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UROLOGY – REVIEW

Effect of GLP-1 receptor agonists on prostate cancer risk reduction: a systematic review and meta-analysis

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Abstract

Background Prostate cancer is one of the most prevalent malignancies among men globally. Glucagon-like peptide 1 receptor agonists (GLP-1 RAs), primarily used for type 2 diabetes mellitus (T2DM) management, have been investigated for their potential effects on cancer risks. This systematic review and meta-analysis aimed to assess the association between GLP-1 RA use and risk reduction of prostate cancer.

Methods A comprehensive literature search was conducted across PubMed, Embase, and Web of Science up to July 30, 2024. Studies that met the inclusion criteria randomized controlled trials, cohort studies, case–control studies, and observational studies assessing the incidence of prostate cancer in GLP-1 RA-treated patients were included. The quality of studies was evaluated using the Newcastle–Ottawa Scale and the Cochrane Risk of Bias tool. Meta-analysis was performed using a random effects model.

Results A total of five studies were included, analyzing data from diverse international contexts. The included studies showed a reduced risk of prostate cancer with both adjusted and unadjusted effect estimates with GLP-1 RAs. The meta-analysis revealed an RR of 0.72 (95% CI: 0.610 to 0.832), indicating a statistically significant 28% reduction in prostate cancer risk associated with GLP-1 RA use compared to placebo or other antidiabetic drugs. Moderate heterogeneity was observed ($I^2 = 51\%$). Sensitivity analysis confirmed the results.

Conclusion The findings suggest a significant protective association between GLP-1 RA use and reduced prostate cancer risk in men, particularly those with T2DM. This supports the potential of GLP-1 RAs not only in diabetes management but also as a strategy to mitigate cancer risk. Further research is required to confirm these findings and explore the underlying mechanisms, considering different dosages, durations of therapy, and patient subgroups based on demographic and metabolic characteristics.

Keywords Prostate cancer · Glucagon-like peptide 1 receptor agonists · Meta-analysis · Systematic review

Introduction

Prostate cancer remains one of the most commonly diagnosed malignancies among men worldwide, posing significant challenges in terms of management and prognosis [1, 2]. The disease's heterogeneity in terms of its pathophysiology and progression necessitates a continuous search for effective treatment and prevention strategies. Amidst evolving therapeutic landscapes, glucagon-like peptide 1 receptor agonists (GLP-1 RAs), primarily utilized for managing type 2 diabetes mellitus (T2DM), have come under scrutiny for their potential influence on cancer risks [3, 4].

The biological mechanism underlying the potential impact of GLP-1 RAs on cancer risk primarily revolves around their modulatory effects on insulin secretion and glucose homeostasis [5]. GLP-1 RAs enhance insulin secretion in a glucose-dependent manner and decrease glucagon secretion, which may indirectly influence cancer risk through pathways related to insulin resistance and hyperinsulinemia

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a known risk factor for various cancers, including prostate cancer [6]. Furthermore, these agents have demonstrated anti-inflammatory effects and influence on cell apoptosis and proliferation, suggesting a possible direct interaction with carcinogenic processes [7].

Risk factors for prostate cancer include age, genetic predisposition, lifestyle, and possibly metabolic disorders such as diabetes [8]. The intersection of diabetes and prostate cancer is particularly complex, as epidemiological studies suggest that diabetes may be associated with a lower risk of prostate cancer [9, 10]. Yet, diabetics have a poorer prognosis if they develop the disease. This paradox highlights the critical need to explore how diabetic treatments, specifically GLP-1 RAs, might influence prostate cancer dynamics.

Several observational studies and clinical trials have provided insights into the cancer-modulatory effects of GLP-1 Ras [11–13]. A previous systematic review indicated a reduced risk of prostate cancer associated with incretin-based drugs; however, it did not account for confounders, such as demographics, underlying conditions, treatment duration, and other variables [14]. This systematic review and meta-analysis will scrutinize the available literature to assess the relationship between GLP-1 RAs and the risk reduction of prostate cancer among men, particularly focusing on those with a history of diabetes.

