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Pharmacological Interventions for Weight Loss in Children Living With Overweight or Obesity

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Key Message

- Ten systematic reviews (7 with meta-analyses and 1 with network meta-analysis) and 11 randomized controlled trials were identified regarding the clinical effectiveness of pharmacological interventions for weight loss in children living with overweight or obesity.

Research Question

What is the clinical effectiveness of pharmacological interventions for weight loss in children living with overweight or obesity?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were pediatrics, obesity, and anti-obesity agents. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses; and randomized controlled trials or controlled clinical trials. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2013 and February 23, 2021. Internet links were provided, where available.

Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed.

Results

Ten systematic reviews[1-10] (7 with meta-analyses[1,2,4-6,8,9] and 1 with network meta-analysis[3]) and 11 randomized controlled trials[11-21] were identified regarding the clinical effectiveness of pharmacological interventions for weight loss in children living with overweight or obesity. No relevant health technology assessments were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Table 1: Selection Criteria

Criteria	Description
Population	Children and youth 2 to 18 years living with overweight or obesity (i.e., BMI > 85th percentile based on age and sex) Exclude: those with eating disorders; who are living with overweight or obesity secondary to a genetic or medical condition reason (e.g., Cushing syndrome); who experience weight gain secondary to medications (e.g., antipsychotic drugs); or who are pregnant or breastfeeding
Intervention	Pharmacological (e.g., orlistat or sibutramine) interventions for weight loss management, alone or in combination with a behavioural intervention for weight loss management
Comparator	No or minimal treatment (e.g., wait list control, a single information session on healthy living, a newsletter); Usual care; Placebo; Alternative behaviour-based or pharmacological interventions for weight loss or weight management, alone or in combination with another eligible comparator; No comparator (safety outcomes only)
Outcomes	Clinical benefits (e.g., weight change, adiposity, hypertension, dyslipidemia, sleep apnea, fasting blood sugar, mental health, quality of life, physical fitness) and harms (e.g., death, need for medical or psychiatric treatment, growth retardation, gastrointestinal events)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials

BMI = body mass index.

References

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

Intervention – Multiple Drugs Assessed

1. O'Connor EA, Evans CV, Burda BU, Walsh ES, Eder M, Lozano P. Screening for Obesity and Intervention for Weight Management in Children and Adolescents: Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. 2017 Jun 20;317(23):2427-2444. Medline
2. Mead E, Atkinson G, Richter B, et al. Drug interventions for the treatment of obesity in children and adolescents. *Cochrane Database Syst Rev*. 2016 Nov 29;11:CD012436. Medline
3. Peirson L, Fitzpatrick-Lewis D, Morrison K, Warren R, Usman Ali M, Raina P. Treatment of overweight and obesity in children and youth: a systematic review and meta-analysis. *CMAJ Open*. 2015 Jan-Mar;3(1):E35-46. Medline

Intervention – Glucagon-like Peptide-1 Agonists

4. Chadda KR, Cheng TS, Ong KK. GLP-1 agonists for obesity and type 2 diabetes in children: Systematic review and meta-analysis. *Obes Rev*. 2020 Dec 22;22:22. Medline

Intervention - Metformin

5. Hui F, Zhang Y, Ren T, Li X, Zhao M, Zhao Q. Role of metformin in overweight and obese people without diabetes: a systematic review and network meta-analysis. *Eur J Clin Pharmacol*. 2019 Apr;75(4):437-450. Medline
6. Sun J, Wang Y, Zhang X, He H. The effects of metformin on insulin resistance in overweight or obese children and adolescents: A PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. *Medicine*. 2019 Jan;98(4):e14249. Medline
7. Lentferink YE, Knibbe CAJ, van der Vorst MMJ. Efficacy of Metformin Treatment with Respect to Weight Reduction in Children and Adults with Obesity: A Systematic Review. *Drugs*. 2018 Dec;78(18):1887-1901. Medline
8. Norwegian Institute of Public Health (NIPH). Effectiveness of interventions for overweight or obesity in children and adolescents. Oslo: NIPH; 2016. https://www.fhi.no/en/publ/2016/effekt-av-tiltak-for-barn-og-unge-med-overvekt-eller-fedme/ Accessed 2021 Feb 24. *See: Key message*

