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Review Article

Smoking Exposure and Severe Hypoglycemia in Diabetes: A PRISMA-ScR Scoping Review of Population-Based Evidence

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Abstract

Background: Hypoglycemia is a major acute complication of diabetes mellitus that limits safe glycemic management. Although smoking is a well-recognized cardiovascular risk factor in diabetes, its role as a risk modifier for severe hypoglycemia has received limited systematic attention. This scoping review aimed to map and synthesize observational and population-based evidence on the association between smoking exposure and hypoglycemia across different diabetes types and severity levels.

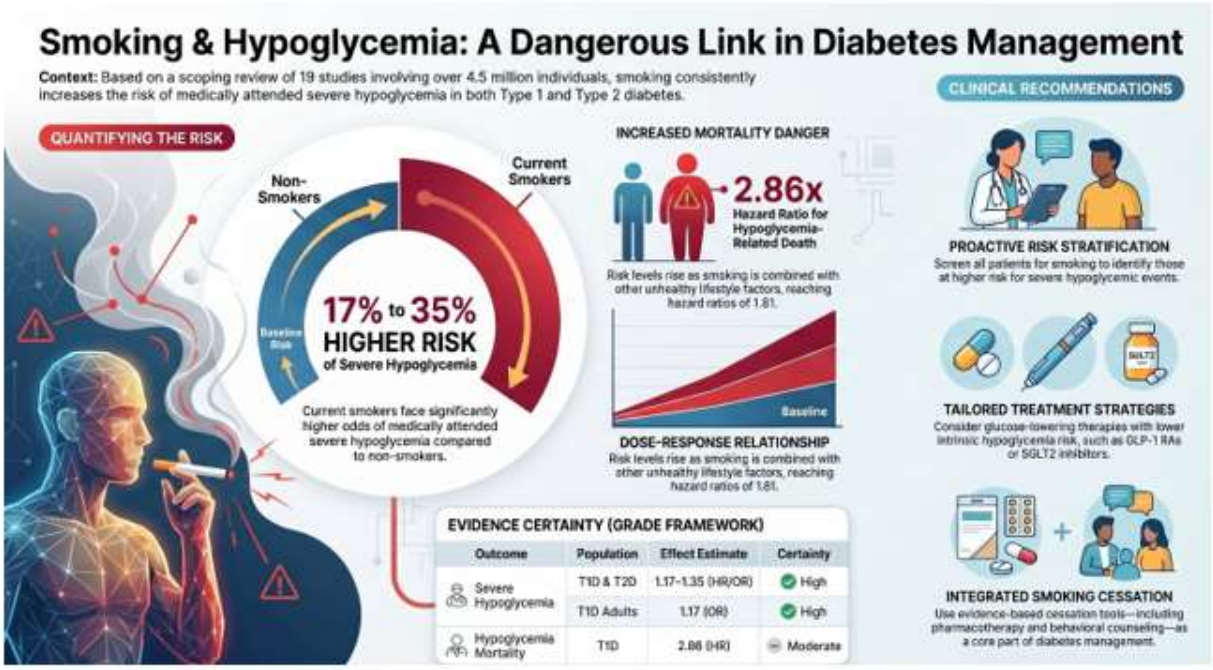
Methods: Conducted in accordance with PRISMA-ScR guidelines, this review systematically searched PubMed and Web of Science databases. From 440 identified records, 234 articles were screened after deduplication, and 19 studies were ultimately included, encompassing nationwide cohort studies, retrospective analyses, cross-sectional investigations, systematic reviews, and health economic models, with a combined population exceeding 4.5 million individuals with type 1 or type 2 diabetes.

Results: Large population-based cohort studies consistently demonstrated an increased risk of medically attended severe hypoglycemia among current smokers (HR/OR range: 1.17–1.35). Lifestyle composite analyses revealed dose-response relationships, with hazard ratios reaching 1.81 when smoking was combined with other unhealthy behaviors. Meta-analytic evidence in type 1 diabetes confirmed smoking as an independent risk factor (OR 1.17; 95% CI: 1.07–1.28). Continuous glucose monitoring studies reported a nearly two-fold higher rate of severe hypoglycemia in smokers. Smoking was also associated with elevated hypoglycemia-related mortality in type 1 diabetes (HR 2.86; 95% CI: 1.57–5.22).

Conclusion: Smoking is a consistent, independent, and modifiable risk factor for severe hypoglycemia in individuals with diabetes mellitus. Integrating smoking cessation into comprehensive diabetes care may reduce acute hypoglycemic complications and associated morbidity and mortality.

Keywords: diabetes mellitus; hypoglycemia; smoking; risk factor; scoping review

Graphical Abstract



Graphical Abstract: The Smoking Risk: Key findings from this scoping review illustrating the quantified risk gradient between smoking and severe hypoglycemia, the biological and behavioral mechanisms involved, and the proposed clinical solutions.

Introduction

Diabetes mellitus (DM) is one of the most prevalent non-communicable diseases globally, affecting an estimated 537 million adults in 2021, with projections of 852.5 million by 2050 [1–3]. In Türkiye specifically, the age-adjusted prevalence of diabetes has risen substantially over the past two decades, with recent forecasts estimating a prevalence of 17.5% by 2030 and 19.2% by 2045 [4, 5]. The increasing disease burden underscores the urgency of identifying modifiable risk factors that can be addressed within routine clinical care.

Hypoglycemia is a major limiting factor in glycemic management for both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) [6]. Severe hypoglycemia (SH) — defined as an episode requiring external assistance for recovery — is associated with significant clinical consequences, including cardiovascular events, arrhythmias, cognitive dysfunction, hospitalization, and mortality [7, 8]. Glycemic variability, which reflects the dynamic interplay between hyperglycemia and hypoglycemia, further amplifies oxidative stress and inflammatory burden [6]. Effective diabetes management therefore requires an integrated approach combining pharmacotherapy optimization with lifestyle modification, including smoking cessation [1, 5].

