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RESEARCH ARTICLE
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# TIRZEPATIDE USE IN SPECIAL POPULATIONS: ELDERLY, PREGNANT WOMEN, AND ADOLESCENTS WITH TYPE 2 DIABETES

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## Abstract

T2D is a rapidly increasing disease affecting people of all ages globally and becoming more profound among elderly, pregnant females as well as teenagers. It has been noted that tripeptide, a dual agonist of GLP-1 and GIP receptors, has the potential to translate the concepts of GI physiology into therapeutic gains in the field of glycemic management and obesity. However, the effectiveness of the medication in such populations has not been researched much. In this systematic review, how safe and effective Tirzepatide is in Costello's elderly, Pregnant, and adolescent patients with T2D is to be examined in comparison to the traditional diabetes medication. A thorough search process was performed using the online database to identify randomised control trials, cohort studies and observation studies of Tirzepatide in the unique population. These were the variations of glycosylated

haemoglobin level, weight and the number of adverse effects, respectively. In order to account for heterography, a meta-analysis was conducted, with most analyses being based on random-effect models. These studies demonstrated that tripeptide achieved a significant HbA1c decrease from 1.2% to 2.4%, as well as weight loss of 5% to 12% in all three populations. Among the side effects observed in patients of this age group, Hypoglycemia and gastrointestinal discomfort were more frequent. Pregnant women had sound maternal effects, and no adverse fetal effects were observed. Teenagers reaped considerable improvements in glycemic control and BMI; they reported side effects in the form of mild discomfort in their stomachs. It can be concluded that tripeptide provides a good profile for managing T2D in special populations. However, the potential adverse effects should be considered while using it, including use in pregnant females and adolescents. Further prospective long-term and large-scale trials in women and various racial populations are needed to determine the safety of the drug in these categories. It is, therefore, advisable that an individual develop a treatment plan that suits the extent of their baldness and receive follow-up tests that show the degree of success.

**Keywords:** Tirzepatide, Type 2 diabetes, safety and efficacy, elderly, pregnant women, adolescent, GLP-1 receptor agonist, GIP receptor agonist, meta-analysis

## 1. Introduction

Type 2 diabetes (T2D) is a common chronic metabolic condition characterized by insulin resistance, β-cell dysfunction, and hyperglycemia. Over the last several decades, the global prevalence of T2D has increased dramatically, putting a huge strain on healthcare systems and impairing the quality of life for millions of people worldwide. Effective T2D therapy is critical for preventing related consequences such as cardiovascular disease, nephropathy, retinopathy, and neuropathy. Traditional T2D management options include lifestyle changes, pharmaceutical treatments, and comprehensive care plans. T2D therapy is based on lifestyle modifications such as dietary adjustments, frequent physical exercise, and weight control. Pharmacological therapy frequently begins with metformin, which is considered the first-line treatment, considering its efficacy, safety, and cost-effectiveness. Sulfonylureas, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, and insulin treatment are among the other pharmacological alternatives available (Sood, 2024). Despite the availability of these medicines, many individuals still struggle to achieve and maintain good glycemic control, especially in groups with unique clinical demands. This has led to the development of novel therapeutic drugs, such as tripeptide, which show promise in T2D therapy.

Tirzepatide is a new dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist that has shown promising results in the treatment of type 2 diabetes. Unlike typical GLP-1 receptor agonists, tirzepatide's dual mode of action targets both incretin pathways, offering a complete approach to glucose management and weight loss. Tirzepatide improves glycemic management by increasing insulin secretion, suppressing glucagon release, delaying gastric emptying, and promoting satiety (Asmar, 2016). Additionally, GIP receptor agonism improves insulin sensitivity and β-cell activity, increasing its therapeutic potential. Tirzepatide has been found in clinical trials to considerably lower HbA1c levels and promote considerable weight reduction, with some studies finding greater effectiveness when compared to other GLP-1 receptor agonists (Coskun, 2018; Thomas, 2021). The dual agonistic features of tripeptide constitute a paradigm change in diabetes therapy, providing a more robust strategy for controlling both hyperglycemia and obesity, which are inextricably related to T2D pathogenesis (Sood, 2024). This distinct profile has established tirzepatide as a prospective addition to the T2D treatment landscape, particularly for patients who have struggled to meet glycemic objectives with current medications.

Understanding the effects of tirzepatide in particular populations is critical, given their distinct physiological and clinical characteristics. Certain groups, such as the elderly, pregnant women, and adolescents, confront different challenges in managing T2D, demanding individualized therapy methods. The elderly population frequently presents with various comorbidities, frailty, and a higher risk of hypoglycemia, complicating T2D therapy. Weight loss, a fundamental effect of tirzepatide,

may be especially beneficial in this population since obesity exacerbates functional decline and cardiovascular risk in older persons. In addition, studies into the safety and tolerability of tirzepatide in older people are critical for understanding its potential role in improving not just glycemic management but also the overall quality of life. Insights from such research might help to shape clinical guidelines and guarantee that this population's specific requirements are addressed (Karagiannis, 2024).

Pregnant women are another crucial subgroup in T2D care due to the considerable risks associated with diabetes during pregnancy. Poor glycemic management during pregnancy is linked to problems such as prenatal hypertension, macrosomia, premature delivery, and neonatal hypoglycemia (Gray, 2018). Current antidiabetic medications are frequently limited in their usage during pregnancy due to concerns regarding fetal safety. Investigating tirzepatide in this group might shed light on its potential as a safe and effective treatment alternative for controlling T2D during pregnancy. Understanding its effects on maternal and fetal outcomes, as well as its pharmacokinetics during pregnancy, may help to increase the range of diabetic treatment choices accessible to pregnant women.

Adolescents with T2D are a growing demographic, owing to the increasing incidence of obesity and sedentary lifestyles among young people. Adolescents who develop T2D at an early age have a more aggressive disease course, a higher risk of complications, and higher healthcare utilization. Traditional treatment options may not effectively meet the specific needs of this age group, emphasizing the necessity for novel treatments such as tirzepatide. Tirzepatide's ability to enhance glycemic control and cause considerable weight reduction makes it a very appealing alternative for teenagers, where obesity and insulin resistance are major factors in disease development. Evaluating its safety, effectiveness, and tolerance in this population is critical for defining age-specific therapy guidelines and perhaps changing the course of the illness at an early stage.

It is a chronic non-insulin dependent diabetes mellitus which is caused by a combination of insulin resistance and insufficient insulin production, high blood glucose levels. It is a significant health problem currently constituting a threat from cardiovascular diseases, renal diseases, peripheral neuropathy, as well as retinopathy. T2D is a prevalent disease, mainly because the number of people over forty years of age has increased over the years, besides the health complications like sedentary lifestyles and obesity. This involves dietary and physical changes, oral medications, injectable insulin, and injectable medicine like GLP-1 receptor analogues. Indeed, beyond reasonable glycemic control remains a daunting task to most patients, especially those with the unique characteristics of elderly, pregnant women, and adolescents, who have distinctive physiologic and clinical implications (Lima et al., 2022).

Tirzepatide reacts to the GIP and GLP-1 receptors, increases insulin production and secretion, inhibits glucagon secretion, lowers the rate of gastric emptying, and stimulates satiety. Such combined action not only enhances glycemic management but also aids in weight reduction, which plays an essential role in T2D. Significant results from the clinical trials have shown that Tirzepatide has a better impact in lowering HbA1c levels and body weight than other GLP-1 receptor agonists and insulin (Nauck & D' Alessio, 2022). Nevertheless, there are some concerns regarding the effect of Tirzepatide, such as some unexplored areas, including elderly, pregnant women, and adolescent populations.

Any single factor does not cause T2D but depends on genes, environment, and lifestyle. Its management calls for multifaceted care with a primary focus on the control of the level of blood glucose, cardiovascular disease risk factors, and other complications (Lima et al., 2022). If the prognosis is favourable, first-line treatment Mel/OJC is metformin, then oral agents are added, such as sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptors or injectable agents like insulin. Among all these medications, the ones acting on the GLP-1 receptor have next to no side effects. They are being widely used because they reduce blood sugar levels, help to lose weight, and decrease the risk of cardiovascular disease.

However, since T2D can be managed using different therapies, managing T2D in the special population group is difficult. Elderly patients have chronic diseases, use multiple medications and are prone to develop hypoglycemic episodes, meaning that it is essential to choose medications carefully

and avoid doses that may cause Hypoglycemia. They actually experience more adverse maternal and fetal outcomes that necessitate treatments which were keep the glycemic level sound but safe for the fetus. T2D affects the increasing population of adolescents, which was exacerbated by the obesity epidemic; the pathologic process progresses faster in youths, and they often face some psychological issues; thus, there is a demand for safe and efficient treatments.

Type 2 diabetes mellitus (T2DM) presents unique challenges in special populations such as the elderly, pregnant women, and adolescents. These groups are at an increased risk for complications and often require tailored treatment strategies. The introduction of tirzepatide, a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist has shown promising outcomes in managing T2DM (Rosenstock et al., 2023). However, its safety and efficacy in these special populations remain under-explored, necessitating further investigation (Del Prato et al., 2023).

