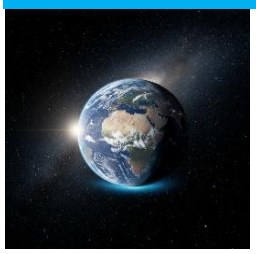
NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ



Quality in Sport. eISSN 2450-3118.

Journal Home Page
https://apcz.umk.pl/QS/index

DROZDOWSKA, Marta, BORYCHOWSKA, Emilia, BYSTROS, Aleksandra, CZUDOWSKA, Michalina, GWÓŹDŹ, Karolina, KURZĄTKOWSKA, Klaudia, MARSZAŁEK, Dominika, MIERZEJEWSKA, Zofia, OCIMEK, Aleksandra and ZAWADZKA, Magdalena. Pharmacological treatment options for obesity in children with insulin resistance: a targeted review. Quality in Sport. 2026;54:70352. eISSN 2450-3118. https://doi.org/10.12775/QS.2026.54.70352

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 l.p. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 28.03.2026. Revised: 30.03.2026. Accepted: 30.03.2026. Published: 10.04.2026.

Pharmacological treatment options for obesity in children with insulin resistance: a targeted review

Marta Antonina Drozdowska (corresponding author)

ORCID: https://orcid.org/0009-0006-3785-2532

Międzyleski Szpital Specjalistyczny w Warszawie: Warsaw, Mazovia, PL

Emilia Borychowska
ORCID: https://orcid.org/0009-0004-5703-2991
Warszawski Szpital Południowy sp. z o.o. ul. Rotmistrza Witolda Pileckiego 99, 02-781, Warszawa, PL

Aleksandra Natalia Bystros
ORCID: https://orcid.org/0009-0009-4117-0624
Międzyleski Szpital Specjalistyczny w Warszawie: Warsaw, Mazovia, PL

Michalina Czudowska
ORCID: https://orcid.org/0009-0002-0035-0150
Mazovian Brodno Hospital in Warsaw, Ludwika Kondratowicza 8, 03-242, Warsaw, PL

Karolina Gwóźdź
ORCID: https://orcid.org/0009-0009-2690-5573
Independent Public Complex of Healthcare Institutions of Marshal Józef Piłsudski in Płońsk: Płońsk, PL

Klaudia Kurzątkowska
ORCID: https://orcid.org/0009-0006-1882-5301
Warszawski Uniwersytet Medyczny: Warsaw, Mazovia, PL

Dominika Marszałek
ORCID: https://orcid.org/0009-0008-2419-1864
Medical University of Warsaw, Żwirki i Wigury 61, 02-091, Warsaw, PL

Zofia Aneta Mierzejewska
ORCID: https://orcid.org/0009-0002-3670-3480
Lazarski University, Warsaw, Mazovia, PL

Aleksandra Ocimek

ORCID: https://orcid.org/0009-0007-9342-8055
Medical University of Warsaw: Warsaw, Mazovia, PL

Magdalena Zawadzka
ORCID: https://orcid.org/0009-0000-2456-9443
Autonomous Public Health Maintenance Organisation J. Sniadecki Voivodship Polyclinical Hospital in Bialystok, PL

Abstract:

Background. Childhood and adolescent obesity is an increasing global health concern. Many obese children develop insulin resistance, which contributes to metabolic complications including type 2 diabetes, dyslipidemia, hypertension, and non-alcoholic fatty liver disease. Although lifestyle modification remains the primary treatment, it is often insufficient in cases of severe obesity or marked insulin resistance. In recent years, pharmacological therapies have been increasingly used in pediatric obesity, but their efficacy and safety in insulin-resistant children are not fully established.

Aim. This review aims to summarize current evidence on pharmacological treatment options for obese children with insulin resistance, with a focus on efficacy, safety, and research gaps relevant to clinical practice.

Material and methods. A literature review was conducted using PubMed, MEDLINE, Scopus, and Web of Science. Studies evaluating pharmacological therapies such as metformin, GLP-1 receptor agonists, and orlistat were included. Randomized controlled trials, systematic reviews, meta-analyses, and observational studies reporting changes in BMI, metabolic parameters, and adverse events were analyzed.