Methods

Study design

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15]. A protocol has been registered in PROSPERO with registration number: CRD42024576645. We employed semi-automated software (Nested-Knowledge, MN, USA) for screening and data extraction.

Data sources and search strategy

A comprehensive search of PubMed, Embase, and Web of Science was performed to identify studies published up to July 30, 2024. The search strategy included a combination of keywords and MeSH terms related to 'GLP-1 receptor agonists' and 'prostate cancer'. We did not employ any language, date filters, or filters based on the type of article. The full search strategy for each database is presented in Table S1.

Eligibility criteria

We included original studies that reported an association between prostate cancer GLP-1 Ras. Any type of GLP-1 Ra was considered. No restrictions were placed on the dose or route of administration. Only male participants were considered. Placebo, no treatment, or other antidiabetic drugs were considered as control groups. Inclusion criteria included randomized controlled trials (RCTs), cohort studies, case–control studies, and observational studies that evaluated the incidence of prostate cancer in patients treated with GLP-1 Ras. Only English language articles were included. Non-peer-reviewed articles, abstracts, conference presentations, and editorials were excluded. Non-human studies and cell studies were also excluded.

Screening

The initial screening of studies was conducted by two independent reviewers who assessed titles and abstracts for relevance based on the inclusion and exclusion criteria specified in the methodology. This initial screening aimed to eliminate studies that clearly did not meet the research objectives or that were outside the scope of this review regarding subject matter, such as studies not focused on GLP-1 Ra or prostate cancer. Studies that passed the initial title and abstract screening were subjected to a full-text review. During this stage, reviewers carefully examined each selected study in detail to confirm its eligibility. This involved checking for the specific use of GLP-1 Ra, the presence of a control group as defined in the methods (placebo, no treatment, or other antidiabetic drugs), and the explicit reporting of prostate cancer outcomes. Any discrepancies between the two reviewers regarding the eligibility of specific studies were resolved through discussion. If a consensus could not be reached, a third, senior reviewer was consulted to make a final decision.

Data extraction and quality assessment

A standardized data extraction form was developed to facilitate a thorough and precise extraction of data from the selected studies. This form was crafted to collect all pertinent details necessary for the systematic review and meta-analysis. The extraction was conducted by two independent reviewers to reduce potential errors and biases, ensuring reliability in the data collection process. The standardized form included several critical fields: study identification (authors, year, country), study design (e.g., randomized controlled trial, cohort study), population characteristics (age, demographics, participant number), details of the intervention (type of GLP-1 RA), control group specifics (type of control, comparable details to the intervention), outcomes measured (number of prostate cancer cases), adjustments for confounders (such as age, BMI, and smoking status), and effect measures, such as hazard ratio (HR) and odds ratio (OR), along with their confidence intervals (CI).

The quality of included studies was assessed using the Newcastle–Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias tool for randomized controlled trials. Studies were rated on the selection of participants, comparability of groups, and ascertainment of outcomes.

Statistical analysis

Meta-analysis was conducted using a random effects model, which accounts for the possibility of variation between studies due to differences in populations, interventions, and other factors. The random effects model, as opposed to a fixed effects model, assumes that the true effect size may vary across studies and provides more conservative estimates with wider confidence intervals, making it suitable for our dataset. We used the DerSimonian and Laird method to estimate between-study variance (τ^2) in the random effects model. To calculate the pooled effect sizes from HRs and ORs with 95% CIs for the association between RA use and prostate cancer risk, we applied inverse-variance weighting. This method assigns greater weight to studies with smaller standard errors (higher precision) and less weight to studies with larger standard errors, ensuring that more precise estimates contribute more to the overall pooled effect size. HR and ORs were pooled together. Heterogeneity among the included studies was assessed using both the Cochran's Q test and the I^2 statistic [16]. The I^2 statistic quantifies the proportion of total variation in study estimates due to heterogeneity rather than chance, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. Sensitivity analyses were performed using a leave-one-out approach, where each study was sequentially removed from the meta-analysis to assess its impact on the overall result [17]. This helped ensure the robustness of the findings as no single study had an undue influence on the pooled effect size. Due to the small number of included studies, we did not formally assess publication bias with funnel plots or Egger's test as these methods require a larger sample size to yield reliable results. Statistical analyses were conducted using R software (version 4.3), utilizing the "meta" and "metafor" packages for conducting the meta-analysis and related statistical assessments.

