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Glucagon-like Peptide-1 Receptor Agonists (GLP-1RAs) are correlated with mitigation of early mortality and cardiorenal risks in Type 1 Diabetes (T1D) patients: Perspectives of the economic impact

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Citation of this article: Chrysanthus Chukwuma Sr (2026) "Glucagon-like Peptide-1 Receptor Agonists (GLP-1RAs) are correlated with mitigation of early mortality and cardiorenal risks in Type 1 Diabetes (T1D) patients: Perspectives of the economic impact." *Epidemiology and Public Health Research*. 1(1); DOI: EPHR.RW.26.001

Submitted: April 15, 2026 **Accepted:** April 20, 2026 **Published:** April 22, 2026

Abstract:
This article presents a comprehensive review of the application of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in type 1 diabetes (T1D), with essential focus on the cardiovascular and renal benefits. This is a timely contribution to the field, especially given the deficiency of long-term data associated with T1D and GLP-1RA application. The discourse of GLP-1RAs outside the confines of their conventional functionality in type 2 diabetes (T2D) management depicts critical demands for further research in this sphere. This work instigates an innovative strategy to explicate the cardiovascular and renal benefits of GLP-1RAs in T1D persons; and integratively articulates the potential of these therapeutic medicatjons to ameliorate major adverse cardiovascular events (MACE) and progression of kidney disease, with nascent perspective in T1D management. The interdisciplinary conglomeration of cardiology, endocrinology, and nephrology enact a conformed strategy to diabetes research and clinical practice. Also, ethical concepts correlated to off-label therapeutic agents prescriptions substantiate and provide a nuanced elucidation of type 1 diabetes patient care. The article exposes significant interdisciplinary aspects in the use of GLP-1RAs in T1D. The ethical instances of off-label drug use depict challenges, issues, opportunities and priorities concerning clinical decision-making, especially with regard to patient autonomy versus traditional care protocols. The evaluation of economic impacts in novel pharmaceutical modalities is opportune and relevant, and requires future work delving into the socio-economic implications on broadening the analytic scope of the healthcare system.
Keywords: medical nuances; hypoglycaemia; risks; ethics; off-label; cardiorenal events; type 2 diabetes

Introduction:

This review grants an insightful exploration of the usage of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in the management of type 1 diabetes (T1D), with a defined emphasis on ameliorating cardiovascular and renal risks. This fills a crucial lacuna in extant diabetic research, particularly regarding long-run outcomes related with GLP-1RA application in T1D, a field conventionally eclipsed by type 2 diabetes research. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are established to substantially enhance cardiometabolic outcomes in type 2 diabetes (T2D) subjects, ameliorating major severe cardiovascular events (MACE) significantly and slowing progression of chronic kidney disease (CKD). These therapeutic agents are embraced as critical, evidence-based therapeutic measures for retarding cardio-renal risk, while providing protection against heart failure, hospitalization, renal decline, and all-cause mortality [1, 2]. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have provided cardiorenal benefits in type 2 diabetes, long-term data for their use in type 1 diabetes (T1D) patients are lacking. Although,

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the practice, teaching and research of medicine have invariably progressed to the detriment of specialties, it is acknowledged that the patient or ailment as a unit, all aspects of the disease or body must be taken into account. It is important that in medical care, the body be observed in parts, but a holistic strategy is fit in therapy and care [3, 4]. So, it ought to be between type 1 diabetes and type 2 diabetes with GLP-1 agonists.

Recent broad-scale investigations highlight that commencing GLP-1RA therapy correlates with a mitigated risk of significantly excruciating cardiovascular and kidney outcomes prioritizing on safety and health [1, 2], improved heart and kidney outcomes for type 1 diabetes using GLP-1 for weight loss. Glucagon-like peptide 1 (GLP-1) receptor agonists lower body weight and enhance glycaemic control. As therapeutics, they have increasingly protected the heart and kidney in persons having diabetes [5]. The extrapolation of these results to such in chronic kidney disease (CKD) is unravelled. Type 1 diabetes patient receiving GLP-1 receptor agonist (GLP-1-RA) medications for loss of weight or improvement of blood-sugar regulation evidenced pronounced diminished risks of MACE. Glucagon-like peptide-1 receptor agonists demonstrate major cardiovascular and kidney outcomes in type 1 diabetes patients. These necessitate burden-sharing and strategic priorities between type 1 diabetes and type 2 diabetes in appropriation of medications in vulnerable populations in equitable distribution of resources [6]. This comprehensive exploration enhances understanding and invites a meaningful dialogue about the future utility of GLP-1 receptor agonists in broader diabetic contexts. This article exhibits interdisciplinary potentialities by integrating insights from endocrinology, cardiology, nephrology, and health economics, depicting it as an essential resource overlapping multiple medical spheres. Thus, this submission argues in a well-articulated trajectory for the re-evaluation of GLP-1 receptor agonists beyond their conventional functionalities in type 2 diabetes management. From evaluating their usage within type 1 diabetes care, this study presents a compelling platform for further research and potential paradigm shifts in therapeutic approaches.

