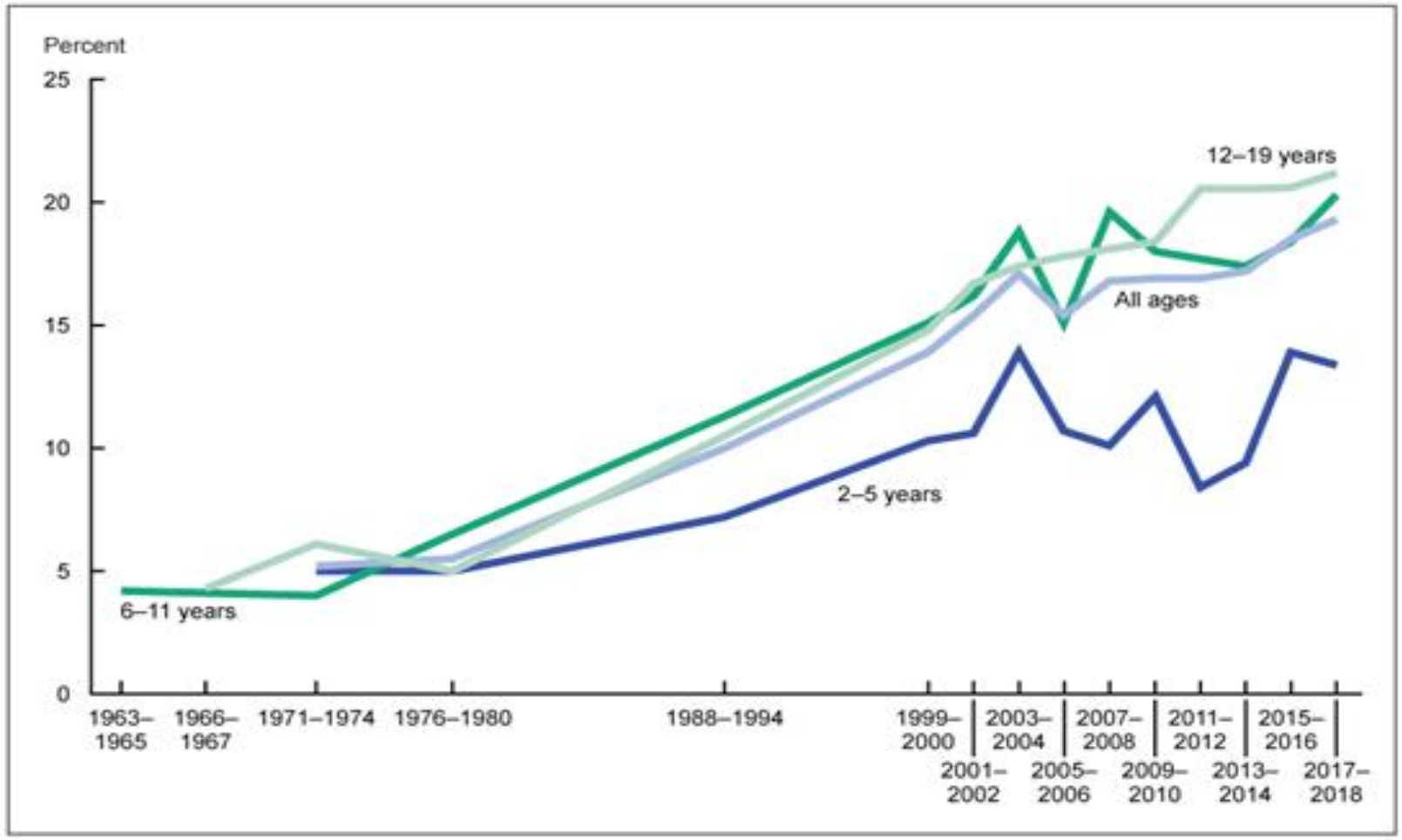
Clinical practice guidelines around anti-obesity medications: pediatrics

