyle interventions.

An additional meta-analysis of RCTs of lifestyle interventions (without an analysis of family involvement) found moderate positive effects from the interventions when compared with no treatment or information-only controls. These effects persisted for an average follow-up period of 15 months (207). Although there was overlap with the Task Force meta-analysis, each study contained reports not covered by the other.

An evidence-based position statement of the American Dietetic Association supports the utility of family-based lifestyle interventions for children and similar multicomponent programs for adolescents (208). These recommendations are consistent with conclusions of a combined CDC and American Medical Association expert committee (209) and an evidence-based review of pharmacological interventions for pediatric obesity that highlighted the importance of concomitant intensive lifestyle interventions, including dietary, exercise, and family counseling (210).

Values and preferences

In making this recommendation, the Task Force placed a high value on promoting healthy, safe pediatric lifestyle modification that included family involvement, with potential wide-reaching benefits.

Remarks

Clinicians should encourage BMI reduction for patients with obesity. A Task Force commissioned meta-analysis demonstrated favorable effects on systolic blood pressure, serum triglycerides, and serum high-density lipoprotein with decreasing BMI or weight (5). When interpreting these data, one must consider that the beneficial effects seen in the 133 RCTs and 16 systematic reviews are for averaged data, not individualized patients; other factors such as age, ethnicity, or genetics may modify individual responses. Very large changes may not be necessary. Although a BMI decrease of 1.5 kg/m^2 (reported in the meta-analysis commissioned by the first Task Force) may seem small, if maintained for the long term, overweight or obese children and adolescents may benefit by maintaining weight as they grow; BMI will decline as linear growth proceeds, and lifestyle modification may reduce fat mass, increase lean body mass, and improve cardiovascular fitness (211). Seven percent weight loss may be a more realistic goal for children and adolescents with extreme obesity. Well-designed RCTs, with large numbers of patients, employing intensive lifestyle intervention and follow-up maintenance programs, will help develop refined techniques. A review of 25 years of behavioral therapy intervention in children and adolescents has demonstrated that long-term weight loss maintenance is possible (212). Other RCTs of diet, physical activity, and/or behavior modification have also demonstrated persistent changes in BMI (212, 213).

Dietary

4.2 We recommend that clinicians prescribe and support healthy eating habits in accordance with the following guidelines of the American Academy of Pediatrics and the US Department of Agriculture:

- decreased consumption of fast foods
- decreased consumption of added table sugar and elimination of sugar-sweetened beverages
- decreased consumption of high-fructose corn syrup and improved labeling of foods containing high-fructose corn syrup
- decreased consumption of high-fat, high-sodium, or processed foods
- consumption of whole fruit rather than fruit juices
- portion control education
- reduced saturated dietary fat intake for children and adolescents >2 years of age
- US Department of Agriculture recommended intake of dietary fiber, fruits, and vegetables
- timely, regular meals, and avoiding constant "grazing" during the day, especially after school and after supper
- recognizing eating cues in the child's or adolescent's environment, such as boredom, stress, loneliness, or screen time
- encouraging single portion packaging and improved food labeling for easier use by consumers. (Ungraded Good Practice Statement)

Evidence

(Refer to section 3.2 for some of the evidence for recommendation 4.2.) Children and adolescents who are overweight are more likely to skip breakfast and consume few large meals per day (214) than do their leaner counterparts who are more likely to consume smaller, more

frequent meals (215). Because snacks tend to be higher in calorie density than meals, frequent snacking (among children and adolescents) is associated with a high intake of fat, sugar, and calories and with overweight (216).

Educating families, children, and adolescents about the need to measure out single snack portions from multiserving packages and place them in single-serving containers can significantly change the amount of food children and adolescents consume (217).

Values and preferences

The committee placed a high value on decreasing snacking and decreasing overall caloric intake to reduce weight gain among children and adolescents.

Remarks

A meta-analysis in children and adolescents suggests that improved weight can be achieved regardless of the macronutrient composition of the diet, and this mirrors similar results found in adults (218). The WHO has recently recommended that adults, children, and adolescents limit sugar to <5% to 10% of total daily energy intake, unless the sugars are contained in fresh fruits and vegetables, which are lower in calories and higher in fiber than processed carbohydrates. The other carbohydrates, which they term "free sugars," include honey; other sweeteners; glucose/fructose; and sugar added by a cook, consumer, or producer. This recommendation was termed "strongly" because of moderate quality evidence that increasing free sugars in one's diet increases body weight, and decreasing free sugars decreases body weight (110).

A dietician familiar with the energy needs of growing children and adolescents should supervise calorie reduction for weight loss or maintenance in patients of this age group. Unbalanced hypocaloric diets (*e.g.*, "fad diets") may be deficient in essential vitamins and minerals.

Physical activity

4.3 We recommend that clinicians prescribe and support the reduction of inactivity and also a minimum of 20 minutes of moderate to vigorous physical activity daily, with a goal of 60 minutes, all in the context of a calorie-controlled diet. (1|⊕⊕◯◯)

Evidence

In the absence of caloric restriction, moderate exercise does not cause weight loss. However, in combination with decreased caloric intake, exercise can achieve and maintain significant weight loss. Studies performed in the school setting have shown beneficial effects of exercise in children and adolescents (204). The beneficial effects of both aerobic exercise and resistance training can be short-lived, and exercise must be sustained over months. Even 20 minutes of aerobic activity 5 days per week over 13 weeks can decrease body and visceral fat (124). Recent studies in Denmark and elsewhere have demonstrated benefits in mild intensity jogging and in small 10- to 15-minute intervals of exercise, which may be more readily achievable (219, 220).

Physical fitness, even without weight loss, may confer health benefits. Improvements in cardiovascular fitness were associated with improvements in body composition and diabetes risk factors in adolescents (220). In addition to improving metabolic fitness, exercise has been linked to improvements in cognitive function and concentration (124). (Refer to section 4.8 regarding school-based interventions to increase activity.)

Values

The Committee placed a high value on losing weight (in the form of body fat) by decreasing caloric intake and increasing energy expenditure.

Remarks

Although current recommendations state that school children and adolescents (who spend about half their waking hours in school) should receive a minimum of 30 to 60 minutes of moderately vigorous physical activity and at least 60 minutes of aerobic (moderate and vigorous) physical activity each school day, only 5% of school districts in the United States have a requirement for a specific amount of physical education (221–225). Clinicians should place emphasis on increasing a child's or adolescent's activity by helping facilitate:

- the ability to safely walk to and from school
- increased use of stairs (and improved signage to indicate their location)
- increased breaks for movement in the classroom
- increased movement during recess and gym.

Moderate to vigorous exercise is defined as causing some increase in breathing and heart rate; in a healthy person this is usually associated with brisk walking, dancing, swimming, or cycling on flat terrain. In exercise physiology terms, the energy expended should be at least 3 metabolic equivalents (85, 226). Moderate exercise allows talking but not singing, and vigorous exercise makes it impossible to sing and difficult to talk. This generalization should help families understand and identify the difference between moderate and vigorous exercise.

The use of motivational interviews to help an older child or adolescent and/or his or her parent set physical fitness or dietary goals may lead to greater success in

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decreasing BMI (218, 219). In spite of limitations inherent in the method, clinicians should assess a patient's readiness for change when determining how to approach the family.

4.4 We suggest that clinicians encourage and support patients to limit nonacademic screen time to 1 to 2 hours per day and decrease other sedentary behaviors, such as digital activities. (2|⊕○○○)

Evidence

The 2009 Cochrane analysis reported that a combined behavioral approach incorporating both dietary and physical activity changes can produce a significant and clinically meaningful reduction in overweight in children and adolescents (204). A meta-analysis commissioned by the original Task Force of 3 randomized trials of interventions for reducing sedentary activity reported imprecise results (*i.e.*, that these interventions had both a favorable and unfavorable impact on obesity outcomes) (182). Both girls and boys demonstrated small decreases in the amount of screen time in a German study, and these decreases did not correlate with increases in physical activity (227).

Values and preferences

The committee placed a high value on limiting digital access time and other efforts to decrease sedentary time. As our ever-increasing digital environment necessitates increased screen time, a plan for the world's children and adolescents should complement necessary screen time with:

- environments that demand and facilitate movement
- monetary incentives for decreased caloric intake (such as taxes on sugar-sweetened beverages).

The committee agrees with research that finds an association with the presence of a television set in a child's bedroom to increased screen time and increase caloric intake while weakening the positive influence of parents on promotion of healthy habits (228, 229).

Psychological complications of overweight and obesity

Psychosocial

4.5 We suggest that the health care team identify maladaptive rearing patterns related to diet and activity and educate families about healthy food and exercise habits. (2|⊕○○○)

4.6 We suggest that the health care team probe for and diagnose unhealthy intrafamily communication patterns and support rearing patterns that seek to enhance the child's or adolescent's self-esteem. (2|⊕○○○)

4.7 We suggest that the health care team evaluate for psychosocial comorbidities and prescribe assessment and counseling when psychosocial problems are suspected. (2|⊕○○○)

Evidence

In section 4 we discuss the importance of involving the whole family, and not just the child or adolescent, in prevention and treatment interventions.

How interactions between parents and children and adolescents and parenting styles contribute to unhealthy lifestyle habits is a subject of investigation (230, 231). An additional factor to overcome before initiating any intervention may be the parents' inability to recognize that their child or adolescent is overweight, particularly for the preschool child (232–234).

Obesity is associated with QOL, with levels measured in obese children and adolescents equivalent to those seen in pediatric cancer or diabetes (235, 236). In addition to low QOL, children and adolescents with obesity have significant psychosocial comorbidities, including poor self-esteem (237–239), increased risk of depression and anxiety (240–242), and higher-than-average risk of eating disorders and substance abuse. Low self-esteem (243) and perceived or actual higher BMIs are associated with increased likelihood of smoking and alcohol consumption (244).

To remove the bias that might be seen in a clinic sample, the Childhood Growth and Development Study in Australia enrolled healthy weight (n = 158), overweight (n = 77), and obese (n = 27) children from the schools and from families asking to be referred (n = 19). Heights, weights, and psychological testing were done in the schools for the school-based cohort (245). Increasing BMI *z* scores were associated with decreasing self-worth and global self-esteem as well as with decreased athletic competency, social acceptance, and dissatisfaction with their physical appearance. These associations were reported as young as age 8 years, but the association with physical appearance was more pronounced in the older group (246). The presence of psychosocial distress in a population of school children and adolescents not seeking clinic referral, as well as those seeking referral, indicates that psychosocial issues are present in both clinical and nonclinical populations of youths who are obese.

A review of the literature found lower QOL scores for social acceptance, family life, physical appearance, school functioning, and physical functioning in all but 2 of the 34 publications included in the study. Factors influencing lower QOL included degree of obesity, symptoms of

depression, lack of social support from classmates/family, and low socioeconomic status (247).

In general, low self-esteem does not seem to be a significant problem until adolescence, as self-esteem is similar between preteen children who are obese and normal weight. During adolescence, however, self-esteem becomes more closely tied to body image, and rapidly plummets, with those adolescent females who have higher BMIs and body image dissatisfaction having the lowest self-esteem (248).

Individuals with eating disorders tend to define self-worth by their body image (249), possibly explaining the association between eating disorders and youths who are overweight and obese. Surveys from 135 Hispanic and African American girls who are obese or overweight revealed that 52% had been teased about their weight by girls and 60% had been teased about their weight by boys. Of those who were teased, 70% skipped meals, dieted, or starved themselves; 12% reported binge eating; and 33% stated they had "emotional" eating. All of the girls surveyed stated they were unhappy about their weight and wanted to be thinner (250). Eating disorders, including binge eating and anorexia nervosa/bulimia, are more commonly seen in those who have depression, anxiety, and disruptive behavior (251, 252).

Parental reaction to their child's weight affects how the child responds. Bullying by peers and families contributes to poor body image and impaired psychosocial functioning (253).

Some may harass their child, letting them know how unattractive he/she is, resulting in worsening body image and poor self-esteem. A retrospective Internet-based study of college students with great concern about their weight, body shape, and eating behaviors revealed that >80% had a history of parents or siblings making negative comments about their weight, shape, or eating behaviors. Most scored above average in psychometric emotional-abuse tests, with positive associations with negative parental comments and higher weight and negative associations with social support and self-esteem (254). Some parents are overly restrictive, potentially causing their children and adolescents to binge when they have access to unrestricted food (255, 256). Alternatively, adolescents with extreme obesity may develop anorexia bulimia, anorexia nervosa, or purging behaviors in an effort to lose weight. A cross-sectional cohort study of adolescents with extreme obesity and their parents found bulimic symptoms did not correlate with the degree of obesity but were associated with maternal psychopathology, including somatization and anxiety (257).

Youths who are obese are more likely to be teased and bullied and are less likely to have a "best friend" or be considered popular by classmates than their thinner peers (258). Parents, teachers, and peers indicate that youths who are obese are more isolated and have poorer social skills than do their thinner counterparts (259). Those with low self-esteem (243) and perceived or actual higher BMIs are more likely to smoke and drink alcohol than those with higher self-esteem (244). Additionally, they are less athletic and less likely to have romantic relationships, contributing to increased teasing, worsening of self-esteem, loneliness, depression, anxiety, and introverted behavior (260).

In general, those who are most obese report more psychological distress (246, 261). Girls become more depressed with increasing BMI than do boys, and some studies indicate that depression in African American boys is not linked to BMI but rather to peer teasing (246, 262). Race and socioeconomic status (in addition to sex) affect how children and adolescents react to obesity; however, there are conflicting reports on the effect of obesity on psychological status in different groups. One study found that African American children have more body image dissatisfaction and anxiety than do their same-weight white counterparts (262), whereas a study of adolescents found that African Americans and Hispanics are less stigmatized than whites (263). High socioeconomic status adolescents who are obese with psychopathology are less likely to seek help at a weight-loss program than are low socioeconomic status adolescents who are obese (252), possibly due to a more negative perception regarding obesity in high socioeconomic status families.

As adolescents who are obese consistently report high rates of depression, anxiety, and binge eating disorders, all overweight patients should be assessed for psychopathology. Assessment and counseling by a psychologist are often indicated. Clinicians should prescribe antidepressant medications with caution, as atypical antipsychotics cause rapid (often extreme) weight gain (264).

Diuretics, diet pills, and self-induced emesis are not uncommonly used to achieve rapid weight loss by adolescents. One study demonstrated that laxative use, self-induced vomiting, and diet pill ingestion were more common in adolescents who are obese compared with those who are normal weight and overweight (265). Six percent of 6957 middle school children and adolescents in North Carolina used diet pills and 7.1% used laxatives or self-induced vomiting. The case prevalence of diet pills was 3.4 in normal weight, 4.1 in overweight, and 9.5 in adolescents who are obese; the case prevalence of laxatives was 1.3, 0.7, and 3.2, respectively; and the case prevalence of self-induced vomiting was 3.4 in normal weight vs 7.6 in adolescents who are obese. Females more commonly abused substances for weight loss, such as

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tobacco, alcohol, and marijuana; they were also more likely to participate in risky sexual behaviors (265). Clinicians should discuss these maladaptive behaviors at clinic visits, as they are potentially harmful. It is important to emphasize moderation rather than restriction and to counsel against risky weight loss strategies

Remarks

As psychosocial issues are so prevalent, providers should psychologically screen all youths who are obese for the presence of mental health issues, asking questions regarding:

- school absences/refusal
- teasing by peers regarding weight/appearance
- persistent anxiety
- depression/self-harm
- anger outbursts
- sexual activity, alcohol, drug use
- eating disorders—purging, anorexia, binge eating
- family functioning/family attitudes about weight and specifically obesity/parent psychopathology.

Parents and/or children and adolescents should complete a mental health screening measure, such as the Pediatric Symptom Checklist (266). Clinicians can review this during patient visits and refer patients to a mental health professional when indicated. Obesity-related mental health issues are a pervasive problem, and a team-based approach is essential, involving school counselors, nurses, and teachers, as well as health care providers. It might also be helpful to consult with school personnel to initiate school-based counseling. A list of local programs (*e.g.*, YMCA, Boys and Girls Clubs) that offer physical activity programs and healthy snacks is also helpful. Behavioral modification is helpful in determining the child's readiness to change and potential barriers to achieving change (264).

Pharmacotherapy

4.8 We suggest pharmacotherapy for children or adolescents with obesity only after a formal program of intensive lifestyle modification has failed to limit weight gain or to ameliorate comorbidities (2|⊕○○○). We recommend against using obesity medications in children and adolescents <16 years of age who are overweight but not obese, except in the context of clinical trials. (1|⊕○○○)

4.9 We suggest that FDA-approved pharmacotherapy for obesity be administered only with a concomitant lifestyle modification program of the highest intensity available and only by clinicians who are experienced in the use of antiobesity agents and are aware of the potential for adverse reactions. (2|⊕○○○)

4.10 We suggest that clinicians should discontinue medication and re-evaluate the patient if the patient does not have a >4% BMI/BMI *z* score reduction after taking antiobesity medication for 12 weeks at the medication's full dosage. (2|⊕○○○)

Evidence

The FDA recently approved a number of weight-loss medications for adults (216, 267, 268) and considers these medications to be appropriate for those ≥16 years of age who have BMI ≥ 30 kg/m^2 or who have BMI ≥ 27 kg/m^2 and at least 1 weight-related comorbid condition (*e.g.*, hypertension or T2DM). However, although the utility of pharmacotherapy in pediatric obesity has been recently reviewed (269–271), there are no published data directly comparing adult and adolescent outcomes for obesity pharmacotherapy.

Physicians should be discouraged from prescribing weight loss medications off-label to those <16 years old because of: 1) the lack of FDA approval for use; 2) the limited number of well-controlled safety and efficacy studies in obese children and adolescents, 3) the limited efficacy demonstrated in adults for most agents, and 4) the need to weigh the relative risk of drug-induced adverse events in children and adolescents against a medication's long-term theoretical potential for reducing obesity-related morbidity and mortality.

Despite these concerns, the negative health impact of pediatric obesity may justify long-term medication. However, pharmacotherapy should only be prescribed in combination with comprehensive lifestyle modification programs (210, 271–274) that have substantial efficacy (270). The limited available evidence suggests the best pediatric pharmacotherapy outcomes are among patients adherent to lifestyle program recommendations (275).

Among pharmacotherapeutic agents approved for adult obesity (Table 5), only orlistat is FDA approved for obesity treatment of ages 12 to 16 years. Orlistat (299–305) inhibits gastrointestinal lipases, reducing adolescent's fat absorption by ~30% (299). Orlistat reduces BMI significantly in adolescents by ~0.7 to 1.7 kg/m^2 (150, 318), but treatment is associated with significant gastrointestinal side effects (Table 5). Orlistat must be taken with each meal, thus reducing its utility in school-attending adolescents. Orlistat appears to affect the absorption of fat-soluble vitamins E and D (299). Available data suggest that ~50% of pediatric patients that are prescribed orlistat discontinued it within 1 month, 75% stop using it by 3 months, and only 10% remain on orlistat after 6 months (319, 320). Given its limited

Table 4. Factors Associated With Prevention of Pediatric Obesity

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
4.2 Increased sugar sweetened beverages intake			
2- to 5-y-old children from various periods of the National Health and Nutrition Examination Surveys	There was a decrease of 57 calories/d intake of sugar-sweetened beverages between 2003–2004 and 2009–2010 with no appreciable change in sugar intake thereafter up to 2011–2012	Ford *et al.*, 2015 (112)	Probable +
Cross-sectional analysis of 4880 children between 3 and 11 y from the National Health and Nutrition Examination Survey between 1999 and 2004	Sugar-sweetened beverage intake was independently associated with decreased HDL, increased C-reactive protein, and increased waist circumference	Kosova *et al.*, 2013 (113)	+
Longitudinal study of 9600 children in the Early Childhood Longitudinal Survey–Birth Cohort	There was a 1.4 odds ratio for being obese if a 5-y-old child drinks 4 or 5 sugar-sweetened beverages per day but no such risk for 2-y-old; however there was a significant influence on drinking sugar-sweetened beverages at 2 y of age and an increase in BMI *z* score during the next 2 y	DeBoer *et al.*, 2013 (114)	+
Randomized controlled study of 224 teenagers that reduced sugar sweetened beverage intake	There was a decrease in the change in BMI and weight at 1 y but no difference at 2 y	Ebbeling *et al.*, 2012 (115)	+
Eighteen-month study of 642 primarily normal-weight Dutch children aged 4 y 10 mo to 11 y 11 mo who were divided into groups receiving 8 ounces of sugar-free drink or 105 kcal containing sugar-sweetened drinks	There was an increased weight gain and increase in BMI in the sugar-sweetened group	de Ruyter *et al.*, 2102 (116)	+
One hundred forty-six 7- to 11-y-olds drinking sugar-free or sugar-sweetened beverages	There was no difference in the level of satiety experienced; the conclusion is that the child will not compensate for all calories missing from nonsweetened drinks, which may partly explain a lower degree of weight gain with nonsweetened drink ingestion	de Ruyter *et al.*, 2012 (116)	+
4.3 Higher level of activity[a]			
Meta-analysis of 11 RCTs of activity ranging in length from 20 min to >1 h/d and ranging in frequency from twice a week to every day of the school week	There was little effect on BMI, but there were decreases in triglycerides and systolic and diastolic blood pressure when the intervention lasted at least 6 mo; total cholesterol, however, did increase during some studies	Cesa *et al.*, 2014 (117); Vasconcellos *et al.*, 2014 (118)	–
Nine randomized controlled pediatric studies (n = 367) included in a meta-analysis	At least 3 mo of exercise in 3 sessions per week of 60 min each led to decreased fasting glucose and insulin and body fat	Garcia-Hermoso *et al.*, 2014 (119)	–
Meta-analysis of 24 studies of fasting insulin levels and 12 studies on insulin resistance in pediatric normal weight overweight and obese	There was a small but positive effect in improving fasting insulin resistance in children, with the greatest effect occurring in those with the highest BMI standard deviation values	Fedewa *et al.*, 2014 (120)	–
Systematic review of 16 studies of school-based jumping exercises	There was small positive effect of bone-targeted exercise on fat mass (SMD, −0.248; 95% CI, −0.406 to −0.089) and lean mass (SMD, 0.159; 95% CI, −0.076 to 0.394), but there are few studies	Nogueira and Hrovat, 2014 (121)	–
Meta-analysis of 40 studies on the effect of resistance training in pediatric overweight or obese	Resistance training in children and adolescents who are overweight and obese appears to generally have very small to small effects on body composition and moderate to large effects on strength	Schranz *et al.*, 2013 (122)	–
Systematic review of 2 aggregate data meta-analyses representing 14 and 17 studies in 481 and 701 boys and girls, respectively	Exercise decreased the percentage of body fat but does not necessarily have an effect on BMI; therefore, replacing fat tissue with muscle may not necessarily be reflected by characteristic clinic-based anthropomorphic data	Kelley and Kelley, 2013 (123)	–

(Continued)

