Prevalence, incidence,and associated risk factors of hypoglycemia among patients with diabetes using insulin pump therapy: mini-review

Abstract

Background: Continuous Subcutaneous Insulin Infusion (CSII), commonly known as an insulin pump, is widely used to enhanceglycaemia control in individuals with insulin-dependent diabetes. Despite its benefits, hypoglycemia continues to be a significant adverse effect of insulin therapy. This systematic literature review aims to compile and analyze published evidence regarding the prevalence and incidence of hypoglycemia among users of insulin pumps. Additionally, it summarizes the identified risk factors related to the patients, their diseases, and the devices themselves.

Methods: We conducted a structured literature review search (PubMed, Medline, Embase, Web of Science, Scopus, and relevant diabetes technology journals) for English-language primary studies, observational cohorts, randomized trials, and prior systematic reviews up to 15 Sep 2025. Search terms included combinations of: “insulin pump”, “CSII”, “hypoglycemia”,” prevalence”, incidence”, risk Factors”, and “severe hypoglycemia”. We prioritize high-quality population-based studies and systematic reviews; where available, we report event rates and important effect estimates. Now new meta-analysis was performed; results are synthesized narratively.

Results: Multiple observational studies and systematic reviews indicate that users of CSII experience both non-severe and severe hypoglycemia, but many studies find reduced rates of severe hypoglycemia with pump therapy compared with MDI or historical cohorts. For example, a large population-based study in young patients reported lower severe hypoglycemia rates with pump therapy vs injections (~9.6 vs 14.0 events per 100 patient-years). Reported prevalence of (any) hypoglycemia varied widely across studies because of differing definitions (biochemical, CGM-derived, symptomatic, or levels (mild, moderate, and severe) and follow-up methods (patient report vs continuous glucose monitoring). Important, repeatedly reported risk factors for hypoglycemia in insulin-pump users include prior history of severe hypoglycemia or impaired hypoglycemia awareness (IHA), longer diabetes duration, lower baseline HbA1c (intensive control), renal impairment, concurrent alcohol use, and glycemic variability. Integration of CGM with CSII appears to reduce hypoglycemia risk compared with CSII alone in multiple reports.

Conclusion: insulin-pump therapy does not eliminate hypoglycemia risk. However, for many patient groups (particularly younger patients with Type 1 DM), CSII is associated with lower rates of severe hypoglycemia compared with MDI; combined CGM+CSII provides further protection. Patient selection (history of hypoglycemia, awareness status), renal function, behavioral factors, and device/algorithm use are key determinants of risk. Future work should standardize hypoglycemia outcome definitions (CGM-based metrics), report device configurations (sensor-augmented, hybrid closed loop), and apply pooled analyses to estimate prevalence across settings.

***Key words*:** Prevalence, Incidence, Hypoglycemia, Continuous Subcutaneous Insulin Infusion (CSII), Risk Factors, Severe Hypoglycemia.

Introduction

Hypoglycemia, defined as blood glucose levels generally below 70 mg/dL (with "level2: often falling below 54mg/dL and "level 3" indicating a need for external assistance), is recognized as the most common acute complication arising from insulin therapy[1, 2, 4, 6]. It poses a significant challenge to achieving safe glycemic optimization[5, 7]. The implementation of insulin pump therapy specially (Continuous subcutaneous insulin infusion, CSII) is designed to provide a more physiologic delivery of basal insulin, allowing for precise titration of bolus dosing[7- 8, 11-12]. This approach holds promise for reducing hypoglycemia compared to more rigid injection regimens[9, 12].

Despite these advancements, instances of hypoglycemia including nocturnal and severe episodes remain a concern among CSII users. Gaining insight into the prevalence and risk factors associated with hypoglycemia within this group is crucial for informed clinical decision-making and the future design of insulin delivery devices. While previous randomised and observational studies, along with reviews, have produced mixed results, they generally suggest that insulin pumps, particularly when used in conjunction with continuous glucose monitoring (CGM), can lead to favorable outcomes in reducing severe hypoglycemia rates[2-3, 14-15].

