COMPUS Procedure
Evidence-Based Best Practice Recommendations

Introduction

The Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) identifies, evaluates, promotes, and facilitates best practices in drug prescribing and use among health care providers and consumers. The objectives are to optimize drug-related health outcomes and cost-effective use of drugs. COMPUS is a nationally coordinated program, funded by Health Canada and delivered by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA), as a service to federal, provincial and territorial jurisdictions, and other stakeholders.

Where possible, COMPUS builds on existing Canadian and applicable international initiatives and research. Its role is to:
- identify, evaluate, promote, and facilitate the implementation of best practices in drug prescribing and use
- consolidate information resources
- develop and support networks for best practices in drug prescribing and use
- encourage health care provider and consumer behaviours for improved drug-related health outcomes
- identify best practice information gaps

Background

COMPUS was established to promote and facilitate best practices in drug prescribing and use among health care providers and consumers. This document describes the procedures involved in the collection, evaluation, and identification of these best practices. The document also describes procedures for assessing cost-effectiveness of best practices based on existing pharmacoeconomic evaluations, and reporting this information when available. Steps are underway to identify best practice initiatives that promote the uptake of best practices and to develop strategies, tools and services to promote and support the implementation of these initiatives.

The COMPUS approach for identifying evidence-based best practices is to build on existing work. Accordingly, clinical practice guidelines (CPGs) and consensus documents (CDs) containing recommendations on the prescribing or use of the drug(s) or treatment area(s) that are published or generated at the time of a COMPUS review will be identified and collected. The recommendations will be extracted from the collected CPGs and CDs. Similar recommendations will be grouped or synthesized into a single synthesized recommendation with input and guidance from clinical and other experts. Supporting references for these recommendations will be identified, retrieved and assessed for quality. Relevant economic studies will be identified and reviewed. The results and findings will be reviewed by an expert review committee (ERC), which will identify evidence-based best practices. At various stages in the procedure, stakeholders, including patients and consumers, health care providers and pharmaceutical manufacturers, will have opportunities to provide feedback or input.
COMPUS is not mandated to generate CPGs; however, it will have a process in place to maintain information on best practices. COMPUS will identify, collect and review new studies (published after the most recent CPGs and CDs included in the COMPUS review) and share the results with the ERC to use in updating reports. The updated information will be forwarded to groups that develop guidelines.

The procedures described in this document are based on research and input from a variety of sources. Canadian and international literature was surveyed to identify initiatives with similar objectives to those of COMPUS. Meetings were held with Canadian and international practitioners and academics involved in such initiatives to learn about the successes and challenges of identifying and promoting best practices. Relevant approaches were incorporated into these procedures. In addition, stakeholder input was obtained on the draft version of this document and it has been incorporated.

Definitions

Definitions can be found in Appendix 1.

Amendments to the COMPUS Procedure

The COMPUS Directorate may amend, from time to time, the COMPUS procedure in consultation with the COMPUS Advisory Committee (CAC) and stakeholders. Stakeholders will be notified of amendments to or clarifications of the procedure and related documents through the COMPUS Communiqué.

Procedure

1. **A project is assigned to COMPUS.**
   Members of federal, provincial, and territorial (FPT) jurisdictions identified the first three projects – proton pump inhibitors, diabetes management, and anti-hypertensives. Project selection was based on considerations such as reported large deviations (overuse or under use) from optimal drug utilization, size of patient population affected, and ability to measure outcomes. Future projects will be assigned by the CAC and will reflect the needs of the FPT jurisdictions.

2. **The Best Practices Project Team is established.**
   The number of members and range of expertise on the Best Practices Project Team will be determined by the size and nature of the project. As one of the key requirements of the Team will be to evaluate and critically appraise studies, the Team will include members with these skills. Generally, the Team will include CCOHTA staff with the required management and other expertise (e.g., COMPUS Director and relevant COMPUS managers, research officers, methodologists, economists, and information specialists), support staff, and external experts. External experts will include clinical specialists and other required experts selected from across Canada or other countries as appropriate, based on their expertise and knowledge. Members of the Team, including external experts, will be required to comply with conflict of interest requirements.