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Table 4. Continued

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
Randomized controlled pediatric study of >200 subjects who experienced 20 or 40 min of fun but nonetheless aerobic activity 5 d/wk during 13 wk	There was a dose response decrease in insulin resistance measured by the area under the curve of an oral glucose tolerance test, decreased total body fat and visceral fat, and a similar improvement in fitness measured by peak VO2; the conclusion is that there is benefit for a child who is obese if the child will actually engage in at least 20 min of aerobic exercise 5 d/wk, (and we expect this may extend to the prevention of obesity)	Davis *et al.*, 2011 (124)	–
4.4 Decreased sleep duration or variation			
A systematic review and unbiased meta-analysis of 11 longitudinal studies of 24,821 children and adolescents	There was a twofold increase in risk for obesity with "short" sleep duration according to sleep standards	Fatima *et al.*, 2015 (125)	+
Sleep duration in a cross-sectional pediatric study (n = 676)	Energy density of the diet, added sugar, and SSBs decreased with increased sleep	Kjeldsen *et al.*, 2014 (126)	+
Variability in sleep duration of 10 min per night	This was positively associated with energy density (P = 0.04), sugar-sweetened beverages intake (P = 0.03), and Children's Sleep Habits Questionnaire score independent of sleep duration	Kjeldsen *et al.*, 2014 (126)	+
One hour decrease in pediatric sleep duration (n = 441) during 200 d	There was a higher intake of added sugar (P = 0.001) and sugar-sweetened beverages (P = 0.002) with no change in energy density of the diet (P = 0.78)	Hjorth *et al.*, 2014 (127); Kjeldsen *et al.*, 2014 (126)	+
Sleeping <10 h at 16 mo of age in 1303 twins	There was a 50 kcal increased intake	Fisher *et al.*, 2014 (128)	+
Increasing pediatric sleep duration an average of 2 h 20 min (n = 37)	There was decreased caloric intake by 134 kcal/d and lowered plasma leptin	Hart *et al.*, 2013 (129)	+
Three hundred eleven term infants; sleep duration at 9 mo, 18 mo, and 3 y of age	There was no relationship between sleep duration and adiposity indicators in 9- to 36-mo-old children: the SKOT cohort	Klingenberg *et al.*, 2013 (130)	None
Eight hundred two 4- to 14-y-old children and adolescents; sleep and intake followed for 7 d	There was no relationship between sleep duration and energy intake, but there was a trend toward a positive association with intake of dietary fiber and vegetables and a negative association with intake of poultry, and a trend toward a negative association with intake of liquid "discretionary calories"	Hoppe *et al.*, 2013 (131)	None
Longitudinal cohort study of 550 children of average age 9.6 y	There was an odds ratio of 2.08 for obesity with <10 h sleep	Chaput *et al.*, 2011 (132)	+
A meta-analysis of 12 studies including 20,003 children	There was a 1.86 odds ratio for obesity with "short" duration of sleep	Cappuccio *et al.*, 2008 (133)	+
4.5 Increased screen time			
Measurements at ~12 y of age of 234 parents from a previously established cohort were compared with 382 of their offspring for screen time and measures of adiposity	Both generations demonstrated a relationship between screen time and obesity at about 12.5 y of age, demonstrating a need to target high-risk families across generations	Steffen *et al.*, 2013 (134)	+
A systematic review of 7 prospective studies on television time and 1 study on computer use	Six studies of varying quality demonstrated a positive relationship between screen time and the development of obesity	te Velde *et al.*, 2012 (135)	+
Seventy children studied every 6 mo during 2 y in a randomized controlled study to decrease television viewing 50% and decrease sedentary activity in the intervention group of 35	The intervention decreased sedentary activity especially in lower socioeconomic group children; there was relationship between decreased television viewing, decreased BMI, and decreased energy, but not increased activity	Epstein *et al.*, 2008 (136)	+

(*Continued*)

Table 4. Continued

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
4.6 Increased family involvement in prevention			
Fifteen RCTs of family-based lifestyle interventions for children and adolescents	Family-based interventions based in behavior theory had more effect than did those theoretically connected to family systems theory	Sung-Chan *et al.*, 2013 (137)	–
A systematic review including 24 studies including parental involvement in long-term weight-control interventions with a nutritional focus	Although there were inadequate data to determine whether parental involvement in prevention programs is important, medium and high levels of parental involvement in obesity treatment programs improved outcomes, suggesting that parental involvement should be studied in prevention	van der Kruk *et al.*, 2013 (138)	Probable +
Fifteen studies (7 were longitudinal) included measures of frequency of family meals although in an inconsistent manner	There was inconsistent and weak evidence of an inverse association between the frequency of family meals and risk of pediatric overweight; there is need for robust longitudinal studies on this topic	Valdes *et al.*, 2013 (139)	None
A systematic review of 9 studies including portion manipulation interventions or portion education/training interventions	Most studies demonstrated increased intake with increased portion size, and that parents can be educated to estimate portion size more accurately, but there were other studies that contradicted both concepts	Small *et al.*, 2013 (140)	–
4.7 Disordered family function or abuse			
Systematic review of 16 cross-sectional and 1 longitudinal study of family function	Lower levels of family functioning, including poor communication, poor behavior control, poor family cohesion, high levels of family conflict, and low family hierarchy values representing low authority, dominance, and decision power, showed low to moderate relationship to the subject's classification of pediatric obese or overweight; however, out of 4 interventional studies only 2 showed that improved family functioning decreased the risk of obesity, but these studies were suboptimal	Halliday *et al.*, 2014 (141)	+
A meta-analysis of 41 studies including 190,285 participants	Pediatric maltreatment was associated with a 1.36 increased risk ratio for pediatric obesity	Danese and Tam, 2014 (142)	+
Systematic review of 36 studies	Interpersonal violence increased the risk of obesity later in life	Midei *et al.*, 2011 (143)	+
Systematic review of 6 prospective and 2 retrospective studies	Stressful environments during childhood and adolescence, including lack of good care, pediatric anxiety disorders, learning difficulties, low school achievement, and childhood/adolescence abuse, increased adult obesity risk, depression in adolescence, and increased the risk for obesity in girls only	Vamosi *et al.*, 2010 (144)	+
4.8 Increased school involvement			
Nine community-based studies (5 RCTs and 4 non-RCTs) of which 1 was conducted only in the community setting, 3 were conducted in the community and school setting, and 5 were conducted in the community setting in combination with at least 1 other setting, such as the home	There was moderate strength of evidence that a combined diet and physical activity intervention in the community with a school component is effective at preventing obesity or overweight	Bleich *et al.*, 2013 (145)	–
A systematic review of 16 studies involving school prevention programs with community involvement	School programs with more community involvement were more successful than those with less community involvement	Krishnaswami *et al.*, 2012 (146)	–

(*Continued*)

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Table 4. Continued

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
Meta-analysis of 37 studies of 27,946 children generally between 6 and 12 y of age	There were beneficial effects of pediatric obesity prevention programs on BMI with school curriculum that includes healthy eating; physical activity and body image; increased sessions for physical activity and the development of fundamental movement skills throughout the school week; improvements in nutritional quality of the food supply in schools; environments and cultural practices that support children eating healthier foods and being active throughout each day; support for teachers and other staff to implement health promotion strategies and activities, as well as parent support and home activities that encourage children to be more active, eat more nutritious foods, and spend less time in screen-based activities; however, weaknesses in studies and potential bias point to the necessity for improved studies in the future	Waters *et al.*, 2011 (147)	–
4.10 Increased breast feeding			
Meta-analysis of 25 studies with a total of 226,508 participants	Breast-feeding was protective of the development of obesity with a dose response effect in 17 studies	Yan *et al.*, 2014 (148); Kramer *et al.*, 2009 (149)	+
A cluster-randomized trial of a breast-feeding promotion intervention of 13,889 subjects (81.5%) followed up at 6.5 y from 31 Belarusian maternity hospitals and affiliated clinics	Although there were substantial increases in the duration and exclusivity of breast-feeding, there was no reduction in obesity at age 6.5 y	Kramer *et al.*, 2009 (149)	None
Meta-analysis of 10 studies of breast-feeding	Five studies showed protective effects and 5 did not; likewise, there were mixed findings on length of breast-feeding and time of introduction of complementary food	Weng *et al.*, 2012 (150)	Mixed
Cohort analyses of 11,998 teenagers from the National Longitudinal Study of Adolescent Health	There was a decreased risk of obesity in girls breast-fed at least 9 mo with similar, but less significant, effects in boys; however, analysis of sibling pairs eliminated any significance from the relationship, demonstrating the effect of confounding effects on cohort analyses	Nelson *et al.*, 2005 (151)	+

Note: Numbers 4.2–4.8 and 4.10 refer to numbered recommendations in the manuscript.

Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; RCT, randomized controlled trial; SKOT, Scottish Childhood Obesity Treatment Trial; SMD, standardized mean difference; TV, television; VO2, oxygen consumption.

[a]Some studies included obese children and adolescents, but results may relate to prevention.

efficacy and low long-term use, orlistat appears of limited benefit in practice.

Additional medications not FDA approved for the treatment of pediatric obesity

Metformin (306–311, 321–334) is not FDA approved for obesity treatment. However, metformin reduces hepatic glucose production, increases peripheral insulin sensitivity, and may reduce appetite (335). Metformin decreases BMI, but with a mean decrease of only 1.16 kg/m^2 over 6 to 12 months (336). Metformin may also possibly be useful in combating the weight gain observed in children and adolescents who are taking atypical psychotropic medications (337, 338) or who have PCOS (324, 331, 339). However, given its limited weight-loss efficacy, metformin is not a considered a weight-loss treatment.

Sibutramine (275, 284, 285, 340–346) was removed from the US market in 2010 because of concerns for

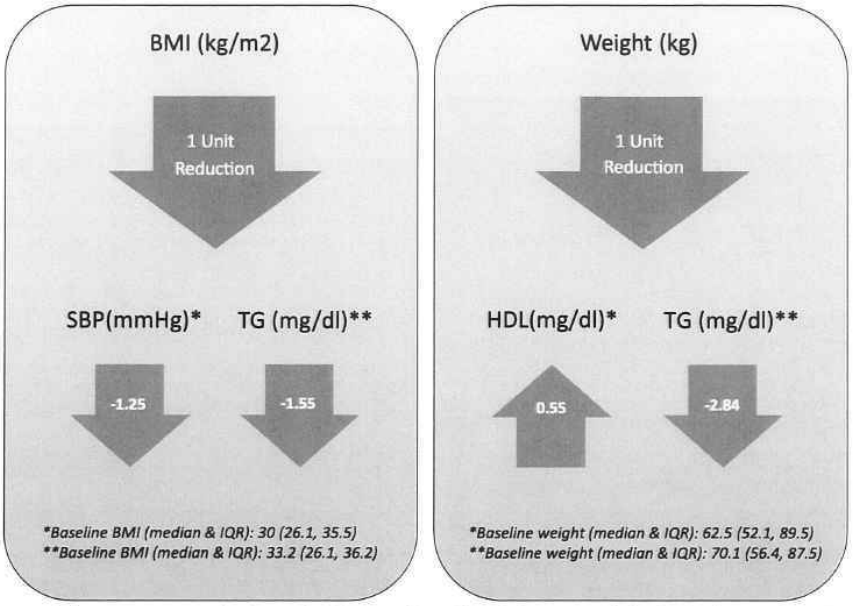

Figure 2. Change in metabolic outcome per unit change in BMI or weight. Abbreviations: HDL, high-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride.

cardiovascular safety but remains available in several other countries.

Other medications approved for obesity treatment of ≥16 years of age or under investigation generally have few relevant pediatric data (297, 298) (Table 5).

Some centrally active, amphetamine-like catecholaminergic and dopaminergic stimulants, such as phentermine and diethylpropion, are FDA approved as short-term monotherapy (a few weeks) for obesity in adults. Recently, lisdexamfetamine dimesylate was FDA approved to treat binge eating in adults (282, 283). Lisdexamfetamine treatment was associated with short-term weight loss, but this medication is not FDA approved for weight management. Because of adverse effect profiles (Table 5), abuse potential (347), and the absence of trials showing long-term weight loss efficacy, none of the amphetamine-like agents is recommended for obesity management in children and adolescents.

Although not FDA approved for the treatment of obesity, GH treatment of children and adolescents with Prader-Willi syndrome, particularly when started early (90), decreases body fat percentage and increases lean body mass (348), with effects that may be sustained for the long term (90). A summary of the benefits and risks of GH treatment (349) and consensus guidelines for GH therapy in Prader-Willi Syndrome are available (350).

Octreotide limits the opening of voltage-gated calcium channels in beta cells (351, 352), decreasing the magnitude of insulin response to glucose (353). In obese adults with insulin hypersecretion, treating with long-acting repeatable octreotide for 6 months resulted in ~2% greater weight loss than in controls (316). Studies have reported weight stabilization, instead of significant weight gain, in children and adolescents with hypothalamic obesity treated with somatostatin analogs (315, 354). Given its side-effect profile, octreotide appears to be potentially beneficial only for those with hypothalamic obesity.

Liraglutide, a glucagon-like peptide 1 analog, is approved for long-term adult obesity treatment; the effective 3 mg dose produced an additional weight loss of 4.5% vs placebo at 1 year, with sustained effects for up to 2 years (355). Small trials suggest that another glucagon-like peptide 1 analog, exenatide, may potentially have efficacy in adolescent obesity; used for >3 months, exenatide reduced BMI by >1 kg/m^2 (compared with control), with continued BMI reduction during a 3-month open-label phase (297, 298).

Leptin therapy in leptin-deficient patients produces significant loss of fat mass (295, 356, 357). Unfortunately, leptin therapy in adults who are not leptin deficient has little effect on body weight (358–360).

Agents that have been recently approved for long-term obesity treatment in adults (Table 5) currently lack pediatric-specific data. The additional weight loss (beyond that achieved with placebo) at 1 year among adults ranges from ~3% (lorcaserin) to ~10% (phentermine plus topiramate) (267), but none is without potential risks. If

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adult patients taking full-dose lorcaserin, bupropion plus naltrexone, liraglutide, or phentermine plus topiramate do not see clinically meaningful weight loss (>3% to 5% of body weight) after 12 weeks, clinicians should discontinue treatment, because significant weight loss after 1 year is unlikely. Similar results were found for adults given orlistat (361). In the largest adolescent orlistat trial (362), 21% of orlistat-treated adolescents decreased their body weight by ≥5% at 12 weeks and went on to decrease body weight by 7.8% after 1 year of treatment; however, those who lost <5% at 12 weeks had a 2.3% weight gain after 1 year (362). Thus, clinicians should discontinue pharmacotherapy agents when sufficient weight loss is not observed after 12 weeks.

Values and preferences

We placed a higher value on avoiding drug side effects and on achieving healthy weight through the incorporation of healthy behaviors. The suggestion to minimize the use of pharmacotherapy in children and adolescents reflects the limited efficacy and small number of long-term pediatric trials for existing agents, along with the imperative to manage pediatric obesity as a serious chronic condition in which long-term success overrides short-term gains.

Remarks

Drug efficacy is based only on reductions of BMI or BMI *z* scores. Antiobesity drugs may have differential effects on obesity-associated comorbidities based on their mechanisms of action. For example, certain medications (*e.g.*, metformin) have more potent effects on glucose tolerance. Clinicians should tailor drug selection to the individual patient and pay strong attention to the patient's concomitant medications, medical conditions, and family history, as well as each medication's efficacy and adverse event profile. The benefits of any drug used to treat pediatric obesity should clearly outweigh its long-term risks. Clinicians should be aware that no obesity medication has been shown to reduce the incidence of cardiovascular morbidity or mortality (267).

The recommendation to discontinue medication when it appears relatively ineffective after 12 weeks of use is consistent with adult obesity pharmacotherapy labeling. The FDA label for liraglutide recommends discontinuation when adults have <4% weight reduction. Most drugs should be discontinued if a 5% decrease in BMI/BMI *z* score does not occur.

Although pediatricians prescribe many medications "off-label", we think pharmacotherapeutic agents not yet approved for the treatment of pediatric obesity should be restricted to large, well-controlled clinical studies.

Bariatric surgery

4.11 We suggest bariatric surgery only under the following conditions:

- the patient has attained Tanner 4 or 5 pubertal development and final or near-final adult height, the patient has a BMI of >40 kg/m^2 or has a BMI of >35 kg/m^2 and significant, extreme comorbidities
- extreme obesity and comorbidities persist despite compliance with a formal program of lifestyle modification, with or without pharmacotherapy
- psychological evaluation confirms the stability and competence of the family unit, psychological distress due to impaired QOL from obesity may be present, but the patient does not have an underlying untreated psychiatric illness
- the patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits
- patient has access to an experienced surgeon in a pediatric bariatric surgery center of excellence providing the necessary infrastructure for patient care, including a team capable of long-term follow-up of the metabolic and psychosocial needs of the patient and family. (2|⊕○○○)

4.12 We suggest against bariatric surgery in preadolescent children; pregnant or breast-feeding adolescents (and those planning to become pregnant within 2 years of surgery); and in any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder. (2|⊕○○○)

Evidence

Clinicians prescribe bariatric procedures for weight loss in adolescents because of the poor success of nonsurgical treatment in achieving and maintaining weight loss in adolescents with extreme obesity.

Indications for weight loss surgery include BMI of >35 kg/m^2 with major comorbidities of obesity (T2DM, moderate to extreme sleep apnea, pseudotumor cerebri, debilitating orthopedic problems, and nonalcoholic steatohepatitis with advanced fibrosis). Patients are also candidates for bariatric surgery if they have a BMI of >40 kg/m^2 with mild comorbidities (hypertension, dyslipidemia, moderate orthopedic problems, mild sleep apnea, nonalcoholic steatohepatitis, and extreme psychological distress that is secondary to their obesity) (363).

Because of the beneficial effects on QOL, social relationships, and depression in studies of adolescents (364–367), some as long as 2 to 3 years in duration (368, 369), proponents of bariatric surgery suggest that extreme psychological distress is an indication for

Table 5. Medications Studied for the Long-Term Treatment of Obesity

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Centrally acting anorexigenic agents				
Phentermine, diethylpropion, and mazindol[a]	Approved only for short-term use in adults	Insomnia, elevation in heart rate, dry mouth, taste alterations, dizziness, tremors, headache, diarrhea, constipation, vomiting, gastrointestinal distress, anxiety, restlessness	Monitor HR, BP. These medications are contraindicated in uncontrolled hypertension, hyperthyroidism, glaucoma, agitated states, history of drug abuse, and MAOIs; use caution when prescribing to patients with even mild hypertension	Rauh and Lipp, 1968 (276); Lorber, 1966 (277); von Spranger, 1965 (278); Andelman *et al.*, 1967 (279); Golebiowska *et al.*, 1981 (280); Komorowski, 1982 (281)
Lisdexamfetamine dimesylate[a]	Not FDA approved for obesity. Approved for binge eating disorder in adults and for attention deficit hyperactivity disorder in patients 6 y of age and older	Dry mouth, sleeplessness (insomnia), increased heart rate, jittery feelings, constipation, anxiety	This medication is contraindicated with MAOIs. There is a risk for sudden death in people who have heart problems or heart defects, and stroke and heart attack in adults. Monitor blood pressure and heart rate. May produce psychotic or manic symptoms, such as hallucinations, delusional thinking, or mania. May worsen peripheral vasculopathy, including Raynaud phenomenon	McElroy *et al.*, 2015 (282); McElroy *et al.*, 2015 (283)
Sibutramine	Withdrawn in the US (increased risk of serious cardiovascular events). Still available in some countries such as Brazil	Tachycardia, hypertension, palpitations, insomnia, anxiety, nervousness, depression, diaphoresis	Monitor HR, BP. Do not use with other drugs, MAOIs	Berkowitz *et al.*, 2003 (275); Godoy-Matos *et al.*, 2005 (284); Berkowitz *et al.*, 2006 (285)
Lorcaserin[a]	Approved for long-term use in adults	Headache, dizziness, fatigue, nausea, dry mouth, cough, and constipation; back pain, cough, hypoglycemia in patients with T2DM	There is a risk for serotonin syndrome or neuroleptic malignant syndrome-like reactions. Evaluate patients for signs or symptoms of valvular heart disease. Euphoria, hallucination, and dissociation have been seen with supratherapeutic doses. Interactions with triptans, MAOIs, including linezolid, SSRIs, SNRIs, dextromethorphan, tricyclic antidepressants, bupropion, lithium, tramadol, tryptophan, and St. John's wort	Smith *et al.*, 2010 (286); Fidler *et al.*, 2011 (287)

(Continued)

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Table 5. Continued

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Liraglutide[a]	Approved for long-term use in adults	Nausea, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase	Monitor heart rate at regular intervals. This medication is contraindicated in patients with a history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2. Discontinue promptly if pancreatitis is suspected	Zinman *et al.*, 2009 (288); Wadden *et al.*, 2013 (289); Astrup *et al.*, 2009 (290)
Phentermine plus topiramate[a]	Approved for long-term use in adults	Paresthesias, dizziness, taste alterations, insomnia, constipation, dry mouth, elevation in heart rate, memory or cognitive changes	This medication is contraindicated in glaucoma, hyperthyroidism, MAOIs. Concerns about teratogenicity (increased risk of oral clefts) mandate effective contraceptive use and pregnancy test monitoring in females. Metabolic acidosis, hypokalemia, and elevated creatinine have been reported, and periodic monitoring is advised. Abrupt withdrawal of topiramate may cause seizures	Garvey *et al.*, 2012 (291); Allison *et al.*, 2011 (292)
Bupropion plus naltrexone[a]	Approved for long-term use in adults	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea	Monitor HR, BP. Do not administer to patients with a history of seizure disorders or with anorexia or bulimia nervosa or to patients who are using opioids or abruptly discontinuing use of alcohol, benzodiazepines, barbiturates, or antiseizure medications. There is potential increased risk of suicidality	Greenway *et al.*, 2010 (293); Padwal, 2009 (294)
Drugs in development or used off-label that may act centrally as anorexigenic medications				
Recombinant human leptin, metreleptin[a]	This drug is under investigation. In monotherapy it was successful for treating leptin deficiency	Headache, abdominal pain	This drug is useful only in leptin deficiency. Antibodies with neutralizing activity have been identified in patients treated with metreleptin. T cell lymphoma has been reported in patients with acquired generalized lipodystrophy. A risk evaluation and mitigation strategy should be in place to prevent inappropriate prescription	Farooqi *et al.*, 2002 (105); Farooqi *et al.*, 1999 (295)

(*Continued*)

Table 5. Continued

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Exenatide[a]	Not FDA approved for obesity	Nausea, vomiting, diarrhea, feeling jittery, dizziness, headache, dyspepsia	Acute pancreatitis, including fatal and nonfatal hemorrhagic or necrotizing pancreatitis, has been reported. Observe patients carefully for signs and symptoms of pancreatitis. Discontinue promptly if pancreatitis is suspected. Contraindicated in patients with severe renal impairment	Rosenstock *et al.*, 2010 (296); Kelly *et al.*, 2013 (297); Kelly *et al.*, 2012 (298)
Drugs affecting nutrient trafficking				
Orlistat	This drug is FDA approved for treatment of obesity in adolescents ≥12 y old	Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, increased defecation, fecal incontinence	This drug is contraindicated in chronic malabsorption syndromes and cholestasis. Cholelithiasis and, rarely, severe liver injury, including hepatocellular necrosis and acute hepatic failure leading to death, have been reported. It decreases drug concentrations of cyclosporine and levothyroxine. Doses should be temporally separated from orlistat. Fat-soluble vitamin absorption is decreased by orlistat. Use with caution in those at risk for renal insufficiency. MVI supplementation is strongly recommended. A low- dose preparation is approved for over-the-counter sale	McDuffie *et al.*, 2002 (299); Zhi *et al.*, 2003 (300); Norgren *et al.*, 2003 (301); Ozkan *et al.*, 2004 (302); McDuffie *et al.*, 2004 (303); Chanoine *et al.*, 2005 (304); Maahs *et al.*, 2006 (305)
Drugs affecting internal milieu/metabolic control				
Metformin[a]	This drug is not FDA approved for obesity. It is approved for ≥10 y of age for T2DM	Nausea, flatulence, bloating, diarrhea; usually resolves	Do not use in renal failure or with i.v. contrast. MVI supplementation is strongly recommended. Potential risk for vitamin B12 deficiency when used long-term. Avoid alcohol intake	Freemark and Bursey, 2001 (306); Atabeck and Pirgon, 2008 (307); Love-Osborne *et al.*, 2008 (308); Wilson *et al.*, 2010 (309); Yanovski *et al.*, 2011 (310); Kendall *et al.*, 2013 (311)
Octreotide (for hypothalamic obesity)[a]	This drug is not FDA approved for obesity	Cholelithiasis (can be prevented by concurrent ursodiol), diarrhea, edema, abdominal cramps, nausea, bloating, reduction in T4 concentrations, decreased GH but normal IGF-I	Monitor fasting glucose, FT4, HbA1c. Useful only for hypothalamic obesity. Ursodiol coadministration is strongly recommended	Gambineri *et al.*, 2005 (312); Haqq *et al.*, 2003 (313); Lustig *et al.*, 2001 (314); Lustig *et al.*, 1999 (315); Lustig *et al.*, 2006 (316)

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Table 5. Continued

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Recombinant human GH[a]	This drug is not FDA approved for obesity. It is FDA approved in Prader-Willi syndrome to increase height velocity	Edema, carpal tunnel syndrome, death in patients with preexisting obstructive sleep apnea	GH should be used only after screening to rule out obstructive sleep apnea in patients with Prader-Willi syndrome. Clinicians must closely monitor pulmonary function, adrenal function, glucose, HbA1c	Shadid and Jensen, 2003 (317)

Note: All agents are contraindicated in pregnancy. See full prescribing information for all adverse effects, cautions, and contraindications. Pharmacotherapy is not usually considered if the BMI is below the 95th percentile, but there are additional factors to consider. If we initiate pharmacotherapy early in the course of obesity, we may prevent extreme weight gain and metabolic complications, but we may treat an excess of children and adolescents, raise the rate of unwarranted side effects, and increase the costs to individuals and to society. Alternatively, if we begin medication late in the course of obesity, we run the risk of runaway weight gain and long-term morbidity. One approach that reconciles these difficulties is to act aggressively with lifestyle intervention in overweight and mildly obese patients to prevent extreme obesity and to consider pharmacotherapy when the risk of complications is high or soon after complications emerge. The tipping point for pharmacotherapy could be if the family history is strongly positive for a major comorbidity. Lifestyle intervention should precede pharmacotherapy and should be maintained during pharmacotherapy. Derived from August *et al.* (86).

