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OPTIMAL THERAPY REPORT

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SUMMARY REPORT: Optimal Prescribing and Use of Insulin Analogues

Supporting Informed Decisions

À l'appui des décisions éclairées

This Summary is based on comprehensive Optimal Therapy Reports on the topic, prepared by the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS), a service of the Canadian Agency for Drugs and Technologies in Health (CADTH). The conclusions were provided by experts. The authors have also considered input from other stakeholders.

The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders and policymakers make well-informed decisions and thereby improve the quality of health care services. The information in this report should not be used as a substitute for the application of clinical judgement in respect of the care of a particular patient or other professional judgement in any decision making process nor is it intended to replace professional medical advice. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up-to-date, CADTH does not make any guarantee to that effect. CADTH is not responsible for any errors or omissions or injury, loss or damage arising from or as a result of the use (or misuse) of any information contained in or implied by the information in this Report.

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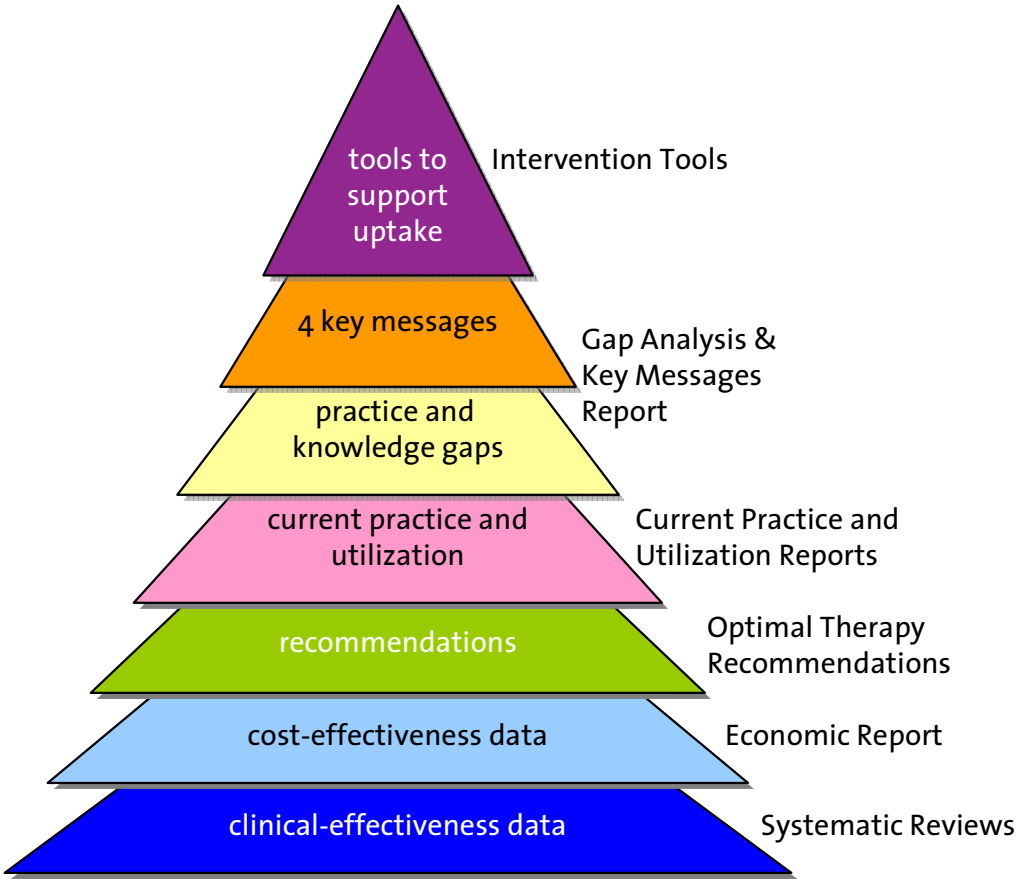
SUMMARY REPORT:
Optimal Prescribing and Use of Insulin Analogues

The Canadian Agency for Drugs and Technologies in Health (CADTH) through its Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) — has released a series of Optimal Therapy Reports on insulin analogues, together with recommendations and intervention tools to support the uptake of this information. These reports and tools are part of the diabetes mellitus topic, a priority area identified by the COMPUS Advisory Committee (CAC).

This summary highlights the work done by COMPUS, from the most concise information available, in user-friendly intervention tools, back through to the evidence on which recommendations and tools were built. The following diagram presents each level of information; the corresponding sections in this summary include a link to the Optimal Therapy Report or tool on the CADTH website.



More information and the full Optimal Therapy Reports and tools may be found on the CADTH website (www.cadth.ca).