Results

Literature search

We initiated our systematic review by identifying a total of 196 records through database searches: 42 from PubMed, 74 from Embase, and 80 from Web of Science. Before screening, we removed 79 duplicate records. The remaining 117 records were then screened for relevance based on title and abstract, leading to the exclusion of 84 records for reasons not meeting the inclusion criteria. The remaining 33 records were sought for full-text retrieval, with all 33 successfully retrieved and assessed for eligibility. Of these, 28 were excluded for various reasons: 11 were non-human studies, 3 reported outcomes not of interest, 3 were review articles, 2 were case studies, 1 involved a different intervention, 7 were not relevant, and 1 did not separately specify the data for GLP-1 RA. Consequently, 5 studies were deemed eligible and included in the final analysis (Fig. 1).

Characteristics of included studies

The characteristics of the included studies are given in Table 1. A total of five studies were evaluated, deriving data from diverse international contexts including the United Kingdom, Denmark, the United States, and a multi-country study encompassing 32 countries. Four of these studies employed a retrospective cohort design, emphasizing longitudinal observation of outcomes following the administration of GLP-1 receptor agonists. One study utilized an RCT design, providing high-quality evidence through controlled intervention and placebo comparison. The populations studied were predominantly male, diagnosed with T2DM, and varied in age across studies. For instance, the UK study focused on males with an average age range from 56.5 to 61.4 years, while the multi-country RCT reported a mean age of 64.3 years. Intervention groups across these studies were treated with various forms of GLP-1 receptor agonists including albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, oral semaglutide, and semaglutide, reflecting a broad spectrum of the medication class. Control groups varied, with some studies comparing GLP-1 RAs against placebos, sulfonylureas, basal insulin, metformin, and DPP4 inhibitors. Sample sizes ranged from several thousand to over six hundred thousand participants, allowing for robust statistical analyses. Outcomes focused on the incidence of prostate cancer, with studies adjusted for multiple confounding factors, such as age, BMI, smoking status, duration of diabetes, and other health and lifestyle variables, to ensure the accuracy of results. The quality assessment of the studies is given in Table S2.

Prostate *cancer* risk with GLP-1 Ras

Several studies have consistently demonstrated a reduced risk of prostate cancer associated with the use of GLP-1RAs, highlighting their protective effects through both unadjusted and adjusted effect estimates. A 2022 study by Lu reported a HR of 0.65 (95% CI: 0.43 to 0.99) for prostate cancer in patients treated with GLP-1RAs compared to those using sulfonylureas after adjusting for HbA1c levels

