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***Review Article***

# Association Between Diabetes and Cancer Risk: A Rapid Review of Cohort Studies Published Since 2013 to 2024.



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## ABSTRACT

### Background
Diabetes mellitus (DM) and cancer are two prevalent and debilitating health conditions worldwide. Emerging evidence suggests that diabetes not only increases the risk of developing various cancers but may also worsen cancer progression and complicate treatment outcomes. This rapid review evaluates existing cohort studies that investigate the progression from diabetes to cancer, with a focus on identifying key factors that potentially influence cancer development in diabetic patients.

### Methods
25 cohort studies from 2013-2024 sourced from Google Scholar, including prospective, retrospective, and clinical studies examining the relative risk of various cancers in diabetic populations were reviewed. The quantitative cancer risk analyses conducted on people with diabetes in these studies were also reviewed. Studies that did not report risk estimates and studies with cross-sectional or case-control designs were excluded.

### Results
The review showed a gradual increase in the number of studies investigating the relationship between diabetes and cancer, with the highest proportion conducted between 2021 (16%) and 2023 (12%). Findings revealed an association of Type 2 DM (T2DM) with a higher risk of pancreatic cancer (OR = 2.50) and colorectal cancer in men (HR = 1.42). Standardized risk ratios (SRR) revealed stronger associations of T2DM with certain cancers, including endometrial cancer (SRR = 1.81).

### Conclusion
When compared with Type 1 DM, T2DM is associated with a higher risk of cancer including pancreatic, colorectal, endometrial, and breast cancers. Obesity, glycaemic control, disease duration, and the effects of therapeutic treatment have been highlighted as factors that contribute to this increased risk. Furthermore, the study emphasizes the importance of tailored approaches to cancer risk management in diabetes patients, considering gender, region, and treatment techniques.

### Recommendations
Future research should investigate the link between diabetes and cancer, emphasizing underexplored cancer types, diabetes medications, gender, region, and socioeconomic status to enhance cancer prevention in diabetic populations.

***Keywords:*** *Diabetes, Cancer risk, Obesity; Glycaemic contro,; Diabetes treatment,; Risk ratio*
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## INTRODUCTION

Diabetes Mellitus and Cancer: Complex Interactions and Risk Factors

Diabetes mellitus (DM) and cancer are among the most prevalent and debilitating health conditions worldwide, each contributing significantly to morbidity and mortality. The growing prevalence of diabetes, alongside the rising incidence of cancer, highlights the need for a deeper understanding of how these two diseases intersect. Emerging evidence suggests that diabetes not only increases the risk of developing various cancers but may also exacerbate cancer progression and complicate treatment outcomes (Paternoster & Falasca, 2020). Given

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the complexity of this relationship, there is an urgent need to explore and synthesize data on how diabetes leads to cancer, particularly through cohort studies that track patient outcomes over time.

Diabetes currently affects over 463 million people globally, with the number projected to rise to 700 million by 2045 (Patil et al., 2023). It encompasses several subtypes, including Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), gestational diabetes, and rarer forms like maturity-onset diabetes of the young (MODY) and secondary diabetes (Marcovecchio, 2017). While diabetes is typically marked by persistent hyperglycemia due to insulin resistance or inadequate insulin secretion, the risk of cancer among diabetic patients appears to be multifactorial, influenced by factors such as obesity, comorbidities, and metabolic dysfunction.

Cancer, on the other hand, remains one of the leading causes of morbidity and mortality worldwide, with 19.3 million new cases and 10 million cancer-related deaths reported in 2020 (Chhikara & Parang, 2023). While cancer development is driven by a variety of genetic, environmental, and lifestyle factors, recent studies have pointed to an elevated cancer risk in individuals with diabetes. This relationship has been widely documented in various cohort studies, with T2DM patients particularly showing a heightened risk for cancers such as pancreatic, liver, colorectal, and breast cancers (Lam et al., 2021).

The Focus of the Review: Diabetes-Induced Cancer in Cohort Studies

The primary aim of this review is to evaluate existing cohort studies that investigate the progression from diabetes to cancer. Cohort studies are invaluable in tracking the long-term outcomes of individuals with diabetes and in establishing correlations between the condition and diverse types of cancer. By examining data from such studies, we aim to clarify the extent of cancer risk among diabetic patients and identify key factors that may influence cancer development in this population.

Epidemiological studies have consistently shown that individuals with diabetes, particularly those with T2DM, have an increased risk of developing various cancers, including pancreatic, liver, colorectal, and breast cancers (Lam et al., 2021). The current review focuses on cohort studies that have followed diabetic patients over extended periods, analyzed the cancer incidence, and highlighted the role of diabetes in cancer development. Through this synthesis, we hope to contribute to a clearer understanding of how diabetes serves as a precursor to cancer, providing insights that could inform clinical practice and preventive strategies.

## METHODOLOGY

### Eligibility Criteria

The inclusion criteria were studies that reported quantitative measures of cancer risk (such as hazard ratios [HR], odds ratios [OR], or relative risks [RR]) in individuals diagnosed with Type 1 Diabetes Mellitus (T1DM) or Type 2 Diabetes Mellitus (T2DM). Studies were required to assess a range of cancer types, including colorectal, pancreatic, breast, lung, and endometrial cancers. Exclusion criteria included studies not reporting risk estimates, studies with cross-sectional or case-control designs, studies presenting only qualitative data and lacking quantitative risk measures, studies lacking an appropriate comparison or control group to assess cancer risk, and studies published before 2013.

### Information Sources

The data for this review was primarily sourced from Google Scholar, a comprehensive and widely used database for academic research. This database was utilized to identify relevant cohort studies published between 2013 and 2024.

### Search Strategy

A comprehensive search strategy was employed to identify studies related to the association between diabetes (T1DM and T2DM) and cancer risk. The search focused on cohort studies published between 2013 and 2024, ensuring that the review was based on more recent evidence.

### Selection Process

Studies were selected based on predefined eligibility criteria. Two reviewers independently screened the studies for inclusion, ensuring that they met the inclusion criteria, and excluded studies that did not meet the requirements, such as those lacking quantitative risk estimates or control groups.

### Data Collection

A systematic data extraction process was employed, gathering information on study design, diabetes subtype, cancer types, and risk estimates. Data was extracted by two independent reviewers to ensure accuracy and consistency, with any discrepancies resolved through discussion.

### Data Items

Data items collected from the included studies included:

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- Study design (prospective, retrospective, or clinical)
- Diabetes subtype (Type 1 or Type 2)
- Cancer types examined (colorectal, pancreatic, breast, lung, and endometrial)
- Quantitative measures of cancer risk (hazard ratios [HR], odds ratios [OR] relative risks [RR])

## Study Risk of Bias Assessment

A risk of bias assessment was not conducted as the scope of this rapid review focused on providing a general overview of the existing literature, rather than conducting an in-depth quality assessment. A risk of bias assessment will be conducted in the future in a more comprehensive systematic review.

