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OPTIMAL THERAPY REPORT

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Gap Analysis and Key Messages for the Prescribing and Use of Insulin Analogues

Supporting Informed Decisions

À l'appui des décisions éclairées

This report is prepared by the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS), a service of the Canadian Agency for Drugs and Technologies in Health (CADTH). This report is based on the comparison of evidence-based recommendations related to the prescribing and use of insulin analogues with current utilization patterns and practices. The intent of this report is to identify areas that may require interventions and information to optimize the prescribing and use of insulin analogues. 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. The information in this report should not be used as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process nor is it intended to replace professional medical advice.

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ABBREVIATIONS

A1C	glycosylated hemoglobin
CAC	COMPUS Advisory Committee
CADTH	Canadian Agency for Drugs and Technologies in Health
CERC	COMPUS Expert Review Committee
COMPUS	Canadian Optimal Medication Prescribing and Utilization Service
NPH	neutral protamine Hagedorn

DEFINITIONS

Bolus dose of insulin: A bolus dose of insulin is the dose of regular or rapid-acting insulin that is injected to cover the food eaten in a meal or a snack. When an insulin pump is used, the bolus is given, in addition to the basal rate, to cover food intake. Bolus doses are also used when blood glucose levels are too high, to lower the amount of glucose in the blood.

Basal dose of insulin: Also known as background insulin, it is the insulin that controls blood glucose levels between meals and overnight. It controls glucose in the fasting state.

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1 INTRODUCTION

In March 2004, the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) was launched by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) — now the Canadian Agency for Drugs and Technologies in Health (CADTH) — as a service to federal, provincial, and territorial jurisdictions and other stakeholders. COMPUS is a nationally coordinated program, funded by Health Canada.

The goal of COMPUS is to optimize drug-related health outcomes and the cost-effective use of drugs by identifying and promoting optimal drug prescribing and use. Where possible, COMPUS builds on existing applicable Canadian and international initiatives and research. COMPUS achieves its goal through three main approaches:

- identifying evidence-based optimal therapy in prescribing and use of specific drugs
- identifying gaps in clinical practice, then proposing evidence-based interventions to address these gaps
- supporting the implementation of these interventions.

Direction and advice are provided to COMPUS through various channels, including:

- the COMPUS Advisory Committee (CAC), which includes representatives from the federal, provincial, and territorial health ministries and related health organizations
- the COMPUS Expert Review Committee (CERC), which is an advisory body that makes recommendations related to the identification, evaluation, and promotion of optimal drug prescribing and use in Canada
- stakeholder feedback.

1.1 CERC

CERC consists of eight Core Members appointed to serve for all topics under consideration during their term of office, and three or more Specialist Experts appointed to provide their expertise in recommending optimal therapy in respect of one or more specific topics. For insulin analogues, four endocrinologists/diabetes specialists were appointed as Specialist Experts. Two of the Core Members are Public Members who bring a lay perspective. The remaining six Core Members hold qualifications as physicians, pharmacists, or health economists or have other relevant qualifications with expertise in one or more areas, such as, but not limited to family practice, institutional or community clinical pharmacy, pharmacoeconomics, clinical epidemiology, drug utilization expertise, methodology, affecting behaviour change (through health professional and/or patient and/or policy interventions), and critical appraisal. The Core Members including Public Members are appointed by the CADTH Board of Directors.

The mandate of CERC is advisory in nature and is to provide recommendations and advice to the COMPUS directorate at CADTH on assigned topics that relate to the identification, evaluation, and promotion of best practices in the prescribing and use of drugs across Canada. The overall perspective used by CERC members in producing recommendations is that of public health care policy makers in pursuit of optimizing the health of Canadians within available health care system resources.

2 ISSUE

CAC has identified management of diabetes mellitus as a priority area for optimal practice initiatives based on the following criteria:

- large deviations from optimal utilization (over- or under-use)
- size of patient populations
- impact on health outcomes and cost-effectiveness
- potential to effect change
- benefit to multiple jurisdictions
- measurable outcomes
- the extent that evidence is available.