Sarah E Barlow, MD, MPH
National Academies Roundtable on Obesity Solutions

March 20, 2024

The prevalence of childhood obesity over the time

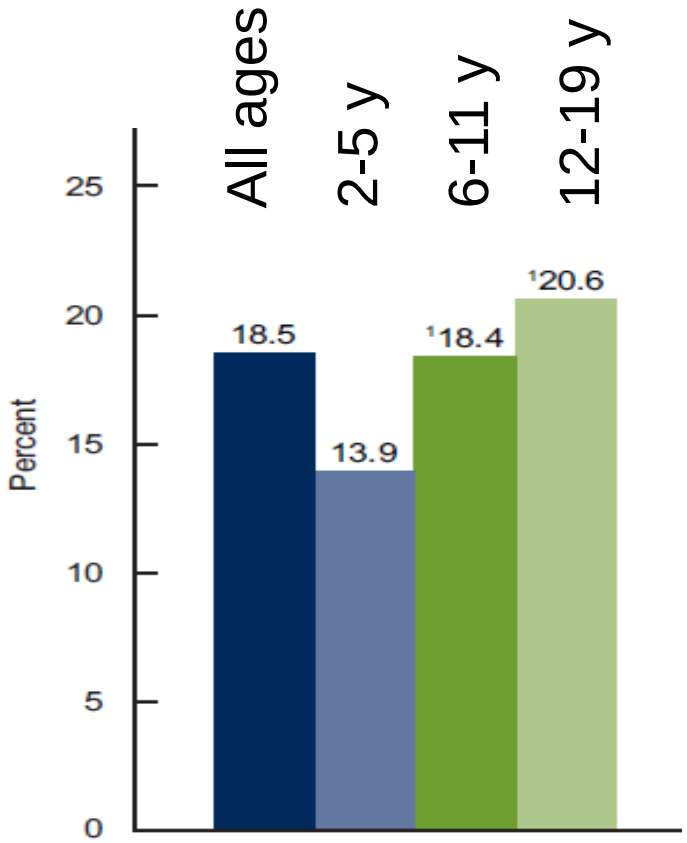


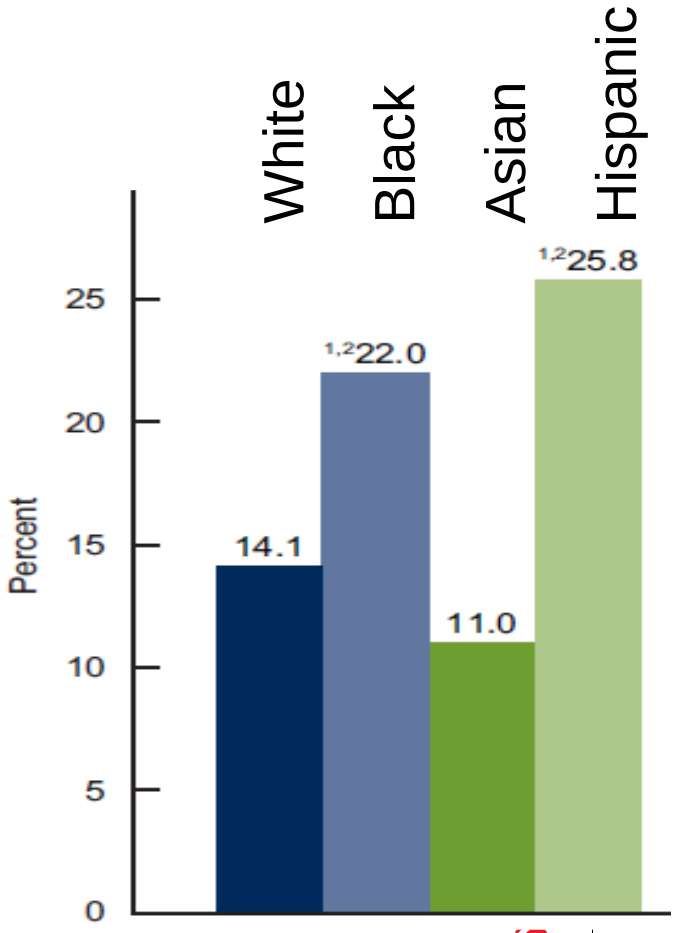
NOTE: Obesity is body mass index (BMI) at or above the 95th percentile from the sex-specific BMI-for-age 2000 CDC Growth Charts.
SOURCES: National Center for Health Statistics, National Health Examination Surveys II (ages 6–11), III (ages 12–17), and National Health and Nutrition Examination Surveys (NHANES) I–III, and NHANES 1999–2000, 2001–2002, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016, and 2017–2018.

Between 1963 to 2018, childhood obesity prevalence increased from 5% to about 21.5%

U.S. Childhood Obesity Epidemic

Obesity prevalence 2-19 years NHANES 2015-2016





Ogden 2017. NCHS data brief no 219. Hyattsville, MD

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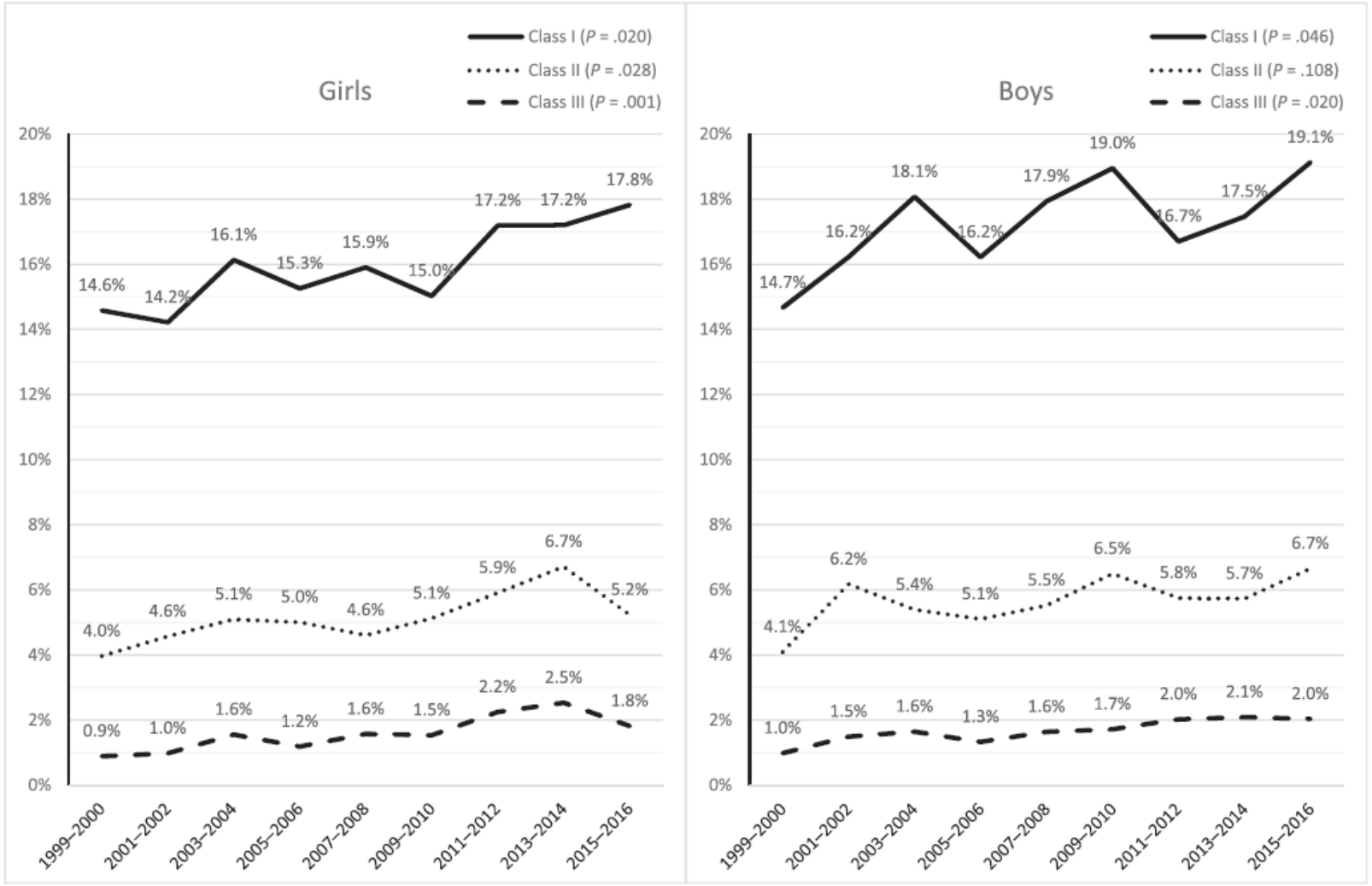
Significant increases for obesity, severe (class 2) obesity and very severe (class 3) obesity in children 1999-2016