Conclusions. Available evidence suggests that pharmacological agents, including metformin, orlistat, GLP-1 receptor agonists, and phentermine/topiramate, can reduce body weight and improve metabolic outcomes in obese children and adolescents with insulin resistance. GLP-1 receptor agonists show the greatest BMI reduction. Safety profiles vary, with gastrointestinal adverse effects being most common. Long-term safety data, particularly in children under 12

years of age, remain limited, highlighting the need for individualized therapy and further research.

Keywords: pediatric obesity, pharmacotherapy, liraglutide, orlistat, GLP-1, insulin resistance

Introduction:

Obesity in children and adolescents is one of the major public health challenges of our time. The prevalence of this condition in the pediatric population continues to increase, which is associated not only with a reduced quality of life but also with a long-term risk of developing metabolic diseases. One of the key disorders that frequently coexists with obesity is insulin resistance, which may predispose affected individuals to the development of type 2 diabetes, metabolic syndrome, arterial hypertension, and non-alcoholic fatty liver disease.

Current epidemiological data on insulin resistance among obese children are limited and highly heterogeneous, largely due to the lack of a standardized definition of insulin resistance. Moreover, there is a paucity of large, comprehensive review studies published in recent years (2015–2025) that specifically focus on insulin resistance in this population.

Table 1. Epidemiological data on overweight and obesity in children and adolescents.

Phenomenon	Epidemiological values
Overweight/obesity in children (5–19 years)	~20% of children aged 5–19 years are overweight or obese (2022) [1]
Number of children with overweight/obesity	~391 million children aged 5–19 years are overweight or obese (2022) [1]
Prognosis	~One-third of children and adolescents may be overweight or obese by 2050 [2]

The primary approach to obesity treatment in children is a comprehensive lifestyle modification, including dietary changes, increased physical activity, and behavioral therapy. However, in cases of advanced obesity or when insulin resistance is pronounced, these strategies often fail to achieve the desired outcomes. In such situations, pharmacological interventions become an

important adjunct to therapy, enabling not only weight reduction but also improvement in tissue insulin sensitivity and overall metabolic profile.

State of knowledge:

Several pharmacological agents have been evaluated in the pediatric population for their efficacy in the treatment of obesity associated with insulin resistance, with **orlistat** and **metformin** being among the most frequently investigated in clinical studies. In a study involving adolescents, orlistat administered for 54 weeks in combination with dietary intervention and behavioral therapy resulted in a significant reduction in BMI compared with placebo [3]. Meta-analyses have also shown that orlistat may contribute to a reduction in waist circumference and a decrease in serum insulin levels in children and adolescents [4].

Metformin, owing to its mechanism of action that improves insulin sensitivity, has been extensively studied in children and adolescents with insulin resistance. In a randomized trial involving children aged 6–12 years, metformin administration led to a reduction in BMI, a decrease in fat mass, and an improvement in metabolic indices, including HOMA-IR [5]. In a long-term study lasting 18 months in adolescents, metformin stabilized BMI and improved body composition compared with placebo; however, changes in insulin resistance were less pronounced [6]. At the same time, prolonged use is associated with certain limitations—data from extension studies indicate that the beneficial effect of metformin on HOMA-IR diminishes or may even disappear over time, which may be related to suboptimal treatment adherence (compliance) or inadequate dosing [7].

Despite these promising findings, several challenges remain, including the limited duration of available studies, the insufficient number of trials focusing specifically on children with insulin resistance, and concerns regarding the safety and long-term tolerability of pharmacological therapies in pediatric patients. Therefore, a thorough analysis of the available evidence is

necessary to determine which pharmacological approaches are most appropriate for use in this specific population.