Type 1 diabetic nephropathy from small print to centre stage

Type 1 diabetic nephropathy is a severe, long-term sequela driven by persistent hyperglycaemia. It depicts clinically with persistent albuminuria, increasing blood pressure, and lowering glomerular filtration rate (GFR), resulting in exorbitant economic costs resulting from management and end-stage renal disease (ESRD) therapy[7]. A pivotal incipient review integrating clinical features and economic effect of Type 1 diabetic nephropathy is "Type I diabetic nephropathy: Clinical characteristics and economic impact" by Chrysanthus Chukwuma Sr, published in 1993 [7]. This article highlights the progression, mortality, and exorbitant costs of end-stage renal disease. The pivotal spheres in the 1993 paper encompass: Clinical characteristics in which the article stated that circa one-third of type 1 diabetic patients develop nephropathy, with persistent proteinuria, declining glomerular filtration rate (GFR), and elevated arterial hypertension. The study pinpointed poor prognosis resulting in increased morbidity and mortality, in that patients with persistent proteinuria are in the precarious situation of high mortality risk within 5–10 years. The article enunciated that the economic burden of end-stage renal disease (ESRD) due to Type 1 diabetic nephropathy was excruciating and over-stretching. The study depicted increasing incidence/prevalence of Type 1 diabetes, especially in northern Europe and the United States of America [7].

It should be emphasised, whereas pathological awareness specific to [8] Kimmelstiel-Wilson detailing nodular renal lesions were established in 1935, but the 1993 research constitutes an incipient or primordial comprehensive review encompassing both clinical management and economic repercussions [7]. Whereas other authors, such as Mogensen in the early 1980s enacted diabetic nephropathy clinical staging, and [8] Kimmelstiel/Wilson in 1936 characterized the pathology, Chukwuma is unarguably the author of any specific article that primordially uncompromisingly introduced economic sphere into the type 1 diabetic nephropathy syndrome [7]. Amongst the long-term diabetes sequelae, nephropathy presents the greatest costs regarding economic burden and human anguish. Irrespective of ardent management, the risk for ESRD in diabetic nephropathy is elevated. Contemporary management modalities and treatments are necessitated [9]. Following certain select neglected descriptions, the currently noticed publication by Paul Kimmelstiel and Clifford Wilson of 1936 explicated nodular renal lesions in merely eight maturity-onset of 48-68 year old diabetic patients [10]. The National Institute of Diabetes and Digestive and Kidney Diseases-supported Kidney Research National Dialogue (KRND) demanded the scientific community to configure and upgrade research objectives for the elucidation of kidney functionality and disease. Diverse high-priority goals for diabetic nephropathy manifested in data and sample collation, hypothesis formulation and testing, as well as translation advancements. The deficiency of rapidly available human samples associated with comprehensive phenotypic, clinical, and demographic data has been a critical impediment. The readily availability of data and biological samples, diverse opportunities are extant to apply newfangled technologies and hypotheses development. Investigating nascent disease trajectories continuously with contemporary tools ought to fundamentally constitute a vast proportion of the investigative team in order for research to be translated for improved diagnosis and treatment. The enacted objectives by the KRND grants research future opportunities to improve the prevention, diagnosis, and therapeutic modalities of type 1 diabetic nephropathy.