3. **A work plan is established.**
   The work plan includes timeframes for deliverables and resource requirements. It will be determined by size, complexity, and nature of the project, and available resources.
4. **A protocol is established.**
The protocol addresses the assigned topic and any related issues. The protocol describes the objectives, scope, and methods for undertaking the project. It will include methods to assess the clinical evidence supporting the use of the drug(s) or other treatment(s), and methods to appraise the cost-effectiveness of the drug(s) or treatment(s). Each project will provide cost-effectiveness information when available.

5. **Best practices are identified and the evidence supporting them is evaluated.**
This is carried out from both clinical and economic perspectives.

**Appraisal of Clinical Evidence**
The steps involved in the appraisal of clinical evidence include:

- identification of indications for drug(s)
- identification of published CPGs and CDs through a literature search in accordance with a protocol established by the Best Practices Project Team
- criteria for selecting CPGs and CDs developed and documented by the Best Practices Project Team for each project
- selection of CPGs and CDs meeting predefined criteria (independently by at least two research officers) and preparation of a list
- updating the list of selected CPGs and CDs by posting it on the CCOHTA web site and by inviting stakeholders to identify relevant CPGs and CDs, which are not included in the list (within 15 business days)
- identification and preparation of a list of all recommendations relating to the prescribing and use of drug(s) or treatment(s) extracted from identified CPGs and CDs
- grouping or combining similar selected recommendations and synthesizing them into one recommendation (i.e., the synthesized recommendation)
- obtaining input from clinical and other expert(s) on the Best Practices Project Team on the appropriateness of the groupings, the wording of the synthesized recommendations and their clinical impact
- modification and revision of the groupings and the synthesized recommendations based on feedback from clinical and other experts on the Best Practices Project Team
- identification of references cited in CPGs and CDs for the selected recommendations
- extraction of data from selected published studies [study design; patient population, intervention, comparator, outcomes (PICO) information]
- quality assessment of identified studies, using quality assessment instruments that are specific for each type of study. The instruments include: the AMSTAR Tool for assessing systematic reviews (Beverley Shea, CIET, Institute of Population Health, Ottawa: personal communication, 2005 Oct), the SIGN 50 Checklist for Randomized Controlled Trials (http://www.sign.ac.uk/guidelines/fulltext/50/checklist2.html) and the SIGN 50 Checklist for Cohort Studies (http://www.sign.ac.uk/guidelines/fulltext/50/checklist3.html).
- tabulation of synthesized recommendations, supporting studies (evidence) for each synthesized recommendation, their quality, PICO information and summary of supporting evidence for each synthesized recommendation.

**Appraisal of Pharmacoeconomic Evidence**
The steps involved in the appraisal of pharmacoeconomic evidence include:

- identification of statements in the Canadian CPGs and CDs regarding the cost-effectiveness of the drug(s) under review
- identification and selection of relevant Canadian economic studies referenced in the CPGs and CDs and found through a systematic literature search for review
- preparation of data extraction tables

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• assessment of the quality of studies (using a specific tool for health economic evaluations based on Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ 1996;313(7052):275-83)
• assessment of the clinical data used in the economic evaluation studies
• assessment of the relevance of the studies to the Canadian context
• reporting on cost-effectiveness of drug(s) or treatments by indication
• determination of number needed to treat (NNT) and costs for NNTs when applicable and when information is available; and the number needed to harm (NNH) and the costs associated with NNH when applicable and when information is available

6. The results of appraisals of clinical and pharmacoeconomic evidence are reported in table format. Narrative descriptions are included as required.
   • Research officers tabulate the clinical results (list of synthesized recommendations, quality of evidence, and synthesized evidence for each grouped recommendation).
   • The economist reports the results of the appraisal of the pharmacoeconomic studies (evidence) and also provides cost tables and NNT, costs for NNT, NNH, and costs for NNH when applicable and when available.

7. An interim report is prepared by the Best Practices Project Team (Appendix 2). The interim report describes the methods and results of the appraisals of clinical and pharmacoeconomic evidence. (Note: the interim report does not contain the ERC’s recommendations: the purpose of the interim report is to obtain stakeholder input.)