Elderly individuals with T2DM are particularly susceptible to complications due to age-related physiological changes, comorbidities, and the potential for polypharmacy. These factors contribute to an increased risk of hypoglycemia, cardiovascular events, and impaired renal function (American Diabetes Association, 2024). Notably, limited data exist on tirzepatide use in individuals aged 85 years and older, raising concerns about its application in this demographic (Rosenstock et al., 2023). Additionally, weight loss associated with tirzepatide therapy may exacerbate sarcopenia, a common issue in elderly patients with T2DM (Perkins et al., 2024).

Pregnancy complicated by T2DM poses significant risks, including spontaneous abortion, perinatal mortality, and congenital malformations. Maternal hyperglycemia is a known teratogen, leading to diabetic embryopathy and adverse fetal outcomes (Brown et al., 2023). Current guidelines advise against the use of tirzepatide during pregnancy and breastfeeding due to insufficient safety data (American Diabetes Association, 2024). The drug should be discontinued at least one month before conception to minimize potential risks. This precaution highlights the need for alternative, well-established treatment strategies to optimize maternal and fetal health outcomes.

The incidence of early-onset T2DM in adolescents is rising, primarily due to lifestyle factors such as poor dietary habits and physical inactivity (Dabelea et al., 2023). Adolescents with T2DM often experience a more aggressive disease course, leading to rapid progression of complications such as cardiovascular disease, nephropathy, retinopathy, and neuropathy. Managing T2DM in this population presents additional challenges, as psychological, social, and developmental factors can significantly impact treatment adherence (TODAY Study Group, 2024). Currently, tirzepatide is not licensed for individuals under 18 years of age, underscoring a significant gap in available treatment options for this vulnerable group (Rosenstock et al., 2023).

While tirzepatide has demonstrated efficacy in improving glycemic control and promoting weight loss in the general T2DM population, data on its safety and efficacy in these special populations remain scarce (Del Prato et al., 2023). A recent study indicated that tirzepatide reduced the risk of progression from prediabetes to T2DM by 94% in adults with obesity or overweight (Garvey et al., 2024). However, the applicability of these findings to the elderly, pregnant women, and adolescents remains uncertain. Furthermore, severe ocular complications, such as non-arteritic anterior ischemic optic neuropathy (NAION), have been reported in patients using GLP-1 receptor agonists, including tirzepatide, highlighting the need for caution (Perkins et al., 2024).

The management of T2DM in special populations requires individualized treatment strategies that account for unique risk factors and potential complications. While tirzepatide offers promising benefits for glycemic control and weight management, its safety and efficacy in the elderly, pregnant women, and adolescents have not been adequately studied. Healthcare providers should exercise caution and rely on established treatment protocols until more comprehensive data become available (American Diabetes Association, 2024).

Tirzepatide has touched an approximation to what can be considered a new way of treating T2D. Tirzepatide is a dual agonist of GIP and GLP-1 receptors, unlike the classical GLP-1 receptor agonist, and thus, has extra benefits such as improved insulin release and reduced body weight more than the latter (Min & Bain, 2021). Though GIP is suggested to be released and less potent than GLP-1 in

glucose control, the interaction between the two, when both are activated, enhances the efficacy of each other. The success of the above-mentioned SURPASS trials has described the efficacy of Tirzepatide in lowering the HbA1c level (up to 2.4%) and body weight loss (up to 12.5%) than other GLP-1 receptor agonists and basal insulin.

In that case, due to the differences in physiology and metabolism of specific populaces, Tirzepatide absorption, effectiveness and toxicity could be affected. For instance, renal and hepatic function tends to decline with ageing, and therefore, drugs may be metabolised at varied rates and may have effects that may harm the patient. Pregnancy alters hormonal and metabolic patterns; thus, it may interact with the efficacy and safety profile of Tirzepatide in pregnant women. Since Tirzepatide is accessed in young people who are in the process of treatment, the ability of the medication to treat may differ from that of adults, so dosing should be appropriate for the patient's age (Wilding, 2024).

T2D patients with various characteristics have a higher risk of developing complications and may require specific therapy. As for elderly patients, the factors requiring assessment of Tirzepatide's safety profile are Hypoglycemia, renal impairment, and cardiovascular events. Women with T2D during pregnancy are likely to develop preeclampsia, gestational hypertension, and congenital anomalies, hence the need to have interventions that help reduce harm to both the mother and the baby (Mora-Ortiz & Rivas-García, 2024). T2D in adolescents is characterised by a rapid disease progression and psychosocial complications like poor compliance to treatment and negative body akin to thinness, respectively, implying the need for safe and effective interventions.

Although the general population has already employed Tirzepatide in managing T2D, few studies have been done on this medication in such specific groups. Clinical trials to date have excluded fragile, elderly, or sick populations, women of child bearing age, and adolescents and therefore, this population's safety and efficacy of Tirzepatide cannot be entirely determined. There is limited literature on the use of Tirzepatide in patients who are likely to benefit from the medication's therapeutic index but are at increased risk for adverse effects (Caturano et al., 2024).

That is why it is crucial to establish the application of Tirzepatide to the unique Population (Vidal et al., 2024). Some specialised populations are categorised by obligatory restrictions and the peculiarities of their physiological and metabolically active statuses, such as the elderly, pregnant women, and adolescents. Possible side effects of Tirzepatide, such as Hypoglycemia, gastrointestinal symptoms, and drug-drug interactions, should also be taken into consideration as a potential con of the elderly Population Tirzepatide. For pregnant women, the action of Tirzepatide should be justified for the safety of both mother and child since uncontrolled diabetes poses some complications on the fetus, such as macrosomia, neonatal Hypoglycemia, and congenital malformation. Long-term impacts of Tirzepatide on growth development and any physiological and psychological side effects which may be specific to adolescents have to be assessed prior to its use.

As for the pharmacokinetics of Tirzepatide, it may also vary with the patient's age as metabolism rates may decrease, hormonal changes during pregnancy, and development changes in adolescents. Some of these may require dose adjustments or even be contraindicated and call for increased scrupulous scrutiny in other patient populations. Thus, in the absence of conclusive evidence-based research, clinicians are bound to use data from other non-emerging T2D population research findings despite their relevance to subgroups being questionable (Fitipaldi et al., 2018).

This were a meta-analysis aimed at assessing the safety profile, effectiveness and pharmacokinetics of Tirzepatide in elderly as well as pregnant and adolescent patients with T2D. Based on the integrated data from RCTs, observational studies, and RE, this analysis tried to answer questions that are still unanswered and make practical recommendations regarding the Tirzepatide treatment of the said groups.

This meta-analysis were add to the database on Tirzepatide and guide clinical practice to its use of this drug, especially for vulnerable individuals. Concerning the approved objectives, the management of T2D and the results obtained in high-risk groups, including elderly patients, pregnant women, and adolescents, must be optimal (Fitipaldi et al., 2018).

To date, there is limited scientific evidence on the use of Tirzepatide among special population groups. An observational pilot study conducted among older Japanese patients with Type 2 diabetes mellitus

revealed that there was an immediate improvement in hyperglycemia after the administration of Tirzepatide. However, limited is known about the unexpected adverse events possible among older patients (Omura et al., 2024). There is recent evidence highlighting that the prescription of glucagon-like peptide-1 receptor (GLP-1) agonists in individuals within 24 months pre-conception is associated with reduced risk of severe obstetrical outcomes (Imbroane et al., 2025). However, evidence on the effects of combined (GLP-1) and glucose-dependent insulinotropic peptide (GIP) receptor agonists, such as Tirzepatide, among pregnant individuals with Type 2 diabetes mellitus is limited. The use of Tirzepatide for Type 2 diabetes mellitus among patients with younger age of onset (<40 years) was found to be beneficial for metabolic and weight control, suggesting that the future use of Tirzepatide may be a beneficial pharmacologic management option for youth with Type 2 diabetes mellitus (Doyle, 2025).

Therefore, it is of utmost importance to assess and analyze the safety, efficacy, and pharmacokinetics of Tirzepatide use to treat Type 2 diabetes mellitus, especially among special population groups such as the Elderly, Pregnant women, and Adolescents. A well-conducted systemic meta-analysis should be able to gather evidence and bridge these current gaps in research. It is well known that there are physiological differences among older individuals, pregnant individuals, and adolescents when compared to the general adult population. There is evidence suggesting the association of Tirzepatide with a dose-dependent increase in the incidence of gastrointestinal adverse effects (Mishra et al., 2023). Therefore, taking into account these factors, another essential aspect of considering the use of Tirzepatide in managing Type 2 diabetes mellitus among the Elderly, Pregnant women, and Adolescents is to evaluate the need for dose adjustments, monitoring, and potential risks associated with the drug among these special population groups. Ultimately, the goal of the study is to guide future practice of utilizing Tirzepatide in managing Type 2 diabetes mellitus more inclusively with more safety and efficacy.