Within diabetes mellitus management, optimal use of insulin analogues was identified by CAC as a priority topic. Given the high prevalence and rising incidence of diabetes in Canada, the optimal prescribing and use of insulin and insulin analogues has the potential to positively impact health outcomes for a large number of patients. Although insulin analogues may have certain clinical advantages compared with conventional insulins, acquisition costs of insulin analogues (i.e., insulin aspart, insulin lispro, insulin detemir, insulin glargine) are greater than those for conventional insulin products (e.g., insulin neutral protamine Hagedorn [NPH], regular human insulin). In view of the increasing number of people who are diagnosed with diabetes mellitus each year, health care providers, consumers, and policy makers require evidence-based information on the optimal use of these agents.

3 OBJECTIVE

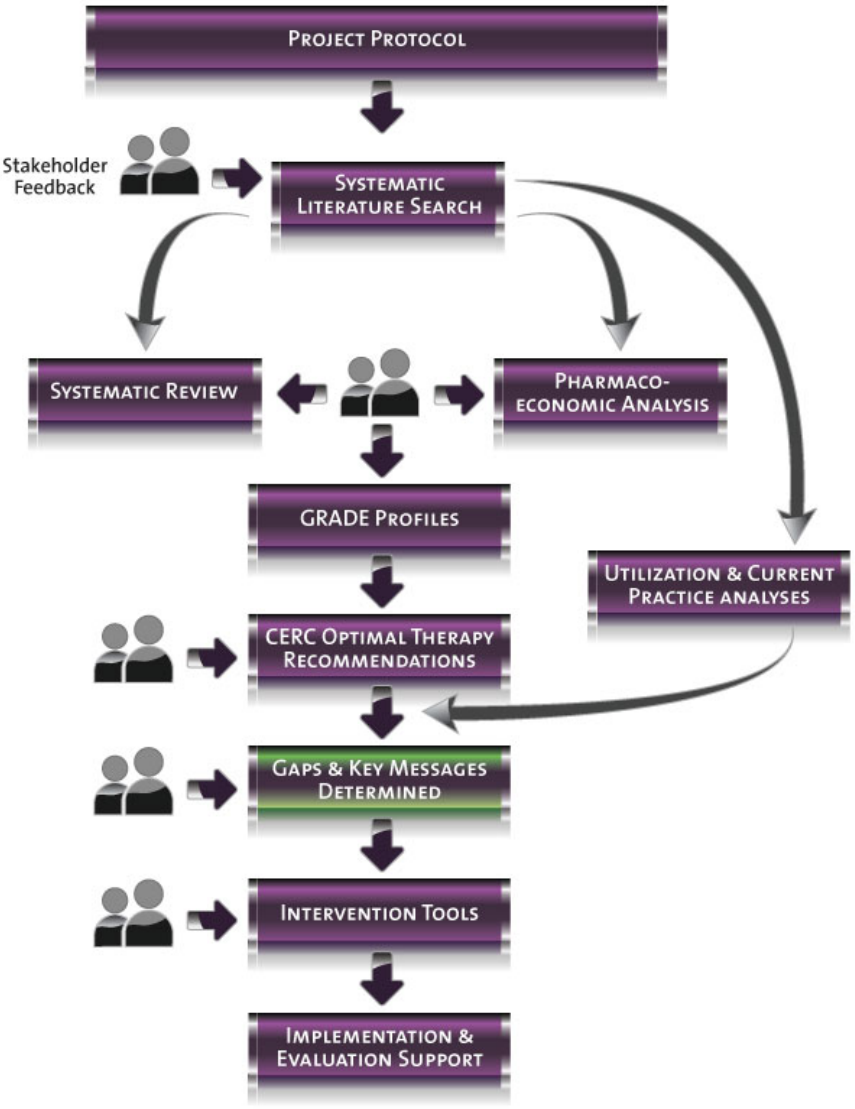
The objective of this report is to present the gaps in practice and prescriber knowledge related to insulin analogues that were identified through comparison of the results of the *Current Utilization of Insulin Products in Canada* Optimal Therapy Report and the *Current Practice Analysis: Insulin Analogues — A Qualitative Analysis of Canadian Physician Perceptions and Use of Insulin Analogues* Optimal Therapy Report with the Optimal Therapy Recommendations developed by CERC. Key messages addressing these gaps are also presented.