Abbreviations: BP, blood pressure; CNS, central nervous system; FT4, (plasma) free thyroxine; HR, heart rate; IV, intravenous; MAOI, monoamine oxidase inhibitor; MVI, multivitamins; SNRI, selective serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin-reuptake inhibitors; T4, thyroxine.

[a]The use for obesity treatment in children and adolescents <16 y of age of these non–FDA-approved agents should be restricted to large, well-controlled studies.

bariatric surgery (368, 370). Most guidelines now include obesity-related psychological distress an indication for bariatric surgery if the adolescent's BMI is >40 kg/m^2 (363, 370).

A psychologist must assess the bariatric surgery candidate to determine the severity of psychological impairment as well as ability to comply with the requirements for successful outcome. It is essential that all potential candidates have a stable home environment with good family support and the ability to carry out the necessary postoperative behaviors—adherence to dietary guidelines (including macronutrient administration) and physical activity recommendations. Adolescents who are unable to give assent; who have untreated or unstable psychiatric issues other than depression; who are substance abusers; or who are pregnant, planning pregnancy, or breastfeeding are not good candidates for bariatric surgery (370). All candidates for bariatric surgery should agree to psychological evaluation before surgery and in the perioperative period (371).

Surgery can be malabsorptive, restrictive, or combination procedures. Laparoscopic adjustable gastric banding (LAGB) (83) is a purely restrictive procedure that isolates the upper stomach by placing an adjustable silicone ring around the entrance to the stomach [Fig. 3(A)] (223). The LAGB procedure has high reoperation and long-term complication rates, which increase with time and thus it is rarely used anymore (373–375).

Malabsorptive procedures decrease intestinal mucosal function by rearranging the anatomy of the intestine, resulting in malabsorption of nutrients. RYGB is a combination procedure in which the surgeon creates a small stomach pouch and the remainder of the stomach is bypassed. The surgeon inserts a segment of the jejunum in the small gastric pouch, which connects to the proximal portion of the jejunum that drains the bypassed portion of the stomach and the duodenum [Fig. 3(C)]. The RYGB has the restrictive properties of a partial gastrectomy while causing malabsorption and "dumping syndrome" by bypassing much of the stomach.

In vertical sleeve gastrectomy (VSG), a surgeon resects ~85% of the stomach, removing the fundus and greater curvature, leaving a narrow gastric remnant [Fig. 3(F)]. There is no rearrangement of the anatomy, making it less likely that patients having VSG will have malabsorption of micronutrients or postoperative bowel obstruction, as compared with RYGB (370). Because VSG has less surgical complications than the RYGB, patients use it with increasing frequency (373, 376). The Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study (a prospective, multisite observational study at 5 academic centers) performed 52 RYGB and 1 VSG in 2008 vs 24 RYGB and 29 VSG in 2011 (377).

In addition to the anatomic effects of the procedures, both RYGB and VSG decrease the orexigenic hormone ghrelin (87, 378, 379) and increase the anorexogenic incretins glucagon-like peptide 1 and peptide YY (380, 381), thus decreasing appetite and improving insulin sensitivity (382).

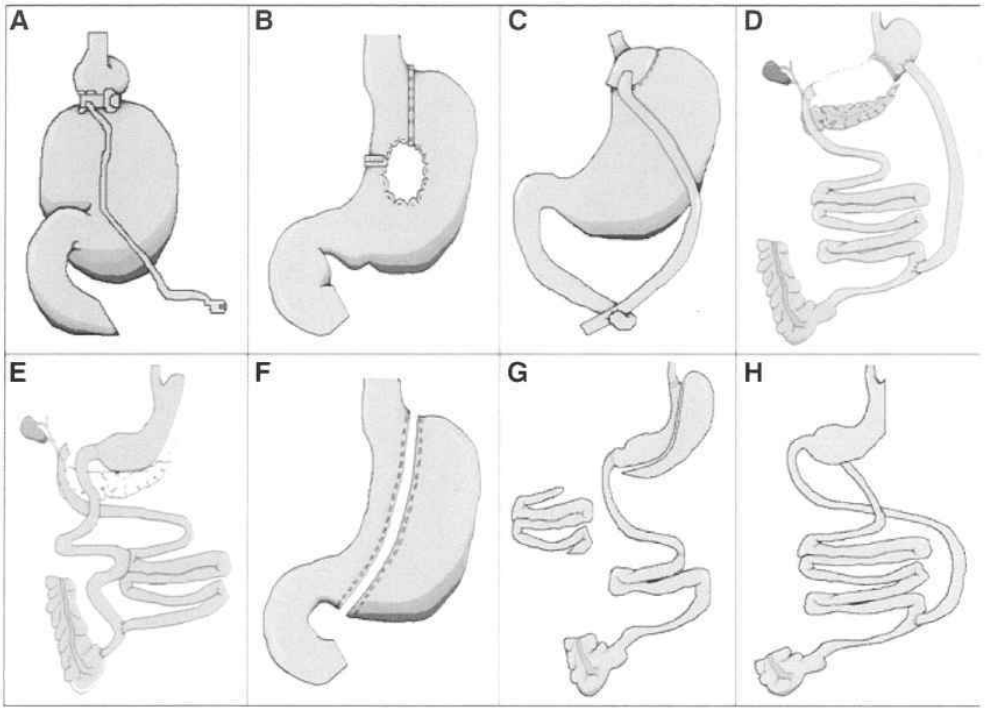

Figure 3. Bariatric surgical procedures. (A) LAGB, (B) vertical banded gastroplasty, (C) RYGB, (D) biliopancreatic diversion, (E) biliopancreatic diversion with duodenal switch, (F) VSG, (G) ileal interposition with sleeve gastrectomy, and (H) Santoro III. (A), (C), and (F) are applicable to section 4 (Bariatric Surgery). [Reproduced from Nandagopal R *et al.* (372), with permission.]

Adolescents having VSG performed between 2008 and 2011 had 61.3% excess weight loss at 1 year (n = 41) and 62.3% excess weight loss at 2 years (n = 8) (383). The largest pediatric study to date found a similar BMI reduction with VSG (37%) (384) as with RYGB (35% to 37%) (385) at 1 year following surgery. This is consistent with the results of the Adolescent Morbid Obesity Study (376), a Swedish study of 81 adolescents with a mean BMI decrease from 45.5 to 29.7 kg/m^2 2 years following RYGB (367). Three-year data from the Teen-LABS study found that the mean BMI decreased overall from 53 to 38 kg/m^2 (a decrease of 27%) with a 28% BMI decrease in those receiving RYGB (n = 161) and a 26% decrease in the teens who had VSG (n = 67) (369).

Regardless of procedure, the percentage of weight loss is independent of initial BMI, so those who are extremely obese will still be obese following surgery (385). Even when obesity persists, most comorbidities associated with obesity improve markedly following the surgery. A study of 22 adolescents who were extremely obese showed positive effects of RYGB on glucose homeostasis parameters with 38% decline in BMI (61 to 39 kg/m^2) 1 year after surgery (386). Positive effects of bariatric surgery have included the reversal of T2DM (387), improvements in glucose homeostasis in nondiabetics (379), improved insulin sensitivity and secretion (388), resolution of sleep apnea (389), improvements in nonalcoholic steatohepatitis (381), improvements in severe arthropathy (371), and improvements in cardiovascular risk factors [dyslipidemia, hypertension, and inflammation (390) and increased adiponeptin and decreased IL-1, IL-8, CRP, and TNF-α (391)], as well as decreased left ventricular mass index, improvements in left ventricular hypertrophy, improvements in diastolic function, and improved rate-pressure product, all of which suggest decreased cardiac workload (392).

The Teen-LABS study indicated that 39% of enrolled patients had more than 4 major comorbid conditions at baseline (376). Three-year follow-up of the patients enrolled in Teen-LABS found a 95% remission of T2DM (19 of 20 teens who had diabetes at the time of surgery), 76% remission of prediabetes (13 of 17 patients), 74% remission of hypertension (56 of 76 with initial high blood pressure), and a 66% normalization of dyslipidemia (84 of 128 patients) (369).

The Teen-LABS study assessed comorbid conditions and surgical complications in the perioperative period in 242 adolescents during the first month following surgery

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(377). There were no procedure-related deaths. Sixty-six percent had laparoscopic RYGB, 28% had VSG, and 6% had LAGB. Major complications occurring within the 30 days following surgery (gastrointestinal leaks, suicidal ideation, anticoagulation for pulmonary embolus) occurred in 7 patients (0.4%), and minor complications occurred in 27 patients (11.2%; 2.5% of patients undergoing RYGB, 3.0% VSG, and 7.1% AGB) (377). The most common complications with both RYGB and VSG were abdominal pain/diarrhea/nausea/dehydration followed by stricture with RYGB and wound infection with VSG (373). Nineteen of 242 patients had major complications within 30 days of surgery (9.3% with RYGB, 4.5% following VSG, and 7.1% with AGB). Late complications occurred in 10% to 15% of patients and included hernias at incision sites, cholelithiasis, small bowel obstruction, stomal stenosis, protein calorie malnutrition, vitamin and mineral deficiencies, and weight regain (376, 377, 393, 394). The Adolescent Morbid Obesity Surgery Study in Sweden had a 33% adverse event rate, with 15% (n = 12) requiring reoperation, 5 for internal hernias, 5 for cholecystectomy, 1 for adhesions, and 1 for pain without surgical findings (364). Seven percent had psychological sequelae, 2 with suicide attempts from medication overdose, 1 with self-destructive behavior and suicidal ideation, and 3 with depression and anxiety. All had psychological problems before surgery. Five patients had excessive use of addictive drugs (none of these patients disclosed the fact that they had preexisting addictions at the time of presurgery assessment) (367). Although most patients have improvement in QOL, self-esteem, anxiety, and depressive symptoms (365), these improvements were not universally maintained at 2 years following surgery (368). Suicidal ideation has been reported, possibly related to unrealistic expectations that their life would be completely different following surgery or to continued poor self-image with weight regain (367). The most recent Teen-LABS study, evaluating 242 adolescents at 3 years after RYGB or VSG, found the mean QOL improved from 63 to 83 based on the total score from the Impact of Weight on Quality of Life–Kids survey (369).

As these procedures all have potential adverse events, it is important to have life-long monitoring for complications. Adherence to prescribed nutritional guidelines is essential for all weight-loss surgery patients postoperatively because low levels of minerals and vitamins can occur due to restricted nutrient intake, decreased gastric acid production, decreased production of intrinsic factor and digestive enzymes, or food intolerance (especially following the dumping syndrome with RYGB) (121, 395). Iron deficiency is the most common mineral deficiency, as RYGB not only causes malabsorption but also has low gastric acid production, further impairing iron absorption (121, 370). Decreased bone mineralization is common, as RYGB decreases cholecalciferol absorption by 25% and calcium and phosphorous concentrations may be low, resulting in significant bone density loss (396). Vitamin deficiencies are common, including deficiencies of vitamins B12, B1, and folate, as RYGB and VSG both reduce the surface of the distal portion of the stomach, resulting in inadequate secretion of intrinsic factor. Annual screening is recommended for patients at risk for developing vitamin deficiencies. As RYGB can result in copper, selenium, and zinc deficiencies, it is recommended that all patients having bariatric surgery receive supplementation with a multivitamin with minerals (370). Patients need to be monitored long term for changes in bone density, hair loss secondary to zinc deficiency, and neurologic complications (363). It is recommended that they avoid alcohol and decrease the intake of sugar and fructose-containing drinks. Despite the importance of nutritional supplementation following bariatric surgery, the Adolescent Morbid Obesity Surgery study found a 67% noncompliance rate with prescribed vitamin and mineral intake at 2 years following surgery. Low ferritin levels were found in 12% of patients before surgery and in 39% of patients 2 years after surgery. Similarly, Vitamin B12 deficiency increased from 1.3% before surgery to 13% after surgery (367). The 3-year follow-up data from the Teen-LABS study found similar results. Low folate levels were found in 3% of youths at baseline and in 8% at 3 years, low vitamin B12 concentrations increased from <1% to 8%, low 25 hydroxyvitamin D levels increased from 37% to 43%, and the percentage of adolescents with low ferritin levels increased from 5% at baseline to 57% at 3 years (369).

These data emphasize the need for a multidisciplinary team that should include a bariatric surgeon, a pediatric obesity specialist to screen and manage the comorbidities, a dietitian to plan the diet and assure adequate nutritional intake, a mental health professional to perform the initial psychological assessment and provide counseling during the postoperative adjustment, a program coordinator to facilitate compliance and follow-up, and a social worker to provide resources to help overcome barriers to care and run support groups (373). Long-term follow-up is essential to maintain compliance with nutritional recommendations.

We agree with the expert panels (226, 227) that suggest bariatric surgery for adolescents with obesity-related comorbid conditions that threaten the adolescent's health—a BMI of >35 kg/m^2 and an extreme comorbidity or a BMI of >40 kg/m^2 and less extreme comorbidity.

Remarks

As adolescents appear to have a greater rate of diabetes resolution and improvement in other obesity-related comorbidities than do adults, it may be beneficial to consider earlier surgery in obese teens, as they likely have less vascular damage than do older individuals.

Values and preferences

The Task Force suggestion of bariatric surgery in adolescents who are extremely obese with serious comorbidities places a high value on amelioration of life-threatening complications and lower value on surgical cost and perioperative complications.

Conclusion

Pediatric obesity remains an ongoing serious international health concern affecting ~17% of US children and adolescents, threatening their adult health and longevity. Pediatric obesity has its basis in genetic susceptibilities influenced by a permissive environment starting *in utero* and extending through childhood and adolescence. Endocrine etiologies for obesity are rare and usually are accompanied by attenuated growth patterns. Pediatric comorbidities are common and long-term health complications often result; screening for comorbidities of obesity should be applied in a hierarchal, logical manner for early identification before more serious complications result. Genetic screening for rare syndromes is indicated only in the presence of specific historical or physical features. The psychological toll of pediatric obesity on the individual and family necessitates screening for mental health issues and counseling as indicated. The prevention of pediatric obesity by promoting healthful diet, activity, and environment should be a primary goal, as achieving effective, long-lasting results with lifestyle modification once obesity occurs is difficult. Although some behavioral and pharmacotherapy studies report modest success, additional research into accessible and effective methods for preventing and treating pediatric obesity is needed. The use of weight loss medications during childhood and adolescence should be restricted to clinical trials. Increasing evidence demonstrates the effectiveness of bariatric surgery in the most seriously affected mature teenagers who have failed lifestyle modification, but it requires experienced teams with resources for long-term follow-up. Adolescents undergoing lifestyle therapy, medication regimens, or bariatric surgery for obesity will need cohesive planning to help them effectively transition to adult care, such as continued necessary monitoring, support, and intervention. Transition programs for obesity are an uncharted area requiring further research for efficacy.

Despite a significant increase in research on pediatric obesity since the initial publication of these guidelines 8 years ago, there remains an unmet need for further study of the genetic and biological factors that increase the risk of weight gain and influence the response to therapeutic interventions. Also needed are more studies to better understand the genetic and biological factors that cause an obese individual to manifest 1 comorbidity vs another or to be free of comorbidities. Continued investigation into the most effective methods of preventing and treating obesity and into methods for changing environmental and economic factors that will lead to worldwide cultural changes in diet and activity should be priorities. Particular attention to determining ways to effect systemic changes in food environs and total daily mobility, as well as methods for sustaining healthy BMI changes, is of importance.

Summary of Changes

Since the publication of the original guidelines 8 years ago there have been an additional 1778 references added to PubMed concerning pediatric obesity. We have incorporated the most relevant data from these to update and enhance the original text.

The epidemiology and definition section contains the latest statistics on trends in childhood obesity, including an apparent recent stabilization of the prevalence. New definitions for extreme obesity are added with a notation that this is the group that continues to rise. The prevalence in ethnic minorities as well a discussion of the limitations of applying the BMI equation to all ethnic groups are addressed.

The evaluation section provides the latest guidelines for utilizing laboratory evaluation for diagnosis and management of comorbidities of obesity. Special emphasis on avoiding endocrine evaluation in most children as well as avoiding measurement of insulin values is provided to prevent unnecessary laboratory testing.

The genetics section has been extensively revised with the latest genomic findings presented in table form and provides guidelines on when to invoke genetic testing in obese children, particularly those with early onset obesity, family history of extreme obesity, and hyperphagia. A combined flowchart demonstrating pathways of diagnosis from history and physical examination to genetic testing is included.

Prevention of obesity is discussed with numerous new studies that support most previous conclusions on lifestyle modification. However, although breast-feeding is beneficial for an infant in numerous ways and was supported as a recommendation to prevent obesity in the

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previous guidelines, recent data weaken support for breast-feeding as a means of preventing obesity and breast-feeding is now a suggestion.

The treatment section focuses on lifestyle changes as the basis of all efforts to treat childhood obesity and supports most previous recommendations and suggestions. A chart demonstrating how much change in systolic blood pressure and lipid values might be expected with a decrease in 1 unit of BMI (kg/m^2) or a decrease of 1 kg of body weight is added.

A discussion of the significant toll childhood obesity takes on the psychological function of a child follows. Guidelines for evaluation of children and access to tools to evaluate child and family function are provided. Referral to appropriate counseling programs is emphasized when psychological problems or aberrant family dynamics are found.

Although noting that all but one of the pharmacological agents targeting obesity are not approved until 16 years of age, agents and their method of action are presented in detail in a table. Lifestyle modification is emphasized as a basis for any additional pharmacological therapy. Should pharmacological therapy be invoked, even off label, guidelines for use and for discontinuation in the case of lack of efficacy are provided. When pharmacotherapy is considered, only clinicians experienced in the use of the agents should use them.

The increasing information on the benefits and risks of bariatric surgery is presented along with a discussion of the types of procedures that might be used. There is emphasis upon contraindications in the use of bariatric surgery in growing children and immature teenagers. Emphasis that procedures should only be carried out in those mature pubertal individuals with severe comorbidities of obesity in the presence of a motivated and compliant patient and family and only in the hands of an experienced surgeon with a dedicated and experienced support team is provided.

The last section sets new goals for future research into the thorny questions of the best method to determine the etiology of childhood obesity and methods to prevent and treat childhood obesity and its comorbidities.

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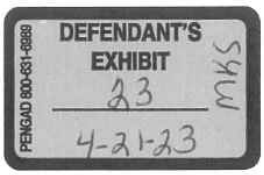

Part 4: Pediatric Basic and Advanced Life Support

2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Collapse All −

1 Top 10 Take-Home Messages

1. High-quality cardiopulmonary resuscitation (CPR) is the foundation of resuscitation. New data reaffirm the key components of high-quality CPR: providing adequate chest compression rate and depth, minimizing interruptions in CPR, allowing full chest recoil between compressions, and avoiding excessive ventilation.
2. A respiratory rate of 20 to 30 breaths per minute is new for infants and children who are (a) receiving CPR with an advanced airway in place or (b) receiving rescue breathing and have a pulse.
3. For patients with nonshockable rhythms, the earlier epinephrine is administered after CPR initiation, the more likely the patient is to survive.
4. Using a cuffed endotracheal tube decreases the need for endotracheal tube changes.

5. The routine use of cricoid pressure does not reduce the risk of regurgitation during bag-mask ventilation and may impede intubation success.
6. For out-of-hospital cardiac arrest, bag-mask ventilation results in the same resuscitation outcomes as advanced airway interventions such as endotracheal intubation.
7. Resuscitation does not end with return of spontaneous circulation (ROSC). Excellent post–cardiac arrest care is critically important to achieving the best patient outcomes. For children who do not regain consciousness after ROSC, this care includes targeted temperature management and continuous electroencephalography monitoring. The prevention and/or treatment of hypotension, hyperoxia or hypoxia, and hypercapnia or hypocapnia is important.
8. After discharge from the hospital, cardiac arrest survivors can have physical, cognitive, and emotional challenges and may need ongoing therapies and interventions.
9. Naloxone can reverse respiratory arrest due to opioid overdose, but there is no evidence that it benefits patients in cardiac arrest.
10. Fluid resuscitation in sepsis is based on patient response and requires frequent reassessment. Balanced crystalloid, unbalanced crystalloid, and colloid fluids are all acceptable for sepsis resuscitation. Epinephrine or norepinephrine infusions are used for fluid-refractory septic shock.

2 Preamble

More than 20 000 infants and children have a cardiac arrest per year in the United States.[1–4] In 2015, emergency medical service–documented out-of-hospital cardiac arrest (OHCA) occurred in more than 7000 infants and children.[4] Approximately 11.4% of pediatric OHCA patients survived to hospital discharge, but outcomes varied by age, with survival rates of 17.1% in adolescents, 13.2% in children, and 4.9% in infants. In the same year, pediatric in-hospital cardiac arrest (IHCA) incidence was 12.66 events per 1000 infant and child hospital admissions, with an overall survival to hospital discharge rate of 41.1%.[4] Neurological outcomes remain difficult to assess across the pediatric age spectrum, with variability in reporting metrics and time to follow-up across studies of both OHCA and IHCA. Favorable neurological outcome has been reported in up to 47% of survivors to discharge.[5] Despite increases in survival from IHCA, there is more to be done to improve both survival and neurological outcomes.[6]

The International Liaison Committee on Resuscitation (ILCOR) Formula for Survival emphasizes 3 essential components for good resuscitation outcomes: guidelines based on sound resuscitation science, effective education of the lay public and resuscitation providers, and implementation of a well-functioning Chain of Survival.[7]

These guidelines contain recommendations for pediatric basic and advanced life support, excluding the newborn period, and are based on the best available resuscitation science. The Chain of Survival (Section 2), which is now expanded to include recovery from cardiac arrest, requires coordinated efforts from medical professionals in a variety of disciplines and, in the case of OHCA, from bystanders, emergency dispatchers, and first responders. In addition, specific recommendations about the training of resuscitation providers are provided in Part 6: Resuscitation Education Science, and recommendations about systems of care are provided in Part 7.

3 Introduction

3.1 Scope of Guidelines

These guidelines are intended to be a resource for lay rescuers and healthcare providers to identify and treat infants and children in the prearrest, intra-arrest, and postarrest states. These apply to infants and children in multiple settings; the community, prehospital, and the hospital environment. Prearrest, intra-arrest, and postarrest topics are reviewed, including cardiac arrest in special circumstances, such as in patients with congenital heart disease.

For the purposes of the pediatric advanced life support guidelines, pediatric patients are infants, children, and adolescents up to 18 years of age, excluding newborns. For pediatric basic life support (BLS), guidelines apply as follows:

- Infant guidelines apply to infants younger than approximately 1 year of age.

- Child guidelines apply to children approximately 1 year of age until puberty. For teaching purposes, puberty is defined as breast development in females and the presence of axillary hair in males.
- For those with signs of puberty and beyond, adult basic life support guidelines should be followed.

Resuscitation of the neonate is addressed in "Part 5: Neonatal Resuscitation" and applies to the newborn typically only during the first hospitalization following birth. Pediatric basic and advanced life support guidelines apply to neonates (less than 30 days old) after hospital discharge.

COVID-19 Guidance

Together with other professional societies, the AHA has provided interim guidance for basic and advanced life support in adults, children, and neonates with suspected or confirmed coronavirus disease 2019 (COVID-19). Because evidence and guidance are evolving with the COVID-19 situation, this interim guidance is maintained separately from the emergency cardiovascular care (ECC) guidelines. Readers are directed to the American Heart Association (AHA) website for the most recent guidance.[8]

3.2 Organization of the Pediatric Writing Committee

The Pediatric Writing Group consisted of pediatric clinicians including intensivists, cardiac intensivists, cardiologists, emergency medicine physicians, medical toxicologists, and nurses. Volunteers with recognized expertise in resuscitation are nominated by the writing group chair and selected by the AHA ECC Committee. The AHA has rigorous conflict of interest policies and procedures to minimize the risk of bias or improper influence during development of the guidelines.[9] Prior to appointment, writing group members and peer reviewers disclosed all commercial relationships and other potential (including intellectual) conflicts. Writing group members whose research led to changes in guidelines were required to declare those conflicts during discussions and abstain from voting on those specific recommendations. This process is described more fully in "Part 2: Evidence Evaluation and Guidelines Development." Disclosure information for writing group members is listed in Appendix 1.

