©IDOSR PUBLICATIONS International Digital Organization for Scientific Research

IDOSR JOURNAL OF SCIENTIFIC RESEARCH 11(2):23-27, 2026. ISSN: 2550-794X

https://doi.org/10.59298/IDOSRJSR/2026/11.2.2327 IDOSRJSR11106

Long-Acting GLP-1 Receptor Agonists for Weight and Glycaemic Control in Adolescents with Type 2 Diabetes

Muhindo Anitah

Department of Pharmacy Kampala International University Uganda
Email: anitah.muhindo@studwc.kiu.ac.ug

ABSTRACT

Type 2 diabetes in adolescents was an escalating global health challenge, with limited pharmacologic options beyond metformin and insulin. Long-acting glucagon-like peptide-1 receptor agonists (GLP-1 RAs) transformed adult diabetes and obesity care, yet their role in youth remains underexplored despite regulatory approvals for liraglutide, exenatide, and dulaglutide in patients aged 10 years and older. This narrative review synthesized current evidence on the efficacy and safety of long-acting GLP-1 RAs for weight and glycaemic control in adolescents with type 2 diabetes, evaluating their clinical utility and implementation considerations. A systematic search of peer-reviewed literature, clinical trial registries, and guideline documents published through early 2026 informed this narrative synthesis. Meta-analytic data from five randomized trials (415 participants) demonstrated that GLP-1 RAs reduce HbA1c by approximately 1.0 percentage point, lower fasting blood glucose by 1.88 mmol/L, and decrease body weight by 1.6 kg compared with placebo. Gastrointestinal adverse events were more frequent but generally tolerable, with low discontinuation rates. Long-acting GLP-1 RAs represented a meaningful therapeutic advance for adolescents with type 2 diabetes, offering dual benefits in glycaemic and weight management. Their integration into pediatric diabetes care requires careful patient selection, dose titration, and monitoring.

Keywords: GLP-1 receptor agonists, Type 2 diabetes, Adolescents, Weight management, Glycaemic control.

INTRODUCTION

Type 2 diabetes in adolescents has emerged as a critical public health concern, with an estimated 41,600 new cases of youth-onset disease worldwide in 2021 alone [1, 2]. In the United States, approximately 1,230 children aged 10 to 19 years were diagnosed with type 2 diabetes in 2017, reflecting a trend of increasing prevalence linked to rising obesity rates, sedentary behavior, and adverse metabolic programming [3]. The pathophysiology of youth-onset type 2 diabetes involves complex interactions among genetic susceptibility, environmental exposures, and metabolic dysfunction, often resulting in more aggressive disease progression and earlier onset of complications compared with adult-onset disease. Historically, therapeutic options for adolescents with type 2 diabetes were restricted to metformin and insulin, both of which have limitations in efficacy, weight effects, and hypoglycaemia risk [4]. The advent of long-acting glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has revolutionized adult diabetes and obesity management, offering sustained glycaemic control, weight reduction, and cardiovascular benefits [5]. In recent years, regulatory agencies have extended approvals for certain GLP-1 RAs, including liraglutide, exenatide, and dulaglutide, to pediatric patients aged 10 years and older with type 2 diabetes. However, adolescents remain an underrepresented population in clinical trials, and evidence specific to this age group is limited compared to adults. This gap creates uncertainty for clinicians seeking to optimize treatment strategies for youth facing a lifetime of diabetes-related morbidity [6]. This narrative review addresses this knowledge gap by synthesizing current evidence on long-acting GLP-1 RAs for weight and glycaemic control in adolescents with type 2 diabetes. The article is organized into five sections. First, we describe the pharmacological mechanisms and approved agents relevant to pediatric use. Second, we present efficacy data from randomized controlled trials and meta-analyses, focusing on HbA1c, fasting glucose, and weight outcomes. Third, we evaluate safety and

tolerability profiles, emphasizing gastrointestinal adverse events and hypoglycaemia risk. Fourth, we discuss clinical implementation considerations, including patient selection, dosing strategies, and integration with lifestyle interventions. Fifth, we highlight evidence gaps and future research directions. The purpose of this review is to provide clinicians and researchers with a comprehensive, evidence-based assessment of long-acting GLP-1 RAs in adolescent type 2 diabetes, facilitating informed decision-making and identifying priorities for future investigation. By consolidating available data and contextualizing findings within current guidelines, this review aims to support the integration of these agents into comprehensive, individualized care for young people with type 2 diabetes.