Currently available pharmacological treatment options for obesity in children:

Orlistat

Orlistat is a pancreatic lipase inhibitor that acts in the gastrointestinal tract by blocking the digestion and absorption of dietary fats, leading to a negative energy balance and weight reduction. Clinical studies in children and adolescents with obesity have demonstrated a moderate decrease in BMI, typically ranging from 0.5 to 1.5 kg/m² over 6–12 months of therapy. Additionally, orlistat may have beneficial effects on total cholesterol and triglyceride levels. The most common adverse effects include steatorrhea, bloating, oily stools, and increased bowel movements, which in most cases resolve after dietary adjustments. Due to its mechanism of action, supplementation with fat-soluble vitamins (A, D, E, K) is recommended. Orlistat is considered relatively safe but requires collaboration with a dietitian and regular monitoring of nutritional status [8][9]. Orlistat is officially approved for use in children and adolescents **aged 12 years and older**, based on clinical trial evidence [10]. Reliable long-term studies in children under 12 years are lacking, representing a significant gap in the literature.

Liraglutide

Liraglutide is a GLP-1 receptor agonist that acts by enhancing glucose-dependent insulin secretion, suppressing glucagon release, delaying gastric emptying, and reducing appetite. Clinical studies have shown that liraglutide can induce a significant reduction in BMI in children and adolescents with obesity, with an average decrease of 4.5–5.6% over 12–56 weeks, along with improvements in insulin sensitivity and metabolic markers. The most common adverse effects include nausea, vomiting, abdominal pain, and constipation, which are generally mild and transient. Liraglutide therapy requires patient monitoring, including liver and kidney function, as well as education on proper injection technique and monitoring for gastrointestinal symptoms. A 2025 meta-analysis including seven randomized controlled trials (totaling 575 patients) assessed the efficacy and safety of liraglutide in children and adolescents with obesity, including participants aged 6–12 years. The authors concluded that liraglutide significantly reduced BMI and body weight while improving metabolic parameters [11].

Semaglutide

Semaglutide is a long-acting GLP-1 receptor agonist that allows for once-weekly administration. Its mechanism of action is similar to that of liraglutide, but due to its prolonged effect, it often produces greater weight reduction. In children and adolescents with obesity, semaglutide has been shown to induce substantial reductions in BMI—often higher than those observed with liraglutide—ranging from 10% to 16% over 68 weeks. The drug also improves insulin sensitivity and metabolic parameters. The most common adverse effects include nausea, vomiting, and constipation, while acute pancreatitis has been reported in rare cases. Due to its high efficacy, semaglutide is increasingly considered a first-line pharmacological option for pediatric obesity in combination with lifestyle modification. According to reviews of large studies and meta-analyses, semaglutide (GLP-1 RA) achieves greater reductions in body weight and BMI compared with placebo and other GLP-1 receptor agonists (including liraglutide) in children and adolescents with obesity [12]. Semaglutide was approved by the FDA in December 2022 for the treatment of obesity in adolescents **aged ≥12 years** [13]. Official approval exists for use in children and adolescents from 12 years of age; for children under 12, reliable clinical data are lacking or very limited in the available literature.

Metformin

Metformin is a biguanide that increases tissue insulin sensitivity, inhibits hepatic gluconeogenesis, and reduces glucose absorption in the intestines. In obese children and adolescents with insulin resistance, metformin induces a moderate reduction in BMI, typically 0.8–2 kg/m², and also improves metabolic parameters such as HOMA-IR, fasting insulin levels, and lipid profile. Adverse effects of metformin are primarily gastrointestinal and include nausea, vomiting, abdominal pain, and diarrhea; less commonly, long-term use may lead to vitamin B12 deficiency. Metformin is particularly indicated for children with insulin resistance who do not respond adequately to non-pharmacological interventions, making it one of the most commonly used medications in this context. Randomized controlled trials have evaluated metformin in children as young as 7 years old (most commonly 9–18 years), indicating that its use in younger age groups is possible, although data in the youngest children (<7 years) are very limited. In most studies, the reduction in BMI and/or body weight was moderate, generally less pronounced than with more potent “weight-loss” agents—typically a decrease in BMI of approximately 1–1.4 kg/m² or a corresponding reduction in BMI z-score [14]. Many studies

have a relatively short duration (6–12 months), which limits the assessment of long-term efficacy and safety [14].