3.3 Methodology and Evidence Review

These pediatric guidelines are based on the extensive evidence evaluation performed in conjunction with the ILCOR and affiliated ILCOR member councils. Three different types of evidence reviews (systematic reviews, scoping reviews, and evidence updates) were used in the 2020 process.[10,11] After review by the ILCOR Science Advisory Committee Chair, the evidence update worksheets were included in Appendix C of the *2020 ILCOR Consensus on CPR and ECC Science With Treatment Recommendations*.[11a] Each of these resulted in a description of the literature that facilitated guideline development. This process is described more fully in "Part 2: Evidence Evaluation and Guidelines Development."[12]

3.4 Class of Recommendation and Level of Evidence

The writing group reviewed all relevant and current AHA Guidelines for Cardiopulmonary Resuscitation (CPR) and ECC and all relevant 2020 *ILCOR Consensus on CPR and ECC Science With Treatment Recommendations* evidence and recommendations to determine if current guidelines should be reaffirmed, revised, or retired or if new recommendations were needed. The writing group then drafted, reviewed, and approved recommendations, assigning to each a Class of Recommendation (COR; ie, strength) and Level of Evidence (LOE; ie, quality, certainty). Criteria for each COR and LOE are described in Table 1.

Table 1. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

Open table in a new window.

3.5 Guideline Structure

The 2020 Guidelines are organized in discrete modules of information on specific topics or management issues.[13] Each modular "knowledge chunk" includes a table of recommendations using standard AHA nomenclature of COR and LOE. Recommendations are presented in order of COR: most potential benefit (Class 1), followed by lesser certainty of benefit (Class 2), and finally potential for harm or no benefit (Class 3). Following the COR, recommendations are ordered by the certainty of supporting LOE: Level A (high-quality randomized controlled trials) to Level C-EO (expert opinion). This order does not reflect the order in which care should be provided.

A brief introduction or short synopsis is provided to contextualize the recommendations with important background information and overarching management or treatment concepts. Recommendation-specific supportive text clarifies the rationale and key study data supporting the recommendations. When appropriate, flow diagrams or additional tables are included. Hyperlinked references are provided to facilitate quick access and review.

3.6 Document Review and Approval

The guideline was submitted for blinded peer review to 5 subject matter experts nominated by the AHA. Peer reviewer feedback was provided for guidelines in draft format and again in final format. The guideline was also reviewed and approved for publication by the AHA Science Advisory and Coordinating Committee and AHA Executive Committee. Disclosure information for peer reviewers is listed in Appendix 2.

3.7 Abbreviations

Abbreviation	Meaning/Phrase
ACLS	advanced cardiovascular life support
AED	automated external defibrillator
ALS	advanced life support
AHA	American Heart Association
BLS	basic life support
COI	conflict of interest
COR	Class of Recommendation
CPR	cardiopulmonary resuscitation
ECC	emergency cardiovascular care
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
ECPR	extracorporeal cardiopulmonary resuscitation

Abbreviation	Meaning/Phrase
EO	Expert Opinion
ETI	endotracheal intubation
FBAO	foreign body airway obstruction
IHCA	in-hospital cardiac arrest
ILCOR	International Liaison Committee on Resuscitation
LD	limited data
LOE	Level of Evidence
MCS	mechanical circulatory support
NR	nonrandomized
OHCA	out-of-hospital cardiac arrest
PALS	pediatric advanced life support
PICO	population, intervention, comparator, outcome
pVT	pulseless ventricular tachycardia
RCT	randomized clinical trial
ROSC	return of spontaneous circulation
SGA	supraglottic airway
TTM	targeted temperature management
VF	ventricular fibrillation

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4 Major Concepts

The epidemiology, pathophysiology, and common etiologies of pediatric cardiac arrest are distinct from adult and neonatal cardiac arrest. Cardiac arrest in infants and children does not usually result from a primary cardiac cause; rather, it is the end result of progressive respiratory failure or shock. In these patients, cardiac arrest is preceded by a variable period of deterioration, which eventually results in cardiopulmonary failure, bradycardia, and cardiac arrest. In children with congenital heart disease, cardiac arrest is often due to a primary cardiac cause, although the etiology is distinct from adults.

Outcomes for pediatric IHCA have improved over the past 20 years, in part because of early recognition, high-quality CPR, postarrest care, and extracorporeal cardiopulmonary resuscitation (ECPR).[1,2] In a recent analysis of the Get With The Guidelines Resuscitation Registry, a large multicenter, hospital-based cardiac arrest registry, pediatric cardiac arrest survival to hospital discharge was 19% in 2000 and 38% in 2018.[2] Survival has increased on average by 0.67% per year, though that increase has plateaued since 2010.[2] New directions of research and therapy may be required to improve cardiac arrest survival. More cardiac arrest events now occur in an intensive care unit (ICU) setting, suggesting that patients at risk for cardiac arrest are being identified sooner and transferred to a higher level of care.[3]

Survival rates from OHCA remain less encouraging. In a recent analysis of the Resuscitation Outcomes Consortium Epidemiological Registry, a multicenter OHCA registry, annual survival to hospital discharge of pediatric OHCA between 2007 and 2012 ranged from 6.7% to 10.2% depending on region and patient age.[4] There was no significant change in these rates over time, consistent with other national registries from Japan and from Australia and New Zealand.[5,6] In the Resuscitation Outcomes Consortium Epidemiological Registry, survival of OHCA was higher in regions with more arrests that were witnessed by emergency medical services and with higher bystander CPR rates, stressing the importance of early recognition and treatment of these patients.[4]

As survival rates from pediatric cardiac arrest increase, there has been a shift with more focus on neurodevelopmental, physical, and emotional outcomes of survivors. Recent studies demonstrate that a quarter of patients with favorable outcomes have global cognitive impairment and that 85% of older children who were reported to have favorable outcomes have selective neuropsychological deficits.[7]

4.1 The Pediatric Chain of Survival

Historically, cardiac arrest care has largely focused on the management of the cardiac arrest itself, highlighting high-quality CPR, early defibrillation, and effective teamwork. However, there are aspects of prearrest and postarrest care that are critical to improve outcomes. As pediatric cardiac arrest survival rates have plateaued, the prevention of cardiac arrest becomes even more important. In the out-of-hospital environment, this includes safety initiatives (eg, bike helmet laws), sudden infant death syndrome prevention, lay rescuer CPR training, and early access to emergency care. When OHCA occurs, early bystander CPR is critical in improving outcomes. In the in-hospital environment, cardiac arrest prevention includes early recognition and treatment of patients at risk for cardiac arrest such as neonates undergoing cardiac surgical procedures, patients presenting with acute fulminant myocarditis, acute decompensated heart failure, or pulmonary hypertension.

Following resuscitation from cardiac arrest, management of the post–cardiac arrest syndrome (which may include brain dysfunction, myocardial dysfunction with low cardiac output, and ischemia or reperfusion injury) is important to avoid known contributors to secondary injury, such as hypotension.[8,9] Accurate neuroprognostication is important to guide caregiver discussions and decision-making. Finally, given the high risk of neurodevelopmental impairment in cardiac arrest survivors, early referral for rehabilitation assessment and intervention is key.

To highlight these different aspects of cardiac arrest management, the Pediatric Chain of Survival has been updated (Figure 1). A separate OHCA Chain of Survival has been created to distinguish the differences between OHCA and IHCA. In both the OHCA and IHCA chains, a sixth link has been added to stress the importance of recovery, which focuses on short- and long-term treatment evaluation, and support for survivors and their families. For both chains of survival, activating the emergency response is followed immediately by the initiation of high-quality CPR. If help is nearby or a cell phone is available, activating the emergency response and starting CPR can be nearly simultaneous. However, in the out-of-hospital setting, a single rescuer who does not have access to a cell phone should begin CPR (compressions-airway-breathing) for infants and children before calling for help because respiratory arrest is the most common cause of cardiac arrest and help may not be nearby. In the event of sudden witnessed collapse, rescuers should use an available automatic external defibrillator (AED), because early defibrillation can be lifesaving.

Figure 1. Pediatric Chains of Survival for in-hospital (top) and out-of-hospital (bottom) cardiac arrest.
CPR indicates cardiopulmonary resuscitation.

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5 Sequence of Resuscitation

Rapid recognition of cardiac arrest, immediate initiation of high-quality chest compressions, and delivery of effective ventilations are critical to improve outcomes from cardiac arrest. Lay rescuers should not delay starting CPR in a child with no "signs of life." Healthcare providers may consider assessing the presence of a pulse as long as the initiation of CPR is not delayed more than 10 seconds. Palpation for the presence or absence of a pulse is not reliable as the sole determinant of cardiac arrest and the need for chest compressions. In infants and children, asphyxial cardiac arrest is more common than cardiac arrest from a primary cardiac event; therefore, effective ventilation is important during resuscitation of children. When CPR is initiated, the sequence is compressions-airway-breathing.

High-quality CPR generates blood flow to vital organs and increases the likelihood of return of spontaneous circulation (ROSC). The 5 main components of high-quality CPR are (1) adequate chest compression depth, (2) optimal chest compression rate, (3) minimizing interruptions in CPR (ie, maximizing chest compression fraction or the proportion of time that chest compressions are provided for cardiac arrest), (4) allowing full chest recoil between compressions, and (5) avoiding excessive ventilation. Compressions of inadequate depth and rate,[1,2] incomplete chest recoil,[3] and high ventilation rates[4,5] are common during pediatric resuscitation.

5.1 Initiation of CPR

Recommendations for Initiation of CPR

COR	LOE	Recommendations
1	C-LD	1. Lay rescuers should begin CPR for any victim who is unresponsive, not breathing normally, and does not have signs of life; do not check for a pulse.[6–20]
2a	C-LD	2. In infants and children with no signs of life, it is reasonable for healthcare providers to check for a pulse for up to 10 s and begin compressions unless a definite pulse is felt.[21–23]
2b	C-EO	3. It may be reasonable to initiate CPR with compressions-airway-breathing over airway-breathing-compressions.[24]

Recommendation-Specific Supportive Text

1. Lay rescuers are unable to reliably determine the presence or absence of a pulse.[6–20]

2. No clinical trials have compared manual pulse checks with observations of "signs of life." However, adult and pediatric studies have identified a high error rate and harmful CPR pauses during manual pulse checks by trained rescuers.[21–23] In 1 study, healthcare provider pulse palpation accuracy was 78%[21] compared with lay rescuer pulse palpation accuracy of 47% at 5 seconds and 73% at 10 seconds.[6]

3. One pediatric study demonstrated only a small delay (5.74 seconds) in commencement of rescue breathing with compressions-airway-breathing compared with airway-breathing-compressions.[24]

Although the evidence is of low certainty, continuing to recommend compressions-airway-breathing likely results in minimal delays in rescue breathing and allows for a consistent approach to cardiac arrest treatment in adults and children.

5.2 Components of High-Quality CPR

Recommendations for Components of High-Quality CPR

COR	LOE	Recommendations
1	B-NR	1. CPR using chest compressions with rescue breaths should be provided to infants and children in cardiac arrest.[25–29]
1	B-NR	2. For infants and children, if bystanders are unwilling or unable to deliver rescue breaths, it is recommended that rescuers should provide chest compressions only.[27,28]
1	C-EO	3. After each compression, rescuers should allow the chest to recoil completely.[2,3,30]
2a	C-LD	4. It is reasonable to use a chest compression rate of ≈100–120/min for infants and children.[31,32]
2a	C-LD	5. For infants and children, it is reasonable for rescuers to provide chest compressions that depress the chest at least one third the anterior-posterior diameter of the chest, which equates to approximately 1.5 inches (4 cm) in infants to 2 inches (5 cm) in children. Once children have reached puberty, it is reasonable to use the adult compression depth of at least 5 cm but no more than 6 cm.[33–36]
2a	C-EO	6. For healthcare providers, it is reasonable to perform a rhythm check, lasting no more than 10 s, approximately every 2 min.
2a	C-EO	7. It is reasonable to ventilate with 100% oxygen during CPR.
2a	C-EO	8. When performing CPR without an advanced airway, it is reasonable for single rescuers to provide a compression-to-ventilation ratio of 30:2 and for 2 rescuers to provide a compression-to-ventilation ratio of 15:2.[25]
2b	C-LD	9. When performing CPR in infants and children with an advanced airway, it may be reasonable to target a respiratory rate range of 1 breath every 2–3 s (20–30 breaths/min), accounting for age and clinical condition. Rates exceeding these recommendations may compromise hemodynamics.[5]

Recommendation-Specific Supportive Text

1. Large observational studies of children with OHCA show the best outcomes with compression-ventilation CPR, though outcomes for infants with OHCA are often poor regardless of resuscitation strategy.[25-29]

2. Large observational studies of children with OHCA show that compression-only CPR is superior to no bystander CPR, though outcomes for infants with OHCA are often poor.[27,28]

3. Allowing complete chest re-expansion improves the flow of blood returning to the heart and thereby blood flow to the body during CPR. There are no pediatric studies evaluating the effect of residual leaning during CPR, although leaning during pediatric CPR is common.[2,3] In 1 observational study of invasively monitored and anesthetized children, leaning was associated with elevated cardiac filling pressures, leading to decreased coronary perfusion pressures during sinus rhythm.[30]

4. A small observational study found that a compression rate of at least 100/min was associated with improved systolic and diastolic blood pressures during CPR for pediatric IHCA.[31] One multicenter, observational study of pediatric IHCA demonstrated increased systolic blood pressures with chest compression rates between 100 and 120/min when compared with rates exceeding 120/min.[32] Rates less than 100/min were associated with improved survival compared to rates of 100 to 120/min; however, the median rate in this slower category was approximately 95/min (ie, very close to 100/min).[32]

5. Three anthropometric studies have shown that the pediatric chest can be compressed to one third of the anterior-posterior chest diameter without damaging intrathoracic organs.[33-35] An observational study found an improvement in rates of ROSC and 24-hour survival, when at least 60% of 30-second epochs of CPR achieve an average chest compression depth greater than 5 cm for pediatric IHCA.[36]

6. Current recommendations include a brief rhythm check every 2 minutes when a monitor or AED is available.

7. There are no human studies addressing the effect of varying inhaled oxygen concentrations during CPR on outcomes in infants and children.

8. The optimum compression-to-ventilation ratio is uncertain. Large observational studies of children with OHCA demonstrated better outcomes with compression-ventilation CPR with ratios of either 15:2 or 30:2 compared with compression-only CPR.[26]

9. One small, multicenter observational study of intubated pediatric patients found that ventilation rates (at least 30 breaths/min in children less than 1 year of age, at least 25 breaths/min in older children) were associated with improved rates of ROSC and survival.[5] However, increasing ventilation rates are associated with decreased systolic blood pressure in children. The optimum ventilation rate during continuous chest compressions in children with an advanced airway is based on limited data and requires further study.

Recommendations 1 and 2 were reviewed in the "2017 American Heart Association Focused Update on Pediatric Basic Life Support and Cardiopulmonary Resuscitation Quality: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[37]

5.3 CPR Technique

COR	LOE	Recommendations
1	C-LD	1. For infants, single rescuers (whether lay rescuers or healthcare providers) should compress the sternum with 2 fingers (Figure 2) or 2 thumbs placed just below the intermammary line.[35-41]

COR	LOE	Recommendations
1	C-LD	2. For infants, the 2-thumb–encircling hands technique (Figure 3) is recommended when CPR is provided by 2 rescuers. If the rescuer cannot physically encircle the victim's chest, compress the chest with 2 fingers.[42–46]
2b	C-LD	3. For children, it may be reasonable to use either a 1- or 2-hand technique to perform chest compressions.[47–49]
2b	C-EO	4. For infants, if the rescuer is unable to achieve guideline recommended depths (at least one third the anterior-posterior diameter of the chest), it may be reasonable to use the heel of 1 hand.

Recommendation-Specific Supportive Text

1. One anthropometric[38] and 3 radiological studies[39–41] found that optimal cardiac compressions occur when fingers are placed just below the intermammary line. One observational pediatric study found that blood pressure was higher when compressions were performed over the lower third of the sternum compared to the midsternum.[41] See Figure 2 for the 2-finger technique.

2. Systematic reviews suggest that the 2-thumb– encircling hands technique may improve CPR quality when compared with 2-finger compressions, particularly for depth.[42,43] However, recent manikin studies suggest that the 2-thumb–encircling hands technique may be associated with lower chest compression fractions (percent of cardiac arrest time that chest compression are provided)[44] and incomplete chest recoil,[45,46] especially when performed by single rescuers. See Figure 3 for the 2-thumb–encircling hands technique.

3. There are no pediatric-specific clinical data to determine if the 1-hand or 2-hand technique produces better outcomes for children receiving CPR. In manikin studies, the 2-hand technique has been associated with improved compression depth,[47] compression force,[48] and less rescuer fatigue.[49]

4. There were no human studies comparing the 1-hand compression versus the 2-thumb–encircling hands technique in infants.

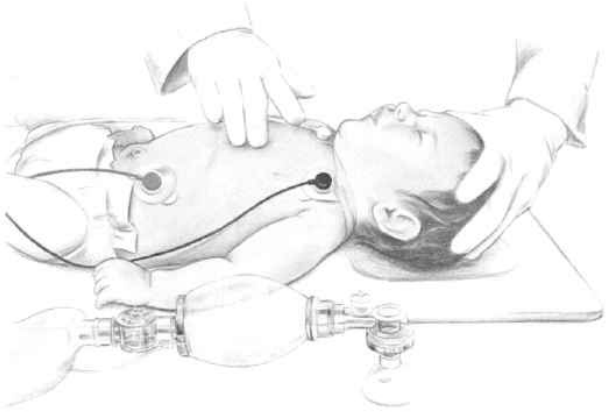

Figure 2. 2-Finger compressions.

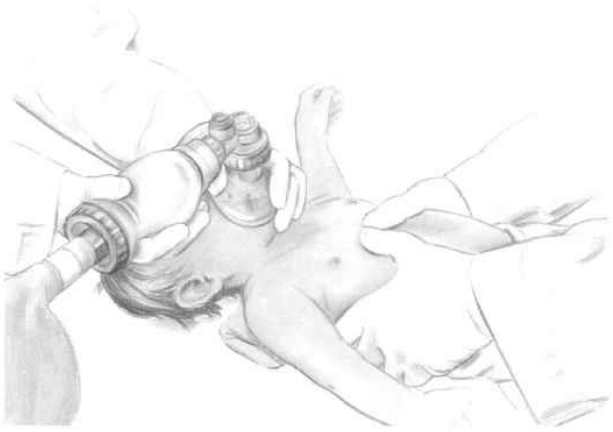

Figure 3. 2-Thumb–encircling hands compressions.

5.4 Support Surfaces for CPR

Recommendations for Support Surfaces for CPR

COR	LOE	Recommendations
1	C-LD	1. During IHCA, when available, activate the bed's "CPR mode" to increase mattress stiffness.[50–53]
2a	C-LD	2. It is reasonable to perform chest compressions on a firm surface.[53–59]
2a	C-LD	3. During IHCA, it is reasonable to use a backboard to improve chest compression depth.[53,55,56,60–62]

Recommendation-Specific Supportive Text

1. "CPR mode" is available on some hospital beds to stiffen the mattress during CPR. Manikin models indicate that mattress compression ranges between 12% and 57% of total compression depth, with softer mattresses being compressed the most.[50–53] This can lead to reduced sternal displacement and a reduction in effective chest compression depth.

2. Manikin studies and 1 pediatric case series show that effective compression depth can be achieved even on a soft surface, providing the CPR provider increases overall compression depth to

compensate for mattress compression.[53–59]

3. Meta-analysis of 6 studies[53,56,60–63] showed a 3-mm (95% CI 1–4 mm) improvement in chest compression depth associated with backboard use when CPR was performed on a manikin placed on a mattress or bed.

5.5 Opening the Airway

Recommendations for Opening the Airway

COR	LOE	Recommendations
1	C-LD	1. Unless a cervical spine injury is suspected, use a head tilt–chin lift maneuver to open the airway.[64]
1	C-EO	2. For the trauma patient with suspected cervical spinal injury, use a jaw thrust without head tilt to open the airway.
1	C-EO	3. For the trauma patient with suspected cervical spinal injury, if the jaw thrust does not open the airway, use a head tilt–chin lift maneuver.

Recommendation-Specific Supportive Text

1. No data directly address the ideal method to open or maintain airway patency. One retrospective cohort study evaluated various head-tilt angles in neonates and young infants undergoing diagnostic MRI and found that the highest proportion of patent airways was at a head-tilt angle of 144 to 150 degrees based on a regression analysis.[64]

2. While no pediatric studies evaluate jaw thrust versus head tilt–chin lift to open the airway, the jaw thrust is widely accepted as an effective way to open the airway, and this maneuver theoretically limits cervical motion compared with the head tilt–chin lift.

3. There are no pediatric studies evaluating the impact of a head tilt–chin lift maneuver to open the airway in a trauma patient with suspected cervical spine injury. However, if providers are unable to open the airway and deliver effective ventilations using a jaw thrust, given the importance of a patent airway, using a head tilt–chin lift maneuver is recommended.

Figures 4, 5, 6, and 7 show, respectively, an infographic for pediatric BLS for lay rescuers, the current pediatric BLS algorithms for healthcare provider, single-rescuer CPR and 2-rescuer CPR, and the current algorithm for pediatric cardiac arrest.

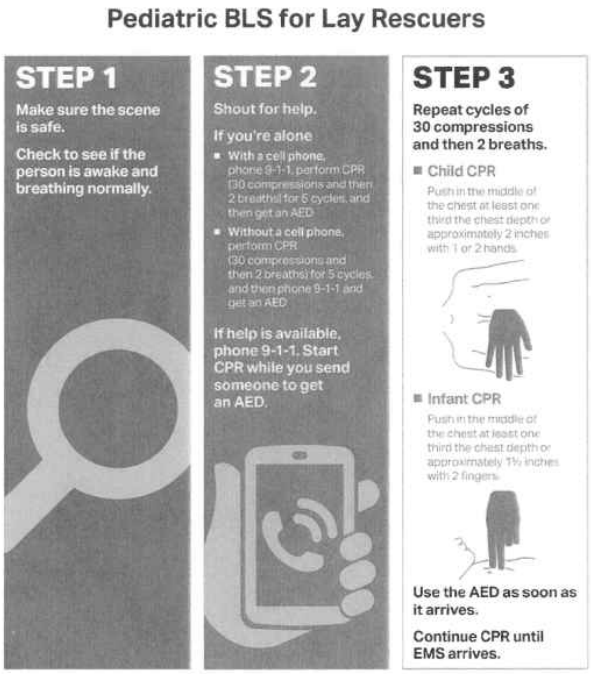

Figure 4. Pediatric BLS for lay rescuers.
AED indicates automated external defibrillator; BLS, basic life support; CPR, cardiopulmonary resuscitation; and EMS, emergency medical services.

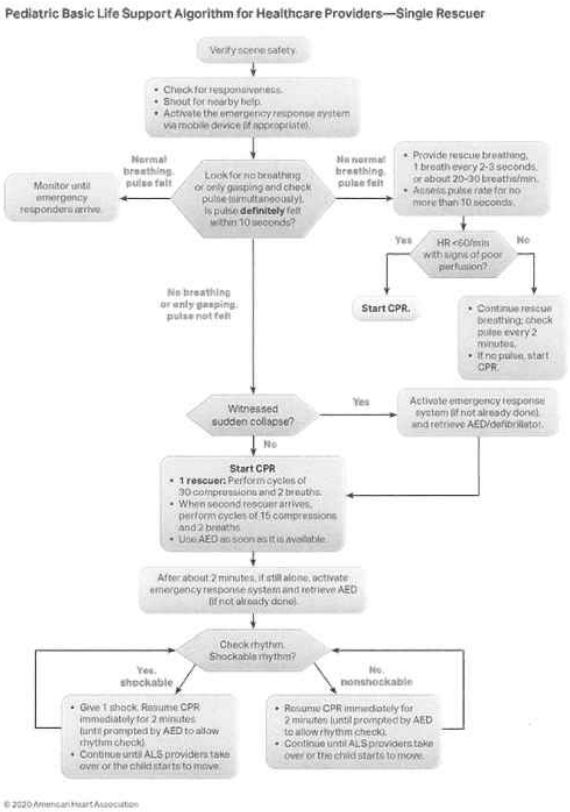

Figure 5. Pediatric Basic Life Support Algorithm for Healthcare Providers—Single Rescuer. AED indicates automated external defibrillator; ALS, advanced life support; CPR, cardiopulmonary resuscitation; and HR, heart rate.