4 PROJECT OVERVIEW

Once a topic is selected, COMPUS undertakes activities related to key areas in the COMPUS procedure. CAC provides advice and guidance throughout the process, from topic identification through to feedback and approval of recommendations and supporting interventions. CERC, as described in Section 1.1, provides expert advice and recommendations on the topic area relating to the identification, evaluation, and promotion of optimal prescribing and use of drugs. A broad range of stakeholders is invited to provide feedback at various stages in the COMPUS process.

To identify and promote the implementation of evidence-based and cost-effective optimal therapy in the prescribing and use of long- and rapid-acting insulin analogues, COMPUS follows the process outlined in the flow chart to the right.

This report represents the presentation of gaps and key messages (green box) after stakeholder feedback. Stakeholder feedback was considered by COMPUS and CERC in the production of the final key messages and ultimately the interventions and tools aimed at optimizing practice related to insulin analogues.



5 METHODS

5.1 Optimal Therapy Recommendations

Recommendations developed by CERC for the optimal prescribing and use of rapid- and long-acting insulin analogues, as well as the methods used in their development, are presented in *Optimal Therapy Recommendations on the Prescribing and Use of Insulin Analogues*.[1] In brief, COMPUS applied the Grades of Recommendation Assessment, Development and Evaluation (GRADE) approach to summarize the available clinical and economic evidence on insulin analogues and facilitate the generation of Optimal Therapy Recommendations by CERC. This process resulted in 14 detailed Optimal Therapy Recommendations, agreed upon through voting by CERC members. The Recommendations included type 1, type 2, and gestational diabetes as well as relevant subpopulations within each category. The overall quality of evidence and strength of recommendation were also decided through voting for each statement.

5.2 Current Utilization Analysis

An analysis of current utilization of insulin analogues in Canada was conducted for COMPUS by IMS Health Consulting using dispensing data from a representative sample of retail pharmacies in Canada.[2] Two types of analyses were conducted for both type 1 and type 2 diabetes: characterization of initial insulin therapy and analysis of switching patterns to insulin analogues for patients initiated on conventional insulins.

The final *Current Utilization of Insulin Products in Canada* Optimal Therapy Report is posted on the CADTH website.

5.3 Current Practice Analysis

The Current Practice analysis was a qualitative study designed to assess physicians' perceptions and beliefs regarding insulin analogues as well as to determine how these agents are typically used in clinical practice.[3] A total of 17 family physicians and five endocrinologists from across Canada were interviewed by telephone by an experienced qualitative researcher using a structured interview guide. A set of case studies was also included to elicit physician responses regarding the choice of insulin in commonly encountered clinical situations. A grounded theory approach was used to analyze responses.

The final *Current Practice Analysis: Insulin Analogues — A Qualitative Analysis of Canadian Physician Perceptions and Use of Insulin Analogues* Optimal Therapy Report is posted on the CADTH website.

5.4 Identification of Practice and Knowledge Gaps

Practice and knowledge gaps related to insulin analogues were identified by CERC members and COMPUS staff through comparison of the *Current Practice Analysis: Insulin Analogues — A Qualitative Analysis of Canadian Physician Perceptions and Use of Insulin Analogues* Optimal Therapy Report and *Current Utilization of Insulin Products in Canada* Optimal Therapy Report with the Optimal Therapy Recommendations developed by CERC. This analysis focused on identifying:

- ***Discrepancies between the Recommendations and actual practice, as indicated by the utilization data and responses in the Current Practice analysis***:
    - Quantitative prescribing patterns (e.g., by type of diabetes, age, whether analogues were used as first- or second-line therapy) from the utilization analysis were compared with the Recommendations. As well, responses to case study descriptions, and spontaneous descriptions of typical situations in which analogues were prescribed, from the Current Practice analysis were compared with the Recommendations to identify discrepancies.[3]

- ***Discrepancies between the Recommendations and perceptions regarding insulin analogues, as indicated by the Current Practice analysis***:
    - Prevalent views regarding the advantages or benefits of insulin analogues and the clinical situations or patient groups for whom they might be useful were compared with the Recommendations to identify perceptions that were not supported by the available evidence.