Phentermine/Topiramate

The combination of phentermine and topiramate (Qsymia, phentermine/topiramate ER) is currently approved by the FDA in the United States for the treatment of obesity in children and adolescents **aged ≥12 years**, including those with insulin resistance. The efficacy of this therapy has been confirmed in randomized clinical trials: in a 56-week study in adolescents aged 12–17 years, an average BMI reduction of 8–10% was achieved compared with placebo, and 39–47% of participants reached a ≥5% reduction in BMI, depending on the dose [15][16][17]. According to the American Academy of Pediatrics guidelines, pharmacological treatment (including phentermine/topiramate) should be considered in children with obesity for whom behavioral interventions have not achieved the desired results, particularly in the presence of metabolic complications such as insulin resistance. The dosing regimen typically begins with 3.75 mg/23 mg for 14 days, then increases to 7.5 mg/46 mg; if necessary, it can be titrated gradually up to a maximum of 15 mg/92 mg. Phentermine acts as a norepinephrine reuptake inhibitor, while topiramate functions as a carbonic anhydrase inhibitor, affecting appetite and satiety. The most common adverse effects include mood changes, insomnia, paresthesia, cognitive disturbances, dry mouth, and constipation. Topiramate is teratogenic, so effective contraception is required in girls of reproductive age. In children with insulin resistance, treatment with phentermine/topiramate may improve metabolic parameters, including lipid profile and blood pressure, and reduce the risk of progression to type 2 diabetes.

Tirzepatide

Tirzepatide is not currently FDA-approved for the treatment of obesity in children and adolescents without type 2 diabetes; however, in the **SURPASS-PEDS** study, it was shown that in children and adolescents with type 2 diabetes, tirzepatide leads to significant reductions in body weight, BMI, and improvements in metabolic parameters, including insulin resistance. In a 52-week observation period, mean reductions in BMI of 8.9–15.1% and body weight of 8.0–13.8% were observed, depending on the dose, along with improvements in lipid profile and blood pressure. These effects are particularly relevant for children with insulin resistance, where weight loss and improved insulin sensitivity may reduce the risk of progression to type 2 diabetes and cardiovascular complications. Tirzepatide is a dual **GIP and GLP-1 receptor**

agonist, allowing synergistic effects on weight reduction and glucose homeostasis. The most common adverse effects are gastrointestinal symptoms, which are generally mild to moderate and tend to resolve during treatment. Tirzepatide may be considered as a therapeutic option for treating obesity in children with insulin resistance, especially in the context of type 2 diabetes. However, it is currently **not approved for use in this population in the USA outside of type 2 diabetes**. Further studies are ongoing to evaluate the safety and efficacy of tirzepatide for obesity treatment in children without type 2 diabetes [18][19].

Recommendations:

Table 2. Key thresholds and recommendations for pharmacological and surgical management of pediatric obesity across major guidelines.

Guidelines /Year Organization		Definition of Obesity / Severe Obesity	Age for Pharmacotherapy	Pharmacotherapy Criteria	Age / Criteria for Metabolic Surgery
AAP	2023	Obesity: ≥95th percentile; Severe: ≥120% of 95th percentile (~99th)	≥12 years if lifestyle interventions insufficient	BMI in obesity/severe obesity range; individual decision	Usually ≥13 years with severe obesity + comorbidities; multidisciplinary assessment

NICE (UK)	2025	Overweight: ≥91st percentile; Obesity: ≥98th percentile	≥12 years (medications not generally <12)	Clinical cut-offs; Orlistat ≥12y; other drugs per license/TA	Selected severe, treatment-resistant cases; specialist multidisciplinary evaluation
Endocrine Society	2017	BMI ≥85th percentile — comorbidities; ≥95th percentile = obesity	Limited to clinical assess trials; adolescents in selected cases	Pharmacotherapy in research context	Considered in mature adolescents after failure of conservative therapy; multidisciplinary care
USPSTF	2024	High BMI: ≥95th percentile	Referral to intensive behavioral programs; pharmacotherapy not routine	≥95th percentile → intensive intervention programs	Not included; guided by local/clinical guidelines
PTLO (Poland)	2024	IOTF cut-offs; obesity per international percentiles	≥12 years + weight >60 kg; lifestyle responsive	Registered drugs: non-li (selected indications)	raglutide, semaglutide severe, resistant obesity + comorbidities; multidisciplinary qualification

The table is intended for **qualitative and comparative purposes**. Exact BMI thresholds (e.g., percentile values, absolute BMI, thresholds for different age groups) and precise criteria for pharmacotherapy and surgery vary between documents and may be updated over time. To obtain precise numerical values and direct citations, reference should be made to the original source guidelines (e.g., AAP 2023, NICE 2025, ESPGHAN 2023, Endocrine Society 2017, USPSTF 2024).