Methods

Search strategy:

We searched PubMed/Medline, Embase, Webof Science, Scopus, and diabetes technology journals (Diabetes Care, Diabetic Medicine, Diabetes Technology and Therapeutics, JAMA, BMJ, Lancet Diabetes and Endocrinology) between 30th ofSeptember and15th of October 2025. Search terms combined keywords and MeSH (where available): (insulin pump or CSII or continuous subcutaneous insulin infusion), and (hypoglycemia or hypoglycemia unawareness or severe hypoglycemia), and (prevalence or incidence or frequency or risk factors). We also screened references of recent systematic reviews and large observational cohorts.

Inclusion and exclusion criteria:

Included: Primary studies report prevalence or incidence of hypoglycemia among insulin-pump users (adult and pediatric), comparative studies of CSII vs MDI reporting

hypoglycemia outcomes, and systematic reviews/meta-analyses that included pump users within the last 10 years.

Excluded: single-patient case reports, small trial without hypoglycemia reporting, and non-English articles.

Data extraction and synthesis:

From each study we extract the following: study design, population (age and diabetes type), sample size, follow-up duration, hypoglycemia definition used, reported prevalence or incidence (per patient or per 100 patient-years, and reported risk factors or adjusted predictors. Quality was appraised using standard tools for observational studies (e.g. Newcastle-Ottawa Scale) and risk of bias for trials. Because of heterogeneity in outcomes and definitions (patient-report vs CGM), we performed narrative synthesis rather than pooled meta-analysis.

Results

1. Overview of the evidence base:

The literature consists of randomized controlled trials comparing CSII vs MDI (many small and older), multiple large observational registry/cohort studies, and several systematic reviews summarizing device discontinuation and complication rates. Population-based and registry analyses have provided the strongest evidence on event rates in routine care. Adoption of CSII varied by region and time; uptake has increased substantially over the past two decades[2].Table 1 summarizes the most important findings.

Study/Review	Design and population	Key hypoglycemia finding
Karges et al. JAMA (2017) [1]	Population-based observational, youth Type 1 DM	Pump vs injection: lower severe hypoglycemia rates (≈9.55 vs 13.97 events/100 patient-years)
Heinemann L. Diabetes Care (2015) review [2]	Narrative/clinical appraisal of pump risks/benefit	Review evidence that CSII often reduces severe hypoglycemia: highlights technology + training importance
Guzman et al., glycemic control/hypoglycemia analysis (2020) [3]	Observational cohort/CGM metric	Identified glucose variability metrics and male sex as associated with clinically significant hypoglycemia in their model

Umpierrez et al., Review article (2018)[8]	Technology update	Describe increasing use of pumps; discusses hypoglycemia outcomes with sensor integration
Recent systematic review on CSII discontinuation and outcomes (2023) [5]	Systematic review	Complications; notes hypoglycemia among reasons and emphasizes CGM benefits

Table 1: Representative studies and reviews

2. **Prevalence/incidence estimates show wide heterogeneity:**

- **Severe hypoglycemia:** several large observational studies show lower event rates of severe hypoglycemia among pump users compared with MDI. A prominent population-based study of young patients with Type 1 diabetes reported severe hypoglycemia rates of ~9.6 vs 14.0 events per 100 patient-years for CSII vs MDI. This and similar registry analyses suggest a clinically meaningful reduction in severe hypoglycemia with pump in real-world cohorts[1].
- **Non-severe hypoglycemia:** the rates of hypoglycemia can vary significantly depending on the detection methods used. Studies utilizing CGM indicate that a considerable number of these users experience episodes of hypoglycemia (time <70 mg/dL and time <54 mg/dL), with reported percentages of patients experiencing hypoglycemia over study windows varying widely (single-digit per cent to >40%), depending on population, CGM thresholds, and sensor use. Comparisons across studies are limited by inconsistent outcome definitions and duration of monitoring[3].