GLP-1 drugs diminish adverse risks in type 1 diabetes

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GLP-1 (glucagon-like peptide-1) is a natural hormone produced in the small intestine, and acts as a messenger that informs the brain and digestive system of the satiety of a person during meal consumption, ameliorates appetite and retards digestion. It also enables the body to release insulin solely with elevated blood sugar level. GLP-1 therapeutic medications imitate these effects, and cause individuals to feel satisfied sooner from meal consumption, reduce meal consumption, with concomitant management of blood sugar concentrations [11]. Prescriptions of GLP-1 medications are usually for individuals having type 2 diabetes, obesity or overweight. Not all GLP-1 medications are safe for consumption, especially in persons presenting advanced kidney disease. These may necessitate the interventions of a nephrologist to determine safe medications or effective alternatives. Also, endocrinologists can provide proper directives in the management of T1D or T2D [12]. A valuable team strategy promotes glycaemic control and weight loss, and concurrently ameliorates unwholesome reactions from GLP-1 agonists [12]. This category of medications belong to diverse pharmacological alternatives for these endocrine disorders. GLP-1 agonists lower serum glucose concentrations, thus manage metabolism in affected patients. Clinicians enhance their understanding appropriately in the prescription of these agonists, take into cognizance defined patient communities, and for care of patients consult with specialists [3, 4]. Recommendations for mixed formulations are in pertinent trajectory with contemporary investigations concerning this category of drugs. These may constitute hallmarks for indications, mechanism of action or function, drug administration, adverse impact profile, and drug contraindications. A formidable interdisciplinary conglomeration of practicing medical nurses, primarycare clinicians, pharmacists, and endocrinologists are necessary to prescribe this category of medications for diabetes patient care, especially in insulin predicament [13, 14].

Recent studies demonstrate that GLP-1 receptor agonists (GLP-1RAs) substantially reduce major cardiovascular events and end-stage kidney disease in type 1 diabetes (T1D) subjects. The drugs provide protective heart and kidney benefits without increased risks of adverse hypoglycaemia or diabetic ketoacidosis, accentuating their potential as crucial appurtenant therapeutic medication for T1D management. A preeminent real-world analysis considers GLP-1 receptor agonists provide cardiac, renal, and weight advantages in type 1 diabetes without inducing hospitalization risk towards diabetic ketoacidosis or aggravated hypoglycaemia. These results suggest GLP-1RAs are advantageous in major severe cardiorenal events in type 1 diabetes patients, without adverse effects on health and safety. Type 1 diabetes (T1D) individuals present higher risks of cardiovascular disease and chronic kidney disease in comparison to populations without type 1 diabetes [2]. There is extant significant usage of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in type 1 diabetes, but there is paucity of data on the long-run clinical outcomes [1]. These suggest that GLP-1RAs are pertinent towards severe cardiorenal episodes in type 1 diabetes, without deteriorating health and safety. GLP-1 receptor agonists diminish the risk of major adverse cardiovascular events (MACE) to the benefit of the kidney. It remains uncertain that GLP-1 receptor agonists are clinically beneficial to kidney outcomes [15]. Incipient GLP-1RA utilisation in type 1 diabetes correlates with diminished risks of major cardiovascular events and end-stage kidney disease, as well as achieving clinically significant weight loss, with minimal hospitalizations for diabetic ketoacidosis or severe hypoglycemia. Although, GLP-1 agonists are admittedly ubiquitous for weight loss and type 2 diabetes management, it is realised that type 1 diabetes patients on these medications off-label ought to be wary of possible excruciating impacts, such as hypoglycaemia and diabetic ketoacidosis (DKA), a deleterious sequelae due to insulin deficiency. Succinctly put, semaglutide (Ozempic) may be of benefit to type 1 diabetes patients. An initial randomized clinical trial indicates that semaglutide intake in type 1 diabetes correlates with improvement of glucose management, weight loss and reduced insulin needs. Individuals having a personal or family history of variations of thyroid cancers, severe allergic reactions to ingredients, or aggravated digestive challenges tend to decline from the use of GLP-1s, as these medications are also not usually of recommendation during pregnancy, and also present restricted safety data while nursing [16].