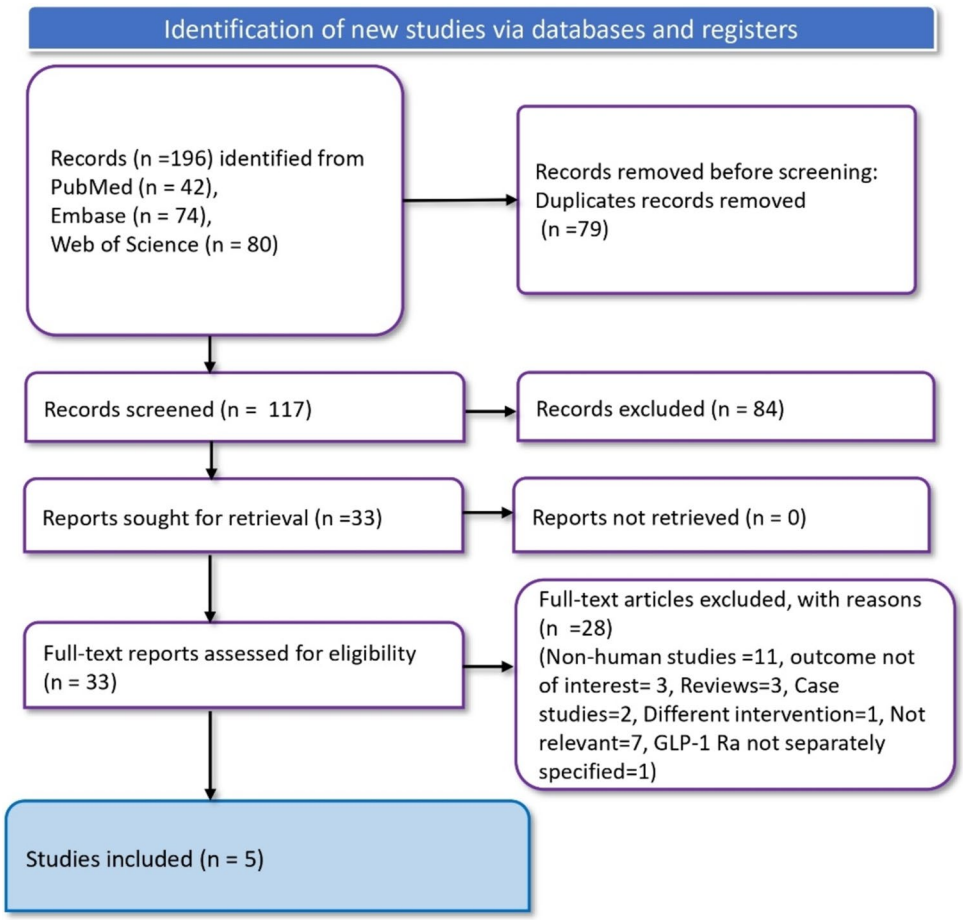

Fig. 1 PRISMA flowchart depicting article selection and screening process

and the duration of diabetes. Similarly, Nauck's 2018 RCT involving patients with diabetes and high cardiovascular risk showed that liraglutide treatment resulted in an HR of 0.54 (95% CI: 0.34 to 0.88) compared to placebo. Skriver in 2023 noted an HR of 0.80 (95% CI: 0.64 to 1.01) when comparing GLP-1RAs with basal insulin. Wang's 2022 research further reinforced these findings, showing an adjusted OR of 0.85 (95% CI: 0.73 to 0.98) for GLP-1RAs versus metformin and providing unadjusted OR for GLP-1RAs compared to sulfonylureas and other treatments which suggested significant protective trends. Additionally, a 2020 study by Wang found an adjusted OR of 0.65 (95% CI: 0.59 to 0.82) for GLP-1RAs compared to DPP-4 inhibitors after adjusting for factors, such as sex, age, smoking status, and BMI. These collective findings indicate a significant protective effect of GLP-1RAs against prostate cancer in patients with diabetes, confirmed across various study designs and adjustments for potential confounders.

Meta-analysis

From five studies, the pooled HRs and ORs for the meta-analysis was 0.72 (95% CI: 0.610 to 0.832), with a prediction interval ranging from 0.610 to 0.832, indicating a statistically significant reduction in prostate cancer risk associated with the use of GLP-1 RAs compared to placebo or other antidiabetic drugs. This effect size reflects the general trend among the included studies, suggesting a protective effect of GLP-1 RAs against prostate cancer (Fig. 2). Heterogeneity among the studies was moderate with an I^2 of 51%, indicating a moderate level of variability in effect sizes that could be due to differences in study populations, interventions, or methods.