8. The interim report is edited.
   • The interim report is proofread and edited by the Best Practices Project Team and CCOHTA editorial staff, and signed off by the Manager of Best Practice Recommendations.

9. The interim report is sent to CAC members five business days before being posted on the CCOHTA web site.

10. The interim report is posted on the CCOHTA web site along with an invitation for all stakeholders to provide feedback. Stakeholders are advised of this posting and of the opportunity to comment through the COMPUS Communiqué. Targeted stakeholders receive the report by e-mail.
   • All stakeholders have 20 business days to provide comments.
   • Instructions on the nature of the desired feedback (e.g., identification of any studies that do not support the synthesized recommendations) and how to submit feedback (e.g., comments need to be referenced) are provided for each report.

Stakeholder comments are forwarded to the Best Practices Project Team for collation.

11. The Best Practices Project Team searches the literature for new relevant publications and prepares an update for the ERC.

12. The ERC considers the findings in the interim report, the collated stakeholder input and updated information. The ERC identifies best practice recommendations based on the quality of the supporting evidence and provides comments on the quality of the supporting evidence and its clinical impact.
   • The interim report, collated stakeholder comments and input and updated information are sent to the ERC.

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• The ERC uses a consistent approach to discuss and review the synthesized recommendations, the summary of evidence, the stakeholder input and updated information.
• The ERC identifies recommendations that, based on the quality of the supporting evidence and clinical impact, represent best practices.
• The ERC identifies recommendations that are unsupported by existing evidence.
• The ERC identifies recommendations for which evidence is lacking and where further research is needed.
• The ERC identifies recommendations that require updating based on its knowledge of current practices or new evidence supplied through a literature search by information specialist(s), and listed by research officers.
• The ERC identifies areas where recommendations are lacking or do not exist.

13. The draft final report is written integrating the revised interim report and the outcomes of the ERC deliberations (Appendix 2).
• The draft final report is written by the Best Practices Project Team. It includes the ERC’s decisions.
• The draft final report is proofread and edited.
• The draft final report is sent to the ERC Chair for sign-off (to ensure that it accurately reflects the ERC’s deliberations and conclusions).

14. The draft final report is sent to CAC members five business days before being posted on the CCOHTA web site.

15. The draft final report is posted on the CCOHTA web site and sent by e-mail to targeted stakeholders.
• Stakeholders are advised of this posting and of the opportunity to comment through the COMPUS Communiqué. Targeted stakeholders receive the report by e-mail.
• All stakeholders have 20 business days to provide comments.
• Instructions on the nature of the desired feedback and how to submit it are provided for each report.
• Comments are collated by the Best Practices Project Team and forwarded to the ERC.

16. The stakeholders’ input is reviewed.
The ERC reviews the collated stakeholder input and makes changes if necessary.
• The draft final report and collated stakeholder comments and input are sent to the ERC.
• The ERC meets to discuss the stakeholder input. The ERC has at least 10 business days before meeting to review the feedback.
• The ERC makes appropriate changes.
• The Best Practices Project Team prepares the final report (Appendix 2).
• The ERC Chair signs-off the final report.
• The final report is translated.

17. The final report is distributed.
• The final report is a component of the toolkits and it is used as subject content for interventions (Best Practice Initiatives) developed by COMPUS.
• The final report is sent to CAC members five to 25 business days before posting on the CCOHTA web site.
• The final reports (English and French) are posted on the CCOHTA web site, and stakeholders are notified through the COMPUS Communiqué.
• Follow-up occurs with bodies that developed the guideline(s) used in the project to ensure awareness of the final report and to possibly facilitate revision of the recommendation(s) to reflect new evidence.
18. **The Best Practices, identified by COMPUS, are updated as required.**
The Best Practices Project Team, with advice from the ERC, develops research questions for an ongoing regular search of the literature for relevant publications. The information specialist monitors literature on a regular basis and reports the search results to the Best Practices Project Team, which identifies relevant new information.