Smoking exacerbates insulin resistance and impairs glycemic control, thereby increasing the risk of microvascular and macrovascular complications, including neuropathy, retinopathy, and cardiovascular disease [9, 10]. Studies in populations without prior diabetes have established that active smoking increases the risk of incident T2DM through multiple mechanisms, including impairment of pancreatic beta-cell function and enhancement of peripheral insulin resistance [11, 12]. In individuals with established diabetes, smoking cessation has been associated with reductions in fasting plasma glucose and HbA1c levels [13]. However, evidence specifically addressing the relationship between smoking and hypoglycemia in diabetes management remains fragmented.

This scoping review aimed to systematically map the multifaceted evidence on the association between smoking exposure and hypoglycemia in individuals with DM. Specifically, we sought to examine: (1) whether smoking is associated with an increased risk of hypoglycemia; (2) whether this risk differs between T1DM and T2DM; (3) whether the association varies according to hypoglycemia severity; and (4) the overall strength, consistency, and certainty of the existing evidence. By integrating these dimensions, this review seeks to inform risk-stratified and proactive clinical strategies for hypoglycemia prevention.

Methods

Study Design and Framework

This scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) framework. The methodology was designed to systematically map the extant literature and identify key evidence regarding the association between smoking and hypoglycemia in individuals with diabetes.

Search Strategy and Information Sources

A systematic literature search was performed in two principal electronic databases: PubMed and Web of Science (WoS). The search strategy incorporated a combination of Medical Subject Headings (MeSH) terms and free-text keywords pertaining to “Diabetes,” “Hypoglycemia,” and “Smoking.”

PubMed (n = 148): (("Diabetes Mellitus"[Mesh] OR diabetes OR "diabetes mellitus") AND ("Hypoglycemia"[Mesh] OR hypoglycemia OR hypoglycaemia) AND ("Smoking"[Mesh] OR smoking OR tobacco OR nicotine))

Web of Science (n = 292): TS=((diabetes OR "diabetes mellitus" OR diabetic*) AND (hypoglycemia OR hypoglycaemia OR "low blood sugar") AND (smoking OR smoker* OR cigarette* OR tobacco OR nicotine OR "tobacco use"))

Study Selection and Eligibility Criteria

Following the initial search, 440 records were identified. After removing 206 duplicates, 234 unique articles remained for title and abstract screening. Of these, 124 were excluded due to wrong outcome (n = 88) or wrong population (n = 36). A further 77 records could not be retrieved in full text. Of 33 articles assessed for full-text eligibility, 14 were subsequently excluded (wrong association, n = 8; wrong study design, n

= 4; other, n = 2), yielding a final sample of 19 studies for synthesis. The complete selection process is depicted in Figure 1 (PRISMA flow diagram).

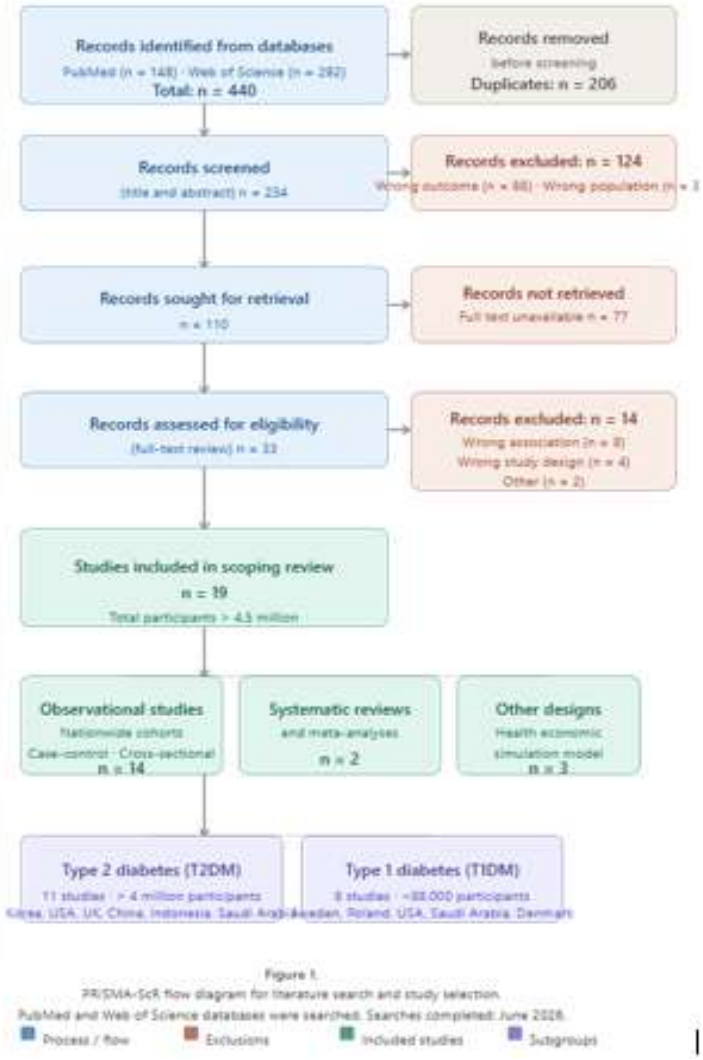


Figure 1: Prisma -ScR flow diagram of study

Predefined inclusion criteria were applied as follows:

Study Design: Primary research studies, including observational designs (prospective and retrospective cohorts, nested case-control, and cross-sectional) and interventional designs, were eligible. Secondary research, including systematic reviews, meta-analyses, and health economic simulation models, was also included to provide a comprehensive mapping of available evidence.

Population: Adults or adolescents with a confirmed diagnosis of any type of diabetes mellitus (T1DM, T2DM, or mixed populations).

Exposure: Smoking or tobacco use, encompassing current, former, or lifetime exposure.