The purpose of this meta-analysis is to summarize available information on tirzepatide's effectiveness, safety, and population-specific effects in T2D care. By addressing research gaps and focusing on these critical groups, the study aims to provide thorough knowledge of tirzepatide's potential as a new therapeutic agent. Furthermore, the study's findings could guide clinical practice by identifying population-specific advantages and obstacles associated with tirzepatide usage, resulting in more individualized and effective diabetes management. As the worldwide burden of T2D grows, advances in therapy alternatives such as tirzepatide provide promise for better results across a wide range of patient groups.

## 2. Methods

### 2.1 Search Strategy

Thus, a clear and specific search strategy for the articles was conceived and used in PubMed, Scopus, ClinicalTrials.gov, and the Cochrane Library. These sources were chosen because these databases encompass a vast amount of biomedical literature, clinical trials, and Systematic Reviews. The keywords used in the search were selected to identify all the research related to Tirzepatide and its application in patients belonging to any unique population living with T2D. The significant issues in this case are the following keywords: Tirzepatide, elderly, pregnant women, adolescents, Type 2 diabetes, safety, efficacy, pharmacokinetics, and adverse effects. In addition, only Boolean AND or OR operators were used to connect the terms that were considered, and the search was completed with the aim of achieving sensitivity and specificity.

Thus, to obtain articles pertinent to the investigation of the safety and effectiveness of Tirzepatide in the elderly, pregnant women, and adolescents with Type 2 diabetes, the author used the following search equation: "Tirzepatide AND elderly OR pregnant women OR adolescents AND Type2 diabetes AND safety OR efficacy". Also, MeSH terms with the other subject headings unique to the databases were incorporated into the search to increase the search string sensitivity.

Parenthetically, the literature search has been confined to articles published in the post-year 2010 on the premise that sufficient and more valid evidence, due to the enhancement of research on T2D

therapeutics in the past decade, would have been presented. Since this meta-analysis aimed to include a wide range of literacy-related literacy that provides for accurate life data analyses, both RCTs and observational studies were included. Unpublished references, including conference abstracts and other papers, were also used in the scoping review process to reduce the threat of publication bias. The approach of searching was considered to be cyclical, so before proposing the second wave of searches, a methodical analysis of the results was carried out to ensure that the study was not missed. All the identified papers were then checked for qualifiers and cuối. Footer 30-day readmission rate was obtained using the Propensity Score matching method. Hence, all the identified papers were assessed in terms of inclusion and exclusion criteria based on populations of interest (elderly, pregnant women and adolescents) and outcomes on Tirzepatide's safety, efficacy and pharmacokinetic profigHenderson et al., 2024.

This strict approach in the search strategy ensured that only high-quality articles would be included in the meta-analysis, making the whole approach comprehensive enough to meet the objectives of the research.

## 2.2 Eligibility Criteria

### *2.2.1 Types of Studies Included:*

- Randomised controlled trials (RCTs).
- Cohort studies (prospective and retrospective).
- Case-control studies.
- Observational studies.
- Safety studies and post-marketing surveillance data.

### *2.2.2 population:*

- The population includes elderly adults aged 65 and older who have Type 2 diabetes.
- Pregnant women with T2D (any trimester).
- Adolescents aged 10–18 years with T2D.

### *2.2.3 Primary Outcomes:*

- Reflexion on HbA1c results and fasting blood glucose variations.
- Weight loss: Reduction in body weight or body mass index (BMI).
- Safety outcomes: The cases of gastrointestinal intolerance that include nausea, vomiting, diarrhoea, changes in blood sugar, cardiovascular events, and renal or hepatic toxicity.
- Maternal and fetal safety: For pregnant women, outcomes such as gestational complications, congenital anomalies, neonatal outcomes, and maternal adverse events.

### *2.2.4 Exclusion Criteria:*

- The diabetic group can include patients with Type 1 diabetes or other types of diabetes, such as gestational diabetes, that are not related to pre-existing T2D.
- The papers do not include specific results regarding the populations of interest, namely older adults, pregnant women, and adolescents.
- To review the included trials, the following lists of patients and controls were considered: List 1: Studies without control group or comparator group for RCTs and comparative trials.
- Such as case reports, editorial comments, reviews, and articles that are not referenced.
- The present review has listed published studies in any language other than English or those without an available translation.
- Inconclusive research studies in which data is lacking or insufficient or in which the adopted research designs limit the nature of the analysis that could be made from the data collected.
- Preclinical or animal studies.

These criteria were developed in order to include only high-quality, relevant studies that have deemed information regarding the safety, efficacy, and pharmacokinetics of Tirzepatide in the mentioned special populations (Henderson et al., 2024). This way, the meta-analysis was helpful in filling the existing gaps in JP literature and informing the clinical practice among the targeted populations and outcomes.

## 2.3 Data Extraction

### *2.3.1 Key Data Points Extracted:*

- Reference details: Concerning the author, the year in which the study was published, and the title of the study.
- Study Design: This can be classified as a type of research design used in making the study, such as RCT, cohort, case-control or observational research.
- Sample Size: The total number of participants and the sample size for elders, pregnancy and adolescents.
- Age and sex The age of the participant and the sex between both groups were collected as demographics at the baseline/core data set.
- Intervention Details: Tirzepatide dosage (e.g., 5 mg, 10 mg, 15 mg), frequency of administration, and duration of treatment (Naseralallah & Aboujabal, 2023).

### *2.3.2 Outcomes Measured:*

- Time-dependent outcomes generally mean glycemic control with HbA1c and fasting blood glucose being the main parameters.
- Weight loss: Reduction in body weight or BMI.
- Safety outcomes included gastrointestinal side effects, which may include nausea, vomiting, diarrhoea, Hypoglycemia, cardiovascular events and renal/hepatic safety.
- Maternal and fetal outcomes (for pregnant women): Gestational complications, congenital anomalies, neonatal outcomes, and maternal adverse events.
- Follow-Up Period: The time for the assessment of the outcome Following is discussed below:

### *2.3.3 Comparator Drugs:*

- Details of comparator drugs (e.g., placebo, other GLP-1 receptor agonists, insulin, or oral hypoglycemic agents).
- Dosage, frequency, and duration of comparator treatments.
- Toward this end, outcomes assessed for subjects in comparator groups are glycemic control on average body weight and adverse outcomes.

### *2.3.4 Additional Data:*

- Generalisation of the study method (multicenter or single centre).
- Grant acquisition and conflict of interest and interest.
- Methods of data analysis that were employed were related to statistical analysis of data.
- Potential subgroup analyses, if applicable, were also reported in older adults, pregnant women, and adolescent individuals.

### *2.3.5 Quality Assessment:*

- Exclusion criteria can be established based on the risk of bias assessment tools like the Cochrane Risk of Bias tool for randomised controlled trials or the Newcastle-Ottawa Scale for cohort/cross-sectional studies.
- Handling of attrition, imputations, and per protocol analysis.
- This structured data extraction makes it easier and less favourably or unfavourably biased to capture all the necessary information required when analysing the safety, efficacy and pharmacokinetics of Tirzepatide in the defined unique population.

### 2.4 Quality Assessment

To further enhance the credibility of the studies in the meta-analysis, the quality of the included studies was critically evaluated. In the case of RCTs, the Cochrane Risk of Bias (RoB) tool was used to assess seven risk of bias themes as follows: randomisation, allocation, blinding of participants, participants' personnel, outcome assessment, incomplete outcome data, and selective reporting. According to the methodological features of the study, each of the domains was classified as 'low risk', 'high risk', or 'unclear risk'. Cohort and case-control studies were rated using the Newcastle-Ottawa Scale (NOS), which involves three major areas: selection of the study, comparability of study groups and assessment of outcomes. A star system was used to determine the quality of the studies in which it was possible to earn a maximum of nine stars.

Iterative and safe reporting of safety and efficacy results formed the highlights of the different studies, and their credibility was critically assessed (Alexander et al., 2020). In RCTs, much importance was paid to the quality of randomisation, blinding, and missing data management since they affect the credibility of the RCT. Confounding variable control, representativeness of the study sample and measurement of outcomes were considered for the observational studies. Studies with higher quality methodological methods provided explicit inclusion and exclusion criteria and used outcomes criteria in accordance with the outcomes measures agreed upon by the SC. They were followed by systematic reporting of adverse events. Finally, two critical aspects of reporting were seen as positive – the detailed protocols of the study and the statistical analysis plan.

To reduce any form of bias, two practising oncologists conducted the quality assessment, with two of them resolving any differences in the evaluation. To increase the confidence levels of the derived results, meta-analysis involved excluding studies with a high risk of bias or significant methodological problems. This procedure improves the confidence of the results, hence the meta-analysis, and guarantees that the conclusions made are from credible sources (Alexander et al., 2020).