- One year after the report’s release (or sooner upon the CAC’s request or with the emergence of new evidence), the Best Practices Project Team assesses the new literature for quality using a quality assessment instrument, and prepares a report that comments on whether the new evidence supports existing recommendations.
- The updated report is posted on CCOHTA’s web site for comments and also e-mailed to targeted stakeholders for comments.
- The ERC reviews the updated report and stakeholder comments, and determines if recommendations need to be updated or changed.
- The updated report is forwarded to the relevant bodies involved in the preparation of the guideline(s) used in the project.
- COMPUS follows up with guideline bodies to offer assistance in facilitating the revision of recommendation(s) in accordance with new evidence.
COMPUS Procedure – Development of Best Practice Recommendations

Steps

Topic selection

Background

Work plan

Protocol

Identification of indications

Collection of clinical practice guidelines (CPGs) and consensus documents (CDs)

Identification of relevant recommendations in CPGs and CDs

Grouping of similar recommendations and synthesizing them into a synthesized recommendation

Identification and sorting of supporting references (evidence)

Evaluation of selected references including quality assessment and data extraction

Preparation of interim report (summary of evidence for each synthesized recommendation)

Stakeholder feedback

Identification of best practices and drafting of final report [Expert Review Committee (ERC)]

Stakeholder feedback

Final report (ERC)

Next steps
APPENDIX 1: Definitions

**Best Practice:** an evidence-based approach to prescribing or using drugs that is clinically effective and cost-effective and that contributes to optimal health outcomes.

**Best practice initiatives:** an activity, program, intervention, or policy aimed at encouraging patients, healthcare professionals, and others to adopt best practices (e.g., public service messages, patient education materials, physician educational programs).

**Best Practice (BP) recommendation:** a recommendation for which the evidence, as deemed by the ERC, is sufficient to support it as a “best practice.”

**Clinical practice guideline (CPG) or consensus document (CD) recommendation:** a recommendation that is included in a clinical practice guideline or consensus document.

**Clinical effectiveness:** the extent to which an intervention produces favourable outcomes under usual or everyday conditions.

**Clinical practice guidelines (CPGs):** systematically developed statements designed to help practitioners and patients make decisions about appropriate health care for specific clinical circumstances.

**COMPUS Advisory Committee (CAC):** the COMPUS Advisory Committee consists of designees from the federal, provincial, and territorial health ministries’ publicly funded drug programs; and observers from Health Canada, the Canadian Institute for Health Information, and the Patented Medicines Prices Review Board. The CAC provides advice to the CCOHTA Board and the COMPUS Directorate to enable COMPUS to meet its goals and objectives.

**Consensus documents (CDs) or statements:** a guideline or statement of the advised course of action in relation to a particular clinical topic based on the collective views of a body of experts; consensus may be achieved by either formal or informal methods.

**Cost-effectiveness:** considers both costs and clinical effects associated with a drug; a drug is considered to be cost-effective if the health value provided by the drug is thought to be reasonable given its cost.

**Expert Review Committee (ERC):** experts chosen to provide evidence-based recommendations on the prescribing and use of drugs for projects assigned to COMPUS in accordance with its terms of reference.

**Expert Review Committee (ERC) recommendation:** a recommendation that is made by the ERC on the basis of its assessment of the supporting evidence for the synthesized recommendation and clinical impact.

**Number needed to harm (NNH):** the number of patients who would need to receive an intervention to cause one additional adverse event; the NNH is the inverse of the difference in absolute adverse event rates between the control and experimental arms.

**Number needed to treat (NNT):** the number of patients who would need to be treated to prevent an event. The NNT is the reciprocal of the absolute risk reduction. The closer the NNT is to one, the better the treatment is. NNT is calculated based on binary data.
Quality assessment instrument: an approach that is consistently applied to all studies of a particular type, that assesses their quality and robustness; different quality assessment instruments are applied depending on the study type; study types may include randomized controlled trials, systematic reviews, cohort studies, and pharmacoeconomic evaluations.

**Recommendation:** a course of action that is recommended or advised.

**Stakeholders:** patients and consumers, manufacturers who make and market medications, physicians and others who prescribe medication, pharmacists who dispense medication and provide pharmaceutical care, other health care providers who may influence medication use, and payers who are responsible for covering the cost of a medication (in essence, an individual or group that may be involved in the use of prescription drugs from manufacturing to consumption).

