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Transforming diabetes care: Latest advancements in treatment and technology

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Abstract

This comprehensive review explores recent advancements in diabetes management, encompassing technological innovations and pharmacological developments. Key findings include the introduction of smart insoles and boots for diabetic foot ulcers, promising non-pharmacological approaches like plant-based α -amylase inhibitors, and the emergence of top choices such as Semaglutide, dulaglutide, and liraglutide among glucagon-like peptide-1 receptor agonists. Innovative drug delivery systems, exemplified by the LG/TD-NF nano formulation, offer potential benefits over traditional injections. Recent guidelines emphasize early detection and personalized treatment plans, with a focus on SGLT2 inhibitors and GLP-1 receptor agonists for type 2 diabetes. Genetic studies have identified unique mutations like m.A5826G linked to type 2 diabetes, providing insights into potential early detection and treatment targets. Overall, these advancements offer hope for improved diabetes management and underscore the importance of continued research and clinical trials to validate their effectiveness and integrate them into standard practice, ultimately enhancing patient outcomes.

Keywords: Diabetes management innovations, smart insoles for diabetic foot ulcers, GLP-1 receptor agonists, SGLT2 inhibitors and genetic mutations in type 2 diabetes

Introduction

Diabetes mellitus, a chronic metabolic disorder characterized by persistent hyperglycaemia, poses a significant global health challenge. Effective management of diabetes is crucial to prevent complications and enhance the quality of life for individuals affected by the condition ^[1]. Recent advancements in diabetes management encompass a broad spectrum of innovations, including sensor technologies, plant-based treatments, pharmacological developments, and personalized medicine approaches ^[2]. This article provides an in-depth review of the latest research and technological advancements in diabetes management, with a focus on their implications for patient care.

Materials and Methods

A comprehensive literature search was conducted using several scientific databases, including Google Scholar, PubMed, Sci-Hub, and dovepress. The search aimed to identify the latest advancements in diabetes management, focusing on both technological innovations and pharmacological developments. The keywords used in the search included "diabetes management," "diabetic foot ulcers," "smart insoles," "plant-based α -amylase inhibitors," "GLP-1 receptor agonists," "nano formulations," "SGLT2 inhibitors," "personalized diabetes treatment," and "mitochondrial mutations in diabetes. Latest developments in footwear, sensor technology, and digital health such as specially made footwear, smart insoles, and Smart Boot enhance offloading and adherence in managing diabetic foot ulcers by reducing foot pressure and integrating smart devices with remote monitoring, feedback mechanisms, gamification, and emotive visual indicators to boost patient engagement and provide personalized care plans while educational and behavioural interventions improve understanding and adherence to offloading regimens ^[3]. Current advancements in the management of diabetes have centred on investigating non-pharmacological substances as substitutes for traditional anti-diabetic medications. In particular, plant-based α -amylase inhibitors have shown promise in controlling postprandial glucose levels while posing few

side effects. These inhibitors work by preventing the absorption of carbohydrates through bioactive components found in different plant extracts that inhibit α -amylase, an enzyme essential to the breakdown of carbohydrates. Although most results are still in the early stages of research based on *in vitro* studies, additional studies and clinical trials are required to confirm the safety and effectiveness of these natural inhibitors before they can be widely used in clinical settings [4].



Fig 1: Smart insoles and a Smart Boot

Blood Urea Nitrogen Correlates with Both Short- and Long-Term Glycaemic Variability in Older Individuals with Type 2 Diabetes Mellitus Who Were admitted: A retrospective investigation

A study discovered a favourable correlation between increased blood urea nitrogen (BUN) levels and both short- and long-term glycaemic variability (GV) in older individuals with T2DM who were hospitalised. Accordingly, there is a correlation between increased blood BUN levels and both short- and long-term GV. In order to guide GV management in clinical practice, BUN levels in elderly individuals with T2DM who were hospitalised can be indicative of and utilised to assess short-term GV and long-term (fasting plasma glucose- glycaemic variability)

FPG-GV [5].

Utilising the Patient Health Questionnaire (PHQ-9) and the International Index of Erectile Function short form (IIEF-5) in a cross-sectional study conducted between January and August 2023, researchers determined the prevalence of depression and erectile dysfunction (ED) among 478 male patients with Type 2 Diabetes (T2D)

With a long history of T2D and an average age of 59.2, the majority of participants were married. According to the study, 52% of the individuals had moderate to severe ED. People with ED tended to be older, had more comorbidities, had been living with type 2 diabetes for longer periods of time, had a worse socioeconomic position, and engaged in less physical exercise. Furthermore, ED was substantially correlated with depression, which was present in over one-third of the population. Additionally, smoking and physical activity levels were lower in those who had depression. The findings highlight the high frequency of ED in men with type 2 diabetes (T2D), and they also found a substantial correlation between ED and depression. Other characteristics that may contribute to ED prevalence in this population include older age, longer disease duration, comorbidities, lower socioeconomic status, and poor lifestyle choices [6].