Outcome: Hypoglycemia of any definition, including severe, symptomatic, CGM-detected, or biochemical episodes.

Language and Availability: Only English-language articles with accessible full-text were included in the final synthesis.

Data Extraction and Synthesis

Data were extracted using a standardized charting form, capturing study characteristics (author, year, country), population details, diabetes type, smoking exposure metrics, hypoglycemia definitions, effect sizes (hazard ratios, odds ratios, incidence rate ratios), and strength of evidence. Given the methodological heterogeneity across exposure measurements, outcome definitions, and analytic approaches, quantitative meta-analysis was not appropriate for the majority of outcomes. Findings were therefore synthesized narratively according to outcome severity and methodological robustness. A GRADE-based certainty of evidence assessment was applied for the key outcomes.

Results

Overview of Study Characteristics

Nineteen studies were included, collectively encompassing over 4.5 million individuals with T1DM, T2DM, or mixed diabetes populations (Table 1). Study designs were heterogeneous, including nationwide prospective cohorts, registry-based analyses, nested case–control studies, cross-sectional investigations, systematic reviews with meta-analyses, and one simulation model. Smoking exposure was primarily self-reported, although several large administrative cohorts utilized health examinations or registry-linked data. Hypoglycemia outcomes ranged from medically attended severe hypoglycemia to self-reported non-severe episodes, impaired awareness of hypoglycemia (IAH), mortality, and

markers of glycemic instability measured by continuous glucose monitoring (CGM).

No.	Study	Design / Data Source	Population	Smoking Exposure	Hypoglycemia Outcome	Main Finding / Effect Estimate	Direct Analysis	Evidence Category	Key Limitations
1	Ahlen et al., 2016 [14]	Nationwide cohort, Sweden	33,915 T1DM + 169,249 matched controls	Current smoking	Death from hypoglycemia or DKA in adults <50 yrs	Smoking: HR 2.86 (95% CI 1.57–5.22) for hypoglycemia/ DKA death	Yes (combined outcome)	T1DM mortality signal	Hypoglycemia and DKA combined; residual confounding
2	Hogendorf et al., 2017 [15]	Cross-sectional; ESPAD questionnaire	209 adolescents with T1DM; 12,114 controls	Lifetime and recent cigarette use	Severe hypoglycemia and DKA	Lifetime smoking associated with higher SH incidence and poorer metabolic control (HbA1c ≥8%)	Yes	T1DM adolescent evidence	Small T1DM sample; self-reported HbA1c; limited statistical power
3	Han et al., 2018 [16]	Nationwide population-based cohort; Korea NHID	1,676,885 adults with T2DM	Current smoking	Severe hypoglycemia (ICD-10 coded)	Current smoking: HR 1.17 (95% CI 1.08–1.26)	Yes	Core SH evidence (T2DM)	No HbA1c data; medically attended events only
4	Jendle et al., 2018 [17]	Health economic simulation (IQVIA CORE Diabetes Model)	1,000 simulated T1DM patients	Smoking subgroup (modelled)	Modelled long-term hypoglycemia outcomes	No direct empirical smoking–hypoglycemia effect estimated	No	Very low-certainty simulation	Simulation only; not empirical; derived from model assumptions
5	Shah et al., 2018 [18]	T1D Exchange registry; cross-sectional	9,481 adults with T1DM	Current smoking prevalence	Acute complications; self-care variables	Higher smoking prevalence in men; smoking–SH association not directly analyzed	No	Contextual T1DM evidence	Cross-sectional; smoking not modelled as SH predictor
6	Cai et al., 2019 [19]	Prospective nationwide cohort; China	5,770 newly diagnosed T2DM	Current smoking	Metabolic target failure; hypoglycemia (secondary)	Smoking associated with metabolic failure; hypoglycemia not directly linked to smoking	Indirect	Metabolic control pathway evidence	Short follow-up (12 months); not designed for smoking–hypoglycemia analysis
7	Yun et al., 2019 [20]	Nationwide population-based cohort; Korea	1.3+ million T2DM adults	Smoking in subgroup analyses	Severe hypoglycemia requiring medical care	Low BMI strongly associated with SH; smoking modified risk patterns (contextual)	Indirect/contextual	Contextual risk-factor evidence	Smoking not the primary exposure; administrative data only

No.	Study	Design / Data Source	Population	Smoking Exposure	Hypoglycemia Outcome	Main Finding / Effect Estimate	Direct Analysis	Evidence Category	Key Limitations
8	van Mark et al., 2020 [21]	Registry-based cross-sectional; DPV/DIVE registries	396,719 older adults with T2DM	Smoking prevalence by age group	SH across age groups	SH more frequent in oldest-old; smoking–SH association not directly modelled	No	Contextual elderly T2DM evidence	Smoking not tested as SH predictor
9	Zaccardi et al., 2020 [22]	UK primary care observational cohort	74,610 adults with T2DM	Current smoking (baseline covariate)	Severe hypoglycemia and cause-specific mortality	SH predicted higher mortality; smoking not tested as SH predictor	No	Contextual mortality evidence	Smoking not primary exposure; residual confounding
10	Jensen et al., 2021 [23]	Randomized trial CGM subanalysis (Onset 5)	49 smokers and 320 non-smokers; T1DM	Daily smoking	CGM-detected hypoglycemia; time in range; SH rate	Smokers: nearly doubled SH rate; higher glycemic variability; increased time in very low glucose	Yes	Objective CGM-based evidence	Small smoker subgroup; limited SH power; European/North American population only
11	Agrawal et al., 2022 [24]	Cross-sectional analysis; Poland	300 T1DM or T2DM patients	Smoking status	Self-reported hypoglycemia	Smoking correlated with increased hypoglycemia risk alongside alcohol use and low BMI	Yes (lower certainty)	Supportive cross-sectional evidence	Small sample; recall bias; cross-sectional design
12	Al-Ma'aitah et al., 2022 [25]	Systematic review and meta-analysis; MENA region	54 studies; 41,079 T2DM adults	Current smoking	Inadequate glycemic control	Smoking associated with poor glycemic control: OR 1.26 (95% CI 1.05–1.52)	Indirect	Metabolic pathway evidence	High heterogeneity; mostly cross-sectional; hypoglycemia not direct outcome
13	Galindo et al., 2022 [26]	Retrospective population-based cohort; USRDS	521,789 U.S. adults with diabetes and ESKD	Tobacco use (self-reported/registry)	Severe hypoglycemic crisis (ED/hospitalization)	Tobacco use: IRR 1.35 (95% CI 1.28–1.43)	Yes	Strong population-based evidence (ESKD)	Diabetes type not differentiated; administrative coding
14	Hassounah et al., 2022 [27]	Cross-sectional questionnaire study; Saudi Arabia	242 T1DM patients	Current smoking	Impaired awareness of hypoglycemia (IAH)	Smoking not significantly associated with IAH ($p = 0.166$)	No significant association	Low-certainty IAH evidence	Small sample; single center; self-reported exposure and outcome