Mechanisms of Action and Approved Long-Acting GLP-1 Receptor Agonists in Adolescents

Glucagon-like peptide-1 is an incretin hormone secreted by intestinal L cells in response to nutrient intake, exerting multiple physiological effects relevant to glucose homeostasis and energy balance [7]. GLP-1 enhances glucose-dependent insulin secretion from pancreatic beta cells, suppresses glucagon release, slows gastric emptying, and promotes satiety through central appetite-regulating pathways in the hypothalamus and brainstem. These mechanisms collectively reduce postprandial glucose excursions, decrease overall caloric intake, and facilitate weight loss. Native GLP-1 has a short half-life due to rapid degradation by dipeptidyl peptidase-4, necessitating the development of longer-acting analogues for clinical use [4]. Long-acting GLP-1 RAs are engineered to resist enzymatic degradation and prolong receptor activation through structural modifications, such as fatty acid side chains (liraglutide), albumin binding (dulaglutide), or fusion to immunoglobulin fragments (exenatide extended-release) [8, 9]. These agents achieve sustained plasma concentrations with once-daily or once-weekly dosing, improving adherence and providing consistent glycaemic and weight benefits. In adolescents, the pathophysiological rationale for GLP-1 RA use parallels that in adults, given the shared mechanisms of insulin resistance, beta-cell dysfunction, and obesity-driven metabolic dysregulation [6]. Three long-acting GLP-1 RAs currently hold regulatory approval for use in pediatric patients with type 2 diabetes. Liraglutide, a once-daily injectable analogue, was approved by the United States Food and Drug Administration in 2019 for adolescents aged 10 years and older, based on the phase 3 trial demonstrating significant HbA1c and weight reductions [10]. Exenatide extended release, administered once weekly, received approval in 2022 for the same age group following a randomized trial showing improved glycaemic control and modest weight loss. Dulaglutide, another once-weekly agent, was approved in 2022 for adolescents aged 10 years and older, supported by a phase 3 trial demonstrating superior HbA1c lowering compared with placebo. These approvals reflect a paradigm shift in pediatric diabetes care, expanding the therapeutic armamentarium beyond metformin and insulin [4].

Efficacy of Long-Acting GLP-1 RAs on Glycaemic Control and Weight in Adolescents

Robust evidence from randomized controlled trials and meta-analyses supports the efficacy of long-acting GLP-1 RAs in improving glycaemic control and reducing body weight in adolescents with type 2 diabetes. A 2024 meta-analysis of five randomized trials encompassing 415 participants aged 10 to 18 years reported that GLP-1 RAs reduced HbA1c by a mean of 1.01 percentage points (95 percent confidence interval, minus 1.26 to minus 0.76) compared with placebo [11]. This magnitude of HbA1c reduction is clinically meaningful, particularly in youth who face heightened risks of microvascular and macrovascular complications due to prolonged exposure to hyperglycaemia [12]. The same meta-analysis demonstrated a significant reduction in fasting blood glucose of 1.88 mmol/L (95 percent confidence interval, minus 2.51 to minus 1.26), indicating improved basal glycaemic control [4]. Weight outcomes are particularly relevant in adolescents, given the strong association between obesity and type 2 diabetes pathogenesis. The meta-analysis reported a mean weight reduction of 1.6 kg (95 percent confidence interval, minus 2.83 to minus 0.36) with GLP-1 RA therapy compared with placebo [13, 14]. Although this effect is modest compared to adult trials, it is clinically significant in the context of pediatric growth trajectories and metabolic health. A 2025 systematic review and meta-analysis of 18 randomized trials in children and adolescents with type 2 diabetes or obesity corroborated these findings, reporting HbA1c reductions of 0.44 percentage points and weight loss of 3.02 kg across diverse populations and treatment durations [6].

Individual trials provide further granularity. The liraglutide trial demonstrated an HbA1c reduction of 1.06 percentage points and weight loss of 1.6 kg over 26 weeks. The exenatide extended-release trial showed an HbA1c reduction of 0.86 percentage points and weight loss of 2.48 kg over 24 weeks [15]. The dulaglutide trial reported HbA1c reductions of 0.8 percentage points over 26 weeks. These data collectively affirm that long-acting GLP-1 RAs confer dual benefits in glycaemic and weight management, addressing two core therapeutic targets in adolescent type 2 diabetes [4].