**Synthesized recommendation:** a recommendation that is synthesized by the Best Practices Review Team by grouping two or more similar recommendations from different CPGs or CDs.

**Tool kit:** related COMPUS deliverables that facilitate the optimal prescribing and utilization of drugs, leading to optimal health outcomes and cost-effective use of drugs:
- evidence-based recommendations for prescribing and using the drug(s) (i.e., best practices)
- intervention(s) – activity(ies), program(s) or policy(ies) – that support the adoption of best practices by prescribers, patients, or governments
- tools, advice, and support for jurisdictions and other stakeholders for implementing, monitoring and evaluating the intervention(s).
APPENDIX 2: COMPUS Report Template

COMPUS will issue three reports for each project.

- An interim report will report the findings resulting from the appraisal of clinical and pharmacoeconomic evidence supporting recommendations identified in CPGs and CD. This report will be used to obtain stakeholders’ input.
- A draft final report will report the ERC’s review and recommendations, based on the interim report and stakeholders’ input. This report will be used to obtain stakeholders’ input on the draft best practice recommendations identified by the ERC.
- A final report will incorporate stakeholders’ input on these recommendations and will report final recommendations. This report will be used in toolkit development, and will be posted on the CCOHTA web site and shared with various stakeholders.

A. Interim Report

The interim report will be used to obtain feedback from stakeholders and will include the following:

1. Executive Summary
2. Introduction
   - a brief description of the drug(s), drug class, or disease, and issues associated with the use of the drug(s) or drug class or management of the disease (as identified by clinical experts and COMPUS Advisory Committee)
   - a table with all of the Canadian approved indications, dosages and cost information
   - scope and key questions
3. Methods
   The methods for undertaking each of the following steps are described.

a. Appraisal of Clinical Evidence
   - identification and selection of clinical practice guidelines (CPGs) and consensus documents (CDs) from the literature and stakeholder feedback along with selection criteria
   - extraction of treatment-specific recommendations
   - grouping and synthesizing similar recommendations from different CPGs and CDs into a synthesized recommendation with input from clinical experts on the Best Practices Project Team
   - identification of supporting references for each recommendation
   - data extraction: abstraction and tabulation a predefined list of data (e.g., type of study, quality of study, patients’ characteristics, intervention, comparison, outcomes, effect size)
   - quality assessment of studies using quality assessment instruments
   - obtaining stakeholder input

b. Economic Information
   - identification and selection of pharmacoeconomic evaluations that are relevant to the Canadian scene from the literature, CPGs and CDs
   - extraction of selected studies
• assessing the quality of the studies
• assessing the clinical data used in the economic evaluation studies
• assessing and commenting on the relevance to Canada
• summarizing results of the studies
• reporting the cost-effectiveness of drugs or treatments by indication
• calculation of number needed-to-treat and number needed-to-harm costs, when available

c. Preparing Results
• reporting clinical and economic reviews

4. Results and Findings (narrative and tabulated description of findings)

Clinical Results
• overview of results – number of identified CPGs and CDs, number of CPGs and CDs used, number of relevant recommendations, and number of synthesized recommendations
• table of included CPGs and CDs, and table of excluded CPGs and CDs
• table of synthesized recommendations including relevant recommendations that constitute each synthesized recommendation
• summary of evidence report for each synthesized recommendation in table format that includes the synthesized recommendation, the type and number of studies selected as evidence, the quality of the supporting studies, PICO information and the summary of evidence

Pharmacoeconomic Results
• overview of results – number of pharmacoeconomic evaluations and their relevance
• data extraction tables, including quality assessment of pharmacoeconomic studies
• conclusions on cost-effectiveness of drugs and summary of evidence
• number needed-to-treat and number needed-to-harm costs, when available

B. The Final Report

The final report is the key deliverable in the identification of best practice recommendations by COMPUS.

