# **DSEN ABSTRACT**

Safety, effectiveness, and cost-effectiveness of long-acting versus intermediate-acting insulin for patients with type 1 diabetes: a systematic review and network meta-analysis

#### **Summary**

The objective of this review was to examine the safety, effectiveness, and costeffectiveness of long-acting insulin compared to intermediate-acting insulin in patients with type 1 diabetes. A total of 38 studies including 27 RCTs were included in the review. Overall, the findings suggest that long-acting insulin analogs are slightly superior to intermediate-acting analogs for glycemic control and harms (weight gain and severe hypoglycemia).

#### **Implications**

Although long-acting insulin is superior to intermediate-acting insulin, it is likely more expensive. As such, patients and their physicians should tailor their choice of insulin according to their preference, cost, and accessibility.

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### What is the current practice in treating type 1 diabetes?

- Hyperglycemia associated with type 1 diabetes has been commonly treated with intermediate-acting insulin such as isphane insulin (NPH) and zinc insulin (lente).
- Evidence suggests, however, that newer long-acting insulin analogs (i.e. glargine and detemir) may be safe and more effective than NPH and lente.

## What was the aim of the study?

• The objective of this systematic review was to examine the safety, effectiveness, and cost-effectiveness of long-acting insulin in patients with type 1 diabetes.

### How was the study conducted?

- The protocol (or plan) for the review was developed and revised with input from researchers, clinicians, and the British Columbia Ministry of Health.
- 3 databases and unpublished literature were searched for randomized controlled trials (RCTs) or non-randomized studies of long- and intermediate-acting insulin in adults with type 1 diabetes.
- The primary outcome of interest was glycosylated hemoglobin (A1C) and secondary outcomes included severe hypoglycemia, serious hyperglycemia, and weight gain.
- Screening of literature search results, data abstraction, and risk-of-bias were conducted independently by two reviewers.
- Random-effects pairwise meta-analysis (MA) and random-effects network metaanalysis (NMA) were conducted based on the availability of evidence.

## What did the study find?

- 38 relevant studies and 1 companion report were identified, including 27 RCTs representing 7,496 patients.
- Glargine once daily, detemir once daily and detemir twice daily significantly reduced A1C compared to NPH once daily in an NMA (26 RCTs).
- In a subgroup analysis (12 RCTs), glargine once daily was significantly more effective compared to NPH once daily for patients with poorly controlled diabetes (A1C>8%).
- Patients receiving detemir once or twice daily experienced significantly fewer episodes of severe hypoglycemia compared to NPH once or twice daily (16 RCTs).
- NPH once daily and detemir once daily caused significantly more weight gain, however, detemir once or twice daily caused significantly less weight gain than NPH once or twice daily (13 RCTs).

This research was funded by CIHR – Drug Safety and Effectiveness Network and conducted by investigators affiliated with the following institutions:



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