Researchers investigated potential causal links between lichen sclerosus (LS), body mass index (BMI), and diabetes mellitus (DM) using information from genome-wide association studies and the FinnGen biological database. In order to fully assess the instrumental variables for DM and BMI and ascertain their influence on LS and vice versa, they employed techniques such as inverse variance weighted (IVW), weighted median, and MR-Egger. The lack of substantial causal relationships between these variables in the results suggests that confounding variables may have influenced earlier observational correlations. This implies that additional investigation is required to clarify these connections [7]. Researchers evaluated seven glucagon-like peptide-1 receptor agonists (GLP-1RAs) marketed in China using a percentage scoring method for safety, efficacy, economy, and pharmacological properties. Based on their high scores of 71.5, 68.9, and 68.7, respectively, these three medications were recommended as the top choices for healthcare organisations looking to introduce GLP-1RAs. This comprehensive health technology assessment was conducted under the guidance of the Rapid Guide for Drug Evaluation and Selection in Chinese Medical Institutions [8].

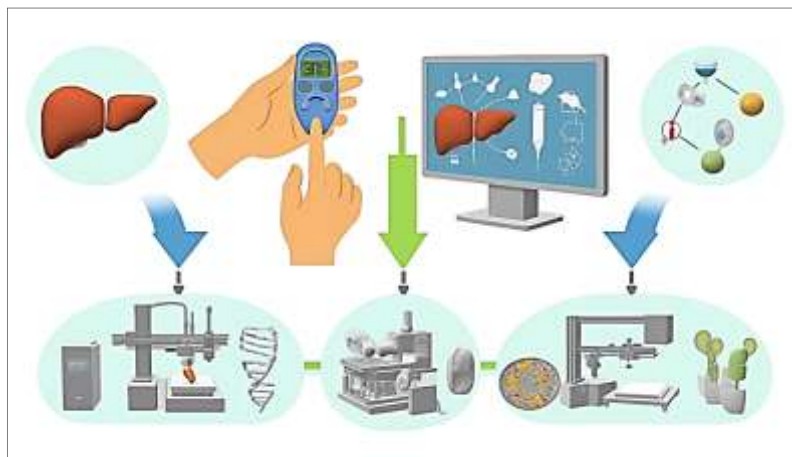


Fig 2: Applications of 3D-printing technology

Ten glucagon-like peptide-1 receptor agonists (GLP-1RAs) were assessed by the Health Technology Assessment for the treatment of Type 2 Diabetes Mellitus, in accordance with the Rapid Guide for Drug Evaluation and Selection in Chinese Medical Institutions (Second Edition, 2023)

The study evaluated the medications based on safety, efficacy, economy, and pharmacological qualities through a systematic assessment of sources such as PubMed, Cochrane, and Embase, in addition to drug labels and clinical guidelines. With scores of 71.5, 68.9, and 68.7, respectively, Semaglutide, dulaglutide, and liraglutide were found to be the top three GLP-1RAs, and healthcare organisations wishing to implement these therapies are advised to choose them ^[9].

Precise control over anatomy and the possibility to bioprint β -cells and pancreas are provided by 3D printing. It helps treat diabetes by enabling transdermal medication delivery using microneedle patches. Pharmaceutical businesses may provide diabetic patients with personalised prescription dosages, and the food industry can create high-fiber, sugar-free items just for them ^[10].

The study unveiled a novel oral nano formulation called LG/TD-NF that targets ASBT and EGFR specifically to promote effective transcytosis through the intestinal epithelium

Bile acid derivatives are used in this formulation to increase the oral bioavailability of peptides. The formulation, which employed a nanoprecipitation process and integrated stabilisers such as labrasol and PEG, demonstrated resistance against enzymatic breakdown in the gastrointestinal tract and improved cellular absorption via bile acid-driven pathways. Compared to subcutaneous injections, this resulted in enhanced absorption and consistent glucose-lowering benefits in diabetic mice. The results highlight this nano formulation's potential to improve patient adherence, facilitate diabetes control, reduce the need for injections, and open the door for further developments in the oral delivery of biologic drugs ^[11].