Sensitivity analysis

Sensitivity analysis conducted for the meta-analysis on the effect of GLP-1 RAs on prostate cancer risk provides a detailed assessment through a leave-one-out approach. This analysis methodically examines the influence of individual studies on the overall pooled HR by omitting each study sequentially. The results from this analysis showed slight variations in the pooled HR, ranging from 0.672 to 0.751, indicating that no single study disproportionately influenced the overall effect estimate (Fig. 3).

Table 1 Characteristics of included studies

Study	Country	Study design	Population characteristics	Age	Intervention	Control	Sample size (intervention)	Sample size (control)	Prostate cancer in GLP group	Prostate cancer in control group	Effect size (95% CI)	Adjusted variables
Lu 2022 [11]	UK	Retrospective cohort study	Males prescribed incretin-based drugs or sulfonylureas	GLP-1Ra = 56.5, sulfonylurea = 61.4	Albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide, semaglutide	Sulfonylureas	5,063	112,955	34	2,157	HR = 0.65 (0.43 to 0.99)	Propensity matched, duration of diabetes and HbA1c
Nauck 2018 [12]	32 countries	RCT	T2DM and high CV risk	64.3	Liraglutide with 1.78 mg	Placebo	4668	4672	26	47	HR = 0.54 (0.34 to 0.88)	Treatment
Skriver 2023 [13]	Denmark	Retrospective cohort study	Men in Denmark aged ≥ 50 years with a first-time prescription for GLP-1RAs or basal insulin	GLP-1 = 62.7, Insulin = 66.7	GLP1Ra	Basal insulin	14,178	21,712	135	322	HR = 0.80 (0.64 to 1.01)	Age, calendar year, education, income, region, comorbid conditions, concomitant drug use, diabetes severity proxies
Wang 2022 [28]	USA	Retrospective cohort study	NA	NA	Liraglutide, exenatide, dulaglutide, albiglutide	Metformin, sulfonylurea	64,230	619,340 (metformin)	74	66 for metformin	GLP-1 Ra VS Metformin = aOR = 0.85 (0.73 to 0.98), GLP-1 Ra VS sulfonylurea = uOR = 0.51(0.46 to 0.57), liraglutide VS Metformin = uOR = 0.61(0.53 to 0.71), exenatide VS Metformin = uOR = 0.68(0.58 to 0.80)	Sex, age (< 65 vs ≥ 65 years old), smoking status, alcohol abuse history, HbA1c around initiation of antidiabetic agents, and BMI

Table 1 (continued)

Study	Country	Study design	Population characteristics	Age	Intervention	Control	Sample size (intervention)	Sample size (control)	Prostate cancer in GLP group	Prostate cancer in control group	Effect size (95% CI)	Adjusted variables
Wang 2020 [29]	USA	Retrospective cohort study	Patients diagnosed with T2DM	NA	GLP1Ra	DPP4i	112,000	3,44,550	NA	NA	aOR = 0.65 (0.59 to 0.82)	Sex, age, smoking status, alcohol abuse history, HbA1c (≤ 9.0% vs > 9.0%) and BMI (< 30 vs ≥ 30 kg/m2)

aOR Adjusted Odds Ratio, *BMI* Body Mass Index, *CV* Cardiovascular, *DPP4i* Dipeptidyl Peptidase-4 Inhibitors, *GLP-1 RA* Glucagon-Like Peptide 1 Receptor Agonist, *GLP-1Ra* Glucagon-Like Peptide 1 Receptor Agonist, *HbA1c* Hemoglobin A1c, *HR* Hazard Ratio, *NA* Not Available, *RCT* Randomized Controlled Trial, *T2DM* Type 2 Diabetes Mellitus, *uOR* Unadjusted Odds Ratio

Discussion

This systematic review and meta-analysis explored the potential protective effects of GLP-1 RAs against prostate cancer in men, particularly those with a history of T2DM. The incidence of prostate cancer mentioned in the article is projected to rise significantly. In 2020, there were approximately 1.4 million new cases of prostate cancer globally. This number is expected to increase to 2.9 million new cases annually by 2040. Our findings suggest a statistically significant reduction in the risk of prostate cancer associated with the use of GLP-1 RAs compared to placebo or other antidiabetic drugs. Our analysis indicates a 28% reduction in prostate cancer risk among users of GLP-1 RAs.