**Table 1: Summary of Studies Investigating the Association Between Diabetes and Cancer Risk**

| Study | Type of Diabetes | Cancer Type(s) | Study Design | Sample Size | Relative Risk/Association | Key Findings |
|---|---|---|---|---|---|---|
| **Ma et al., 2018** | Type 2 Diabetes (T2D) | Colorectal Cancer (CRC) | Cohort Study | 87,523 women, 47,240 men | HR = 1.42 (men), HR = 1.17 (women) | T2D is associated with increased CRC risk in men (HR: 1.42) but has a weaker, non-significant association in women (HR: 1.17). |
| **Mao et al., 2022** | Type 1 (T1D) and Type 2 Diabetes | All-site cancer, Breast cancer, Liver cancer | Prospective Cohort Study | 15,286 (T2D: 15,054, T1D: 232) | aHR = 1.15 for all-site cancer, aHR = 1.44 for breast cancer, aHR = 1.37 for liver cancer | High HbA1c variability and obesity increase the risk of all-site, breast, and liver cancer, with a higher risk in obese patients with high HbA1c variability. |
| **Zhang et al., 2013** | Type 1 and Type 2 Diabetes | Endometrial Cancer (EC) | Meta-Analysis of Cohort Studies | 21 studies, 12,195 EC cases, 575 deaths | SRR = 1.81 for EC incidence, SRR = 1.23 for EC mortality | DM is linked to a significantly increased risk of EC incidence (SRR: 1.81), but no significant association with EC mortality (SRR: 1.23). |
| **George et al., 2022** | Type 2 Diabetes (New-onset and Long-standing) | Pancreatic Cancer (PC) | Cohort Study (Mendelian Randomization and Mediation Analysis) | 2,018 PC cases, 1,540 controls | OR = 2.50 for T2DM vs. non-T2DM, OR = 6.39 for NODM, OR = 3.69 for insulin users | T2D, especially new onset, is significantly associated with increased pancreatic cancer risk. No causal effect of long-standing T2D on PC; PC likely causes |

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| | | | | | | new-onset T2D. |
| **Conway et al., 2024** | Type 2 Diabetes | Pancreatic Cancer (PC) | Cohort Study (Southern Community Cohort Study) | 73,378 participants (15,913 with diabetes) | HR = 1.54 for diabetes vs. no diabetes, HR = 1.51 African Americans, HR = 1.78 Whites | Diabetes is associated with increased PC risk in both African Americans (HR = 1.51) and Whites (HR = 1.78). Duration of diabetes did not show a clear trend in risk. |
| **Jacobson et al., 2021** | Hyperglycaemia (Impaired Fasting Glucose) | Pancreatic Cancer (PC) | Nested Case-Control Study (Northern Sweden Health and Disease Study) | 182 cases, 728 controls (matched) | OR = 1.30 for increased fasting glucose, OR = 1.77 for impaired fasting glucose (≥6.1 mmol/L) | Elevated fasting glucose levels (especially ≥6.1 mmol/L) are associated with increased PC risk. Stronger association in non-smokers and non-diabetics. |
| **Wu et al., 2022** | Type 2 Diabetes | All-cause cancer, cardiovascular diseases (CVD), CKD, Pneumonia | Prospective Cohort Study (Hong Kong) | 360,202 participants (6-year follow-up) | PAF for all risk factors: 51.6% (18-54 years), 35.3% (≥75 years) | Blood pressure control is most important in the younger age group (18-54 years), with CKD and CVD dominating in older age groups (≥75 years). |
| **Parsons, 2023** | Type 2 Diabetes | Breast Cancer (BC) | Cohort Study | 157,298 newly diagnosed with breast cancer (13,908 with T2D) | HR = 1.12 (12% increased risk of BC mortality), HR = 1.21 (21% increased risk of all-cause mortality) | T2D was associated with a greater risk of breast cancer-related and all-cause mortality, with an increased risk among patients in the highest HbA1c category. |
| **Stan et al., 2023** | Type 2 Diabetes | Lung Cancer (LC) | Case-Control Study (10-year period, Romania) | 162 patients (81 with LC and T2D) and 81 controls | LC incidence: 13.79%, LC mortality: 18.59% | Higher incidence of lung adenocarcinoma in T2D patients. The duration of cancer treatment and survival rates were influenced by the presence of |

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| | | | | | | diabetes. |
| **Jensen et al., 2022** | Type 2 Diabetes | Obesity-related Cancer (OBC) | Retrospective Cohort Study (United Kingdom) | 7,708 patients with T2D | HR = 1.60 for women, HR = 2.37 for men (stable obesity) | Patients who lost weight after T2D diagnosis had higher risks for OBC (in men) and higher all-cause mortality (both genders) than those with stable obesity. |
| **Wang et al., 2020** | Type 1 and Type 2 Diabetes | Non-Hodgkin's Lymphoma (NHL) | Meta-analysis of Cohort Studies | 20 studies | T2D: RR = 1.20, T1D: RR = 1.55 | A moderate increase in the risk of NHL in patients with type 1 and 2 DM. |
| **Yu X et al., 2024** | Type 1 Diabetes | Lung Cancer (LC) | Cohort Study (Mendelian Randomization Analysis) | 520,580 participants (18,942 cases and 501,638 controls) | OR = 1.040, 95% CI: 1.010–1.072, p = 0.009 | Potentially causal effect of T1DM on lung squamous cell carcinoma (LUSC), highlighting the importance of metabolites as risk factors. |
| **Urpilainen et al., 2018** | Type 2 Diabetes | Ovarian Cancer (OC) | Cohort Study (Finland, 1998–2011) | 421 cases | HR = 0.72 (95% CI: 0.56–0.93) for OC | Inconclusive findings on the association between metformin and ovarian cancer survival. Some evidence for improved prognosis with pre-diagnostic statin use. |
| **Shlomai G et al., 2016** | Type 2 Diabetes | All-site Cancer | Case Study (Preclinical and Clinical Data) | Not supplied | Not supplied | T2D is associated with increased risk and greater mortality from many cancer types. Metformin use may decrease cancer incidence and mortality. |
| **Ma RCW et al., 2014** | Type 2 Diabetes | All-site Cancer | Prospective Cohort (Chinese) | 5,900 T2D patients (429 developed cancer) | aHR = 2.41 (95% CI: 1.23–4.69) | T2D-related variants increased cancer risk in patients with diabetes. |
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| **Tang Z et al., 2022** | Type 2 Diabetes | Pancreatic Cancer (PC) | Retrospective Cohort Study (China Medical University) | 238 patients (72 with T2D) | 5-year OS: 11.4% for T2D, 16.3% for non-T2D | T2D is associated with a lower 5-year overall survival (OS) in patients with PC. |
| **Carstensen et al., 2016** | Type 1 Diabetes | All-site Cancer | Retrospective Cohort Study | 9,149 (4,040 men, 5,109 women) | 1.01 (men), 1.07 (women) | Type 1 diabetes was associated with differences in cancer risk, varying by duration of diabetes. |
| **Hsu et al., 2015b** | Type 1 Diabetes | All-cause Cancer | Retrospective Cohort Study | 760 patients | SIR = 1.13 | Type 1 diabetes was associated with a 13% increase in risk of all-cause cancer incidence. |
| **Feng X et al., 2020** | Type 2 Diabetes | Prostate Cancer (PC) | Prospective Study (28 years of follow-up) | 49,392 diabetic men (6,733 cancer incidents) | HR = 0.82 (total prostate cancer risk) | Men with diabetes had lower risks of prostate cancer (all stages). |
| **Roy A et al., 2021** | New-onset and Long-standing Diabetes | Pancreatic Cancer (PC) | Retrospective Study | Not Supplied | Not Supplied | Long-standing diabetes is a risk factor for PC; new-onset diabetes in elderly patients may indicate underlying PC. |
| **Alharmoodi et. al, 2024** | Non-specific | Breast Cancer (BC) | Retrospective Cohort Study (UAE) | 131 BC patients (98.47% women), average age 54.2 years, 22.14% diabetic | Not applicable | There is no substantial link between diabetes and the stage of breast cancer diagnosis after adjusting for age and comorbidities. |
| **Larsson et. al, 2016** | Type 2 Diabetes (T2D) | Biliary Tract Cancer (BTC), Gallbladder Cancer (GC) | Cohort Study | 70,832 Swedish adults (55.9% men, aged 45-83 years) | HR = 1.79 for extrahepatic BTC, HR = 2.24 for gallbladder cancer | High consumption of sweetened beverages may increase the risk of BTC, particularly gallbladder cancer. |
| **Pearson-Stuttard et al., 2021** | Type 2 Diabetes (T2D) | Common Cancers | Meta-analyses of Observational Studies | 20 studies with 29 meta-analyses | Positive associations for colorectal, hepatocellular, gallbladder, breast, endometrial, and | Strong observational evidence for the association between T2DM and multiple common |