Type 1 diabetic individuals who used GLP-1 receptor agonist (GLP-1-RA) drugs for weight loss or improved blood-sugar control exhibited pronounced mitigated risks of major cardiovascular events and end-stage kidney disease without much ado in aggravated safety issues[1]. The results suggest that the five-year risk of major cardiovascular events, for instance, heart attacks or any cardiac dysfunctionality and the risk of end-stage kidney disease fell by 15% and 19%, respectively, whereas the patients on GLP-1-RA drugs like semaglutide (Ozempic) and tirzepatide (Mounjaro) are not deleterious to T1D patients, without aggravated risk of adverse hypoglycaemia or diabetic ketoacidosis. The risks of side effects of particular concern for type 1 diabetes patients using GLP-1-RAs, severe hypoglycaemia and diabetic ketoacidosis; an advetse insulin deficiency, producing accumulated acid in the blood, were not elevated in patients utilising these medications. Type 1 diabetes patients encounter increased lifespan risks of cardiovascular and kidney disorders. Chronic excess blood sugar augments atherosclerosis, culminating in heart attacks and strokes, as well as enhanced blood-sugar concentrations which have the potential to derange the urine-filtering mechanisms of kidneys. Select GLP-1-RA clinical trials have determined these outcomes in type 1 diabetic patients. These results suggest that physicians take immense care in the selection of type 1 diabetes patients who will be recipients of the medications, with the patients appropriately adjusting their insulin dosages. Glucagon-like peptide 1 (GLP-1) receptor agonists improve cardiac and kidney outcomes in diabetic patients; but their efficacy in persons presenting decreased estimated glomerular filtration rate (eGFR) has not been concretised. A study evaluated the effects of GLP-1 receptor agonists on kidney and cardiovascular outcomes in patients with chronic kidney disease (CKD) [17]. It was observed that Glucagon-like peptide 1 (GLP-1) receptor agonists lessen body weight and enhance glycaemic control. Also, they have been identified to protect

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the heart and kidney in diabetic individuals. However, the translation of these results to chronic kidney disease (CKD) patients has not been concretised. A meta-analysis exploration on data from clinical trials on CKD patients unravelled that GLP-1 receptor agonists are likely to retard kidney disease progression and diminish the risk of heart disease, stroke, and mortality. These suggest that GLP-1 receptor agonists provide numerous kidney and cardiovascular opportunities and priorities to CKD individuals.

Benefits of GLP-1 in type 1 diabetes and type 2 diabetes management

GLP-1 agonists, such as liraglutide and semaglutide are essentially received approval for Type 2 Diabetes (T2D) for the improvement of glycaemic regulation, weight loss promotion, and cardiovascular risk reduction. However, in Type 1 Diabetes (T1D), the agonists are employed off-label as adjuncts to insulin for glycaemic variability improvement, total diurnal insulin dose decrement, and weight management assistance, but envisaging an elevated hypoglycaemic and diabetic ketoacidosis (DKA) risk [18, 19]. GLP-1 analogue usage is a research precinct with conducive haemoglobin A1c and weight loss outcome in type-1 diabetes mellitus (T1DM) patients. Exorbitant costs and tolerability constitute formidable impediments for the prescription of these drugs [20, 21]. GLP-1 receptor agonists are approved or recommended to ameliorate cardiovascular risk. These medications do not lower the opportunities for cardiovascular events and hypoglycaemia but exhibit the potentialities in retarding chronic kidney disease (CKD) progression. Thus, the GLP-1 receptor agonists, semaglutide and liraglutide significantly enhance beneficial outcomes in type 2 diabetes due to diminishing of cardiovascular mortality, cardiac failure, and kidney disease progression, and concomitant provision of metabolic benefits. Furthermore, emerging evidence indicates that these agents enhance cardiovascular and renal outcomes in type 1 diabetes patients [22].

Initially, GLP-1 receptor agonists were produced for therapy in type 2 diabetes, with transformative impact on its management, and have been increasingly effective for glycaemic regulation, bodyweight decrement and an infinitesimal risk of inducing hypoglycaemia. GLP-1 receptor agonists mitigate risks for extremely severe cardiovascular events, such as non-fatal myocardial infarction, stroke, and cardiovascular mortality, and the admission risk to or within hospital for cardiac failure [23]. The medications abate albuminuria and retard the deterioration in glomerular filtration rate, thus forestalling or impeding kidney failure. Also, GLP-1 receptor agonists like liraglutide and semaglutide including the dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor co-agonist tirzepatide are approved for obesity treatment. Clinical trials of the drugs have established benefits for diverse obesity-associated states: type 2 diabetes prevention; risk for major severe cardiovascular events; cardiac failure, particularly with conserved ejection fraction; reversal of steatosis and blockage of fibrosis in steatotic hepatic disease; and symptomatic progress in obstructive sleep apnoea and knee osteoarthritis. Nowadays, progress encompass investigation of nascent indications, such as neurodegenerative disorders and substance abuse disorders with probable evidence of efficacy, and the production of small-molecule GLP-1 receptor agonists for oral therapy for enhanced convenience. Dual GLP-1–glucagon and GLP-1–amylin, and triple GIP–GLP-1–glucagon receptor agonists instigating disparate receptors tend to provide higher efficacy than mono-agonists, particularly for weight loss. It has been suggested that certain clinical development programmes present an increased burden of perturbing gastrointestinal events, which necessitate that dose-escalation regimens be optimised for acceptable manageability [22]. The formulation of incretin-based medications was conducted based on the therapeutic potential of GLP-1, and have evolved to reach increasingly effective and broadly utilised medications type 2 diabetes and obesity therapy and comorbidities sequelae [24]