Prevalence of severe obesity 2015-2016

Class 2 = 5.2% (F), 6.7% (M)

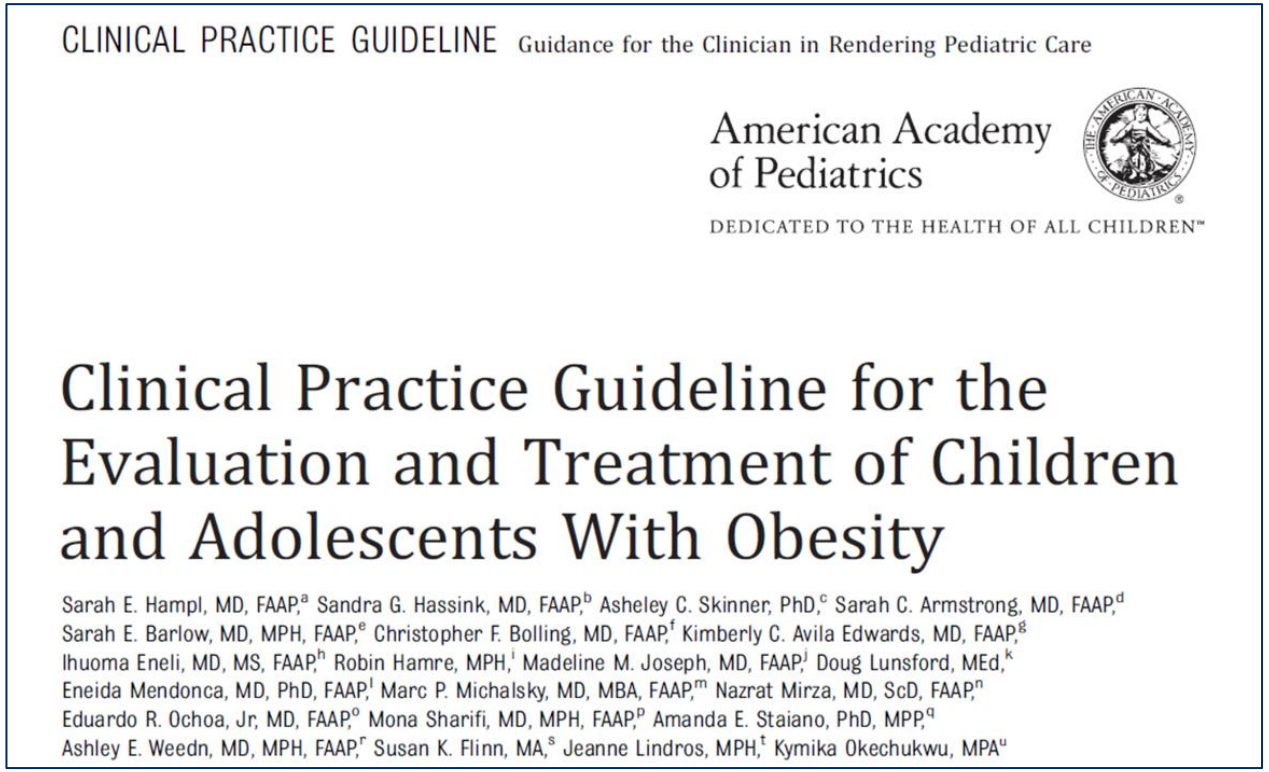
Class 3 = 1.8% (F). 2.0% (M)

Skinner 2018. *Pediatrics* 141:e20173459

Absolute numbers

	Total Population*	Obesity (~20%)	Severe obesity (~5%)
5-9 yo	20,000,000	4,000,000	1,000,000
10-14 yo	22,000,000	4,400,000	1,100,000
15-19 yo	22,000,000	4,400,000	1,100,000

* 2020 US census data



CLINICAL PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity

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Released January 2023

Hampl 2023 *Pediatr* 151(2):e2022060640

Clinical Practice Guideline process and scope

Literature review on these questions:

1. What is the risk of comorbidities among children with obesity?
2. What are clinic-based, effective treatments for obesity