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| | | | | | pancreatic cancers | cancers. |
| **Ling et al., 2020** | Type 2 Diabetes (T2D) | All-site Cancer | Meta-analysis of Cohort Studies | 151 cohorts | Findings suggest a causal association between T2D and liver, pancreatic, and endometrial cancer incidence. | Compelling evidence for T2D-related cancer risks, especially for liver, pancreatic, and endometrial cancers. |
| **Tsilidis et al, 2015** | Type 2 diabetes | All site | Meta-analyses of observational studies | - | The summary random effects estimates were significant at P=0.05 in 20 meta-analyses (74%), and all reported increased risks of developing cancer for participants with versus without diabetes. | Though type 2 diabetes has been extensively studied regarding the risk of developing cancer and cancer mortality and strong claims of significance exist for most of the studied associations, only a minority of these associations have robust supporting evidence without hints of bias. |

## DATA CATEGORIZATION AND OVERVIEW

### Categorization by Diabetes Type

Five studies focus on T1DM, exploring various cancers including Lung Cancer (LC), non-Hodgkin's Lymphoma (NHL), and All-site Cancer. Nineteen studies examine T2DM, with a focus on cancers such as Colorectal Cancer (CRC), Pancreatic Cancer (PC), Breast Cancer (BC), and Endometrial Cancer (EC), among others. One study addressed BC in individuals with non-specific diabetes, without distinguishing between T1DM and T2DM. See Figure 1

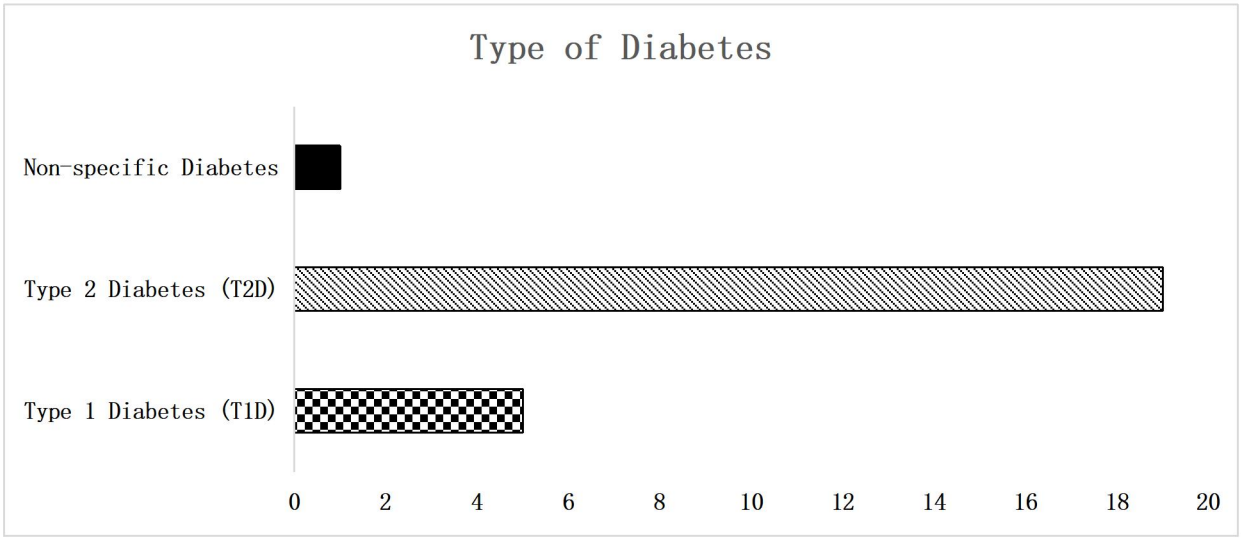


**Figure 1: Categorization by Diabetes Type**

## Categorization by Cancer Type

As depicted in Figure 2 below, PC is the most frequently investigated, with 6 studies examining its association with diabetes. BC follows closely, with 4 studies exploring this link. Other cancers, including CRC, LC, and EC, have also been studied, though with fewer investigations.