Safety and Adverse Effects:

Regular monitoring of drug-specific adverse effects is recommended for each medication.

Orlistat: The most common adverse effects are gastrointestinal, including steatorrhea, urgent bowel movements, oily or fatty stools, bloating with discharge, and fecal leakage. Long-term use may lead to deficiencies in fat-soluble vitamins (A, D, E, K).

Liraglutide: Gastrointestinal symptoms are the most common, including nausea, vomiting, diarrhea, constipation, dyspepsia, and abdominal pain. These effects are most frequent during dose escalation. Less commonly, headache and dizziness may occur. There is a potential risk of pancreatitis and gallstones. The American Academy of Pediatrics also highlights a theoretical risk of thyroid C-cell tumors in individuals with a predisposition.

Semaglutide: The most common adverse effects are nausea, vomiting, diarrhea, constipation, abdominal pain, and dyspepsia. The frequency of gastrointestinal symptoms is similar to liraglutide, but semaglutide more often causes abdominal pain and gallstones. The American Academy of Pediatrics notes a potential risk of thyroid C-cell tumors.

Phentermine/Topiramate: The most common adverse effects include dry mouth, paresthesia, cognitive disturbances (slow thinking, difficulty concentrating), insomnia, headache, dizziness, constipation, and irritability. Phentermine may increase blood pressure and cause palpitations, while topiramate is teratogenic.

Metformin: Gastrointestinal symptoms are the most frequent, including nausea, vomiting, abdominal pain, and diarrhea. Rarely, lactic acidosis may occur. Renal function should be monitored.

The safety of pharmacological therapy for obesity in children with insulin resistance should be monitored at least **monthly during the first three months of treatment**, and thereafter at least **quarterly**, with more frequent visits if adverse effects occur or dose adjustments are required. At each visit, the occurrence of typical adverse effects should be assessed: gastrointestinal symptoms (orlistat, liraglutide, semaglutide, tirzepatide), cognitive and psychiatric disturbances (phentermine/topiramate), fat-soluble vitamin deficiencies (orlistat),

and the risk of rare but serious complications such as pancreatitis, gallstones, or thyroid C-cell tumors (GLP-1 RAs, tirzepatide).

Routine monitoring should include laboratory tests: blood glucose, renal and liver function, electrolytes, fat-soluble vitamins (with orlistat), blood pressure and ECG (with phentermine/topiramate), and hypoglycemia monitoring when used concurrently with other antidiabetic medications. Due to limited long-term safety data (beyond 12–17 months) for all drugs in the pediatric population, the monitoring plan should be **individualized** [20].

Limitations of current evidence:

Despite the growing number of studies on the use of pharmacological treatment for obesity in children with insulin resistance, the available scientific evidence remains significantly limited. Most studies have a relatively short follow-up period (usually 6–12 months), which makes it difficult, if not impossible, to reliably assess the long-term efficacy and safety of therapy, particularly with regard to its effects on growth, pubertal development, and metabolism. Data on the durability of weight loss after discontinuation of treatment are also lacking.

Many studies include heterogeneous populations, often comprising mixed groups of children with obesity and varying degrees of insulin resistance or without its clear diagnosis, which substantially limits the ability to draw conclusions specific to this patient group. The majority of available data concern children older than 12 years, whereas studies including younger children are scarce, restricting the formulation of evidence-based therapeutic recommendations for this age group.

Another important limitation is the lack of direct head-to-head comparative trials between different pharmacological agents, which prevents precise determination of which therapy is the most effective and safest. Most meta-analyses rely on comparisons with placebo rather than between active treatments. Furthermore, many studies are conducted under strictly controlled conditions, which may not reflect the real-world effectiveness and tolerability of treatment in routine clinical practice, where factors such as treatment adherence, drug availability, and multidisciplinary support play a significant role.