The 2024 Standards of Medical Care in Diabetes from the American Diabetes Association introduce significant updates aimed at enhancing diabetes management and care

Key revisions include the implementation of serum C-peptide screening and islet-related autoantibody testing for early detection of Type 1 diabetes, especially among first-degree relatives, with recommendations for using teplizumab to delay disease onset. There's an increased focus on screening for non-alcoholic fatty liver disease (NAFLD) due to its association with obesity and potential link to heart disease. The cardiovascular treatment guidelines now suggest evaluating peripheral artery disease in high-risk groups using the ankle-brachial index and screening for silent heart failure with BNP and NT-proBNP markers. For Type 2 diabetes management, there is a strong endorsement for using SGLT2 inhibitors and GLP-1 receptor agonists, especially in patients with concurrent heart failure, cardiovascular disease, or chronic kidney disease. Newly recommended lipid management pharmaceuticals include inclisiran and bempedoic acid. Additionally, the guidelines emphasize the importance of continuous glucose monitoring devices, like the FreeStyle

Libre 2, for enhancing patient monitoring and management. The guidelines advocate for personalized treatment plans, moving towards more customized approaches that prioritize non-insulin medications such as tirzepatide or GLP-1 receptor agonists, unless immediate insulin therapy is required. Overall, these updated guidelines integrate the latest research and clinical advancements to improve treatment outcomes for individuals with diabetes ^[12].

In a study examining the connection between insulin resistance and serum vitamin E levels in patients with type 2 diabetes mellitus (T2DM), 242 people were examined, 119 of them had T2DM. By using the homeostasis model assessment method (HOMA-IR) to quantify insulin resistance, the study discovered that lower serum vitamin E levels significantly increased the likelihood of insulin resistance. With blood levels below 10,575.23 ng/mL posing a danger, logistic regression revealed that vitamin E is an independent factor affecting insulin resistance in T2DM patients. On the other hand, increased vitamin E levels had advantages in preventing insulin resistance ^[13].

Prevalence of Sensorineural Hearing Impairment and Associated Factors among T2DM Patients in the Amhara Region, Northwest Ethiopia, 2022: A Multi-Centered Cross-Sectional Study

The study's main objective was to evaluate the prevalence of sensorineural hearing impairment (SNHI) and the risk factors for it in individuals with type 2 diabetes mellitus (T2DM) in Northwest Ethiopia. It was held in May and June of 2022 and had 846 participants from referral hospitals that were both comprehensive and specialised. 50.49% of people were found to have SNHI. Age, the length of diabetes, hyperlipidemia, and hypertension were significant risk variables that were found, however regular exercise protected against SNHI. The study emphasises how important it is for T2DM patients in the area to have regular hearing exams and physical activity ^[14].

In this study, a four-generation Han Chinese family with type 2 diabetes mellitus (T2DM) was found to have a unique mitochondrial mutation, m.A5826G. A vital location that is essential for tRNA processing and function is impacted by this mutation, which is located at the intersection of mitochondrial tRNACys and tRNATyr. Biochemical, genetic, and clinical examinations were carried out, including PCR-Sanger sequencing and testing for mitochondrial function in hybrid cell lines. Results showed that ATP generation and mitochondrial membrane potential were significantly reduced in cells with the m.A5826G mutation, and reactive oxygen species levels were elevated, suggesting mitochondrial malfunction. Through its insights into the pathophysiology of mitochondrial diabetes and possible targets for early detection and treatment, this work advances our understanding of the genetic and molecular foundation of the condition. ¹⁵This study looked at the connection between genetic variations of N-6 adenine-specific DNA methyltransferase 1 (N6AMT1) and gestational diabetes mellitus (GDM) in 1303 pregnant Chinese women. According to the study, changes in serum folate and vitamin B12 levels were linked to specific N6AMT1 genetic variations that had a substantial impact on GDM risk. More specifically, when adequate folate levels were present, some genotypes were linked to a lower risk of

GDM, however when certain genotypes were combined with low vitamin B12 levels, the risk of GDM rose. According to the findings, blood folate and vitamin B12

have a significant role in regulating the genetic risk of GDM linked to N6AMT1 variations [16].