Clinical Practice Guideline process and scope

16,000 abstracts

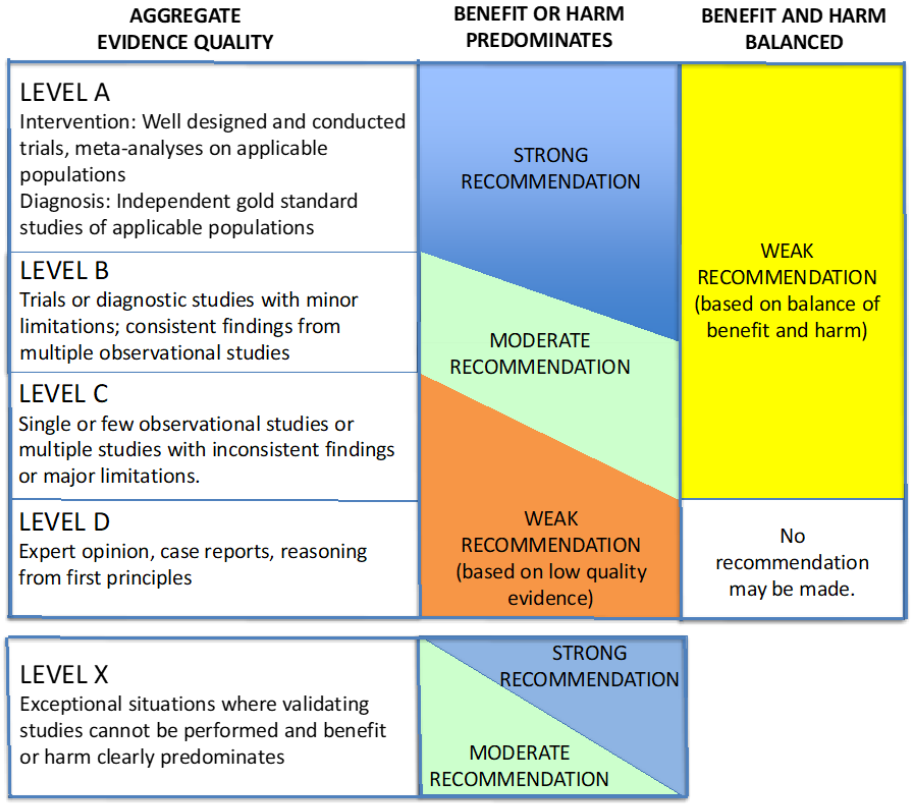
1642 full text articles

382 studies included

2 technical reports

11
Consensus Statements

13
Key Action Statements



Comment on language in Key Action Statements

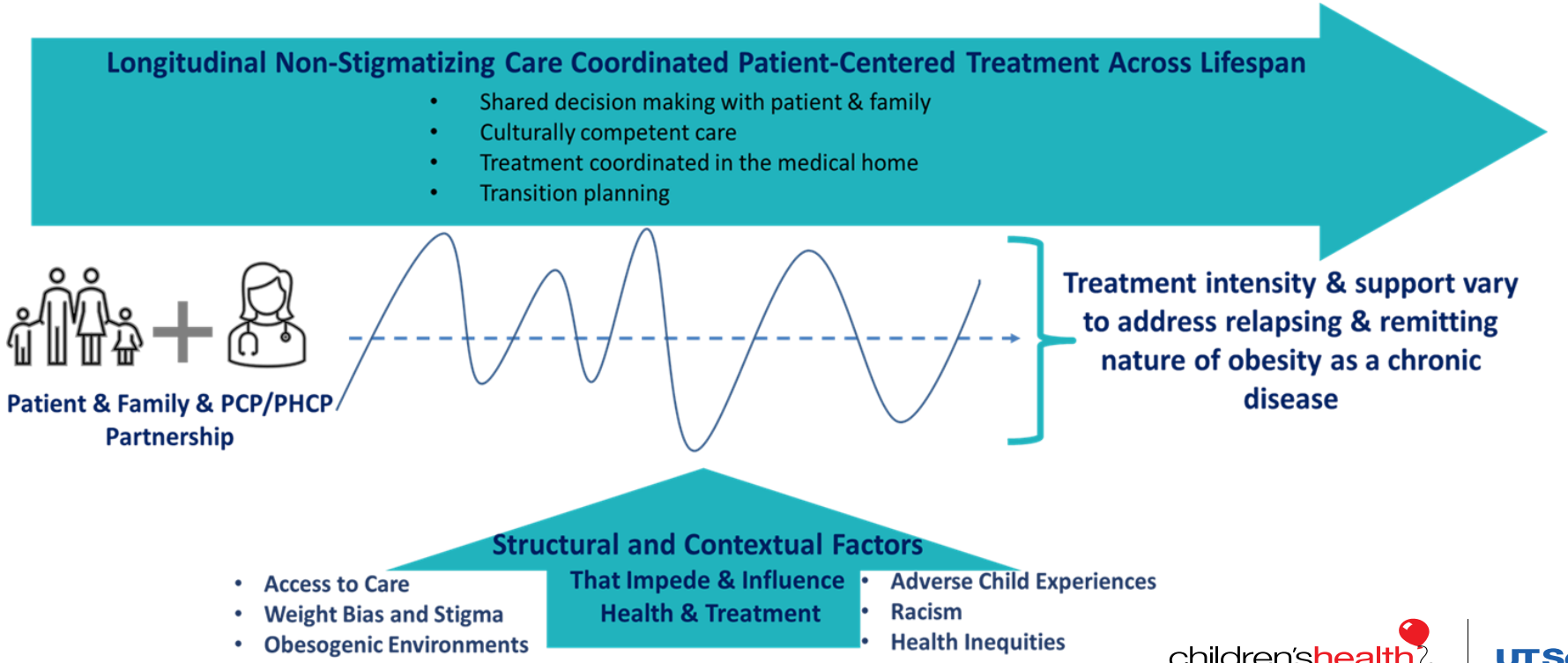
"Using 3 levels of recommendation is supported by research into the obligation level conveyed by terms commonly found in clinical practice guidelines. Despite a large number of descriptive terms, the obligation levels cluster into 3 distinct levels:

must conveys the highest obligation level, **may** the lowest, and **should** an intermediate level."