Tools to support uptake

Optimal Therapy Tools: *Series of tools to support uptake*

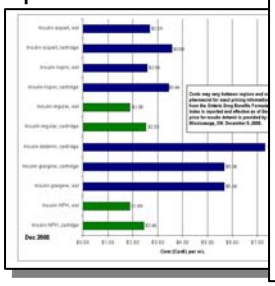
Four key messages

Optimal Therapy Report: *Gap Analysis and Key Messages for the Prescribing and Use of Insulin Analogues*

A menu of intervention tools were developed based on the key messages targeted to improve the prescribing and use of insulin analogues. Input from experts and potential users aided in the selection of tools based on the best available evidence.

Examples:

- didactic presentations for prescribers and pharmacists
- interactive presentations for prescribers and pharmacists
- optimal therapy newsletter
- project highlights brochure
- prescribing aid (with cost information)
- academic detailing upskilling document.



Key messages including "**should/can**" correspond to **strong** optimal therapy recommendations*

Key messages including "**may**" correspond to **weak** optimal therapy recommendations*

*based upon quality of evidence, weighing the balance of benefits versus harms, and identifying underlying values and preferences

Key Messages (When Choosing an Insulin):

Bolus insulin therapy:

- In patients with type 1 diabetes, either regular human insulin or rapid-acting insulin analogues **can** be considered as first-line therapy (except in adolescent patients).
- In adolescent patients with type 1 diabetes, rapid-acting insulin analogues **may** be considered as first-line therapy.
- In patients with type 2 diabetes requiring bolus insulin, regular human insulin **may** be considered first. Although the evidence is limited and inconsistent, patients who are experiencing significant hypoglycemia while taking human insulin **may** benefit from rapid-acting insulin analogues.

Basal insulin therapy:

- In patients with type 1 or type 2 diabetes requiring basal insulin, insulin NPH **should** be considered first. Although the evidence is limited and inconsistent, patients who are experiencing significant hypoglycemia while taking insulin NPH **may** benefit from long-acting insulin analogues.

CADTH works with Canadian jurisdictions in using COMPUS materials to facilitate their uptake and implementation. Support for implementation and evaluation, including adaptation of intervention tools to meet user requirements, is available through CADTH's COMPUS program.

Practice and knowledge gaps

Optimal Therapy Report: *Gap Analysis and Key Messages for the Prescribing and Use of Insulin Analogues*

In comparing the Optimal Therapy Report recommendations with both the *Current Practice Analysis: Insulin Analogues* report and the *Current Utilization of Insulin Products in Canada* report, three major gaps emerge:

Practice and knowledge gaps are identified through comparison of current practice and utilization information with optimal therapy recommendations.

Practice Gap:

1. Current practice of initial use of long-acting insulin analogues is inconsistent with Optimal Therapy Recommendations.

Knowledge Gap:

2. Prescribers are uncertain of the benefits (if any) of insulin analogues compared with human insulin.
3. Prescribers are uncertain how to prescribe and use insulin analogues.

The identified gaps lend themselves well to the development and implementation of interventions and tools to potentially change prescribing behaviour related to insulin analogues.

Current practice and utilization

Optimal Therapy Reports:

Current practice analysis: insulin analogues. A qualitative analysis of Canadian physician perceptions and use of insulin analogues

Current utilization of insulin products in Canada

The objective of the **Current Practice Analysis Report** was to foster an understanding of how insulin analogues are currently being prescribed and used in Canada, and to describe physician beliefs and perceptions regarding these drugs.

To determine **Current Utilization** patterns of human insulins and insulin analogues in Canada, a retrospective utilization analysis of insulin agents was performed regarding the numbers of prescriptions, market share, and costs in Canada over an 18-month period between February 2005 and July 2006.

Both of these Optimal Therapy Reports were used, together with the COMPUS Expert Review Committee (CERC) Optimal Therapy Recommendations, in the production of key messages and intervention tools.

Recommendations

Optimal Therapy Report: *Optimal Therapy Recommendations for the Prescribing and Use of Insulin Analogues*

The COMPUS Expert Review Committee (CERC) produced 16 recommendations on the use of insulin analogues in various populations, including:

- pre-adolescents
- adolescents
- adults
- pregnant women, with type 1 and type 2 diabetes
- pregnant women with gestational diabetes.

Summary of CERC Recommendations:

When a bolus insulin† is required, either regular human insulin or the rapid-acting insulin analogues (i.e., insulin aspart and insulin lispro) are **recommended**‡ in most patients with type 1 diabetes, with the exception of adolescents. In adolescents with type 1 diabetes, a rapid-acting insulin analogue is **suggested** over regular human insulin. When a bolus insulin is required for patients with type 2 diabetes, regular human insulin is **suggested** over the rapid-acting insulin analogues. If a rapid-acting insulin analogue is used, CERC **recommends** that either insulin aspart or insulin lispro be used.

When a basal insulin§ is required, insulin NPH is **recommended**** over the long-acting insulin analogues (i.e., insulin glargine and insulin detemir) in most patients with type 1 and type 2 diabetes. If a long-acting insulin analogue is used, CERC **recommends** that either insulin glargine or insulin detemir can be used.