No.	Study	Design / Data Source	Population	Smoking Exposure	Hypoglycemia Outcome	Main Finding / Effect Estimate	Direct Analysis	Evidence Category	Key Limitations
15	Settles et al., 2022 [28]	Nested case-control study; U.S. IQVIA claims data	3,153 case-control pairs; insulin-treated T2DM	Current or history of smoking	SH requiring emergency care	Smoking independently associated with SH: OR 1.28 (95% CI 1.08–1.52)	Yes	Core SH evidence	Emergency-care events only; pharmacy claims may not reflect actual intake
16	Yun et al., 2022 [29]	Nationwide longitudinal cohort; Korea	1,490,233 T2DM adults	Current smoking and lifestyle composite	Severe hypoglycemia requiring medical care	Current smoking: HR 1.28 (95% CI 1.23–1.34); lifestyle dose-response up to HR 1.81	Yes	Very strong population-based evidence	Lifestyle self-reported; HbA1c and medication dose unavailable
17	Naser et al., 2025 [30]	Retrospective cross-sectional; Saudi Arabia hospital	396 hospitalized patients with hypoglycemia	Ex-smoker/current smoker status	Hospitalization cost, length of stay, ICU admission	Ex-smokers: 4.4-fold higher hospitalization costs; smoking as incident risk factor not analyzed	No/indirect	Health economic burden evidence	Single-center; retrospective; cost/burden outcome not incident hypoglycemia risk
18	Veryanti et al., 2025 [31]	Cross-sectional outpatient study; Jakarta, Indonesia	501 T2DM outpatients; five hospitals	Current smoking vs. non-smoking	Any self-reported hypoglycemia (previous 3 months)	Non-smoking associated with higher reported hypoglycemia (OR 2.2; 95% CI 1.3–3.6); likely confounded	Yes (inconsistent result)	Low-certainty/conflicting evidence	Self-reported; cross-sectional; probable confounding by insulin use and treatment intensity
19	Zhang et al., 2025 [32]	Systematic review and meta-analysis	31 studies; 54,634 T1DM adults	Current smoking	Overall hypoglycemia risk in T1DM	Smoking: pooled OR 1.17 (95% CI 1.07–1.28)	Yes	Core T1DM meta-analytic evidence	Heterogeneity in hypoglycemia definitions; many cross-sectional studies included

Table 1: presents the full evidence base, organized chronologically. Table 2 provides a GRADE summary of evidence by outcome category.

Abbreviations: T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; SH, severe hypoglycemia; IAH, impaired awareness of hypoglycemia; HR, hazard ratio; OR, odds ratio; IRR, incidence rate ratio; CI, confidence interval; CGM, continuous glucose monitoring; ESKD, end-stage kidney disease; DKA, diabetic ketoacidosis; ED, emergency department; MENA, Middle East and North Africa; USRDS, United States Renal Data System; NHID, National Health Insurance Database.

Severe Hypoglycemia Requiring Medical Attention

The most consistent and methodologically robust evidence was derived from large population-based cohort studies examining medically attended SH. Han et al. [16] utilized a nationwide South Korean cohort of over 1.6 million adults with T2DM and demonstrated that current smoking was independently associated with an increased risk of SH (HR 1.17; 95% CI: 1.08–1.26), after adjustment for multiple confounders including age, sex, body mass index, comorbidities, and pharmacotherapy. Yun et al. [29] substantially extended this evidence in a cohort of 1,490,233 Korean adults with T2DM, confirming an adjusted HR of 1.28 (95% CI: 1.23–1.34) for current smokers. Critically, this study further demonstrated a dose-response relationship: the co-occurrence of smoking with other unhealthy lifestyle behaviors (heavy alcohol consumption, physical inactivity) was associated with an HR of 1.81, establishing a lifestyle risk-gradient model for SH prevention.

In a U.S. population-based cohort of 521,789 adults with diabetes and end-stage kidney disease (ESKD), Galindo et al. [26] reported that

tobacco use was independently associated with a significantly higher rate of severe hypoglycemic crises requiring emergency department visits or hospitalization (IRR 1.35; 95% CI: 1.28–1.43). Settles et al. [28], using a nested case–control design of insulin-treated T2DM patients, identified smoking as a previously underrecognized risk factor for medically attended SH (OR 1.28; 95% CI: 1.08–1.52), independent of established predictors including age, comorbidities, and insulin type.

Evidence in Type 1 Diabetes

Dedicated T1DM evidence was provided by several complementary studies. Ahlen et al. [14], in a nationwide Swedish cohort of 33,915 individuals with T1DM, found that smoking was a significant independent predictor of death attributed to hypoglycemia or diabetic ketoacidosis in adults younger than 50 years (HR 2.86; 95% CI: 1.57–5.22). While the combined outcome definition limits precise attribution to hypoglycemia alone, the magnitude of this effect was clinically substantial. Hogendorf et al. [15] reported, in a cross-sectional study of Polish adolescents with T1DM, that lifetime smoking was associated with higher SH incidence and worse metabolic control compared with non-smokers.

