

# Health Technologies for the Improvement of Chronic Disease Management: A Review of the Medical Advisory Secretariat Evidence-Based Analyses Between 2006 and 2011

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Health Quality Ontario (HQO) is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. HQO works with clinical experts, scientific collaborators and field evaluation partners to develop and publish research that evaluates the effectiveness and cost-effectiveness of health technologies and services in Ontario.

Based on the research conducted by HQO and its partners, the Ontario Health Technology Advisory Committee (OHTAC) — a standing advisory sub-committee of the HQO Board — makes recommendations about the uptake, diffusion, distribution or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders and policy-makers.

This research is published as part of Ontario Health Technology Assessment Series, which is indexed in CINAHL, EMBASE, MEDLINE, and the Centre for Reviews and Dissemination. Corresponding OHTAC recommendations and other associated reports are also published on the HQO website. Visit <http://www.hqontario.ca> for more information.

## About the *Ontario Health Technology Assessment Series*

To conduct its comprehensive analyses, HQO and/or its research partners reviews the available scientific literature, making every effort to consider all relevant national and international research; collaborates with partners across relevant government branches; consults with clinical and other external experts and developers of new health technologies; and solicits any necessary supplemental information.

In addition, HQO collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social, and legal issues relating to the intervention assist in making timely and relevant decisions to optimize patient outcomes.

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## Disclaimer

This report was prepared by HQO or one of its research partners for the Ontario Health Technology Advisory Committee and developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to HQO. It is possible that relevant scientific findings may have been reported since completion of the review. This report is current to the date of the literature review specified in the methods section, if available. This analysis may be superseded by an updated publication on the same topic. Please check the HQO website for a list of all publications: [http://www.hqontario.ca/en/mas/mas\\_ohtas\\_mn.html](http://www.hqontario.ca/en/mas/mas_ohtas_mn.html).

# Abstract

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## Background

As part of ongoing efforts to improve the Ontario health care system, a mega-analysis examining the optimization of chronic disease management in the community was conducted by Evidence Development and Standards, Health Quality Ontario (previously known as the Medical Advisory Secretariat [MAS]).

## Objective

The purpose of this report was to identify health technologies previously evaluated by MAS that may be leveraged in efforts to optimize chronic disease management in the community.

## Data Sources

The *Ontario Health Technology Assessment Series* and field evaluations conducted by MAS and its partners between January 1, 2006, and December 31, 2011.

## Review Methods

Technologies related to at least 1 of 7 disease areas of interest (type 2 diabetes, coronary artery disease, atrial fibrillation, chronic obstructive pulmonary disease, congestive heart failure, stroke, and chronic wounds) or that may greatly impact health services utilization were reviewed. Only technologies with a moderate to high quality of evidence and associated with a clinically or statistically significant improvement in disease management were included. Technologies related to other topics in the mega-analysis on chronic disease management were excluded. Evidence-based analyses were reviewed, and outcomes of interest were extracted. Outcomes of interest included hospital utilization, mortality, health-related quality of life, disease-specific measures, and economic analysis measures.

## Results

Eleven analyses were included and summarized. Technologies fell into 3 categories: those with evidence for the cure of chronic disease, those with evidence for the prevention of chronic disease, and those with evidence for the management of chronic disease.

## Conclusions

The impact on patient outcomes and hospitalization rates of new health technologies in chronic disease management is often overlooked. This analysis demonstrates that health technologies can reduce the burden of illness; improve patient outcomes; reduce resource utilization intensity; be cost-effective; and be a viable contributing factor to chronic disease management in the community.

# Plain Language Summary

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People with chronic diseases rely on the health care system to help manage their illness. Hospital use can be costly, so community-based alternatives are often preferred. Research published in the *Ontario Health Technology Assessment Series* between 2006 and 2011 was reviewed to identify health technologies that have been effective or cost-effective in helping to manage chronic disease in the community. All technologies identified led to better patient outcomes and less use of health services. Most were also cost-effective. Two technologies that can cure chronic disease and 1 that can prevent chronic disease were found. Eight technologies that can help manage chronic disease were also found. Health technologies should be considered an important part of chronic disease management in the community.

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# List of Abbreviations

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<b>AAD</b>	Antiarrhythmic drug
<b>AF</b>	Atrial fibrillation
<b>ARAT</b>	Action research arm test
<b>ARI</b>	Acute respiratory illness
<b>BIA</b>	Budget impact analysis
<b>BMI</b>	Body mass index
<b>BPD</b>	Biliopancreatic diversion
<b>BPH</b>	Benign prostatic hyperplasia
<b>CAD</b>	Coronary artery disease
<b>CAP</b>	Community-acquired pneumonia
<b>CHF</b>	Congestive heart failure
<b>CI</b>	Confidence interval
<b>CIMT</b>	Constraint-induced movement therapy
<b>COPD</b>	Chronic obstructive pulmonary disease
<b>CSII</b>	Continuous subcutaneous insulin infusion
<b>EBA</b>	Evidence-based analysis
<b>EECP</b>	Enhanced external counterpulsation
<b>FEV<sub>1</sub></b>	Forced expiratory volume in 1 second
<b>FIM</b>	Functional independence measure
<b>FMA</b>	Fugl-Meyer motor assessment
<b>FTE</b>	Full-time equivalent
<b>FY</b>	Fiscal year
<b>HR</b>	Hazard ratio
<b>GI</b>	Gastrointestinal
<b>HRQOL</b>	Health-related quality of life
<b>ICD</b>	Implantable cardioverter defibrillator
<b>ICER</b>	Incremental cost-effectiveness ratio
<b>ICU</b>	Intensive care unit
<b>IMV</b>	Invasive mechanical ventilation
<b>INAHTA</b>	International Agency for Health Technology Assessment/Centre for Review and Dissemination
<b>IQR</b>	Interquartile range
<b>LOS</b>	Length of stay
<b>LTC</b>	Long-term care
<b>MAS</b>	Medical Advisory Secretariat
<b>MI</b>	Myocardial infarction

<b>NA</b>	Not applicable
<b>NPPV</b>	Noninvasive positive pressure ventilation
<b>NPWT</b>	Negative pressure wound therapy
<b>NR</b>	Not reported
<b>NRT</b>	Nicotine replacement therapy
<b>NSVT</b>	Non-sustained ventricular tachycardia
<b>ODEM</b>	Ontario Diabetes Economic Model
<b>OHTAC</b>	Ontario Health Technology Advisory Committee
<b>OHTAS</b>	<i>Ontario Health Technology Assessment Series</i>
<b>OR</b>	Odds ratio
<b>OT</b>	Occupational therapy
<b>PATH</b>	Programs for Assessment of Technologies in Health
<b>PCI</b>	Percutaneous coronary intervention
<b>PT</b>	Physiotherapy
<b>PVP</b>	Photoselective vaporization of the prostate
<b>QALY</b>	Quality-adjusted life-year
<b>RCT</b>	Randomized controlled trial
<b>RNAO</b>	Registered Nurses' Association of Ontario
<b>RR</b>	Relative risk
<b>SCD</b>	Sudden cardiac death
<b>SD</b>	Standard deviation
<b>SIS</b>	Stroke impact scale
<b>STEMI</b>	ST-segment elevation myocardial infarction
<b>THETA</b>	Toronto Health Economics and Technology Assessment
<b>TURP</b>	Transurethral resection of the prostate
<b>WMD</b>	Weighted mean difference

# Background

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In July 2011, the Evidence Development and Standards (EDS) branch of Health Quality Ontario (HQO) began developing an evidentiary framework for avoidable hospitalizations. The focus was on adults with at least 1 of the following high-burden chronic conditions: chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), atrial fibrillation, heart failure, stroke, diabetes, and chronic wounds. This project emerged from a request by the Ministry of Health and Long-Term Care for an evidentiary platform on strategies to reduce avoidable hospitalizations.

After an initial review of research on chronic disease management and hospitalization rates, consultation with experts, and presentation to the Ontario Health Technology Advisory Committee (OHTAC), the review was refocused on optimizing chronic disease management in the outpatient (community) setting to reflect the reality that much of chronic disease management occurs in the community. Inadequate or ineffective care in the outpatient setting is an important factor in adverse outcomes (including hospitalizations) for these populations. While this did not substantially alter the scope or topics for the review, it did focus the reviews on outpatient care. HQO identified the following topics for analysis: discharge planning, in-home care, continuity of care, advanced access scheduling, screening for depression/anxiety, self-management support interventions, specialized nursing practice, and electronic tools for health information exchange. Evidence-based analyses were prepared for each of these topics. In addition, this synthesis incorporates previous EDS work, including *Aging in the Community* (2008) and a review of recent (within the previous 5 years) EDS health technology assessments, to identify technologies that can improve chronic disease management.

HQO partnered with the Programs for Assessment of Technology in Health (PATH) Research Institute and the Toronto Health Economics and Technology Assessment (THETA) Collaborative to evaluate the cost-effectiveness of the selected interventions in Ontario populations with at least 1 of the identified chronic conditions. The economic models used administrative data to identify disease cohorts, incorporate the effect of each intervention, and estimate costs and savings where costing data were available and estimates of effect were significant. For more information on the economic analysis, please contact either Murray Krahn at [murray.krahn@theta.utoronto.ca](mailto:murray.krahn@theta.utoronto.ca) or Ron Goeree at [goereer@mcmaster.ca](mailto:goereer@mcmaster.ca).

HQO also partnered with the Centre for Health Economics and Policy Analysis (CHEPA) to conduct a series of reviews of the qualitative literature on “patient centredness” and “vulnerability” as these concepts relate to the included chronic conditions and interventions under review. For more information on the qualitative reviews, please contact Mita Giacomini at [giacomini@mcmaster.ca](mailto:giacomini@mcmaster.ca).

The Optimizing Chronic Disease Management in the Outpatient (Community) Setting mega-analysis series is made up of the following reports, which can be publicly accessed at <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ohtas-reports-and-ohtac-recommendations>.

- Optimizing Chronic Disease Management in the Outpatient (Community) Setting: An Evidentiary Framework
- Discharge Planning in Chronic Conditions: An Evidence-Based Analysis
- In-Home Care for Optimizing Chronic Disease Management in the Community: An Evidence-Based Analysis
- Continuity of Care: An Evidence-Based Analysis
- Advanced (Open) Access Scheduling for Patients With Chronic Diseases: An Evidence-Based Analysis
- Screening and Management of Depression for Adults With Chronic Diseases: An Evidence-Based Analysis
- Self-Management Support Interventions for Persons With Chronic Diseases: An Evidence-Based Analysis
- Specialized Nursing Practice for Chronic Disease Management in the Primary Care Setting: An Evidence-Based Analysis
- Electronic Tools for Health Information Exchange: An Evidence-Based Analysis
- Health Technologies for the Improvement of Chronic Disease Management: A Review of the Medical Advisory Secretariat Evidence-Based Analyses Between 2006 and 2011
- Optimizing Chronic Disease Management Mega-Analysis: Economic Evaluation
- How Diet Modification Challenges Are Magnified in Vulnerable or Marginalized People With Diabetes and Heart Disease: A Systematic Review and Qualitative Meta-Synthesis
- Chronic Disease Patients' Experiences With Accessing Health Care in Rural and Remote Areas: A Systematic Review and Qualitative Meta-Synthesis
- Patient Experiences of Depression and Anxiety With Chronic Disease: A Systematic Review and Qualitative Meta-Synthesis
- Experiences of Patient-Centredness With Specialized Community-Based Care: A Systematic Review and Qualitative Meta-Synthesis

## Objective of Review

The purpose of this review was to identify health technologies evaluated by the Medical Advisory Secretariat (MAS; now known as Evidence Development and Standards, Health Quality Ontario) between 2006 and 2011 that can effectively improve the management of chronic disease in the community.

As part of a larger mega-analysis examining chronic disease management in the community, (1) a review was conducted of MAS evidence-based analyses (EBAs) that showed statistical or clinical improvements in chronic disease management, with specific focus on the following 7 chronic conditions:

- type 2 diabetes
- coronary artery disease (CAD)
- atrial fibrillation (AF)
- chronic obstructive pulmonary disease (COPD)
- congestive heart failure (CHF)
- stroke
- chronic wounds

# Review of Evidence-Based Analyses

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## Research Question

What MAS-reviewed health technologies are effective and cost-effective in optimizing chronic disease management in the outpatient setting (i.e., in the community)?

## Selection of Evidence-Based Analyses

### Literature Search

A review was conducted of *Ontario Health Technology Assessment Series* (OHTAS) reports published between January 1, 2006, and December 31, 2011. (2) Field evaluations conducted by the Programs for Assessment of Technologies in Health (PATH) and the Toronto Health Economics and Technology Assessment (THETA) Collaborative were also reviewed. (3;4) EBAs were independently reviewed to identify health technologies that align with the objective of improving chronic disease management, with a focus on those in the 7 areas of interest (type 2 diabetes, CAD, AF, COPD, CHF, stroke, and chronic wounds).

### Inclusion Criteria

EBAs were initially selected based on information in the title and executive summary. The full texts of potentially relevant analyses were then reviewed. Analyses of technologies that led to a statistically or clinically significant improvement in chronic disease management (with moderate to high quality evidence for at least 1 of the primary outcomes based on the GRADE process described below), or that were cost-effective, were included.

### Exclusion Criteria

Analyses related to the screening or monitoring of disease were excluded. Analyses related to multidisciplinary care, rehabilitation programs, and self-management were also excluded, because they are discussed as part of the Optimizing Chronic Disease Management in the Community (Outpatient) Setting mega-analysis. (1)

### Outcomes of Interest

The following outcomes of interest were extracted (where reported):

- hospital utilization
  - hospitalizations
  - rehospitalizations
  - length of stay (LOS)
  - emergency department use
- mortality
- health-related quality of life (HRQOL)
- functional status
- disease-specific measures
- economic analysis measures

- incremental cost-effectiveness ratio (ICER)
- budget impact analysis (BIA)
- post-intervention downstream events avoided (e.g., adverse events, health services utilization)

## Methodology of Evidence-Based Analyses

The EBAs follow a consistent review process. A brief description of the MAS approach to systematic reviews and economic evaluations is provided below (the methodologies of individual reports are available in the OHTAS). (2)

### Literature Search

A literature search was performed for each EBA using at least 3 of the following databases: OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database to identify potential studies. Search dates varied by individual review. Prior to each literature search, specific inclusion and exclusion criteria and outcomes of interest were defined. Search strategies for individual EBAs are described in Appendices 1 and 2.

### Statistical Analysis

When possible, results were pooled using Review Manager. (5) When applicable, continuous and dichotomous data were pooled using a random- or fixed-effects model to calculate relative risk (RR), odds ratio (OR), or weighted mean difference. When data could not be pooled, results were summarized descriptively. Statistical methods for individual EBAs are described in Appendix 2.

### Quality of Evidence

The quality of the body of evidence<sup>1</sup> for each outcome was examined according to the GRADE Working Group criteria. (6) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology. (Note: The GRADE Working Group updated its criteria in the fall of 2011; not all EBAs included in this review will reflect the update.)

Study design was the first consideration; the starting assumption was that randomized controlled trials are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (6) For more detailed information, please refer to the latest series of GRADE articles. (6)

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<sup>1</sup> *Quality* refers to the criteria such as adequacy of allocation concealment, blinding, and follow-up. *Consistency* refers to the similarity of estimates of effect across studies. If there are important and unexplained inconsistencies in the results, confidence in the estimate of effect for that outcome decreases. Differences in direction of effect, magnitude of the difference in effect, and significance of the differences guide decisions about whether important inconsistency exists. *Directness* refers to the extent to which interventions and outcome measures are similar to those of interest.

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

- High** Further research is very unlikely to change confidence in the estimate of effect
- Moderate** Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
- Low** Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate
- Very Low** Any estimate of effect is very uncertain

## **Economic Analysis**

Details of specific economic analyses can be found in the individual EBAs. (2)

### ***Cost-Effectiveness Analysis***

When possible, costs, quality-adjusted life-years (QALYs), and ICERs for each intervention were assessed. Cohorts aligned with the patient populations from the research trials were examined as part of the literature search. Additionally, analyses and models were populated using clinical parameters and summary estimates from the EBAs. Unless otherwise indicated, the perspective of all analyses was that of a publicly funded health care system.

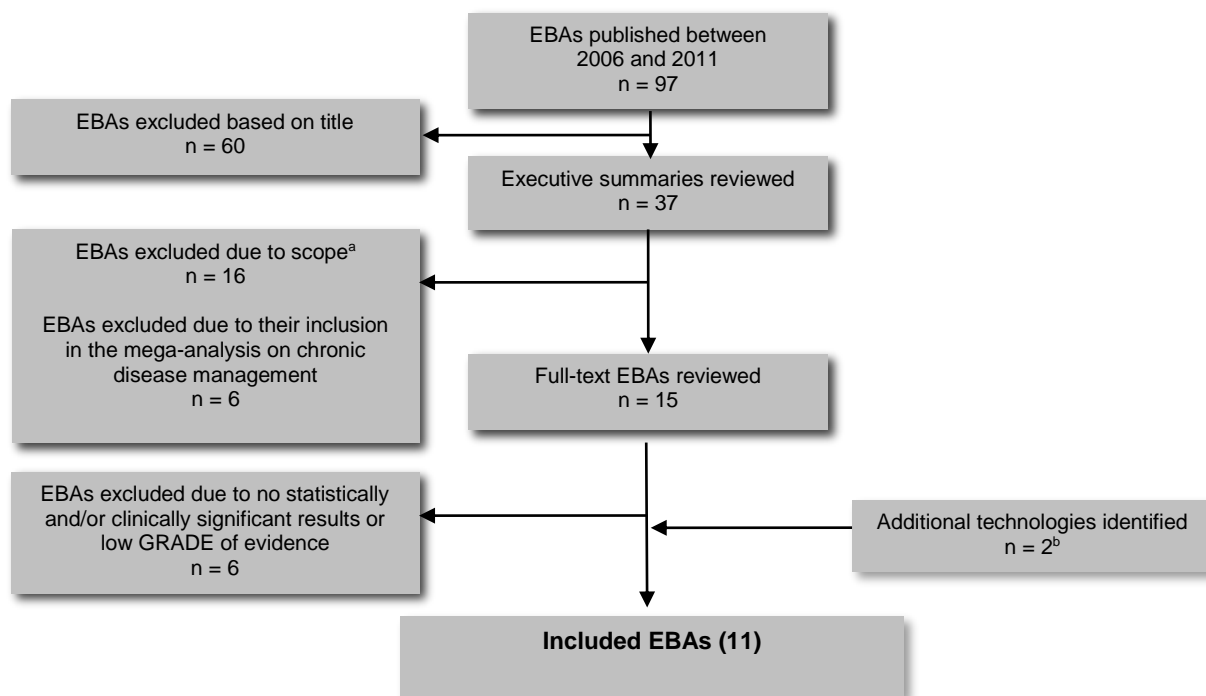
### ***Budget Impact Analysis***

When possible, a BIA was conducted to project potential costs, incremental costs, and resource utilization for the Ontario health care system if the technology under review were implemented. Budget impact analyses often considered relevant resources already in place. Often, several assumptions were required to calculate potentially impacted populations; these assumptions were guided by the literature, population-based administrative data, and expert opinion.



## Results of Review

The OHTAS search yielded 97 publications completed between January 1, 2006, and December 31, 2011. A total of 9 health technologies were identified for review (Figure 1 and Table 1). Additionally, 1 health technology assessment evaluating photoselective vaporization of the prostate (PVP) was included based the results of an ongoing field evaluation, which demonstrated a significant reduction in hospitalizations and associated cost savings. As well, 1 EBA evaluating implantable cardioverter defibrillators (ICDs) from 2005 was included due to ongoing data collection resulting from an Ontario Health Technology Advisory Committee (OHTAC) recommendation. Appendix 3 lists excluded EBAs and the rationale for their exclusion.