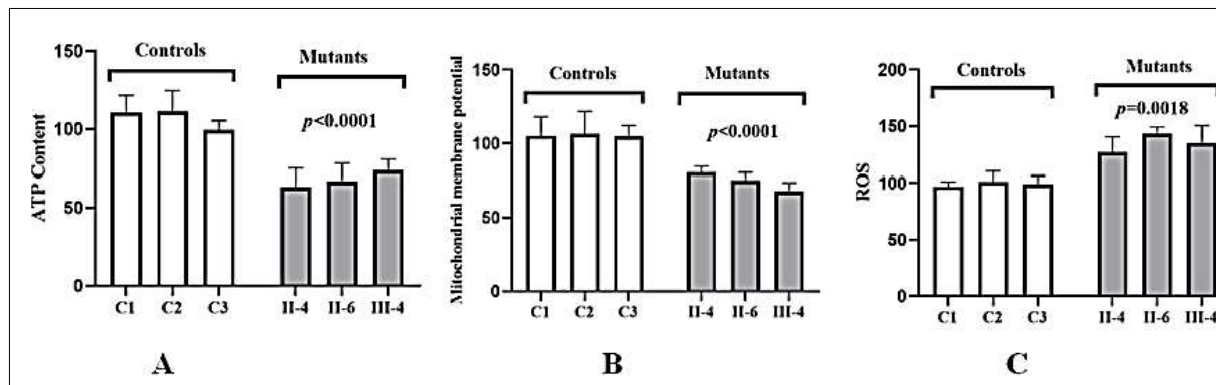


Fig 3: Analyses of mitochondrial functions in cybrids. (A) ATP analysis; (B) Analysis of MMP; (C) ROS measurement

Current Status of Medication Beliefs and Adherence in Patients with T2DM (as per Mortelmans’s study)

The chart shows that elderly patients have a significantly higher belief score, indicating stronger beliefs in the necessity of their medication compared to T2DM patients. The pie chart for medication adherence scores of T2DM patients shows a distribution based on conceptual adherence categories.

Poor (<5): The percentage of patients with scores indicating poor adherence.

Moderate (5-7): The largest segment represents patients whose adherence scores fall into the moderate category.

Excellent (>7): A smaller segment of patients who demonstrate excellent adherence to their medication [17].

In a study done from 2022 to 2023 at Tianjin Medical University General Hospital, researchers looked at the

connection between type 2 diabetes (T2D) and uric acid excretion in 228 individuals who had hyperuricemia (HUA). Every participant's anthropometric, biochemical, and demographic data were gathered for the study. Fractional excretion of uric acid (FEUA) was computed using blood uric acid and creatinine levels, while urine uric acid excretion (UUAЕ) was determined enzymatically from a 24-hour urine collection. Results showed that 48.7% of participants were obese and 13.4% of patients had T2D. In comparison to the in these individual control group, the obese group showed a greater UUAЕ and a lower FEUA ($p < 0.05$) ($p < 0.05$). FEUA was found to have a significantly higher connection ($p < 0.001$) with the probability of T2D. Furthermore, it was discovered that there was a positive correlation between BMI and UUAЕ in the outpatients, but a negative correlation between BMI and FEUA. The study found that among HUA patients, elevated FEUA levels were substantially linked to T2D, emphasising the need of routinely measuring FEUA for precise diagnosis and effective treatment of T2D in these individuals [18].

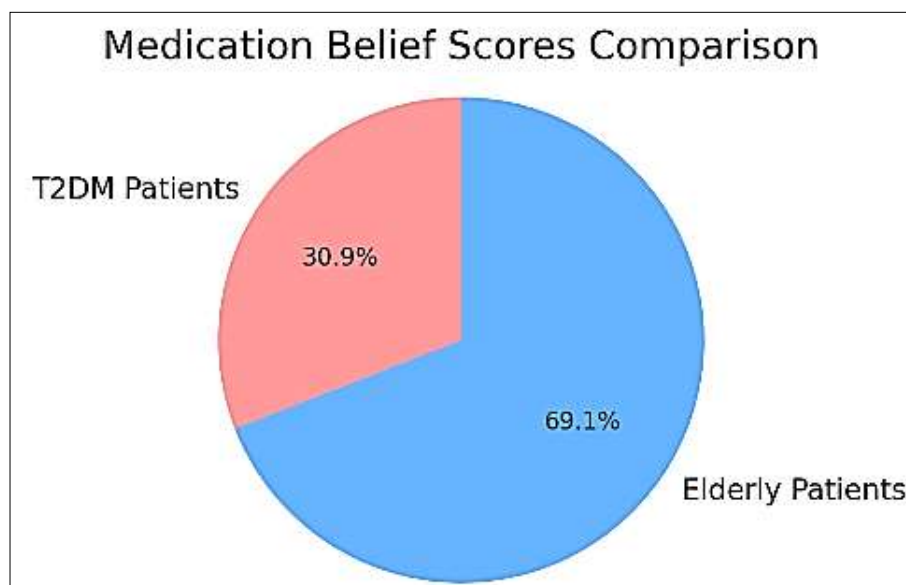


Fig 4: Pie chart illustrating the comparison of medication belief scores between T2DM patients and elderly patients