Rosenfield 2013 clinical Practice Guideline Development Manual, Third Edition
IOM (Institute of Medicine)

Treatment Key Action Statement: Overview

KAS 9. Pediatricians and other PHCPs **should treat** overweight (BMI ≥85th percentile to <95th percentile) and obesity (BMI ≥95th percentile) in children and adolescents, **following the principles of the medical home** and the **chronic care model**, using a **family-centered** and **non-stigmatizing** approach that acknowledges **obesity's biologic, social, and structural drivers.**



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Treatment Key Action Statement: Health Behavior and Lifestyle

KAS 11. Pediatricians and other PHCPs

<u>should</u> provide or refer children **6 y and older** (Grade B) and

<u>may</u> provide or refer children 2 through 5 y of age (Grade C) with overweight (BMI ≥85th percentile to <95th percentile) and obesity (BMI ≥95th percentile)

to intensive health behavior and lifestyle treatment.

Health behavior and lifestyle treatment is more effective with greater contact hours; the most effective treatment includes 26 hours or more of face-to-face, family-based, multi-component treatment over 3- to 12- mo

Evidence for comprehensive behavior-based programs for childhood obesity

Hours of Contact

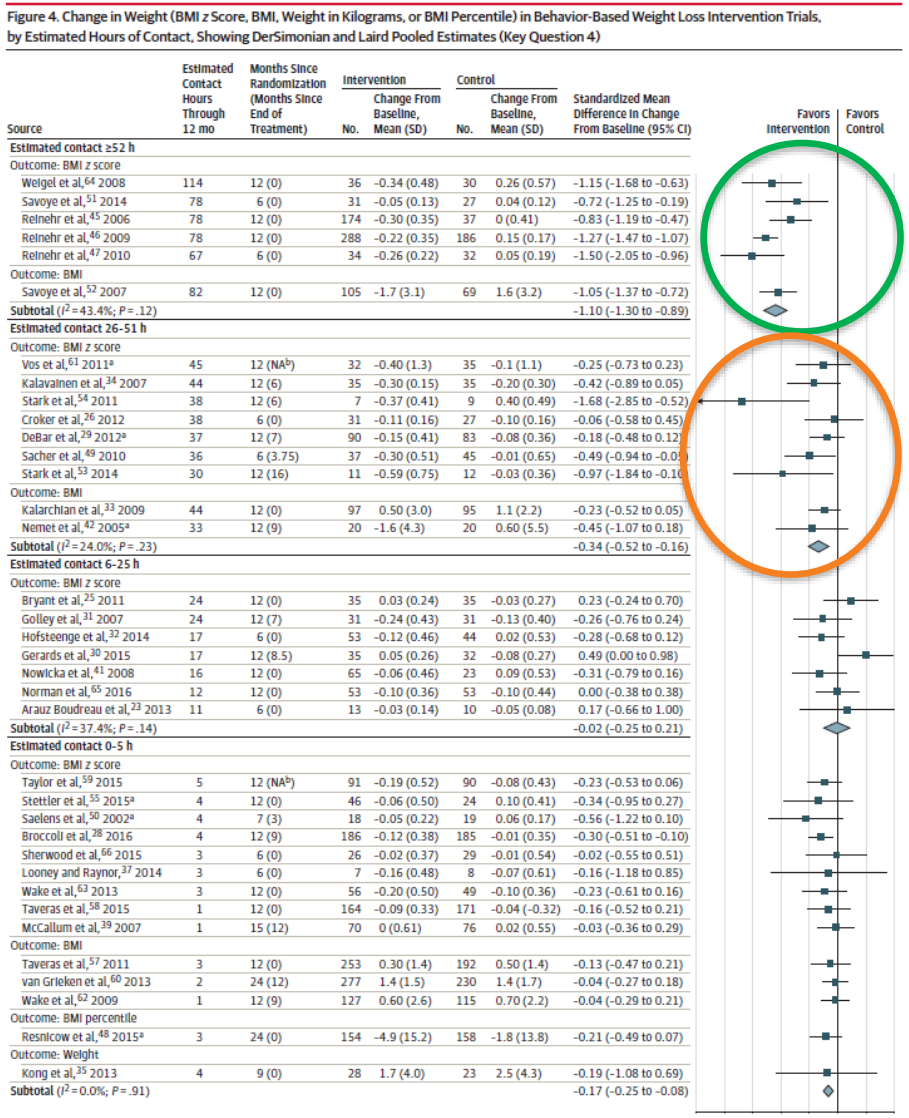
≥ 52

26 – 52

6 – 25

1 – 5.9

Figure 4. Change in Weight (BMI *z* Score, BMI, Weight in Kilograms, or BMI Percentile) in Behavior-Based Weight Loss Intervention Trials, by Estimated Hours of Contact, Showing DerSimonian and Laird Pooled Estimates (Key Question 4)