The most methodologically rigorous T1DM-specific evidence was provided by a recent meta-analysis by Zhang et al. [32], which synthesized data from 31 studies comprising 54,634 adults with T1DM and confirmed smoking as an independent risk factor for hypoglycemia (pooled OR 1.17; 95% CI: 1.07–1.28). This finding, derived through standardized pooled analysis, confirms the biological plausibility and statistical robustness of the smoking–hypoglycemia association in T1DM populations.

CGM-Detected Hypoglycemia and Glycemic Variability

Jensen et al. [23] provided objective, sensor-derived evidence from a sub-analysis of a randomized trial (Novo Nordisk Onset 5). Among 49 smokers and 320 non-smokers with T1DM receiving continuous subcutaneous insulin infusion, smokers exhibited a 4.7-fold increased risk of not achieving glycemic targets (95% CI: 1.5–15.4), increased time in hyperglycemia, decreased time in range, and a nearly two-fold higher rate of SH. CGM median profiles also revealed an elevated risk of morning hypoglycemia in smokers, suggesting a temporal pattern potentially related to nocturnal nicotine withdrawal effects on counterregulatory hormone release.

Non-Severe and Self-Reported Hypoglycemia

Evidence for non-severe and self-reported hypoglycemia was heterogeneous and of lower certainty. Agrawal et al. [24] demonstrated a positive correlation between smoking and hypoglycemia in a cross-sectional analysis of 300 Polish patients with T1DM or T2DM; however, the small sample size and cross-sectional design limit causal inference. Notably, Veryanti et al. [31] reported a paradoxical inverse association, with non-smoking independently associated with higher self-reported hypoglycemia risk (OR 2.2; 95% CI: 1.3–3.6) in a cohort of Indonesian outpatients. This result is likely confounded by differences in treatment intensity, with non-smoking patients potentially receiving more aggressive glucose-lowering pharmacotherapy, and illustrates the methodological challenges inherent to cross-sectional self-report designs.

GRADE Evidence Summary

Outcome	No. Studies	Key Studies	Participants	Effect Estimate	Certainty (GRADE)	Key Comments
Severe Hypoglycemia (Medical/ER)	7	Han 2018 [16]; Galindo 2022 [26]; Settles 2022 [28]; Yun 2022 [29]; Yun 2019 [20]; van Mark 2020 [21]; Zaccardi 2020 [22]	>4.5 million	HR/OR 1.17–1.35	HIGH	Consistent risk across large cohorts; dose-response relationship observed
Severe Hypoglycemia (T1DM Adults)	3	Ahlen 2016 [14]; Hogendorf 2017 [15]; Zhang 2025 meta-analysis [32]	~88,000	OR 1.17 (95% CI 1.07–1.28)	HIGH	Meta-analysis confirmed smoking as independent T1DM risk factor
CGM-Detected Hypoglycemia	1	Jensen 2021 [23]	369	~2-fold increase	MODERATE	Objective CGM-based evidence; strengthens biological plausibility; small smoker subgroup
Hypoglycemia-Related Mortality (T1DM)	1	Ahlen 2016 [14]	33,915	HR 2.86 (95% CI 1.57–5.22)	MODERATE	Outcome combined hypoglycemia + DKA; strong clinical signal
Metabolic Instability (HbA1c ≥7%)	1	Al-Ma'aitah 2022 [25]	41,079	OR 1.26 (95% CI 1.05–1.52)	MODERATE	Poor glycemic control may predispose to hypoglycemia through indirect pathway
Non-Severe / Self-Reported	4	Agrawal 2022 [24]; Hogendorf 2017 [15]; Veryanti 2025 [31]; Cai 2019 [19]	~6,800	OR 0.45–2.56	LOW	Heterogeneous definitions; recall bias; cross-sectional designs
Impaired Awareness (IAH)	1	Hassounah 2022 [27]	242	p = 0.166 (NS)	LOW	Self-reported outcomes; small sample; imprecision noted

Outcome	No. Studies	Key Studies	Participants	Effect Estimate	Certainty (GRADE)	Key Comments
Modelled Risk (Simulation)	1	Jendle 2018 [17]	1,000 (simulated)	No direct effect estimated	VERY LOW	Indirect modeling; no empirical data on smoking-hypoglycemia link

Table 2: presents the GRADE summary of evidence across the principal outcome categories. Consistent, large-effect-size evidence from multiple population-based cohorts supports high certainty for medically attended SH in both T1DM and T2DM, while CGM-based evidence was rated moderate certainty due to limited sample sizes in the smoker subgroup. Evidence for non-severe and self-reported hypoglycemia was rated low certainty, reflecting methodological heterogeneity and risk of bias.

Discussion

This scoping review synthesizes evidence from 19 studies encompassing over 4.5 million individuals to examine the association between smoking and hypoglycemia in diabetes. The findings demonstrate that smoking is consistently associated with an increased risk of SH requiring medical attention, with effect estimates ranging from HR/OR 1.17 to 1.35 across large-scale population-based cohorts. This association was observed in both T1DM and T2DM populations, with high-certainty evidence supporting smoking as an independent and modifiable risk factor for clinically attended SH. In contrast, evidence for non-severe, self-reported, and CGM-detected hypoglycemia remained heterogeneous and of lower certainty.