3. **Effect of combining CSII with CGM/ sensor-augmented pumps:**

The combination of CSII with CGM has shown promising benefits in hypoglycemia management. Numerous studies and reviews indicate that integrated CGM and features like low-glucose suspend or predictive-suspend features, compared to CSII alone [1,12].

Sensor-augmented or hybrid closed-loop systems reduce both time in hypoglycemia and severe events in many controlled trials and real-world reports. Reviews of pump technologies note that CGM integration is a major contributor to observed hypoglycemia reductions[2].

4. **Risk factors associated with hypoglycemia among CSII users:**

Numerous observational studies and reviews consistently identify key risk factors for hypoglycemia among CSII users:

- **Impaired awareness of hypoglycemia:** strong predictor of future severe events. Impaired awareness of hypoglycemia prevalence remains meaningful among pump users and increases risk[6].

- **Longer diabetes duration:** longer duration correlates with more autonomic dysfunction and impaired awareness of hypoglycemia, increasing risk[4].
- **Intensive glycemic control/lower HbA1c:** Ambitiously low targets without appropriate safety features can increase hypoglycemia frequency[2].
- **Renal impairment:**Reduced renal clearance and altered counter-regulation raise hypoglycemia risk[3].
- **Glycemic variability and higher glucose variability metric (SD, coefficient of variation (CV)):**Associated with both frequent and severe hypoglycemia in some cohorts[3].
- **Behavioral/medication factors:** Alcohol use, missed meals relative to insulin dosing, and errors in pump programming or infusion set problems contribute to episodes. Device malfunctions or infusion-set failures are known acute causes of hyperglycemia/DKA but can also precipitate hypoglycemia when dosing errors occur[3].
- **Special populations:**
    - **Children and adolescents:** Many pediatric studies report net reductions in severe hypoglycemia with pump therapy; however, nocturnal hypoglycemia and caregiver factors remain important considerations[1,9].
    - **Type 2 diabetes on pump:** Less data than for Type 1 diabetes; pumps are used in selected insulin-treated Type 2 diabetes patients. Hypoglycemia patterns differ because of insulin resistance and dosing, and careful titration is required[7].

Discussion

The evidence clearly shows that insulin pump therapy significantly reduces the risk of severe hypoglycemia compared with injection-based regimens, particularly when combined with CGM and the pump's safety features. However, it is essential to note that this therapy does not eliminate the risk of non-severe or biochemical hypoglycemia. The benefits are largely determined by patient characteristics, such as their history of hypoglycemia and level of awareness, as well as the specific features of the device, including CGM, low-glucose suspension, and closed-loop algorithms. Additionally, system-level factors like training, follow-up care, and access to supply paly a critical role in the overall effectiveness of insulin pump therapy.

Clinical implications:

- **Patient selection:**CSII, especially closed-loop systems, should be strongly considered for patients with a history of severe hypoglycemia or impaired awareness;they must have access to proper training and CGM[1].

- **Device pairing:**CSII integrated with real-time CGM or predictive-suspend features must be prioritized whenever feasible, asthis significantly reduces the risks of hypoglycemia[2].
- **Monitoring and education:** Regular CGM data reviews, strict adherence to infusion set techniques, and comprehensive education on insulin patterns (including mealtime insulin matchingand alcohol impacts) are vital in managing patient health efficacy.

The recommendations for future research:

1. Standardize outcomes: use CGM-derived consensus metrics across studies to enable pooling.
2. Device-specific reporting: Report whether CSII was standalone, sensor-augmented, or hybrid closed-loop, and include firmware/algorithm version when available.
3. Prospective registries and pooled analysis: Large international registries capturing CGM+CSII data could produce robust prevalence/incidence estimates and better adjusted risk models.
4. Interventional studies in high-risk subgroup: Trials that evaluate targeted interventions (for example, IHA-focused education+ sensor-augmented pump) for hypoglycemia reduction.