**Figure 1: Analysis Flow Chart**

Abbreviations: EBA, evidence-based analysis; OHTAC, Ontario Health Technology Advisory Committee.

<sup>a</sup>Includes technologies used for screening and monitoring diseases and conditions.

<sup>b</sup>Additional technologies identified were a field evaluation resulting in a significant reduction in hospitalizations and associated cost savings; and an EBA from 2005 with ongoing data collection resulting from an OHTAC recommendation.

**Table 1: Included Evidence-Based Analyses**

<b>Year; Volume (Number)</b>	<b>Title</b>
<b>Type 2 Diabetes</b>	
2009;9(22)	Bariatric Surgery for People With Diabetes and Morbid Obesity: An Evidence-Based Analysis (7)
<b>Coronary Artery Disease</b>	
2010;10(17)	Primary Angioplasty and Thrombolysis for the Treatment of Acute ST-Segment Elevated Myocardial Infarction: An Evidence Update (8)
<b>Atrial Fibrillation</b>	
2006;6(7)	Ablation for Atrial Fibrillation: An Evidence-Based Analysis (9)
<b>Chronic Obstructive Pulmonary Disease</b>	
2012;12(3)	Influenza and Pneumococcal Vaccinations for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Review (10)
2012;12(4)	Smoking Cessation for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis (11)
2012;12(8)	Noninvasive Positive Pressure Ventilation for Acute Respiratory Failure Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis (12)
<b>Congestive Heart Failure</b>	
2005;5(14)	Implantable Cardioverter Defibrillators—Prophylactic Use: An Evidence-Based Analysis (13)
<b>Stroke</b>	
2011;11(6)	Constraint-Induced Movement Therapy for Rehabilitation of Arm Dysfunction After Stroke in Adults: An Evidence-Based Analysis (14)
<b>Chronic Wounds</b>	
2009;9(2)	Pressure Ulcer Prevention: An Evidence-Based Analysis (15)
2010;10(23)	Negative Pressure Wound Therapy: An Evidence-Update (16)
<b>Other</b>	
2013;in press (17)	Photoselective Vaporization for the Treatment of Benign Prostatic Hyperplasia

## **Bariatric Surgery for People With Diabetes and Morbid Obesity: An Evidence-Based Analysis**

### ***Background***

Clinically severe or morbid obesity is commonly defined by a body mass index (BMI) of at least 40 kg/m<sup>2</sup>, or a BMI of at least 35 kg/m<sup>2</sup> with the presence of comorbid conditions, such as type 2 diabetes, cardiovascular disease, or arthritis. Obesity is associated with the development of several diseases, including type 2 diabetes. Surgery for morbid obesity is usually considered a last resort for people who have attempted first-line medical management (e.g., diet, behaviour modification, increased physical activity, and drugs) but who have not permanently lost weight.

Numerous surgical options are available for people with morbid obesity. Bariatric surgery can be grouped into 2 general types—malabsorptive and restrictive—both of which can be performed laparoscopically or as open surgery. Malabsorptive techniques work by bypassing parts of the gastrointestinal tract to limit the absorption of food (e.g., biliopancreatic diversion, Roux-en-Y gastric bypass); restrictive techniques decrease the size of the stomach for the patient to feel satiated with a smaller amount of food (e.g., gastroplasty, gastric banding).

### ***Results***

An EBA was conducted to examine the effectiveness and cost-effectiveness of bariatric surgery for the management of diabetes in people with morbid obesity. (7) When possible, results were further stratified by type of bariatric surgery (malabsorptive or restrictive).

The primary outcome of interest was the improvement or resolution of type 2 diabetes, generally defined as the disappearance of diabetes, being able to discontinue all diabetes-related medications, or being able to maintain blood glucose levels in the normal range. A summary of the results is presented in Table 2.

**Table 2: Bariatric Surgery for People With Diabetes and Morbid Obesity—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Disease-Specific Measures		
Intervention	Comparator		Δ HbA1c, % (range) <sup>a</sup>	Mean Improvement/Resolution of Diabetes	Adverse Events
Bariatric surgery	No control arm evaluated  Recovery <sup>b</sup> Usual care (no surgery)	Adults with type 2 diabetes and morbid obesity	-2.70 (-5.0 to -0.70)	Resolution and/or improvement <sup>c</sup> 86.0% (95% CI 78.4–93.7)  Resolution <sup>d</sup> 76.8% (95% CI 70.7–82.9)  Recovery <sup>b</sup> OR 8.42 (95% CI 5.7–12.5) at 2 years OR 3.45 (95% CI 1.6–7.3) at 10 years	Postoperative complications Mortality: 0.25% Other (e.g., bleeding, embolism, wound complications, deep infections): 13% Complications requiring re-surgery: 2.2%
Number of studies (sample size)			1 meta-analysis of 134 studies	Resolution and/or improvement <sup>c</sup> 1 meta-analysis of 134 studies  Recovery <sup>b</sup> 1 observational study (n = 4,047 at 2 years and n = 1,703 at 10 years)	1 observational study (n = 4,047 at 2 years and n = 1,703 at 10 years)
GRADE			Moderate	Moderate	NR
<b>Subgroup Analyses</b>					
Malabsorptive interventions	No control arm evaluated		Gastric bypass: -3.99 (-5.0 to -0.70)	Resolution and/or improvement <sup>c</sup> Gastric bypass: 93.2% (95% CI 79.3–100.0)  Resolution <sup>b</sup> Gastric bypass: 83.7% (95% CI 77.3–90.1) BPD/duodenal switch: 98.9% (95% CI 96.8–100.0)	Operative 30-day mortality: 0.5% gastric bypass 1.1% BPD or duodenal switch
Number of studies (sample size)			1 meta-analysis of 134 studies	1 meta-analysis of 134 studies	1 meta-analysis of 134 studies
Restrictive interventions	No control arm evaluated		-1.34 (-1.60 to -0.94)	Resolution and/or improvement <sup>c</sup> 90.8% (95% CI 76.2–100.0)  Resolution <sup>b</sup> 71.6% (95% CI 55.1–88.2)	Operative 30-day mortality: 0.1%
Number of studies (sample size)			1 meta-analysis of 134 studies	1 meta-analysis of 134 studies	1 meta-analysis of 134 studies

Abbreviations: BPD, biliopancreatic diversion; CI, confidence interval; HbA1c, glycated hemoglobin; NR, not reported; OR, odds ratio.

<sup>a</sup>From baseline to follow-up.

<sup>b</sup>Fasting plasma glucose level of < 126 mg/dL (7.0 mmol/L).

<sup>c</sup>Studies reporting a combination as well as studies that used only the term “improved,” but not the studies reporting only resolution.

<sup>d</sup>Studies reporting diabetes disappeared or no longer required therapy.

### ***Economic Analysis***

A cost-effectiveness analysis was conducted using the Ontario Diabetes Economic Model (ODEM). The ODEM was populated using the Ontario Diabetes Database and various other linked databases to measure the prevalence and incidence of complications, healthcare resource utilization (e.g., inpatient and outpatient hospitalizations, outpatient visits, prescription drugs, emergency department visits, and home care), and death. The baseline characteristics for the cohort were obtained from the literature, and the effectiveness of bariatric surgery was taken from the EBA.

The ODEM was used to identify the ICER and the incremental number of events avoided per 1,000 people, based on the implementation of bariatric surgery over a 40-year time horizon. Results from the cost-effectiveness analysis for bariatric surgery compared to usual care are shown in Table 3.

**Table 3: Bariatric Surgery for People With Diabetes and Morbid Obesity—Summary of ODEM<sup>a</sup>**

Technology Reviewed		Population	ICER (Cost/QALY)	Incremental Number of Events Avoided per 1,000 Population	Ontario Health System Impact, Number of Events Avoided <sup>b</sup>
Intervention	Comparator				
Bariatric surgery	Usual care (no surgery)	Adults with type 2 diabetes and morbid obesity	\$15,697/QALY	Ischemic heart disease: 16.1 MI: 80.8 Heart failure: 181.8 Stroke: 52.3 Amputation: 17.5 Blindness: 24.4 Renal failure: 0.1	Ischemic heart disease: 2,757 MI: 13,839 Heart failure: 31,137 Stroke: 8,957 Amputation: 2,997 Blindness: 4,179 Renal failure: 17

Abbreviations: ICER, incremental cost-effectiveness ratio; MI, myocardial infarction; ODEM, Ontario Diabetes Economic Model; QALY, quality-adjusted life-year.

<sup>a</sup>All costs in Canadian dollars. Based on a 40-year time horizon.

<sup>b</sup>Assuming 171,275 adults with morbid obesity and type 2 diabetes.

### ***OHTAC Recommendation<sup>2</sup>***

OHTAC made the following recommendation after considering the findings above:

- OHTAC recommends improving access to bariatric surgery for morbidly obese adults with diabetes. Priority for bariatric surgery should be given to morbidly obese people (BMI > 35 kg/m<sup>2</sup>) with diabetes over morbidly obese people without diabetes.

### ***Conclusions: Impact on Chronic Disease Management***

Based on moderate-quality evidence, bariatric surgery has shown effectiveness in resolving diabetes in adults with morbid obesity. Moderate-quality evidence also found a statistically significant reduction in glycated hemoglobin (HbA1c) of 2.70% among patients receiving bariatric surgery, which is a clinically meaningful outcome. A 1% reduction in HbA1c is associated with a 10% reduction in diabetes-related mortality and a 25% reduction in microvascular endpoints. Overall, these results indicate that bariatric surgery can significantly improve the management of type 2 diabetes in the morbidly obese population, as well as resolve the disease itself.

Diabetes is a highly prevalent chronic metabolic disorder, affecting an estimated 8.8% of Ontario's population (in 2005). Clinically, diabetes is the leading cause of blindness, end-stage renal disease, and nontraumatic amputation in Canadian adults and is a significant cause of cardiovascular complications,

<sup>2</sup>Note: this is part of a recommendation for the larger diabetes evidentiary platform.

hypertension, stroke, cataracts, and glaucoma. Among people with type 2 diabetes, approximately 52% have a BMI  $\geq 30$  kg/m<sup>2</sup>, and 23% have a BMI  $\geq 35$  kg/m<sup>2</sup>.

The ODEM indicated that bariatric surgery had a significant impact on downstream events associated with diabetes and obesity. With an estimated 171,275 morbidly obese adults with type 2 diabetes in Ontario, bariatric surgery is predicted to prevent an additional 13,839 myocardial infarctions (MIs), 31,137 heart failures, 8,957 strokes, 2,997 amputations, 4,179 cases of blindness and 17 renal failures over a 40-year time horizon. Hospital utilization associated with these complications would also be expected to decrease. Overall, bariatric surgery among morbidly obese people with type 2 diabetes was found to be a cost-effective intervention, with an ICER of \$15,697 (Cdn) per QALY.

## **Primary Angioplasty and Thrombolysis for the Treatment of Acute ST-Segment Elevated Myocardial Infarction: An Evidence Update**

### ***Background***

ST-segment elevation myocardial infarction (STEMI) is 1 type of acute coronary syndrome associated with CAD. A STEMI is identified using an electrocardiogram when a patient experiences chest pain. The best treatment for patients with evolving acute MI (such as that experienced with a STEMI) has been under debate among cardiologists. Percutaneous coronary intervention (PCI) involves surgical treatment to open a blocked artery and restore blood flow. Angioplasty is 1 type of PCI (*primary angioplasty* when performed on patients with an acute MI), and stenting is another type. PCIs are an alternative to thrombolysis (the administration of clot-dissolving drug therapy) for patients with STEMI.

### ***Results***

An EBA was conducted to examine the effectiveness of PCI versus thrombolysis for the treatment of people with an acute MI. (8) Two examinations of PCI had statistically significant findings with moderate-quality evidence for at least 1 of the primary outcomes:

- primary PCI versus in-hospital thrombolysis
- routine early PCI (after thrombolysis) versus thrombolysis (and rescue PCI if needed)

The primary outcomes of interest were reductions in mortality, reinfarction, and stroke. A summary of the results of the effectiveness analysis is presented in Table 4.

Three evaluations of PCI were not supported by the evidence, and therefore not included in this review.

- There was low quality evidence for the use of primary PCI versus prehospital thrombolysis.
- There were no statistically significant findings for the use of facilitated PCI (with thrombolytics and glycoprotein IIb/IIIa [GpIIb/IIIa]) versus the use of primary PCI (with GpIIb/IIIa prior to PCI).
- There were no statistically significant findings for the use of rescue PCI after initial thrombolysis versus repeat thrombolysis.

**Table 4: Percutaneous Coronary Intervention—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Mortality OR (95% CI)	Disease-Specific Measures			
Intervention	Comparator			Reinfarction OR (95% CI)	Stroke OR (95% CI)	Composite Outcome of Mortality, Reinfarction, or Stroke OR (95% CI)	Complications: Major Bleeding OR (95% CI)
Primary PCI	In-hospital thrombolysis	Patients with acute STEMI and door-to-needle time ≤ 30 minutes and door-to-balloon time ≤ 90 minutes	0.87 (0.61–1.24)	0.27 (0.16–0.45)	0.59 (0.29–1.22)	0.56 (0.42–0.75)	NR
Number of studies (sample size)			4 RCTs (1,985)	4 RCTs (1,985)	3 RCTs (1,845)	4 RCTs (1,985)	—
Overall GRADE: Moderate							
Routine early PCI after thrombolysis	Thrombolysis (and rescue PCI as needed)	Patients with acute STEMI	0.73 (0.47–1.14)	0.55 (0.38–0.80)	0.88 (0.36–2.11)	0.64 (0.49–0.83)	1.11 (0.69–1.79)
Number of studies (sample size)			6 RCTs (2,294)	6 RCTs (2,294)	6 RCTs (2,294)	6 RCTs (2,294)	6 RCTs (2,294)
Overall GRADE: Moderate							

Abbreviations: CI, confidence interval; NR, not reported; OR, odds ratio; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; STEMI, ST-segment elevation myocardial infarction.



### ***Economic Analysis***

The cost for a PCI in Ontario is approximately \$5,000 (Cdn) per procedure. (8) PCI procedures and associated costs for fiscal year 2008–2009 are shown in Table 5. Provincial programs pay for PCIs but do not differentiate between types of PCI performed. Costs that exceed the cost per procedure are absorbed by hospital budgets and physician billing through the Ontario Schedule of Physician Benefits.

**Table 5: Percutaneous Coronary Intervention—Ontario Costs, Fiscal Year 2008/2009<sup>a</sup>**

<b>Angioplasty Volumes</b>	<b>Cost per Procedure</b>	<b>Angioplasty Cost</b>	<b>Stent Volumes<sup>b</sup></b>	<b>Cost per Procedure</b>	<b>Stent Cost</b>	<b>Total Cost</b>
19,993	\$4,915	\$98,265,595	4,998	\$2,338	\$11,685,909	\$109,951,504

<sup>a</sup>All costs in Canadian dollars.

<sup>b</sup>Ontario funds drug-eluting stents at 25% of angioplasty volumes.

By comparison, expert opinion estimates the cost of a dose of tenecteplase (a thrombolytic agent) at approximately \$2,700 (Cdn).

Although an economic analysis was not conducted at the time of this EBA, an analysis was conducted as part of a previous EBA on PCI and thrombolytic agents in 2004. (18) This earlier analysis estimated a cost savings to the Ontario hospital budget of between \$2,820 (Cdn) and \$5,259 (Cdn) per capita due to reduced hospitalizations for acute MI with primary angioplasty.

### ***OHTAC Recommendations***

OHTAC made the following recommendations after considering the findings above:

- Hospitals must provide timely access to reperfusion (within 90 minutes for primary PCI or within 30 minutes for thrombolysis) for optimal outcomes in patients with STEMI.
- For patients undergoing thrombolytic reperfusion, attempts should be made to refer them subsequently to a PCI facility with a level of urgency most appropriate for the patient's condition. In particular, patients who are eligible for rescue PCI should be transferred in a timely manner. The routine use of thrombolysis is followed immediately by PCI (facilitated PCI) should not be encouraged due to increased risk of major bleeding.
- When indicated, thrombolysis should be administered as first-line treatment if it is unlikely that primary PCI will be available within the maximum recommended delay (as stated above) for patients being considered for primary PCI.
- Thrombolysis should be available in ambulances for those Ontarians who do not have timely access to a PCI facility or an emergency room due to their geographic location.
- There is uncertainty regarding: 1) the number of STEMI patients in Ontario who receive no reperfusion treatment; and 2) the penetration rate and timeliness of primary PCI and thrombolysis in Ontario. Therefore, through the LHINs, referral and PCI hospitals should be asked to work together with other key partners to track information on the timeliness, management, and outcomes of STEMI patients in Ontario, and these data should be publicly reported back to all hospitals and other relevant stakeholders who are involved in or have a responsibility for the optimal management of STEMI patients.
- Through continuing education, health professionals should follow state-of-the-art thrombolysis management in order to maintain skills related to the timely use of thrombolysis, where appropriate.

### ***Conclusions: Impact on Chronic Disease Management***

Based on moderate-quality evidence, primary PCI has significant advantages over in-hospital thrombolysis. Additionally, based on moderate-quality evidence, routine early PCI has advantages over thrombolysis (with rescue PCI as needed). Advantageous treatment for an acute MI among patients presenting with STEMI significantly reduced rates of mortality, reinfarction, stroke, or a composite outcome of the 3.

Currently, the penetration rate and timeliness of primary PCI versus thrombolysis in Ontario is unknown. It has been demonstrated by 1 study that timeliness of treatment is more important than choice of treatment. Approximately 50% of all patients receive primary PCI or thrombolysis within the recommended periods ( $\leq 90$  minutes for thrombolysis and  $\leq 30$  minutes for PCI). However, the Cardiac Care Network provincial primary PCI registry showed that in 2008–2009, the median door-to-balloon time in Ontario was 101 minutes. Additionally, it should be noted that in 2004, an estimated 50% of STEMI patients in Ontario self-presented to local hospitals rather than calling emergency medical services.

Cardiovascular disease is the leading cause of death among residents of Ontario, with most cardiovascular disease mortality due to acute MI. The estimated number of patients with STEMI in Ontario in 2003 was 1,100. A 2004 economic analysis estimated a cost savings of between \$2,820 (Cdn) and \$5,259 (Cdn) due to reduced hospitalizations for acute MI. The total costs for angioplasty and stenting in Ontario in fiscal year 2008–2009 was \$110 million (Cdn), with total costs unknown for thrombolytic interventions. The estimated cost per treatment for a thrombolytic agent is \$2,700 (Cdn), while stenting costs are \$2,338 (Cdn) per procedure and angioplasty is \$4,915 (Cdn).

## **Ablation for Atrial Fibrillation: An Evidence-Based Analysis**

### ***Background***

Currently, the first-line therapy for AF is medical therapy with antiarrhythmic drugs (AADs). There are several AADs available, because no AAD is effective for all patients; however, AADs have critical adverse effects that can aggravate existing arrhythmias. The drug selection process frequently involves trial and error until the patient's symptoms subside.

Ablation has been frequently described as a cure for AF (compared with drug therapy, which controls AF but does not cure it). Ablation involves directing an energy source at cardiac tissue. For instance, radiofrequency energy uses heat to burn tissue near the source of the arrhythmia. The purpose is to create an area of scar tissue so that the aberrant electrical pathways no longer exist. There are 2 methods of ablation: catheter ablation and surgical (operative) ablation. Radiofrequency energy was the most commonly used ablation technique at the time of this EBA. *Catheter ablation* involves inserting a catheter through the femoral vein to access the heart and burn abnormal foci of electrical activity by direct contact or by isolating them from the rest of the atrium. *Surgical ablation* is minimally invasive, performed via direct visualization or with the assistance of a special scope for patients with lone AF.