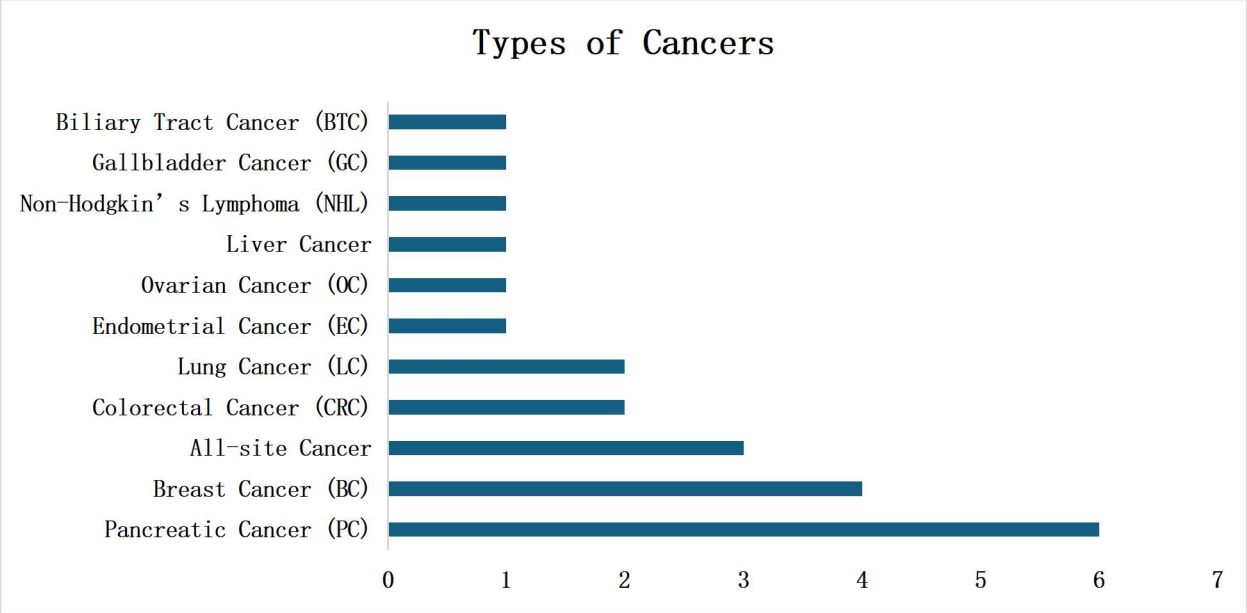


**Figure 2: Distribution of cancer types studied about diabetes**

## Categorization by Study Design

Cohort Studies are the most common design, comprising 13 studies. Meta-analyses follow with 5 studies, pooling data from multiple sources. Case-control studies and Retrospective Cohort Studies are less frequent, with 3 studies each. See Figure 3:

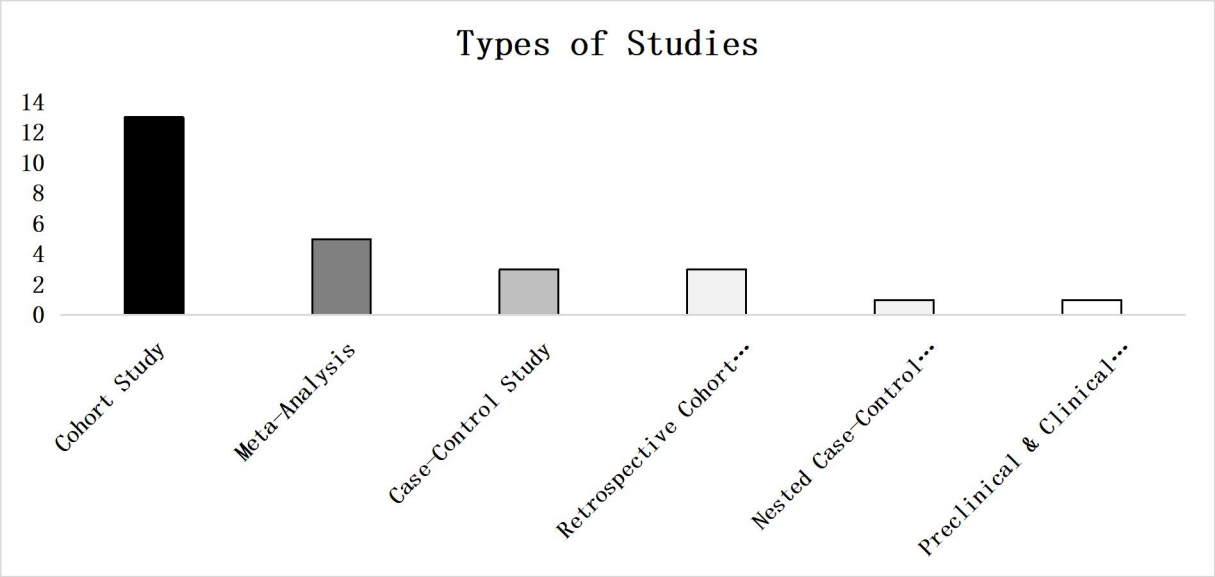


**Figure 3: Distribution of study designs in diabetes and cancer research**

## Risk / Association Summary

The following summary, Table 2, presents the RR, HR), OR, and associations observed in the studies, providing insight into the strength of the diabetes-cancer link. For instance, T2DM is associated with a higher risk of PC (OR = 2.50) and CRC in men (HR = 1.42). Standardized Risk Ratios (SRR) reveal stronger associations in certain cancers, such as EC (SRR = 1.81 for incidence). Some studies, like the one on BC in the United Arab Emirates, report no significant association between diabetes and cancer stage.

| Diabetes Type | Cancer Type(s) | Key Findings |
|---|---|---|
| T1D | Lung Cancer (LC) | OR = 1.04 for lung squamous cell carcinoma (LUSC) |
| T1D | Non-Hodgkin's Lymphoma (NHL) | RR = 1.55 for NHL |
| T2D | Colorectal Cancer (CRC) | HR = 1.42 for men, HR = 1.17 for women |
| T2D | Breast Cancer (BC) | HR = 1.12 for BC mortality, HR = 1.21 for all-cause mortality |
| T2D | Pancreatic Cancer (PC) | OR = 2.50 for T2D vs non-T2D, OR = 6.39 for new-onset diabetes |
| T2D | Endometrial Cancer (EC) | SRR = 1.81 for incidence, SRR = 1.23 for mortality |
| T2D | Liver Cancer | aHR = 1.37 for liver cancer risk |
| T2D | All-site Cancer | aHR = 1.15 for all-site cancer risk |
| Non-specific Diabetes | Breast Cancer (BC) | There is no substantial link between diabetes and BC stage (UAE study) |

**Table 2: HR, OR, and SRR indicate the strength of the association between diabetes and cancer.**

## Distribution of Studies by Country/Region

As shown in Figure 4 below, the studies are geographically diverse, with the United States of America (USA) contributing the most, with 5 studies conducted across various locations and populations. China follows with 4 studies, primarily focusing on PC and EC within the Chinese population. Sweden is represented by 3 studies, concentrating on Pancreatic Cancer and T1DM. The United Kingdom (UK) has 2 studies, examining Obesity-related Cancer and All-Site Cancer. Additionally, studies from Finland, Romania, UAE, Hong Kong, Italy, Taiwan, and Canada each contribute one study to the overall dataset, highlighting the global scope of research in this area.