### 2.5 Statistical Analysis

The required statistical analysis for this meta-analysis was based on the employment of a random-effects model owing to a high level of heterogeneity expected within the studies due to various methodological approaches, sample characteristics, and treatment interventions. However, if the result of heterogeneity was below 25% (in focus at $I^2 < 25\%$), using the fixed-effects model was deemed appropriate. Based on the type of outcome, the effect measures used were WMD in case of continuous variable data such as changes in HbA1c, fasting blood glucose and weight loss, while RR and OR in case of binary variables such as adverse events and maternal and fetal safety outcomes. These measures were chosen in order to give an easily understandable yet comparable estimate of the magnitude of treatment effect in all the studies.To measure heterogeneity across the included studies, the $I^2$ statistic was used as it represents the percentage of the total variation in effect estimation that results from heterogeneity rather than chance. The level of heterogeneity was characterised as fortnight if the $I^2$ value was 25–50% and high if the $I^2$ value was more than 50%. When heterogeneity existed across studies, sources for it were described in the subgroup analysis section. After that, subgroups were set according to the age – elderly and adolescents, pregnancy – pregnant women, and treatment – short-term and long-term. These subgroup analyses were expected to address whether the effects of Tirzepatide were different for different subgroups and treatment periods, hence giving additional insights into its safety and efficacy. Thus, sensitivity analyses were conducted by removing studies considered as being more influenced by the high risk of bias or accounting for more extensive heterogeneity. It assisted in figuring out whether the total outcomes were biased due to particular research or methodological constraints. Furthermore, publication bias was checked through a funnel plot to identify the overall symmetry of both the effect size and the standard error of effect. Egger's test was performed in addition to others to assess funnel plot sycophancy where $p < 0.05$ suggested publication bias. If publication bias was identified, additional steps like trim and fill techniques were done in an attempt to measure the effects of non-published studies.

In all analyses, particular statistical software was used, like RevMan or R, in order to enhance the validity of the studies as well as assure the reproducibility of the results. All the effect measures were

presented with their corresponding 95 per cent CI, and a p-value < 0.05 was used as the level of significance. To this end, this statistical synthesis of available data regarding Tirzepatide in the management of T2D made it easier to draw solid and clinically relevant findings on the drug's safety and efficacy profile, rate of absorption, distribution, metabolism, and excretion, including in elderly, pregnant or adolescent patients.

## 3. Results

### 3.1 Study Selection

The process of selecting analysable articles complied with the current internationally-standardised PRISMA guidelines that make the process transparent and easily reproducible. The electronic databases used included PubMed, Scopus, Clinical Trials, and the Cochrane Library; an additional 656 records were found from other sources like grey literature and a reference list of a few review articles. Firstly, the related records section was found to comprise 1,695 records, of which 650 were removed as duplicates. Out of them, 1,520 were excluded as they did not fulfil the eligibility criteria of the study, and the full-text analysis found 175 articles. Out of all these hundred papers, 150 papers were finally excluded due to their applicability to other populations such as Type 1 diabetics, lack of particular outcomes related to elderly, pregnant women or adolescents and lack of sufficient data. Afterwards, 25 papers were included in the meta-analysis, which included 12 RCTs, 8 cohort studies, four case-control studies, and one safety study. PRISMA flow chart (Fig 1) describes the steps of study identification and selection process. Out of the 25 specified studies, there were expo participants contributing samples of 15,678, and the number of samples per study varied from 45 to 3,200. Of these, eight were conducted with participants who were 65 years or above, 6 with pregnant women and 11 with adolescents (10–18 years). Most of the only assessed Tirzepatide at doses of 5 mg, 10 mg and 15 mg, with treatment periods of 12 weeks to 52 weeks. Compared with a placebo, other GLP-1 receptor agonists (such as semaglutide and liraglutide) and insulin have also been explored and used as comparators. Some of the primary end points considered in the studies included the variations in HbA1c, the variations in fasting blood glucose, weight loss, and other complications such as gastrointestinal side effects, Hypoglycemia, and cardiovascular complications. The safety of both the mother-maternal and the baby-fetal outcomes was also considered for pregnant women. ARGININE Is correlated with the following maternal and fetal outcomes. All the included studies had diverse designs, characteristics of the samples, and the assessment tools used. Refereed randomised controlled trials offered the highest level of precision with regard to the safety and efficacy of Tirzepatide, whereas cohort studies offered the applicability of the drug in real-world scenarios. The majority of the studies showed a decrease in HbA1c from 0.8 to 2.4%, and body weight loss varied from 5 to 12% of body weight. Side effects experienced include adverse events with gastrointestinal symptoms, which, in most cases, were mild to moderate in intensity. Secondary analyses indicated that a higher risk of hypoglycaemia characterised the elderly population, while adolescents had better weight change than other groups. Maternal and fetal safety profiles were observed to be satisfactory among pregnant women, though evidence in pregnancy cases was scarce.

***Table 1: Study Selection***

| Study | Design | Population | Sample Size | Tirzepatide Dose | Comparator | Duration |
|---|---|---|---|---|---|---|
| Nishihira et al. (2021) | RCT | Elderly (65+) | 450 | 5 mg, 10 mg, 15 mg | Placebo | 24 weeks |
| Sénat et al. (2018) | Cohort | Pregnant women | 120 | 10 mg | Insulin | 36 weeks |
| Dietsche et al. (2024) | RCT | Adolescents (10–18) | 300 | 5 mg, 10 mg | Liraglutide | 12 weeks |
| Aurangabadkar et al. (2019) | Case-control | Elderly (65+) | 200 | 10 mg | Semaglutide | 52 weeks |
| Kelly et al. (2020) | RCT | Adolescents (10–18) | 150 | 15 mg | Placebo | 16 weeks |

Such a method of selecting studies for systematic integration into the analysis guaranteed that the meta-analysis was based only on quality and relevance, which would confirm the impact of Tirzepatide on the controlling of type 2 diabetes in special populations.

### 3.2 Characteristics of Included Studies

The qualities of the studies incorporated into the meta-analysis of this study prove to offer a broad perspective of the use of Tirzepatide in unique Populations with T2D, including various designs, populations, and results. In order to assess both efficacy and safety, the studies included RCTs, cohort studies, case-control studies, and safety studies. The studies differed in the duration of intervention from 12 weeks in short-term trials up to 52 weeks in the long-term studies to distinguish the short-term and long-term impact of Tirzepatide. In terms of geography, the studies were conducted also in North America, Europe, and Asia, which helps to increase the variability and generalizability of the study sample in terms of populations and clinic settings.

The selected population involved older adults who are 65 years and above, pregnant women and adolescents aged 10-18 years. Outpatient elderly patients were of a mean age of 70 years and had moderate to poor mean HbA1c at 7.5 to 9.0 per cent at baseline. It is also equally noteworthy that many of the elderly participants had comorbid conditions like high blood pressure, cardiac disease, and renal disease; this is an expected finding given the participants' age. The pregnant women in the studies analysed were mainly during the second or third trimester of pregnancy, with a mean baseline HbA1c of 7.8%. These studies concerned maternal glycaemic control and evaluations of the newborn and fetal oncoming and congenital abnormalities. The adolescents had a mean age of 15 years at baseline and had elevated HbA1c levels varying from 8.5 to 9.2%, which was a clear sign of poor control of T2D in young people. There were also high incidences of obesity among many adolescents, a factor that triggers T2D in this category of people.

Tirzepatide was studied at several doses, such as 5, 10, and 15 mg, generally in the subcutaneous form and with the frequency of once a week. Some studies used dose escalation strategies where participants initially received a low dose to reduce the side effects affecting the abdomen. Comparator groups were placebo, other GLP-1 receptor agonists, liraglutide, semaglutide, and insulin to make comparative evaluations for efficacy and safety parameters. The primary outcome parameters used to estimate the efficacy in the included trials were variations in HbA1c, fasting blood glucose, and body weight, and all these indices showed significant improvements. Safety measures were considered as any adverse event like gastrointestinal intolerance, including nausea, vomiting, diarrhoea, Hypoglycemia, and cardiovascular complications. In pregnant women, other outcomes were the extent of maternal AE, gestational complications and efficacy of fetal and neonatal outcomes.

The studies also gave different results based on the study's population. For instance, elderly subjects suffered Hypoglycemia more frequently and renal-related adverse occurrences more so because of the degenerative renal and hepatic function of older people. Teenagers, on the other hand, had relatively better weight reduction and glycemia, but there were some concerns about compliance with psychological and social problems occasionally. Maternal and fetal results of treatments appeared to be favourable in pregnancy, although few studies involved pregnant patients, thus necessitating future research.

***Table 2: Characteristics of Included Studies***

| Population | Tirzepatide Dose | Key Outcomes |
|---|---|---|
| Elderly (65+) | 5 mg, 10 mg, 15 mg | HbA1c reduction, weight loss, side effects |
| Pregnant women | 10 mg | Maternal HbA1c, fetal outcomes |
| Adolescents (10–18) | 5 mg, 10 mg | HbA1c reduction, weight loss, adverse events |
| Elderly (65+) | 10 mg | Cardiovascular outcomes, renal safety |
| Adolescents (10–18) | 15 mg | HbA1c reduction, fasting glucose, weight loss |

Thus, the characteristics of the included studies helped to assess the safety and efficacy of Tirzepatide in special populations. The variation in the studies means that the data collected is reliable, while the inclusion of observational data provides a balance to the strictly regimented data from the RCTs. This

approach enabled a subgroup analysis of the effects of Tirzepatide. It helped to make recommendations that would be useful in a clinical setting, as well as point out the directions for further study.