### ***Results***

An EBA was conducted to examine the effectiveness of ablation therapies among patients with atrial fibrillation or flutter. (9) Three separate groups were evaluated:

- catheter ablation as first-line treatment for AF and atrial flutter
- ablation in patients with drug-refractory AF who *do not* require additional surgery
- ablation in patients with drug-refractory AF who require additional heart surgery

The primary outcome of interest was freedom from arrhythmia, measured as the proportion of the treatment group free of arrhythmia and compared to the proportion free of arrhythmia in the control group. A summary of the results from the effectiveness analysis is presented in Table 6.

Additionally, there was 1 observation study (n = 1,171) included in the EBA that examined mortality, complication rates, and HRQOL among individuals who received ablation versus those with drug-refractory AF when no additional heart surgery was required. The ablation group had a mortality rate of 6.5% versus the drug therapy group, which had a mortality rate of 14.3%. Additionally, the ablation group had a complication rate of 9.2% versus the drug therapy group, which had a complication rate of 20.1%. Finally, this study found a significantly improved HRQOL ( $P = 0.004$ ) in the ablation group versus the drug therapy group.

**Table 6: Ablation for Atrial Fibrillation—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	HRQOL	Disease-Specific Measures	
Intervention	Comparator			Long-Term Freedom From Arrhythmia RR (95% CI)	Complications <sup>a</sup>
<b>First-Line Treatment With Ablation</b>					
Catheter ablation	Medical therapy	Patients with AF or atrial flutter	Ablation: significant improvement Medical therapy: no significant difference	AF: 0.24 (0.09–0.59) Atrial flutter: 0.35 (0.17–0.72)	No substantial long-term adverse effects were reported among patients undergoing catheter ablation
Number of studies (sample size)			2 RCTs (131)	2 RCTs (131)	2 RCTs (131)
GRADE			NR	Moderate	NR
<b>Ablation for Drug Refractory Fibrillation, No Additional Surgery Required</b>					
Catheter radiofrequency ablation	Drug therapy	Drug-refractory AF, no additional heart surgery required	Significantly greater improvement in general health score with ablation ( $P = 0.007$ )	0.32 (0.21–0.43)	Ablation: 5 atrial flutter, 2 stroke, 1 transient phrenic paralysis, 1 pericardial effusion, 1 groin hematoma Drug therapy: 1 transischemic attack, 2 cancer (1 death), 1 sudden cardiac death, side effects of medical therapy of nausea, sinus node dysfunction and hypothyroidism
Number of studies (sample size)			1 RCT (30)	3 RCTs (313)	3 RCTs (313)
GRADE			NR	Moderate	NR
<b>Ablation for Drug Refractory Fibrillation, Additional Heart Surgery Required</b>					
Radiofrequency surgical ablation with mitral valve surgery	Mitral valve surgery	Drug-refractory AF, additional heart surgery required	NR	0.13 (0.05–0.30)	Ablation: 6 deaths, 1 reoperation for bleeding, 1 late pericardial tamponade, 1 postoperative pacemaker Mitral valve surgery: 4 deaths, 1 reoperation for bleeding, 2 late pericardial tamponade, 1 postoperative pacemaker
Number of studies and study type (sample size)			—	2 RCTs (97)	2 RCTs (97)
GRADE			—	High	NR
Surgical ablation maze plus mitral valve surgery	Mitral valve surgery	Drug-refractory AF, additional heart surgery required	Marked improvement after surgery, no difference between groups	0.30 (0.11–0.79)	Ablation: 1 stroke, 1 inotropic drugs due to intra-operative MI Mitral valve surgery: 1 death, 1 stroke
Number of studies (sample size)			1 RCT (35)	2 RCTs (62)	2 RCTs (62)
GRADE			NR	High	NR

Technology Reviewed		Population	HRQOL	Disease-Specific Measures	
Intervention	Comparator			Long-Term Freedom From Arrhythmia RR (95% CI)	Complications <sup>a</sup>
Microwave ablation and heart surgery	Heart surgery	Drug-refractory AF, additional heart surgery required	NR	0.30 (0.13–0.70)	Ablation: 1 death Heart surgery: 1 death
Number of studies (sample size)			—	1 RCT (43)	1 RCT (43)
GRADE			—	Moderate	NR
Linear atrial cryoablation of left atrium	Pulmonary vein cryoablation	Drug-refractory AF, additional heart surgery required	NR	0.53 (0.39–0.73)	Ablation: 4 deaths Pulmonary vein cryoablation: 1 death
Number of studies (sample size)			—	1 RCT (105)	1 RCT (105)
GRADE			—	Moderate	NR

Abbreviations: AF, atrial fibrillation; CI, confidence interval; HRQOL, health-related quality of life; MI, myocardial infarction; NR, not reported; RR, relative risk; RCT, randomized controlled trial.

<sup>a</sup>Includes, but not limited to: death, transient ischemic attack, ischemic stroke, hemorrhagic stroke, congestive heart failure, myocardial infarction, or peripheral embolism. *Causes of patient deaths*

Ablation group, n: perioperative, 2; heart failure, 1; renal bleeding, 1; mediastinitis, 1; sudden cardiac death, 1; severe lung fibrosis, 1; valvular endocarditis, 1; hemorrhagic stroke, 1; multiorgan failure, 1; traffic accident, 1; cerebral air embolism of unknown origin, 1. Control group, n: perioperative, 1; refractory heart failure, 1; gastrointestinal complication, 1; sudden cardiac death, 1; stroke, 1; severe chronic obstructive bronchial disease, 1.

### ***Economic Analysis***

An Ontario-based economic analysis was conducted to assess the costs of ablation for AF. The analysis was developed in conjunction with the EBA on advanced mapping systems for catheter ablation, and thus the economic analysis includes the costs of advanced mapping systems in addition to the costs of ablation procedures. (9) Hospital costs were based on data from the Ontario Case Costing Initiative, with nonhospital costs obtained from the Provider Services Branch of the Ontario Ministry of Health and Long-Term Care (physician services), local health care institutions (device costs), and the Ontario Drug Benefit formulary (drug costs). Results from the economic analysis are presented in Table 7.

**Table 7: Ablation for Atrial Fibrillation—Per-Patient Costing Estimates and Avoided Hospitalizations<sup>a</sup>**

Intervention	Comparator	Per-Patient Costing Analysis			
		Up-Front Cost (Year 1)	Cumulative Annual Cost of Ablation	Cumulative Annual Cost of Medical Treatment	Cumulative Annual Cost Difference (Ablation–Medical Treatment)
Ablation for atrial fibrillation	Medical treatment	Ablation:	Year 1: \$22,465	Year 1: \$6,475	Year 1: –\$15,990
		\$22,465	Year 2: \$24,560	Year 2: \$13,080	Year 2: –\$11,480
		Medical	Year 3: \$26,697	Year 3: \$19,817	Year 3: –\$6,880
		treatment:	Year 4: \$28,876	Year 4: \$26,688	Year 4: –\$2,188
		\$6,475	Year 5: \$31,100	Year 5: \$33,697	Year 5: \$2,597

<sup>a</sup>All costs in Canadian dollars.

### ***OHTAC Recommendation***

OHTAC made the following recommendation after considering the findings above:

- OHTAC recommends increased access to ablation with advanced mapping so the prevalent population with drug-refractory atrial fibrillation can be treated over 5 years.

### ***Conclusions: Impact on Chronic Disease Management***

Based on moderate to high quality evidence, catheter ablation as a first-line treatment for AF has been shown to result in greater long-term freedom from arrhythmia than medical treatment alone. Several studies also identified a significant increase in HRQOL and a decrease in mortality among patients receiving ablation. As such, ablation for AF results in a direct impact on chronic disease management by avoiding downstream effects and health services utilization.

Atrial fibrillation is a highly prevalent chronic condition that is often associated with other diseases, such as high blood pressure, abnormal heart muscle function, chronic lung diseases, and CHF. AF is associated with higher morbidity and mortality, because it increases the risk of stroke and other thromboembolic events and CHF. AF increases the risk of stroke 4- to 5-fold in all age groups, leading to 10% to 15% of all ischemic strokes, and 25% of strokes in patients age 80 years or older. The rate of hospitalization for AF in Canada is approximately 583 per 100,000 people and for patients discharged alive, 3% are readmitted for stroke within 1 year. There is an indication that the prevalence of complex arrhythmias is increasing in Ontario. Average annual hospital admissions with a diagnosis of AF or flutter rose from 43,680 in 2000 to 50,640 in 2004.

Ablation provides an opportunity to cure AF, as opposed to treating it with drugs or electrical cardioversion. Results from the economic analysis estimate an average annual cost savings of \$971 (Cdn) per treated patient due to avoided hospitalizations related to stroke and CHF, and approximately \$700

(Cdn) per treated patient in annual cost savings due to the reduced use of anticoagulants and antiarrhythmics. Since 78% (76,000/98,000) of the Ontario population with AF is over the age of 65, cost savings due to reduced medication use will largely accrue directly to the Ontario Drug Benefit program. When physician fees, other drug costs, and diagnostic testing are factored into the costing estimates, the added up-front cost of ablation, compared to treatment with medical therapy alone, is recouped at 4.5 years after the procedure. Since baseline life expectancy remains in excess of 5 years for most individuals with AF treated with advanced mapping ablation, they will survive beyond the point at which the added up-front costs are recouped.

## **Influenza and Pneumococcal Vaccinations for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Review**

### ***Background***

#### *Influenza Vaccination*

The selection of influenza viruses for seasonal influenza vaccine is based on the type of influenza viruses that circulated during the previous year. Every year, the World Health Organization convenes technical meetings and makes recommendations about the selection of virus strains. In Canada, there are currently 5 trivalent influenza vaccines authorized for use by injection.

#### *Pneumococcal Vaccination*

*Streptococcus pneumoniae*, also known as pneumococcus, is an encapsulated Gram-positive bacterium that colonizes in the nasopharynx of healthy children and adults. The current pneumococcal polysaccharide vaccines are targeted to prevent diseases caused by 23 of the most common serotypes of *Streptococcus pneumoniae*. Canada-wide estimates suggest that approximately 90% of cases of pneumococcal bacteria and meningitis are caused by these 23 serotypes.

The United States Centers for Disease Control and Prevention provided recommendations for the use of the vaccine among all adults aged 65 years and older and among adults aged 19 to 64 years with underlying medical conditions that put them at greater risk for serious pneumococcal infection, including chronic lung disease (COPD), emphysema, and asthma.

### ***Results***

An EBA was conducted to determine the effectiveness of the influenza vaccination and the pneumococcal vaccination in patients with COPD in reducing the incidence of influenza-related illness or pneumococcal pneumonia. (10) Results were stratified by type of vaccination: influenza vaccination or pneumococcal vaccination.

The primary outcome of interest for the influenza vaccination was episodes of acute respiratory illness (ARI) due to the influenza virus. The primary outcome of interest for the pneumococcal vaccination was time to the first episode of community-acquired pneumonia (CAP) of pneumococcal or unknown etiology. Secondary outcomes for both vaccination types were rate of hospitalization and mechanical ventilation, mortality rate, and adverse events. A summary of the results is presented in Table 8.



**Table 8: Vaccinations for COPD—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Mortality	Hospital Utilization			Disease-Specific Measures		
Intervention	Comparator			Hospitalization	Length of Stay	Incidence Density of Influenza-Related ARI, RR (95% CI)	First Episode of CAP	Mechanical Ventilation RR (95% CI)	Adverse Events
Influenza vaccination	No vaccination	COPD patients	NR	<i>Influenza-related ARI</i> RR 0.41 (95% CI 0.08–2.02)	NR	0.2 (0.06–0.70)	NA	0.15 (0.01–2.75)	<i>Local</i> 27% vaccinated 6% control ( <i>P</i> = 0.002)  <i>Systemic</i> 76% vaccinated 81% control ( <i>P</i> = 0.5)
Number of studies (sample size)			—	1 RCT (125)	—	1 RCT (125)	—	1 RCT (125)	1 RCT (125)
GRADE			—	Low	—	High	—	Low	Low
Pneumococcal vaccination	No vaccination	COPD patients	No significant difference (19% in both groups)	<i>CAP-related</i> 76% vaccinated 81% control ( <i>P</i> = 0.59)	9.5 days vaccinated, 12 days control ( <i>P</i> = 0.16)	NA	<i>Pneumococcal and unknown etiology</i> RR 0.76 (95% CI 0.46–1.24) <sup>a</sup>  <i>Pneumococcal pneumonia</i> 0% vs. 1.68%; log rank test 5.03 ( <i>P</i> = 0.025) <sup>a</sup>  <i>Time to first episode of CAP</i> log rank test 1.15 ( <i>P</i> = 0.28)	NR	No reported local or systemic reactions in either group
Number of studies (sample size)			1 RCT (596)	1 RCT (596)	1 RCT (596)	—	1 RCT (596)	—	1 RCT (596)
GRADE			NR	Low	NR	—	High	—	Low
<b>Subanalyses by Age and Severity<sup>b</sup> of COPD for Incidence of ARI and CAP</b>									
Influenza vaccination	No vaccination	Mild COPD				0.2 (0.003–1.3)			
		Moderate COPD				0.5 (0.05–3.8)			
		Severe COPD				0.1 (0.003–1.1)			
Pneumococcal vaccination	No vaccination	COPD < 65 years					RR 0.24 (95% CI 0.07–0.80)		
		COPD > 65 years					RR 1.14 (95% CI 0.62–2.07)		
		Mild–moderate COPD					RR 1.11 (95% CI 0.53–2.32)		
		Severe COPD					RR 0.52 (95% CI 0.27–1.01)		
		Severe COPD < 65 years					RR 0.09 (95% CI 0.01–0.65)		

Abbreviations: ARI, acute respiratory illness; CAP, community-acquired pneumonia; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in 1 second; NA, not applicable; NR, not reported; RCT, randomized controlled trial; RR, relative risk.

<sup>a</sup>No GRADE reported for outcome.

<sup>b</sup>Mild COPD, FEV<sub>1</sub> ≥ 70% predicted; moderate COPD, FEV<sub>1</sub> 50%–69% predicted; severe COPD, FEV<sub>1</sub> < 50% predicted).

### ***Economic Analysis***

A cost-effectiveness analysis was not conducted, because the appropriate inputs were not reported in the published literature.

### ***OHTAC Recommendations<sup>3</sup>***

OHTAC made the following recommendations after considering the findings above:

- OHTAC recommends maximizing the use of pneumococcal and influenza vaccines in patients with COPD, ensuring that vaccination reflects the established guidelines and recommendations for immunization.
- OHTAC recommends that any barriers to making the pneumococcal vaccine easily available through physician offices should be removed, thereby making the pneumococcal vaccine more accessible to patients.
- Other opportunities to optimize access to influenza and pneumococcal vaccines, including patients with acute exacerbations of COPD admitted to hospital, should be explored.

### ***Conclusions: Impact on Chronic Disease Management***

In 2007, the age- and sex- standardized prevalence of COPD among Ontarians was estimated at 9.5%. Both influenza and pneumonia can lead to acute exacerbations of COPD, which are a major cause of morbidity and mortality in COPD patients. The prevention of these 2 conditions among individuals with COPD is predicted to significantly reduce acute exacerbations, as well as hospitalizations related to ARI and pneumonia.

#### ***Influenza Vaccination***

Based on high quality evidence, influenza vaccination significantly reduces the risk of acquiring influenza-related ARI in patients with COPD. No significant difference was found between the vaccination and non-vaccination groups for rates of hospitalization due to episodes of influenza-related ARI and mechanical ventilation episodes. However, this was based on low quality evidence from a single study, which did not have sufficient power for these outcomes. Although there were insufficient data to show a significant reduction in hospitalizations or mechanical ventilation episodes, this would be expected as a result of the significant reduction in ARIs subsequent to influenza vaccination.

The effectiveness of the influenza vaccination for patients with COPD is important for the management of the disease in the community. Influenza is a global threat, with 3 pandemics occurring in the 20th century and a fourth pandemic of H1N1 influenza in 2009. Complications of influenza infection include viral pneumonia, secondary bacterial pneumonia, and other secondary bacterial infections, such as bronchitis, sinusitis, and otitis media. Rates of serious illness due to influenza viruses are particularly high among older people and patients with chronic conditions such as COPD, often resulting in hospitalization and in some cases, death. Influenza infection can also lead to exacerbation of COPD or underlying heart disease.

#### ***Pneumococcal Vaccination***

Based on high quality evidence, pneumococcal vaccination significantly reduces the risk of acquiring pneumococcus pneumonia in patients with COPD, but does not significantly reduce the risk of acquiring CAP of pneumococcal or unknown etiology. However, for pneumonia of unknown etiology and pneumococcus, there were significant reductions in CAP among patients aged < 65 years, as well as among those with severe COPD. There was no statistically significant difference among study groups for total hospitalizations or LOS, but this was based on a single study with low quality evidence for these outcomes. Mortality rates were similar between individuals with and without vaccination. Although there is sparse evidence evaluating the impact of pneumococcal vaccination on hospitalizations, the observed

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<sup>3</sup> Note: These are part of a larger recommendation for COPD.

reduction in pneumococcus pneumonia would be expected to reduce overall hospitalizations among this population.

The effectiveness of the pneumococcal vaccination in preventing CAP is of importance in managing patients with COPD. The rate of pneumococcal pneumonia in developed countries remains unknown due to the lack of accurate diagnostic tests. However, in the United States Veterans' Administration Trial, among people aged 55 years and older, the incidence of pneumococcal pneumonia per 1,000 person years was 1.7 in people with no underlying disease, 3.4 in those with 1 underlying disease, and 15 in those with 3 underlying diseases. Pneumococcus bacteria can cause illnesses such as otitis media and sinusitis, and may even become more aggressive and affect other areas of the body such as the lungs, brain, joints, and bloodstream. More severe infections caused by pneumococcus include pneumonia, bacterial sepsis, meningitis, peritonitis, arthritis, osteomyelitis, and in rare cases endocarditis and pericarditis. Individuals with underlying medical conditions, including those chronic lung or heart disease, are at higher risk for acquiring pneumococcal pneumonia.

## **Smoking Cessation for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis**

### ***Background***

Airflow limitation in individuals with COPD is usually progressive and is generally associated with an abnormal inflammatory response to noxious particles or gases. Tobacco smoke is the main risk factor for COPD and COPD-associated morbidity.

Smoking cessation is the process of discontinuing the practice of inhaling a smoked substance. Smoking cessation strategies include both pharmacological and nonpharmacological (behavioural or psychosocial) approaches. The basic components of smoking cessation interventions include simple advice, written self-help materials, individual and group behavioural support, telephone quit lines, nicotine replacement therapy (NRT), and antidepressants. Smoking cessation can help to slow or halt the progression of COPD.

### ***Results***

An EBA was conducted to examine the effectiveness and cost-effectiveness of smoking cessation interventions for patients with COPD in comparison to usual care or placebo. (11)

The primary outcome of interest was abstinence from smoking. A summary of the results from the primary analysis is presented in Table 9.

Additionally, there was 1 trial with long-term follow-up, which examined mortality and lung function (using forced expiratory volume in 1 second [FEV<sub>1</sub>]). This study found that patients with COPD who were sustained quitters from smoking had a RR of mortality of 0.54 compared with those who did not quit. Quitters were also found to have improved lung function compared with non-quitters, with a difference in FEV<sub>1</sub> of 11.68 mL at 1-year follow-up and 3.33 mL at 2-year follow-up.