Source	Estimated Contact Hours Through 12 mo	Months Since Randomization (Months Since End of Treatment)	Intervention No.	Intervention Change From Baseline, Mean (SD)	Control No.	Control Change From Baseline, Mean (SD)	Standardized Mean Difference in Change From Baseline (95% CI)
Estimated contact ≥52 h							
Outcome: BMI *z* score							
Weigel et al,[64] 2008	114	12 (0)	36	-0.34 (0.48)	30	0.26 (0.57)	-1.15 (-1.68 to -0.63)
Savoye et al,[51] 2014	78	6 (0)	31	-0.05 (0.13)	27	0.04 (0.12)	-0.72 (-1.25 to -0.19)
Reinehr et al,[45] 2006	78	12 (0)	174	-0.30 (0.35)	37	0 (0.41)	-0.83 (-1.19 to -0.47)
Reinehr et al,[46] 2009	78	12 (0)	288	-0.22 (0.35)	186	0.15 (0.17)	-1.27 (-1.47 to -1.07)
Reinehr et al,[47] 2010	67	6 (0)	34	-0.26 (0.22)	32	0.05 (0.19)	-1.50 (-2.05 to -0.96)
Outcome: BMI							
Savoye et al,[52] 2007	82	12 (0)	105	-1.7 (3.1)	69	1.6 (3.2)	-1.05 (-1.37 to -0.72)
Subtotal (I^2 = 43.4%; P = .12)							-1.10 (-1.30 to -0.89)
Estimated contact 26-51 h							
Outcome: BMI *z* score							
Vos et al,[61] 2011[a]	45	12 (NA[b])	32	-0.40 (1.3)	35	-0.1 (1.1)	-0.25 (-0.73 to 0.23)
Kalavainen et al,[34] 2007	44	12 (6)	35	-0.30 (0.15)	35	-0.20 (0.30)	-0.42 (-0.89 to 0.05)
Stark et al,[54] 2011	38	12 (6)	7	-0.37 (0.41)	9	0.40 (0.49)	-1.68 (-2.85 to -0.52)
Croker et al,[26] 2012	38	6 (0)	31	-0.11 (0.16)	27	-0.10 (0.16)	-0.06 (-0.58 to 0.45)
DeBar et al,[29] 2012[a]	37	12 (7)	90	-0.15 (0.41)	83	-0.08 (0.36)	-0.18 (-0.48 to 0.12)
Sacher et al,[49] 2010	36	6 (3.75)	37	-0.30 (0.51)	45	-0.01 (0.65)	-0.49 (-0.94 to -0.05)
Stark et al,[53] 2014	30	12 (16)	11	-0.59 (0.75)	12	-0.03 (0.36)	-0.97 (-1.84 to -0.10)
Outcome: BMI							
Kalarchian et al,[33] 2009	44	12 (0)	97	0.50 (3.0)	95	1.1 (2.2)	-0.23 (-0.52 to 0.05)
Nemet et al,[42] 2005[a]	33	12 (9)	20	-1.6 (4.3)	20	0.60 (5.5)	-0.45 (-1.07 to 0.18)
Subtotal (I^2 = 24.0%; P = .23)							-0.34 (-0.52 to -0.16)
Estimated contact 6-25 h							
Outcome: BMI *z* score							
Bryant et al,[25] 2011	24	12 (0)	35	0.03 (0.24)	35	-0.03 (0.27)	0.23 (-0.24 to 0.70)
Golley et al,[31] 2007	24	12 (7)	31	-0.24 (0.43)	31	-0.13 (0.40)	-0.26 (-0.76 to 0.24)
Hofsteenge et al,[32] 2014	17	6 (0)	53	-0.12 (0.46)	44	0.02 (0.53)	-0.28 (-0.68 to 0.12)
Gerards et al,[30] 2015	17	12 (8.5)	35	0.05 (0.26)	32	-0.08 (0.27)	0.49 (0.00 to 0.98)
Nowicka et al,[41] 2008	16	12 (0)	65	-0.06 (0.46)	23	0.09 (0.53)	-0.31 (-0.79 to 0.16)
Norman et al,[65] 2016	12	12 (0)	53	-0.10 (0.36)	53	-0.10 (0.44)	0.00 (-0.38 to 0.38)
Arauz Boudreau et al,[23] 2013	11	6 (0)	13	-0.03 (0.14)	10	-0.05 (0.08)	0.17 (-0.66 to 1.00)
Subtotal (I^2 = 37.4%; P = .14)							-0.02 (-0.25 to 0.21)
Estimated contact 0-5 h							
Outcome: BMI *z* score							
Taylor et al,[59] 2015	5	12 (NA[b])	91	-0.19 (0.52)	90	-0.08 (0.43)	-0.23 (-0.53 to 0.06)
Stettler et al,[55] 2015[a]	4	12 (0)	46	-0.06 (0.50)	24	0.10 (0.41)	-0.34 (-0.95 to 0.27)
Saelens et al,[50] 2002[a]	4	7 (3)	18	-0.05 (0.22)	19	0.06 (0.17)	-0.56 (-1.22 to 0.10)
Broccoli et al,[28] 2016	4	12 (9)	186	-0.12 (0.38)	185	-0.01 (0.35)	-0.30 (-0.51 to -0.10)
Sherwood et al,[66] 2015	3	6 (0)	26	-0.02 (0.37)	29	-0.01 (0.54)	-0.02 (-0.55 to 0.51)
Looney and Raynor,[37] 2014	3	6 (0)	7	-0.16 (0.48)	8	-0.07 (0.61)	-0.16 (-1.18 to 0.85)
Wake et al,[63] 2013	3	12 (0)	56	-0.20 (0.50)	49	-0.10 (0.36)	-0.23 (-0.61 to 0.16)
Taveras et al,[58] 2015	1	12 (0)	164	-0.09 (0.33)	171	-0.04 (-0.32)	-0.16 (-0.52 to 0.21)
McCallum et al,[39] 2007	1	15 (12)	70	0 (0.61)	76	0.02 (0.55)	-0.03 (-0.36 to 0.29)
Outcome: BMI							
Taveras et al,[57] 2011	3	12 (0)	253	0.30 (1.4)	192	0.50 (1.4)	-0.13 (-0.47 to 0.21)
van Grieken et al,[60] 2013	2	24 (12)	277	1.4 (1.5)	230	1.4 (1.7)	-0.04 (-0.27 to 0.18)
Wake et al,[62] 2009	1	12 (9)	127	0.60 (2.6)	115	0.70 (2.2)	-0.04 (-0.29 to 0.21)
Outcome: BMI percentile							
Resnicow et al,[48] 2015[a]	3	24 (0)	154	-4.9 (15.2)	158	-1.8 (13.8)	-0.21 (-0.49 to 0.07)
Outcome: Weight							
Kong et al,[35] 2013	4	9 (0)	28	1.7 (4.0)	23	2.5 (4.3)	-0.19 (-1.08 to 0.69)
Subtotal (I^2 = 0.0%; P = .91)							-0.17 (-0.25 to -0.08)

