Diabetes, Metabolic Syndrome and Obesity

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EDITORIAL

Revolutionizing Diabetes Care: From Tech to Therapeutics

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Introduction

Diabetes mellitus remains a health challenge, with not only type 2 diabetes (T2D) but also type 1 diabetes (T1D) on the rise globally. Despite the previous developments in diabetes technologies and therapeutics, many people with diabetes are still not able to achieve glycemic goals. However, recent years have seen eye-opening advancements in diabetes management. From continuous glucose monitoring (CGM) to in-development continuous dual glucose and ketone monitoring (CGKM), automated insulin delivery (AID) systems to in-development fully closed loop systems, weekly basal insulin to alternate insulin delivery methods such as inhaled insulin, and weekly dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) agonists to in-development triple agonists, many technologies and therapeutics have been developed or are currently in development. This review explores the latest advancements in diabetes technology and therapeutics, highlighting their clinical implications, current limitations, and future directions in improving outcomes for individuals with diabetes. In this review, we categorized the developments into therapeutics and technologies.

Recent Developments in Therapeutics

Inhaled Insulin in Pediatrics and Adults

Inhaled insulin represents a needle-free alternative for meals and correction of high glucose in both adult and pediatric patients. Delivered as a dry powder via an oral inhaler, inhaled insulin, such as Afrezza® (FDA approved for adults in 2014), is rapidly absorbed in the neutral pH of the lungs, reaching the bloodstream much faster than subcutaneous injections.[1] Its onset of action is approximately 12 minutes, with a short duration of action of 1.5 to 3 hours, making it ideal for postprandial glucose control and reducing the risk of insulin stacking and hypoglycemia.[2–4]

For adults with T1D or T2D, inhaled insulin has demonstrated comparable efficacy to rapid-acting injectable insulin, with added benefits such as reduced weight gain and improved patient satisfaction.[5–8] It is typically used alongside a long-acting basal insulin to provide comprehensive glucose management. Recent studies, including the INHALE-1 trial, which was presented at the American Diabetes Conference in 2025, have extended these findings to pediatric populations. In children aged 4–17 years old with T1D, inhaled insulin showed non-inferior glycemic control compared to injected analogs, with favorable safety outcomes and higher preference scores among patients and caregivers. A recent case series evaluated the use of inhaled insulin in pregnancy and found that it appears to be safe and may be a feasible and acceptable alternative to injectable rapid-acting insulin during pregnancy; however, controlled studies are required before using inhaled insulin routinely in this population.[9]

Inhaled insulin is contraindicated for individuals with chronic lung conditions like asthma or chronic obstructive pulmonary disease (COPD) due to the risk of bronchospasm.[10] Although minimal changes in pulmonary function have been seen with inhaled insulin,[11] spirometry testing is required prior to initiation and periodically throughout treatment to monitor lung function. The goal includes a forced expiratory volume in one second (FEV1) ≥ 70% of predicted. A ≥ 20%

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decline in FEV1 from baseline may warrant discontinuation of therapy. Overall, inhaled insulin offers a fast-acting, discreet, and patient-friendly option that may improve adherence and quality of life for people managing diabetes across age groups.

GLP-1 Use in T1D

The prevalence of obesity is growing in those living with T1D despite the historical phenotype being characterized by low to normal weight.[12] While the reasons for this increasing body mass index (BMI) include lifestyle concerns similar to the general population, some are unique to the T1D population, like the necessary intake of extra carbohydrates to avoid hypoglycemia.[13,14] Many people with T1D are failing to reach glycemic targets even with high doses of insulin that can contribute to subsequent weight gain.[15] This in turn can lead to additional insulin resistance, resulting in a vicious cycle.[13] Given these difficulties, there is significant interest in the use of adjuvant medications for this population, particularly ones that can also help with weight loss. With the positive impact of GLP-1 in those with T2D, there has been a growing interest in the use for those with T1D.