Several interacting biological and behavioral mechanisms plausibly underlie the observed association. Nicotine acutely stimulates catecholamine release, promoting transient hyperglycemia, but chronic smoking-induced insulin resistance may lead to compensatory increases in exogenous insulin dosing, elevating the background risk of hypoglycemia [9, 10]. Smoking also impairs sympatho-adrenal counterregulatory responses to hypoglycemia, potentially blunting glucagon secretion and epinephrine-mediated glucose recovery [14, 23]. Furthermore, smoking-associated irregular meal patterns, increased alcohol co-use, psychological distress, and lower adherence to self-management behaviors create a behavioral risk milieu that compounds the pharmacological risk [24, 29]. The lifestyle composite analysis by Yun et al. [29] exemplifies this interaction, with an escalating HR from 1.28 for smoking alone to 1.81 when combined with heavy drinking and physical inactivity.

The findings of this review carry several important clinical implications. First, smoking should be formally recognized as an independent and modifiable risk factor for SH and routinely assessed within comprehensive diabetes care frameworks. Current clinical guidelines, while emphasizing smoking cessation for cardiovascular and microvascular risk reduction [33], rarely highlight hypoglycemia prevention as a specific clinical indication. Incorporating hypoglycemia risk as an additional benefit of cessation may enhance patient motivation and prioritize cessation efforts in clinical encounters.

Second, patients with diabetes who smoke may benefit from intensified hypoglycemia prevention strategies, including structured education on hypoglycemia recognition and management, more frequent glucose monitoring, and preferential use of glucose-lowering agents with lower intrinsic hypoglycemia risk, such as GLP-1 receptor agonists or SGLT2 inhibitors, where clinically appropriate [34, 35]. For insulin-treated patients, proactive review of insulin regimens, dose adjustments, and integration of CGM technology may further mitigate smoking-related hypoglycemia risk, as supported by the CGM-based evidence of Jensen et al. [23].

Third, smoking cessation interventions should be proactively offered and integrated into routine diabetes care pathways. Evidence-based cessation strategies, including pharmacotherapy with nicotine replacement, varenicline, and bupropion, behavioral counseling, and digital health interventions, have demonstrated efficacy in the general population [36, 37]. Importantly, clinicians should anticipate and address challenges specific to diabetes, including transient glycemic variability during cessation, weight gain, and psychological distress [38, 39]. Cessation benefits for diabetes patients extend well beyond hypoglycemia risk reduction, encompassing clinically meaningful reductions in cardiovascular events, cancer risk, microvascular complications, and all-cause mortality [13, 40].

Finally, the health economic burden of SH is substantial. Naser et al. [30] demonstrated that ex-smokers hospitalized for hypoglycemia incurred 4.4-fold higher costs than non-smokers, underscoring the economic case for proactive smoking cessation as an acute safety and cost-reduction strategy within diabetes care systems.

Strengths and Limitations

The strengths of this review include the systematic search strategy, adherence to PRISMA-ScR guidelines, inclusion of diverse study designs from multiple healthcare systems, synthesis of data from over 4.5 million participants, and application of GRADE criteria to assess certainty of evidence. The inclusion of CGM-based and meta-analytic evidence further strengthens the evidence mapping.

Several limitations warrant acknowledgment. First, restriction to English-language publications may have introduced language bias, potentially excluding relevant studies from non-English-speaking countries. Second, the scoping review methodology prioritizes breadth over depth and does not include a formal risk of bias assessment; a systematic review with risk of bias evaluation would be warranted for primary outcomes. Third, heterogeneity in hypoglycemia definitions across studies — ranging from ICD-coded hospitalizations to self-reported symptomatic episodes to CGM-detected glucose values below 70 mg/dL — complicates direct comparisons. Adoption of standardized definitions, such as those proposed by the International Hypoglycemia Study Group [41], would facilitate future synthesis. Fourth, smoking exposure was predominantly self-reported across studies, introducing social desirability and misclassification bias; biochemical validation (e.g., cotinine measurement) was rarely employed. Fifth, as the majority of included studies were observational, causal inference is limited by residual confounding and potential reverse causation.

Conclusion

This scoping review provides high-certainty evidence that current smoking is associated with a consistent and clinically significant increase in the risk of severe hypoglycemia in individuals with T1DM and T2DM. The consistency of findings across large population-based cohorts, the demonstration of dose-response relationships, and the biological plausibility of multiple mechanistic pathways collectively support smoking as an independent and modifiable risk factor for severe hypoglycemic events requiring medical attention. Evidence for non-severe hypoglycemia, impaired awareness, and CGM-detected hypoglycemia remains more limited and of lower certainty.

From a clinical perspective, these findings underscore the importance of integrating smoking cessation into comprehensive diabetes care as a pragmatic acute safety strategy to reduce hypoglycemia risk, complementing established interventions such as patient education, intensified glucose monitoring, and pharmacotherapy optimization. From

a public health perspective, population-level smoking cessation programs and policy-level tobacco control measures may yield meaningful reductions in hypoglycemia-related morbidity, mortality, and healthcare expenditure in individuals with diabetes. Future interventional research incorporating hypoglycemia as a primary endpoint in diabetes-specific smoking cessation trials is needed to formally quantify the clinical and economic benefits of cessation for hypoglycemia prevention.

Declarations

Authors' Contributions

MMB conceived the study, designed the search strategy, conducted the literature search, performed data extraction and synthesis, and drafted the manuscript. IS contributed to the literature search, data extraction, and critical revision of the manuscript for important intellectual content. MAB provided clinical expertise, supervised the conceptual framework, critically revised the manuscript, and approved the final version for submission. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare no competing interests.

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This research received no external funding.

Ethical Compliance

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the relevant institutional and/or national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. As this is a scoping review of published literature and no primary data were collected, additional ethical approval was not required.

Data Access Statement

No primary data were generated or analyzed during this scoping review. All data supporting the conclusions of this review are drawn from the published literature included in the reference list.