**Table 9: Smoking Cessation Strategies for Patients With COPD—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Disease-Specific Measures
Intervention	Comparator	Abstinence Rates RR (95% CI)
<b>Counselling</b>		
Counselling	Usual care	5.85 (3.81–8.97)
Number of studies (sample size)		2 RCTs (501)
GRADE		Moderate
<b>Subgroups by Intensity</b>		
Intensive counselling (≥ 90 minutes)	Usual care	7.70 (4.64–12.79)
Number of studies (sample size)		1 RCT (443)
GRADE		Moderate
Minimal counselling (< 90 minutes)	Usual care	1.56 (0.65–3.72)
Number of studies (sample size)		1 RCT (58)
GRADE		Moderate
<b>Counselling + NRT</b>		
Counselling + NRT	Usual care	4.28 (3.51–5.20)
Number of studies (sample size)		3 RCTs (6,342)
GRADE		Moderate
<b>Subgroups by Intensity</b>		
Intensive counselling (≥ 90 minutes) + NRT	Usual care	4.41 (3.60–5.39)
Number of studies (sample size)		1 RCT (5,887)
GRADE		Moderate
Minimal counselling (< 90 minutes) + NRT	Usual care	2.11 (0.90–4.91)
Number of studies (sample size)		2 RCTs (455)
GRADE		Moderate
Minimal counselling (< 90 minutes) + antidepressant	Usual care	1.91 (0.65–5.61)
Number of studies (sample size)		1 RCT (184)
GRADE		Low
Minimal counselling (< 90 min) + NRT + antidepressant	Usual care	2.25 (0.87–5.85)
Number of studies (sample size)		1 RCT (424)
GRADE		Low
<b>NRT</b>		
NRT	Placebo	3.01 (1.02–8.89)
Number of studies (sample size)		1 RCT (183)
GRADE		Moderate
<b>Antidepressant</b>		
Antidepressant	Placebo	2.09 (1.35–3.24)
Number of studies (sample size)		2 RCTs (596)
GRADE		Moderate
<b>Subgroups by Specific Antidepressant</b>		
Nortriptyline	Placebo	2.54 (0.87–7.44)
Number of studies (sample size)		1 RCT (100)
GRADE		Moderate
Bupropion	Placebo	2.01 (1.24–3.24)
Number of studies (sample size)		2 RCTs (496)
GRADE		Moderate

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; NRT, nicotine replacement therapy; RCT, randomized controlled trial; RR, relative risk.

### ***Economic Analysis***

An economic evaluation was conducted to assess the cost-effectiveness and health system impact of COPD treatment strategies. The cost-effectiveness of smoking cessation therapies was assessed in comparison to usual care among individuals with COPD. Costing estimates were based on expert opinion and physician billing in the 2011 Ontario Schedule of Physician Benefits. Ontario currently pays for intensive counselling via physician billing—translating to a current burden of \$8.4 (Cdn) million—and bupropion through the Ontario Drug Benefit formulary—translating to a current burden of \$1.9 (Cdn) million. The burden of NRT was projected to be \$10.4 (Cdn) million, with future expenditures of up to \$0.9 (Cdn) million in years 1 to 3 for incident cases. Results from the economic analysis are presented in Table 10.

**Table 10: Smoking Cessation Strategies for Patients With COPD—Summary of Ontario Economic Analysis<sup>a</sup>**

<b>Intervention</b>	<b>Comparator</b>	<b>ICER (Cost/QALY)</b>	<b>Budget Impact</b>
Intensive counselling	Usual care	Dominant	\$10.4 million for Ontario to fund NRT <sup>b</sup>
Intensive counselling + NRT	Placebo	Dominant	
NRT	Usual care	Dominant	
Bupropion	Placebo	Dominant	

Abbreviations: COPD, chronic obstructive pulmonary disease; ICER, incremental cost-effectiveness ratio; NRT, nicotine replacement therapy; QALY, quality-adjusted life-year.

<sup>a</sup>All costs in Canadian dollars.

<sup>b</sup>Based on an estimated 51,029 highly motivated moderate to severe COPD smokers, as estimated by a clinical expert.

### ***OHTAC Recommendations<sup>4</sup>***

OHTAC made the following recommendations after considering the findings above:

- OHTAC strongly endorses evidence-based strategies aimed at encouraging smoking cessation in patients with COPD.
- Intensive counselling ( $\geq 90$  minutes) is the most effective and cost-effective strategy, and should continue to be encouraged.
- OHTAC recommends that consideration should be made to providing training programs to health care professionals involved in providing intensive counselling.
- OHTAC recommends bupropion or nicotine replacement therapies for smoking cessation.

### ***Conclusions: Impact on Chronic Disease Management***

Based on moderate quality evidence, smoking cessation therapies have shown effectiveness in achieving prolonged abstinence from smoking in patients with COPD compared with usual care. Abstinence rates are significantly higher in patients with COPD receiving intensive counselling ( $\geq 90$  minutes) or a combination of intensive counselling and NRT. Based on limited and moderate quality evidence, abstinence rates are significantly higher in patients with COPD receiving NRT compared with placebo. As well, based on moderate quality evidence, abstinence rates are significantly higher in patients with COPD receiving the antidepressant bupropion compared to placebo. Interventions resulting in the abstinence from smoking are important for the management of COPD in the community. Prior studies have found abstinence from smoking to result in improved outcomes among individuals with COPD. One study demonstrated that the benefit to lung function gained during a smoking intervention program compared to usual care persisted for 11 years after the start of the study.

<sup>4</sup> Note: These are part of a larger recommendation for COPD.

It is estimated that 50% of older smokers develop COPD, and more than 80% of COPD-associated morbidity is attributed to tobacco smoking. According to the Canadian Community Health Survey, 38.5% of Ontarians who smoke have COPD. Despite severe symptoms—including shortness of breath, cough, and sputum production—the majority of patients with COPD are unable to quit smoking on their own. Each year only about 1% of smokers succeed in quitting on their own. Smoking cessation can help to slow or halt the progression of COPD.

An Ontario-based economic analysis found that intensive counselling ( $\geq 90$  minutes) with or without NRT was a dominant strategy (less expensive and more effective) in comparison to usual care. As well, NRT or bupropion compared to usual care or placebo were found to be dominant strategies for achieving smoking abstinence in patients with COPD. Given currently funded healthcare resources in Ontario, the budget impact to fund NRT for Ontario would be \$10.4 million (Cdn).

# **Noninvasive Positive Pressure Ventilation for Acute Respiratory Failure Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis**

## ***Background***

Respiratory failure occurs when the respiratory system cannot oxygenate the blood and/or remove carbon dioxide from the blood. It can be either acute or chronic and is classified as either hypoxemic (type I) or hypercapnic (type II). Acute hypercapnic respiratory failure frequently occurs in COPD patients experiencing acute exacerbations of COPD; it occurs due to a decrease in the drive to breathe, typically due to increased work to breathe in COPD patients.

Noninvasive positive pressure ventilation (NPPV) provides ventilatory support through a facial or nasal mask and reduces inspiratory work; it may be used intermittently for short periods of time to treat respiratory failure. Unlike more invasive forms of respiratory support, patients do not require sedation, airway defense mechanisms and swallowing functions are maintained, and trauma to the trachea and larynx are avoided. NPPV does not allow direct access to the airway to drain secretions and requires patient cooperation.

NPPV may also be used to wean patients from invasive mechanical ventilation (IMV) via the gradual removal of ventilation support until the patient can breathe spontaneously. Following extubation from IMV, acute respiratory failure may recur, leading to extubation failure and the need for reintubation. Reintubations have been associated with increased risk of nosocomial pneumonia and mortality. To avoid such complications, the use of NPPV has been proposed to help prevent acute respiratory failure recurrence and/or to treat respiratory failure when it recurs, thereby reducing the need for reintubation.

## ***Results***

An EBA was conducted to examine the effectiveness and safety of NPPV. A total of 5 comparisons were conducted, of which 2 had moderate to high quality evidence for chronic disease management. (12)

- NPPV plus usual care versus usual care alone for the treatment of acute hypercapnic respiratory failure due to exacerbations of COPD, where usual care typically consists of supplemental oxygen and a variety of medications, such as bronchodilators, corticosteroids, and antibiotics aimed to facilitate adequate oxygenation and treat the cause of the exacerbation
- NPPV compared with IMV for weaning persons with COPD from mechanical ventilation, where IMV involves sedating the patient, creating an artificial airway through endotracheal intubation, and attaching the patient to a ventilator

The outcomes of interest were mortality, intubation rates, length of hospital and intensive care unit stay, HRQOL, breathlessness, duration of mechanical ventilation, weaning failure, complications, and NPPV tolerance and compliance. A summary of the results is presented in Table 11.

Three evaluations of NPPV were not supported by the evidence:

- There was insufficient evidence to draw conclusions on the comparison of NPPV versus IMV for the treatment of acute respiratory failure among patients who have failed IMV, due to inconsistent and low to very low quality evidence.
- There was low quality evidence that showed a nonsignificant reduction in rate of reintubation for NPPV compared to usual care for the treatment of acute respiratory failure after extubation from IMV. As such, there was inadequate evidence to draw conclusions on the effectiveness of NPPV for the treatment of acute respiratory failure among these individuals.
- No evidence evaluated NPPV for the prevention of acute respiratory failure after extubation from IMV.



**Table 11: NPPV for Patients With COPD—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Mortality	Hospital Utilization, Length of Stay	HRQOL	Disease-Specific Measures				
Intervention	Comparator					Endotracheal Intubation	Duration of Mechanical Ventilation	Weaning Failure	Tolerance/Compliance	Complications
NPPV + usual care	Usual care	COPD patients with acute respiratory failure due to acute exacerbations	<i>In-hospital</i> RR 0.53 (95% CI 0.35–0.81)	WMD –2.68 days (95% CI –4.41 to –0.94)	No significant difference in quality of sleep or general well-being <sup>a</sup>	RR 0.38 (95% CI 0.28–0.50)	NA	NA	NPPV intolerance 5%–29% Compliance with NPPV decreased over time	Overall, fewer complications with NPPV (e.g., pneumonia, sepsis, GI disorders, or bleeds)
Number of studies (sample size)			9 RCTs (917)	11 RCTs (1,000)	1 RCT (60)	11 RCTs (1,000)	—	—	<i>Intolerance</i> 8 RCTs <i>Compliance</i> 2 RCTs	5 RCTs
GRADE			Moderate	Moderate	NR	Moderate	—	—	NR	Low
Weaning from IMV using NPPV	IMV	COPD patients invasively ventilated who failed T-piece weaning trials	RR 0.47 (95% CI 0.23–0.97)	<i>In ICU</i> WMD –5.21 days (95% CI –11.60 to 1.18)	Poor sleep quality in NPPV group	NA	WMD –3.55 days (95% CI –8.55 to 1.44)	Significant reduction	NR	<i>Nosocomial pneumonia</i> RR 0.14 (95% CI 0.03–0.71)
Number of studies (sample size)			2 RCTs (80)	2 RCTs (80)	1 RCT (50)	—	2 RCTs (80)	1 RCT (50)	—	2 RCTs (80)
GRADE			Moderate	Low	NR	—	Low	Moderate	—	Moderate

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; HRQOL, health-related quality of life; ICU, intensive care unit; IMV, invasive mechanical ventilation; NPPV, noninvasive positive pressure ventilation; NA, not applicable; NR, not reported; RCT, randomized controlled trial; RR, relative risk; WMD, weighted mean difference.

<sup>a</sup>Based on visual analogue scale.

## Economic Analysis

An economic evaluation was conducted to assess the cost-effectiveness and health system impact of COPD treatment strategies. Two economic evaluations were conducted for NPPV for the treatment of acute respiratory failure due to acute exacerbations of COPD:

- NPPV plus usual care versus usual care for first-line treatment
- NPPV for weaning from IMV

A cost-utility analysis using a Markov model with a lifetime horizon was conducted to estimate the ICER for each intervention. Costs for acute inpatient, day surgery, and ambulatory care cases were obtained from the Ontario Case Costing Initiative. The cost for usual medical care for a COPD hospitalization was obtained from Canadian literature. Based on average LOS reported in the trials, total costs for the hospitalization episode of each arm were calculated and cost savings were reported. Results from the cost-effectiveness model and budget impact analyses for NPPV are shown in Table 12.

**Table 12: NPPV for Patients With COPD—Summary of Ontario Economic Analysis<sup>a</sup>**

Technology Reviewed		Population	ICER (Cost/QALY)	Budget Impact Analysis
Intervention	Comparator			Cost Savings to Province From Hospital Perspective
NPPV + usual care	Usual care	COPD patients with acute respiratory failure due to acute exacerbations	Dominant	\$42 million <sup>b</sup>
Weaning from IMV using NPPV	Pressure support IMV	COPD patients invasively ventilated who fail T-piece weaning trials	Dominant	\$12 million <sup>c</sup>

Abbreviations: COPD, chronic obstructive pulmonary disease; ICER, incremental cost effectiveness ratio; IMV, invasive mechanical ventilation; NPPV, noninvasive positive pressure ventilation; QALY, quality-adjusted life-year.

<sup>a</sup>All costs in Canadian dollars.

<sup>b</sup>Based on estimated 11,163 patients who can benefit from NPPV (assuming 10%–20% of the patient population at risk is eligible for ventilation, and 50%–60% choose to be ventilated).

<sup>c</sup>Based on estimated 1,435 patients can benefit from weaning with NPPV (assuming 10%–20% of the patient population at risk is eligible for ventilation, and 50%–60% choose to be ventilated, and 15% will fail spontaneous breathing tests).

## OHTAC Recommendations<sup>5</sup>

OHTAC made the following recommendations after considering the findings above:

- OHTAC recommends the use of NPPV as an adjunct to usual medical care as a first line treatment for patients with acute respiratory failure due to acute exacerbations of COPD who do not require immediate access to IMV. NPPV should be made widely available with appropriate support systems and human resources for this indication.
- OHTAC recommends the use of NPPV to wean COPD patients who have failed spontaneous breathing tests following IMV.
- OHTAC recommends that patient preferences regarding mechanical ventilation be sought prior to acute respiratory decompensation, and should serve as a guide for the provision of this service.

<sup>5</sup> Note: These are part of a larger recommendation for COPD.

### ***Conclusions: Impact on Chronic Disease Management***

Based on moderate quality evidence, NPPV plus usual medical care significantly reduced the need for endotracheal intubation, in-hospital mortality, and the mean length of hospital stay in comparison to usual care alone. Low quality evidence also showed a lower rate of complications among individuals receiving NPPV and usual medical care. Additionally, moderate quality evidence showed that weaning from IMV using NPPV resulted in significant reductions in mortality, nosocomial pneumonia, and weaning failure compared to weaning with IMV. There was low quality evidence that weaning from IMV with NPPV resulted in a nonsignificant reduction in mean LOS and mean duration of mechanical ventilation compared to the IMV group. There was insufficient evidence to draw conclusions on the comparison of NPPV versus IMV for patients who have failed IMV. Overall, these results indicate that NPPV for the treatment of acute respiratory failure due to acute exacerbations of COPD can greatly improve the management of COPD, with a direct impact on reducing mortality and hospitalizations.

In 2007, the age- and sex- standardized prevalence of COPD among Ontarians was estimated at 9.5%. Persons with COPD typically have impaired oxygenation due to loss of alveolar volume and impaired ventilation from dead space and poor respiratory mechanics, putting them at high risk of developing respiratory failure when faced with additional pulmonary challenges such as an acute exacerbation. Acute respiratory failure develops quickly, and can lead to life-threatening changes in arterial blood gases and acid-base status.

The economic analysis found NPPV plus usual medical care to be a dominant strategy (i.e., more effective and less costly) when compared to usual medical care alone. This was reflected by clinical evidence showing significant in-hospital days avoided in individuals receiving NPPV. Assuming 10% to 20% of the COPD patient population at risk is eligible for ventilation and 50% to 60% will choose to be ventilated, this would correspond to an estimated 11,163 patients in Ontario who could benefit from NPPV. Overall, this would translate to a cost savings from the hospital perspective of \$42 million (Cdn). Weaning with NPPV was also found to be a dominant strategy compared to weaning with IMV (as reflected by reduced inpatient mortality in the study group). With 15% of patients estimated to fail spontaneous breathing tests, an estimated 1,435 patients could benefit from weaning with NPPV, translating to a cost savings from the hospital perspective of \$12 million (Cdn).

## Implantable Cardioverter Defibrillators—Prophylactic Use: An Evidence-Based Analysis

### Background

An ICD is a battery-powered device that monitors heart rhythm and can deliver an electric shock to restore normal sinus rhythm when potentially fatal arrhythmias are detected, thus preventing sudden cardiac death (SCD). Devices are implanted in the pectoral region and last from 5 to 8 years before they need to be replaced. Primary prevention of SCD with an ICD involves identification of and preventative therapy for patients who are at high risk for SCD, including individuals with ischemic heart disease, and in particular those with CHF.

### Results

An EBA was conducted to examine the effectiveness, safety, and cost-effectiveness of ICDs for the primary prevention of SCD. (13) The primary outcomes of interest were all-cause mortality, adverse effects, and HRQOL. The EBA did not report findings for adverse effects and HRQOL.

A summary of the results from the effectiveness analysis is presented in Table 13. Results were reported by individual RCT, and not combined due to differing patient populations.

**Table 13: ICDs for Prophylactic Use—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Mortality Hazard Ratio (95% CI)
Intervention	Comparator		
ICD	Conventional therapy	Ischemic cardiomyopathy, prior MI, ejection fraction $\leq 0.35$ , NSVT identified by electrophysiological screening	0.46 (0.26–0.82)
Number of studies (sample size)			1 RCT (196)
GRADE			Moderate
ICD	Conventional therapy	Ischemic cardiomyopathy, prior MI, ejection fraction $\leq 0.30$	0.69 (0.51–0.93)
Number of studies (sample size)			1 RCT (1,232)
GRADE			Low
ICD	Conventional therapy	Ischemic and nonischemic cardiomyopathy, ejection fraction $\leq 0.35$	0.77 (0.62–0.96)
Number of studies (sample size)			1 RCT (2,521)
GRADE			Moderate

Abbreviations: CI, confidence interval; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; NSVT, non-sustained ventricular tachycardia; RCT, randomized controlled trial.

## ***Economic Analysis***

### ***Cost-Effectiveness***

A literature review was conducted to identify studies that evaluated the cost-effectiveness of ICDs.

Sanders et al reviewed the cost-effectiveness of ICDs based on 8 individual trial populations. Two randomized controlled trials (RCTs) found that ICDs did not reduce risk of death, and that they were more expensive and less effective than control therapy. Six other RCTs found ICD use to add between 1.01 and 2.99 QALYs, and between \$68,300 (US) and \$101,500 (US) in comparison to controls. The cost per QALY ranged from \$34,000 (US) to \$70,200 (US) across trials. Sensitivity analyses showed that this cost-effectiveness ratio would remain below \$100,000 (US) per QALY as long as the ICD reduced mortality for 7 or more years.

Using a societal perspective and data from the RCT evaluating ischemic individuals with an ejection fraction  $\leq 0.30$ , the Blue Cross Blue Shield Technology Evaluation Centre found the ICER for ICDs relative to conventional therapy to be \$50,900 (US) per QALY.

### ***Budget Impact Analysis***

An Ontario BIA was conducted based on the study populations of the 3 major RCTs evaluated in the EBA in order to analyze options for implementing ICDs for primary prevention of SCD. Costs included in the analysis were for hospital, physician services, drugs, and downstream cost savings due to avoidance of healthcare utilization. Results from the BIA are presented in Table 14.

**Table 14: ICDs for Prophylactic Use—Summary of Ontario Budget Impact Analysis Based on Individual Trial Populations<sup>a</sup>**

Technology Reviewed		Population	Estimated Number of Individuals in Ontario	Total Cost in Ontario, \$ Millions
Intervention	Comparator			
ICD	Conventional therapy	Ischemic cardiomyopathy, prior MI, ejection fraction $\leq 0.35$ , NSVT identified by electrophysiological screening	4,740	~\$156
		Ischemic cardiomyopathy, prior MI, ejection fraction $\leq 0.30$	(> 4,740)	> \$156
		Ischemic and nonischemic cardiomyopathy, ejection fraction $\leq 0.35$	~23,700	~\$770

Abbreviations: ICD, implantable cardiac defibrillator; MI, myocardial infarction; NSVT, non-sustained ventricular tachycardia.

<sup>a</sup>All costs in Canadian dollars.