Previous studies on older formulations of GLP-1, like liraglutide and exenatide, showed modest improvements in hemoglobin A1c (HbA1c) and weight loss.[16] However, due to the increased risk of mild ketosis with liraglutide with lack of significant glycemic improvements, it was not filed for FDA approval for T1D.[17,18] However, interest has been renewed with the increased effectiveness of the newer GLP-1 agents (semaglutide) and the GIP/GLP1 dual agonists (tirzepatide) on weight loss. In retrospective studies of overweight and obese adults with T1D, those taking semaglutide or tirzepatide showed greater improvements in weight and HbA1c when compared to matched controls without increased adverse effects.[18–21] Additionally, retrospective, uncontrolled data in youth with T1D have been promising in regard to weight loss, improved glycemia, and insulin dose reduction.[22] Off-label use of GLP-1 and dual agonists has been increasingly common for those with T1D. However, additional research into the safety and efficacy through double blinded randomized control trials is required prior to FDA approval and subsequent widespread use.

Dual, Triple GLP-1 Agonists for Weight Loss, T2D, and MASH

The expanding worldwide obesity epidemic is associated with multiple significant comorbidities. Metabolic syndrome, with abdominal obesity, T2D, and abnormal lipid profile, is increasingly common. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) (formerly non-alcoholic fatty liver disease) affects a quarter of adults globally.[23] Insulin resistance in adipocytes from weight gain can lead to dysregulated lipolysis.[24] Excessive delivery of these fatty acids to the liver can then drive hepatic de novo lipogenesis.[25] Steatosis, or accumulation of fat in the liver, can progress to the fibrosis and cirrhosis, characteristic of Metabolic Dysfunction-Associated Steatohepatitis (MASH) (formerly non-alcoholic steatohepatitis). MASH can subsequently advance to end stage liver disease and may require transplantation.[25]

Currently, there are no pharmacologic interventions specifically targeting MASLD or MASH, with lifestyle modification and weight loss remaining the cornerstone of treatment. However, the improvements seen with weight loss can be significant, with much of the fibrosis resolving with 10% weight loss.[23] GLP-1RAs have been studied in the treatment of T2D, where it helps promote insulin secretion from the pancreatic β-cells, decrease glucagon secretion delaying gastric emptying, and improving glucose uptake in adipose tissues and skeletal muscles.[24] They have also been studied for the treatment of complications from T2D, including MASH[26] where some histologic improvements have been seen with semaglutide use.[25] However, dual and triple agents show greater potential for weight loss, glycemic management, and treatment of MASH due to the additional mechanisms of action, particularly ones including glucagon receptor agonists. Glucagon agonists stimulate hepatic beta oxidation of fatty acids, reduce lipogenesis, and leads to greater energy expenditure than GLP-1 alone. This may allow for greater liver fat reduction and weight loss than single agents.[23]

Studies of dual (Pemvidutide [GLP-1/glucagon receptor dual agonists][23] and triple (Retatrutide [GLP-1, GIP, and glucagon receptor agonist][25] have shown promise in the treatment of T2D and MASH. Liver fat reductions appear greatest with triple agonists or GLP/glucagon dual agonists compared to GIP/GLP-1 dual agonists,[25] though all showed improvement compared to placebo groups.[27,28]

Weekly Basal Insulins

Basal insulin therapy is the mainstay of glycemic management in T1D and insulin-treated T2D. After the introduction of insulin degludec and long-acting insulin glargine (U300), a new era has opened in basal insulin management. The idea of weekly injections was tempting, as previously introduced weekly GLP-1 therapies improved adherence, convenience and glycemic outcomes. Weekly basal insulins are engineered for ultra-long action through molecular modifications that extend their half-life and maintain stable pharmacokinetic (PK) and pharmacodynamic (PD) profiles. There are currently two weekly basal insulins under development (some approved in Europe and Asia but no FDA approval as of October 2025).