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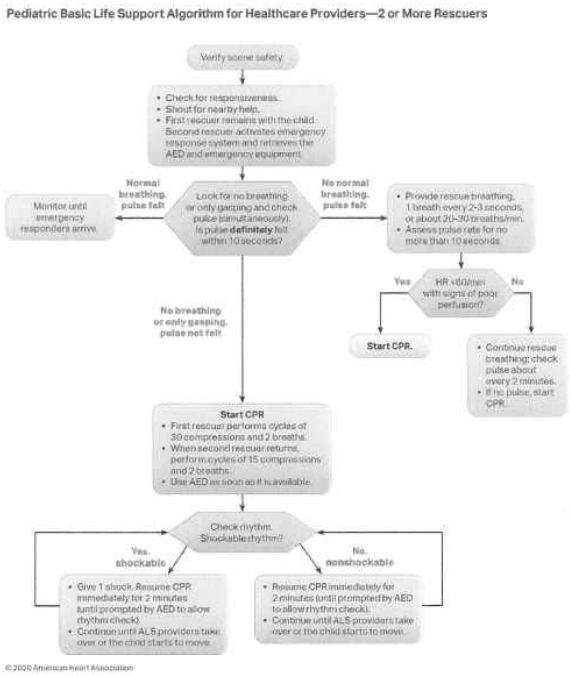

Figure 6. Pediatric Basic Life Support Algorithm for Healthcare Providers—2 or More Rescuers. AED indicates automated external defibrillator; ALS, advanced life support; CPR, cardiopulmonary resuscitation; and HR, heart rate.

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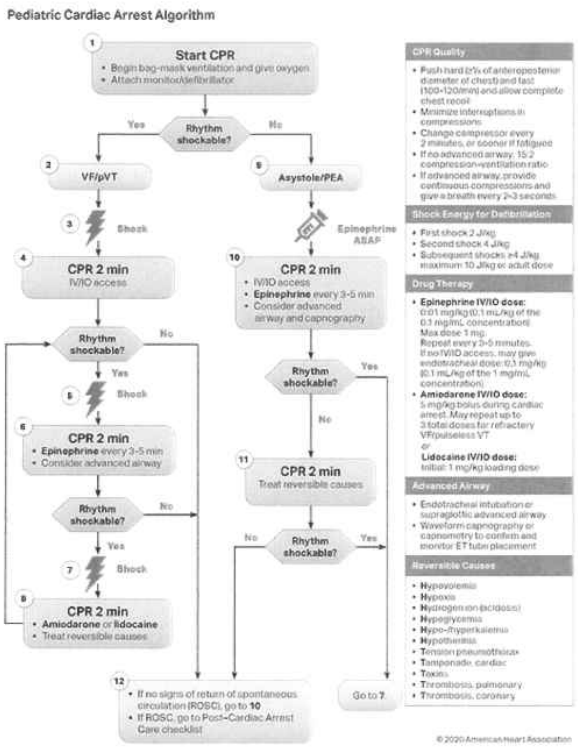

Figure 7. Pediatric Cardiac Arrest Algorithm.
ASAP indicates as soon as possible; CPR, cardiopulmonary resuscitation; ET, endotracheal; HR, heart rate; IO, intraosseous; IV, intravenous; PEA, pulseless electrical activity; and VF/pVT, ventricular fibrillation/pulseless ventricular tachycardia.

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5.6 References

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6 Advanced Airway Interventions During CPR

Most pediatric cardiac arrests are triggered by respiratory deterioration. Airway management and effective ventilation are fundamental to pediatric resuscitation. Although the majority of patients can be successfully ventilated with bag-mask ventilation, this method requires interruptions in chest compressions and is associated with risk of aspiration and barotrauma.

Advanced airway interventions, such as supraglottic airway (SGA) placement or endotracheal intubation (ETI), may improve ventilation, reduce the risk of aspiration, and enable uninterrupted compression delivery. However, airway placement may interrupt the delivery of compressions or result in a malpositioned device. Advanced airway placement requires specialized equipment and skilled providers, and it may be difficult for professionals who do not routinely intubate children.

COR	LOE	Recommendation
2a	C-LD	1. Bag-mask ventilation is reasonable compared with advanced airway interventions (SGA and ETI) in the management of children during cardiac arrest in the out-of-hospital setting.[1–6]

Recommendation-Specific Supportive Text

1. A clinical trial and 2 propensity-matched retrospective studies show that ETI and bag-mask ventilation achieve similar rates of survival with good neurological function and survival to hospital discharge in pediatric patients with OHCA.[1–3] Propensity-matched retrospective studies also show similar rates of survival with good neurological function and survival to discharge when comparing SGA with bag-mask ventilation in pediatric OHCA.[2,3] No difference was observed in outcomes between SGA and ETI.[2,3] There are limited data to compare outcomes between bagmask ventilation versus ETI in the management of IHCA,[4] and there are no hospital-based studies of SGA. The data are not sufficient to support a recommendation for advanced airway use in IHCA. There may be specific circumstances or populations in which early advanced airway interventions are beneficial.

This recommendation was reviewed in the "2019 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[5]

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7 Drug Administration During CPR

Vasoactive agents, such as epinephrine, are used during cardiac arrest to restore spontaneous circulation by optimizing coronary perfusion and maintaining cerebral perfusion, but the benefit and optimal timing of administration remain unclear.[1,2] Antiarrhythmics reduce the risk of recurrent ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT) following defibrillation and may improve defibrillation success. Routine use of sodium bicarbonate and calcium is not supported by current data.[3–7] However, there are specific circumstances when their administration is indicated, such as electrolyte imbalances and certain drug toxicities.

Medication dosing for children is based on weight, which is often difficult to obtain in an emergency setting. There are numerous approaches to estimating weight when an actual weight cannot be obtained.[8]

7.1 Drug Administration During Cardiac Arrest

Recommendations for Drug Administration During Cardiac Arrest

COR	LOE	Recommendations
2a	C-LD	1. For pediatric patients in any setting, it is reasonable to administer epinephrine. IV/IO is preferable to endotracheal tube (ETT) administration.[2,9–11]
2a	C-LD	2. For pediatric patients in any setting, it is reasonable to administer the initial dose of epinephrine within 5 min from the start of chest compressions.[12–16]
2a	C-LD	3. For pediatric patients in any setting, it is reasonable to administer epinephrine every 3–5 min until ROSC is achieved.[17,18]

COR	LOE	Recommendations
2b	C-LD	4. For shock-refractory VF/pVT, either amiodarone or lidocaine may be used.[19,20]
3: Harm	B-NR	5. Routine administration of sodium bicarbonate is not recommended in pediatric cardiac arrest in the absence of hyperkalemia or sodium channel blocker (eg, tricyclic antidepressant) toxicity.[5–7,21–25]
3: Harm	B-NR	6. Routine calcium administration is not recommended for pediatric cardiac arrest in the absence of documented hypocalcemia, calcium channel blocker overdose, hypermagnesemia, or hyperkalemia.[3,4,23]

Recommendation-Specific Supportive Text

1. There are limited data in pediatrics comparing epinephrine administration to no epinephrine administration in any setting. In an OHCA study of 65 children, 12 patients did not receive epinephrine due to lack of a route of administration, and only 1 child had ROSC.[9] An OHCA study of 9 children who had cardiac arrest during sport or exertion noted a survival rate of 67%, of whom 83% did not receive epinephrine. All survivors received early chest compressions (within 5 minutes) and early defibrillation (within 10 minutes), and the initial cardiac arrest rhythm was a shockable rhythm.[9] Intravenous/intraosseous (IV/IO) administration of epinephrine is preferred over ETT administration when possible.[10,11]

2. One retrospective observational study of children with IHCA who received epinephrine for an initial nonshockable rhythm demonstrated that, for every minute delay in administration of epinephrine, there was a significant decrease in ROSC, survival at 24 hours, survival to discharge, and survival with favorable neurological outcome.[12] Patients who received epinephrine within 5 minutes of CPR compared to those who received epinephrine more than 5 minutes after CPR initiation were more likely to survive to discharge.[12] Four observational studies of pediatric OHCA demonstrated that earlier epinephrine administration increased rates of ROSC,[13,14] survival to ICU admission,[14] survival to discharge,[14,16] and 30-day survival.[15]

3. One observational study demonstrated an increased survival rate at 1 year in the group that was administered epinephrine at an interval of less than 5 minutes.[17] One observational study of pediatric IHCA demonstrated that an average epinephrine administration interval of 5 to 8 minutes and of 8 to 10 minutes was associated with increased odds of survival compared with an epinephrine interval of 1 to 5 minutes.[18] Both studies[17,18] calculated the average interval of epinephrine doses by averaging all doses over total arrest time, which does not account for potential differences in dosing intervals throughout resuscitations of varying duration. No studies of pediatric OHCA on frequency of epinephrine dosing were identified.

4. Two studies examined drug therapy of VF/pVT in infants and children.[19,20] In Valdes et al, administration of lidocaine, but not amiodarone, was associated with higher rates of ROSC and survival to hospital admission.[19] Neither lidocaine nor amiodarone significantly affected the odds of survival to hospital discharge; neurological outcome was not assessed. A propensity-matched study of an IHCA registry demonstrated no difference in outcomes for patients receiving lidocaine compared with amiodarone.[20]

5. A recent evidence review identified 8 observational studies of sodium bicarbonate administration during cardiac arrest.[5–7,21–25] Bicarbonate administration was associated with worse survival outcomes for both IHCA and OHCA. There are special circumstances in which bicarbonate is used, such as the treatment of hyperkalemia and sodium channel blocker toxicity, including from tricyclic

antidepressants.

6. Two observational studies examining the administration of calcium during cardiac arrest demonstrated worse survival and ROSC with calcium administration.[4,23] There are special circumstances in which calcium administration is used, such as hypocalcemia, calcium channel blocker overdose, hypermagnesemia, and hyperkalemia.[3]

Recommendation 4 was reviewed in "2018 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[26]

7.2 Weight-Based Dosing of Resuscitation Medications

Recommendations for Weight-Based Dosing of Resuscitation Medications

COR	LOE	Recommendations
1	C-EO	1. For resuscitation medication dosing, it is recommended to use the child's body weight to calculate resuscitation drug doses while not exceeding the recommended dose for adults.[27–31]
2b	B-NR	2. When possible, inclusion of body habitus or anthropomorphic measurements may improve the accuracy of length-based estimated weight.[6]
2b	C-LD	3. If the child's weight is unknown, a body length tape for estimating weight and other cognitive aids to calculate resuscitation drug dosing and administration may be considered.[29,32,33]

Weight-Based Dosing of Resuscitation Medications

1. There are many theoretical concerns about the use of actual body weight (especially in overweight or obese patients).[27–29] However, there are no data about the safety and efficacy of adjusting medication dosing in obese patients. Such adjustments could result in inaccurate dosing of medications.[30,31]

2. Several studies suggest that inclusion of body habitus or anthropometric measurements further refines and improves weight estimations using length-based measures.[6] However, there is considerable variation in these methods, and the training required to use these measures may not be practical in every context.

3. Cognitive aids can assist in the accurate approximation of body weight (described as being within 10% to 20% of measured total body weight). Several recent studies demonstrated high variability of weight estimates, with a tendency toward underestimation of total body weight yet closely approximating ideal body weight.[29,32,33]

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8 Management of VF/pVT

The risk of VF/pVT steadily increases throughout childhood and adolescence but remains less frequent than in adults. Cardiac arrest due to an initial rhythm of VF/pVT has better rates of survival to hospital discharge with favorable neurological function than cardiac arrests due to an initial nonshockable rhythm. Shockable rhythms may be the initial rhythm of the cardiac arrest (primary VF/pVT) or may develop during the resuscitation (secondary VF/pVT). Defibrillation is the definitive treatment for VF/pVT. The shorter the duration of VF/pVT, the more likely that the shock will result in a perfusing rhythm. Both manual defibrillators and AEDs can be used to treat VF/pVT in children. Manual defibrillators are preferred when a shockable rhythm is identified by a healthcare provider because the energy dose can be titrated to the patient's weight. AEDs have high specificity in recognizing pediatric shockable rhythms. Biphasic, instead of monophasic, defibrillators are recommended because less energy is required to achieve termination of VF/pVT, with fewer side effects. Many AEDs are equipped to attenuate (reduce) the energy dose to make them suitable for infants and children younger than 8 years of age.

8.1 Energy Dose

Recommendations for Energy Dose

COR	LOE	Recommendations
2a	C-LD	1. It is reasonable to use an initial dose of 2–4 J/kg of monophasic or biphasic energy for defibrillation, but, for ease of teaching, an initial dose of 2 J/kg may be considered.[1-7]
2b	C-LD	2. For refractory VF, it may be reasonable to increase the defibrillation dose to 4 J/kg.[1-7]
2b	C-LD	3. For subsequent energy levels, a dose of 4 J/kg may be reasonable, and higher energy levels may be considered, though not to exceed 10 J/kg or the adult maximum dose.[1-7]

Recommendation-Specific Supportive Text

1. 2, and 3. A systematic review[1] demonstrated no relationship between energy dose and any outcome. No randomized controlled trials were available, and most studies only evaluated the first shock. An IHCA case series of 71 shocks in 27 patients concluded that 2 J/kg terminated VF, but neither the subsequent rhythm nor the outcome of the resuscitation was reported.[2] A small case series of prolonged OHCA observed that 2 to 4 J/kg shock terminated VF 14 times in 11 patients, resulting in asystole or pulseless electric activity, with no survivors to hospital discharge.[3] In 1 observational study of IHCA,[4] a higher initial energy dose of more than 3 to 5 J/kg was less effective than 1 to 3 J/kg in achieving ROSC. Three small, observational studies of pediatric IHCA[3,5] and OHCA[6] found no specific initial energy dose that was associated with successful defibrillation. One study suggested that 2 J/kg was an ineffective dose, especially for secondary VF.[7]

8.2 Coordination of Shock and CPR

Recommendations for Coordination of Shock and CPR

COR	LOE	Recommendations
1	C-EO	1. Perform CPR until the device is ready to deliver a shock.[8-12]

COR	LOE	Recommendations
1	C-EO	2. A single shock followed by immediate chest compressions is recommended for children with VF/pVT.[13,14]
1	C-EO	3. Minimize interruptions of chest compressions.[13,15]

Recommendation-Specific Supportive Text

1. There are currently no pediatric data available regarding the optimal timing of CPR prior to defibrillation. Adult studies demonstrate no benefit of a prolonged period of CPR prior to initial defibrillation.[8–12]

2. There are currently no pediatric data concerning the best sequence for coordination of shocks and CPR. Adult studies comparing a 1-shock protocol versus a 3-shock protocol for treatment of VF suggest significant survival benefit with the single-shock protocol.[13,14]

3. Prolonged pauses in chest compressions decrease blood flow and oxygen delivery to vital organs, such as the brain and heart, and are associated with lower survival.[13,15]

8.3 Defibrillator Paddle Size, Type, and Position

Recommendations for Defibrillator Paddle Size, Type, and Position

COR	LOE	Recommendations
1	C-EO	1. Use the largest paddles or self-adhering electrodes that will fit on the child's chest while still maintaining good separation between the pads/paddles.[16–18]
2b	C-LD	2. When affixing self-adhering pads, either anterior-lateral placement or anterior-posterior placement may be reasonable.[7,19]
2b	C-LD	3. Paddles and self-adhering pads may be considered equally effective in delivering electricity.[20]

Recommendation-Specific Supportive Text

1. Larger pad or paddle size decreases transthoracic impedance, which is a major determinant of current delivery.[16–18]

2. One human and 1 porcine study demonstrated no significant difference in shock success or ROSC when comparing anterior-lateral with anterior-posterior position.[7,19]

3. One study demonstrated no significant difference in median time to shock with paddles compared with self-adhesive pads.[20]

8.4 Type of Defibrillator

COR	LOE	Recommendations
1	C-LD	1. When using an AED on infants and children <8 y old, use of a pediatric attenuator is recommended.[21–32]
1	C-EO	2. For infants under the care of a trained healthcare provider, a manual defibrillator is recommended when a shockable rhythm is identified.[33,34]
2b	C-EO	3. If neither a manual defibrillator nor an AED equipped with a pediatric attenuator is available, an AED without a dose attenuator may be used.[26–28,30,35]

Recommendation-Specific Supportive Text

1. Shockable rhythms are infrequent in infants.[21,22] Studies of rhythm identification algorithms have demonstrated high specificity for shockable rhythms in infants and children.[23–25] Although there are no direct comparisons between pediatric attenuator and nonattenuator AED-delivered shocks, multiple case reports and case series document shock success with survival when a pediatric attenuator was used.[26–32]

2. There are no specific studies comparing manual defibrillators with AEDs in infants or children. Manual defibrillators are preferred for in-hospital use because the energy dose can be titrated to the patient's weight. In adults, use of an AED in hospitals did not improve survival,[33] and the perishock pauses needed for rhythm analysis were prolonged.[34]

3. AEDs without pediatric modifications deliver 120 to 360 Joules, exceeding the recommended dose for children weighing less than 25 kg. However, there are reports of safe and effective AED use in infants and young children when the dose exceeded 2 to 4 J/kg.[26–28,30,35] Because defibrillation is the only effective therapy for VF, an AED without a dose attenuator may be lifesaving.

8.5 References

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9 Assessment of Resuscitation Quality

Initiating and maintaining high-quality CPR is associated with improved rates of ROSC, survival, and favorable neurological outcome, yet measured CPR quality is often suboptimal.[1–3] Noninvasive and invasive monitoring techniques may be used to assess and guide the quality of CPR. Invasive arterial blood pressure monitoring during CPR provides insight to blood pressures generated with compressions and medications.[4] End-tidal CO_2 ($ETCO_2$) reflects both the cardiac output produced and ventilation efficacy and may provide feedback on the quality of CPR.[5] A sudden rise in $ETCO_2$ may be an early sign of ROSC.[6] CPR feedback devices (ie, coaching, audio, and audiovisual devices) may improve compression rate, depth, and recoil within a system of training and quality assurance for high-quality CPR. Point of care ultrasound, specifically echocardiography, during CPR has been considered for identification of reversible causes of arrest. Technologies that are under evaluation to assess resuscitation quality include noninvasive measures of cerebral oxygenation, such as using near infrared spectroscopy during CPR.

Recommendations for the Assessment of Resuscitation Quality

COR	LOE	Recommendations
2a	C-LD	1. For patients with continuous invasive arterial blood pressure monitoring in place at the time of cardiac arrest, it is reasonable for providers to use diastolic blood pressure to assess CPR quality.[4]
2b	C-LD	2. $ETCO_2$ monitoring may be considered to assess the quality of chest compressions, but specific values to guide therapy have not been established in children.[7,8]
2b	C-EO	3. It may be reasonable for the rescuer to use CPR feedback devices to optimize adequate chest compression rate and depth as part of a continuous resuscitation quality improvement system.[9,10]
2b	C-EO	4. When appropriately trained personnel are available, echocardiography may be considered to identify potentially treatable causes of the arrest, such as pericardial tamponade and inadequate ventricular filling, but the potential benefits should be weighed against the known deleterious consequences of interrupting chest compressions.[11–13]

Recommendation-Specific Supportive Text

1. A prospective observational study of pediatric patients with invasive arterial blood pressure monitoring during the first 10 minutes of CPR demonstrated higher rates of favorable neurological outcome if the diastolic blood pressure was at least 25 mm Hg in infants and at least 30 mm Hg in children.[4] Of note, the cut points for diastolic blood pressure tracings were analyzed using post hoc waveform analysis; therefore, prospective evaluation is needed.

2. A single-center, retrospective study of in-hospital CPR in infants found that $ETCO_2$ values between 17 and 18 mm Hg had a positive predictive value for ROSC of 0.885.[7] A prospective, multicenter observational study of IHCA did not find an association between mean $ETCO_2$ and outcomes.[8]

3. A simulation trial of pediatric healthcare providers demonstrated a significant improvement in chest compression depth and rate compliance when they received visual feedback (compared to no feedback), although overall compression quality remained poor.[9] One small observational study of 8 children with IHCA did not find an association between CPR with or without audiovisual feedback and survival to discharge, although feedback decreased excessive compression rates.[10]

4. Several case series evaluated the use of bedside echocardiography to identify reversible causes of cardiac arrest, including pulmonary embolism.[11,12] One prospective observational study of children (without cardiac arrest) admitted to an ICU reported good agreement of estimates of shortening fraction and inferior vena cava volume between emergency physicians using bedside limited echocardiography and cardiologists performing formal echocardiography.[13]

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10 Extracorporeal Cardiopulmonary Resuscitation

Extracorporeal cardiopulmonary resuscitation (ECPR) is defined as the rapid deployment of venoarterial extracorporeal membrane oxygenation (ECMO) for patients who do not achieve sustained ROSC. It is a resource-intense, complex, multidisciplinary therapy that traditionally has been limited to large pediatric medical centers with providers who have expertise in the management of children with cardiac disease. Judicious use of ECPR for specific patient populations and within dedicated and highly practiced

environments has proved successful, especially for IHCA with reversible causes.[1] ECPR use rates have increased, with single-center reports in both adults and children suggesting that application of this therapy across broader patient populations may improve survival after cardiac arrest.[2–4]

There are no studies of ECPR demonstrating improved outcomes following pediatric OHCA.

Recommendation for the Use of Extracorporeal Cardiopulmonary Resuscitation

COR	LOE	Recommendation
2b	C-LD	1. ECPR may be considered for pediatric patients with cardiac diagnoses who have IHCA in settings with existing ECMO protocols, expertise, and equipment.[5,6]

Recommendation-Specific Supportive Text

1. One observational registry study of ECPR for pediatric IHCA after cardiac surgery demonstrated that ECPR was associated with higher rates of survival to hospital discharge than conventional CPR.[5] A propensity-matched analysis of ECPR compared with conventional CPR using the same registry found that ECPR was associated with favorable neurological outcome in patients with IHCA of any etiology.[6] There is insufficient evidence to suggest for or against the use of ECPR for pediatric patients experiencing OHCA or pediatric patients with noncardiac disease experiencing IHCA refractory to conventional CPR.

This recommendation was reviewed in the "2019 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[7]

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11 Post–Cardiac Arrest Care Treatment and Monitoring

Successful resuscitation from cardiac arrest results in a post–cardiac arrest syndrome that can evolve in the days after ROSC. The components of post–cardiac arrest syndrome are (1) brain injury, (2) myocardial dysfunction, (3) systemic ischemia and reperfusion response, and (4) persistent precipitating pathophysiology.[1,2] Post–cardiac arrest brain injury remains a leading cause of morbidity and mortality in adults and children because the brain has limited tolerance of ischemia, hyperemia, or edema. Pediatric post–cardiac arrest care focuses on anticipating, identifying, and treating this complex physiology to improve survival and neurological outcomes.

Targeted temperature management (TTM) refers to continuous maintenance of patient temperature within a narrowly prescribed range while continuously monitoring temperature. All forms of TTM avoid fever, and hypothermic TTM attempts to treat reperfusion syndrome by decreasing metabolic demand, reducing free radical production, and decreasing apoptosis.[2]

Identification and treatment of derangements—such as hypotension, fever, seizures, acute kidney injury, and abnormalities of oxygenation, ventilation, and electrolytes—are important because they may impact outcomes.

11.1 Post–Cardiac Arrest Targeted Temperature Management

Recommendations for Post–Cardiac Arrest Targeted Temperature Management

COR	LOE	Recommendations
1	A	1. Continuous measurement of core temperature during TTM is recommended.[3,4]
2a	B-R	2. For infants and children between 24 h and 18 yr of age who remain comatose after OHCA or IHCA, it is reasonable to use either TTM of 32°C–34°C followed by TTM of 36°C–37.5°C or only TTM of 36°C–37.5°C.[3,4]

Recommendation-Specific Supportive Text

1. and 2. Two pediatric randomized clinical trials of TTM (32°C–34°C for 48 hours followed by 3 days of TTM 36°C–37.5°C versus TTM 36°C–37.5°C for a total of 5 days) after IHCA or OHCA in children with coma following ROSC found no difference in 1-year survival with a favorable neurological outcome.[3,4] Hyperthermia was actively prevented with TTM. Continuous core temperature monitoring was used for the 5 days of TTM in both trials.

Recommendations 1 and 2 were reviewed in the "2019 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[5]

11.2 Post–Cardiac Arrest Blood Pressure Management

Recommendations for Post–Cardiac Arrest Blood Pressure Management

COR	LOE	Recommendations
1	C-LD	1. After ROSC, we recommend that parenteral fluids and/or vasoactive drugs be used to maintain a systolic blood pressure greater than the fifth percentile for age.[6–9]

COR	LOE	Recommendations
1	C-EO	2. When appropriate resources are available, continuous arterial pressure monitoring is recommended to identify and treat hypotension.[6–9]

Recommendation-Specific Supportive Text

1. and 2. Two observational studies demonstrated that systolic hypotension (below 5th percentile for age and sex) at approximately 6 to 12 hours following cardiac arrest is associated with decreased survival to discharge.[6,7] Another observational study found that patients who had longer periods of hypotension within the first 72 hours of ICU post–cardiac arrest care had decreased survival to discharge.[8] In an observational study of patients with arterial monitoring during and immediately after cardiac arrest, diastolic hypertension (above 90th percentile) in the first 20 minutes after ROSC was associated with an increased likelihood of survival to discharge.[9] Because blood pressure is often labile in the post–cardiac arrest period, continuous arterial pressure monitoring is recommended.