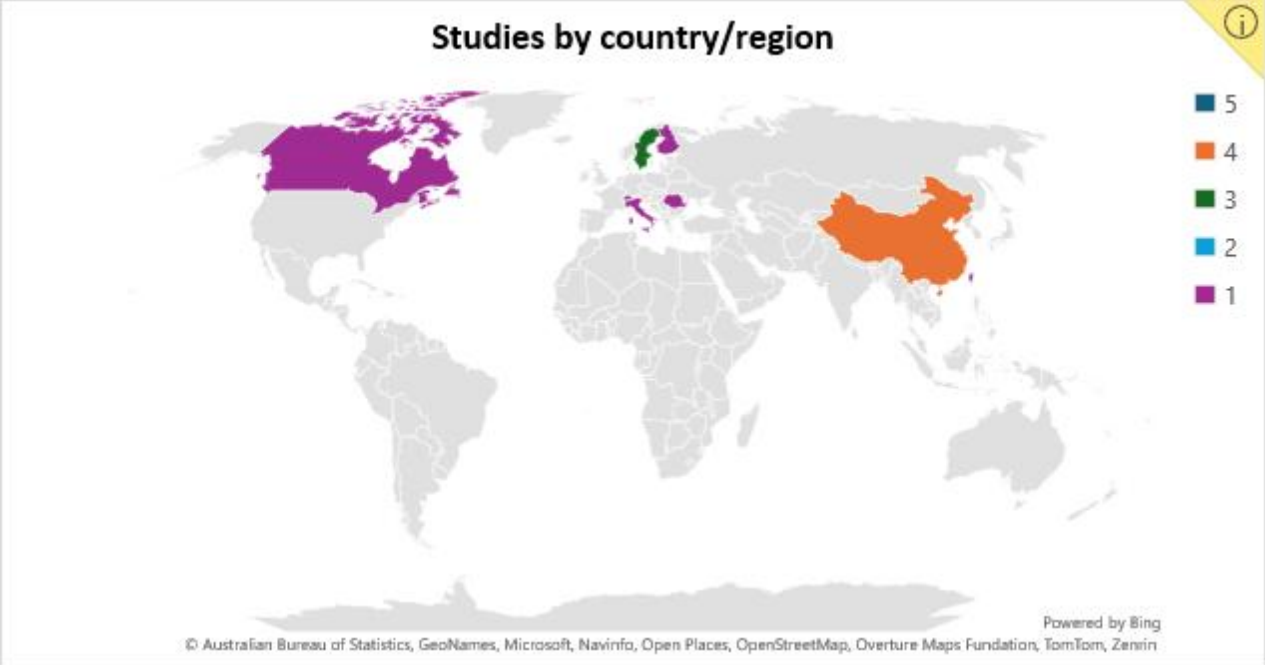


**Figure 4: Distribution of Studies by Country/Region**

## Distribution of Studies by Year of Publication (Out of 25 Studies)

The data highlights a gradual increase in the number of studies published over the years, with the highest proportion of studies from 2021 and 2023 (16% and 12%, respectively). See Figure 5.

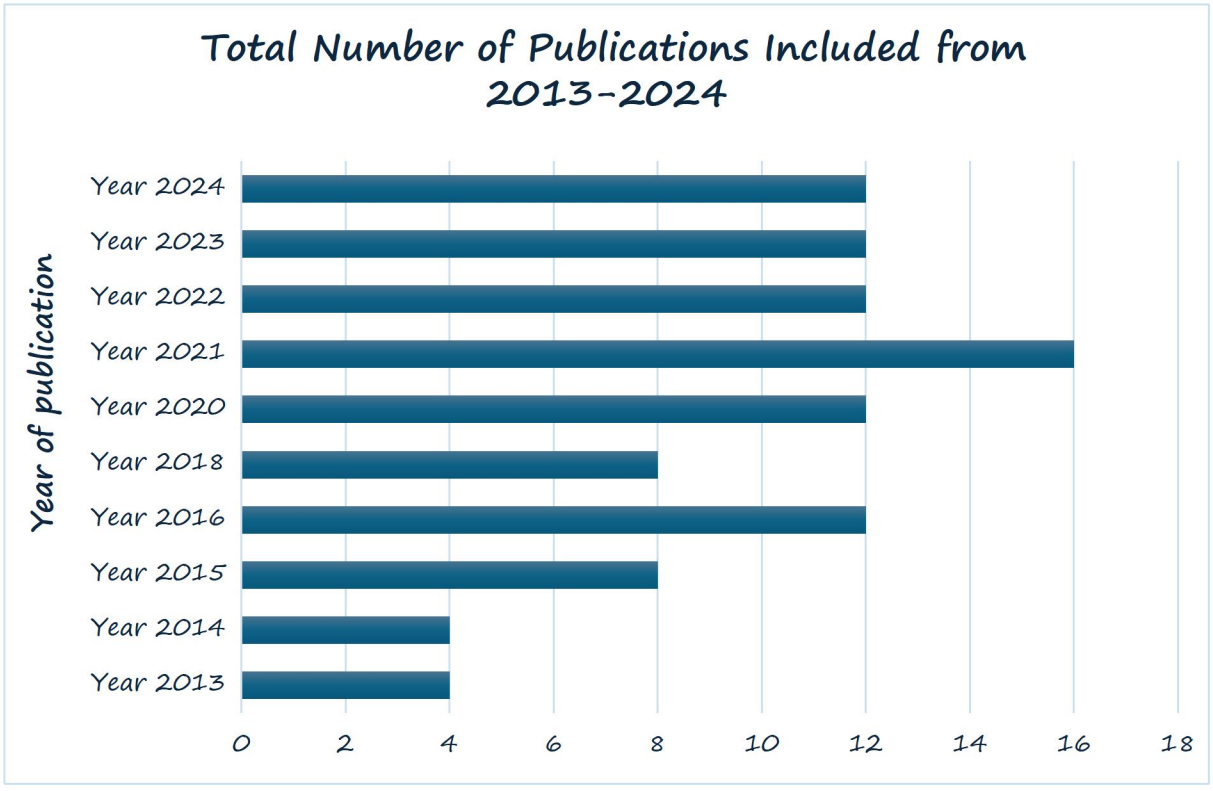

**Figure 5: shows the percentage of studies included in the review, categorized by year of publication.**

## DISCUSSION



This study aimed to explore the intricate relationship between diabetes and cancer by synthesizing findings from a cohort of research studies. The growing global prevalence of both diabetes and cancer necessitates a deeper understanding of how these conditions intersect, and this review offers valuable insights into the multifaceted links between them.

### Categorization by Diabetes Type

The analysis of studies based on diabetes type reveals significant trends in the relationship between diabetes and cancer. T2DM emerges as the primary focus of research, due to its higher prevalence and longer disease duration. As illustrated in Figure 1, T2DM is consistently linked to a wide range of cancers, including colorectal cancer, pancreatic cancer, breast cancer, and endometrial cancer, with 19 studies investigating its associations. T1DM, while less frequently studied, is still implicated in certain cancers such as LC, NHL, and all-site cancer. This discrepancy in research focus likely stems from the fact that T2DM has stronger, more well-established connections to cancer risk, as well as its higher incidence and prolonged duration compared to T1DM. Interestingly, one study analyzing breast cancer in a cohort of individuals with unspecified diabetes, without differentiating between T1DM and T2DM, underscores a gap in our understanding of the specific risks posed by each type of diabetes.