Glucagon-like peptide-1 (GLP-1) receptor agonists are incretin analogues which enhance glucose-mediated insulin discharge and are recommended for type 2 diabetes mellitus and obesity management. GLP-1 receptor agonists and GLP-1 and glucose-dependent insulinotropic peptide agonists present multiple mechanisms of action, decreased gastric emptying, glucagon secretion suppression, beneficial alterations in the intestinal microbiome, and invariable impacts on hypothalamic nuclei for satiety enhancement which induced weight dissipation. In addition to the the beneficial impacts of GLP-1 receptor agonists on blood glucose concentrations and body weight, expansive randomized, regulated trials have demonstrated that GLP-1 receptor agonists diminish cardiovascular risk and retard progression to renal failure in individuals at high risk, and with type 2 diabetes. Excruciating side effects due to GLP-1 receptor agonists are predominantly gastrointestinal but could involve muscle and bone mass dissipation. Challenges and issues concern long-term adherence, weight reversal following therapy disruption, and the functional consequences of muscle and bone mass dissipation, with. suggestions for further uses per GLP-1 receptor agonists [25]. Incretin hormones, such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), are essential regulators of glucose homeostasis, energy equilibrium, and metabolic communication between organs. Even though, medications based on incretins are precisely determined for type 2 diabetes, their physiological importance and therapeutic potential in type 1 diabetes are unclear. In T1D, the autoimmune degradation of pancreatic β-cells immensely depreciates but does not eradicate insulin development, but diverse extraneous pancreatic functions of incretins persist, such as impacts on gastric emptying, glucagon secretion, appetite, inflammation, and cardiovascular actions. The increasing prevalence of overweight, obesity, and insulin resistance within T1D subjects has highlighted interest in investigating incretin-based therapies as adjuncts to insulin medications. Increasing research and evidence suggest significant role of incretins in defined T1D persons, but large-scale, properly established randomized controlled trials are pertinent to establish their long-run efficacy and safety [26].

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Economic impact of GLP-1 RAs use in type 1 diabetes patients

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide and liraglutide, are incessantly used off-label for the treatment of type 1 diabetes (T1D), essentially to deal with insulin-associated weight gain and enhance glycaemic control. Although, clinical benefits are provided including weight decrement and diminished HbA1c, the economic impact is highlighted by elevated acquisition costs, astronomically increased financial burden on insurers, amid potential, though not yet completely acknowledged, cost offsets due to ameliorated diabetes sequelae [11]. Glucagon-like peptide-1 (GLP-1) receptor agonists, although, essentially consented to for Type 2 Diabetes (T2D) and obesity, have been valuable as adjunct therapies in Type 1 Diabetes (T1D) for sequelae management. Although, their application in T1D is off-label, studies suggest they can revert weight appropriation, improve A1c concentrations, and decrease insulin needs, with resultant potential long-run economic advantages by abating concomitant sequelae, such as cardiovascular disorders and nephropathy [27]. Type 1 diabetes insulin therapy is connected with weight acquisition. Glucagon-like peptide 1 (GLP-1) agonists, which decrease blood glucose and induce weight loss, may revert this tendency and abate hemoglobin A1c concentrations. GLP-1 agonists effectively reverse the trajectory of body weight acquisition and improve A1c concentrations in Type 1 diabetic patients.