11.3 Post–Cardiac Arrest Oxygenation and Ventilation Management

Recommendations for Post–Cardiac Arrest Oxygenation and Ventilation Management

COR	LOE	Recommendations
2b	C-LD	1. It may be reasonable for rescuers to target normoxemia after ROSC that is appropriate to the specific patient's underlying condition.[10–13]
2b	C-LD	2. It may be reasonable for rescuers to wean oxygen to target an oxyhemoglobin saturation between 94% and 99%.[10–12,14]
2b	C-LD	3. It may be reasonable for practitioners to target a partial pressure of carbon dioxide ($Paco_2$) after ROSC that is appropriate to the specific patient's underlying condition, and limit exposure to severe hypercapnia or hypocapnia.[10,11,14]

Recommendation-Specific Supportive Text

1. and 2. Because an arterial oxyhemoglobin saturation of 100% may correspond to a Pao_2 between 80 and approximately 500 mm Hg, it is reasonable to target an oxyhemoglobin saturation between 94% and 99%. Three small observational studies of pediatric IHCA and OHCA did not show an association between hyperoxemia and outcome.[10,11,13] In a larger observational study of pediatric IHCA and OHCA patients, the presence of normoxemia compared with hyperoxemia after ROSC was associated with improved survival to pediatric ICU discharge.[12]

3. One observational study demonstrated that both hypercapnia and hypocapnia after ROSC were associated with increased mortality.[11] One small observational study demonstrated no association between hypercapnia ($Paco_2$ greater than 50 mm Hg) or hypocapnia ($Paco_2$ less than 30 mm Hg) and outcome.[10] Another observational study of pediatric IHCA, showed hypercapnia ($Paco_2$ 50 mm Hg or greater) was associated with decreased survival to hospital discharge.[14] Because hypercapnia and hypocapnia impact cerebral blood flow, normocapnia should be the focus after ROSC while accounting for patients who have chronic hypercapnia.

11.4 Post–Cardiac Arrest EEG Monitoring and Seizure Treatment

Recommendations for Post–Cardiac Arrest EEG Monitoring and Seizure Treatment

COR	LOE	Recommendations
1	C-LD	1. When resources are available, continuous electroencephalography (EEG) monitoring is recommended for the detection of seizures following cardiac arrest in patients with persistent encephalopathy.[15–18]
1	C-LD	2. It is recommended to treat clinical seizures following cardiac arrest.[19,20]
2a	C-EO	3. It is reasonable to treat nonconvulsive status epilepticus following cardiac arrest in consultation with experts.[19,20]

Recommendation-Specific Supportive Text

1. Nonconvulsive seizures and nonconvulsive status epilepticus are common after pediatric cardiac arrest.[15–18] The American Clinical Neurophysiology Society recommends continuous EEG monitoring for encephalopathic patients after pediatric cardiac arrest.[15] Nonconvulsive seizures and nonconvulsive status epilepticus cannot be detected without EEG monitoring.[15]

2. and 3. There is insufficient evidence to determine whether treatment of convulsive or nonconvulsive seizures improves neurological and/or functional outcomes after pediatric cardiac arrest. Both convulsive and nonconvulsive status epilepticus are associated with worse outcomes.[17] The Neurocritical Care Society recommends treating status epilepticus with the goal of stopping convulsive and electrographic seizure activity.[19]

Figure 8 shows the checklist for post–cardiac arrest care.

Components of Post–Cardiac Arrest Care	Check
Oxygenation and ventilation	
Measure oxygenation and target normoxemia 94%-99% (or child's normal/appropriate oxygen saturation).	☐
Measure and target P_{aCO_2} appropriate to the patient's underlying condition and limit exposure to severe hypercapnia or hypocapnia.	☐
Hemodynamic monitoring	
Set specific hemodynamic goals during post–cardiac arrest care and review daily.	☐
Monitor with cardiac telemetry.	☐
Monitor arterial blood pressure.	☐
Monitor serum lactate, urine output, and central venous oxygen saturation to help guide therapies.	☐
Use parenteral fluid bolus with or without inotropes or vasopressors to maintain a systolic blood pressure greater than the fifth percentile for age and sex.	☐
Targeted temperature management (TTM)	
Measure and continuously monitor core temperature.	☐
Prevent and treat fever immediately after arrest and during rewarming.	☐
If patient is comatose apply TTM (32°C-34°C) followed by (36°C-37.5°C) or only TTM (36°C-37.5°C).	☐
Prevent shivering.	☐
Monitor blood pressure and treat hypotension during rewarming.	☐
Neuromonitoring	
If patient has encephalopathy and resources are available, monitor with continuous electroencephalogram.	☐
Treat seizures.	☐
Consider early brain imaging to diagnose treatable causes of cardiac arrest.	☐
Electrolytes and glucose	
Measure blood glucose and avoid hypoglycemia.	☐
Maintain electrolytes within normal ranges to avoid possible life-threatening arrhythmias.	☐
Sedation	
Treat with sedatives and anxiolytics.	☐
Prognosis	
Always consider multiple modalities (clinical and other) over any single predictive factor.	☐
Remember that assessments may be modified by TTM or induced hypothermia.	☐
Consider electroencephalogram in conjunction with other factors within the first 7 days after cardiac arrest.	☐
Consider neuroimaging such as magnetic resonance imaging during the first 7 days.	☐

Figure 8. Post–cardiac arrest care checklist.

11.5 References

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12 Prognostication Following Cardiac Arrest

Early and reliable prognostication of neurological outcome in pediatric survivors of cardiac arrest is essential to guide treatment, enable effective planning, and provide family support. Clinicians use patient and cardiac arrest characteristics, postarrest neurological examination, laboratory results, neurological imaging (eg, brain computed tomography and MRI), and EEG to guide prognostication. At this time, no single factor or validated decision rule has been identified to reliably predict either favorable or unfavorable outcome within 24 to 48 hours of ROSC. EEG, neuroimaging, and serum biomarkers when used alone predict outcome with only moderate accuracy, and more data are needed before applying these to individual patients.

Recommendations for Prognostication Following Cardiac Arrest

COR	LOE	Recommendations
2a	B-NR	1. EEG in the first week post cardiac arrest can be useful as 1 factor for prognostication, augmented by other information.[1–8]
2a	B-NR	2. It is reasonable for providers to consider multiple factors when predicting outcomes in infants and children who survive cardiac arrests.[1,7,9–21]
2a	B-NR	3. It is reasonable for providers to consider multiple factors when predicting outcomes in infants and children who survive cardiac arrests after nonfatal drowning (ie, survival to hospital admission).[22–39]

Recommendation-Specific Supportive Text

1. Eight retrospective observational studies demonstrate that EEG background patterns are associated with neurological outcomes at discharge.[1–8] The presence of sleep spindles,[3,4,8] normal background,[2] and reactivity[7,8] is associated with favorable outcomes. Burst suppression and flat or attenuated EEG patterns are associated with unfavorable neurological outcome.[1,2,5,8] However, these associations do not reach the high degrees of sensitivity and specificity needed to use EEG as a stand-alone modality for neuroprognostication.

2. Several studies demonstrate the association of clinical history, patient characteristics, physical examination, imaging, and biomarker data with neurological outcome following cardiac arrest.[1,7,9–19] To date, no single factor has demonstrated sufficient accuracy to prognosticate outcome. Elevated serum lactate, pH, or base deficit measured within the first 24 hours after cardiac arrest are associated with unfavorable outcome;[9,11,12,16–18,20,21] however, specific cutoff values are unknown.

3. Shorter submersion times are associated with better outcomes after pediatric nonfatal drowning.[22–25] There is no clear association between patient age,[23,26–31,39] water type,[30,32,33] water temperature,[23,25,34,35]

emergency medical services response times[35,36] or witnessed status,[36–39] and neurological outcome following nonfatal drowning. No single factor accurately predicts prognosis after nonfatal drowning.

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13 Post–Cardiac Arrest Recovery

Survivors are at significant risk for both short-term and long-term physical, neurological, cognitive, emotional, and social morbidity.[3] Many children who survive a cardiac arrest with a grossly "favorable outcome" have more subtle and sustained neuropsychological impairment.[4] The full impact of brain injury on children's development may not be fully appreciated until months to years after the cardiac arrest. Furthermore, because children are raised by caregivers, the impact of morbidity following cardiac arrest affects not only the child but also the family.

Recovery has been introduced as the sixth link in the Chain of Survival to acknowledge that survivors of cardiac arrest may require ongoing integrated medical, rehabilitative, caregiver, and community support in the months to years after their cardiac arrest (see Figure 9).[3] Recent scientific statements from the AHA and ILCOR highlight the importance of studying long-term neurological and health-related quality-of-life outcomes.[5,6]

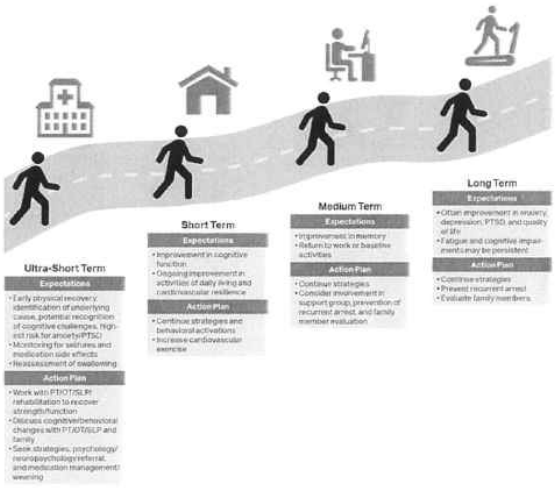

Figure 9. Road map to recovery.[3]

Recommendations for Post-Cardiac Arrest Recovery

COR	LOE	Recommendations
1	C-LD	1. It is recommended that pediatric cardiac arrest survivors be evaluated for rehabilitation services.[4,7–11]
2a	C-LD	2. It is reasonable to refer pediatric cardiac arrest survivors for ongoing neurological evaluation for at least the first year after cardiac arrest.[3,5,10–15]

Recommendation-Specific Supportive Text

1. Two randomized controlled trials of TTM for comatose children after IHCA or OHCA with a primary outcome of neurobehavioral outcome at 1 year[7,8] showed that new morbidity is common.[9–11] Many children who survived to 1 year with a favorable neurobehavioral outcome on Vineland Adaptive Behavior Scales-II (VABS-II) had global cognitive impairment or selective neuropsychological deficits.[4]

2. Two randomized controlled trials of TTM for pediatric cardiac arrest demonstrated that neurological function improves for some survivors during the first year after cardiac arrest.[10,11] Several case series of longer-term outcomes (more than 1 year after cardiac arrest) demonstrate ongoing cognitive, physical, and neuropsychological impairments.[12–14] Recent statements from the AHA highlight the importance of follow-up after discharge, because patient recovery continues during the first year after cardiac arrest.[3,5,6,15] It is unclear what impact ongoing childhood development has on recovery following pediatric cardiac arrest.

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14 Family Presence During Resuscitation

Over the past 20 years, the practice of maintaining family presence during resuscitation has increased. Most parents surveyed indicate that they would desire to be present during their child's resuscitation. Older data suggest a lower incidence of anxiety and depression and more constructive grief behaviors among parents who were present when their child died.[1]

Recommendations for Family Presence During Resuscitation

COR	LOE	Recommendations
1	B-NR	1. Whenever possible, provide family members with the option of being present during the resuscitation of their infant or child.[2–10]
1	B-NR	2. When family members are present during resuscitation, it is beneficial for a designated team member to provide comfort, answer questions, and support the family.[11,12]
1	C-LD	3. If the presence of family members is considered detrimental to the resuscitation, family members should be asked in a respectful manner to leave.[13,14]

Recommendation-Specific Supportive Text

1. Qualitative studies generally show that there can be benefits for families if they are permitted to be present during the resuscitation of their children. Parents stated that they believed their presence brought their child comfort and that it helped them to adjust to the loss of their child.[2] Other surveys of parents reported that they desired to be present to understand what was happening, to know that all that could be done was being done, and to keep physical contact with their child.[3,4] However, not all parents who were present for their child's resuscitation would choose to do so again.[5] Some concerns have been raised about family presence during resuscitation, such as trauma for the family, interference with procedures, impact on technical performance, and concern for teaching and clinical decision-making, but these have not been supported by the available evidence.[6–8] Experienced providers are more likely than trainees to support family presence.[9,10]

2. The presence of a facilitator to support the family is helpful.[11,12] It is important that the family have a dedicated team member during the resuscitation to help process the traumatic event, but this is not always feasible. Lack of an available facilitator should not prevent family presence at the resuscitation.

3. Most surveys indicate family presence is not disruptive during resuscitation, although some providers feel increased stress.[13] Providers with significant experience with family presence acknowledge occasional negative experiences.[14]

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15 Evaluation of Sudden Unexplained Cardiac Arrest

Hypertrophic cardiomyopathy, coronary artery anomalies, and arrhythmias are common causes of sudden unexplained cardiac arrest in infants and children. Up to one third of young patients who do not survive sudden unexplained cardiac arrest have no abnormalities found on gross and microscopic autopsy.[1–4] Postmortem genetic evaluation ("molecular autopsy") is increasingly used to inform etiology of sudden unexplained cardiac arrest.[5] In addition to providing an explanation for the arrest, genetic diagnosis can identify inheritable cardiac disease, such as channelopathy and cardiomyopathy, enabling screening and preventive measures for relatives.

Recommendations for the Evaluation of Sudden Unexplained Cardiac Arrest

COR	LOE	Recommendations
1	C-EO	1. All infants, children, and adolescents with sudden unexpected cardiac arrest should, when resources allow, have an unrestricted, complete autopsy, preferably performed by a pathologist with training and experience in cardiovascular pathology. Consider appropriate preservation of biological material for genetic analysis to determine the presence of inherited cardiac disease.[6–21]
1	C-EO	2. Refer families of patients who do not have a cause of death found on autopsy to a healthcare provider or center with expertise in inherited cardiac disease and cardiac genetic counseling.[6–12,17,18,20–25]
1	C-EO	3. For infants, children and adolescents who survive sudden unexplained cardiac arrest, obtain a complete past medical and family history (including a history of syncopal episodes, seizures, unexplained accidents or drowning, or sudden unexpected death before 50 yr of age), review previous electrocardiograms, and refer to a cardiologist.[16,17,19–21]

Recommendation-Specific Supportive Text

1. In 7 cohort studies, mutations causing channelopathies were identified in 2% to 10% of infants with sudden infant death syndrome.[6–12] Among children and adolescents with sudden unexplained cardiac arrest and a normal autopsy, 9 cohort studies report identification of genetic mutations associated with channelopathy or cardiomyopathy.[13–21]

2. In 7 cohort studies[17,18,20,22–25] and 1 population-based study[21] of screening using clinical and laboratory (electrocardiographic, molecular genetic screening) investigations, 14% to 53% of first- and second-degree relatives of patients with sudden unexplained cardiac arrest had inherited, arrhythmogenic disorders. In 7 cohort studies, mutations causing channelopathies were identified in 2% to 10% of infants with sudden infant death syndrome.[6–12]

3. Several cohort studies report the utility of obtaining a complete past medical and family history after sudden unexplained cardiac arrest as well as review of prior electrocardiograms. A small case series suggested that specific genetic screening of family members was directed by the clinical history.[20] Three

small cohort studies and 1 population- based study reported relevant clinical symptoms or medical comorbidities, such as seizure, syncope, palpitations, chest pain, left arm pain, and shortness of breath, among patients who had a sudden unexplained cardiac arrest and their family members.[16,17,19,21]

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16 Resuscitating the Patient in Shock

Shock is the failure of oxygen delivery to meet tissue metabolic demands and can be life threatening. The most common type of pediatric shock is hypovolemic, including shock due to hemorrhage. Distributive, cardiogenic, and obstructive shock occur less frequently. Often, multiple types of shock can occur simultaneously; thus, providers should be vigilant. Cardiogenic shock in its early stages can be difficult to diagnose, so a high index of suspicion is warranted.

Shock progresses over a continuum of severity, from a compensated to a decompensated (hypotensive) state. Compensatory mechanisms include tachycardia and increased systemic vascular resistance (vasoconstriction) in an effort to maintain cardiac output and end-organ perfusion. As compensatory mechanisms fail, hypotension and signs of inadequate end-organ perfusion develop, such as depressed mental status, decreased urine output, lactic acidosis, and weak central pulses.

Early administration of intravenous fluids to treat septic shock has been widely accepted based on limited evidence. Mortality from pediatric sepsis has declined in recent years, concurrent with implementation of guidelines emphasizing the role of early antibiotic and fluid administration.[1] Controversies in the management of septic shock include volume of fluid administration and how to assess the patient's response, the timing and choice of vasopressor agents, the use of corticosteroids, and modifications to treatment algorithms for patients in sepsis-related cardiac arrest. Previous AHA guidelines[2] have considered large studies of patients with malaria, sickle cell anemia, and dengue shock syndrome; however, these patients require special consideration that make generalization of results from these studies problematic.

Resuscitation guidance for children with hemorrhagic shock is evolving, as crystalloid-then-blood paradigms are being challenged by resuscitation protocols using blood products early in resuscitation. However, the ideal resuscitation strategy for a given type of injury is often unknown.

16.1 Fluid Resuscitation in Shock

Recommendations for Fluid Resuscitation in Shock

COR	LOE	Recommendations
1	C-LD	1. Providers should reassess the patient after every fluid bolus to assess for fluid responsiveness and for signs of volume overload.[3–5]
2a	B-R	2. Either isotonic crystalloids or colloids can be effective as the initial fluid choice for resuscitation.[6]
2a	B-NR	3. Either balanced or unbalanced solutions can be effective as the fluid choice for resuscitation.[7–9]
2a	C-LD	4. In patients with septic shock, it is reasonable to administer fluid in 10-mL/kg or 20-mL/kg aliquots with frequent reassessment.[4]

Recommendation-Specific Supportive Text

1. Although fluids remain the mainstay initial therapy for infants and children in shock, especially in hypovolemic and septic shock, fluid overload can lead to increased morbidity.[3] In 2 randomized trials of patients with septic shock, those who received higher fluid volumes[4] or faster fluid resuscitation[5] were more likely to develop clinically significant fluid overload characterized by increased rates of mechanical ventilation and worsening oxygenation.

2. In a systematic review, 12 relevant studies were identified, though 11 assessed colloid or crystalloid fluid resuscitation in patients with malaria, dengue shock syndrome, or "febrile illness" in sub-Saharan Africa.[6] There was no clear benefit to crystalloid or colloid solutions as first-line fluid therapy in any of the identified studies.

3. One pragmatic, randomized controlled trial compared the use of balanced (lactated Ringer's solution) to unbalanced (0.9% saline) crystalloid solutions as the initial resuscitation fluid and showed no difference in relevant clinical outcomes.[7] A matched retrospective cohort study of pediatric patients with septic shock showed no difference in outcomes,[8] though a propensity-matched database study showed an association with increased 72-hour mortality and vasoactive infusion days with unbalanced crystalloid fluid resuscitation.[9]

4. In a small, randomized controlled study, there were no significant differences in outcomes with the use of 20 mL/kg as the initial fluid bolus volume (compared with 10 mL/kg); however, the study was limited by a small sample size.[4]

16.2 Resuscitating a Patient in Septic Shock

Recommendations for Resuscitating a Patient in Septic Shock

COR	LOE	Recommendations

COR	LOE	Recommendations
2a	C-LD	1. In infants and children with fluid-refractory septic shock, it is reasonable to use either epinephrine or norepinephrine as an initial vasoactive infusion.[1,10–14]
2a	C-EO	2. For infants and children with cardiac arrest and sepsis, it is reasonable to apply the standard pediatric advanced life support algorithm compared with any unique approach for sepsis-associated cardiac arrest.[15]
2b	B-NR	3. For infants and children with septic shock unresponsive to fluids and requiring vasoactive support, it may be reasonable to consider stress-dose corticosteroids.[12,16–19]
2b	C-LD	4. In infants and children with fluidrefractory septic shock, if epinephrine or norepinephrine are unavailable, dopamine may be considered.[10–12]

Recommendation-Specific Supportive Text

1. Two randomized controlled trials comparing escalating doses of dopamine or epinephrine demonstrated improvement in timing of resolution of shock[10] and 28-day mortality[11] with the use of epinephrine over dopamine. Both studies were conducted in resource-limited settings, and the doses of inotropes used may not have been directly comparable, limiting conclusions from the studies. Medications that increase systemic vascular resistance, such as norepinephrine, may also be a reasonable initial vasopressor therapy in septic shock patients.[1,12–14] Recent international sepsis guidelines recommend the choice of the medications to be guided by patient physiology and clinician preferences.[1]

2. No studies support deviations from standard life-support algorithms to improve outcomes in patients with sepsis-associated cardiac arrest. Sepsis-associated cardiac arrest is associated with worse outcomes than other causes of cardiac arrest.[15]

3. A meta-analysis[20] showed no change in survival with corticosteroid use in pediatric septic shock, though a more recent randomized controlled trial suggested a shorter time to reversal of shock with steroid use.[17] Two observational studies[18,19] suggested there may be specific subpopulations, based on genomics, that would either benefit or experience harm from steroid administration, though these subpopulations are difficult to identify clinically. Patients at risk for adrenal insufficiency (eg, those on chronic steroids, patients with purpura fulminans) are more likely to benefit from steroid therapy.[12]

4. In situations when epinephrine or norepinephrine are not available, dopamine is a reasonable alternative initial vasoactive infusion in patients with fluid-refractory septic shock.[10,11] Patients with vasodilatory shock may require a higher dose of dopamine.[14]

16.3 Resuscitating the Patient in Cardiogenic Shock

COR	LOE	Recommendations

COR	LOE	Recommendations
1	C-EO	1. For infants and children with cardiogenic shock, early expert consultation is recommended.
2b	C-EO	2. For infants and children with cardiogenic shock, it may be reasonable to use epinephrine, dopamine, dobutamine, or milrinone as an inotropic infusion.

Recommendation-Specific Supportive Text

1. and 2. Cardiogenic shock in infants and children is uncommon and associated with high mortality rates. No studies were identified comparing outcomes between vasoactive medications. For patients with hypotension, medications such as epinephrine may be more appropriate as an initial inotropic therapy. Because of the rarity and complexity of these presentations, expert consultation is recommended when managing infants and children in cardiogenic shock.

16.4 Resuscitating the Patient in Traumatic Hemorrhagic Shock

Recommendation for Resuscitating the Patient in Traumatic Hemorrhagic Shock

COR	LOE	Recommendation
2a	C-EO	1. Among infants and children with hypotensive hemorrhagic shock following trauma, it is reasonable to administer blood products, when available, instead of crystalloid for ongoing volume resuscitation.[21-27]

Recommendation-Specific Supportive Text

1. There are no prospective pediatric data comparing the administration of early blood products versus early crystalloid for traumatic hemorrhagic shock. A scoping review identified 6 recent retrospective studies that compared patient outcomes with the total volume of crystalloid resuscitation received in the first 24 to 48 hours among children with hemorrhagic shock.[21-25,28] Four studies reported no differences in survival to 24 hours, survival at 30 days with good neurological outcome, or survival to discharge.[21,24,25,28] Large-volume resuscitation was associated with increased hospital/ICU length of stay in 5 of the 6 studies.[22-25,28] One study reported lower survival to hospital discharge among children who received more than 60 mL/kg crystalloid compared to lower volume groups.[22] Despite limited pediatric data, recent guidelines for adults from the Eastern Association for the Surgery of Trauma,[26] the American College of Surgeons, and the National Institute for Health and Care Excellence[27] suggest the early use of balanced ratios of packed red blood cells, fresh frozen plasma, and platelets for trauma-related hemorrhagic shock.[29]

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17 Treatment of Respiratory Failure

Respiratory failure occurs when a patient's breathing becomes inadequate and results in ineffective oxygenation and ventilation. This can occur due to disordered control of breathing, upper airway obstruction, lower airway obstruction, respiratory muscle failure, or parenchymal lung disease. Providing assisted ventilation when breathing is absent or inadequate, relieving foreign body airway obstruction (FBAO), and administering naloxone in opioid overdose can be lifesaving.

Suffocation (eg, FBAO) and poisoning are leading causes of death in infants and children. Balloons, foods (eg, hot dogs, nuts, grapes), and small household objects are the most common causes of FBAO in children,[1-3] whereas liquids are common among infants.[4] It is important to differentiate between mild FBAO (the patient is coughing and making sounds) and severe FBAO (the patient cannot make sounds). Patients with mild FBAO can attempt to clear the obstruction by coughing, but intervention is required in severe obstruction.

In the United States in 2017, opioid overdose caused 79 deaths in children less than 15 years old and 4094 deaths in people age 15 to 24 years.[5] Naloxone reverses the respiratory depression of narcotic overdose,[6] and, in 2014, the US Food and Drug Administration approved the use of a naloxone autoinjector by lay rescuers and healthcare providers. Naloxone intranasal delivery devices are also available.