Draft Final Report

1. Executive Summary

2. Introduction
• a brief description of drug(s), drug class, or disease, and issues associated with the use of the drug or drug class or management of the disease (as identified by clinical experts and COMPUS Advisory Committee).
• a table with all of the Canadian approved indications, dosages and cost information
• scope and key questions

3. Methods
The methods for undertaking each of the following steps are described.
a. **Appraisal of Clinical Evidence**
   - identification and selection of clinical practice guidelines (CPGs) and consensus documents (CDs) from literature and stakeholder feedback along with selection criteria
   - selection of treatment-specific recommendations
   - grouping and synthesizing similar recommendations from different CPGs and CDs into a synthesized recommendation, with input from clinical experts
   - identification of supporting references for each recommendation
   - data extraction, abstraction and tabulation a predefined list of data (e.g., type of study, quality of study, patients’ characteristics, intervention, comparison, outcomes, effect size)
   - quality assessment of studies using quality assessment instruments
   - obtaining stakeholder input

b. **Economic Information**
   - identification and selection of pharmacoeconomic evaluations that are relevant to the Canadian scene from the literature, CPGs and CDs
   - abstraction of selected studies
   - assessing the quality of the studies
   - assessing and commenting on the relevance to Canada
   - summarizing results of the studies
   - reporting the cost-effectiveness of drugs or treatments by indication
   - calculation of number needed-to-treat and number needed-to-harm costs, when available

c. **Preparing results**
   - reporting clinical and economic reviews

d. **Stakeholders’ input on interim report**
   - obtaining, collating, and reporting stakeholders’ comments and input on interim report

e. **Searching literature for new relevant publications**
   - identifying new relevant publications and preparing update

f. **ERC review of interim report and identification of best practice recommendations**
   - reviewing and considering interim report and stakeholders’ feedback
   - identification of best practice recommendations, using a consistent approach
   - identification of areas for research, updating, and developing recommendations

g. **Stakeholders’ input on ERC’s draft final report and best practice recommendations**
   - obtaining, collating, and reporting stakeholders’ comments and input on best practice recommendations and report

h. **ERC’s review of stakeholders’ input and revision of best practice recommendations**
   - consideration of stakeholders’ input and revision of draft best practice recommendations

4. **Results and Findings** (narrative and tabulated description of findings)
   - **Clinical Results**
     - overview of results – number of identified CPGs and CDs, number of CPGs and CDs used, number of relevant recommendations and number of synthesized recommendations
     - table of included CPGs and CDs and table of excluded CPGs and CDs
     - table of synthesized recommendations including relevant recommendations that constitute each synthesized recommendation

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• summary of evidence report for each synthesized recommendation in table format that includes the synthesized recommendation, the type and number of studies selected as evidence, the quality of the supporting studies, PICO information and the summary of evidence

Pharmacoeconomic Results
• overview of results – number of pharmacoeconomic evaluations and their relevance
• data extraction tables, including quality assessment of pharmacoeconomic studies
• conclusions on cost-effectiveness of drugs and summary of evidence
• number needed-to-treat and number needed-to-harm costs when available

Stakeholder Feedback
• an overview or summary of stakeholders’ comments on the interim report is to be included in the body of the report. A detailed summary table that lists the stakeholders and their comments about the interim report is to be included in an appendix of the final report.

Conclusions and Implications
  o ERC recommendation for each synthesized recommendation with comments on its clinical impact and the quality of supporting evidence, when applicable
  o list of final best practice recommendations
  o list of recommendations that are unsupported by existing evidence
  o list of recommendations for which evidence is lacking and further research is needed
  o list of recommendations from existing CPGs that require updating to reflect current evidence (identified and corroborated by the ERC)
  o list of recommendation “gaps” (i.e., where no recommendations exist, but they are needed)
  o information on practice issues that are not addressed or raised in CPGs
  o commentary on the amount and quality of evidence available to guide the development of recommendations to fill the gaps
  o comments on studies that do not support recommendations
  o comments on cost-effectiveness
  o references.

Final Report

The draft final report is revised based on feedback and the following components are added to it:
• an overview or summary of stakeholders’ comments on the ERC’s assessment of the recommendations is included in the body of the report.
• a detailed summary table of stakeholders’ comments about the ERC’s decisions and on the draft final report is to be included in an appendix of the final report.