While the exact mechanisms remain under investigation, several biological pathways have been proposed to explain how GLP-1 RAs may contribute to a reduced risk of prostate cancer. GLP-1 RAs are primarily used to manage T2DM by improving glycemic control and promoting weight loss. Insulin resistance and obesity are significant risk factors for prostate cancer. By enhancing insulin sensitivity and reducing body weight, GLP-1 RAs may indirectly lower the risk of prostate cancer [5, 18]. Studies have shown that patients using GLP-1 RAs exhibit lower rates of obesity-associated cancers, including prostate cancer, compared to those using insulin [5]. These agents regulate glucose homeostasis and insulin secretion in a glucose-dependent manner, exert anti-inflammatory effects, and influence cellular processes, such as apoptosis and proliferation. Given the established role of chronic inflammation and deregulated cell cycle processes in cancer development, these mechanisms are critical [19]. Moreover, the modulation of insulin resistance and hyperinsulinemia by GLP-1 RAs could indirectly reduce cancer risk, considering that insulin resistance is a known risk factor for various cancers, including prostate cancer [5]. Research indicates that GLP-1 RAs can exert direct antitumor effects on prostate cancer cells. For instance, in vitro studies have demonstrated that treatment with GLP-1 RAs can inhibit the proliferation of prostate cancer cell lines [20]. Specifically, exposure to GLP-1 RA Exendin-4 resulted in a significant reduction in tumor volume in preclinical models45. This suggests that GLP-1 signaling may interfere with the growth and survival of cancer cells. Androgens play a crucial role in the development and progression of prostate cancer through their interaction with androgen receptors (AR) [21]. GLP-1 RAs may modulate AR signaling pathways, thereby impacting prostate cancer growth. They have been observed to enhance sensitivity to antiandrogen therapies, potentially making existing treatments more effective. This modulation could

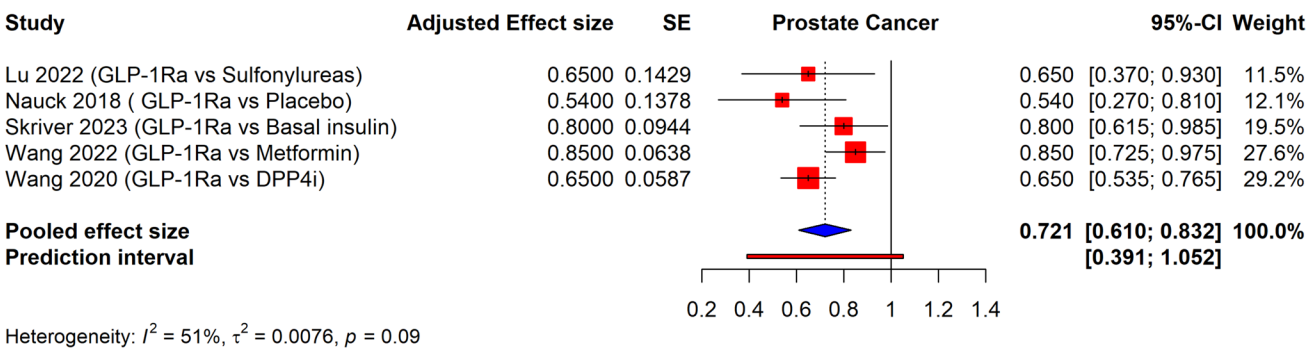

Fig. 2 Meta-analysis showing pooled risk of prostate cancer with GLP-1Ra compared to placebo and other antidiabetic drugs