This article explores the increasing prevalence of obesity in type 1 diabetes (T1D), the dilemma patients encounter to achieve optimal glycaemic control with extant therapies [28]. The evidence undergirding the usage of glucagon-like peptide-1 receptor agonists (GLP-1RA) as potential adjunctive therapy to decrease weight and foster insulin resistance in T1D is strongly appreciated. Potential benefits have to be taken into cognizance per hypoglycaemic risk and limited long-run data [29]. Advanced glycaemic control and weight management research using GLP-1 agonists like liraglutide in T1D subjects indicated a significant reduction in weight and A1c, thus mitigating the metabolic and economic encumbrance of insulin-induced weight gain.

GLP-1 agonists have decreased the basal insulin needs, essentially diminishing the diurnal cost of insulin therapy in T1D patients. As in T2D, GLP-1 receptor agonists, GLP-1 RAs and dual GIP/GLP-1 agonists like tirzepatide in T1D are associated with ameliorating cardiovascular risk and microvascular sequelae risks as well as renal events, suggesting cardiorenal protection. An expansive retrospective analysis indicated that T1D patients on GLP-1 therapies depreciated all-cause mortality and less hospitalizations, minimal healthcare utilizations and emergency department encountres in comparison to controls [30]. The research depicted pronounced benefits in the use of GLP-1 RA analogues as adjunctive therapy in T1D, with lower rates of healthcare resource. A potential economic flaw is diabetic ketoacidosis (DKA) risk. A significant precipitation of insulin doses on the start of a GLP-1 agonist can culminate in high blood ketones, thus spiking DKA risk and consequential emergency, and high-cost care. Type 1 diabetic patients as unravelled in a two-year investigation, where subjects who were recipients of the medications exhibited decreased all-cause mortality and minimal healthcare utilisation are as compared to controls. Diabetic ketoacidosis (DKA) and hypoglycemia rates showed similarities between groups. GLP-1 receptor agonists, such as semaglutide, liraglutide are incessantly employed off-label for type 1 diabetes (T1D) weight dissipation, presenting pronounced decrements in body weight in a period of an excess of 6–12 months, lower HbA1c, and lessen daily insulin requirements. Inasmuch as they are effective in weight management and insulin sensitivity, FDA-approval has not been granted for T1D, necessitating prudent, stringent and ardent medical supervision to attend to elevated risks of hypoglycaemia and diabetic ketoacidosis (DKA). Insulin constitutes the major hormone the body requires to control the quantity of sugar is in the blood. In non-diabetic, other hormones including GLP-1, glucagon and amylin, also assist with appetite, digestion and sugar equilibrium.

The immune system destroys the cells which produce insulin in type 1 diabetes. The GLP-1, amylin and glucagon hormones also derail, causing it more cumbersome to manage hunger and blood sugar. GLP-1 receptor agonists (GLP-1s) were initially employed to assist type 2 diabetic subjects. They assist to lower blood sugar, retard digestion and induce satiety. Currently, scientists are investigating whether GLP-1s are also capable of helping type 1 diabetes subjects, not substituting insulin, assisting other hormones of the body to conduct their jobs in a more proficient trajectory [31].

Ethical considerations and practices using GLP-1 agonists in TID

Speculations are rife regarding multiple spectra of insulin, cardiorenal and weight loss in type 1 diabetes sequelae with vulnerability to a specific therapeutic strategy, and also potentially routine issues necessitating empirical medication strategies [32]. This article explores hallmarks and principles of formulating preventive modalities in the management of type 1 diabetes mellitus in order to systematise the structures conventionally implementing its prevention and treatment using GLP-1 agonists in a safe mode in cognizance of unpredictable sequelae and consequences which may constitute aggravated economic burden. There is paramount interest in the consumption of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in type 1 diabetes, but data on the long-run clinical outcomes are sparse. Persons presenting with type 1 diabetes (T1D) are more susceptible to increased risks of cardiovascular and chronic kidney diseases in comparison to non-diabetic individuals [2, 33].