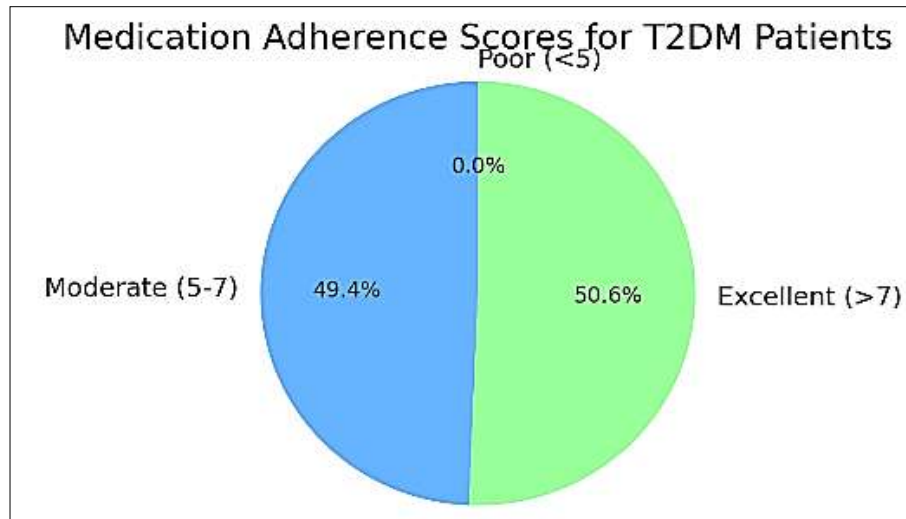


Fig 5: The pie chart for medication adherence scores of T2DM patients shows a distribution based on conceptual adherence categories

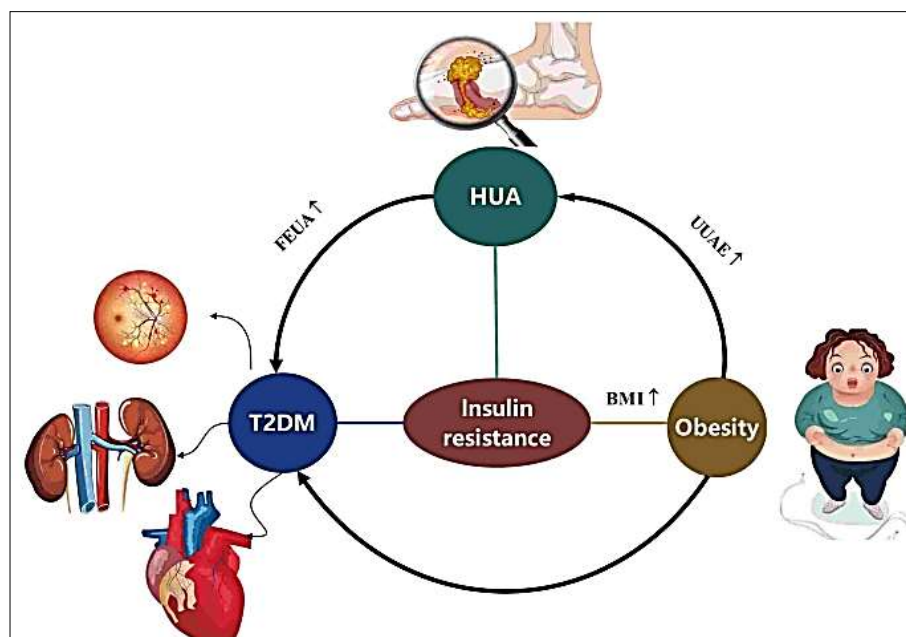


Fig 6: Diagram illustrating the interconnected relationship between hyperuricemia, insulin resistance, obesity, and type 2 diabetes

The American Society of Pain and Neuroscience (ASPN) has established the SWEET Guideline, which provides extensive evidence-based treatment recommendations for painful diabetic neuropathy (PDN)

The guidelines were derived from a global evaluation of research that was conducted starting in 2000. This guideline classifies treatments into several tiers according to their effectiveness: topical treatments such as capsaicin 8% based on effectiveness; TCAs and SNRIs as second-line; oral therapy containing gabapentinoids as first-line; and various interventional approaches, which begin with spinal cord stimulation trials and may proceed to permanent implants if successful. Through the customisation of treatment protocols based on patient responses, the guideline seeks to improve the safe and effective management of PDN [19].

Effects of Semaglutide on Metabolic Results in Patients with Diabetes Mellitus: A Real-World Study

49 T2DM patients who received care in a specialised care facility were part of the group. Through a 3-, 6-, and 12-month follow-up, their weight, renal function, adverse

events, and glucose outcomes were assessed.