36 randomized controlled studies, arranged by hours of contact.

"Comprehensive, intensive behavioral interventions (≥ 26 contact hours) in children and adolescent 6 years and older who have obesity can result in improvements in weight status for up to 12 months."

USPSTF: Screening for obesity in children and adolescents. *JAMA* 2017. 317:2417

Characteristics of comprehensive, intensive behavior and lifestyle interventions (IHBLT)

Components

- Eating and nutrition to establish healthy, sustainable patterns
- Physical activity to establish healthy sustainable patterns
- Behavior change strategies
- Family engagement
- Dosage of 26 hours or more over 3-12 months

Implementation

- Group OR individual OR both
- Healthcare setting OR community with linkage to healthcare
- Face-to-face OR virtual

Impact of IHBLT on BMI measures and co-morbidities

The CPG reviewed impact of IHBLT

- Change in BMI measures:
  - -0.5 to -2 kg/m^2 when 26-51 hours
- Improvement in cardiovascular risk factors
  - blood pressure, insulin and glucose, obstructive sleep apnea and NAFLD
- Impact on mental health:
  - limited studies show no worsening of mental health, but IHBLT studies generally excluded youth with serious mental health disorders (more research needed)
- Risk of eating disorders:
  - IHBLT may reduce disordered eating (more research needed)

Hampl 2023 *Pediatr* 151(2):e2022060640

Treatment Key Action Statement: Pharmacotherapy

KAS 12. Pediatricians and other PHCPs

should offer adolescents 12 y and older with obesity (BMI ≥95th percentile)

weight loss pharmacotherapy, according to medication indications, risks, and benefits, as an **adjunct to health behavior and lifestyle treatment**.

Weight-loss medications with FDA approval in adolescents

1. Liraglutide (daily GLP-1 agonist) FDA-approved 12/4/2020
   - 56-week DBRPCT* of 251 12-17 yo
   - -4.3% BMI vs +0.4% in placebo
   - Side effects: nausea, abdominal pain
2. Phentermine and topiramate: FDA-approved 6/27/2022
   - 56-week DBRPCT* of 223 12-17 yo
   - -4.8% and -7.1% BMI vs +3.3% in placebo
   - Side effects: increased blood pressure, fatigue, cognitive slowing, teratogenicity
3. Semaglutide (weekly GLP-1 agonist) FDA approved 1/3/2023
   - 56-week DBRPCT* of 201 12-17 yo
   - -16.1% BMI vs +0.6% in placebo
   - Side effects: nausea, abdominal pain

* Double-Blind Randomized Placebo-Controlled Trial

Kelly NEJM 2020
Kelly NEJM 2022
Weghuber NEJM 2022

Success and Harms of pharmaceutical treatment of pediatric obesity

Success (benefits)

- Adiposity reduction
- Metabolic health (current and future)
- Improved quality and quantity of nutritional intake
- Improved physical activity
- Improved quality of life
- Improved mental health

Harm

- Physical:
  - Loss of muscle mass
  - Linear growth limitation
  - Excessive or too rapid weight loss
  - Decreased bone mass and bone mineral density
- Mental and emotional health
  - Disordered eating (uncovering or worsening)
  - Lack of improved QOL/worse QOL
  - Negative impact on other mental health
- Inequitable access

Should…but Can't?

Intensive Health Behavior and Lifestyle Treatment (IHBLT)

- Poor fit with healthcare structure of individual office visits
- More practical to deliver in community setting (adequate space, use of health educators or other non-physicians, availability outside of typical office hours, location close to families)
- Community setting is barrier to insurance coverage as it now exists

Should…but Can't?