- ***Knowledge deficits with respect to the optimal use of insulin analogues (e.g., the patient groups and clinical situations in which analogues are most likely to confer benefit; strategies for initiation, switching, and dosing; the application of evidence to individual patients) identified in the Current Practice analysis.***

5.5 Identification of Key Messages

Once gaps in practice and knowledge related to insulin analogues were identified, the gaps were scrutinized to determine their relevancy to the optimal prescribing and use of insulin analogues. For example, could addressing the gap through interventions and targeted tools potentially impact on the gap, or was the gap unlikely to be amenable to change? Did the gap lend itself to the development and implementation of interventions, or was it difficult to address in a meaningful way? Would addressing the gap make a discernable difference in the prescribing and use of insulin analogues? If a number of gaps were identified, it would also be necessary to prioritize, allowing a focused approach to addressing the gaps in practice and knowledge related to insulin analogues.

After identifying the highest priority gaps most relevant to the optimal prescribing and use of insulin analogues, key messages related to the gaps were developed based on the associated Optimal Therapy Recommendation. In developing the key messages, consideration was given to the associated barriers to change and how those barriers could potentially be overcome as well as factors favouring change (i.e., enablers). The usability and acceptability of these key messages were tested through focus groups held in cities across Canada composed of target audience members (those to whom the key messages are directed in an effort to effect change and optimize the prescribing and use of insulin analogues). Identified target audiences include prescribers (physicians), diabetes educators, pharmacists, and patients.

Interventions and tools will be developed based on the final key messages.

6 GAPS

The prescribing of insulins requires the consideration of many factors. Two patients who clinically appear very similar may use completely different insulin regimens because of the interplay of variables related to both the patient and the prescriber. These include prescriber perceptions and beliefs about the available insulins, patient lifestyle concerns, and available health care and financial resources. This makes the

prescribing and use of insulins, including insulin analogues, an individualized, unique endeavour for each patient. A one-size-fits-all approach is not possible; and context, together with quantifiable parameters related to the management of diabetes (e.g., glycosylated hemoglobin [A1C] levels, incidence of hypoglycemia (nocturnal, severe, overall), body mass index or weight gain, satisfaction surveys, quality of life indices), is important. As a result, the gaps related to insulin analogue prescribing and use are both qualitative (gaps in knowledge related to perceptions and beliefs about insulin analogues) as well as quantitative (X% of prescribers prescribe insulin A).

In comparing the Optimal Therapy Recommendations with both the *Current Practice Analysis: Insulin Analogues* report and the *Current Utilization of Insulin Products* report, three major themes emerge:

- The current practice of initial use of long-acting insulin analogues represents a practice gap. Long-acting insulin analogues are prescribed as initial therapy for a proportion of both type 1 and type 2 diabetes patients initiated on insulin. Overall, about 10.5% of patients in each population are initiated on a long-acting insulin analogue either alone or in combination with a bolus insulin. Analysis by age revealed that long-acting insulin analogue use is higher among younger patients. For example, about 14% of patients with type 2 diabetes younger than 65 years of age initiated on insulin are prescribed a long-acting insulin analogue compared with about 7% of those older than 65 years of age. The Optimal Therapy Recommendations advise that NPH insulin be used as initial basal insulin therapy in the majority of patients with either type 1 and type 2 diabetes.

- Prescribers are uncertain of the benefits (if any) of insulin analogues compared with human insulin. This represents a knowledge gap.

  Although endocrinologists report being more convinced of the merits and benefits of insulin analogues, including patient lifestyle issues and to a lesser degree clinical benefits, family doctors and general practitioners report being much less certain. Knowledge of insulin analogues varied greatly among all prescribers. They did not report concerns regarding the safety or side effects of the insulin analogues, rather their uncertainty focused on the effect of insulin analogues on:
  - Quality of life
  - Glycemic control
    - A1C levels
    - Hypoglycemia (i.e., nocturnal hypoglycemia)
  - Patient satisfaction and/or lifestyle
  - Weight gain
  - Cost of treatment.