Insulin Icodec developed by Novo Nordisk showed non-inferiority in HbA1c reduction compared to standard of care basal insulin (insulin glargine U100/300 and degludec) in T1D and T2D in several ONWARDS trials.[29–33] Recently, FDA rejected its approval for T1D citing increased risk of hypoglycemia. In the ONWARDS 6 trial, adults with T1D receiving insulin icodec had higher rates of level two and level three hypoglycemia than adults receiving once-daily insulin degludec.[34] HbA1c changes from baseline to 26 weeks were similar between the two groups.

Insulin efsitora alfa developed by Eli Lilly showed non-inferiority in HbA1c reduction compared to standard of care basal insulin (insulin glargine U100 and degludec) in T2D in several QWINT trials.[35,36] In the QWINT 5 trial, rates of combined level two or level three severe hypoglycemia were higher with efsitora compared with degludec.[35] Remaining Phase 3 trials are ongoing.

Weekly insulins have a potential to be used first in T2D, and likely in the near future in T1D. It may be combined with GLP-1 analogs and decrease the injections for insulin-dependent people with diabetes. Titration complexity, loading dose, missing dose mitigation, cost and accessibility after marketing are limitations.

Recent Developments in Technology

New Developments in CGM Space

CGMs have undergone significant advancements in recent years, reshaping diabetes care through smarter, more accurate, and more accessible technology. These advancements are driven by innovations in wearable devices, sensor miniaturization, and digital health integration. The use of CGMs in routine care has significantly improved glycemic control[37,38] and is now recommended as part of standard diabetes management.[39]

Newer devices, such as the Dexcom G7, Abbott FreeStyle Libre 3 Plus, and MiniMed Simplera, offer faster warm-up times, smaller profiles, all-in-one functionality, and enhanced connectivity with smart phones and AID systems.[40] Beyond routine diabetes management, CGMs are increasingly being adopted by non-insulin users and individuals focused on metabolic health.[41,42] Modern CGMs additionally now include AI-powered tools like photo-based meal logging and predictive glucose analytics, helping users better understand how food and lifestyle choices affect their glucose levels.[40]

A unique system, the Eversense 365 CGM, features a 365-day subcutaneously implanted sensor with a removable transmitter.[43] This design offers an alternative system that may reduce the burden of wear, including minimizing pain and discomfort associated with frequent subcutaneous insertion (every 7–15 days) and mitigating skin irritation from adhesives designed to be worn for extended periods of time.

Further innovations in the CGM space include the exploration of non-invasive glucose monitoring methods, such as light-based technologies (eg, spectroscopy and fluorescence),[44,45] electromagnetic approaches (eg, microwave and radiofrequency),[45,46] and biofluid-based sensors (eg, sweat, tears, saliva).[47] More research is needed in these areas to ensure sufficient accuracy for insulin dosing decisions.

Additionally, integrating multiple analytes into a single sensor, such as lactate and ketones, provides richer information for health management. Among these, continuous ketone monitoring (CKM) has made the most progress[48,49] with anticipated commercial availability in 2026. However, further research is needed to assess the real-world utility of continuous ketone data, its impact on diabetes-related outcomes (including diabetic ketoacidosis (DKA) and glycemic control) and its integration into AID algorithms.

CGM data are essential for the functionality of AID systems, AI-based dosing algorithms, and glucose tracking tools and individually improves glycemic control for people with diabetes. CGMs are evolving from simple monitoring

devices into intelligent health platforms, integrating with wearables, electronic health records, and telemedicine to enable personalized, proactive diabetes management.

New Developments in AID Space

AID systems have seen remarkable advancements, transforming diabetes management through smarter, more adaptive algorithms. These systems integrate CGMs with insulin pumps and algorithms to mimic the function of a healthy pancreas through glucose-responsive automatic insulin delivery. While use of CGM alone has shown significant improvements in glycemic control in people with diabetes, AID systems are able to achieve even further improvements[50] and are currently being recommended as the standard of care for people with T1D,[39] and becoming more widely used in people with T2D not succeeding on current medical management.