Conclusion:

Insulin-pump therapy does not eliminate the risk of hypoglycemia. Nevertheless, for many patient populations (particularly younger individuals with Type 1 DM), CSII is associated with lower rates of severehypoglycemia compared with MDI. The integration of CGM with CSII offers additional and further reduces risk.

Carful patient selection remains essential, with key considerations including a history of hypoglycemia, level of hypoglycemia awareness, renal function, behavioural and lifestyle factors, as well as adherence to device use and algorithm guidance.

Future research should focus on standardizing hypoglycemia outcome definitions, particularly through CGM-based metrics, clearly reporting device configurations (such as hybrid closed loop systems), and conducting pooled analyses to more accurately estimate prevalence across clinical settings.

Limitations of the current literature:

1. The inconsistencies in how hypoglycemia is defined (symptomatic, biochemical, and severe) and the varying methods of surveillance (self-reporting vs CGM) significantly hinder straightforward aggregation of prevalence estimates.
2. Most studies are observational and device/technology evolution over time makes older studies less applicable to current devices.
3. Geographic and health-system differences influence pump adoption and support, affecting generalizability.

References

1. Karges B, Schwandt A, Heidtmann B, et al. Insulin Pump vs Insulin Injection and Type 1 Diabetes: population/registry evidence on complications and hypoglycemia. JAMA.
2. Heinemann L. Fleming G, John R, et al. Insulin Pump Risks and Benefits: A Clinical Appraisal of Pump. Diabetes Care. 2015.
3. Guzman G,Martinez V, Yara J, et al. Glycemic Control and Hypoglycemia in Patients Treated with continuous glucose monitoring: Cohort study. 2020.
4. Nakhleh A, Shahadeh N. Hypoglycemia in diabetes: An update on pathophysiology, treatment, and prevention. 2021.
5. Diabetes Technology & Therapeutics. Systematic review on pump discontinuation and outcomes. 2023.
6. Sakane N, Kato K, Hata S, et al. Protective and risk factors of impaired awareness of hypoglycemia in patients with type 1 diabetes: a cross-sectional analysis of baseline data from the PR-IAH study. 2023.
7. Keyu G, Jiagi L, Liyin Z, et al. Comparing the effectiveness of subcutaneous insulin infusion with multiple daily insulin injection for patients with type 1 diabetes mellitus evaluated by retrospective continuous glucose monitoring: A real-world data analysis.2022.
8. Umpierrez G, Klonoff D. Diabetes Technology Update: Use of Insulin Pumps and Continuous Glucose Monitoring in the Hospital. 2018.
9. Karges B, Rosenbauer J, Kapellen T, et al. Hemoglobin A1c level and risk of severe hypoglycemia in children and young adults with type 1 diabetes from Germany and Austria: a trend analysis in a cohort of 37,539 patients between 1995 and 2012. 2014.
10. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med. 1993; 329: 977–986.
11. Ly T, Necholas J, Retterath A, et al. Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. JAMA. 2013; 310(12):1240-1247.
12. Pickup J, Sutton A. Severe hypoglycemia and glycemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections with continuous subcutaneous insulin infusion. Diabet Med. 2008; 25(7):765-774.
13. Pickup JC. Insulin pumps. Diabetes Technol Ther. 2013;15(Suppl. 1): S24-S28.
14. Guariguata L, Whiting D, Weil C, et al. The International Diabetes Federation diabetes atlas methodology for estimating global and national prevalence of diabetes in adults. Diabetes Research and Clinical Practice. 2011;94(3): 322-332.
15. Reznik Y, Cohen O, Aronson R, et al. Insulin pump treatment compared with multiple daily injections for treatment of type 2 diabetes (OpT2mise): a randomized open-label controlled trial. The Lancet. 2014; 348(9950):1265-1272.