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They provide protective advantages against cardiovascular mortality, cardiac failure, and renal depreciation without augmenting hypoglycaemic risk. The pivotal presentations on GLP-1 RAs for cardiorenal health. In cardiovascular disease, GLP-1RAs, such as semaglutide, liraglutide) decrease MACE, cardiac failure, hospitalization, mortality, with cardio-protective impacts more than glucose decrement. For renal protection, these therapeutic agents decrease CKD progression, diminishing albuminuria and retarding kidney functionality decline, enabling them to be effective for the management of diabetic kidney disease. A recent investigation indicated that benefits in Type 1 diabetes (T1D) revealed GLP-1RAs decreased 5-year risk of cardiovascular incidents and end-stage kidney disease without augmenting ketoacidosis or adverse hypoglycaemia. The mechanism of action of GLP-1RAs involve diminishing inflammation, oxidative stress, and fibrosis, which are significant in impeding diabetic cardiomyopathy and nephropathy [1]. As combination therapies, GLP-1RAs with SGLT2 inhibitors result in additive advantages, producing abatement in cardiovascular mortality or cardiac failure, and decrement in the progression of kidney disease.

The prevalent GLP-1 Receptor Agonists encompass Semaglutide (Ozempic/Wegovy), Tirzepatide (Mounjaro - a GIP/GLP-1 receptor agonist), Liraglutide (Victoza), Exenatide and (Byetta/Bydureon). These therapeutic agents increasingly diminish cardiovascular and renal sequelae, thus, presenting them as crucial ingredients for the management of high-risk diabetic kidney disease patients [34]. Conversely, GLP-1s can elevate the risks of hypoglycaemia (low blood sugar) and SGLT-2s of adverse life-threatening sequelae addressed as diabetic ketoacidosis (DKA) [35]. Certain type 1 diabetic patients elect to consume these medications “off-label” from the directives of their healthcare providers [36]. As the discourse relates to the risks associated with off-label usage, it is concerned with the ethical obligations of medical practitioners and prescriptions of these medications. This necessitates an expansive in-depth evaluation of potential conflicts between clinical benefits and ethical prescription practices [3,4].

Discussion

This article focuses on a comprehensive review on the cardiovascular and renal benefits of GLP-1 receptor agonists in Type 1 Diabetes subjects. It tends to bridge the gap in the pronounced emphasis on Type 2 Diabetes in the extant scientific and medical literature. The study posits that GLP-1RAs offer significant preventive modalities against major adverse cardiovascular events (MACE) and kidney disease progression in T1D patients. Leveraging an interdisciplinary strategy, the article evaluates ethical nuance, clinical decision-making, and economic impact, especially in off-label drug applications and patient autonomy, as envisaged in the sphere of non-infectious or non-communicable diseases [1, 4, 5, 8].

Non-communicable diseases are an increasing aetiology of morbidity, comorbidities, and mortality globally [37, 38]. The issue is whether it is safe or dangerous to take GLP-1 if a patient presents a heart condition. Evidence exists than expected, GLP-1 consumption can be safer for cardiovascular therapy in select high-risk patients, however, the encompassing safety spectrun remains conditional on the patient taking the drug, extent or magnitude of the period of intake, and the expected prognosis or outcome. The cardiovascular benefits of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) may present body mass index variations (BMI), but indications on BMI-specific outcomes are not pellucid [15, 39]. A sustained decrement in eGFR by a 50% minimum or the closest equivalent, or mortality due to kidney failure. The main cardiovascular outcome was MACE, constituting cardiovascular mortality, non-fatal myocardial infarction or its stroke equivalent. Evidence that GLP-1 receptor agonists significantly diminishes clinically critical kidney events, kidney failure, and cardiovascular events abound [15]. Adequate research is necessary to determine if cardiovascular benefits of GLP-1RAs are sustainable with incessant consumption, but when accompanied by disruptions in intake, they may progressively be excoriated and reverted to the status quo of increased risk of cardiovascular events [40]. Glucagon-like peptide-1 receptor agonists (GLP1-RAs) are anti-hyperglycaemic agents, with cardioprotective effects, but their renal protective impacts are unclear. An assessment of the impacts of GLP1-RAs on renal outcomes in diabetic and non-diabetic [41] individuals indicated that GLP1-RAs exhibited cardiovascular and renal benefits.