Anti-Obesity Medications

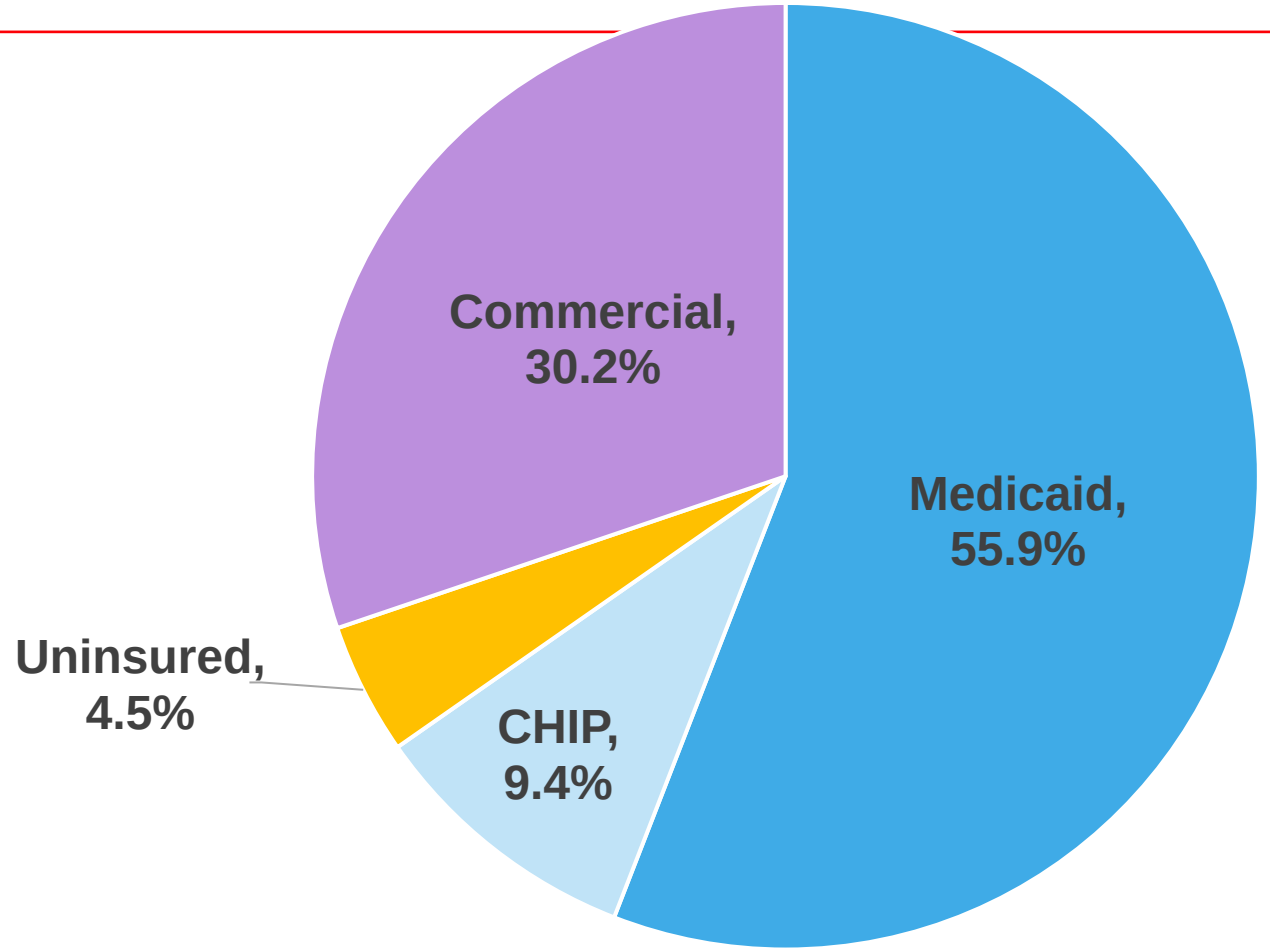
- Should be prescribed as "an adjunct to health behavior and lifestyle treatment"
  - Medication studies included healthy lifestyle support in all arms
  - However, publications do not describe lifestyle support
- Insurance often does not cover. Commercial insurances exclude AOM from benefits (often in response to employer requests). Medicaid and CHIP similarly exclude it in many states.
- Shortages nationally
- Primary care pediatricians face implementation challenges, especially with injectables

Implementation and equity

Gap between children who would benefit from treatment and children who receive it

- Reasons include:
  - Insurance coverage, difficulty of treatment path, stigma about obesity, structural racism, cultural values, bias within healthcare system, unfamiliarity of providers with treatment, lack of availability

Healthcare coverage for U.S. children (< 18 years) in 2022



Conmy AB, Peters C, De Lew N, Sommers BD. Children's Health Coverage Trends: Gains in 2020-2022 Reverse Previous Coverage Losses. (Issue Brief No. HP-2023-07). Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. March 2023

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RE AIM applied to obesity treatment

Reach	Patient representativeness	Who are offered and who use IHBLT, medication, surgery, etc. Aim for inclusion across socio-demographic groups including race, ethnicity, and income; also rural vs urban setting
Effectiveness	Patient outcome in clinical setting	What are “real life” outcomes of weight, BMI metrics, body composition, bone health, quality of life, mental health, nutritional health?
Adoption	Organizations’ barriers and supports for adopting treatments	What do providers/staff/practices/larger organizations need to provide treatment? Staff, space, schedule, EHR changes. Who allocates resources and champions new programs?
Implementation	How well do organizations deliver new treatments?	Once treatment adopted (IHBLT, medication), is it offered consistently and with appropriate supports and monitoring?
Maintenance	After it is established, is treatment maintained?	What are factors that allow a treatment to continue after funding ends or a champion leaves?

Summary points

- The CPG identifies evidence from efficacy studies and does not modify Key Action Statements based on the constraints of healthcare structure
- AOM needs to be available in pediatrics:
  - Many adolescents (and children) have obesity have current and future chronic health conditions. Many have severe obesity
  - Lifestyle interventions are beneficial but inadequate when obesity is severe
- AOM should be used
  - Price and availability challenges are similar to those in adult medicine
  - Lifestyle support is part of AOM treatment but is hard to implement, with insurance structure one important barrier

Future directions

- Improve affordability of AOM and improve insurance coverage (state by state for Medicaid)
- Implement IHBLT outside current healthcare structure, with insurance coverage
  - CDC is leading some initiatives in this area
  - CDC has developed a list of high quality IHBLT
- Support training primary pediatric providers to prescribe medication and ensure patients receive appropriate lifestyle support
- Conduct studies of AOM and mental health, eating disorder risk, muscle mass, and bone health, especially when/if AOM is approved for pre-adolescents

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Thank you