17.1 Treatment of Inadequate Breathing with a Pulse

Recommendations for Treatment of Inadequate Breathing With a Pulse

COR	LOE	Recommendations
1	C-EO	1. For infants and children with a pulse but absent or inadequate respiratory effort, provide rescue breathing.[7]
2a	C-EO	2. For infants and children with a pulse but absent or inadequate respiratory effort, it is reasonable to give 1 breath every 2 to 3 s (20–30 breaths/min).[7]

Recommendation-Specific Supportive Text

1. and 2. There are no pediatric-specific clinical studies evaluating the effect of different ventilation rates on outcomes in inadequate breathing with a pulse. One multicenter observational study found that high ventilation rates (at least 30/min in children younger than 1 year of age, at least 25/min in children older than 1 year) during CPR with an advanced airway for cardiac arrest were associated with improved ROSC and survival.[7] For the ease of training, the suggested respiratory rate for the patient with inadequate breathing and a pulse has been increased from 1 breath every 3 to 5 seconds to 1 breath every 2 to 3 seconds to be consistent with the new CPR guideline recommendation for ventilation in patients with an advanced airway.

17.2 Foreign Body Airway Obstruction

Recommendations for Foreign Body Airway Obstruction

COR	LOE	Recommendations
1	C-LD	1. If the child has mild FBAO, allow the victim to clear the airway by coughing while observing for signs of severe FBAO.[4,8,9]
1	C-LD	2. For a child with severe FBAO, perform abdominal thrusts until the object is expelled or the victim becomes unresponsive.[4,8,9]
1	C-LD	3. For an infant with severe FBAO, deliver repeated cycles of 5 back blows (slaps) followed by 5 chest compressions until the object is expelled or the victim becomes unresponsive.[4,9–12]
1	C-LD	4. If the infant or child with severe FBAO becomes unresponsive, start CPR beginning with chest compressions (do not perform pulse check). After 2 min of CPR, activate the emergency response system if no one has done so.[13]

COR	LOE	Recommendations
1	C-LD	5. For the infant or child with FBAO receiving CPR, remove any visible foreign body when opening the airway to provide breaths.[13–15]
3: Harm	C-LD	6. Do not perform blind finger sweeps.[13–15]

Recommendation-Specific Supportive Text

1. and 2. There are no high-quality data to support recommendations regarding FBAO in children. Many FBAOs are relieved by allowing the patient to cough or, if severe, are treated by bystanders using abdominal thrusts.[4,8,9]

3. Observational data primarily from case series support the use of back blows[4,9,10] or chest compressions[10,11] for infants. Abdominal thrusts are not recommended for infants given the potential to cause abdominal organ injury.[12]

4. Once the victim is unconscious, observational data support immediate provision of chest compressions whether or not the patient has a pulse.[11]

5. and 6. Observational data suggest that the risk of blind finger sweeps outweighs any potential benefit in the management of FBAO.[13–15]

17.3 Opioid-Related Respiratory and Cardiac Arrest

Recommendations for Opioid-Related Respiratory and Cardiac Arrest

COR	LOE	Recommendations
1	C-LD	1. For patients in respiratory arrest, rescue breathing or bag-mask ventilation should be maintained until spontaneous breathing returns, and standard pediatric basic or advanced life support measures should continue if return of spontaneous breathing does not occur.[17,18]
1	C-EO	2. For patients known or suspected to be in cardiac arrest, in the absence of a proven benefit from the use of naloxone, standard resuscitative measures should take priority over naloxone administration, with a focus on high-quality CPR (compressions plus ventilation).[16,20]
1	C-EO	3. Lay and trained responders should not delay activating emergency response systems while awaiting the patient's response to naloxone or other interventions.[21,22]

COR	LOE	Recommendations
2a	B-NR	4. For a patient with suspected opioid overdose who has a definite pulse but no normal breathing or only gasping (ie, a respiratory arrest), in addition to providing standard pediatric basic life support or advanced life support, it is reasonable for responders to administer intramuscular or intranasal naloxone.[23–36]

Recommendation-Specific Supportive Text

1. Initial management should focus on support of the patient's airway and breathing. This begins with opening the airway followed by delivery of rescue breaths, ideally with the use of a bag-mask or barrier device.[17,18] Provision of life support should continue if return of spontaneous breathing does not occur.

2. Because there are no studies demonstrating improvement in patient outcomes from administration of naloxone during cardiac arrest, provision of CPR should be the focus of initial care.[20] Naloxone can be administered along with standard advanced cardiovascular life support care if it does not delay components of high-quality CPR.

3. Early activation of the emergency response system is critical for patients with suspected opioid overdose. Rescuers cannot be certain that the person's clinical condition is due to opioid-induced respiratory depression alone. This is particularly true in first aid and BLS, where determination of the presence of a pulse is unreliable.[21,22] Naloxone is ineffective in other medical conditions, including overdose involving nonopioids and cardiac arrest from any cause. Patients who respond to naloxone administration may develop recurrent central nervous system and/or respiratory depression and require longer periods of observation before safe discharge.[37–40]

4. Twelve studies examined the use of naloxone in respiratory arrest, of which 5 compared intramuscular, intravenous, and/or intranasal routes of naloxone administration (2 RCT[23,24] and 3 non-RCT[25–27]) and 9 assessed the safety of naloxone use or were observational studies of naloxone use.[28–36] These studies report that naloxone is safe and effective in treatment of opioid-induced respiratory depression and that complications are rare and dose related.

These recommendations were taken from Part 3: Adult Basic and Advanced Life Support[41] and further supported by a 2020 ILCOR evidence update.[42] There were no pediatric data supporting these recommendations; however, due to the urgency of the opioid crisis, the adult recommendations should be applied to children.

Figures 10 and 11 are algorithms for opioid-associated emergencies for lay responders and healthcare providers.

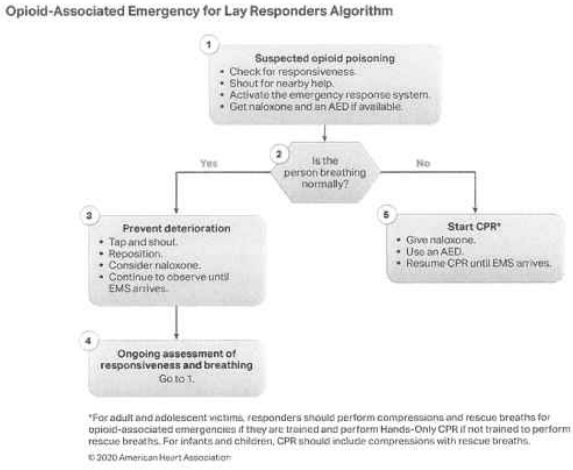

Figure 10. Opioid-Associated Emergency for Lay Responders Algorithm.
AED indicates automated external defibrillator; CPR, cardiopulmonary resuscitation; and EMS, emergency medical services.

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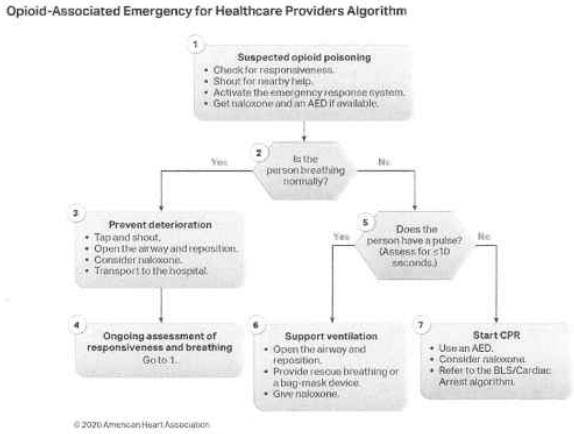

Figure 11. Opioid-Associated Emergency for Healthcare Providers Algorithm.
AED indicates automated external defibrillator; BLS, basic life support; and CPR, cardiopulmonary resuscitation.

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18 Intubation

It is important to select appropriate equipment and medications for pediatric intubation. Uncuffed ETTs were historically preferred for young children because the normal pediatric airway narrows below the vocal cords, creating an anatomic seal around the distal tube. In the acute setting and with poor pulmonary compliance, uncuffed ETTs may need to be changed to cuffed ETTs. Cuffed tubes improve capnography accuracy, reduce the need for ETT changes (resulting in high-risk reintubations or delayed compressions), and improve pressure and tidal volume delivery. However, high pressure in the cuff can cause airway mucosal damage. Although several studies have identified that cuffed tube use may actually decrease airway trauma by decreasing tube changes, attention must be made to selecting the correct tube size and cuff inflation pressure.[1] ETT cuff pressures are dynamic during transport at altitude[2] and with increasing airway edema.

Intubation is a high-risk procedure. Depending on the patient's hemodynamics, respiratory mechanics, and airway status, the patient can be at increased risk for cardiac arrest during intubation. Therefore, it is important to provide adequate resuscitation before intubation.

Cricoid pressure during bag-mask ventilation and intubation has historically been used to minimize the risk of gastric contents refluxing into the airway, but there are concerns that tracheal compression may impede effective bag-mask ventilation and intubation success.

Confirmation of ETT placement in patients with a perfusing rhythm is not reliably achieved by auscultation of breath sounds, mist in the tube, or chest rise. Either colorimetric detector or capnography ($ETCO_2$) can be used to assess initial ETT placement. In patients with decreased pulmonary blood flow from low cardiac output or cardiac arrest, $ETCO_2$ may not be as reliable.

18.1 Use of Cuffed Endotracheal Tubes for Intubation

Recommendations for the Use of Cuffed Endotracheal Tubes for Intubation

COR	LOE	Recommendations
1	C-EO	1. When a cuffed ETT is used, attention should be paid to ETT size, position, and cuff inflation pressure (usually <20–25 cm H_2O).[3]
2a	C-LD	2. It is reasonable to choose cuffed ETTs over uncuffed ETTs for intubating infants and children.[4–15]

Recommendation-Specific Supportive Text

1. A retrospective study including 2953 children noted that, with 25 cm H_2O of pressure to the airway and a slight leak around the ETT, there were no cases of clinically significant subglottic stenosis, and the incidence of stridor requiring reintubation was less than 1%.[3]

2. Three systematic reviews, 2 randomized controlled trials, and 2 retrospective reviews support the safety of cuffed ETTs and the decreased need for ETT changes.[4–10] These studies were almost entirely performed in the perioperative patient population, and intubation was performed by highly skilled airway providers. Thus, ETT duration may have been shorter than in critically ill patients. The use of cuffed ETTs is associated with lower reintubation rates, more successful ventilation, and improved accuracy of capnography without increased risk of complications.[7,9–13] Cuffed ETTs may decrease the risk of aspiration.[14,15]

18.2 The Use of Cricoid Pressure During Intubation

Recommendations for the Use of Cricoid Pressure During Intubation

COR	LOE	Recommendations
2b	C-LD	1. Cricoid pressure during bag-mask ventilation may be considered to reduce gastric insufflation.[16,17]
3: No Benefit	C-LD	2. Routine use of cricoid pressure is not recommended during endotracheal intubation of pediatric patients.[16,17]
3: Harm	C-LD	3. If cricoid pressure is used, discontinue if it interferes with ventilation or the speed or ease of intubation.[16,17]

Recommendation-Specific Supportive Text

1. 2, and 3. A retrospective, propensity score–matched study from a large pediatric ICU intubation registry showed that cricoid pressure during induction and bag-mask ventilation before tracheal intubation was not associated with lower rates of regurgitation.[17] A study from the same pediatric ICU database reported external laryngeal manipulation was associated with lower initial tracheal intubation success.[16]

18.3 Atropine Use for Intubation

Recommendations for Atropine Use for Intubation

COR	LOE	Recommendations
2b	C-LD	1. It may be reasonable for practitioners to use atropine as a premedication to prevent bradycardia during emergency intubations when there is higher risk of bradycardia (eg, when giving succinylcholine).[18,19]
2b	C-LD	2. When atropine is used as a premedication for emergency intubation, a dose of 0.02 mg/kg of atropine, with no minimum dose, may be considered.[20]

Recommendation-Specific Supportive Text

1. The 2019 French Society of Anesthesia and Intensive Care Medicine guidelines state that atropine "should probably" be used as a preintubation drug in children 28 days to 8 years with septic shock, with hypovolemia, or with succinylcholine administration.[18,19]

2. One nonrandomized, single-center intervention study did not identify an association between atropine dosing less than 0.1 mg and bradycardia or arrhythmias.[20]

18.4 Monitoring Exhaled CO_2 in Patients with Advanced Airways

Recommendations for Monitoring Exhaled CO_2 in Patients With Advanced Airways

COR	LOE	Recommendations
1	C-LD	1. In all settings, for infants and children with a perfusing rhythm, use exhaled CO_2 detection (colorimetric detector or capnography) for confirmation of ETT placement.[21–27]
2a	C-LD	2. In infants and children with a perfusing rhythm, it is beneficial to monitor exhaled CO_2 (colorimetric detector or capnography) during out-of-hospital and intra/interhospital transport.[21,22,28–30]

Recommendation-Specific Supportive Text

1. Although there are no randomized controlled trials linking use of $ETCO_2$ detection with clinical outcomes, the Fourth National Audit Project of the Royal College of Anesthetists and Difficult Airway Society concluded that the failure to use or inability to properly interpret capnography contributed to adverse events, including ICU-related deaths (mixed adult and pediatric data).[21,22] One small randomized study showed that capnography was faster than clinical assessment in premature newborns intubated in the delivery room.[23] There was no difference in patient outcomes between qualitative (colorimetric) and quantitative (capnography or numeric display) $ETCO_2$ detectors.[24–27]

2. Adult literature suggests monitoring and correct interpretation of capnography in intubated patients may prevent adverse events.[21,22,28] This has been demonstrated in simulated pediatric scenarios, in which capnography increased provider recognition of possible ETT dislodgement.[29,30]

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19 Management of Bradycardia

Bradycardia associated with hemodynamic compromise, even with a palpable pulse, may be a harbinger for cardiac arrest. As such, bradycardia with a heart rate of less than 60 beats per minute requires emergent evaluation for cardiopulmonary compromise. If cardiopulmonary compromise is present, the initial management in the pediatric patient requires simultaneous assessment of the etiology and treatment by supporting airway, ventilation, and oxygenation. If bradycardia with cardiopulmonary compromise is present despite effective oxygenation and ventilation, CPR should be initiated immediately. Outcomes are better for children who receive CPR for bradycardia before progressing to pulseless arrest.[1] Correctable factors that contribute to bradycardia (ie, hypoxia, hypotension, hypoglycemia, hypothermia, acidosis, or toxic ingestions) should be identified and treated immediately.

COR	LOE	Recommendations
1	C-LD	1. If bradycardia is due to increased vagal tone or primary atrioventricular conduction block (ie, not secondary to factors such as hypoxia), give atropine.[2,3,6,7]

COR	LOE	Recommendations
1	C-LD	2. If the heart rate is <60 beats/min with cardiopulmonary compromise despite effective ventilation with oxygen, start CPR.[1,10]
1	C-EO	3. If bradycardia persists after correction of other factors (eg, hypoxia) or responds only transiently, give epinephrine IV/IO. If IV/IO access is not available, give endotracheally if present.[1,11]
2b	C-LD	4. Emergency transcutaneous pacing may be considered if bradycardia is due to complete heart block or sinus node dysfunction unresponsive to ventilation, oxygenation, chest compressions, and medications, especially in children with congenital or acquired heart disease.[12–16]

Recommendation-Specific Supportive Text

1. Two adult studies[2,4] and 2 pediatric studies[6,7] demonstrate that atropine is effective to treat bradycardia due to vagal stimulation, atrioventricular block, and intoxication. There is no evidence that atropine should be used for bradycardia due to other causes.

2. Two retrospective analyses from the same database showed children who received CPR for bradycardia and poor perfusion had better outcomes than children who suffered pulseless cardiac arrest and received CPR.[1,10] The longer the time between the initiation of CPR for bradycardia and the loss of a pulse, the lower the chance of survival.

3. There are limited pediatric data regarding the treatment of bradycardia. A recent retrospective, propensity-matched study of pediatric patients with bradycardia with a pulse found that patients who received epinephrine had worse outcomes than patients who did not receive epinephrine.[11] However, due to limitations of the study, further research on the impact of epinephrine on patients with bradycardia and a pulse is required.

4. There are limited data about transcutaneous pacing for refractory bradycardia in children.[12–16] In patients with complete heart block or sinus node dysfunction, especially when caused by congenital or acquired heart disease, emergency transcutaneous pacing may be considered. Pacing is not useful for asystole or bradycardia due to postarrest hypoxic or ischemic myocardial insult or respiratory failure.

Figure 12 shows the algorithm for pediatric bradycardia with a pulse.

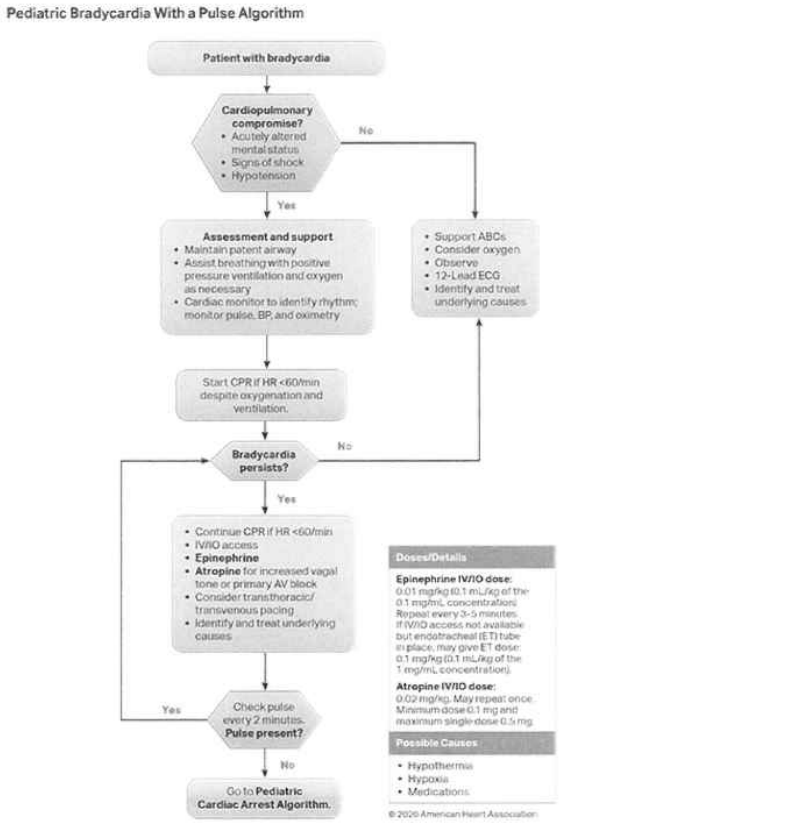

Figure 12. Pediatric Bradycardia With a Pulse Algorithm.
ABC indicates airway, breathing, and circulation; AV, atrioventricular; BP, blood pressure; CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; HR, heart rate; IO, intraosseous; and IV, intravenous.

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20 Tachyarrhythmias

Regular, narrow-complex tachyarrhythmias (QRS duration 0.09 seconds or less) are most commonly caused by re-entrant circuits, although other mechanisms (eg, ectopic atrial tachycardia, atrial fibrillation) sometimes occur. Regular, wide-complex tachyarrhythmias (greater than 0.09 seconds) can have multiple mechanisms, including supraventricular tachycardia (SVT) with aberrant conduction or ventricular tachycardia.

The hemodynamic impact of SVT in the pediatric patient can be variable, with cardiovascular compromise (ie, altered mental status, signs of shock, hypotension) occurring in the minority of patients. In hemodynamically stable patients, re-entrant SVT can often be terminated with vagal maneuvers.[1,2] Adenosine remains the preferred medication to treat SVT in infants and children with a palpable pulse who do not respond to vagal maneuvers. For patients with hemodynamically stable wide-complex tachycardia and those in whom SVT recurs after initial successful treatment, expert consultation is important to diagnose etiology and customize treatment.

In hemodynamically unstable patients with SVT or wide-complex tachycardia, synchronized cardioversion should be considered.

20.1 Treatment of Supraventricular Tachycardia with A Pulse

COR	LOE	Recommendations
1	C-LD	1. If IV/IO access is readily available, adenosine is recommended for the treatment of SVT.[3-6]

COR	LOE	Recommendations
1	C-EO	2. For hemodynamically stable patients whose SVT is unresponsive to vagal maneuvers and/or IV adenosine, expert consultation is recommended.[5-15,17]
2a	C-LD	3. It is reasonable to attempt vagal stimulation first, unless the patient is hemodynamically unstable or it will delay chemical or electric synchronized cardioversion.[1,2,4]
2a	C-LD	4. If the patient with SVT is hemodynamically unstable with evidence of cardiovascular compromise (ie. altered mental status, signs of shock, hypotension) it is reasonable to perform electric synchronized cardioversion starting with a dose of 0.5 to 1 J/kg. If unsuccessful, increase the dose to 2 J/kg.[5,8,15]
2b	C-LD	5. For a patient with unstable SVT unresponsive to vagal maneuvers, IV adenosine, electric synchronized cardioversion and for whom expert consultation is not available, it may be reasonable to consider either procainamide or amiodarone.[12,15]

Recommendation-Specific Supportive Text

1. Intravenous adenosine remains generally effective for terminating re-entrant SVT within the first 2 doses.[3–6] Of 5 retrospective observational studies on the management of tachyarrhythmias (4 single center, 1 multicenter), none directly compared adenosine to other drugs.[6–9,17]

2. For patients with hemodynamically stable SVT that is refractory to vagal maneuvers or adenosine, consideration of alternative second-line agents should be guided by expert consultation, given potential proarrhythmic and life-threatening hemodynamic collapse with the administration of multiple antiarrhythmic agents. Multiple medications have been used as second-line agents for the management of adenosine-refractory SVT, including intravenous verapamil, β-blockers, amiodarone, procainamide, and sotalol.[5–15,17] Few comparative studies exist.

3. Vagal maneuvers are noninvasive, have few adverse effects, and effectively terminate SVT in many cases; exact success rates for each type of maneuver (ie, ice water to face, postural modification) are unknown.[5] Although improved success rates have been reported with a postural modification to the standard Valsalva maneuver in adults,[1] published pediatric experience with this technique is very limited. Upside-down positioning may be an additional form of a vagal maneuver that is effective in children.[2]

4. Direct current synchronized cardioversion remains the treatment of choice for patients with hemodynamically unstable SVT (ie, with cardiovascular compromise characterized by altered mental status, signs of shock, or hypotension) and those with SVT unresponsive to standard measures. However, these cases are uncommon, and there are few data reporting outcomes from cardioversion of SVT.[5,8,15] Consider administering sedation prior to synchronized cardioversion if resources are available and definitive therapy is not delayed.

5. Procainamide and amiodarone are moderately effective treatments for adenosine-resistant SVT.[12] There may be a small efficacy advantage favoring procainamide; adverse effects are frequent with both therapies. Intravenous sotalol was approved by the US Food and Drug Administration for the treatment of SVT in 2009. Only 3 reports describe its use in acute or subacute supraventricular tachyarrhythmias, with a 60% to 100% termination rate of SVT and atrial tachyarrhythmias.[9,13,14] In the aforementioned studies, IV sotalol was administered under the guidance of pediatric

electrophysiologists in the critical care or pediatric cardiology unit. Due to its potential proarrhythmic properties, it is unknown whether IV sotalol can be safely given in other settings. There is currently insufficient evidence in support for or against the use of IV sotalol for refractory SVT.

20.2 Treatment of Wide-Complex Tachycardia with a Pulse

Recommendations for Treatment of Wide-Complex Tachycardia With a Pulse

COR	LOE	Recommendations
1	C-LD	1. If the patient with a wide-complex tachycardia is hemodynamically stable, expert consultation is recommended prior to administration of antiarrhythmic agents.[18]
2a	C-EO	2. If the patient with a wide-complex tachycardia is hemodynamically unstable with evidence of cardiovascular compromise (ie, altered mental status, signs of shock, hypotension), it is reasonable to perform electric synchronized cardioversion starting with a dose of 0.5–1 J/kg. If unsuccessful, increase the dose to 2 J/kg.

Recommendation-Specific Supportive Text

1. The occurrence of wide-complex tachycardia (QRS duration more than 0.09 s) with a pulse is rare in children and may originate from either the ventricle (ventricular tachycardia) or atria (SVT with aberrant conduction).[18] Both pediatric and adult studies have identified potential populations at risk of proarrhythmic complications from antiarrhythmic therapies, including patients with underlying cardiomyopathies, long-QT syndrome, Brugada syndrome, and Wolff-Parkinson-White syndrome.[19–23]

2. Electric direct current synchronized cardioversion should be provided urgently for the treatment of children with wide-complex tachycardia of either atrial or ventricular origin who are hemodynamically unstable with a pulse. Cardiovascular compromise is a key factor in determining the use of electric therapy instead of primary pharmacological management. There is insufficient evidence describing the incidence of wide-complex tachycardias with a pulse and hemodynamic stability, and there is no support for or against the use of specific antiarrhythmic drugs in the management of children with wide-complex tachycardia with a pulse.