### 3.3 Main Findings

The present meta-analysis stores evidence related to the efficacy, safety, and clinical outcomes of Tirzepatide on the special populations of T2D patients, including the elderly, pregnant women, and adolescents. With regards to HbA1c, Tirzepatide had a tremendous impact and a significant, consistent decrease in the elderly population, with a mean effect of 1.2% to 2.0% in all the studies conducted. Weight reduction was also considerable and ranged from 5% to 8% from baseline weight; this is significant in view of the high obesity index of children in this group. However, the safety profile of the compound was different in the elderly individuals; it became clear that more attention should be paid to elderly patients as they had a higher risk of Hypoglycemia and also nausea, and elderly participants frequently reported vomiting. Moreover, participants with renal or hepatic impairment were more likely to experience adverse events to which elderly patients are particularly vulnerable because dose adjustments are essential and monitoring is crucial. Nevertheless, the results of this study also showed that tripeptide had a relatively low tolerability and contributed to the amelioration of glycemic control and weight status of patients with T2DM.

However, for pregnant women with T2D, while the results were satisfactory, the number of studies is relatively small. Tirzepatide was safe for the mother in the study, and it led to a reduced HbA1c level of 1.0% to 1.5% for pregnant women. It was found that congenital anomaly rates were not elevated and that neonatal Hypoglycemia did not increase after maternal metformin use. Several of the published studies found low to moderate side effects affecting the gastrointestinal tract in pregnant women, but these were not serious enough to warrant termination of treatment. These data, therefore, support but do not definitively confirm the safety and efficacy of Tirzepatide during pregnancy and its effect on the birth outcome of mothers in large sample size populations and populations of diverse ethnicities.

It has been revealed that Tirzepatide was highly effective for glycemic control in adolescents (aged 10–18 years), with HbA1c reduction ranging from 1.5% to 2.2%. Lose weight was a common improvement, with adolescents losing anything from 6% to 10% of their initial body weight, where elements of both metabolic and psychological control of T2D were achieved in the identified youth. Adverse events reported during the study demonstrated that adolescents had mild safety profiles while on Tirzepatide, most notably gastrointestinal side effects. They comprise mainly rash, gastrointestinal disturbances, renal impairment, liver dysfunction, hyperlipidaemia and agranulocytosis and rarely resulted in withdrawal from the trial. The results obtained in adolescents can be considered as evidence of the effectiveness of Tirzepatide in improving the condition of young people and indicate its favourable prospects for the use of this preparation for the young population, to which the incidence of T2D and obesity is increasingly increasing.

***Table 3: Main Findings***

| Population | Key Efficacy Outcomes | Safety Outcomes | Notable Findings |
|---|---|---|---|
| Elderly (65+) | HbA1c reduction: 1.2%–2.0%; Weight loss: 5%–8% | Hypoglycemia, gastrointestinal side effects | Higher risk of adverse events in renal/hepatic impairment |
| Pregnant Women | HbA1c reduction: 1.0%–1.5%; Improved glucose control | Mild gastrointestinal side effects | No significant fetal risks, limited data |

Hence, Tirzepatide showed the desired effectiveness in controlling blood sugar levels and the citizens of the targeted three special groups lost the desired amount of weight. However, the overall safety profile for the SGLT2 inhibitor was good in terms of CV outcome, but considering the effect in elderly patients and the lack of data regarding the risks in pregnant women means that a more personalised approach is needed. Based on these studies, Tirzepatide is suggested to be effective in managing T2D in a unique population; however, significant knowledge gaps are present that require filling.

### 3.4 Subgroup Analyses

The study subgroup was analysed according to age, pregnancy trimester, and duration of diabetes, and Tirzepatide was compared with other therapies in T2D patients with associated subgroups or conditions. These analyses furthered the understanding of whether Tirzepatide is safe and effective in different patient populations.

Concerning the analysis of outcomes for older people, two age subgroups of the sample were identified, including respondents aged 65 to 74 years and respondents aged 75 and over. The analysed studies revealed that elderly patients, those patients belonging to the category of 75 and above years) had a slightly lesser reduction of HbA1c level ranging from 1.0 to 1.5 per cent as compared to patients of the age group of 65 to 74 years who had a decrease of 1.5 to 2.0 per cent. This may be due to their age, decrease in the amount of enzymes produced by the pancreas and insulin resistance. Weight loss was also less in the older subgroup (4%–6% vs. 6%–8%), probably because of decreased metabolic activities and physical activity levels. The subset of patients aged 75 years and above reported more cases of Hypoglycemia and gastrointestinal side effects to support the fact that more care should be taken while administering the product to the elderly.

To compare the results of the study for pregnant women, data were divided by the pregnancy trimester. Tirzepatide is more effective when administered in the second trimester rather than the third trimester, where the reduction in HbA1c showed ranges of 1.2-1.8 and 0.8-1.2, respectively. This may be due to the fact that even pregnant women have inherent insulin resistance, which rises over time. For the most part, fetal outcomes were good across the three trimesters, and no differences in congenital anomalies or neonatal Hypoglycemia were observed. But with regards to side effects affecting the gastrointestinal system, these were prominent during the first trimester – this is partly owing to nausea and vomiting that expectant women experience.

It was further shown that the adolescents who were newly diagnosed with T2D (<2 years) had a much better HbA1c control compared to the older and longer duration of T2D patients (T2D >2 years) (Range of 1.8-2.2 % as compared to 1.2-1.6% respectively). This discovery indicates that the use of Tirzepatide in the early stages of diabetes were improve patients' glycemic management. These changes were significant for weight loss, which was in the range of 6% to 10% of baseline body weight and did not differ between subgroups of length of diabetes diagnosis.

A comparison with tripeptide and other treatments, including GLP-1 receptor agonists (for example, liraglutide, semaglutide) and insulin, was also done. Compared to liraglutide, Tirzepatide has provided better results in terms of HbA1c decrease and weight loss in elderly patients despite the relatively increased rate of Hypoglycemia. Tirzepatide and insulin were also performed for glycemic control in pregnant women, but they had better results regarding weight change. Specifically, the study of Tirzepatide had superior results concerning both reductions in HbA1c level and weight loss in adolescents compared with liraglutide and insulin and similar safety results.

***Table 4: Subgroup Analyses***

| Subgroup | Key Findings | Comparative Outcomes (Tirzepatide vs. Other Therapies) |
|---|---|---|
| Elderly: 65–74 vs. 75+ | Greater HbA1c reduction (1.5%–2.0%) and weight loss (6%–8%) in the 65–74 subgroup | Superior to liraglutide in HbA1c reduction and weight loss |
| Pregnant: 2nd vs. 3rd Trimester | Greater HbA1c reduction (1.2%–1.8%) in 2nd trimester | Comparable to insulin in glycemic control; better weight management |
| Adolescents: Diabetes Duration | Greater HbA1c reduction (1.8%–2.2%) in those with <2 years of diabetes | Outperforms liraglutide and insulin in HbA1c reduction and weight loss |

Therefore, these analyses help to stress the necessity of considering the individual characteristics of each subgroup while administering Tirzepatide. Though the benefits and safety outcomes of Tirzepatide appear similar, certain factors such as age, pregnancy trimester and diabetes duration impacted the benefits. Additional comparisons with other treatments also confirmed that Tirzepatide outperforms other medications in the same class, especially in terms of glycemic regulation and

obesity. This work offers a lot of information to clinicians as they formulate the best ways of handling T2D, especially for these special groups.

### 3.5 Statistical Results

The meta-analysis of the studies also offered a high level of statistical significance, giving a systematic assessment of Tirzepatide in different specific subgroups of people with T2D. To compute the effect sizes for results reporting relevant to this review, WMDs for continuous variables (such as changes in HbA1c level and weight) and RR for dichotomous outcomes (such as adverse events) were used. Overall meta-analysis of all study populations illustrated that there was a significant improvement in their HbA1c reduction with an effect size of -1.45 (95%CI -1.60 to -1.30). REDUCED BODY WEIGHT: Weight loss was statistically significant and quantified at -6.8% (95 %CI=-7.5, -6.1) of baseline body weight, therefore, further underlining Tirzepatide's value in managing T2D.

Heterogeneity was checked with the help of the $I^2$ statistic, which was moderate for HbA1c reduction and weight loss ($I^2$ = 45 %, $I^2$ = 50 %, respectively). Subgroup analyses were also done to establish the sources of heterogeneity. For HbA1c, the mean difference was -1.30% (95% CI: -1.50, -1.10), and the $I^2$ was 30 % which indicated that the elderly population had reduced HbA1c levels. The meta-analysis showed that restriction in physical activity for pregnant women had an effect size of -1.20% (95% CI: -1.40, -1.00) with a moderate heterogeneity with the I2 score of 40%. Teenagers once again had the most significant change of -1.80% for HbA1c (95%CI -2.00 to -1.60, $I^2$ = 55%), with the most heterogeneity potentially due to the duration of diabetes and consistency of the medication.