AI Disclosure

During the preparation of this manuscript, the authors used Google Gemini (Google LLC, Mountain View, CA, USA) and Notebook LM (Google LLC) as AI-assisted tools to support initial literature organization, thematic structuring, and language refinement. All AI-generated suggestions were critically reviewed, verified against the primary literature, and substantially revised by the authors. AI tools were not used for study design, literature search execution, data extraction, statistical analysis, or interpretation of results. The authors take full responsibility for the integrity and accuracy of all content in this publication.

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References

1. Alshahrani A, Kabel AM, Alsuwat M, Ashour AM. (2022). The Impact of Smoking Cessation on the Control of Diabetes Mellitus and Blood Pressure in Saudi Arabia: A Prospective Randomized Controlled Clinical Trial. Med. Sci., 26(125), 1-14.
2. Magliano DJ, Boyko EJ; IDF Diabetes Atlas 11th Edition Scientific Committee. (2025). IDF Diabetes Atlas, 11th ed. Brussels: International Diabetes Federation.
3. International Diabetes Federation. (2025). IDF Diabetes Atlas 11th Edition — Middle-East & North Africa (MENA) Fact Sheet. Brussels: International Diabetes Federation.
4. Satman I, Omer B, Tutuncu Y, Kalaca S, Gedik S, Dinccag N, et al. (2013). Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur. J. Epidemiol., 28(2), 169-180.
5. Satman I, Bayirlioglu S, Okumuş F, Erturk N, Yemenici M, Cinemre S, et al. (2023). Estimates and forecasts on the burden of prediabetes and diabetes in adult and elderly population in Turkiye. Eur. J. Epidemiol., 38(3), 313-323.
6. Ceriello A, Monnier L, Owens D. (2019). Glycaemic variability in diabetes: clinical and therapeutic implications. Lancet Diabetes Endocrinol., 7(3), 221-230.
7. Echouffo-Tcheugui JB, Daya N, Lee AK, Tang O, Ndumele CE, Windham BG, et al. (2021). Severe hypoglycemia, cardiac structure and function, and risk of cardiovascular events among older adults with diabetes. Diabetes Care, 44(1), 248-254.
8. Frier BM. (2014). Hypoglycaemia in diabetes mellitus: epidemiology and clinical implications. Nat. Rev. Endocrinol., 10(12), 711-722.
9. Braffett BH, Rice MM, Young HA, Lachin JM. (2019). Mediation of the association of smoking and microvascular complications by glycemic control in type 1 diabetes. PLoS One, 14(7), e0219654.
10. Arnold SV, Khunti K, Tang F, Chen H, Cid-Ruzafa J, Cooper A, et al. (2021). Incidence rates and predictors of microvascular and macrovascular complications in patients with type 2 diabetes: Results from the longitudinal global DISCOVER study. Am. Heart J., 236, 80-88.
11. Pan A, Wang Y, Talaei M, Hu FB, Wu T. (2015). Relation of active, passive, and quitting smoking with incident type 2 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol., 3(12), 958-967.
12. Artese A, Stamford BA, Moffatt RJ. (2019). Cigarette smoking: an accessory to the development of insulin resistance. Am. J. Lifestyle Med., 13(6), 602-605.
13. Lycett D, Nichols L, Ryan R, Farley A, Roalfe A, Mohammed MA, et al. (2015). The association between smoking cessation and glycaemic control in patients with type 2 diabetes: a THIN database cohort study. Lancet Diabetes Endocrinol., 3(6), 423-430.
14. Ahlen E, Pivodic A, Wedel H, Dahlqvist S, Kosiborod M, Lind M. (2016). Glycemic Control, Renal Complications, and Current Smoking in Relation to Excess Risk of Mortality in Persons with Type 1 Diabetes. J. Diabetes Sci. Technol., 10(5), 1006-1014.
15. Hogendorf AM, Fendler W, Sieroslawski J, Bobeff K, Wegrewicz K, Malewska KI, et al. (2017). Alcohol and cigarette use among adolescents with type 1 diabetes. Eur. J. Pediatr., 176(6), 713-722.
16. Han K, Yun JS, Park YM, Ahn YB, Cho JH, Cha SA, et al. (2018). Development and validation of a risk prediction model for severe hypoglycemia in adult patients with type 2 diabetes: a nationwide population-based cohort study. Clin. Epidemiol., 10, 1545-1559.
17. Jendle J, Ericsson A, Hunt B, Valentine WJ, Pollock RF. (2018). Achieving good glycemic control early after onset of diabetes: a cost-effectiveness analysis in patients with type 1 diabetes in Sweden. Diabetes Ther., 9(1), 87-99.
18. Shah VN, Wu M, Polsky S, Snell-Bergeon JK, Sherr JL, Cengiz E, et al. (2018). Gender differences in diabetes self-care in adults with type 1 diabetes: findings from the T1D Exchange clinic registry. J. Diabetes Complications, 32(10), 961-965.