### Categorization by Cancer Type

When examining the types of cancer most frequently studied about diabetes, pancreatic cancer emerges as the most investigated cancer, with six studies focusing on its association with both T1DM and T2DM (see Figure 2). BC follows closely, with four studies, while CRC, LC, and EC are also explored, albeit to a lesser extent. This distribution reflects the established link between diabetes, especially T2DM, and cancers like pancreatic, which has a particularly strong association with T2DM. The data suggests that more research is needed to examine other cancer types that may have significant, yet less explored, connections to diabetes, such as liver cancer and non-Hodgkin's lymphoma.

### Categorization by Study Design

The study designs employed across the literature are dominated by cohort studies, which account for 13 of the studies reviewed (see Figure 3). These longitudinal studies are essential for examining causal relationships, particularly in chronic diseases like diabetes and cancer. Meta-analyses also feature prominently, pooling data from multiple sources to strengthen the statistical power and generalizability of the findings. Case-control and retrospective cohort studies, which are less frequent, contribute valuable insights but are limited in establishing causality. The predominance of cohort studies underscores the need for long-term, population-based research to investigate the complex links more thoroughly between diabetes and cancer over time.

### Relative Risk / Association Summary

The strength of the association between diabetes and cancer is quantitatively assessed through various statistical metrics, including RR, HR, OR, and SRR, as summarized in Table 2. Findings consistently show that T2DM is associated with a significantly increased risk of developing various cancers. For instance:

Pancreatic cancer has a 2.50-fold increased risk for individuals with T2DM (George et al., 2022).

Colorectal cancer in men shows a 1.42-fold higher risk (Ma et al., 2018), though the association in women is weaker (HR = 1.17).

Endometrial cancer has a 1.81-fold increased risk in those with T2DM for incidence (SRR = 1.81), though the link to mortality is less pronounced (SRR = 1.23).

Breast cancer research indicates a 1.12-fold higher risk of breast cancer-related mortality in T2DM patients (Parsons, 2023), particularly among those with poor glycemic control.

In contrast, studies examining T1DM reveal weaker associations, with modest increases in risk for lung squamous cell carcinoma (OR = 1.04) and non-Hodgkin's lymphoma (RR = 1.55). These findings underscore the more pronounced and consistent risk observed in T2DM patients, particularly for cancers like pancreatic cancer, colorectal cancer, and endometrial cancer.

### Distribution of Studies by Country/Region

The geographical distribution of the studies reviewed shows widespread international interest in the relationship between diabetes and cancer, as shown in Figure 4. The USA leads in the number of studies (5), with research spanning diverse populations and cancer types. China follows with four studies, focused on pancreatic and endometrial cancers within the Chinese population. Sweden contributes three studies, concentrating on pancreatic cancer and T1DM. Other countries such as Finland, Romania, UAE, Hong Kong, Italy, Taiwan, and Canada each contribute one study. This global representation highlights both regional differences in diabetes prevalence and cancer types, as well as the need for broader research to understand the global burden of diabetes-related cancers.

### Distribution of Studies by Year of Publication

The temporal trends in the volume of research on diabetes and cancer, as depicted in Figure 5, reveal a gradual increase in publications over time. Notably, the highest proportion of studies was published in 2021 (16%), followed by 2023 (12%). This uptick in research may reflect growing recognition of the importance of understanding the diabetes-cancer link, especially given the rising global prevalence of both conditions. Furthermore, the delayed publication of large, complex cohort studies accounts for the more recent surge in research activity. These trends suggest that future studies will continue to refine our understanding of the relationship between diabetes and cancer, potentially leading to novel insights and therapeutic strategies.

### Literature Synthesis: The Link Between Diabetes and Cancer Risk

The relationship between diabetes and cancer has been widely explored, with T2DM showing a consistently stronger and more significant association with various cancer types, such as PC, CRC, EC, and BC. In contrast, T1DM has weaker associations, though certain cancers like lung squamous cell carcinoma and NHL still show modestly increased risks.

### Key themes emerging from the synthesized literature include

### The Stronger Association Between T2DM and Cancer

T2DM is more strongly linked to PC (OR = 2.50), CC (HR = 1.42 in men), EC (SRR = 1.81), and BC (HR = 1.12). This suggests that the chronic nature of T2DM, along with metabolic factors such as hyperglycemia, insulin resistance, and obesity, contributes to heightened cancer risk.

### Impact of Obesity and HbA1c Variability

Obesity and fluctuating HbA1c levels are significant modifiers of cancer risk in T2DM patients. Obesity, especially in men, is associated with a higher risk of obesity-related cancers (HR = 2.37), and poor glycaemic control exacerbates cancer susceptibility.

### Disease Duration and Onset

New-onset T2DM is particularly linked to pancreatic cancer (OR = 6.39), while long-standing diabetes shows a more moderate increase in risk. The timing of diabetes onset is crucial in determining the extent of cancer risk.

### Gender Differences

Gender plays a key role in the diabetes-cancer link, with men showing higher cancer risks, particularly for colorectal and obesity-related cancers. Men with T2DM also face higher risks of obesity-related cancers (HR = 2.37) compared to women.

### Role of T1DM

Although T1DM is less frequently associated with cancer risk, it still demonstrates moderate increases in the risk for lung squamous cell carcinoma and NHL.

### Treatment Effects

Metformin, a common treatment for T2DM, may offer protective benefits against certain cancers, such as PC and EC, while the role of insulin therapy remains contentious, with some studies suggesting it may promote cancer cell growth in poorly controlled diabetes.

### Geographical Variations

Geographic differences in the relationship between diabetes and cancer highlight the influence of regional factors such as genetics, lifestyle, and healthcare practices. Countries like Sweden and China have identified distinctive patterns of cancer risk in T2DM populations, underscoring the need for region-specific research.

## CONCLUSION

Three conclusions can be drawn from this review on the relationship between diabetes and cancer risk. First, the evidence strongly supports the significant link of T2DM to an increased risk of several cancers, particularly pancreatic, colorectal, endometrial, and breast cancers. The studies reviewed consistently show a stronger and more established connection between T2DM and cancer risk compared to T1DM, which is associated with a more modest increase in cancer risk, primarily for cancers like lung squamous cell carcinoma and NHL. This suggests that the long-term metabolic changes associated with T2DM, including insulin resistance and obesity, are key factors driving cancer risk.

Second, the review identified several critical factors influencing the diabetes-cancer relationship, including obesity, glycaemic control (as measured by HbA1c variability), disease duration, and treatment effects. Obesity and poor glycaemic control, particularly in men, significantly exacerbate cancer risk in individuals with T2DM. The relationship between new-onset diabetes and pancreatic cancer was particularly striking, indicating that early onset of T2DM may serve as a stronger predictor of cancer risk. Furthermore, treatments like metformin appear to offer some protective effects against certain cancers, while insulin therapy remains controversial, with some

studies suggesting it may increase cancer risk in poorly controlled patients.