### ***OHTAC Recommendations***

OHTAC made the following recommendations after considering the findings above:

- OHTAC recommends that conditional and reviewable funding be provided for up to 1,600 ICDs per year over the next 2 years to be used in a field evaluation examining the use of ICDs for primary prevention of SCD. The field evaluation will explore/verify the wide QRS interval as a screen to risk-stratify patients with ischemic heart failure who could derive most benefit from ICDs in the primary prevention of SCD.
- OHTAC recommends that hospitals funded to provide ICD services be expected to participate in the field evaluation and to collect and report ICD data to the database.
- OHTAC recommends that eligibility criteria for patients to receive an ICD for primary prevention include only patients with an ejection fraction  $\leq 30\%$  and on optimized medical therapy.
- OHTAC recommends that the ministry support an ICD database for the purpose of monitoring utilization, patient characteristics, uptake, and long-term outcomes.
- OHTAC recommends that ICDs be inserted at advanced arrhythmia centres with the involvement of a cardiac electrophysiologist. ICD centres must insert a minimum of 100 devices annually.
- OHTAC recommends that the ministry revise the current ICD funding rate to reflect changes in practice, replacement devices and follow-up costs.
- OHTAC will appoint an expert panel to make recommendations regarding the integration of technologies to treat HF, excluding drugs.

### ***Conclusions: Impact on Chronic Disease Management***

Based on low to moderate quality evidence, ICDs were found to be effective for the primary prevention of SCD when compared to individuals receiving conventional therapy. Quality of evidence was dependent upon the individual RCT and the patient population evaluated for ICD use. The strongest evidence and greatest relative reduction in mortality (54%) was for the RCT evaluating ICD use among individuals with ischemic cardiomyopathy, prior MI, ejection fraction  $\leq 0.35$ , and non-sustained ventricular tachycardia (NSVT) by electrophysiological screening to identify high-risk patients. Overall, the clinical evidence suggested that ICDs can significantly improve the management of CAD and HF patients in the community by reducing the risk of mortality due to SCD. The risk of SCD is higher in patients with chronic HF than in any other definable subset of patients in cardiovascular medicine, with a 5-fold higher risk than in the general population.

The true mortality burden of SCD is not well established. Various sources have estimated the annual number of deaths in the United States to be between 184,000 and 462,000, accounting for a mean of 1 to 2 deaths per 1,000 adults aged over 35 years annually, and 50% of all heart-related deaths. Survival rates following an outside-of-hospital cardiac arrest in Ontario range from 0% to 11.8%. Most SCDs are caused by acute fatal arrhythmias or abnormal heart rhythms (ventricular tachycardia and ventricular fibrillation).

Although a cost-effectiveness analysis was not conducted, prior economic analyses based on the specific RCTs evaluated in the EBA found ICDs to be generally cost-effective compared to conventional treatment (\$34,000–\$70,200 [US] per QALY). An Ontario BIA showed that overall costs are highly dependent on the eligible patient population. Using a broad implementation strategy, providing ICD implantation for all individuals in Ontario with HF and left ventricular ejection fraction  $\leq 0.30$ , would cost the province as much as \$770 million (Cdn). Due to a high number needed to treat at 5 years, a high prevalent population, and a high budget impact, the overall strength of this recommendation was stated to be weak. Providing ICDs only for ischemic patients with left ventricular ejection fraction  $\leq 0.35$ , as well as screening for NSVT, was estimated to cost approximately \$156 million (Cdn), and was found to be a moderate strength recommendation when considered in conjunction with the effectiveness data. However, using a similar

base population of ischemic patients with left ventricular ejection fraction  $\leq 0.30$  and *without* the additional screening for NSVT, was found to result in greater costs and greater numbers needed to treat. Therefore, although ICDs are effective in preventing SCD, uptake and diffusion of the device for primary prevention of SCD needs to be optimized to identify those at true risk of SCD and who might benefit most to be generalizable to the Ontario prevalent population.

## **Constraint-Induced Movement Therapy for Rehabilitation of Arm Dysfunction After Stroke in Adults: An Evidence-Based Analysis**

### ***Background***

Rehabilitation interventions are the cornerstones of care and recovery after stroke. Constraint-induced movement therapy (CIMT) is a behavioural approach to neurorehabilitation. The major components of CIMT include i) intense repetitive task-oriented training of the impaired limb; ii) immobilization of the unimpaired arm; and iii) shaping. With task-oriented training, people may train the affected arm for several hours a day for up to 10 to 15 consecutive days. With immobilization, the unaffected arm may be restrained for up to 90% of waking hours. With shaping, the difficulty of training tasks is progressively increased as performance improves and encouraging feedback is provided immediately when small gains are achieved.

### ***Results***

An evidence-based analysis was conducted to examine the effectiveness and cost-effectiveness of CIMT for persons with arm dysfunction after a stroke. (14)

The primary outcome of interest was arm motor function, with secondary outcomes assessing arm motor impairment; activities of daily living based on the functional independence measure (FIM); perceived motor function (self-reported amount and quality of arm use); and HRQOL. When possible, analyses were further stratified by intensity and duration of treatment, restraint position, and time from onset of stroke. A summary of the results for the effectiveness analysis is presented in Table 15: .



**Table 15: CIMT for Stroke Rehabilitation—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Health Quality				Disease-Specific Measures	
Intervention	Comparator		HRQOL, Mean Difference in Final SIS (95% CI)	Functional Status, Mean Difference in FIM (95% CI)	Perceived Motor Function, Mean Difference in Amount of Arm Use (95% CI)	Perceived Motor Function, Mean Difference in Quality of Arm Use (95% CI)	Arm Motor Function, Mean Difference in ARAT (95% CI)	Arm Motor Impairment, Mean Difference in FMA (95% CI)
CIMT	Usual care (PT or OT)	Adults with arm dysfunction after stroke	3.9 (−5.6 to 13.5)	3.6 (−0.22 to 7.44)	1.1 (0.6–1.7)	0.97 (0.7–1.3)	13.6 (8.7–18.6)	6.5 (2.3–10.7)
Number of studies (sample size)			2 RCTs (66)	4 RCTs (128)	8 RCTs (241)	8 RCTs (241)	4 RCTs (43)	8 RCTs (169)
GRADE			Very low	Low	Low	Low	Moderate	Low
<b>Subgroup Analyses of CIMT</b>								
Program: high intensity/short duration	Usual care		NR	3.6 (−0.22 to 7.44)	0.95 (0.77–1.1)	0.84 (0.64–1.1)	13.6 (8.7–18.6)	4.1 (2.1–6.1)
Number of studies (sample size)			—	4 RCTs (128)	7 RCTs (231)	7 RCTs (231)	4 RCTs (43)	4 RCTs (126)
Program: low intensity/long duration	Usual care		NR	NR	2.4 (2.1–2.6)	1.5 (1.1–1.9)	NR	11.0 (6.3–15.7)
Number of studies (sample size)			—	—	1 RCT (10)	1 RCT (10)	—	4 RCT (57)
Restraint position: hand	Usual care		NR	NR	0.93 (0.72–1.15)	0.96 (0.7–1.2)	NR	4.1 (2.1–6.1)
Number of studies (sample size)			—	—	6 RCTs (188)	6 RCTs (188)	—	4 RCTs (126)
Restraint position: hand and arm	Usual care		NR	3.6 (−0.22 to 7.44)	1.67 (0.34–3.0)	0.98 (−0.07 to 2.0)	13.6 (8.7–18.6)	11.0 (6.3–15.7)
Number of studies (sample size)			—	4 RCTs (128)	2 RCTs (53)	2 RCTs (53)	4 RCTs (43)	4 RCTs (57)
Time from onset of stroke: 1–12 months	Usual care		NR	3.6 (−0.22 to 7.44)	1.3 (0.52–2.1)	1.0 (0.6–1.4)	13.6 (8.7–18.6)	9.5 (3.6–15.4)
Number of studies (sample size)			—	4 RCTs (128)	4 RCTs (126)	4 RCTs (126)	4 RCTs (43)	4 RCTs (44)
Time from onset of stroke: > 12 months	Usual care		NR	NR	0.90 (0.54–1.25)	0.86 (0.48–1.3)	NR	3.5 (1.1–6.0)
Number of studies (sample size)			—	—	4 RCTs (115)	4 RCTs (115)	—	3 RCTs (100)

Abbreviations: ARAT, action research arm test score; CI, confidence interval; CIMT, constraint-induced movement therapy; FIM, functional independence measure; FMA, Fugl-Meyer motor assessment; HRQOL, health-related quality of life; NR, not reported; OT, occupational therapy; PT, physiotherapy; RCT, randomized controlled trial; SIS, stroke impact scale.

## Economic Analysis

An Ontario-based cost impact analysis was developed to assess the costs associated with CIMT for rehabilitation of arm dysfunction after stroke in adults in Ontario. The costs of providing CIMT for inpatient stroke rehabilitation of arm dysfunction were based on both the duration and intensity of the program; the costs were calculated in addition to current rehabilitation care in Ontario. Table 16 shows the total costs of combining current rehabilitation care and CIMT for stroke inpatients in Ontario in fiscal year 2011.

**Table 16: CIMT for Stroke Rehabilitation—Annual Incremental Costs<sup>a</sup>**

Description	Per Patient Cost		Total CIMT-Eligible Patient Costs (\$ and FTEs)			
	Total Care Hours	Total Cost	FY 2011 (Low) <sup>a</sup> , Millions	FY 2011 (High) <sup>a</sup> , Millions	Average Annual, Millions	FTEs <sup>b</sup>
<b>2-Week CIMT Comparisons (10 Days of Care)</b>						
Ontario (current care)	5.0	\$177	\$0.06	\$0.12	\$0.09	1.5
Low-intensity CIMT (2 h/day)	25.0	\$884	\$0.31	\$0.62	\$0.46	7.6
Medium-intensity CIMT (3 h/day)	35.0	\$1,238	\$0.43	\$0.86	\$0.65	10.7
High-intensity CIMT (3.5 h/day)	40.0	\$1,415	\$0.49	\$0.99	\$0.74	12.2
<b>3-Week CIMT Comparisons (15 Days of Care)</b>						
Ontario (current care)	7.5	\$265	\$0.09	\$0.19	\$0.14	2.3
Low-intensity CIMT (2 h/day)	30.0	\$1,061	\$0.37	\$0.74	\$0.56	9.2
Medium-intensity CIMT (3 h/day)	45.0	\$1,592	\$0.56	\$1.11	\$0.83	13.7
High-intensity CIMT (3.5 h/day)	52.5	\$1,857	\$0.65	\$1.30	\$0.97	16.0

Abbreviations: CIMT, constraint-induced movement therapy; FTE, full-time equivalent; FY, fiscal year.

<sup>a</sup>All costs in Canadian dollars.

<sup>b</sup>Note: *Low* and *high* refer to cost estimations based on 349 and 698 CIMT-eligible patients, respectively; FTE represents full-time equivalent figures obtained by dividing the average annual costs by the average annual income of occupational therapists or physiotherapists.

## OHTAC Recommendations

OHTAC made the following recommendations after considering the findings above:

- CIMT shows short-term effectiveness on arm function and should be considered in the stroke rehabilitation regimen beginning no earlier than 1 month after the onset of stroke.
- Contextualization of these findings in terms of the management of stroke rehabilitation in Ontario is required.
- OHTAC supports the 2010 Institute for Clinical Evaluative Sciences *Ontario Stroke Evaluation Report* recommendations regarding access and tracking of outpatient stroke rehabilitation care in the province.

## Conclusions: Impact on Chronic Disease Management

Based on moderate quality evidence, CIMT was found to significantly improve arm motor function measured with the action research arm test compared to usual care delivered with the same intensity and duration. Significant differences were also found for arm motor impairment and perceived motor function (amount of use and quality of use). There was a nonsignificant effect found for functional status using the FIM score or HRQOL outcome measures. The nonsignificant effect found with the FIM score and the HRQOL score may be a factor of a nonresponsive outcome measure (FIM scale) and/or a type II statistical error from an inadequate sample size. The quality of evidence was low for all secondary outcome measures except HRQOL, which was very low. Overall, these findings suggest that CIMT may

be an important technology for the overall management of stroke in the community by improving arm motor function, but current evidence is not sufficient to suggest that these improvements translate to improved HRQOL or functional status.

Stroke is the leading cause of adult neurological disability in Canada, with 300,000 people or 1% of the population living with its effects. In Ontario, there were 19,395 persons with stroke (this includes intracerebral hemorrhage, ischemic stroke, subarachnoid hemorrhage, and transient ischemic attack) presenting to emergency departments in 2007/2008, with 15,514 admitted to the hospital. It is estimated that up to 85% of persons experiencing a complete stroke have residual arm dysfunction, which will interfere with their ability to live independently. Clinical experts estimated that approximately 40% of stroke inpatients would require rehabilitation for arm dysfunction and about 5% to 10% of these patients would be eligible for CIMT programs specifically. As a result, the annual volume of CIMT-eligible stroke patients in Ontario in fiscal year 2011 was estimated to be in the range of 349 to 698 patients.

Economic utility analyses estimates an average annual cost for Ontario to implement CIMT of \$0.46 million to \$0.97 million (Cdn) for 2 to 3 weeks of therapy. However, CIMT need not occur only in an inpatient setting. According to expert consultation, CIMT would be administered *after* 30 days of inpatient care. In Ontario's current care model, for the first 30 days of inpatient stroke rehabilitation, approximately 10 hours would be spent with patients. Therefore, total costs for CIMT (including current care) is estimated to range from \$0.59 million (Cdn) for a 2-week low-intensity program and an estimated 349 CIMT-eligible stroke patients to \$1.22 million (Cdn) for a 3-week high-intensity program and 698 CIMT eligible stroke patients.

## **Pressure Ulcer Prevention: An Evidence-Based Analysis**

### ***Background***

A pressure ulcer is defined as a localized injury to the skin/and or underlying tissue, occurring most often over a bony prominence and caused by pressure, shear, or friction—either alone or in combination. Those at risk for developing pressure ulcers include the elderly and critically ill, as well as persons with neurological impairments and those with conditions associated with immobility. Pressure ulcers are graded or staged along a 4-point classification system denoting severity. Stage I represents the beginnings of a pressure ulcer and stage IV consists of tissue loss with exposed bone, tendon, and/or muscle.

Numerous health technologies have been developed for the prevention of pressure ulcers, some of which are currently being used in Ontario. These technologies include various mattress types, skin cleaning procedures, and alternative care schedules for patients.

### ***Results***

An EBA was conducted to examine the effectiveness of pressure ulcer preventative interventions. (15) A total of 14 analyses were conducted as part of the EBA, of which 3 health technologies were identified as falling within the scope of this summary report:

- alternative foam mattress—a number of alternative mattresses comprised of unique foam types and densities have entered the health care market targeting the prevention of pressure ulcers
- repositioning schedule—Registered Nurses' Association of Ontario (RNAO) 2005 nursing best practice guidelines state that individuals restricted to bed be repositioned at least every 2 hours or sooner. Given advancements in high-quality foam mattresses, alternative repositioning schedules have been proposed
- dry vesico-elastic polymer pad (gel pad)—an alternative to the standard operating table mattress

The primary outcome measure in each analysis was the incidence of pressure ulcers measured as the number (proportion) of participants developing a new pressure ulcer. The effectiveness of alternative repositioning schedules and gel pads alone were based on low quality data, but were included in this review because of optimal cost-effectiveness and positive OHTAC recommendations. (19;20) A summary of the results from the effectiveness analysis is presented in Table 17.

Other interventions examined in the EBA were not included this summary report as they showed no statistically or clinically significant findings based on moderate to high quality data for at least 1 of the primary outcomes of interest. These included the following:

- alternative mattresses (air suspension bed in the intensive care unit, Micropulse System alternating mattress used intraoperatively and postoperatively, alternating pressure mattresses and alternating pressure overlays). The evidence did not support the superiority of 1 particular type of alternative foam mattress
- sheepskin (specifically Australian sheepskin)
- risk assessment and allocation of pressure-relieving equipment according to the person's level of pressure ulcer risk
- structured skin care protocols or pH-balanced cleansers among persons with urinary and/or fecal incontinence
- nutritional supplementation

**Table 17: Technologies for Pressure Ulcer Prevention—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population	Disease-Specific Measures
Intervention	Comparator		Incidence of Pressure Ulcers, RR (95% CI)
Alternative foam mattress	Standard foam mattress	Patients admitted to an acute care setting	0.31 (0.21–0.46)
Number of studies (sample size)			4 RCTs (801)
GRADE			Moderate
Repositioning every 4 hours plus a pressure redistribution mattress	Standard care (2- or 3-hour turning schedule with a standard mattress)	Patients admitted to an acute care setting	0.70 (0.52–0.93)
Number of studies (sample size)			1 RCT (187)
GRADE			Low
Dry vesico-elastic polymer pad (gel pad)	Standard operating table foam mattress	Patients in a perioperative and operative setting with surgeries of at least 90 minutes in duration	0.53 (0.33–0.85)
Number of studies (sample size)			1 RCT (416)
GRADE			Low

Abbreviations: CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.

### ***Economic Analysis***

Using the low-moderate quality effectiveness data from the EBAs, a cost-effectiveness analysis was conducted for each of the 3 health technologies evaluated for the prevention of pressure ulcers (alternative foam mattresses, alternative turning schedules, and gel pads) (Table 18). A Markov cohort model was developed to simulate the natural history of pressure ulcers. The model was structured to be consistent with the current biologic and clinical understanding of the development and management of pressure ulcers. The first economic analysis examined the use of alternative foam mattresses or alternative turning schedules for the prevention of pressure ulcers in a long-term care (LTC) setting using a lifetime horizon. The second evaluated gel-filled overlays in operating rooms for hospitalized patients undergoing planned major surgical procedures using a 1-year time horizon. Analyses were conducted from the Ontario public health system perspective.

#### ***Alternative Foam Mattresses or Alternative Turning Schedules in LTC***

On the assumption that approximately 46% of LTC facility beds in Ontario currently use alternative foam mattresses, it was assumed that approximately 48,600 cases remain at risk for pressure ulcers. Introduction of alternative foam mattresses to all Ontario LTC beds is estimated to have a 1-time cost of \$22 million (Cdn). (20) Table 18 summarizes the cost-effectiveness and health system implications of alternative foam mattress or alternative turning schedules for the prevention of pressure ulcers in LTC.

#### ***Gel Pads in Operating Rooms***

On the assumption that approximately 8% to 20% of operating room tables are currently equipped with gel-filled overlays, approximately 121,000 to 140,000 inpatient surgical cases remain at risk for pressure-ulcers intraoperatively. The implementation of gel-filled overlays to cover all remaining operating room tables in Ontario would cost approximately \$1.6 to \$1.9 million (Cdn). Table 18 summarizes the cost-

effectiveness and health system implications of alternative operating room gel-filled overlays for pressure ulcer prevention.

*Updated Economic Analysis*

Since the EBA was published, THETA has updated the economic analyses on pressure ulcer prevention in LTC facilities and in the operating room based on an updated knowledge base. The updated economic analysis for alternative foam mattresses in the LTC setting reported an estimated 1,597 facility-acquired pressure ulcer cases averted per year, saving approximately \$1.3 million (Cdn) in health care costs. (21) Similarly, the updated economic analysis evaluating gel pads in operating rooms reported 974 pressure ulcer cases prevented per year, with an estimated \$500,000 (Cdn) savings per year. (22)

**Table 18: Technologies for Pressure Ulcer Prevention—Summary of Economic Evaluation<sup>a</sup>**

Technology Reviewed		Population	ICER: Cost/QALY	Aggregated QALYs Gained	Net Pressure-Ulcer Related Healthcare Cost Savings Per Year, <sup>a</sup> Millions	Events Avoided	
Intervention	Comparator					Pressure-Ulcer Cases Averted	Reduction in Pressure Ulcer- Related Deaths
Alternative foam mattress	Standard foam mattress	Patients admitted to a LTC setting	\$6,328/QALY	173 <sup>b</sup>	\$17.3 <sup>b</sup>	2,984 <sup>b</sup>	NR
Repositioning every 4 hours plus a pressure redistribution mattress	Standard care (2- or 3-hour turning schedule with a standard mattress)	Patients admitted to a LTC setting	\$5,234/QALY (Dominant when assuming a cost saving due to reduction in personal support worker time)	192 <sup>b</sup>	\$19.7 <sup>b</sup>	3,381 <sup>b</sup>	47% over 5 years (intervention: 270 deaths estimated; control: 508 deaths projected)
Dry vesico-elastic polymer pad (gel pad)	Standard operating-table foam mattress	Patients in a perioperative and operative setting with surgical duration ≥ 90 minutes	Dominant (Mean QALY increase of 0.00003; mean cost savings of \$224)	3.8–4.4 <sup>c</sup>	\$26–\$29 <sup>c</sup>	4,233–4,868 <sup>c</sup>	No change in absolute life expectancy

Abbreviations: ICER, incremental cost-effectiveness ratio; LTC, long-term care; NR, not reported; QALY, quality-adjusted life-year.