Summary:

Pharmacological treatment of obesity in children and adolescents with insulin resistance appears to be an increasingly important component of comprehensive therapeutic management, particularly when lifestyle modification interventions prove insufficient. Currently available evidence indicates that several drug classes—most notably metformin, orlistat, GLP-1 receptor agonists (liraglutide and semaglutide), and the combination of phentermine with topiramate—can lead to significant reductions in BMI and improvements in metabolic parameters, including tissue insulin sensitivity.

At present, GLP-1 receptor agonists, particularly semaglutide, demonstrate the greatest efficacy in body weight reduction. Metformin remains a valuable option for children with predominant insulin resistance, especially in the presence of concomitant disturbances of glucose metabolism, although its effect on body weight is moderate. Orlistat and the phentermine/topiramate combination represent alternative therapeutic options; however, they require careful monitoring for adverse effects.

Despite these promising results, pharmacological treatment should be used as an adjunct to intensive behavioral and dietary interventions and delivered within a multidisciplinary care framework. Given the limited number of long-term studies and the insufficient data on younger children, therapeutic decisions should be individualized, taking into account metabolic profile, age, degree of obesity, and potential adverse effects.

Further well-designed studies with long-term follow-up are necessary to determine optimal pharmacological strategies for treating obesity with insulin resistance in the pediatric population and to develop precise, evidence-based clinical guidelines.

Disclosures:

Authors' contribution:

Conceptualisation: Marta Drozdowska, Magdalena Zawadzka

Methodology: Marta Drozdowska, Magdalena Zawadzka

Software: Aleksandra Bystros, Dominika Marszałek

Check: Karolina Gwóźdź, Dominika Marszałek
Formal analysis: Aleksandra Bystros, Aleksandra Ocimek
Investigation: Zofia Aneta Mierzejewska, Michalina Czudowska
Resources: Zofia Aneta Mierzejewska, Michalina Czudowska
Data curation: Emilia Borychowska, Karolina Gwóźdź
Writing - rough preparation: Emilia Borychowska, Klaudia Kurzątkowska
Writing - review and editing: Marta Drozdowska, Klaudia Kurzątkowska
Visualisation: Aleksandra Ocimek
Project administration: Marta Drozdowska

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The study did not receive special funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Not applicable.

Conflict Of Interest: The authors declare no conflict of interest.

References:

[1] United Nations Children's Fund (UNICEF), Feeding Profit. How food

environments are failing children. Child Nutrition Report 2025, UNICEF, New York, September 2025.
[2] Global, regional, and national prevalence of child and adolescent overweight and obesity, 1990–2021, with forecasts to 2050: a forecasting study for the Global Burden of Disease Study 2021 Kerr, Jessica A et al. The Lancet, Volume 405, Issue 10481, 785 - 812

[3] Chanoine JP, Hampl S, Jensen C, Boldrin M, Hauptman J. Effect of orlistat on weight and body composition in obese adolescents: a randomized controlled trial. JAMA. 2005 Jun 15;293(23):2873-83. doi: 10.1001/jama.293.23.2873. Erratum in: JAMA. 2005 Sep 28;294(12):1491. PMID: 15956632.
[4] Nikniaz Z, Nikniaz L, Farhangi MA, Mehralizadeh H, Salekzamani S. Effect of Orlistat on anthropometrics and metabolic indices in children and adolescents: a systematic review and meta-analysis. BMC Endocr Disord. 2023 Jul 7;23(1):142. doi: 10.1186/s12902-023-01390-7. PMID: 37420181; PMCID: PMC10327388.
[5] Yanovski JA, Krakoff J, Salaita CG, McDuffie JR, Kozlosky M, Sebring NG, Reynolds JC, Brady SM, Calis KA. Effects of metformin on body weight and body composition in obese insulin-resistant children: a randomized clinical trial. Diabetes. 2011 Feb;60(2):477-85. doi: 10.2337/db10-1185. Epub 2011 Jan 12. PMID: 21228310; PMCID: PMC3028347.
[6] 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 Aug 29;6(8):e228. doi: 10.1038/nutd.2016.37. PMID: 27571249; PMCID: PMC5022149.
[7] Lentferink YE, van der Aa MP, van Mill EGAH, Knibbe CAJ, van der Vorst MMJ. Long-term metformin treatment in adolescents with obesity and insulin resistance, results of an open label extension study. Nutr Diabetes. 2018 Sep 10;8(1):47. doi: 10.1038/s41387-018-0057-6. PMID: 30197416; PMCID: PMC6129504.
[8] Boland CL, Harris JB, Harris KB. Pharmacological management of obesity in pediatric patients. Ann Pharmacother. 2015 Feb;49(2):220-32. doi: 10.1177/1060028014557859. Epub 2014 Nov 3. PMID: 25366340.
[9] Zhou XL, Wu W, Zhang L, Lin H, Zhao NN, Li YJ, Huang K, Dong GP, Fu JF. [A meta-analysis of efficacy and safety of anti-obesity medications in the treatment of childhood obesity].

