PROTOCOL BRIEF

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Comparative Efficacy and Safety of Intermediate-acting, Long-acting and Biosimilar insulins for Type 1 Diabetes Mellitus: A Systematic Review and Network Meta-Analysis

Rationale

Type 1 Diabetes Mellitus (T1DM) is managed with a basal-bolus insulin regimen. Three choices for basal insulin exist: long-acting, intermediate-acting, and biosimilars. The objective of this study is to compare the clinical effectiveness and safety of intermediate-acting, long-acting and biosimilar insulins for patients with T1DM.

Implications

This study aims to provide patients with T1DM and their physicians with recommendations to help tailor insulin treatment regimens. The results of this study are expected to contribute to discussions on the World Health Organization's List of Essential Medicines and inform clinical practice guidelines worldwide.

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Background

- The incidence of Type 1 Diabetes Mellitus (T1DM) is increasing globally every year and is managed with a basal-bolus insulin regimen. Three choices for basal insulin exist: long- and intermediate-acting insulin, as well as biosimilar insulins.

Objective

- To compare the comparative effectiveness and safety of intermediate-/long-acting insulin products and intermediate-/long-acting biosimilar insulin products in patients with T1DM.
- To determine whether intermediate- and long-acting biosimilar insulin products can be used as a replacement for reference intermediate- and long-acting insulin (including insulin analogues) products when the latter products are not available (due to cost or supply issues).

Methodology

- A systematic review will be conducted, guided by the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement for network meta -analysis.
- Our eligibility criteria are outlined using the PICOST framework as follows:

  Population: Adults (at least 18 years of age) with T1DM

  Interventions: Long- or intermediate-acting insulins and insulin analogues, and biosimilar insulins.

  Comparators: Long- or intermediate-acting insulins and insulin analogues, biosimilar insulins, and no treatment

  Outcomes: Glycemic control, efficacy outcomes (mortality, diabetes-related morbidity, and health-related quality of life), harms outcomes (total adverse events, serious adverse events, withdrawals due to adverse events, and notable harms), and cost (using effectiveness studies).

  Study Designs: Experimental, quasi-experimental, and observational study designs, as well as cost-effectiveness analyses and cost-utility analyses.
- The literature search will be executed in MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials. Grey literature will be identified by searching public health websites, drug regulatory websites and clinical trial registries.
- Title and abstract screening, full-text screening, and data abstraction will be conducted in duplicate. All discrepancies will be resolved by discussion or involvement of a third reviewer.
- The analysis will predominantly be conducted using network meta-analyses.

Knowledge Translation Strategy

- The summary of results will be sent to the Canadian Institutes of Health Research Drug Safety and Effectiveness Network, Health Canada, the Canadian Agency for Drugs and Technologies in Health, and the World Health Organization policy-makers in the form of a 1-page policy brief. We will also submit the results as a presentation at a relevant conference and as a paper for publication in an open-access, peer-reviewed journal.

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