AID systems currently FDA approved in the US include the Tandem t: slim X2 and Mobi pumps with Control-IQ+ technology, the MiniMed™ 780G with Smart Guard, the Insulet Omnipod® 5 (OP5) system, the Beta Bionics iLet, and the newest FDA approved system from Sequel Med Tech and Tidepool Loop, the twiist™ AID system.[40] Clinical trials with these systems have shown significant reductions in HbA1c in both adult and pediatric patients with T1D (other than twiist which received FDA approval through modern mechanisms and have not conducted clinical trials in T1D and T2D though data has been published on the real-world use of the Tidepool Loop algorithm).[51–56] Several systems have additionally received recent FDA approval for T2D (Insulet's OP5, Tandem's Control-IQ+, and MiniMed's 780G) and their efficacy have been shown in recent clinical trials.[57,58]

AID systems are continuing to advance, with improved opportunities to tighten glycemic control (such as with the twiist AID system, which features more tunable parameters than any other device currently available), and reduce burden (such as with the iLet AID system, which requires only weight to initiate and does not utilize specific carbohydrate counting for mealtime insulin dosing). The next step in AID system development is moving towards a fully closed-loop system, which requires little to no user interaction and no food insulin bolusing.[59,60] Early work with a variety of fully closed-loop systems has been promising.[61–63] Additional advancements in AID systems, which may further support the move towards a fully closed-loop system, include the use of multiple hormones, such as insulin along with glucagon or pramlintide.[64–67] These innovations mark a shift toward more personalized, seamless, and user-friendly diabetes care, bringing us closer to a future where insulin therapy is intuitive, automated, and less intrusive.

AID Use in T2D

AID systems have led to significant glycemic improvements for people living with T1D across all age groups and health statuses.[68–70] Given the marked glycemic and quality of life improvements with this technology, there has been interest in the use for people living with T2D who are not currently meeting the glycemic target on multiple medical therapies. However, there has been hesitation in the use of these systems due to psychological factors, particularly related to a fear of hypoglycemia, unfamiliarity with the systems, and lack of experience with prandial insulin.[71] Across multiple countries and systems, the use of any AID system for people with T2D is associated with improvements in HbA1c, time in range (70–180 mg/dL),[72–74] and both daytime and overnight glycemic control.[74] There were no increases in severe hypoglycemia or diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS), including in older adults.[75] In some studies, but not all, those with the highest baseline HbA1c had some increased weight gain with the use of AID, potentially due to increased insulin administration.[57,72]

Benefits of AID systems are seen across a variety of subgroups, including those not previously receiving prandial insulin. Intensive carbohydrate counting education does not appear to be required.[74] Additionally, frequent hyperglycemia correction insulin dosing or engagement with the pump does not appear to be necessary for glycemic improvement, as the system's ability to automatically increase insulin delivery based on rise in glucose levels via basal insulin changes or autocorrections may be more useful for glycemic control compared to mealtime announcement. These systems also appear safe for people with T2D on other medical therapies like GLP-1 and sodium-glucose cotransporter 2 (SGLT-2) inhibitors.[74] Participants reported high satisfaction with the AID systems,[73] especially related to sleep quality.[57] AID systems remain a viable source for those living with T2D. There is the potential for improvements in both glycemic control and quality of life, without a need for additional education around carb counting. Additional study, particularly in the younger population,[24] is required.

Conclusions

Recent years have witnessed a shift in diabetes management driven by advancements in technology and therapeutics. The improvements in CGM and AID systems, as well as digital health technologies, have shaped the treatment of diabetes. Advances in diabetes and obesity medications with additional benefits with cardiorenal protection opened a new era in preventing long-term complications. The next phase is to bring these therapeutic options to the people in need through increased insurance coverage and decreased cost. In summary, the evolving landscape of diabetes technology and therapeutics not only improves glycemic control but also transforms the lived experience of people with diabetes.

Data Sharing Statement

Data sharing is not applicable to this article as no data were created or analyzed in this study.

Author Contributions

H.K.A, L.A.W and E.C.C – Conceptualization, Writing – original draft and Writing – review and editing. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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