19. Cai X, Hu D, Pan C, Li G, Lu J, Ji Q, et al. (2019). The risk factors of glycemic control, blood pressure control, lipid control in Chinese patients with newly diagnosed type 2 diabetes: a nationwide prospective cohort study. Sci. Rep., 9(1), 7709.
20. Yun JS, Park YM, Han K, Cha SA, Ahn YB, Ko SH. (2019). Association between BMI and risk of severe hypoglycaemia in type 2 diabetes. Diabetes Metab., 45(1), 19-25.
21. van Mark G, Tittel SR, Sziegoleit S, Putz FJ, Durmaz M, Bortscheller M, et al. (2020). Type 2 diabetes in older patients: an analysis of the DPV and DIVE databases. Ther. Adv. Endocrinol. Metab., 11, 2042018820958296.
22. Zaccardi F, Ling S, Lawson C, Davies MJ, Khunti K. (2020). Severe hypoglycaemia and absolute risk of cause-specific mortality in individuals with type 2 diabetes: a UK primary care observational study. Diabetologia, 63(10), 2129-2139.
23. Jensen MH, Cichosz SL, Hirsch IB, Vestergaard P, Hejlesen O, Seto E. (2021). Smoking is Associated with Increased Risk of Not Achieving Glycemic Target, Increased Glycemic Variability, and Increased Risk of Hypoglycemia for People with Type 1 Diabetes. J. Diabetes Sci. Technol., 15(4), 827-832.
24. Agrawal S, Makuch S, Drozdz M, Dudzik T, Domanski I, Poreba R, et al. (2022). The impact of hypoglycemia on patients with diabetes mellitus: a cross-sectional analysis. J. Clin. Med., 11(3), 748.
25. Al-Ma'aitah OH, Demant D, Jakimowicz S, Perry L. (2022). Glycaemic control and its associated factors in patients with type 2 diabetes in the Middle East and North Africa: an updated systematic review and meta-analysis. J. Adv. Nurs., 78(8), 2257-2276.
26. Galindo RJ, Ali MK, Funni SA, Dodge AB, Kurani SS, Shah ND, et al. (2022). Hypoglycemic and hyperglycemic crises among U.S. adults with diabetes and end-stage kidney disease: population-based study, 2013-2017. Diabetes Care, 45(1), 100-107.
27. Hassounah G, Abdullah Aljohani AE, Al Sharhani R, Al Aljoulni M, Robert AA, Al Goudah AH, et al. (2022). Prevalence of impaired awareness of hypoglycemia and its risk factors among patients with type 1 diabetes in Saudi Arabia. Diabetes Metab. Syndr., 16(1), 102351.
28. Settles J, Kan H, Child CJ, Gorritz M, Multani JK, McGuiness CB, et al. (2022). Previously unrecognized risk factors for severe hypoglycaemia requiring emergency medical care in insulin-treated type 2 diabetes: results from a real-world nested case-control study. Diabetes Obes. Metab., 24(7), 1235-1244.
29. Yun JS, Han K, Park YM, Han E, Lee YH, Ko SH. (2022). Adherence to healthy lifestyle behaviors as a preventable risk factor for severe hypoglycemia in people with type 2 diabetes: a longitudinal nationwide cohort study. J. Diabetes Investig., 13(9), 1533-1542.
30. Naser AY, Qadus S, AlOsaimi HM, AlFayez A, Bin Huwayshil H, Al Harbi LA, et al. (2025). Cost of hospitalization and length of stay of hypoglycemic events in hospitalized patients with diabetes mellitus: a cross-sectional study. Medicine (Baltimore), 104(11), e41840.
31. Veryanti P, Sauriasari R, Sartika RAD, Elya B. (2025). Factors influencing hypoglycemia in type 2 diabetes mellitus outpatients with state health insurance at regional general hospitals in Jakarta, Indonesia. Curr. Diabetes Rev., 21(1).
32. Zhang Q, Zhou H, Lin R, Hu L, Zhu X. (2025). Risk factors for hypoglycaemia in adults with type 1 diabetes: a systematic review and meta-analysis. BMC Endocr. Disord., 26(1), 21.
33. Elsayed NA, Aleppo G, Bannuru RR, Beverly EA, Bruemmer D, Collins BS, et al. (2024). 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: Standards of Care in Diabetes—2024. Diabetes Care, 47(Suppl. 1), S77-S110.
34. Standl E, Ceriello A, McGuire DK, Schnell O, Holman RR. (2025). Clinical perspectives of new insights and tools to minimize the hypoglycaemia burden connected with type 2 diabetes pharmacotherapy. Cardiovasc. Diabetol., 24(1), 441.
35. Mathieu C, Martens PJ, Vangoitsenhoven R. (2021). One hundred years of insulin therapy. Nat. Rev. Endocrinol., 17(12), 715-725.
36. Li WHC, Wang MP, Lam TH, Cheung YT, Cheung DY, Suen YN, et al. (2017). Brief intervention to promote smoking cessation and improve glycemic control in smokers with type 2 diabetes: a randomized controlled trial. Sci. Rep., 7(1), 45902.
37. Reid RD, Malcolm J, Wooding E, Geertsma A, Aitken D, Arbeau D, et al. (2018). Prospective, cluster-randomized trial to implement the Ottawa model for smoking cessation in diabetes education programs in Ontario, Canada. Diabetes Care, 41(3), 406-412.
38. Kos K. (2020). Cardiometabolic morbidity and mortality with smoking cessation, review of recommendations for people with diabetes and obesity. Curr. Diabetes Rep., 20(12), 82.
39. Sepulveda E, Poinhos R, Nata G, Gaspar N, Freitas P, Vicente SG, et al. (2025). Relationship between severe hypoglycemia or impaired awareness of hypoglycemia and diabetes-related health status, global cognition, and executive functions in adults with type 1 diabetes without severe anxiety or depression. Diabetes Res. Clin. Pract., 221, 112004.
40. Liu G, Hu Y, Zong G, Pan A, Manson JE, Rexrode KM, et al. (2020). Smoking cessation and weight change in relation to cardiovascular disease incidence and mortality in people with type 2 diabetes: a population-based cohort study. Lancet Diabetes Endocrinol., 8(2), 125-133.
41. Heller SR, Buse JB, Ratner R, Seaquist E, Bardtrum L, Hansen CT, et al. (2020). Redefining hypoglycemia in clinical trials: validation of definitions recently adopted by the American Diabetes Association/European Association for the Study of Diabetes. Diabetes Care, 43(2), 398-404.
42. Thankappan K, Mini GK, Daivadanam M, Vijayakumar G, Sarma PS, Nichter M. (2013). Smoking cessation among diabetes patients: results of a pilot randomized controlled trial in Kerala, India. BMC Public Health, 13(1), 47.
43. Register SJ, Harrington KF, Agne AA, Cherrington AL. (2016). Effectiveness of non-primary care-based smoking cessation interventions for adults with diabetes: a systematic literature review. Curr. Diabetes Rep., 16(9), 81.

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