Figure 13 shows the algorithm for pediatric tachycardia with a pulse.

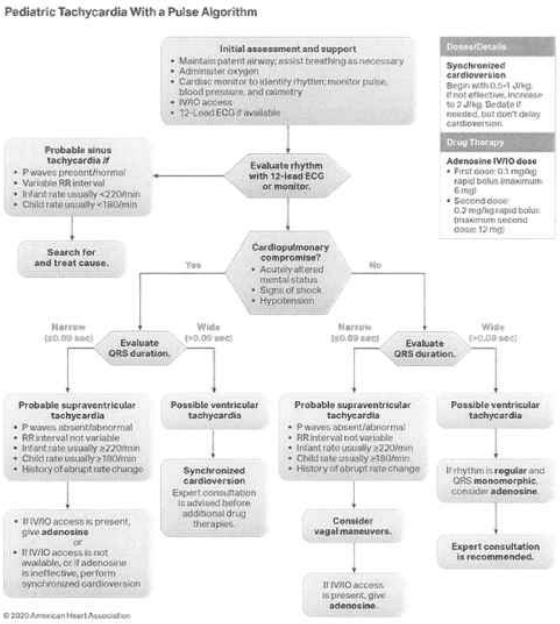

Figure 13. Pediatric Tachycardia With a Pulse Algorithm.
CPR indicates cardiopulmonary resuscitation; ECG, electrocardiogram; IO, intraosseous; and IV, intravenous.

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20.3 References

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21 Treatment of Myocarditis and Cardiomyopathy

Fulminant myocarditis can result in decreased cardiac output with end-organ compromise; conduction system disease, including complete heart block; and persistent supraventricular or ventricular arrhythmias, which can ultimately result in cardiac arrest.[1] Because patients can present with nonspecific symptoms such as

abdominal pain, diarrhea, vomiting, or fatigue, myocarditis can be confused with other, more common disease presentations. Outcomes can be optimized by early diagnosis and prompt intervention, including ICU monitoring and therapy. Sudden onset of heart block and multifocal ventricular ectopy in the patient with fulminant myocarditis should be considered a prearrest state. Treatment with external or intracardiac pacing or antiarrhythmic drugs may not be successful, and early transfer to a center capable of providing extracorporeal life support (ECLS) or mechanical circulatory support (MCS), such as temporary or implanted ventricular assist devices, is recommended.[2,3]

Noninfectious causes of cardiomyopathy in children include dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, and miscellaneous (rare) forms of cardiomyopathy that include arrhythmogenic right ventricular dysplasia and mitochondrial and left ventricular noncompaction cardiomyopathies. Cardiomyopathy patients who present in acute decompensated heart failure refractory to mechanical ventilation and vasoactive administration have undergone preemptive MCS in the form of ECMO, short-term percutaneous ventricular assist device, or long-term implantable ventricular assist device prior to or during cardiac arrest.[4,5]

For patients who have worsening clinical status or incessant ventricular arrhythmias, ECLS can be lifesaving when initiated prior to cardiac arrest. ECLS also offers an opportunity to wean inotropic support, assist myocardial recovery, and serve as a bridge to cardiac transplantation if needed. The use of ECLS and MCS have improved outcomes from acute myocarditis, with a high possibility of partial or complete recovery of myocardial function.[2,6]

Recommendations for Treatment of Myocarditis and Cardiomyopathy

COR	LOE	Recommendations
1	C-LD	1. Given the high risk of cardiac arrest in children with acute myocarditis who demonstrate arrhythmias, heart block, ST-segment changes, and/or low cardiac output, early consideration of transfer to ICU monitoring and therapy is recommended.[1,7,8]
2a	B-NR	2. For children with myocarditis or cardiomyopathy and refractory low cardiac output, prearrest use of ECLS or MCS can be beneficial to provide end-organ support and prevent cardiac arrest.[9,10]
2a	B-NR	3. Given the challenges to successful resuscitation of children with myocarditis and cardiomyopathy, once cardiac arrest occurs, early consideration of ECPR can be beneficial.[9]

Recommendation-Specific Supportive Text

1. Three retrospective studies have evaluated predictors of worse outcome in fulminant myocarditis, noting increased incidence of cardiac arrest and the need for ECLS in this high-risk population.[1,7,8] In 1 study, nearly half of fulminant myocarditis patients required CPR, and nearly one third received MCS.[7] Even modest decreases in left ventricular ejection fraction are associated with the need for invasive circulatory support.[8]

2. The prognosis for patients with fulminant myocarditis who receive ECLS or MCS can be good. In 1 study, 13 (46%) of 28 children requiring MCS survived without transplant.[9] One study noted that outcomes for ECPR patients cannulated with a diagnosis of myocarditis are superior to other arrest and illness categories leading to ECPR (ie, patients without congenital heart disease), noting myocarditis as a precannulation factor associated with improved survival.[10] In the pre–cardiac arrest cardiomyopathy patient, newer forms of temporary circulatory support devices provide alternate and potentially improved support for decompensated heart failure requiring bridge to transplantation. These devices may provide a survival

benefit over ECMO.[4,5]

3. In 1 study, 95% of children with myocarditis who were placed on ECLS (n=15) or MCS (n=1) after cardiac arrest were alive 6 months later.[9]

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22 Resuscitation of the Patient with a Single Ventricle

The complexity and variability in pediatric congenital heart disease pose unique challenges during resuscitation. Children with single-ventricle heart disease typically undergo a series of staged palliative operations. The objectives of the first palliative procedure, typically performed during the neonatal period, are (1) to create unobstructed systemic blood flow, (2) to create an effective atrial communication to allow for atrial level mixing, and (3) to regulate pulmonary blood flow to prevent overcirculation and decrease the volume load on the systemic ventricle (Figure 14). During the second stage of palliation, a superior cavopulmonary anastomosis, or bidirectional Glenn/hemi-Fontan operation, is performed to create an anastomosis, which aids in the redistribution of systemic venous return directly to the pulmonary circulation (Figure 15). The Fontan is the final palliation, in which inferior vena caval blood flow is baffled directly to the pulmonary circulation, thereby making the single (systemic) ventricle preload dependent on passive flow across the pulmonary vascular bed (Figure 16).

Neonates and infants with single-ventricle physiology have an increased risk of cardiac arrest as a result of (1) increased myocardial work as a consequence of volume overload, (2) imbalances in relative systemic (Qs) and pulmonary (Qp) blood flow, and (3) potential shunt occlusion.[1,2] Depending on the stage of repair, resuscitation may require control of pulmonary vascular resistance, oxygenation, systemic vascular resistance, or ECLS.

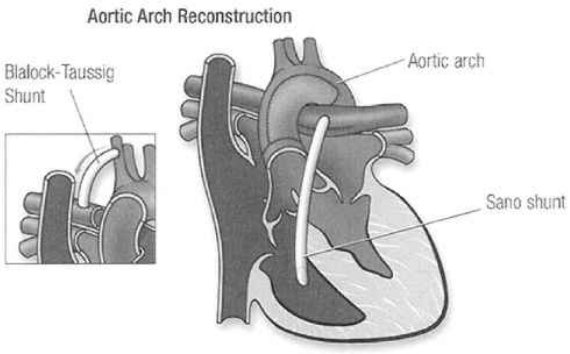

Figure 14. Stage I palliation for single ventricle with a Norwood repair and either a Blalock-Taussig Shunt from the right subclavian artery to the right pulmonary artery or a Sano shunt from the right ventricle to pulmonary artery.

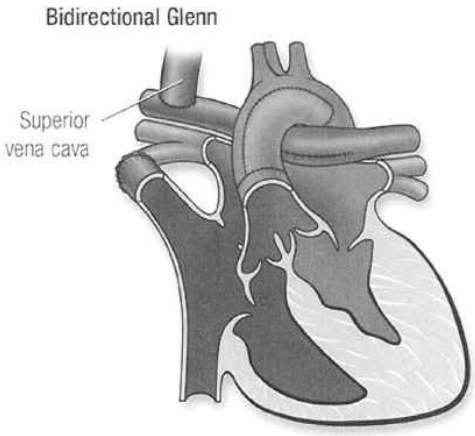

Figure 15. Stage II palliation for single ventricle with a bidirectional Glenn shunt connecting the superior vena cava to the right pulmonary artery.

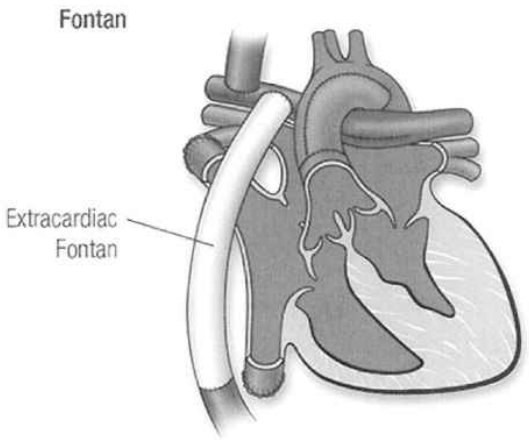

Figure 16. Stage III Fontan single ventricle palliation with an extracardiac conduit connecting the inferior vena cava to the right pulmonary artery.

22.1 Preoperative and Postoperative Stage I Palliation (Norwood/Blalock-Taussig Shunt or Sano Shunt)

Recommendations for the Treatment of Preoperative and Postoperative Stage I Palliation (Norwood/Blalock-Taussig Shunt or Sano Shunt)

COR	LOE	Recommendations
2a	B-NR	1. Direct (superior vena cava catheter) and/or indirect (near infrared spectroscopy) oxygen saturation monitoring can be beneficial to trend and direct management in the critically ill neonate after stage I Norwood palliation or shunt placement.[5]
2a	C-LD	2. In the patient with an appropriately restrictive shunt, manipulation of pulmonary vascular resistance may have little effect, whereas lowering systemic vascular resistance with the use of systemic vasodilators (α-adrenergic antagonists and/or phosphodiesterase type III inhibitors), with or without the use of oxygen, can be useful to increase systemic oxygen delivery (DO_2).[4,5]
2a	C-LD	3. For neonates prior to stage I repair with pulmonary overcirculation and symptomatic low systemic cardiac output and delivery of oxygen (DO_2), it is reasonable to target a Pa_{CO2} of 50–60 mm Hg. This can be achieved during mechanical ventilation by reducing minute ventilation or by administering analgesia/sedation with or without neuromuscular blockade.[5,7]

COR	LOE	Recommendations
2a	C-LD	4. ECLS after Stage I Norwood palliation can be useful to treat low systemic DO_2.[8,9]
2a	C-EO	5. In the situation of known or suspected shunt obstruction, it is reasonable to administer oxygen, vasoactive agents to increase shunt perfusion pressure, and heparin (50–100 U/kg bolus) while preparing for catheter-based or surgical intervention.[2]

Recommendation-Specific Supportive Text

1. In the early postoperative period, noninvasively measured regional cerebral and somatic saturations, via near infrared spectroscopy, can predict outcomes of early mortality and ECLS use following stage I Norwood palliation. There are retrospective data that postoperative near infrared spectroscopy measures may be targets for goal-directed interventions.[3]

2. Afterload reduction using vasodilators (sodium nitroprusside or phentolamine), with or without a phosphodiesterase type III inhibitor (eg, milrinone), reduces systemic vascular resistance, serum lactate, arterial venous oxygen difference, and the need for ECPR in the postoperative period for shunt-dependent single-ventricle patients.[4,5]

3. In the period before single-ventricle palliation, cautious use of controlled hypoventilation can reduce Qp:Qs by increasing pulmonary vascular resistance, narrowing the arterial-venous oxygen difference, and increasing cerebral oxygen delivery. Simple hypoventilation can also increase the pulmonary vascular resistance but can be associated with unwanted atelectasis or respiratory acidosis.[6,7]

4. For cardiac arrest before or after Stage I palliation repair, the use of ECPR is associated with improved survival. In 2 observational studies, 32% to 54% of neonates requiring ECPR survived, and, in 1 study, the odds of survival improved in cardiac arrest patients managed with ECPR.[8,9]

5. Treatment of acute shunt obstruction can include administration of oxygen, vasoactive agents (eg, phenylephrine, norepinephrine, epinephrine) to maximize shunt perfusion pressure, anticoagulation with heparin (50–100 U/kg bolus), shunt intervention by catheterization or surgery, and ECLS.[2]

22.2 Postoperative Stage II (Bidirectional Glenn/Hemi-Fontan) and III (Fontan) Palliation

Recommendations for the Treatment of Postoperative Stage II (Bidirectional Glenn/Hemi-Fontan) and Fontan Palliation

COR	LOE	Recommendations
2a	B-NR	1. For patients in a prearrest state with superior cavopulmonary anastomosis physiology and severe hypoxemia due to inadequate Qp, ventilatory strategies that target a mild respiratory acidosis and a minimum mean airway pressure without atelectasis can be useful to increase cerebral and systemic arterial oxygenation.[10]

COR	LOE	Recommendations
2b	B-NR	2. ECLS in patients with superior cavopulmonary anastomosis or Fontan circulation may be considered to treat low DO_2 from reversible causes or as a bridge to a ventricular assist device or surgical revision.[11]

Recommendation-Specific Supportive Text

1. In patients immediately following bidirectional Glenn placement, a ventilation strategy with higher $Paco_2$ improved oxygenation.[10]

2. In 1 retrospective analysis of the Extracorporeal Life Support Organization database, among infants in whom a bidirectional Glenn had been placed and in whom ECLS was required, survival was similar in patients who had cardiac arrest before ECLS (16/39, 41%) and those who did not (26/64, 41%).[11]

These topics were reviewed previously in "Cardiopulmonary Resuscitation in Infants and Children With Cardiac Disease: A Scientific Statement From the American Heart Association."[12]

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23 Recommendation for Treatment of the Child with Pulmonary Hypertension

Pulmonary hypertension is a rare disease in infants and children that is associated with significant morbidity and mortality. In the majority of pediatric patients, pulmonary hypertension is idiopathic or associated with chronic lung disease; congenital heart disease; and, rarely, other conditions, such as connective tissue or thromboembolic disease.[1] Pulmonary hypertension occurs in 2% to 20% of patients following congenital heart disease surgery, with substantial morbidity and mortality.[2] Pulmonary hypertension occurs in 2% to 5% of pediatric patients after cardiac surgery,[3] and 0.7% to 5% of all cardiovascular surgical patients experience postoperative pulmonary hypertensive crises.[4] Pulmonary hypertensive crises are acute rapid increases in pulmonary artery pressure accompanied by right-sided (or single-ventricle) heart failure. During pulmonary hypertensive crises, the right ventricle fails, and the increased afterload on the right ventricle produces increased myocardial oxygen demand at the same time that the coronary perfusion pressure and coronary blood flow decrease. The elevated left ventricle and right ventricle pressures lead to a fall in pulmonary blood flow and left-sided heart filling, with a resultant fall in cardiac output. Inotropic agents can be administered to improve right ventricle function, and vasopressors can be administered to treat systemic hypotension and improve coronary artery perfusion pressure. Once cardiac arrest has occurred, outcomes can be improved in the presence of an anatomic right-to-left shunt that permits left ventricle preload to be maintained without pulmonary blood flow.[2] These crises are life threatening and may lead to systemic hypotension, myocardial ischemia, cardiac arrest, and death. Because acidosis and hypoxemia are both potent pulmonary vasoconstrictors, careful monitoring and management of these conditions are critical in the management of pulmonary hypertension. Treatment should also include the provision of adequate analgesics, sedatives, and muscle relaxants. Pulmonary vasodilators, including inhaled nitric oxide, inhaled prostacyclin, inhaled and intravenous prostacyclin analogs, and intravenous and oral phosphodiesterase type V inhibitors (eg, sildenafil) are used to prevent and treat pulmonary hypertensive crises.[5–8]

Recommendation for Treatment of the Child with Pulmonary Hypertension

COR	LOE	Recommendations
1	B-R	1. Inhaled nitric oxide or prostacyclin should be used as the initial therapy to treat pulmonary hypertensive crises or acute right-sided heart failure secondary to increased pulmonary vascular resistance.[9–12]
1	B-NR	2. Provide careful respiratory management and monitoring to avoid hypoxia and acidosis in the postoperative care of the child with pulmonary hypertension.[13–15]

COR	LOE	Recommendations
1	C-EO	3. For pediatric patients who are at high risk for pulmonary hypertensive crises, provide adequate analgesics, sedatives, and neuromuscular blocking agents.[2,11,16,17]
2a	C-LD	4. For the initial treatment of pulmonary hypertensive crises, oxygen administration and induction of alkalosis through hyperventilation or alkali administration can be useful while pulmonary-specific vasodilators are administered.[13–15]
2b	C-LD	5. For children who develop refractory pulmonary hypertension, including signs of low cardiac output or profound respiratory failure despite optimal medical therapy, ECLS may be considered.[11,18–23]

Recommendation-Specific Supportive Text

1. Treatment with inhaled nitric oxide reduces the frequency of pulmonary hypertensive crises and shortens time to extubation.[5] In patients with atrioventricular septal defect repair and severe postoperative pulmonary hypertension, inhaled nitric oxide administration is associated with reduced mortality.[7,10] Inhaled prostacyclin transiently produces pulmonary vasodilation and improves oxygenation, but the alkalinity of the drug can irritate airways, and precise dosing can be complicated by drug loss in the nebulization circuit.[11,12]

2. Two physiological reviews and 1 randomized clinical trial have demonstrated that hypercarbia, hypoxemia, acidosis, atelectasis, and ventilation-perfusion mismatch can all lead to increases in pulmonary vascular resistance and, hence, elevation of pulmonary artery pressures in the immediate postoperative period.[13–15]

3. Two observational studies looking at select high-risk postoperative cardiac patients found an attenuation in the stress response in those patients receiving fentanyl in the postoperative period.[2,11,16,17]

4. Two physiological reviews and 1 randomized clinical trial have demonstrated that hypercarbia, hypoxemia, acidosis, atelectasis, and ventilation-perfusion mismatch can all lead to increases in pulmonary vascular resistance and, hence, elevation of pulmonary artery pressures in the immediate postoperative period.[13–15]

5. ECLS has been used in children with pulmonary vascular disease after cardiopulmonary collapse or low cardiac output.[18,19] Although outcomes remain poor in certain populations,[20] advances in technology of extracorporeal devices may allow for bridging to MCS or to transplantation.[21] Although patients with pulmonary hypertension who require ECLS have a high mortality rate, provision of ECLS can be lifesaving.[11,22,23]

These topics were reviewed previously in "Cardiopulmonary Resuscitation in Infants and Children With Cardiac Disease: A Scientific Statement From the American Heart Association"[2] and "Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society."[1]

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24 Management of Traumatic Cardiac Arrest

Unintentional injuries are the most common cause of death among children and adolescents.[1] Although many organizations have established trauma care guidelines,[2–4] the management of traumatic cardiac arrest is often inconsistent. Cardiac arrest due to major blunt or penetrating injury in children has a very high mortality rate.[5–8] Thoracic injury should be suspected in all thoracoabdominal trauma because tension pneumothorax, hemothorax, pulmonary contusion, or pericardial tamponade may impair hemodynamics, oxygenation, and ventilation.

Recommendations for the Management of Traumatic Cardiac Arrest

COR	LOE	Recommendations
1	C-EO	1. In pediatric traumatic cardiac arrest, evaluate for and treat potential reversible causes, such as hemorrhage, tension pneumothorax, and pericardial tamponade.[9,10]
2b	C-LD	2. In pediatric cardiac arrest secondary to penetrating injury with a short transport time, it may be reasonable to perform resuscitative thoracotomy.[11–18]

Recommendation-Specific Supportive Text

1. Early correction of reversible causes by reducing delays in the delivery of trauma-specific interventions may increase survival following penetrating traumatic cardiac arrest.[9,10] Guidelines for cardiac arrest due to trauma recommend hemorrhage control, restoration of circulating blood volume, opening the airway, and relieving tension pneumothorax. These measures should be performed simultaneously with conventional resuscitation.

2. Recent systematic reviews,[11–14] multicenter retrospective studies,[15,16] and single-center retrospective studies[17] recommend emergent thoracotomy for pediatric patients who present pulseless after penetrating thoracic injury. There is no evidence to support emergent thoracotomy for infants and children with blunt injury who are without signs of life.[14,18]

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25 Critical Knowledge Gaps and Ongoing Research

During the literature review process, we identified several critical knowledge gaps related to pediatric basic and advanced life support. These topics are either current areas of ongoing research or lack significant pediatric evidence to support evidence-based recommendations. In addition, we identified topics for which systematic or scoping reviews are in process by the ILCOR Basic Life Support or Pediatric Life Support Task Forces and elected not to make premature recommendations until these reviews are available.

As is so often the case in pediatric medicine, many recommendations are extrapolated from adult data. This is particularly true for the BLS components of pediatric resuscitation. The causes of pediatric cardiac arrest are very different from cardiac arrest in adults, and pediatric studies are critically needed. Furthermore, infants, children, and adolescents are distinct patient populations. Dedicated pediatric resuscitation research is a priority given the more than 20 000 infants, children, and adolescents who suffer cardiac arrest in the United States each year.

Critical knowledge gaps are summarized in Table 2.

Table 2. Critical Knowledge Gaps Due to Insufficient Pediatric Data

What is the optimal method of medication delivery during CPR: IO or IV?
What is the optimal method to determine body weight for medication administration?
In what time frame should the first dose of epinephrine be administered during pulseless cardiac arrest?
With what frequency should subsequent doses of epinephrine be administered?
With what frequency should epinephrine be administered in infants and children during CPR who are awaiting ECMO cannulation?
Are alternative compression techniques (cough CPR, fist pacing, interposed abdominal compression CPR) more effective alternatives to CPR?
With what frequency should the rhythm be checked during CPR?
What is the optimal method of airway management during OHCA–bag-mask ventilation, supraglottic airway, or endotracheal tube?
What is the optimal F_{IO2} to administer during CPR?
What is the optimal ventilation rate during CPR in patients with or without an advanced airway? Is it age dependent?
What is the optimal chest compression rate during CPR? Is it age dependent?
What are the optimal blood pressure targets during CPR? Are they age dependent?
Can echocardiography improve CPR quality or outcomes from cardiac arrest?
Are there specific situations in which advanced airway placement is beneficial or harmful in OHCA?
What is the appropriate timing of advanced airway placement in IHCA?
What is the role of ECPR for patients with OHCA and IHCA due to noncardiac causes?
What is the optimal timing and dosing of defibrillation for VF/pVT?
What clinical tools can be used to help in the decision to terminate pediatric IHCA and OHCA resuscitation?
What is the optimal blood pressure target during the post–cardiac arrest period?

CPR indicates cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; F_{IO2}, fraction of inspired oxygen; IHCA, in-hospital cardiac arrest; IO, intraosseous; IV, intravenous; OHCA, out-of-hospital cardiac arrest; pVT, pulseless ventricular tachycardia; SVT, supraventricular tachycardia; and VF, ventricular fibrillation.

Table 2. Critical Knowledge Gaps Due to Insufficient Pediatric Data

Should seizure prophylaxis be administered post cardiac arrest?
Does the treatment of postarrest convulsive and nonconvulsive seizure improve outcomes?
What are the reliable methods for postarrest prognostication?
What rehabilitation therapies and follow-up should be provided to improve outcomes post arrest?
What are the most effective and safe medications for adenosine-refractory SVT?
What is the appropriate age and setting to transition from (1) neonatal resuscitation protocols to pediatric resuscitation protocols and (2) from pediatric resuscitation protocols to adult resuscitation protocols?

CPR indicates cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; F_{IO2}, fraction of inspired oxygen; IHCA, in-hospital cardiac arrest; IO, intraosseous; IV, intravenous; OHCA, out-of-hospital cardiac arrest; pVT, pulseless ventricular tachycardia; SVT, supraventricular tachycardia; and VF, ventricular fibrillation.

26 Article Information

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26.3 Disclosures

Appendix 1. Writing Group Disclosures

Open table in a new window.

Appendix 2. Reviewer Disclosures

Open table in a new window.

Applying Class of Recommendations and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION

CLASS 1 (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS 2a (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS 2b (WEAK) — Benefit > Risk

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS 3: No Benefit (WEAK) — Benefit = Risk

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:

LEVEL (QUALITY) OF EVIDENCE

LEVEL A

- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)

- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)

- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

- Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews,

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.