Finally, the study emphasizes the need for further research to better understand the complex and variable nature of the diabetes-cancer link. Addressing the geographical variations in the findings, as well as exploring under-researched cancer types, will be crucial in advancing our knowledge of diabetes-related cancer risks. Moreover, the findings highlight the importance of considering factors such as gender differences, regional healthcare practices, and treatment strategies in developing effective strategies to mitigate cancer risk in diabetes patients. By overcoming these challenges, future research can help refine public health strategies and clinical practices aimed at reducing cancer risk in individuals with diabetes, improving both the quality of life and long-term health outcomes for affected populations.

## LIMITATIONS OF THE STUDY

While this rapid review provides valuable insights into the relationship between diabetes and cancer, several limitations should be considered. The inability to conduct a meta-analysis due to the heterogeneity of the studies and the rapid review process restricts the ability to draw definitive conclusions. Moreover, the reliance on published studies may introduce publication bias. Nonetheless, this review offers a focused summary of the current evidence and emphasizes the need for further research to fully elucidate the complex links between diabetes and cancer.

## RECOMMENDATIONS

Future research should focus on long-term studies to explore the causal mechanisms linking diabetes to cancer, particularly underexplored cancer types, and the impact of diabetes treatments like metformin and insulin. Additionally, addressing gender and regional disparities e.g., low- and middle-income countries, while promoting strategies for better obesity and glycaemic control, is essential for reducing cancer risk in diabetic populations.

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## CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

## ABBREVIATIONS

**HR** = Hazard Ratio
**aHR** = Adjusted Hazard Ratio
**OR** = Odds Ratio
**SRR** = Standardized Rate Ratio
**RR** = Relative Risk
**SIR** = Standardized Incidence Ratio
**OS** = Overall Survival
**T2D** = Type 2 Diabetes
**T1D** = Type 1 Diabetes
**DM** = Diabetes Mellitus
**NODM** = New-Onset Diabetes Mellitus
**BC** = Breast Cancer
**CRC** = Colorectal Cancer
**PC** = Pancreatic Cancer
**EC** = Endometrial Cancer
**NHL** = Non-Hodgkin's Lymphoma
**LC** = Lung Cancer
**OBC** = Obesity-Related Cancer
**BTC** = Biliary Tract Cancer
**GC** = Gallbladder Cance

## DATA AVAILABILITY

All data utilized in the review has been included (See Table 1).

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## AUTHOR CONTRIBUTIONS



SP and NT collected the data. SP cleaned and analyzed the data and wrote the draft manuscript. ZNJ and NT supervised all stages of the review, reviewed the draft manuscript, and provided general supervision and mentorship.

## REFERENCES

1. Alharmoodi, F., Al Ameri, M.A., Alblooshi, M., Shanbhag, N.M., Almheiri, M.H. and Sumaida, A.B., 2024. Exploring the Relationship Between Diabetes and Breast Cancer in the United Arab Emirates. Cureus, 16(2). DOI: 10.7759/cureus.54787 https://doi.org/10.7759/cureus.54787
2. Carstensen, B., Read, S.H., Friis, S., Sund, R., Keskimäki, I., Svensson, A.M., Ljung, R., Wild, S.H., Kerssens, J.J., Harding, J.L. and Magliano, D.J., 2016. Cancer incidence in persons with type 1 diabetes: a five-country study of 9,000 cancers in type 1 diabetic individuals. Diabetologia, 59, pp.980-988. https://doi.org/10.1007/s00125-016-3884-9 PMid:26924393 PMCid:PMC4826427
3. Chhikara, B.S. & Parang, K., 2023, 'Global Cancer Statistics 2022: the trends projection analysis', Chemical Biology Letters, 10(1), 451.
4. Conway, R.B., Hudson, A.G., Munro, H., Fu, D., McClain, D.A., and Blot, W.J., 2024. Diabetes and pancreatic cancer risk in a multiracial cohort. Diabetic Medicine, 41(4), p.e15234. https://doi.org/10.1111/dme.15234 https://doi.org/10.1111/dme.15234 PMid:37779225
5. Feng, X., Song, M., Preston, M.A., Ma, W., Hu, Y., Pernar, C.H., Stopsack, K.H., Ebot, E.M., Fu, B.C., Zhang, Y., Li, N., Dai, M., Liu, L., Giovannucci, E.L. & Mucci, L.A., 2020, 'The association of diabetes with risk of prostate cancer defined by clinical and molecular features', British Journal of Cancer, 123(4), 657-665. https://doi.org/10.1038/s41416-020-0910-y PMid:32467600 PMCid: PMC7435261
6. George, S., Jean-Baptiste, W., Yusuf Ali, A., Inyang, B., Koshy, F.S., George, K., Poudel, P., Chalasani, R., Goonathilake, M.R., Waqar, S. & Mohammed, L., 2022, 'The Role of Type 2 Diabetes in Pancreatic Cancer', Cureus. DOI: 10.7759/cureus.26288 https://doi.org/10.7759/cureus.26288
7. Hsu, P.C., Lin, W.H., Kuo, T.H., Lee, H.M., Kuo, C. & Li, C.Y., 2015a, 'A population-based cohort study of all-cause and site-specific cancer incidence among patients with type 1 diabetes mellitus in Taiwan', Journal of Epidemiology, 25(9), 567-573. https://doi.org/10.2188/jea.JE20140197 PMid:26212724 PMCid: PMC4549608
8. Jacobson, S., Dahlqvist, P., Johansson, M., Svensson, J., Billing, O., Sund, M. and Franklin, O., 2021. Hyperglycemia as a risk factor in pancreatic cancer: A nested case-control study using prediagnostic blood glucose levels. Pancreatology, 21(6), pp.1112-1118. https://doi.org/10.1016/j.pan.2021.05.008 PMid:34049822
9. Jensen, B.W., Watson, C., Geifman, N., Baker, J.L., Badrick, E. & Renehan, A.G., 2022, 'Weight Changes in Type 2 Diabetes and Cancer Risk: A Latent Class Trajectory Model Study', Obesity Facts, 15(2), 150-159.https://doi.org/10.1159/000520200 PMid:34903697 PMCid:PMC9021620
10. Lam, B.Q., Srivastava, R., Morvant, J., Shankar, S. & Srivastava, R.K., 2021, Association of diabetes mellitus and alcohol abuse with cancer: Molecular mechanisms and clinical significance, Cells, 10(11). https://doi.org/10.3390/cells10113077 PMid:34831299 PMCid: PMC8620339
11. Larsson, S.C., Giovannucci, E.L. & Wolk, A., 2016, Sweetened Beverage Consumption and Risk of Biliary Tract and Gallbladder Cancer in a Prospective Study, Journal of the National Cancer Institute, 108(10). https://doi.org/10.1093/jnci/djw125 PMid:27281756
12. Ling, S., Brown, K., Miksza, J.K., Howells, L., Morrison, A., Issa, E., Yates, T., Khunti, K., Davies, M.J. and Zaccardi, F., 2020. Association of type 2 diabetes with cancer: a meta-analysis with bias analysis for unmeasured confounding in 151 cohorts comprising 32 million people. Diabetes care, 43(9), pp.2313-2322. https://doi.org/10.2337/dc20-0204 PMid:32910779
13. Ma, Y., Yang, W., Song, M., Smith-Warner, S.A., Yang, J., Li, Y., Ma, W., Hu, Y., Ogino, S., Hu, F.B. and Wen, D., 2018. Type 2 diabetes and risk of colorectal cancer in two large US prospective cohorts. British Journal of Cancer, 119(11), pp.1436-1442. https://doi.org/10.1038/s41416-018-0314-4 PMid:30401889 PMCid: PMC6265303
14. Ma, R.C.W., So, W.Y., Tam, C.H.T., Luk, A.O., Ho, J.S.K., Wang, Y., Lam, V.K., Lee, H.M., Kong, A.P., Tong, P.C. and Xu, G., 2014. Genetic variants for type 2 diabetes and new-onset cancer in Chinese with type 2 diabetes. Diabetes Research and Clinical Practice, 103(2), pp.328-337. https://doi.org/10.1016/j.diabres.2013.12.016 PMid:24468095
15. Mao, D., Lau, E.S., Wu, H., Yang, A., Shi, M., Fan, B., Tam, C.H., Chow, E., Kong, A.P., Ma,