<sup>a</sup>All costs in Canadian dollars.

<sup>b</sup>Not including 1-time implementation costs of \$22 million for alternative foam mattress and repositioning in LTC facilities, and \$2 million for gel-filled overlays in operating rooms.

<sup>c</sup>Assuming a current use of alternative foam mattresses of 46% in Ontario LTC facilities.

<sup>d</sup>Assuming a current use of gel-filled overlays of 8%–20% in Ontario operating departments.

### ***OHTAC Recommendations<sup>6</sup>***

OHTAC made the following recommendations after considering the findings above:

- For the prevention of pressure ulcers, OHTAC recommends that a high quality foam mattress be provided to all persons in an acute care setting.
- For the prevention of pressure ulcers, a high quality support surface (foam or gel) should be used during surgical procedures of greater than 90 minutes in duration. Strongest evidence exists for using a gel pad for this population.
- For the prevention of pressure ulcers, a high quality foam mattress should be provided to all residents in long-term care facilities. The Community Care Access Centre (CCAC) should use the Pressure Ulcer Risk Score (PURS) to assess a client's risk for developing a pressure ulcer.
- Where risk is identified, a high-density foam mattress should be used to prevent the development of pressure ulcers.
- There is low quality evidence to suggest that persons using a high quality foam mattress may be turned at a minimum of every 4 hours. Therefore, OHTAC recommends a field study be undertaken to determine the optimal turning schedule (2 hour versus 4 hour) for persons using a high-density foam mattress. Until better evidence is available, all healthcare facilities should follow the current RNAO 2005 nursing best practice guidelines, which state that individuals restricted to bed be repositioned at least every 2 hours or sooner if at high risk for pressure ulcers. This complies with the current Ontario long-term care home standard.

### ***Conclusion: Impact on Chronic Disease Management***

There is moderate quality evidence that an alternative foam mattress is effective in preventing the development of pressure ulcers compared with a standard hospital foam mattress. Overall, there remains a paucity of moderate or high quality evidence in the literature to also support many of the other preventative interventions, including alternative repositioning strategies and gel pad mattresses. Until better quality evidence is available, pressure ulcer preventive care must be guided by expert opinion for interventions where low or very low quality evidence supports the effectiveness of such interventions.

The prevalence of pressure ulcers at stage 1 or greater in health care settings in Ontario (2004) ranged from 13.1% to 53.3% with non-acute health care settings having the highest prevalence rate. An economic analysis model estimated lifetime probability of pressure ulcers at 49.2% and the probability of pressure ulcer-related death at 0.08%. (19;20) Pressure ulcers are treatable if found early, but left untreated they are associated with adverse health outcomes and in rare instances, can lead to fatal infections. Furthermore, pressure ulcers can delay functional recovery, impair HRQOL, and cause complications that require hospitalization and prolonged LOS.

The use of alternative foam mattresses, both with and without 4-hourly turning/repositioning, was found to be economically attractive as a preventative measure of pressure ulcers for individuals in LTC (ICERs: \$6,328 [Cdn] per QALY and \$5,234 [Cdn] per QALY, respectively). Overall, the economic evaluation found these strategies to improve the management of pressure ulcers by avoiding approximately 3,000 pressure ulcer cases and gaining nearly 200 QALYs. The implementation of alternative foam mattresses in addition to 4-hour repositioning was also predicted to decrease pressure ulcer-related deaths by 47%. After accounting for an implementation cost of nearly \$22 million (Cdn), alternative foam mattresses resulted in a total healthcare cost savings of \$17 million (Cdn) alone, or \$20 million (Cdn) with the addition of a 4-hourly turning schedule.

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<sup>6</sup>Note: These are part of a larger recommendation for the evidentiary platform for pressure ulcers.



Gel-filled overlays are currently used in 8% to 20% of operating departments in Ontario (an estimated 2,205 operating tables). The expanded use of gel-filled overlays to cover all operating tables would result in greater health benefits, with a substantial reduction in healthcare costs. Based on the economic evaluation, the implantation cost was estimated at approximately \$2 million (Cdn) and resulted in the prevention of 4,233 to 4,868 cases of pressure ulcers per year, with a corresponding gain in HRQOL. Direct healthcare costs would be reduced and result in a cost saving to hospitals' annual budgets.

## **Negative Pressure Wound Therapy: An Evidence Update**

### ***Background***

Negative pressure wound therapy (NPWT) is a procedure that uses negative pressure to create suction and drain the wound of exudates (i.e., fluid, cells, and cellular waste that has escaped from blood vessels and seeped into tissue). The procedure subsequently influences the shape and growth of the surface tissues in a way that helps healing. Negative pressure wound therapy may be used for patients with chronic and acute wounds; subacute wounds (dehisced incisions); chronic diabetes-related wounds or pressure ulcers; meshed grafts (before and after); or flaps.

### ***Results***

An EBA was conducted to assess the effectiveness of NPWT for chronic wound treatment. (16) Two separate groups were evaluated:

- patients with diabetic foot ulcer
- patients hospitalized for skin grafting

The primary outcome of interest was proportion of patients who achieved complete wound closure. Secondary outcomes included HRQOL, median time to complete wound closure, reduction in wound area, graft survival/loss, the proportion of patients with granulation tissue formation, mean time to achieve 76% to 100% granulation tissue formation, and rates of secondary amputations and adverse events. A summary of the results from the effectiveness analysis is presented in Table 19.

**Table 19: NPWT for Treatment of Chronic Wounds—Summary of Outcomes and GRADE Quality of Evidence**

Technology Reviewed		Population (Type of Wound)	Health Quality		Hospital Length of Stay Median Days (Range)	Disease Specific Measures							
Intervention	Comparator		HRQOL	Pain Scores		Complete (100%) Wound Closure		Reduction in Wound Area, cm <sup>2</sup>	Granulation Formation/ Wound Bed Preparation			Rates of Secondary Amputation	Adverse Events <sup>a</sup>
						Proportion of Patients, %	Median Time, Days		Graft Survival/Loss	% of Patients Achieving 76%–100%	Median Time to Achieve 76%–100%, days		
<b>Diabetic Foot Ulcers</b>													
NPWT	Usual care	Foot ulcer	NR	NR	NR	NPWT 43.2 Usual care 28.9 ( <i>P</i> = 0.007)	NPWT 96 (95% CI 75–114) Usual care not estimable ( <i>P</i> = 0.001)	NPWT 4.3 Usual care 2.5 ( <i>P</i> = 0.021)	NR	NPWT 70.8 Usual care 36.4 ( <i>P</i> = 0.019)	NPWT 56 Usual care 114 ( <i>P</i> = 0.022)	Significantly lower in NPWT group	Significantly higher in NPWT group
Number of studies (combined sample size)			—	—	—	1 RCT (341)	1 RCT (341)	1 RCT (341)	—	1 RCT (341)	1 RCT (341)	1 RCT (341)	1 RCT (341)
NPWT	Usual care	Foot amputation	NR	NR	NR	NPWT 56 Usual care 39 ( <i>P</i> = 0.04)	NPWT 56 (IQR 26–92) Usual care 77 (IQR 40–112) ( <i>P</i> = 0.005)	NR	NR	NR	NPWT 42 (IQR 40–56) Usual care 84 (IQR 57–112) ( <i>P</i> = 0.002)	Non-significant, fewer amputations in NPWT	No difference
Number of studies (combined sample size)			—	—	—	1 RCT (162)	1 RCT (162)	—	—	—	1 RCT (162)	1 RCT (341)	1 RCT (341)
GRADE <sup>b</sup>			—	—	—	Moderate	Moderate	—	—	—	NR	NR	NR
<b>Skin Grafting</b>													
NPWT	Usual care	Leg ulcers	Lower in NPWT group in first week ( <i>P</i> = 0.031); no difference at end of study	Lower in NPWT group in first week; no difference at end of study	Equal to complete healing time (discharge only upon complete healing)	NR	NPWT 29 (95% CI 26–33) Usual care 45 (95% CI 36–54) ( <i>P</i> = 0.0001)	NR	Graft survival (% ± SD) NPWT 83 ± 14 Usual care 70 ± 31 ( <i>P</i> = 0.011)	NR	NPWT 7 (95% CI 5.7–8.3) Usual care 17 (95% CI 10–24) ( <i>P</i> = 0.005)	None	Significantly higher in NPWT group
Number of studies (combined sample size)			1 RCT (60)	1 RCT (60)	1 RCT (60)	—	1 RCT (60)	—	1 RCT (60)	—	1 RCT (60)	1 RCT (60)	1 RCT (60)
GRADE			NR	NR	NR	—	Moderate	—	NR	—	NR	NR	NR
NPWT	Usual care	Ulcers caused by wounds	NR	NR	NPWT 13.5 (11–22) Usual care 17 (10–31) ( <i>P</i> = 0.01)	NR	NR	NR	Graft loss (%) NPWT 0 (95% CI 0–62) Usual care 12.8 (95% CI 0–75.9) ( <i>P</i> < 0.001)	NR	NR	None	NR
Number of studies (combined sample size)			—	—	1 RCT (60)	—	—	—	1 RCT (60)	—	—	1 RCT (60)	—
GRADE			—	—	NR	—	—	—	Moderate	—	—	NR	—

Abbreviations: CI, confidence interval; HRQOL, health-related quality of life; IQR, interquartile range; NPWT, negative pressure wound therapy; NR, not reported; RCT, randomized controlled trial; SD, standard deviation.

<sup>a</sup>Adverse events includes but is not limited to: wound infection, pain, osteomyelitis, staphylococcus infection, and bleeding at donor site.

<sup>b</sup>GRADE of quality of evidence was conducted for body of evidence related to NPWT among individuals with diabetic foot ulcers.

### ***Economic Analysis***

An economic analysis was not conducted for NPWT. However, other studies reported NPWT as cost saving compared to control treatment regimens. One study found the incremental cost difference of NPWT for the treatment of diabetic foot ulcers to be \$12,852 (US) based on total costs to achieve complete healing. Using an intention-to-treat sample size, the incremental cost difference was \$9,915 (US). Additionally, 1 study examined NPWT for the treatment of chronic leg ulcers. This study reported a cost savings of \$1,571 (US) for the average cost of treatment, accounting for disposables such as bandages and personnel time including nursing costs when NPWT is used in comparison to usual care.

### ***OHTAC Recommendations***

OHTAC made the following recommendations after considering the findings above:

- Negative pressure wound therapy is an effective option in the management of diabetes foot ulcers.
- Negative pressure wound therapy is an appropriate option for use following skin grafting of medium sized (around 30 cm<sup>2</sup>) vascular ulcers and burns.
- To optimize patient outcomes and safety, appropriate guidelines should be adhered to in the application of this technology.

### ***Conclusion: Impact on Chronic Disease Management***

There is moderate quality evidence that NPWT is an effective option in the management and treatment of certain chronic wounds. As a result, NPWT has been shown to decrease hospital LOS, and may lead to other downstream health care utilization savings due to faster and more complete healing.

Chronic wounds are most often found in elderly people and in people with immunological or chronic disease. They may lead to deficits in function or HRQOL, amputation, or even death. One systematic review reported that the prevalence of lower limb ulcers ranged from 0.12% to 0.32% in the general population, which translates to between 15,600 and 41,600 people in Ontario (in 2004). Among patients with diabetes, 15% are thought to have foot ulcers at some time during their lives, typically due to peripheral neuropathy and vascular disease, deformity, or infection. This equates to approximately 105,000 people in Ontario.

Negative pressure wound therapy is currently being used across many health sectors in Ontario, and is widely diffused. In 2004, there were about 380 NPWT units rented from the manufacturer in Ontario: 152 systems were rented by CCACs, 110 by LTC facilities and 103 by hospitals. NPWT is typically performed by nurses or enterostomal therapists. In 2006, it was estimated that home care agencies use 40% of NPWT systems in Ontario, followed by LTC facilities (29%) and hospitals (27%), and it is believed that estimates have not changed dramatically since that time. While an economic analysis was not conducted, reported cost savings ranged from \$1,517 to \$12,852 (US) per patient when NPWT was used compared to usual care.

## Photoselective Vaporization for the Treatment of Benign Prostatic Hyperplasia

### Background

Traditional treatment of benign prostatic hyperplasia (BPH) includes watchful waiting, pharmacotherapy, and surgical procedures. The gold standard for the surgical treatment and management of BPH is transurethral resection of the prostate (TURP), which is a slice-by-slice resection of prostatic tissue performed through the urethra. However, new options for the surgical treatment and management of BPH have become available in the last decade to reduce the morbidity associated with TURP. These options include monopolar and bipolar electrovaporization, transurethral microwave thermotherapy, transurethral needle ablation of prostate, and laser treatments such as YAG laser and potassium titanyl phosphate laser, also known as PVP.

The PVP procedure involves laser energy, which is strongly absorbed by hemoglobin and penetrates only 1 to 2 mm of tissue. Heat is thus concentrated into a small volume and prostatic tissue is ablated by rapid vaporization of cellular water instantaneously and with improved hemostasis, leaving only a 2 mm rim of coagulated tissue. One of the proposed benefits of PVP is the ability to successfully discharge patients on the day of surgery.

In 2006, OHTAC made the recommendation that a field evaluation be conducted on PVP given the uncertainty of the best technology and the likelihood of increasing diffusion of PVP. We present a summary of this field evaluation. (23)

### Results

A field evaluation was conducted by research partners at PATH, McMaster University (Hamilton, Ontario, Canada), to examine the effectiveness of PVP for BPH versus the current gold standard treatment of TURP. (17)

The primary outcomes of the analysis were change from baseline on the international prostate symptom score, urinary flow rate, post-void residual, prostate-specific antigen, sexual health inventory for men score, and HRQOL at 6 months. Other outcomes of interest included the proportion of patient admissions after the procedure and number of hospitalization days (if admitted).

Overall, there was no significant difference in the change from baseline to 6-month follow-up for the disease-specific clinical measures evaluated, with only changes in post-void residual favouring PVP ( $P = 0.018$ ). A summary of the results for hospital utilization and HRQOL at 6 months is presented in Table 20.

**Table 20: PVP Versus TURP for the Treatment of BPH—Summary of Outcomes**

Technology Reviewed		Population	Hospital Utilization		Health Quality
Intervention	Comparator		Admissions	Mean Length of Stay (SD) in days (If Admitted)	HRQOL at 6 Months
PVP	TURP	Patients with BPH requiring surgical treatment	PVP 7.1% TURP 100%	PVP 2.0 (0.5) TURP 2.5 (0.5) ( $P = 0.02$ )	No significant difference between groups ( $P = 0.13$ )

Abbreviations: BPH, benign prostatic hyperplasia; PVP, photoselective vaporization of the prostate; HRQOL, health-related quality of life; TURP, transurethral resection of the prostate.

### ***Economic Analysis***

An economic analysis was conducted to evaluate the 6-month expected costs and QALYs associated with PVP and TURP (Table 21). Total costs per case were based on hospital, physician/anaesthesiologist and device costs. (17)

A budget impact analysis was conducted from an Ontario Ministry of Health Perspective to assess the annual costs of TURP and PVP, and the difference in costs between procedures. It was assumed that 5,000 individuals underwent TURP per year, with costs associated with PVP based on a 100% substitution rate for TURP. The total number of hospital admissions and patient days were also evaluated.

**Table 21: PVP Versus TURP for Treatment of BPH—Summary of Economic Evaluation<sup>a</sup>**

Technology Reviewed		Population	Expected Direct Cost, 6 Months	Expected QALY, 6 Months	ICER: Cost/QALY	Annual Budget Impact Analysis <sup>b</sup>	Annual Impact on Hospitalizations <sup>b</sup>
Inter-vention	Com-parator						
PVP	TURP	Patients with BPH requiring surgical treatment	PVP \$3,891	PVP 0.447	PVP Dominates	PVP \$16,876,259.85	Hospital admissions 4,644
			TURP \$4,863 ( <i>P</i> < 0.001)	TURP 0.437 ( <i>P</i> = 0.508)		TURP \$22,808,250.00	
						Cost difference with PVP -\$5,931,990.15	Total bed days 11,790 Bed days per patient 2.4

Abbreviations: BPH, benign prostatic hyperplasia; ICER, incremental cost effectiveness ratio; PVP: photoselective vaporization of the prostate; TURP, transurethral resection of the prostate; QALY, quality-adjusted life-year.

<sup>a</sup>All costs in Canadian dollars.

<sup>b</sup>Assuming 5,000 TURPs per year.

### ***Conclusion: Impact on Chronic Disease Management***

Based on evidence from a field evaluation, PVP has been shown to be both safe and effective over a 6-month follow-up period for the treatment of BPH. No significant differences were found in clinical or HRQOL outcomes between PVP and TURP.

BPH is 1 of the most common conditions for which male patients seek treatment, with 40% to 50% of men having the condition by age 50 to 59 years and 80% in those over age 80 years. Without treatment, complications of BPH can include upper tract dilatation and hydronephrosis, chronic renal failure, bladder wall hypertrophy, bladder stones, bladder diverticula, and urinary infection.

The use of PVP in place of TURP for the treatment of BPH has been shown to directly improve chronic disease management. PVP has been shown to be both safe and effective based on long-term follow-up data, and results in substantially fewer hospital admissions and lower costs. Conservative estimates of PVP predict a \$6.5 million (Cdn) annual savings to the province of Ontario, with 4,600 avoided hospitalizations and 11,800 avoided hospital days each year. Additionally, given that PVP is an outpatient, noninvasive procedure it is likely to be preferred by patients; this was seen over the course of this field evaluation, which faced challenges with recruitment for the TURP arm of the trial, with patients opting for PVP as part of the informed-consent process.

## Summary of Results

A number of individual health technologies have demonstrable effectiveness and cost-effectiveness related to the management of chronic disease in the community setting. The final technologies selected for review can be categorized into 3 groups: (1) technologies related to the cure of a chronic disease; (2) technologies related to the prevention of a chronic disease; and (3) technologies related to the management of chronic disease.

Potentially of greatest clinical benefit are technologies that have been shown to be curative or preventative in nature. Bariatric surgery among morbidly obese adults with diabetes was shown to result in significant reductions in HbA1c levels, as well as the resolution of the disease itself. Similarly, ablation procedures for atrial fibrillation resulted in significant freedom from arrhythmias and improved HRQOL.

Alternative foam mattresses had evidence supporting their effectiveness in the prevention of pressure ulcers. Additionally, alternative foam mattresses plus alternative turning/repositioning schedules in LTC facilities and specialized gel pads in operating rooms had demonstrated cost-effectiveness, and even cost savings under certain circumstances. By preventing or curing these diseases, it is possible to reduce the need for long-term management by the health care system and directly prevent downstream complications.