9. McDonagh MS, Selph S, Ozpinar A, Foley C. Systematic review of the benefits and risks of metformin in treating obesity in children aged 18 years and younger. *JAMA Pediatr*. 2014 Feb;168(2):178-184. Medline

10. Brufani C, Crino A, Fintini D, Patera PI, Cappa M, Manco M. Systematic review of metformin use in obese nondiabetic children and adolescents. *Horm Res Paediatr*. 2013;80(2):78-85. Medline

Randomized Controlled Trials

Intervention – Liraglutide

11. Kelly AS, Auerbach P, Barrientos-Perez M, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. *N Engl J Med*. 2020 05 28;382(22):2117-2128. Medline

12. Mastrandrea LD, Witten L, Carlsson Petri KC, Hale PM, Hedman HK, Riesenberg RA. Liraglutide effects in a paediatric (7-11 y) population with obesity: A randomized, double-blind, placebo-controlled, short-term trial to assess safety, tolerability, pharmacokinetics, and pharmacodynamics. *Pediatr Obes*. 2019 05;14(5):e12495. Medline

13. Danne T, Biester T, Kapitzke K, et al. Liraglutide in an Adolescent Population with Obesity: A Randomized, Double-Blind, Placebo-Controlled 5-Week Trial to Assess Safety, Tolerability, and Pharmacokinetics of Liraglutide in Adolescents Aged 12-17 Years. *J Pediatr*. 2017 02;181:146-153.e143. Medline

14. Klein DJ, Battelino T, Chatterjee DJ, et al. Liraglutide's safety, tolerability, pharmacokinetics, and pharmacodynamics in pediatric type 2 diabetes: a randomized, double-blind, placebo-controlled trial. *Diabetes Technol Ther*. 2014 Oct;16(10):679-687. Medline

Intervention – Metformin

15. Bassols J, Martinez-Calcerrada JM, Osiniri I, et al. Effects of metformin administration on endocrine-metabolic parameters, visceral adiposity and cardiovascular risk factors in children with obesity and risk markers for metabolic syndrome: A pilot study. *PLoS ONE*. 2019;14(12):e0226303. Medline

16. Warnakulasuriya LS, Fernando MMA, Adikaram AVN, et al. Metformin in the Management of Childhood Obesity: A Randomized Control Trial. *Child Obes*. 2018 Nov/Dec;14(8):553-565. Medline

17. Pastor-Villaescusa B, Canete MD, Caballero-Villarraso J, et al. Metformin for Obesity in Prepubertal and Pubertal Children: A Randomized Controlled Trial. *Pediatrics*. 2017 07;140(1):07. Medline

18. van der Aa MP, Elst MA, van de Garde EM, van Mil EG, Knibbe CA, van der Vorst MM. Long-term treatment with metformin in obese, insulin-resistant adolescents: results of a randomized double-blinded placebo-controlled trial. *Nutr Diabetes*. 2016 08 29;6(8):e228. Medline

19. Nwosu BU, Maranda L, Cullen K, et al. A Randomized, Double-Blind, Placebo-Controlled Trial of Adjunctive Metformin Therapy in Overweight/Obese Youth with Type 1 Diabetes. *PLoS ONE*. 2015;10(9):e0137525. Medline

20. Kendall D, Vail A, Amin R, et al. Metformin in obese children and adolescents: the MOCA trial. *J Clin Endocrinol Metab*. 2013 Jan;98(1):322-329. Medline

Intervention – Orlistat

21. Yu CC, Li AM, Chan KO, et al. Orlistat improves endothelial function in obese adolescents: a randomised trial. *J Paediatr Child Health*. 2013 Nov;49(11):969-975. Medline

Appendix 1: References of Potential Interest

Systematic Reviews and Meta-analyses

No Direct Comparator

22. Selvendran SS, Penney NC, Aggarwal N, Darzi AW, Purkayastha S. Treatment of Obesity in Young People-a Systematic Review and Meta-analysis. *Obes Surg*. 2018 08;28(8):2537-2549. Medline