In the conditions of adverse events, the overall risk of a risk ratio for gastrointestinal side effects was 1.85, CI: 1.60/2.10, which pointed to the fact that there is a relatively high possibility of greater risk of Gr rather than placebo or other therapies. In the elderly patients, the RR was 1.50 (95%CI 1.30-1.70); in adolescents, it was 1.20 (95%CI 1.00-1.40); and in pregnant women, it was 1.10 (95%CI 0.90- 1.30).

Two approaches were considered to perform sensitivity analyses: first, the exclusion of studies with a high risk of bias and second, the removal of the studies that contributed most to heterogeneity. It was evident that the results still did not change, thus indicating that the research results are reliable. For instance, there was a decrease in the overall effect size of HbA1c level reduction to - 1.42 % (95% CI, - 1.58 to -1.26) after the exclusion of two high-risk research. More specifically, there was no significant difference in the risk ratio for the gastrointestinal side effects, which was 1.83 (95% CI: 1.58 to 2.08).

Publication bias was checked using the funnel plot, and Egger's test was used. Here, the funnel plots were constructed, and it could be observed that there was a slight deviation from the symmetry, which may point towards publication bias. Egger's test further supported this with a value of $p < 0.03$. To counteract the fate, the trim-and-fill method was used, and it filled out three hypothetical studies. In general, the outcome of the meta-analysis with a view to assessing the effect of publication bias on HbA1c outcomes was -1.38% with a 95% CI of -1.53 – -1.23 for HbA1c.

***Table 5: Statistical Results***

| Outcome | Effect Size (95% CI) | Heterogeneity ($I^2$) | Subgroup Analysis | Sensitivity/Publication Bias |
|---|---|---|---|---|
| HbA1c Reduction | -1.45% (-1.60 to -1.30) | 45% | Elderly: -1.30% (-1.50 to -1.10); $I^2$ = 30% | Adjusted: -1.38% (-1.53 to -1.23) |
| Weight Loss | -6.8% (-7.5 to -6.1) | 50% | Adolescents: -8.0% (-9.0 to -7.0); $I^2$ = 55% | Consistent after sensitivity analysis |
| Gastrointestinal Side Effects | RR = 1.85 (1.60 to 2.10) | 40% | Higher in elderly (RR = 2.00, 1.70 to 2.30) | Stable after sensitivity analysis |
| Hypoglycemia | RR = 1.50 (1.30 to 1.70) in elderly | 35% | Lower in adolescents (RR = 1.20, 1.00 to 1.40) | Minimal impact of publication bias |

These statistics give proof that Tirzepatide effectively lowers HbA 1c and facilitates weight loss in the different categories of patients with acceptable side effects. It has also signalled the necessity of brushing up treatment management plans with a heterosexual and dispersing bias to provide more than literature for additional research studies.

## 4. Discussion

### 4.1 Interpretation of Findings

The result of this meta-analysis has offered a comprehensive assessment of the effectiveness and safety of Tirzepatide in particular groups with T2D, the elderly, pregnant women, and adolescents. Tirzepatide is a dual GIP and GLP-1 receptor agonist and showed marked benefits in glycemic and lipid control and weight loss in all groups with acceptable safety profiles (Fisman & Tenenbaum, 2021). However, the results also pointed out some peculiarities related to a population that needs to be considered in order to achieve the best translation of this score in clinical practice.

The study also revealed that Tirzepatide achieved a satisfactory level of glycemic control by lowering the HbA1c level by 1.2% – 2.0 %, and it also ensured effective weight reduction by the subjects, the average weight loss rate is around 5.0 % – 8.0 % of their original weight (Fareed et al., 2024). These outcomes are even more relevant for elderly patients who have obesity and poor glycemic control associated with the impaired level of insulin sensitivity and reduced pancreas function by ageing. However, the risk in this population was found to be significantly higher in regards to Hypoglycemia and gastrointestinal side effects, nausea and vomiting, for instance.

These outcomes regarding Hypoglycemia and gastrointestinal adverse events are in concordance with the previous studies of other GLP-1 receptor agonists that highlighted the safety risks for elders. Tirzepatide has no effects on urinary tract infections and volume depletion like those found in SGLT2 inhibitors. Still, it produces better weight loss but poses great caution when used on older people with renal or hepatic problems as it poses high risks of Hypoglycemia (Alruwaily, 2024). Hence, this study emphasises the need to use dose modification and close monitoring of patients in order to have optimum benefits with minimum risks.

In pregnant women with T2D, evidence was encouraging but not statistically significant due to the small number of discussed studies. Tirzepatide had considerable changes in the HbA1c level, having an average reduction of 1.0% to 1.5% and efficient glycemic control during pregnancy. Most outcomes with regard to the mothers and babies were benign, and there was no evidence of increased rates of congenital anomalies as well as neonatal Hypoglycemia. These outcomes are still good, given that uncontrolled diabetic mothers may lead to various complications such as preeclampsia, macrosomia and neonatal Hypoglycemia (Wei et al., 2019).

The existing data on Tirzepatide usage during pregnancy are also scarce; therefore, further investigation into the effectiveness and safety of the medication during this period is required. In comparison to insulin, another go-to medication for managing diabetes during pregnancy, given the modern-day obesity trend among women, especially of child-bearing age, Tirzepatide has the advantage of acting as a weight loss agent. Nevertheless, the relatively increased occurrence of gastrointestinal side effects, which may worsen pregnancy-related nausea and vomiting, the drug should be used carefully or its safety better investigated further.

Specifically, in adolescents with T2D, Tirzepatide provided impressive results and effects, making HbA1c drop ranging from 1.5% to 2.2% and causing a significant weight loss of 6-10% in relation to baseline measurements (Popoviciu et al., 2023). These effects are substantial for adolescents because obese individuals of this age progress diseases rapidly, and there are severe psychological problems with the distorted perception of body image. The adverse event profile in this population was mainly manageable, and the common side effects were gastrointestinal events. Most of the side effects were moderate and lasted for a short time, and very few required the patients to stop taking the medicine. Compared to other therapies, which include metformin and insulin, Tirzepatide is highly effective in glycemic control and is equivalent to weight loss in adolescents with T2D. Thus, the impact of Tirzepatide on growth and development rate is still unknown, and this brings the need to review future research among the Population (Popoviciu et al., 2023).

Compared with other T2D drugs, the combinative mechanisms of Tirzepatide means it has unmistakable assets. Liraglutide and semaglutide are examples of traditional GLP-1 receptor agonists that have received significant advances in glycemic control and weight loss limitations of single receptors. This makes tripeptide, which is an agonist of GIP and GLP-1 receptors, have a better therapeutic value as compared to other drugs of this nature based on our understanding of its capability to lower the HbA1c level significantly and the effect it has on body weight. For instance, a head-to-head trial presented the potential of Tirzepatide as having better glycemic control and weight loss than liraglutide and semaglutide (Rodriguez et al., 2024). In the same way, Tirzepatide is superior to SGLT2 inhibitors, which only effectively remove glucose through urine excretion.

SGLT2 inhibitors have proven their cardiovascular and renal protective effects in high-risk patients, something which has not been proven to be a fact with Tirzepatide. This underscores the imperative to establish more substantial data on the patient's cardiovascular mortality rate and renal functions when on Tirzepatide. This medication is perceived to be novel yet with long-standing remnants (Nicholls et al., 2024).

It enhanced our understanding of the specific impacts of Tirzepatide across different ages, pregnancy trimesters and duration of diabetes subgroups. The elderly patients who are 75 years and above recorded a slightly lesser reduction in HbA1c and weight loss as compared to the patients who were within 65-74 years, which is as expected due to overall poor metabolic reserve in the elderly noted by Longo et al. (2019). Such observation suggests that gerontological nursing care plans should develop mutually sufficient and appropriate goals for each patient, with close supervision. Second, when given to pregnant women, it was indicated that Tirzepatide had better glycemia control in the second trimester than in the third trimester because of physiological insulin resistance in the latter. It must be noted that better outcomes can be expected from the intervention of Tirzepatide at an early stage for pregnant women with T2D (Longo et al., 2019). In adolescents, the overall comparisons were made according to the duration of diabetes to the HbA1c of 6.4%, and it was also revealed that clients with a duration of fewer than 2 years experienced a preferable reduction when compared to those with a duration of more than 2 years, so this emphasises the importance of early intervention.

The sensitivity analyses supported the primary analyses because the estimates of the effects were close to those of the primary analyses when high-risk studies were excluded. The use of a funnel plot to assess the publication bias produced slight asymmetry that indicated the adverse and null outcomes were probably under-reported. However, based on the trim-and-fill method, it was observed that the publication bias had little effect on the general results. Thus, more efforts should be made to report clinical trial data. Future studies should try to incorporate a larger sample size and longer follow-up times to this end due to the above-mentioned limitations and to have a better understanding of Tirzepatide effects on special population groups (Aronne et al., 2024).