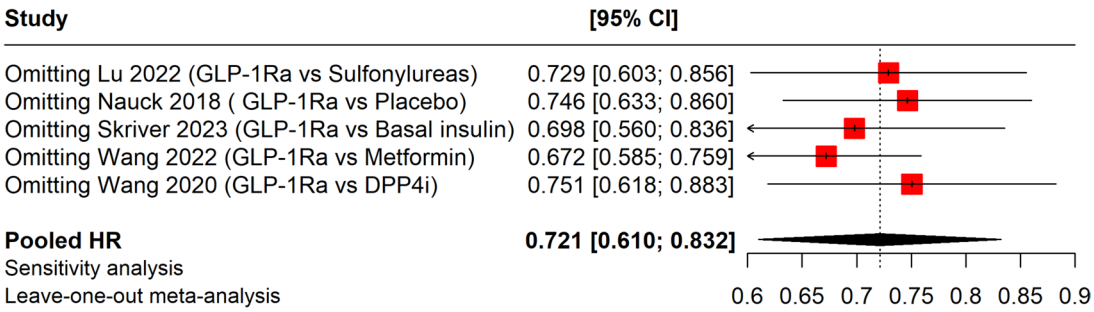

Fig. 3 Sensitivity analysis

be particularly beneficial for patients with androgen-sensitive tumors. The tumor microenvironment plays a critical role in cancer progression and metastasis. GLP-1 RAs may influence this microenvironment by altering metabolic pathways and immune responses, which can affect tumor growth dynamics [22]. By creating an unfavorable environment for tumor cells, these agents may contribute to reduced cancer incidence.

Previous studies and systematic reviews have demonstrated a relationship between diabetes treatments and cancer risks. A previous meta-analysis indicated that incretin-based drugs might reduce the risk of prostate cancer although they calculated unadjusted risks [14]. Unlike previous reviews, we considered confounding factors adjusted by the included studies. Our findings align with a subset of literature indicating that incretin-based therapies, including GLP-1 RAs, might offer protective benefits against cancer development. Notably, our analysis contributes to the literature by focusing specifically on prostate cancer and providing a robust statistical synthesis of available evidence, which adjusts for numerous potential confounders, such as demographics, comorbid conditions, and treatment durations. When considering other types of cancers, GLP-1 RAs showed different results. Surprisingly, a meta-analysis indicated that GLP-1 RA treatment could be associated with a moderate increase in relative risk for thyroid cancer in clinical trials, with a small increase in absolute risk [23]. As for pancreatic cancer, no significant effect was found by another systematic review [24].

The relationship between T2DM and prostate cancer risk is complex and somewhat contradictory. Some studies indicate that men with diabetes have an increased risk of developing prostate cancer, with a hazard ratio of 1.52 for all tumor grades compared to normoglycemic men, suggesting a significant elevation in risk [25]. However, diabetic patients often present with lower prostate-specific antigen (PSA) levels, which may lead to underdiagnosis of prostate cancer [26]. Conversely, other research has reported a decreased risk of prostate cancer among diabetic men [27]. From a clinical practice perspective, incorporating GLP-1 RAs into the treatment regimen for diabetic patients, especially those at higher risk of prostate cancer, could provide added preventive benefits. However, further investigation is required to establish clear guidelines on how these medications can be optimized for cancer prevention in daily practice. This approach may offer a valuable strategy for reducing cancer risk while maintaining effective diabetes control. Future research should focus on larger, well-designed randomized controlled trials to confirm the protective effects of GLP-1 RAs against prostate cancer. Additionally, studies should explore the impact of different dosages and durations of GLP-1 RA therapy on cancer risk, as well as investigate

specific patient subgroups, such as those with varying levels of glycemic control or those already diagnosed with prostate cancer. Understanding these nuances will help refine treatment strategies and provide a clearer understanding of the potential role of GLP-1 RAs in cancer prevention.