  In addition, prescribers voiced concerns that the evidence related to insulin analogues focused on A1C levels but that other factors such as fear of hypoglycemia and lifestyle were just as important — if not more so — to patients.

- Prescribers, in particular family doctors and general practitioners, are uncertain how to prescribe and use insulin analogues. This includes initiating, switching to, and adjusting the insulin analogues. This represents a knowledge gap.

  Whereas endocrinologists reported feeling confident in the prescribing and use of insulin analogues, other prescribers reported a lack of confidence in this area, although it varied greatly among the prescribers. The use of insulin analogues in diabetes management is a practice in evolution. Insulin analogues have been available for less than a decade; and many prescribers, especially family doctors

and general practitioners, have only started to use these agents in the last year or two. Although many prescribers report at least an awareness of the evidence related to insulin analogues, it was felt that the evidence did not offer enough in terms of practical advice on how to prescribe and use these agents, especially taking into consideration factors such as patient lifestyle and possible resistance to change. This resulted, at least in some cases, in a reliance on pharmaceutical representatives to guide treatment decisions in addition to local endocrinologists.

The identified gaps lend themselves well to the development and implementation of interventions and tools to potentially change prescribing and use behaviour related to insulin analogues. According to the Current Practice analysis, prescribers recognize that there are gaps in knowledge about insulin analogues and are looking for further information and guidance — a powerful enabler to the uptake of key messages aimed at these gaps. Given that the practice and use of insulin analogues is still evolving, intervening now is much more likely to result in behaviour change than waiting until prescribing and use behaviours are strongly established and entrenched. Potential barriers, such as preconceived perceptions of insulin analogues, limited prescriber time, specialist influence on practice, or pharmaceutical marketing techniques may need to be overcome. By providing evidence and information to fill the identified knowledge gaps while considering potential enablers and barriers, patients with diabetes may receive optimal insulin therapy.

7 KEY MESSAGES

Based on the identified gaps and the corresponding CERC Recommendations on Insulin Analogues, the following are the key messages:

When choosing an insulin…

Bolus insulin therapy:

- In patients with type 1 diabetes, either regular human insulin or rapid-acting insulin analogues may 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. 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. In patients experiencing significant hypoglycemia while using insulin NPH, long-acting insulin analogues may be considered.

Notes:

- *During interviews and focus groups, some health care professionals suggested that when compared with human insulins, insulin analogues result in meaningful differences in A1C levels, patient satisfaction and convenience, adherence to treatment, weight gain, long-term complications, and quality of life. No definitive evidence to support these beliefs was found.*
- *When considering the various treatment options, the COMPUS Optimal Therapy Recommendations, which include clinical- and cost-effective information, should be taken into account along with each patient's unique situation.*

8 TARGET AUDIENCES

The Current Practice analysis reveals that family doctors/general practitioners indicate the most uncertainty about insulin analogues and therefore represent an important target audience. However other prescribers such as endocrinologists represent another key target audience especially considering their influence on the prescribing of others. Diabetes educators play an important role in diabetes care and often shape the prescribing of those with whom they work closely. This makes diabetes educators a third target audience for the insulin analogue key messages. The key messages will also be of interest to policy and decision makers who must make formulary decisions on the use and coverage of insulin analogues for drug plans and in hospitals. Patients play an important role in the management of their diabetes, and the importance of the key messages to this target audience must not be overlooked. Finally, researchers in the area of diabetes will also find important information in the key messages, indicating where further research is required.

9 NEXT STEPS

Stakeholder feedback on the draft gap analysis and key messages to optimize the prescribing and use of insulin analogues was collated and considered by COMPUS and CERC in the production of the final key messages. Development of interventions and tools to disseminate the messages and effect change will be based on final key messages. As with the key messages, the interventions and tools will be based on the best available evidence with input from experts (both clinical and educational).

10 REFERENCES

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