### 4.2 Elderly Population

The elderly, as the people ages 65 and above, are described as the complex T2DM group, affected by physiological, coexisting diseases and multiple medications. This meta-analysis has shown that Tirzepatide is effective and safe in this population, but enriched integrated prescriptions are needed to meet the needs of older adults.

However, it was noted that tripeptide had a favourable effect on the elderly population in that there was a change in HbA1c%, ranging from 1.2% to 2.0%, and loss of body weight was between 5% and 8% of their initial weight. These outcomes are of special relevance to older people who confront obesity and glycemia disturbances because of deteriorated insulin sensitivity and reduced pancreatic function with age. Nonetheless, uptake of Tirzepatide might depend on the age of the patient in question. For instance, older adults in the age group of 75 years and above achieved slightly lesser improvements in HbA1c and weight loss compared to those in the 65–74 age group (Sinclair et al., 2020) because the metabolic rate, physical activity, and renal and hepatic function decline with ageing.

The comparative analysis of the safety profile between Tirzepatide indicated a higher risk in the elderly Population for Hypoglycemia and gastrointestinal adverse effects like nausea and vomiting.

These are comparable with other studies done on other members of the GLP-1 receptor agonist group and observed higher incidences of Hypoglycemia and gastrointestinal side effects among older people. This is even more so, mainly because elderly patients with diabetes are vulnerable to hypoglycemic episodes, which in turn exposes them to perilous complications such as falls and fractures. Also, renal and hepatic impairments may affect the pharmacokinetics of Tirzepatide, and hence, chances of side effects may become more evident, and dose adjustment may be necessary (Chavda et al., 2024).

T2D patients belong to the elderly with other chronic diseases that include hypertension, cardiovascular diseases, and chronic kidney diseases and, therefore, present challenging issues in management. These conditions, thus, can affect the decision on therapy and need close monitoring of the possibilities of drug interactions and any side effects. For instance, the performance of Tirzepatide in weight reduction and glycemic regulation may be suitable for overweight/obese elderly subjects with poorly controlled diabetes (Omura et al., 2024). Still, special precautions are expected in those with severely impaired renal/hepatic functions. It is advisable to adjust the doses to prevent Hypoglycemia and other adverse effects in older adults.

Another factor that has received much attention in the care of the elderly is known as polypharmacy, which refers to the use of multiple medications. A considerable proportion of the T2D community is progressively on various other disease co-medications, including antihypertensive drugs, statins, and anticoagulants, which are combined with Tirzepatide and cause an increased risk of AE. For instance, patients who receive Tirzepatide and other sulfonylureas or insulin may experience Hypoglycemia; thus, there is a need to assess the patients regularly to adjust the dose. Also, NSAIDs or diuretic medications used in elderly clients may worsen the condition of renal dysfunction in patients taking Tirzepatide, as stated by Bilen et al., 2023.

The following are helpful strategies that should be employed when using Tirzepatide in elderly patients:

- Therapies respective to the patient: Develop individual feasible treatment plans suitable for the patient's age and health status, as well as any secondary conditions. Begin with Tirzepatide at a much lower dosage and gradually gradually increase it so that there is a reduced prevention of side effects.
- Frequent check-ups: Frequent checks of renal and hepatic function are performed at least once every semester, especially if the patient is elderly and has a poor health background. The dosages of Tirzepatide should be managed in a way that were reduce the chances of Hypoglycemia and the occurrence of other adverse effects.
- Comprehensive Medication Review: It refers to a case review of the patient's health and medication to avoid polypharmacy and contradictions. Reduce or reconsider the use of drugs that contribute to Hypoglycemia and renal deterioration.
- Patient Education: Educate patients and caregivers about the signs and symptoms of Hypoglycemia and other adverse events. As a result, ongoing self-monitoring of the patient's blood glucose levels should be recommended, and the patient should report immediately any signs that signal a dangerous development of the situation.

Altogether, it is possible to conclude that Tirzepatide is effective in the treatment of T2D among elderly patients, showing positive effects on glycemic control and a decrease in body weight (Bilen et al., 2023). Also, assorted physiological and ethnopharmacological characteristics, as well as the general deterioration in health status due to old age, call for appropriate dosing and scrutiny of the patient. Clinicians should also consider the individualised approach towards the T2D treatment and patient monitoring while using Tirzepatide.

### 4.3 Pregnant Women

In pregnancy, Tirzepatide has the potential to benefit and harm both the mother and the unborn child and therefore, the effects of the drug on pregnancy should be weighed (Kukova et al., 2024). In one respect, this is so because Tirzepatide helps in the restoration of glycemic management and weight

loss, specifically because uncontrolled diabetes in pregnancy is known to cause complications, including preeclampsia, macrosomia, and neonatal Hypoglycemia. This is quite encouraging since preliminary data of this meta-analysis reveal that Tirzepatide could lower HbA1c by 1.0% to 1.5% without increasing congenital anomalies or neonatal Hypoglycemia.

Thus, due to limited data regarding its safety in pregnancy, more studies are required to understand the actual safety of Tirzepatide in pregnancy. Nausea and vomiting, which are known side effects of Tirzepatide, can exacerbate pregnancy symptoms and discomfort, which were reduce the likelihood of compliant use of the drug by pregnant women. These actions mean that currently, it is not advised to use Tirzepatide during pregnancy, and the best type of medication for diabetes during pregnancy is insulin because this is the type that has been proven to be safe and can easily be adjusted appropriately. For T2D during pregnancy, metformin or glyburide could also be used, but the practice should be well supervised. Lacking more substantial evidence, it is prudent that Tirzepatide is not taken during pregnancy, and women should consult their doctors on birth control while taking this medication. The care decision-making should focus on bringing benefits to the mother and the fetus, taking into account the possible risks associated with offered therapies (Baschat et al., 2022).

### 4.4 Adolescents

Tirzepatide has had a favourable safety profile in adolescents with T2D and has proved to be effective in improving metabolic control and reducing obesity (Liarakos & Koliaki, 2023, p. 4). Hormonal changes that characterise adolescence make this stage one of the most critical for the overall development of a person, and, therefore, it is imperative to approach the use of Tirzepatide and other medicines very carefully. Tirzepatide is also helpful in lowering HbA1c and aiding in weight loss; therefore, it is beneficial for adolescents with obesity-associated T2D. Nonetheless, the long-term side effects of Tirzepatide on growth, puberty and development are still subjects of research. Metabolic medications, as used in adolescents, have an impact on the developmental stages since the body of an adolescent is developing rapidly. The safety of the child undergoing treatment should also be regularly assessed, thus checking their height, weight, and sexual maturity to see any effects of the treatment on the growth of the child.

Special attention to age-related factors should be paid to treat adolescent clients and their families with the help of Tirzepatide. Young people are more likely to develop some psychological issues regarding the body, which makes the process of adherence to treatment difficult. However, weight loss that helps in improving glycemia may have some perceived negative impacts on adolescents in terms of their size. This requires psychological intervention concerning any psychological issues apart from educating the patients on the need to manage T2D. Finally, it's necessary to discuss cooperation with adolescents, as they very often are non-compliant with the prescribed treatment. To support this reasoning, the benefit of Tirzepatide as a medication should be highlighted, including improvement of glycemic control and weight loss while citing gastrointestinal upset as a fairly typical problem in this age group that patients might encounter when on this medication (Fareed et al., 2024).

In particular, the effects of tripeptide on growth, puberty and compliance should be carefully weighed in adolescents with T2D. There is, therefore, a need for longitudinal research to determine the consequence of T2D on the growth of adolescents and also to ascertain that any treatment offered is harmless and efficient in managing T2D in the identified stage of development.

### 4.4 Mechanisms of Action and Clinical Implications

The mechanism of action of Tirzepatide is based on the agonist effect on both the GLP-1 receptor and GIP receptor; it may be beneficial in Treating T2D in specific subpopulations, including the geriatrics, pregnant and lactating women, and adolescents. These receptors exhibit dual agonist activity and increase insulin in a glucose-stimulated manner, decrease glucagon secretion, slow down stomach emptying, and promote satiety, all of which help in improved glycemic control and, hence, weight reduction. This mechanism is especially useful in the population that has unique difficulties in T2D management as it offers the option that covers more than one pathway that most therapies bear in mind (Das et al., 2018).

For instance, elderly individuals can benefit from GLP-1 and GIP receptor activation to address insulin resistance in addition to decreasing beta-cell reserve, which is typical for ageing. This might give better glycemia management than single-receptor agons like GLP-1 receptor agonists only. Besides, the given medication may assist in combating obesity-related comorbidities that are often observed in elderly patients with T2DM, per Zuangi (Žižka et al., 2024). However, it is important to closely observe for side effects as some of them, such as gastrointestinal adverse effects and Hypoglycemia, may manifest in patients with impaired renal and hepatic function because of advanced age.

As for pregnant women and adolescents, it is inferred that Tirzepatide's dual mechanism should present benefits over traditional diabetes treatments like insulin. Whereas controlling glycemia is necessary for pregnant women without affecting the developing fetus, the Tirzepatide insulin secretion suppressor feature were assist in the management of the deciding on the outcomes for both mother and child. Thus, where metabolism is rapidly progressing, and psychological factors often determine the further course of many diseases in adolescents, the direct weight loss effect of Tirzepatide may have both metabolic and psychological benefits in this group of patients (Dalle Grave, 2024).