The third category of technologies either greatly supported the management of chronic disease in the community or were associated with a reduction of hospital utilization. Primary angioplasty, or PCI, as an alternative to thrombolytic treatments for patients presenting with STEMI reduced mortality, stroke, reinfarction and severe adverse events, including major bleeding rates. Influenza and pneumococcal vaccinations resulted in significant management of COPD, as they were associated with a decrease in influenza-related ARI and pneumococcal pneumonia among COPD patients, respectively. This would be expected to reduce hospitalizations related to these events, as well as the need for mechanical ventilation. Smoking cessation strategies for smokers with COPD (consisting of at least 1 of counselling, NRT or antidepressants) demonstrated significantly improved prolonged abstinence from smoking compared with usual care or placebo. Cessation from smoking among patients with COPD has been associated with decreased mortality and improved lung function. NPPV to manage acute exacerbations in COPD was associated with a significant decrease in mortality, hospital LOS, and complications in comparison to usual care. When NPPV was used to assist in weaning patients off the more invasive IMV it resulted in a decrease in mortality, hospital LOS, weaning failure, and nosocomial pneumonia rates. ICDs have shown significant evidence in reducing overall mortality for CAD and CHF patients. CIMT for the rehabilitation of arm dysfunction after stroke resulted in improved health outcomes, including improved arm motor function and reduced arm motor impairment. As well, CIMT demonstrated further improvement in both self-reported amount and quality of arm use. NPWT was shown to be an effective option in the management and treatment of certain chronic wounds. It decreased hospital LOS and may lead to other downstream health care utilization savings due to faster and more complete healing. Finally, PVP for BPH is a noninvasive procedure that results in a decrease in hospitalizations, hospital LOS, and significant cost savings in comparison to TURP.

Findings and corresponding results of the outcomes of interest for all technologies reviewed are summarized in Table 22.

**Table 22: Summary of Results**

Disease	Health Technology	Mortality	Hospital Utilization		Health Quality	Disease-Specific Measures	Economic Evaluation <sup>a</sup>
			LOS	Hospitalizations			
<b>Technologies for the Cure of Disease</b>							
<b>Diabetes</b>	Bariatric surgery for people with diabetes and morbid obesity	—	—	—	—	Resolution of diabetes (76.8%; 95% CI 70.7–82.9) <i>GRADE: Moderate</i>  Clinically significant reduction in HbA1c (–2.7%; range –5.0 to –0.70) <i>GRADE: Moderate</i>	ICER: \$15,697/QALY <i>Complications avoided</i> Heart disease: 2,757 MI: 13,839 HF: 31,137 Stroke: 8,957 Amputation: 2,997 Blindness: 4,179 Renal failure: 17
<b>Atrial Fibrillation</b>	First-line treatment of ablation for AF of flutter (vs. drug therapy)	—	—	—	Significant improvement <i>GRADE: NR</i>	Significant freedom from arrhythmia (RR 0.24; 95% CI 0.09–0.59) <i>GRADE: Moderate</i>	Annual cost savings per patient starting from 4.5 years post-ablation forward
	Ablation for drug-refractory AF when no other heart surgery required (vs. drug therapy)	—	—	—	Significant improvement ( $P < 0.05$ ) <i>GRADE: NR</i>	Significant freedom from arrhythmia (RR 0.32; 95% CI 0.21–0.43) <i>GRADE: Moderate</i>	—
	Ablation for drug-refractory AF when additional heart surgery required (vs. heart surgery alone)	—	—	—	No difference <i>GRADE: NR</i>	Significant freedom from arrhythmia (range RR 0.13–0.53) <i>GRADE: Moderate–High</i>	—
<b>Technologies for the Prevention of Disease</b>							
<b>Chronic Wounds</b>	Alternative foam mattresses (vs. standard mattresses)	—	—	—	—	Significant prevention of pressure ulcers (RR 0.31; 95% CI 0.21–0.46) <i>GRADE: Moderate</i>	ICER: \$6,328/QALY (in LTC) Annual pressure ulcer–related cost savings: \$17.3 million Pressure ulcer cases averted: 2,984
	Repositioning every 4 hours plus a alternative foam mattress (vs. 2–3 h)	—	—	—	—	Significant prevention of pressure ulcers (RR 0.70; 95% CI 0.52–0.93) <i>GRADE: Low</i>	ICER: \$5,234/QALY (in LTC) (Dominant when also assuming a reduction in personal support worker time) Annual pressure ulcer–related cost savings: \$19.7 million Pressure ulcer cases averted: 3,381 Projected 47% reduction in pressure ulcer–related deaths over 5 years



Disease	Health Technology	Mortality	Hospital Utilization		Health Quality	Disease-Specific Measures	Economic Evaluation <sup>a</sup>
			LOS	Hospitalizations			
	Dry vesico-elastic polymer pad (gel pad) (vs. standard mattress)	—	—	—	—	Significant prevention of pressure ulcers for surgeries > 90 minutes (RR 0.53; 95% CI 0.33–0.85) <i>GRADE: Low</i>	ICER: Dominant (in operating room) Annual pressure ulcer–related cost savings: \$26 million–\$29 million Pressure ulcer cases avoided: 4,233–4,868 Projected no change in absolute life expectancy
<b>Technologies for the Management of Disease</b>							
<b>Coronary Artery Disease</b>	Primary PCI (vs. in-hospital thrombolysis)	No difference (OR 0.87; 95% CI 0.61–1.24) <i>GRADE: Moderate</i>	—	—	—	Significant reduction in composite outcome of mortality, reinfarction, and stroke (OR 0.56; 95% CI 0.42–0.75) <i>GRADE: Moderate</i>	Cost savings per capita: \$2,820–\$5,259
	Routine early PCI (vs. thrombolysis and rescue PCI as needed)	No difference (OR 0.73; 95% CI 0.47–1.14) <i>GRADE: Moderate</i>	—	—	—	Significant reduction in composite outcome of mortality, reinfarction, and stroke (OR 0.64; 95% CI 0.49–0.83) <i>GRADE: Moderate</i>	—
<b>Chronic Obstructive Pulmonary Disease</b>	Influenza vaccination <sup>b</sup> (vs. no vaccination)	—	—	No difference (RR 0.41; 95% CI 0.08–2.02) <i>GRADE: Low</i>	—	Significant reduction in ARI (RR 0.2; 95% CI 0.06–0.70) <i>GRADE: High</i> No difference in mechanical ventilation (RR 0.15; 95% CI 0.01–2.75) <i>GRADE: Low</i>	—
	Pneumococcal vaccination <sup>b</sup> (vs. no vaccination)	No difference <i>GRADE: NR</i>	No difference (P = 0.16) <i>GRADE: NR</i>	No difference (P = 0.59) <i>GRADE: Low</i>	—	Significant 1.7% reduction in pneumococcal pneumonia (P = 0.025) <i>GRADE: High</i> Significant reduction in CAP among < 65 years (RR 0.24; 95% CI 0.07–0.80) <i>GRADE: NR</i>	—
	Smoking cessation <sup>b</sup> strategies, including a combination of counselling, NRT, and antidepressants (vs. usual care or placebo)	—	—	—	—	Significant improvement in prolonged smoking abstinence (range RR 2.01–7.70, depending on intervention) <i>GRADE: Moderate</i>	ICER: Dominant for all cessation strategies modelled Budget impact for Ontario to fund NRT: \$10.4 million

Disease	Health Technology	Mortality	Hospital Utilization		Health Quality	Disease-Specific Measures	Economic Evaluation <sup>a</sup>
			LOS	Hospitalizations			
	NPPV + usual care (vs. usual care)	Significant reduction (RR 0.53; 95% CI 0.35–0.81) GRADE: Moderate	Significant reduction (WMD –2.68; 95% CI –4.41 to –0.94) GRADE: Moderate	—	No significant difference in quality of sleep and general well-being GRADE: NR	Significant reduction in endotracheal intubation (RR 0.38 (95% CI 0.28–0.50) GRADE: Moderate  Fewer complications GRADE: Low	ICER: Dominant  Cost savings to Ontario from hospital perspective: \$42 million
	Weaning from IMV using NPPV (vs. IMV)	Significant reduction (RR 0.47; 95% CI 0.23–0.97) GRADE: Moderate	No difference (WMD –5.21; 95% CI –11.60 to 1.18) GRADE: Low	—	Poor sleep quality in NPPV group GRADE: NR	No difference in duration of mechanical ventilation (WMD –3.55; 95% CI –8.55 to 1.44) GRADE: Low  Significant reduction in weaning failure GRADE: Moderate  Significant reduction in nosocomial pneumonia (RR 0.14; 95% CI 0.03–0.71) GRADE: Moderate	ICER: Dominant  Cost savings to Ontario from hospital perspective: \$12 million
<b>Congestive Heart Failure</b>	ICD (vs. conventional therapy)	Significant reduction (range HR 0.46–0.77) GRADE: Low–Moderate	—	—	—	—	ICER: \$34,000/QALY–\$70,200/QALY (US)  Total cost: \$156 million–\$770 million
<b>Stroke</b>	CIMT (vs. usual care)	—	—	—	No difference in HRQOL GRADE: Very low  No difference in functional status GRADE: Low  Significantly improved perceived arm motor function, quality of use (MD 0.97; 95% CI 0.7–1.3) and amount of use (MD 1.1; 95% CI 0.6–1.7) GRADE: Low	Significant improvement in measured arm motor function (ARAT MD 13.6; 95% CI 8.7–18.6) and decreased impairment (FMA MD 6.5; 95% CI 2.3–10.7) GRADE: Low–Moderate	Average annual implementation cost: \$0.46 million–\$0.97 million
<b>Chronic Wounds</b>	NPWT (vs. usual care)	—	Significant reduction of 3.5 days among patients with a skin graft (P = 0.01) GRADE: NR	—	First week: lower (P = 0.031) End of study: no difference GRADE: NR	Significantly greater proportion of complete wound closure (P < 0.05) GRADE: Moderate  Significantly greater graft survival (P = 0.01) and less graft loss (P < 0.001) GRADE: NR	Annual cost savings: \$1,571 (US) —\$12,852 (US), per patient

Disease	Health Technology	Mortality	Hospital Utilization		Health Quality	Disease-Specific Measures	Economic Evaluation <sup>a</sup>
			LOS	Hospitalizations			
<b>Benign Prostatic Hyperplasia</b>	PVP (vs. TURP)	—	Significant reduction (PVP 2 days, TURP 2.5 days)	Significant reduction (PVP 7.1%, TURP 100%)	No difference	No difference	ICER: dominant Annual cost savings: \$6 million Hospitalizations avoided: 4,644 hospital admissions, 11,790 bed days

Abbreviations: AF, atrial fibrillation; ARAT, action research arm test; ARI, acute respiratory illness; CAP, community-acquired pneumonia; CI, confidence interval; CIMT, constraint-induced movement therapy; COPD, chronic obstructive pulmonary disease; EBA, evidence-based analysis; FMA, Fugl-Meyer motor assessment; HR, hazard ratio; HRQOL, health-related quality of life; ICD, implantable cardioverter defibrillator; ICER, incremental cost-effectiveness ratio; IMV, invasive mechanical ventilation; LOS, length of stay; LTC, long-term care; MD, mean difference; MI, myocardial infarction; NPPV, noninvasive positive pressure ventilation; NPWT, negative pressure wound therapy; NRT, nicotine replacement therapy; OR, odds ratio; PCI, percutaneous coronary intervention; PVP, photoselective vaporization of the prostate; QALY, quality-adjusted life-year; RR, relative risk; TURP, transurethral resection of the prostate; WMD, weighted mean difference.

<sup>a</sup>All costs in Canadian dollars unless otherwise stated.

<sup>b</sup>Manages COPD by preventing potentially complex adverse events.

## **Summary of Technologies Excluded Due to No Statistically or Clinically Significant Findings**

The focus of this summary report was to identify technologies reviewed that could be leveraged to optimize chronic disease management in the community. Six EBAs related to the populations of interest were excluded from the summary due to no statistically and/or clinically significant findings or low GRADE quality of evidence for the outcomes of interest. This section summarizes these 6 technologies, as their implementation may result in unnecessary expenses absorbed by the health care system.

### **Continuous Subcutaneous Insulin Infusion Pumps for Adults With Type 2 Diabetes**

There was low quality of evidence demonstrating that the efficacy of continuous subcutaneous insulin infusion (CSII) pumps was not superior to multiple daily injections (MDIs) among adults with type 2 diabetes. (24) Additionally, there were no differences in the number of mild and severe hypoglycemic episodes when comparing CSII pumps to MDI. There were conflicting findings with respect to improved HRQOL for patients with CSII pumps, and significant limitations of the literature exist. Limitations included the fact that all studies were sponsored by insulin pump manufacturers, prior treatment regimens varied, types of insulin used varied by study (NPH versus glargine), and the generalizability of studies may not reflect the eligible patient population in Ontario, as participants were not necessarily on MDI prior to study entrance.

OHTAC did not recommend that Ontario support expanding the CSII pump program to adults with type 2 diabetes.

### **Hospital-at-Home for Acute Exacerbations Among Individuals With COPD**

There was low quality evidence showing no significant differences in hospital readmissions between individuals in the hospital-at-home and inpatient care groups. (25) However, the number of days to hospital readmission was increased in the hospital-at-home group compared with the inpatient care group. As well, there was very low quality of evidence that showed no significant difference in mortality, HRQOL, or patient caregiver satisfaction between the hospital-at-home and inpatient groups. There was also insufficient evidence to determine the impact on lung function and LOS of hospital-at-home compared with inpatient care.

There was insufficient evidence for OHTAC to make a recommendation for the strategy of hospital-at-home for the treatment of acute exacerbations.

### **Long-Term Oxygen Therapy for Individuals With COPD**

Long-term oxygen therapy (LTOT) was examined in comparison to no oxygen therapy among individuals with COPD. (26) Results were stratified among patients with severe hypoxemia ( $\text{PaO}_2 \leq 55$  mmHg) and mild to moderate hypoxemia ( $55 < \text{PaO}_2 \leq 60$  mmHg). Among patients with severe hypoxemia, there was low quality evidence that LTOT decreased all-cause mortality, but this was based on borderline statistical significance. Based on very low quality evidence, LTOT resulted in a significant improvement in  $\text{FEV}_1$ , and based on low to very low quality evidence, LTOT showed a significant improvement in HRQOL. Low quality evidence showed an increase in hospitalizations in the LTOT group compared with the no-oxygen group, but no difference in hospital LOS between the 2 groups. Among patients with mild to moderate hypoxemia, there was low quality evidence that showed no difference in mortality in the LTOT group compared with the no-oxygen group at 3 and 7 years of follow-up. Very low quality evidence showed nonsignificant improvements in % predicted  $\text{FEV}_1$ , endurance time, and dyspnea in the LTOT group compared with the no-oxygen group.

Overall, based on societal values in the decision determinants, OHTAC recommended that LTOT should continue to be provided to COPD patients with severe resting hypoxemia (<55 mm Hg).

### **Noninvasive Positive Pressure Ventilation for Chronic Respiratory Failure in COPD**

NPPV was evaluated in comparison to no ventilation plus usual care among stable persons with COPD. (12) There was moderate quality evidence showing a nonsignificant difference in mortality, lung function after 3 months, functional exercise capacity after 3 months, and hospitalizations. Additionally, there was low quality evidence supporting clinically and statistically significant improvements in functional exercise capacity for the first 3 months of treatment and a beneficial impact on dyspnea in the NPPV group compared with the usual care group. There was insufficient evidence to draw conclusions about the impact of NPPV on HRQOL.

Overall, OHTAC did not recommend the use of NPPV for chronic respiratory failure in stable COPD patients due to its lack of clinical effectiveness.

### **Enhanced External Counterpulsation**

There was insufficient evidence to support the effectiveness and safety of enhanced external counterpulsation (EECP) for the treatment of patients with refractory stable Canadian cardiovascular society classification III-IV angina or HF. (27) The overall quality of evidence was low for patients with angina and HF, as there were uncertainties due to methodological limitations in study design (study quality and directness). As well, the corresponding risk/uncertainty increased due to a budget impact of approximately \$26.6 million (Cdn) or \$166 million (Cdn), respectively, while the cost-effectiveness of EECP was unknown and difficult to estimate considering that there were no high-quality studies of effectiveness.

### **Management of Chronic Pressure Ulcers**

Numerous strategies were evaluated for the management of chronic pressure ulcers, but evidence was generally based on small RCTs with methodological flaws. (15) The type of nonsurgical debridement used did not appear to have a significant impact on the complete healing of ulcers. No significant difference in debridement abilities was detected among nonsurgical debridement agents, with 3 exceptions (papain urea was better than collagenase, calcium alginate was better than dextranomer, and addition of streptokinase/streptodornase improved the debridement ability of hydrogel). There were no significant differences among modern dressings in influencing complete healing of pressure ulcers, with 2 exceptions (hydrocolloid dressing was associated with more complete healing than saline gauze, as was hydrogel or hydropolymer when compared with hydrocolloid dressing). There was evidence that polyurethane foam dressing and hydrocellular dressing have better absorbency and less difficult removal than hydrocolloid dressings. Efficacy of topical growth factors in the treatment of pressure ulcers has not been established, and the use of platelet-derived growth factor has been associated with higher mortality from cancers. Additionally, there were no significant differences in complete healing between specialized beds and mattresses, with 3 exceptions (alternative pressure mattresses with a heel guard were superior to ones without, profiling beds were superior to flat based beds, and air-fluidized beds were associated with more improved ulcers than other low pressure beds or mattresses). Supplementation of standard hospital diet with protein, ascorbic acid (500 mg twice daily), or multivitamin supplements was associated with a significantly greater or faster reduction in the size of pressure ulcers, but did not result in a significant increase in the proportion of healed pressure ulcers. There was evidence to suggest that electrotherapy may improve healing of pressure ulcers, but no firm conclusion can be drawn. There was no evidence that other adjunctive physical therapies (electromagnetic therapy, ultrasound therapy, ultrasound therapy in conjunction with ultraviolet C light, LLL therapy, and NPWT) would improve the healing of pressure

ulcers. There was preliminary evidence that suggested multidisciplinary wound care teams may have an impact on the healing of pressure ulcers and length of hospitalization in the acute care setting, but no firm conclusion could be drawn.

OHTAC recommended that a field evaluation be undertaken to determine the effectiveness of a multidisciplinary wound care team for wound healing. It was also recommended that an expert panel review those therapies whose effectiveness is supported by low quality evidence to advise on which therapies would benefit from a field evaluation. Until better evidence is available, OHTAC recommended that all healthcare services should follow best clinical practice for the treatment of pressure ulcers.

# Conclusions

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This review highlights the important role of health technologies in improving community-based care for chronic disease. Eleven health technologies were identified with a meaningful reduction in health resource utilization. All technologies summarized in this report significantly improved patient-level outcomes and were often associated with decreased mortality and hospital utilization. Additionally, most of the technologies identified were highly cost-effective, with numerous technologies shown to be both more effective and less costly than their comparators.

Potentially of greatest clinical impact are those technologies with direct evidence for the cure or prevention of chronic disease. Technologies such as bariatric surgery for diabetes, ablation for AF, alternative mattresses for pressure wounds, and smoking cessation for COPD are associated with long-term freedom from disease, which would be expected to result in significant reductions in disease-related mortality, hospitalizations and hospital LOS.

Health technologies can provide an effective and cost-effective means to decrease burden of illness and improve patient outcomes, which would in turn reduce resource utilization intensity. As such, health technologies are a viable contributing factor to the management of chronic disease and should be considered as an integral component of community health care.