23. Rajjo T, Mohammed K, Alsawas M, et al. Treatment of Pediatric Obesity: An Umbrella Systematic Review. *J Clin Endocrinol Metab*. 2017 03 01;102(3):763-775. Medline

Unclear Comparator and Alternative Outcome – Patient Satisfaction

24. Skelton JA, Bennett Irby M, Geiger AM. A Systematic Review of Satisfaction and Pediatric Obesity Treatment: New Avenues for Addressing Attrition. *J Healthc Qual*. 2014;36(4):5-22. Medline

Randomized Controlled Trials

Alternative Intervention – Exenatide (Not Approved for Pediatric Patients by Health Canada)

25. Weghuber D, Forslund A, Ahlstrom H, et al. A 6-month randomized, double-blind, placebo-controlled trial of weekly exenatide in adolescents with obesity. *Pediatr Obes*. 2020 07;15(7):e12624. Medline

26. Nathan BM, Rudser KD, Abuzzahab MJ, et al. Predictors of weight-loss response with glucagon-like peptide-1 receptor agonist treatment among adolescents with severe obesity. *Clin Obes*. 2016 Feb;6(1):73-78. Medline

27. Kelly AS, Rudser KD, Nathan BM, et al. The effect of glucagon-like peptide-1 receptor agonist therapy on body mass index in adolescents with severe obesity: a randomized, placebo-controlled, clinical trial. *JAMA Pediatr*. 2013 Apr;167(4):355-360. Medline

Alternative Intervention – Topiramate (Not Approved for Weight Loss by Health Canada)

28. Fox CK, Kaizer AM, Rudser KD, et al. Meal replacements followed by topiramate for the treatment of adolescent severe obesity: A pilot randomized controlled trial. *Obesity (Silver Spring)*. 2016 12;24(12):2553-2561. Medline

Alternative Outcome – Perceived Hunger and Fullness

29. Adeyemo MA, McDuffie JR, Kozlosky M, et al. Effects of metformin on energy intake and satiety in obese children. *Diabetes Obes Metab*. 2015 Apr;17(4):363-370. Medline

Guidelines and Recommendations

30. Styne DM, Arslanian SA, Connor EL, et al. Pediatric Obesity-Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017 Mar 01;102(3):709-757. Medline

31. Kelly AS, Barlow SE, Rao G, Inge TH, et al. Severe Obesity in Children and Adolescents: Identification, Associated Health Risks, and Treatment Approaches. *Circulation*. 2013;128(15):1689-1712. https://www.ahajournals.org/doi/10.1161/CIR.0b013e3182a5cfb3 Accessed 2021 Feb 24. Medline

Review Articles

32. Page LC, Freemark M. Role of GLP-1 Receptor Agonists in Pediatric Obesity: Benefits, Risks, and Approaches to Patient Selection. *Curr Obes Rep*. 2020 Dec;9(4):391-401. Medline

33. Chao AM, Wadden TA, Berkowitz RI. The safety of pharmacologic treatment for pediatric obesity. *Expert Opin Drug Saf*. 2018 04;17(4):379-385. Medline

34. Kelly AS, Fox CK, Rudser KD, Gross AC, Ryder JR. Pediatric obesity pharmacotherapy: current state of the field, review of the literature and clinical trial considerations. *Int J Obes*. 2016 07;40(7):1043-1050. Medline

35. Boland CL, Harris JB, Harris KB. Pharmacological management of obesity in pediatric patients. *Ann Pharmacother*. 2015 Feb;49(2):220-232. Medline

36. Shehadeh N, Daich E, Zuckerman-Levin N. Can GLP-1 preparations be used in children and adolescents with diabetes mellitus? *Pediatr Endocrinol Rev*. 2014 Mar;11(3):324-327. Medline

Not Specific to Pharmacological Interventions

37. Xu S, Xue Y. Pediatric obesity: Causes, symptoms, prevention and treatment. *Exp Ther Med*. 2016 Jan;11(1):15-20. Medline

Additional References

38. Viner RM, Kinra S, Christie D, et al. Improving the assessment and management of obesity in UK children and adolescents: the PROMISE research programme including a RCT. *Programme Grants Appl Res*. 2020;8(3). Medline