Safety and Tolerability Profiles in Adolescents

The safety and tolerability of long-acting GLP-1 RAs in adolescents are generally favorable, with gastrointestinal adverse events being the most frequently reported side effects. The 2024 meta-analysis reported significantly higher odds of nausea (odds ratio 2.15, 95 percent confidence interval 1.17 to 3.95), vomiting (odds ratio 2.23, 95 percent confidence interval 1.19 to 4.18), and diarrhea (odds ratio 1.81, 95 percent confidence interval 1.01 to 3.25) in GLP-1 RA recipients compared with placebo [16]. Abdominal pain did not differ significantly between groups. These events are typically mild to moderate in severity, occur early in treatment, and often resolve with continued

use or dose titration [4]. Hypoglycaemia risk was elevated in the GLP-1 RA group, with an odds ratio of 2.03 (95 percent confidence interval 1.16 to 3.54) for any hypoglycaemic episode defined as plasma glucose less than or equal to 3.9 mmol/L [17]. This risk is likely attributable to concurrent insulin use in some trials, as GLP-1 RAs alone have minimal hypoglycaemia risk due to their glucose-dependent mechanism of action. No significant differences in serious adverse events or treatment discontinuations were observed between GLP-1 RA and placebo groups, supporting the overall tolerability of these agents in adolescents [4]. Long-term safety data in youth remain limited, but adult studies and post-marketing surveillance have not identified new safety signals with extended use. A 2025 systematic review of long-term GLP-1 RA use in obesity management reported acceptable safety profiles over 40 to 120 weeks, with gastrointestinal events being the primary concern. Continued monitoring and pharmacovigilance are essential as these agents become more widely used in pediatric populations [6].

Clinical Implementation Considerations

Integrating long-acting GLP-1 RAs into adolescent diabetes care requires thoughtful patient selection, dosing strategies, and multidisciplinary support [18, 19]. Current guidelines recommend considering GLP-1 RAs as second-line therapy when glycaemic targets are not achieved with metformin, with or without long-acting insulin. Candidates typically include adolescents with suboptimal glycaemic control, excess weight, or both, who may benefit from the dual effects of these agents. Contraindications include personal or family history of medullary thyroid carcinoma, multiple endocrine neoplasia type 2, and severe gastrointestinal disease [6]. Dosing should follow a gradual titration schedule to minimize gastrointestinal adverse events. For liraglutide, initiation at 0.6 mg daily with weekly increments to the target dose of 1.8 mg is recommended. Exenatide extended release starts at 2 mg weekly, and dulaglutide begins at 0.75 mg weekly, with adjustments based on tolerability and efficacy. Patient and caregiver education on injection technique, storage, and potential side effects is critical for adherence and safety [6]. Multidisciplinary care involving endocrinologists, dietitians, diabetes educators, and mental health professionals optimizes outcomes. Combining GLP-1 RAs with structured lifestyle interventions, including medical nutrition therapy and physical activity, enhances weight loss and metabolic benefits. Regular monitoring of HbA1c, weight, renal function, and adverse events ensures timely intervention and dose optimization. Cost and access remain barriers in some settings, necessitating advocacy for equitable availability of these therapies [6].

Evidence Gaps and Future Research Directions

Despite promising evidence, significant knowledge gaps persist regarding long-acting GLP-1 RAs in adolescents with type 2 diabetes. Most trials have short follow-up durations (5 to 26 weeks), limiting understanding of long-term efficacy, safety, and impact on diabetes-related complications. Larger, longer-duration trials are needed to assess durability of glycaemic and weight benefits, effects on cardiovascular and renal outcomes, and potential for diabetes remission [6]. Head-to-head comparisons between different GLP-1 RAs are lacking, precluding definitive conclusions about relative efficacy and safety. Subgroup analyses by age, sex, ethnicity, and baseline metabolic characteristics are limited, hindering personalized treatment approaches [20]. The underrepresentation of indigenous and black populations, who bear a disproportionate burden of youth-onset type 2 diabetes, further limits generalizability [4]. Future research should prioritize long-term outcome trials, real-world effectiveness studies, and investigations into biomarkers predicting treatment response. Exploration of combination therapies, such as GLP-1 RAs with sodium-glucose cotransporter-2 inhibitors or dual incretin agonists, may offer additional benefits. Finally, implementation science research is needed to optimize delivery models, address cost barriers, and ensure equitable access to these therapies for all adolescents with type 2 diabetes [6].