With improvement in survival, there are increasing number of persons with type 1 diabetes reaching the age where irreversible failure of kidney action can impair health and clinical outcomes. Inasmuch as conventional care has significantly decreased the incidence of rapid-progressive kidney disease featuring fulminant albuminuria, and patient improved survival rate, these identical interventions have not retarded kidney functional decline in several patients. The urgency exists for the development of a different strategy to type 1 diabetes with early kidney protection relying on glucose control and certain novel renoprotective modalities, including glucagon-like peptide 1 receptor agonists, aldosterone antagonists, and sodium–glucose cotransporter 2 inhibitors. Regarding an individual therapy, it has been demonstrated in type 2 diabetes and kidney disease, inducing select clinicians to introduce agents off-label in type 1 diabetes patients, due to the exigency involved. Prior to the translation of such significant benefits to type 1 diabetes subjects, the risk of adverse impacts, the balance of efficacy and safety ought to be verifiable in clinical trials, as well as the potential role of adjunctive therapy in type 1 diabetes for the improvement of kidney outcomes [42] and functionality. The leading aetiology of mortality in type 1 diabetes is End-stage renal disease (ESRD), historically, in the mid-years of diabetes duration circa 35 years, accounting for over 50% mortality. Following 35 years duration, cardiovascular disease (CVD) constitutes the leading aetiology of mortality, accounting for two-thirds of overall mortalities. The central or peripheral GLP-1 administration elevates blood

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pressure and heart rate, probably via the activation of brainstem autonomic nuclei and increasing vagus nerve action, thus enhancing heart rate. This submission delves into the multipronged spheres of GLP-1 receptor agonists for type 1 diabetes subjects, with particular focus on cardiovascular and renal protection, the work contributes to extant literature, conventionally overshadowed by insights and hallmarks of type 2 diabetes [43], by investigating the explicit utility of these therapeutic agents. The study posits GLP-1RAs not merely as a therapeutic partner in managing glycaemic control and weight parameters but as a preventive approach against cardiovascular events and kidney failure. Furthermore, potential economic consequences and risks, such as hypoglycaemia and ketoacidosis are addressed, contextualizing GLP-1RAs as an intricately complex but beneficial enhancement to T1D management, specialists and leadership functionalities [3, 4, 12, 44-46].

GLP-1 agonists, such as semaglutide and liraglutide in type 1 diabetes iabetes (T1D) is generally referred as an "off-label" practice because the drugs are formally approved for type 2 diabetes (T2D) and obesity. Their application in T1D, mostly as an adjunct to insulin in the obesity scourge, decreases insulin dose, or enhances glycaemic stability, elicits intricately complex ethical polemics concerning evidence, health, safety, and equitable access [27]. GLP-1 receptor agonists are specifically given in this wise: exenatide two times a day, exenatide extended-release (ER) once a week, lixisenatide once a day, liraglutide once a day, dulaglutide once a week, semaglutide once a week, and oral semaglutide once a day [47]. These GLP-1 agonists They well-renowned therapeutic alternatives for T2DM treatment. Although, there are extant health benefits and guideline recommendations for these medicinal agents, both the patients and healthcare specialists are disinclined to initiate these therapeutic agents [3,4, 48].

Conclusion

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) applications are correlated with mitigated risks for cardiovascular (CV) and renal events including early mortality in type 1 diabetes. This review explores the transect of therapeutic care using GLP-1 drugs in type 1 diabetic patients, with reflections and perspectives on type 2 diabetes, and the economic impact on medication costs. Perspicuously, there are multiple spectra of insulin issues in type 1 diabetes with vulnerability to a specific therapeutic strategy, and also potentially routine insulin issue necessitating empirical medications. This article explores hallmarks and principles of formulating preventive modalities in the management of type 1 diabetes mellitus in order systematized the structures conventionally implementing its prevention and treatment globally with the application of GLP-1 agonists in a safe mode in cognizance with unpredictable sequelae and consequences which may constitute aggravated economic burden.

This article offers an insightful exploration of the usage of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in the management of type 1 diabetes (T1D), with a defined emphasis on ameliorating cardiovascular and renal risks. This fills a crucial lacuna in extant diabetic research, particularly regarding long-run outcomes related with GLP-1RA application in T1D, a field conventionally eclipsed by type 2 diabetes research. This work is exemplary for its encompasding endeavour in bridging the research lacuna between the usage of GLP-1RAs in type 1 versus type 2 diabetes. It harnesses a novel strategy in positing the cardiovascular and renal protective impacts of these agonists in T1D management, providing significant ambient for clinical practices. The rigorous and resilient presentation of both clinical and potential economic impacts supplement an essential ingredient to the discourse surrounding chronic disease management. The inclusion of both physiological mechanisms and real-world clinical applications provides a resilient fundamental hallmark for future studies.

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