†Faster-acting insulin that provides the boost of insulin needed to stop the rise in blood glucose levels that occurs after meals. ‡For most pre-adolescents and pregnant women with type 1 diabetes and women with gestational diabetes, CERC suggests that either regular human insulin or the rapid-acting insulin analogues can be used. §Longer-acting insulin that controls blood glucose levels between meals and overnight.
***For most children with type 1 diabetes, CERC suggests that insulin NPH* or Neutral protamine Hagedoran, an intermediate-acting insulin, *be used in preference to long-acting insulin analogues.*

Legend (strength of a recommendation)

"Recommends" equates to a strong recommendation*
"Suggests" equates to a weak recommendation*

** based upon quality of evidence, weighing the balance of benefits versus harms, and identifying underlying values and preferences*

COMPUS applied the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to summarize the available evidence and facilitate the generation of optimal therapy recommendations by CERC.

Summary of Research Gaps

Part of the COMPUS process is to outline gaps in research. The following gaps in research related to the prescribing and use of insulin analogues were identified:

Populations and comparisons with insufficient evidence:

- comparative trial of insulin analogues versus conventional insulins in children and pregnant women with type 2 diabetes
- long-acting insulin analogues in pregnant women
- studies comparing insulin analogues to conventional insulins in First Nation populations.

Outcomes with insufficient evidence:

- the effect of the insulin analogues on long-term microvascular and macrovascular diabetes complications
- potential benefits of the insulin analogues regarding quality of life (in particular, increased convenience and reduced fear of hypoglycemia).

The identification of these gaps will contribute to the planning of future research. In the long-term, results from this research will lead to improved clinical practice and better outcomes for patients with diabetes.

Cost-effectiveness data:

Optimal Therapy Report: *An Economic Evaluation of Insulin Analogues for the Treatment of Patients with Type 1 and Type 2 Diabetes Mellitus in Canada*

Cost-effectiveness data about the use of insulin analogues were derived from pharmacoeconomic analyses conducted by CADTH using the Center for Outcomes Research and Education (CORE) diabetes model. The results of these analyses are presented in an Economic Report: *An Economic Evaluation of Insulin Analogues for the Treatment of Patients with Type 1 and Type 2 Diabetes Mellitus in Canada*.

A summary interpretation of the data by COMPUS: the cost-effectiveness of insulin analogues depends on the type of insulin analogue and whether the patient receiving the treatment has type 1 or type 2 diabetes. With the exception of rapid-acting insulin analogues in type 1 diabetes, routine use of insulin analogues, especially long-acting analogues in type 2 diabetes, is unlikely to represent an efficient use of finite health care resources. (*CMAJ* 2009;180(4):400-7)

Clinical-effectiveness data:

Optimal Therapy Reports:
Rapid-acting Insulin Analogues for the Treatment of Diabetes Mellitus: Meta-analyses of Clinical Outcomes

Long-acting Insulin Analogues for the Treatment of Diabetes Mellitus: Meta-analyses of Clinical Outcomes

The clinical evidence for the insulin analogue topic was derived from two systematic reviews conducted by CADTH's COMPUS program: *Rapid-acting Insulin Analogues for the Treatment of Diabetes Mellitus: Meta-analyses of Clinical Outcomes*, and *Long-acting Insulin Analogues for the Treatment of Diabetes Mellitus: Meta-analyses of Clinical Outcomes*. These reviews were updates on the rapid-acting insulin analogues (*Short-acting Insulin Analogues for Diabetes Mellitus: Meta-analysis of Clinical Outcomes and Assessment of Cost-effectiveness, March 2007)* and long-acting insulin analogues (*Long-acting Insulin Analogues for Diabetes Mellitus: Meta-analysis of Clinical Outcomes and Assessment of Cost-effectiveness, October 2007)* from CADTH's Health Technology Assessment program. A further update of the literature search was conducted for studies published between the search cut-off date of the COMPUS systematic reviews April 2007 and September 2008 to identify any additional evidence that addressed existing recommendations or research gaps. Although the systematic reviews included all relevant data from peer-reviewed articles, as well as abstracts and grey literature, CERC based its recommendations only on evidence from peer-reviewed studies. Results from abstracts and grey literature were assessed separately by the committee to determine their impact on the recommendations.

A summary interpretation of the data by COMPUS: rapid-and long-acting insulin analogues offer little benefit relative to conventional insulins in terms of glycemic control or reduced hypoglycemia. Long-term, high-quality studies are needed to determine whether insulin analogues reduce the risk of long-term complications of diabetes. (*CMAJ* 2009;180(4):385-97)

Stakeholder feedback is sought at key points in the COMPUS process. This ensures that the end products, the intervention tools, are useful to those seeking to optimize the prescribing and use of drugs.

For further information, please visit the CADTH web site: www.cadth.ca.