Findings

Considerable variations were noted in the evaluation of the outcome: decrease in the levels of glycosylated haemoglobin (MD -2.74 CI -1.95) to -3.52 after half a year), body weight (MD -7.11 CI -5.97 to -8.24), albumin-to-creatinine ratio, and fasting plasma glucose levels. Throughout the course of the treatment, the outcomes held true. The majority of the adverse event rate (16.3%) were gastrointestinal in nature.

- **Change in HbA1c:** Show the reduction in HbA1c levels over time at 3, 6, and 12 months.
- **Fasting Plasma Glucose:** Illustrate changes in fasting plasma glucose levels at the same time points.
- **Body Weight:** Depict changes in body weight over the 12-month period.
- **ACR (Albumin-Creatinine Ratio):** Show trends in ACR changes which reflect renal function.
- **Treatment Discontinuation and Adverse Events:** Highlight the rates of treatment discontinuation and the prevalence of adverse events over the course of the study [20].

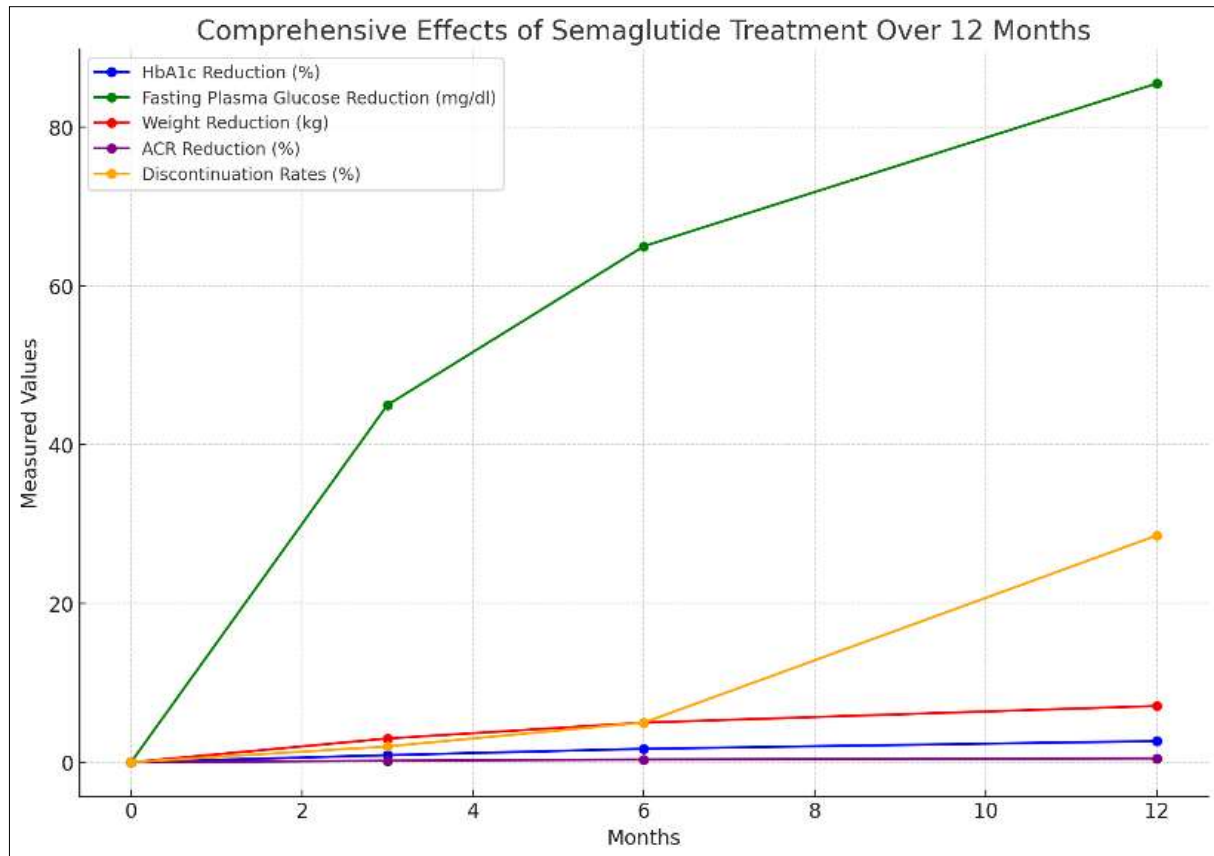


Fig 7: Comprehensive Effects of Semaglutide Treatment Over 12 Months

Optimizing Animal Models for Studying the Impact of Multiple Sclerosis on Tendinous Structures