CONCLUSION

Long-acting GLP-1 receptor agonists represent a significant therapeutic advance for adolescents with type 2 diabetes, offering clinically meaningful reductions in HbA1c and body weight with acceptable safety profiles. Their integration into pediatric diabetes care expands treatment options beyond metformin and insulin, addressing the dual challenges of hyperglycaemia and obesity that drive disease progression and complications.

Evidence from randomized trials and meta-analyses demonstrates that GLP-1 RAs reduce HbA1c by approximately 1 percentage point, lower fasting glucose, and facilitate modest weight loss in youth. Gastrointestinal adverse events are common but generally tolerable, with low discontinuation rates. Implementation requires careful patient selection, gradual dose titration, and multidisciplinary support to maximize benefits and minimize risks. Significant evidence gaps remain, particularly regarding long-term outcomes, comparative efficacy between agents, and generalizability to diverse populations. Future research should prioritize extended follow-up trials, head-to-head comparisons, and implementation strategies to optimize access and adherence. Clinicians should consider long-acting GLP-1 receptor agonists as second-line therapy for adolescents with type 2 diabetes who have inadequate glycaemic control or excess weight on metformin, with individualized dosing and monitoring to ensure safety and efficacy.

REFERENCES

1. Pappachan, J.M., Fernandez, C.J., Ashraf, A.P.: Rising tide: The global surge of type 2 diabetes in children and adolescents demands action now. World J Diabetes. 15, 797–809 (2024). https://doi.org/10.4239/wjd.v15.i5.797
2. Perng, W., Conway, R., Mayer-Davis, E., Dabelea, D.: Youth-Onset Type 2 Diabetes: The Epidemiology of an Awakening Epidemic. Diabetes Care. 46, 490–499 (2023). https://doi.org/10.2337/dci22-0046
3. Nadeau, K.J., Mayer-Davis, E.J., Gubitosi-Klug, R., Zeitler, P.S., Kahn, S.E., Dabelea, D., SEARCH, TODAY, RISE, and DISCOVERY study groups: Youth-Onset Type 2 Diabetes: What We've Learned From Key Youth-Onset Type 2 Diabetes Studies, What We Still Don't Know, and Why It Is Important. Diabetes Care. 48, 1136–1149 (2025). https://doi.org/10.2337/dc25-0001
4. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.A. (2025). Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obesity Medicine, 2025; 100622. https://doi.org/10.1016/j.obmed.2025.100622.
5. Krishnamoorthy, R., Gatasheh, M.K., Subbarayan, S., Vijayalakshmi, P., Uti, D.E.: Protective Role of Jimson Weed in Mitigating Dyslipidemia, Cardiovascular, and Renal Dysfunction in Diabetic Rat Models: *In Vivo* and *in Silico* Evidence. Natural Product Communications. 19, 1934578X241299279 (2024). https://doi.org/10.1177/1934578X241299279
6. Berman, C., Vidmar, A.P., Chao, L.C.: Glucagon-like Peptide-1 Receptor Agonists for the Treatment of Type 2 Diabetes in Youth. touchREV Endocrinol. 19, 38–45 (2023). https://doi.org/10.17925/EE.2023.19.1.38
7. Wang, X., Liu, H., Chen, J., Li, Y., Qu, S.: Multiple Factors Related to the Secretion of Glucagon-Like Peptide-1. International Journal of Endocrinology. 2015, 651757 (2015). https://doi.org/10.1155/2015/651757
8. Min, J.S., Jo, S.J., Lee, S., Kim, D.Y., Kim, D.H., Lee, C.B., Bae, S.K.: A Comprehensive Review on the Pharmacokinetics and Drug–Drug Interactions of Approved GLP-1 Receptor Agonists and a Dual GLP-1/GIP Receptor Agonist. Drug Design, Development and Therapy. 19, 3509–3537 (2025). https://doi.org/10.2147/DDDT.S506957