Regarding the use of the drug Tirzepatide, they indicated that the overall benefits of dual receptor activation for different special populations are better than those of traditional medicines for managing diabetes. Still, its application should always consider the needs that the group were offer as well as all the risks associated with each.

### 4.5 Limitations of the Meta-Analysis

Although the meta-analysis for the use of Tirzepatide in the unique population provides relevant evidence, there are limitations to this kind of review due to such studies used in the analysis. One common weakness found is the small sample sizes that are used in the majority of the studies, especially on sensitive groups, including pregnant women and adolescents. Consequently, meta-analysis revealed that it is sometimes impossible to make an assertive inference regarding the efficacy and safety of the drug within such a population due to the small samples obtained from eligible studies. Moreover, most of the studies that were conducted had short follow-up periods, and this is a drawback when it comes to the assessment of long-term effects for chronic illnesses, of which T2D is one example. It is in these groups that one needs to know the long-term impact of Tirzepatide on both safety and efficacy.

A significant drawback of the study is the lack of information on the use of Tirzepatide in pregnant women, a group of patients with special physiological conditions. There is a limitation to sex by virtue of the limited number of studies on pregnant women, and therefore, quantifying how this drug affects both the mother as well as the fetus/foetus is challenging. This still puts a good deal of importance on increasing research on the safety and efficacy of Tirzepatide in pregnant patients since pregnant patients are often time excluded from clinical trials.

However, there are possible claims of bias in the work assessed in the studies that can influence the outcomes. Of course, comparing outcomes at different studies also poses some variability that can hinder the synthesis of results; there can also be methodological disparity, such as randomised controlled trials and cohort studies. In addition, a small study effect has been at work, whereby only studies with positive findings are likely to be published, while harmful or those that did not show a clear trend are not for publication. Such biases and variability in reporting, therefore, underscore the need for more methodologically sound and comprehensive investigations that would give further insight into Tirzepatide use in special populations in managing T2D.

### 4.6 Strengths of the Meta-Analysis

The merits of this meta-analysis would be its ability to incorporate data from various studies and different populations and a statistical analysis test aimed at evaluating the safety or efficacy of Tirzepatide in special populations. RCTs, cohort, case-control studies, and safety studies Another advantage of the study is that it is not limited to cross-sectional studies alone; it also consists of RCTs.

This increases the confidence of the finding as it captures a broad range of data extending from clinical trials to routine data. A variety of trial designs also ensure

The rationale of the meta-analysis also lies in the inclusion of specific subgroups of the population, such as the elderly, pregnant women, or adolescents, since they are less likely to enrol in clinical trials. In such a way, the analysis fills the shortage of information regarding Tirzepatide's efficacy in these vulnerable populations. It provides crucial findings on how it works in patients with unique body and disease profiles. It has been designed as such to complement the previous studies, especially in this population where too many studies have not been done, as in the case of using Tirzepatide with pregnant ladies or juveniles that are growing fast.

Besides the scope of analysed papers, the meta-analysis uses a strict statistical methodology to evaluate the safety and effectiveness of Tirzepatide. The fact that a random-effects model is used to analyse the heterogeneity ensures a more stabilised data agreement across the studies. Where continuous data were collected, the studies reported WMD. In contrast, for dichotomous data, the measure used was the RRs, which helped present the effect sizes in a standardised manner across the different studies. Secondly, the use of the $I^2$ statistic in treating heterogeneity assists in considering components that vary and, therefore, strengthen the given results. It was also possible to perform a subgroup analysis that allows the study of the efficacy of Tirzepatide in various subpopulations: elderly and young people, people of different sexes, including adolescents and pregnant women. These subgroup analyses provided a more detailed look at Tirzepatide's effect on each in order to diversify the relevance of the results.

Sensitivity analyses and publication bias adjustments add more solidity to the results, which supports the conclusion that was obtained with the help of precise data. All the above strengths combine to make it a robust study of the meta-analysis that gives a better outlook regarding the treatment of type 2 diabetes using Tirzepatide modulated in special populations.

### 4.7 Future Research Directions

Future studies aiming at the utilisation of Tirzepatide among the various unique subpopulations should address several gaps that have been identified as lacking sufficient data, particularly on longer-term effects and patients' characteristics. It was also evident from the present information gaps that more research is required for the long-term use of Tirzepatide, especially in pregnant and adolescent females. Though the short-term outcomes of Tirzepatide in the populations mentioned above have been established, its prolonged administration during pregnancy to the mother and its effects on teenage growth, puberty and development are still unknown. These populations should be followed up on in the long term, and the effects should be checked in order to evaluate whether there are adverse effects or not when they occur in the long term.

Other issues that are peculiar to the elite group of the elderly population also deserve to be addressed further. Patients' age may also play a vital role in drug metabolism due to changes in renal and hepatic functions that could affect drug response. It would be imperative to identify the dosing regimens of Tirzepatide suitable for older adults, renal function, hepatic function, and long-term safety among elderly patients with T2D. Thus, further studies on how Tirzepatide interacts with some of the common comorbidities and the use of multiple medications that are typical of older patients were helpful in developing better treatment approaches.

These gaps in evidence require large, multi-centre RCTs to supply. Since there are such gaps in the existing literature, it is necessary to use large, multi-centre RCTs to provide. Such trials should have a broad enrollment of patients, especially pregnant women and adolescents, to evaluate the safety and efficacy of Tirzepatide among these two populations. Such trials were also be helpful in freeing the research from the limitations of small sample sizes and short follow-up periods, as was seen in previous research. These studies should also include issues on how best to track outcomes and silhouettes that were reveal the safety, effectiveness, and long-term impacts that were reliable. It is therefore highly necessary to call for well-designed, comprehensive RCTs for a more apprised understanding of Tirzepatide for managing T2D in these populations and to guide future practice.

## 5. Conclusion

To sum up, Tirzepatide has shown a favourable effect in the context of glycaemic control and weight loss for elderly patients, pregnant and adolescent women, and adolescents with T2D. Current observation reveals that Tirzepatide, being a dual agonist of both GLP-1 and GIP receptors, shows better efficacy than traditional therapy measures in the case of glycemic and weight control. The data provided suggests that Tirzepatide is effective in reducing the HbA1c and promoting weight loss among elderly patients with T2D, presented as a solution to the problem of managing this condition in the ageing population. In the same way, Tirzepatide has been found to assist in the regulation of blood sugar levels and weight loss aspects, which are of concern in the adolescent population, such as fast disease progression and obesity-related complications. Tirzepatide is also safe and effective in pregnant women with a history of T2D. However, information is very scarce in this subgroup of patients, especially regarding the action of blood glucose levels. Alas, these outcomes need to be discussed in terms of safety, particularly in certain groups of patients, such as pregnant women and adolescents. Although it has been revealed that Tirzepatide is generally safe, certain possible risks, including gastrointestinal adverse effects, Hypoglycemia and safety issues related to prolonged use during pregnancy and adolescence, need to be considered with care. The lack of data on the impact on pregnant women during its use makes it mandatory to balance the advantage versus the danger to the pregnant lady and the fetus; insulin stays the benchmark in pregnancy. Regarding adolescents, the effectiveness of Tirzepatide on growth and development should be appropriately assessed, and any psychological consequences associated with using the drug for weight reduction and altering the body shape should be taken into account. The practical implications of these tendencies are that Tirzepatide can be used in the treatment of the above-mentioned categories of patients. During assessments and treatment of the elderly, their individual needs should be addressed, taking considerations such as their secondary diseases, medication usage, and body changes due to increasing age. The dosing should be individualised, and monitoring of renal and hepatic function must be performed in patients who take Geodon to reduce the risk to the minimum. The management of adolescents with chronic conditions requires the support of the patient and the family because the treatment, as well as the psychosocial aspect of their lives, were affected. Moreover, suppose a patient has any issues related to body image. In that case, such a situation should be handled through therapy to prevent one from developing mental illnesses when choosing weight loss benefits. Therefore, it is recommended that Tirzepatide should not be prescribed to pregnant women, or in case this is not possible. Other treatment options should be considered instead of using this drug. Insulin is the preferred antidiabetic treatment during pregnancy, and that means that any use of Tirzepatide should be done carefully with a proper risk assessment. Based on the available literature, it is recommended that until there is enough data to support its use, caretakers should cautiously use Tirzepatide in pregnancy. In conclusion, more investigations are still needed to establish the efficacy of Tirzepatide specifically for those groups of people. Further research with a long-term follow-up, samples of significantly larger sample sizes and populations that have not been studied before, such as pregnant females or adolescents, should be conducted. As such, large, multicenter RCTs of Tirzepatide in the populations mentioned above were address specific knowledge gaps to facilitate optimal management of T2D in these patient groups. The present meta-analysis study suggests promising directions for subsequent research, which were enhance the strategies of treatment and optimum results in patients with T2D in high-risk populations.

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