# Acknowledgements

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# Appendices

## Appendix 1: Search Strategies of Individual EBAs

A list of the databases and search dates utilized by the individual analyses that are included in this summary, further details can be accessed in each individual summary. (2)

**Table A1: Search Strategies of Individual EBAs**

Year; Volume (Number)	Title	Databases Searched	Search Dates
<b>Type 2 Diabetes</b>			
2009;9(22)	Bariatric Surgery for People with Diabetes and Morbid Obesity: An Evidence Based Analysis	OID MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, CINAHL, the Cochrane Library, INAHTA	January 1996 to December 2004
<b>Coronary Artery Disease</b>			
2010;10(17)	Primary Angioplasty and Thrombolysis for the Treatment of Acute ST-Segment Elevated Myocardial Infarction (STEMI): An Evidence Update	Update of 2004 EBA; OVID MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, Wiley Cochrane, INAHTA	Original Search: 1966 to October 2003  Updated Search: 1996 to 2009
<b>Atrial Fibrillation</b>			
2006;6(7)	Ablation for Atrial Fibrillation: An Evidence-Based Analysis	The Cochrane Library, MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, Medscape and Current Controlled Trials	1966 to March 1, 2006
<b>Chronic Obstructive Pulmonary Disease</b>			
2012;12(3)	Influenza and Pneumococcal Vaccinations for Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Review	OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, the Cochrane Library, INAHTA	January 1, 2000, to July 5, 2010
2012;12(4)	Smoking Cessation for Patients With Chronic Obstructive Pulmonary Disease: An Evidence-Based Analysis	OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, the Cochrane Library, Centre for Reviews and Dissemination	1950 to June 2010

Year; Volume (Number)	Title	Databases Searched	Search Dates
2012;12(8)	Noninvasive Positive Pressure Ventilation for Acute Respiratory Failure Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, Wiley Cochrane, INAHTA	January 1, 2004 to December 3, 2010
<b>Congestive Heart Failure</b>			
2005;5(14)	Implantable Cardioverter Defibrillators—Prophylactic Use: An Evidence-Based Analysis	Update of 2004 EBA; updated search included: Cochrane Database of Systematic Reviews, ACP Journal Club, DARE, INAHTA, EMBASE, MEDLINE, reference sections from reviews and extracted articles	January 2003 to May 2005
<b>Stroke</b>			
2011;11(6)	Constrained-Induced Movement Therapy for Rehabilitation of Arm Dysfunction After Stroke in Adults: An Evidence-Based Analysis	OVID MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, OVID EMBASE, CINAHL, the Cochrane Library, Centre for Reviews and Dissemination	January 1, 2008, to January 21, 2011
<b>Chronic Wounds</b>			
2009;9(2)	Pressure Ulcer Prevention: An Evidence-Based Analysis	OVID MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, the Cochrane Library, CINAHL	January 1, 2006, to February 14, 2010
2010;10(22)	Negative Pressure Wound Therapy: An Evidence Update	OVID MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, CINAHL, the Cochrane Library, INAHTA	January 1, 2006, to February 14, 2010
<b>Other</b>			
In Progress	PVP vs. TURP for the treatment of benign prostatic hyperplasia	This was a field evaluation; no literature search was conducted	NA

Abbreviations: EBA, evidence-based analysis; INAHTA, International Agency for Health Technology Assessment/Centre for Review and Dissemination; NA, not applicable; PVP, photoselective vaporization of the prostate; TURP, transurethral resection of the prostate.

## Appendix 2: Inclusion/Exclusion Criteria and Statistical Analyses of Individual EBAs

Table A2: Inclusion/Exclusion Criteria and Statistical Analyses of Individual EBAs

Year; Volume (Number)	Title	Inclusion Criteria	Exclusion Criteria	Statistical Analyses
<b>Diabetes</b>				
2009;9(22)	Bariatric Surgery for People with Diabetes and Morbid Obesity: An Evidence-Based Analysis	Data on the effectiveness or cost-effectiveness of bariatric surgery for the improvement of diabetes Systematic reviews, RCTs and observational controlled prospective studies that had > 100 patients Meta-analyses	Duplicate publications (superseded by another publication by the same investigator group, with the same objective and data) Non-English-language articles Non-systematic reviews, letters, and editorials Animal and in vitro studies Case reports, case series Studies that did not examine the outcomes of interest	No statistical analyses were conducted, as outcomes were based on a published meta-analysis of 134 studies and a single observational study
<b>Coronary Artery Disease</b>				
2010;10(17)	Primary Angioplasty and Thrombolysis for the Treatment of Acute ST-Segment Elevated Myocardial Infarction (STEMI): An Evidence Update	Systematic reviews of RCTs, meta-analyses of RCTs and RCTs Trial had to include, for the primary angioplasty arm, primary coronary stenting and option of using glycoprotein IIb/IIIa Thrombolysis group had to have received the accelerated regimen of alteplase in hospital and been offered rescue angioplasty Heparin and Aspirin had to have been offered to all patients and antiplatelet agents administered for at least 1 month after MI	Trials that are not consistent with practice standards in Ontario	No statistical analyses were conducted, as outcomes are summaries by RCT or systematic review

Year; Volume (Number)	Title	Inclusion Criteria	Exclusion Criteria	Statistical Analyses
<b>Atrial Fibrillation</b>				
2006;6(7)	Ablation for Atrial Fibrillation: An Evidence-Based Analysis	<p>Systematic reviews of RCTs, meta-analyses of RCTs, and RCTs</p> <p>&gt; 20 patients included in the study</p> <p>Studies reported in English</p> <p>Studies with follow-up of at least a mean of 6 months</p> <p>Studies that reported baseline characteristics of patients in treatment groups (such as age, gender, duration of symptoms, left ventricular ejection fraction, etc.)</p> <p>Studies that reported at least 1 of the aforementioned outcomes of interest</p>	<p>Studies that included pacing therapy as a part of the treatment</p> <p>Studies including patients who had previous ablation procedures</p> <p>Studies including children (patients &lt; 18 years)</p> <p>Nonhuman studies</p> <p>Studies in a language other than English</p> <p>Nonrandomized studies, prospective case series, case reports, retrospective studies, editorials, and letters</p>	No statistical analyses were conducted as outcomes are summarized by RCT or systematic review
<b>Chronic Obstructive Pulmonary Disease</b>				
2012;12(3)	Influenza and Pneumococcal Vaccinations for Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Review	<p>Studies comparing clinical efficacy of influenza vaccine or pneumococcal vaccine with no vaccine or placebo</p> <p>RCTs published between January 1, 2000, and January 31, 2011</p> <p>Studies included patients with COPD only</p> <p>Studies investigating the efficacy of the types of vaccines approved by Health Canada</p> <p>English language studies</p>	<p>Non-RCTs</p> <p>Studies investigating vaccines for other diseases</p> <p>Studies comparing different variations of vaccines</p> <p>Studies in which patients received 2 or more types of vaccines</p> <p>Studies comparing different routes of administering vaccines</p> <p>Studies not reporting clinical effectiveness of the vaccine or studies reporting immune response only</p> <p>Studies investigating the efficacy of vaccines not approved by Health Canada</p>	Results were pooled using Review Manager 5 Version 5.1. Continuous data were pooled to calculate RRs using the Mantel-Haenszel method and a random-effects model. When data could not be pooled, the results were summarized descriptively.

Year; Volume (Number)	Title	Inclusion Criteria	Exclusion Criteria	Statistical Analyses
2012;12(4)	Smoking Cessation for Patients With Chronic Obstructive Pulmonary Disease: An Evidence-Based Analysis	<p>English language, full reports from 1950 to week 3 of June 2010</p> <p>RCTs, systematic reviews and meta-analyses, or non-RCTs with controls</p> <p>A proven diagnosis of COPD</p> <p>Adult patients (<math>\geq 18</math> years)</p> <p>A smoking cessation intervention that comprised at least 1 of the treatment arms</p> <p><math>\geq 6</math> months' abstinence as an outcome</p> <p>Patients followed for <math>\geq 6</math> months</p>	<p>Case reports</p> <p>Case series</p>	<p>Due to excessive clinical heterogeneity across interventions, studies were first grouped into categories of similar interventions and then statistically pooled as appropriate. When possible, pooled estimates (RR for abstinence with 95% CI) were calculated using a fixed-effects model. Remaining studies were reported separately.</p>
2012;12(8)	Noninvasive Positive Pressure Ventilation for Acute Respiratory Failure Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	<p>English language full reports</p> <p>HTAs, systematic reviews, meta-analyses, and RCTs</p> <p>Studies performed exclusively in patients with a diagnosis of COPD or studies performed with patients with a mix of conditions if results are reported for COPD patients separately</p> <p>Patient population: (Question 1) patients with acute hypercapnic respiratory failure due to an exacerbation of COPD; (Question 2a) COPD patients being weaned from IMV; (Questions 2b and 2c) COPD patients who have been extubated from IMV</p>	<p>&lt; 18 years age</p> <p>Animal studies</p> <p>Duplicate publications</p> <p>Grey literature</p> <p>Studies examining noninvasive negative pressure ventilation</p> <p>Studies comparing modes of ventilation</p> <p>Studies comparing patient-ventilation interfaces</p> <p>Studies examining outcomes not listed below such as physiologic effects including heart rate, arterial blood gases, and blood pressure</p>	<p>When possible, results were pooled using Review Manager 5 Version 5.1; otherwise, the results were summarized descriptively. Dichotomous data were pooled into RRs using random-effects models and continuous data were pooled using weighted mean differences with a random-effects model. Analyses using data from RCTs were done using intention-to-treat protocols. <i>P</i> values &lt; 0.05 were considered significant. Post hoc sample size calculations were performed using STATA 10.1.</p> <p>A priori subgroup analyses were planned for severity of respiratory failure, location of treatment (ICU or hospital ward), and mode of ventilation with additional subgroups as needed based on the identified literature. For the severity of respiratory failure subgroups, the mean pH level was used to classify a study as mild (<math>\text{pH} \geq 7.35</math>), moderate (<math>7.30 \leq \text{pH} &lt; 7.35</math>), severe (<math>7.25 \leq \text{pH} &lt; 7.30</math>),</p>

Year; Volume (Number)	Title	Inclusion Criteria	Exclusion Criteria	Statistical Analyses
				and very severe (pH < 7.25) respiratory failure. For those studies that presented the mean pH for each study group separately, and the mean pH of the 2 arms fall into separate categories, the higher category was used.
<b>Congestive Heart Failure</b>				
2005;5(14)	Implantable Cardioverter Defibrillators— Prophylactic Use: An Evidence-Based Analysis	English-language articles (January 2003–May 2005). Journal articles that report primary data on the effectiveness or cost-effectiveness of prophylactic ICD, treatment obtained in a clinical setting, or analysis of primary data maintained in registries or databases Clearly described study design Systematic reviews, RCTs, non-RCTs, and/or cohort studies that have ≥ 20 patients, and studies on cost-effectiveness	Studies that are duplicate publications (superseded by another publication by the same investigator group, with the same objective and data) Non-English-language articles Nonsystematic reviews, letters, and editorials Animal and in vitro studies Case reports Studies that do not examine the outcomes of interest	No statistical analyses were conducted; outcomes are summarized by RCT or systematic review
<b>Stroke</b>				
2011;11(6)	Constrained-Induced Movement Therapy for Rehabilitation of Arm Dysfunction After Stroke in Adults: An Evidence-Based Analysis	Systematic reviews of RCTs with or without meta-analysis Study participants 18 years of age and older with arm dysfunction after stroke Studies comparing the use of CIMT with occupational therapy and/or physiotherapy rehabilitative care (usual care) to improve arm function Studies which described CIMT as having the following 3 components: i) restraining unimpaired arm and/or wrist with a sling, hand splint or cast; ii) intensive training with functional task practice of the affected arm; and iii) application of shaping methodology during training	Narrative reviews, case series, case reports, controlled clinical trials Letters to the editor Grey literature Non-English-language publications	Where appropriate, a meta-analysis was undertaken to determine the pooled-estimate of effect of CIMT compared with usual care for explicit outcomes using Review Manager 5 version 5.0.25. Mean difference was used as the pooled summary estimate for continuous data where the outcome among pooled studies was measured by the same scale. The degree of statistical heterogeneity among studies was assessed by the I <sup>2</sup> -statistic for each outcome. A fixed or random effects model was used. An I <sup>2</sup> > 50% was considered as substantial

Year; Volume (Number)	Title	Inclusion Criteria	Exclusion Criteria	Statistical Analyses
		<p>No restriction was placed on intensity or duration of treatment otherwise</p> <p>Duration and intensity of therapy equal in treatment and control groups</p> <p>Therapy beginning a minimum of 1 month after stroke</p> <p>Published 2008 to 2011</p>		heterogeneity, for which a subgroup analysis was undertaken
<b>Chronic Wounds</b>				
2009;9(2)	Pressure Ulcer Prevention: An Evidence-Based Analysis	<p>English-language systematic reviews and RCTs that meet the following description: Patients: in any setting, with 1 or more pressure ulcers; Interventions: nondrug and nonsurgical treatments for pressure ulcers, including local wound therapy, adjunctive physical therapies, pressure relieving support surfaces, nutrition therapy, and multidisciplinary wound care teams; Comparison: an intervention versus a placebo, a sham treatment or another intervention; Outcome of interest: proportion of ulcers that healed completely (closed), percent change in surface area/volume, rate of change in surface area, mean time to achieve complete healing, change in the amount of exudate, granulation, PSST score, PUSH score, treatment-related adverse events, and absorbency and ease of removal</p> <p>Clinical controlled trials or other observational studies if RCTs are not available</p> <p>Sample ≥10 ulcers</p>	<p>Studies on acute wounds or chronic wounds other than pressure ulcers</p> <p>Studies with only subjective outcomes</p> <p>Nonsystematic reviews or case reports (except where indicated)</p> <p>Opinion articles or letters to the editor that provided no primary data</p> <p>Studies for which results have already been reported or for which a more current update is available</p> <p>Full text articles in a language other than English</p> <p>Studies on surgical reconstruction of pressure ulcers</p>	The individual study results were not amenable to meta-analysis because of different study designs and outcome measures used

Year; Volume (Number)	Title	Inclusion Criteria	Exclusion Criteria	Statistical Analyses
2010;10(22)	Negative Pressure Wound Therapy: An Evidence Update	RCTs published between 2000 and 2010 Sample size $\geq 30$ Inclusion of homogenous type of wounds Commercially marketed NPWT systems Human subjects English language	Non-RCTs Sample size $<30$ Studies included a variety of wound types Studies used home-made negative pressure systems Studies included patients with abdominal wall loss Studies on open fractures/high-energy trauma Studies on wounds at the donor site of the graft	No statistical analyses were conducted; outcomes were summarized by RCT or systematic review
<b>Other</b>				
In Progress	PVP versus TURP for benign prostatic hyperplasia	This was a field evaluation; no literature review was conducted	—	—

Abbreviations: CI, confidence interval; CIMT, constraint-induced movement therapy; COPD, chronic obstructive pulmonary disease; EBA, evidence-based analysis; HTA, health technology assessment; ICD, implantable cardioverter defibrillator; ICU, intensive care unit; IMV, invasive mechanical ventilation; MI, myocardial infarction; NPPV, noninvasive positive pressure ventilation; NPWT, negative pressure wound therapy; PVP, photoselective vaporization of the prostate; RCT, randomized controlled trial; RR, relative risk; STEMI, ST-segment elevation myocardial infarction; TURP, transurethral resection of the prostate.



## Appendix 3: Excluded EBAs

Excluded EBAs conducted between 2006 and 2011 that were related to 1 of the disease areas of interest but did not meet other inclusion criteria.

**Table A3: Excluded EBAs**

Year; Volume (Number)	Title	Reason for Exclusion
<b>Type 2 Diabetes</b>		
2011;11(4)	Continuous Glucose Monitoring for Patients With Diabetes: An Evidence-Based Analysis ( <i>type 1 diabetes</i> )	The patient population falls beyond the scope of the summary review
2009;9(13)	Optical Coherence Tomography For Age-Related Macular Degeneration And Diabetic Macular Edema: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2009;9(20)	Continuous Subcutaneous Insulin Infusion (CSII) Pumps For Type 1 And Type 2 Adult Diabetic Populations: An Evidence-Based Analysis	No statistical and/or clinically significant results supporting the technology were found for the population of interest
2009;9(21)	Behavioural Interventions for Type 2 Diabetes: An Evidence-Based Analysis	The EBA falls under the scope of 1 of the major drivers of the larger mega-analysis
2009;9(23)	Community-Based Care for the Management of Type 2 Diabetes: An Evidence-Based Analysis	The EBA falls under the scope of 1 of the major drivers of the larger mega-analysis
2009;9(24)	Home Telemonitoring for Type 2 Diabetes: An Evidence-Based Analysis	The technology falls beyond the scope of the summary review
<b>Coronary Artery Disease</b>		
2010;10(7)	Non-Invasive Cardiac Imaging Technologies for the Diagnosis of Coronary Artery Disease: A Summary of Evidence-Based Analyses	Technologies for screening purposes are beyond the scope of the summary review
2010;10(8)	Single Photon Emission Computed Tomography for the Diagnosis of Coronary Artery Disease: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2010;10(9)	Stress Echocardiography for the Diagnosis of Coronary Artery Disease: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2010;10(10)	Stress Echocardiography With Contrast for the Diagnosis of Coronary Artery Disease: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2010;10(11)	64-Slice Computed Tomographic Angiography for the Diagnosis of Intermediate Risk Coronary Artery Disease: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2010;10(12)	Cardiac Magnetic Resonance Imaging for the Diagnosis of Coronary Artery Disease: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2010;10(13)	Use of Contrast Agents With Echocardiography in Patients With Suboptimal Echocardiography: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review

<b>Year; Volume (Number)</b>	<b>Title</b>	<b>Reason for Exclusion</b>
2006;6(12)	Intravascular Ultrasound to Guide Percutaneous Coronary Interventions: An Evidence-Based Analysis	Technology not related to outcomes associated with larger mega-analysis
<b>Atrial Fibrillation</b>		
2006;6(8)	Advanced Electrophysiologic Mapping Systems: An Evidence-Based Analysis	Technology not related to outcomes associated with larger mega-analysis
<b>Chronic Obstructive Pulmonary Disease</b>		
2012;12(5)	Community-Based Multidisciplinary Care for Patients With Stable Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	The EBA falls under the scope of 1 of the major drivers of the larger mega-analysis
2012;12(6)	Pulmonary Rehabilitation for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	The EBA falls under the scope of 1 of the major drivers of the larger mega-analysis
2012;12(7)	Long-Term Oxygen Therapy for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	No statistical and/or clinically significant results supporting the technology were found for the population of interest
2012;12(9)	Noninvasive Positive Pressure Ventilation for Chronic Respiratory Failure Patients With Stable Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	No statistical and/or clinically significant results supporting the technology were found for the population of interest
2012;12(10)	Hospital-at-Home Programs for Patients With Acute Exacerbations of Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	No statistical and/or clinically significant results supporting the technology were found for the population of interest
2012;12(11)	Home Telehealth for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis	The technology falls beyond the scope of the summary review
<b>Congestive Heart Failure</b>		
2010;10(15)	Magnetic Resonance Imaging (MRI) for the Assessment of Myocardial Viability: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2010;10(16)	Positron Emission Tomography for the Assessment of Myocardial Viability: An Evidence-Based Analysis	Technologies for screening purposes are beyond the scope of the summary review
2006;6(5)	Enhanced External Counterpulsation (EECP): An Evidence-Based Analysis	No statistical and/or clinically significant results supporting the technology were found for the population of interest
<b>Stroke</b>		
No technologies related to stroke were excluded		
<b>Chronic Wounds</b>		
2009;9(3)	Management of Chronic Pressure Ulcers: An Evidence-Based Analysis	No statistical and/or clinically significant results supporting the technology were found for the population of interest

Year; Volume (Number)	Title	Reason for Exclusion
<b>Other</b>		
2009;9(12)	Point-of-Care International Normalized Ratio (INR) Monitoring Devices for Patients on Long-Term Oral Anticoagulation Therapy: An Evidence-Based Analysis	The technology falls beyond the scope of the summary review
2009;9(17)	Community-Based Care for the Specialized Management of Heart Failure: An Evidence-Based Analysis	The EBA falls under the scope of 1 of the major drivers of the larger mega-analysis
2009;9(17)	Community-Based Care for Chronic Wound Management: An Evidence-Based Analysis	The EBA falls under the scope of 1 of the major drivers of the larger mega-analysis

Abbreviations: EBA, evidence-based analysis.

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