9. Saran, A., Raisinghani, R., Paliwal, S., Sharma, S.: GLP-1R agonists: recent advances, current gaps, and future challenges. Mol Divers. 30, 101–112 (2026). https://doi.org/10.1007/s11030-025-11195-6
10. Kohut, T., Panganiban, J.: Liraglutide with Lifestyle Intervention in Adolescents with Overweight/Obesity, Nonalcoholic Fatty Liver Disease, and Type II Diabetes Mellitus. JPGN Rep. 2, e141 (2021). https://doi.org/10.1097/PG9.0000000000000141
11. Chadda, K.R., Cheng, T.S., Ong, K.K.: GLP-1 agonists for obesity and type 2 diabetes in children: Systematic review and meta-analysis. Obesity Reviews. 22, e13177 (2021). https://doi.org/10.1111/obr.13177
12. Ikpozu, E.N., Offor, C.E., Igwenyi, I.O., Obaroh, I.O., Ibiam, U.A., Ukaidi, C.U.A.: RNA-based diagnostic innovations: A new frontier in diabetes diagnosis and management. Diabetes & Vascular Disease Research. 22, 14791641251334726 (2025). https://doi.org/10.1177/14791641251334726
13. Wong, H.J., Sim, B., Teo, Y.H., Teo, Y.N., Chan, M.Y., Yeo, L.L.L., Eng, P.C., Tan, B.Y.Q., Sattar, N., Dalakoti, M., Sia, C.-H.: Efficacy of GLP-1 Receptor Agonists on Weight Loss, BMI, and Waist Circumference for Patients With Obesity or Overweight: A Systematic Review, Meta-analysis, and Meta-regression of 47 Randomized Controlled Trials. Diabetes Care. 48, 292–300 (2025). https://doi.org/10.2337/dc24-1678
14. Orandi, B.J., Chen, Y., Li, Y., Charyton, D., Lentine, K.L., Lee, B.P., Ali, N., DeMarco, M.P., Weintraub, M.A., Bae, S., Lonze, B.E., Ren-Fielding, C.J., Lofton, H., Gujral, A., Segev, D.L., McAdams-DeMarco, M.: GLP-1 Receptor Agonist Outcomes, Safety, and Body Mass Index Change in a National Cohort of Patients on Dialysis. CJASN. 20, 1100–1110 (2025). https://doi.org/10.2215/CJN.0000000750
15. Herold, K.C., Reynolds, J., Dziura, J., Baidal, D., Gaglia, J., Gitelman, S.E., Gottlieb, P.A., Marks, J., Philipson, L.H., Pop-Busui, R., Weinstock, R.S.: Exenatide extended release in patients with type 1 diabetes with and without residual insulin production. Diabetes Obes Metab. 22, 2045–2054 (2020). https://doi.org/10.1111/dom.14121
16. Chang, B.-H., Hoaglin, D.C.: Meta-analysis of Odds Ratios: Current Good Practices. Med Care. 55, 328–335 (2017). https://doi.org/10.1097/MLR.0000000000000696
17. Kamalinia, S., Josse, R.G., Donio, P.J., Leduc, L., Shah, B.R., Tobe, S.W.: Risk of any hypoglycaemia with newer antihyperglycaemic agents in patients with type 2 diabetes: A systematic review and meta-analysis. Endocrinology, Diabetes & Metabolism. 3, e00100 (2020). https://doi.org/10.1002/edm2.100
18. Moiz, A., Peters, T.M., Tsoukas, M.A., Yu, O.H.Y., Filion, K.B., Eisenberg, M.J.: Balancing the benefits and risks of GLP-1 receptor agonists: a clinical guide for shared decision-making. eClinicalMedicine. 96, (2026). https://doi.org/10.1016/j.eclinm.2026.103991

19. Alum, E.U. Optimizing patient education for sustainable self-management in type 2 diabetes. *Discov Public Health* **22**, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5

20. Moiz, A., Filion, K.B., Toutounchi, H., Tsoukas, M.A., Yu, O.H.Y., Peters, T.M., Eisenberg, M.J.: Efficacy and Safety of Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss Among Adults Without Diabetes. Ann Intern Med. 178, 199–217 (2025). https://doi.org/10.7326/ANNALS-24-01590

CITE AS: Muhindo Anitah (2026). Long Acting GLP-1 Receptor Agonists for Weight and Glycaemic Control in Adolescents with Type 2 Diabetes. IDOSR JOURNAL OF SCIENTIFIC RESEARCH 11(2):23-27. https://doi.org/10.59298/IDOSRJSR/2026/11.2.2327