To study the impact of multiple sclerosis (MS) on tendinous structures and the associated molecular mechanisms, creating appropriate animal models is crucial. While rats are traditionally used, other animals that closely mimic human conditions should be considered. The two primary rodent models for MS research are diet-induced obesity (DIO) and monogenic models. Monogenic models, such as db/db mice and Zucker obese rats, exhibit high susceptibility to obesity, glucose intolerance, and insulin resistance, which affect tendon structure and function. The Goto-Kakizaki (GK) rat model is valuable for studying type 2 diabetes-related tendon issues due to early hyperglycaemia and DM complications. However, single-gene models do not fully capture MS's entire pathophysiology and are costly to model. DIO models, derived from high-fat, sugar, and salt diets in animals like C57BL/6J mice and Sprague-Dawley rats, mimic human central obesity, insulin resistance, and dyslipidaemia. These models exhibit tendon changes, such as sparse collagen fiber organization and inflammatory cell infiltration. A comprehensive animal model for MS research should balance the advantages of both monogenic and DIO models [21].

In 1073 pregnant women, this study evaluated the predictive power of four insulin resistance indicators for gestational diabetes mellitus (GDM). Anthropometric measurements, lipid profiles, and an oral glucose tolerance test (OGTT) at 24-28 weeks were conducted throughout the first trimester

Groups for GDM and Normal Glucose Tolerance (NGT) were created from the participants. The findings indicated that although TC/HDL-C was not higher, people with GDM

had higher levels of TyG, TG/HDL-C, and LDL-C/HDL-C. The TyG index, which has an AUC of 0.692, similar to HOMA-IR's 0.703, has been identified as an independent risk factor for insulin resistance. When it came to GDM prediction, TG/HDL-C and TyG ratios outperformed HOMA-IR in specificity. According to the study's findings, women who are at risk for GDM can be identified with the aid of the TyG index and TG/HDL-C, with the TyG index having a higher predictive capacity [22].

This study investigated the efficacy of DR10627, a novel dual GLP-1 and GIP receptor agonist, for treating obesity and type 2 diabetes mellitus

In vitro, DR10627 activated both GLP-1R and GIPR in transfected CHO cells. In cynomolgus monkeys, the drug had a terminal half-life of approximately 4.19–5.8 hours. Oral glucose tolerance tests (OGTTs) in Sprague-Dawley (SD) rats showed significant improvement. In diabetic (db/db) mice, DR10627 demonstrated a potent glucose-lowering effect, surpassing liraglutide at comparable doses. In diet-induced obesity (DIO) mice, DR10627 significantly enhanced weight loss, lipid reduction, and metabolic improvement compared to liraglutide. The preclinical assessment concluded that DR10627 effectively lowers glucose levels and improves metabolism and body weight [23].

A total cerebral small vessel disease (CSVD) burden score was used in a study to create and evaluate a nomogram to predict moderate vascular cognitive impairment (VCI) in individuals with type 2 diabetes mellitus (T2DM)

Based on a variety of indicators, 322 participants were divided into groups for mild and normal cognitive

functioning. Age, education, serum homocysteine level, HbA1c level, and overall CSVD burden score were all included in the nomogram, which demonstrated good accuracy, calibration, and clinical value. Decision curve analysis indicates that it can accurately estimate the likelihood of moderate VCI in people with type 2 diabetes.²⁴ Young Men Diagnosed with Diabetes Show Increased Association with Albuminuria Prevalence of Albuminuria by Age Group: The left bar chart shows that the prevalence of albuminuria is higher among T2D patients diagnosed

under the age of 45 compared to those diagnosed over the age of 45. Risk Factors Odds Ratios by Gender: The right bar chart presents the odds ratios for various risk factors segmented by gender. Significant values are shown in full opacity, while non-significant values (originally None, replaced with 0 for visualization and faded) represent the factors for which data wasn't significant or available. Notable findings are the increased odds for age at diagnosis under 45, BMI, and SBP in male patients, whereas disease duration and HbA1c are significant for female patients^[25].