Zhonghua Yi Xue Za Zhi. 2025 Nov 11;105(41):3783-3790. Chinese. doi: 10.3760/cma.j.cn112137-20250416-00945. PMID: 41218895.

[10] Chao AM, Wadden TA, Berkowitz RI. The safety of pharmacologic treatment for pediatric obesity. Expert Opin Drug Saf. 2018 Apr;17(4):379-385. doi: 10.1080/14740338.2018.1437143. Epub 2018 Feb 7. PMID: 29411652.

[11] Dong J, Liu M, Liu Z. Long-term administration of liraglutide for weight management in pediatric patients under 18 years: evidence from 7 randomized controlled trials. Pediatr Res. 2025 Nov 3. doi: 10.1038/s41390-025-04537-5. Epub ahead of print. PMID: 41184626.

[12] Liu L, Shi H, Shi Y, Wang A, Guo N, Tao H, Nahata MC. Comparative Efficacy and Safety of Glucagon-like Peptide-1 Receptor Agonists in Children and Adolescents with Obesity or Overweight: A Systematic Review and Network Meta-Analysis. Pharmaceuticals. 2024; 17(7):828. https://doi.org/10.3390/ph17070828

[13] Rehman R. Role of glucagon-like peptide-1 receptor agonists in pediatric obesity and metabolic dysfunction associated steatotic liver disease. World J Clin Pediatr 2025; 14(3): 105731 [PMID: 40881096 DOI: 10.5409/wjcp.v14.i3.105731]

[14] Park MH, Kinra S, Ward KJ, White B, Viner RM. Metformin for obesity in children and adolescents: a systematic review. Diabetes Care. 2009 Sep;32(9):1743-5. doi: 10.2337/dc09-0258. Epub 2009 Jun 5. PMID: 19502540; PMCID: PMC2732169.

[15] Dhillon S. Phentermine/Topiramate: Pediatric First Approval. *Paediatr Drugs*. 2022;24(6):715-720. doi:10.1007/s40272-022-00532-z

[16] Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet*. 2011;377(9774):1341-1352. doi:10.1016/S0140-6736(11)60205-5

[17] Yang S, Xin S, Ju R, Zang P. Pharmacological interventions for addressing pediatric and adolescent obesity: A systematic review and network meta-analysis. *PLoS One*. 2025;20(2):e0314787. Published 2025 Feb 27. doi:10.1371/journal.pone.0314787

[18] Hannon TS, Chao LC, Barrientos-Pérez M, et al. Efficacy and safety of tirzepatide in children and adolescents with type 2 diabetes (SURPASS-PEDS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2025;406(10511):1484-1496. doi:10.1016/S0140-6736(25)01774-X

[19] Corrao S, Pollicino C, Maggio D, Torres A, Argano C. Tirzepatide against obesity and insulin-resistance: pathophysiological aspects and clinical evidence. *Front Endocrinol (Lausanne)*. 2024;15:1402583. Published 2024 Jun 24. doi:10.3389/fendo.2024.1402583

[20] Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity *Pediatrics* (2023) 151 (2): e2022060640. Volume 151, Issue 2 February 2023.