R.C. and Luk, A., 2022. Risk associations of long-term HbA1c variability and obesity on cancer events and cancer-specific death in 15,286 patients with diabetes-A prospective cohort study. The Lancet Regional Health-Western Pacific, 18. https://doi.org/10.1016/j.lanwpc.2021.100315 PMid:35024653 PMCid: PMC8669375

16. Marcovecchio, M.L., 2017, Complications of acute and chronic hyperglycemia, US Endocrinology, 13(1), 17-21. https://doi.org/10.17925/USE.2017.13.01.17
17. Parsons, K., 2023. The association between pre-existing type 2 diabetes on breast cancer-related and all-cause mortality among women with breast cancer. McGill University (Canada).
18. Paternoster, S. & Falasca, M., 2020, 'The intricate relationship between diabetes, obesity, and pancreatic cancer', Biochimica et Biophysica Acta (BBA) - Reviews on Cancer, 1873(1), 188326. https://doi.org/10.1016/j.bbcan.2019.188326 PMid:31707038
19. Patil, S.R., Chavan, A.B., Patel, A.M., Chavan, P.D. & Bhopale, J.V., 2023, 'A Review on Diabetes Mellitus its Types, Pathophysiology, Epidemiology and its Global Burden', Journal for Research in Applied Sciences and Biotechnology, 2(4), 73-79. https://doi.org/10.55544/jrasb.2.4.9
20. Pearson-Stuttard, J., Papadimitriou, N., Markozannes, G., Cividini, S., Kakourou, A., Gill, D., Rizos, E.C., Monori, G., Ward, H.A., Kyrgiou, M. and Gunter, M.J., 2021. Type 2 diabetes and cancer: an umbrella review of observational and Mendelian randomization studies. Cancer Epidemiology, Biomarkers & Prevention, 30(6), pp.1218-1228. https://doi.org/10.1158/1055-9965.EPI-20-1245 PMid:33737302 PMCid: PMC9398112
21. Roy, A., Sahoo, J., Kamalanathan, S., Naik, D., Mohan, P. and Kalayarasan, R., 2021. Diabetes and pancreatic cancer: Exploring the two-way traffic. World Journal of Gastroenterology, 27(30), p.4939. https://doi.org/10.3748/wjg.v27.i30.4939 PMid:34497428 PMCid: PMC8384733
22. Shlomai, G., Neel, B., LeRoith, D. and Gallagher, E.J., 2016. Type 2 diabetes mellitus and cancer: the role of pharmacotherapy. Journal of Clinical Oncology, 34(35), pp.4261-4269.https://doi.org/10.1200/JCO.2016.67.4044 PMid:27903154 PMCid: PMC5455318
23. Stan, M.C., Mireştean, C.C., Stoica, D., Popescu, F.C. & Bădulescu, F., 2023, 'Lung cancer and type 2 diabetes experience in Dolj County (southwest region of Romania) - a clinical, bioclinical and pathological study', Romanian Journal of Morphology and Embryology, 64(3), 411-417. https://doi.org/10.47162/RJME.64.3.12 PMid:37867358 PMCid: PMC10720928
24. Tang, Z., Xu, W. and Zhang, M., 2022. Association between type 2 diabetes and 5-year overall survival in early-stage pancreatic cancer: a retrospective cohort study. PeerJ, 10, p.e14538. https://doi.org/10.7717/peerj.14538 PMid:36530401 PMCid: PMC9753753
25. Tsilidis, K.K., Kasimis, J.C., Lopez, D.S., Ntzani, E.E. and Ioannidis, J.P., 2015. Type 2 diabetes and cancer: umbrella review of meta-analyses of observational studies. Bmj, 350.https://doi.org/10.1136/bmj.g7607 PMid:25555821
26. Urpilainen, E., Marttila, M., Hautakoski, A., Arffman, M., Sund, R., Ilanne-Parikka, P., Arima, R., Kangaskokko, J., Puistola, U., Hinkula, M. and Läärä, E., 2018. Prognosis of ovarian cancer in women with type 2 diabetes using metformin and other forms of antidiabetic medication or statins: a retrospective cohort study. BMC Cancer, 18, pp.1-9.https://doi.org/10.1186/s12885-018-4676-z PMid:30055585 PMCid:PMC6064082
27. Wang, Y., Liu, X., Yan, P., Bi, Y., Liu, Y., and Zhang, Z.J., 2020. Association between type 1 and type 2 diabetes and risk of non-Hodgkin's lymphoma: a meta-analysis of cohort studies. Diabetes & Metabolism, 46(1), pp.8-19. https://doi.org/10.1016/j.diabet.2019.04.006 PMid:31039401
28. Wu, H., Lau, E.S., Yang, A., Zhang, X., Fan, B., Ma, R.C., Kong, A.P., Chow, E., Chan, J.C. and Luk, A., 2022. 1208-P: Age-Specific Association between Risk Factors and All-Cause and Cause-Specific Mortality in People with Type 2 Diabetes. Diabetes, 71(Supplement_1). https://doi.org/10.2337/db22-1208-P
29. Yu, X., Fu, B., Sun, T. and Sun, X., 2024. The causal relationship between diabetes mellitus and lung cancer: two-sample Mendelian randomization and mediation analysis. Frontiers in Genetics, 15, p.1449881. https://doi.org/10.3389/fgene.2024.1449881 PMid:39655224 PMCid: PMC11625780
30. Zhang, Z.-H., Su, P.-Y., Hao, J.-H. & Sun, Y.-H., 2013, 'The Role of Preexisting Diabetes Mellitus on Incidence and Mortality of Endometrial Cancer: A Meta-Analysis of Prospective Cohort Studies', International Journal of Gynecologic Cancer, 23(2), 294. https://doi.org/10.1097/IGC.0b013e31827b8430 PMid:23287960

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