The relationship between diabetes mellitus (DM) and the risk of prostate cancer (PCa) has generated considerable interest, revealing a complex interplay of factors. Some studies suggest that men with diabetes face an increased risk of developing prostate cancer, with hazard ratios indicating a significant elevation in risk for all tumor grades. However, diabetic patients often exhibit lower prostate-specific antigen (PSA) levels, which may lead to fewer biopsies and potentially underdiagnosis of PCa, complicating the understanding of actual incidence rates. Duration of diabetes and glycemic control also play crucial roles; longer durations and poorer control are associated with higher risks of high-grade PCa. Interestingly, certain antidiabetic medications, particularly metformin, may mitigate this risk, prompting hypotheses about how glucose metabolism influences PCa development. Despite these findings, not all research supports a direct link between DM and increased PCa risk—some studies have found no significant difference in incidence rates between diabetic and non-diabetic populations, suggesting that other factors like obesity or lifestyle choices might also be at play. Overall, while evidence points to an increased risk of prostate cancer among diabetic patients, particularly those with poor glycemic control, the relationship remains multifaceted and warrants further investigation to unravel the underlying mechanisms involved.

The strengths of this review include adherence to stringent PRISMA guidelines, a comprehensive search strategy without language or date restrictions, and rigorous data extraction and quality assessment procedures. Despite the strengths of our analysis, several limitations warrant careful consideration. First, the inherent limitations of observational studies, which formed the majority of the included data, present challenges, such as potential residual confounding and biases in effect estimation. While we accounted for several known confounders, unmeasured variables may have influenced the observed association between GLP-1 RAs and prostate cancer risk. For instance, lifestyle factors, such as diet, physical activity, and socioeconomic status, were not consistently controlled for across studies, leaving room for potential bias in the effect estimates. Additionally, although RCTs provide higher-quality evidence, their limited representation in this meta-analysis restricted our ability to make definitive conclusions regarding causality. Only one RCT was included, and the remainder were observational studies, which are more prone to selection bias and confounding. This reliance on non-randomized data emphasizes the need for further high-quality RCTs to validate our findings and to better assess the long-term effects of GLP-1 RAs on prostate cancer risk. Another limitation pertains to the relatively small number of studies included in the analysis, which affects the robustness of the pooled estimates. The limited sample size reduced the statistical power to detect more subtle effects and restricted our ability to perform more detailed subgroup analyses. The studies also varied in terms of their control groups, with some comparing GLP-1 RAs to placebos, while others used different antidiabetic drugs such as sulfonylureas or metformin. This heterogeneity in the comparator groups introduces variability in the results, making it difficult to generalize the findings across different clinical contexts. Moreover, the duration of GLP-1 RA therapy and dosages varied among the studies, potentially affecting the consistency of the observed outcomes. Long-term effects of GLP-1 RA use on prostate cancer risk remain unclear as most studies did not assess the impact of prolonged exposure to the medication. It would be beneficial for future research to explore the effects of different dosages and durations of therapy to better understand their relationship with cancer risk. Subgroup analyses based on patient characteristics, such as age, race, and baseline metabolic status, were limited due to the lack of consistent reporting in the included studies. These factors are known to influence both cancer risk and the efficacy of diabetic treatments, so more detailed stratified analyses in future studies would provide valuable insights into the populations that might benefit most from GLP-1 RA therapy in terms of cancer prevention.

Conclusion

Our analysis suggests a significant association between GLP-1 RA use and reduced risk of prostate cancer in men, especially those with T2DM. These findings support the potential role of GLP-1 RAs not only in diabetes management but also as a component of a strategy to mitigate cancer risk. Further high-quality, diverse, and long-term studies are needed to confirm these findings and elucidate the underlying mechanisms at play.

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Data availability The data is with the authors and available on request.

Declarations

Conflicts of interest The authors declare no competing interests.

Ethics approval and consent to participate Not applicable.

Consent to participate Not applicable since this is a review and not involved any human.

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