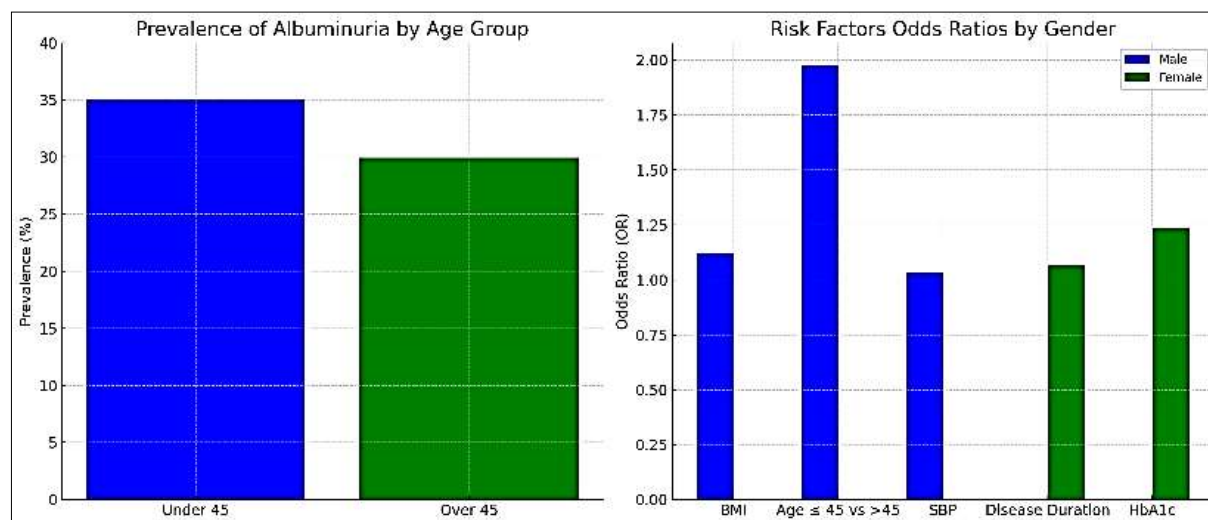


Fig 8: Albuminuria Prevalence and Risk Factor Variability by Age and Gender in Type 2 Diabetes Patients

In people with type 2 diabetes and obesity, the study looked at the connections between short-chain fatty acids (SCFAs), glucose, and insulin secretion

The findings indicated that butyrate rose following weight loss and that there was an inverse relationship between obesity and glucose metabolism and butyrate and propionate. Studies on animals bolster the function of SCFAs in maintaining metabolic health and controlling weight. Human research, however, is scarce and contradictory. Propionate and butyrate were found to have detrimental effects on glucose metabolism and obesity in this investigation, with butyrate levels rising following weight loss. More extensive research is required to comprehend the function of SCFAs in metabolic disorders and how they relate to obesity^[26].

Discussion

The management of diabetic foot ulcers has seen significant improvements with the introduction of smart insoles and smart boots^[27]. These devices utilize sensor technology to reduce foot pressure and incorporate remote monitoring feedback mechanisms, gamification, and emotive visual indicators to enhance patient adherence and engagement^[28]. Non-pharmacological approaches, particularly plant-based α -amylase inhibitors, have shown promise in controlling postprandial glucose levels with minimal side effects^[29]. These inhibitors, derived from various plant extracts, prevent carbohydrate absorption by inhibiting α -amylase, an enzyme crucial for carbohydrate breakdown^[30]. Pharmacological advancements have focused on glucagon-like peptide-1 receptor agonists (GLP-1RAs), with Semaglutide, dulaglutide, and liraglutide emerging as top choices based on their safety, efficacy, and economic profiles. These medications are recommended for healthcare

organizations seeking effective treatments for type 2 diabetes mellitus (T2DM)^[31].

Innovative drug delivery systems, such as the LG/TD-NF nano formulation, have been developed to improve the oral bioavailability of peptides and enhance glucose-lowering effects^[32]. This formulation, utilizing bile acid derivatives, has demonstrated resistance to enzymatic breakdown and improved cellular absorption, offering potential benefits over traditional subcutaneous injections^[33].

Recent guidelines from the American Diabetes Association emphasize the importance of early detection and personalized treatment plans. Key updates include serum C-peptide screening, islet-related autoantibody testing, and recommendations for using teplizumab to delay the onset of type 1 diabetes. For type 2 diabetes, the guidelines strongly endorse SGLT2 inhibitors and GLP-1 receptor agonists, particularly in patients with heart failure, cardiovascular disease, or chronic kidney disease^[34].

Research has also explored the genetic and molecular foundations of diabetes. A study on a Han Chinese family identified a unique mitochondrial mutation, m.A5826G, linked to type 2 diabetes. This mutation affects tRNA processing, leading to mitochondrial dysfunction and providing insights into potential early detection and treatment targets^[35].

Conclusion

The advancements in diabetes management highlighted in this review demonstrate a multifaceted approach to tackling this complex condition. From technological innovations in diabetic foot care to promising plant-based treatments and personalized pharmacological interventions, these developments offer hope for improved patient outcomes. Continued research and clinical trials are essential to

validate these findings and integrate them into standard practice, ultimately enhancing the quality of life for individuals living with diabetes.

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