Quality-Based Procedures: Clinical Handbook for **Chronic Obstructive Pulmonary Disease (Acute and Postacute)**

Health Quality Ontario &
Ministry of Health and Long-Term Care

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(This handbook includes, in its acute phase, an update of the Clinical Handbook for Chronic Obstructive Pulmonary Disease, published in April 2013.)

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

About Health Quality Ontario

Health Quality Ontario 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. Health Quality Ontario 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 Health Quality Ontario and its partners, the Ontario Health Technology Advisory Committee (OHTAC)—a standing advisory subcommittee of the Health Quality Ontario 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.

Rapid reviews, evidence-based analyses and their corresponding OHTAC recommendations, and other associated reports are published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About the Quality-Based Procedures Clinical Handbooks

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding initiative, Health Quality Ontario works with multidisciplinary expert advisory panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Disclaimer

The content in this document has been developed through collaborative efforts between the Ministry of Health and Long-Term Care, the Evidence Development and Standards branch at Health Quality Ontario, and the expert advisory panels on COPD. The template for the Quality-Based Procedures Clinical Handbook and all content in the "Purpose" and "Introduction to Quality-Based Procedures" sections were provided in standard form by the Ministry. All other content was developed by HQO with input from the expert advisory panels. As it is based in part on rapid reviews and expert opinion, this handbook may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its reports. In addition, it is possible that other relevant scientific findings may have been reported since completion of the handbook and/or rapid reviews. This report is current to the date of the literature search specified in the Research Methods section of each rapid review. This handbook may be superseded by an updated publication on the same topic. A list of all HQO's Quality-Based Procedures Clinical Handbooks is available at: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/clinical-handbooks.

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List of Abbreviations

AGREE	Appraisal of Guidelines for Research & Evaluation
ARF	Acute respiratory failure
BODE	A COPD index using body mass index, airflow obstruction, dyspnea, and exercise capacity
CAT	COPD Assessment Test
CIHI	Canadian Institute for Health Information
COPD	Chronic obstructive pulmonary disease
CTS	Canadian Thoracic Society
ECFAA	Excellent Care for All Act
ED	Emergency department
Expert advisory panels	Expert Advisory Panel on Episodes of Care for Acute COPD Expert Advisory Panel on Episodes of Care for Post-Acute Community-Based Care for COPD Patients
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HIG	Health-based allocation model inpatient group
HQO	Health Quality Ontario
HSFR	Health system funding reform
ICD-10-CA	International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canadian Edition
ICES	Institute for Clinical Evaluative Sciences
LACE	A COPD index using length of stay, acuity of admission, comorbidity, and emergency department visits
LHIN	Local health integration network
LOS	Length of stay
MMRC	Modified Medical Research Council dyspnea scale
MRDx	Most responsible diagnosis
NICE	National Institute for Health and Care Excellence[1]
NRT	Nicotine replacement therapy
OHTAC	Ontario Health Technology Advisory Committee
PBF	Patient-based funding
PCP	Primary care provider

[1] Prior to 2013, NICE was known as the National Institute for Health and Clinical Excellence. In this handbook, we cite NICE evidence from 2010 and use the name in effect at that time.

PR	Pulmonary rehabilitation
QBP	Quality-based procedure

Preface

This document has been developed through collaborative efforts between the Ministry of Health and Long-Term Care, Health Quality Ontario (HQO), and the HQO Expert Advisory Panels on the Continuum of Care for COPD (the "expert advisory panels").

The content in the following "Purpose" and "Introduction" sections were provided in standard form by the ministry. All other content was developed by HQO with input from the expert advisory panel.

The content of this Clinical Handbook was developed to conform with the specific deliverables agreed upon by the ministry and HQO.

In the area of quality-based procedures, HQO will:

1. Take a provincial leadership role in knowledge translation related to QBP work.

2. Include in their analyses consultations with clinicians and scientists who have knowledge and expertise in identified priority areas, either by convening a reference group or engaging an existing resource of clinicians/scientists.

3. Work with the reference group to:
    a. Define the population/patient cohorts for analysis and refine inclusion and exclusion criteria for the QBP, using data to review utilization and length of stay trends.
    b. Develop clinical best practices for defined QBP including transition to the community.
    c. Seek consensus on a set of evidence-based clinical pathways and standards of care for each episode of care.

4. Submit to the ministry within the deadlines set by the Agreement, a draft report and clinical handbook, including:
    a. A summary of HQO's clinical engagement process.
    b. Guidance on the real-world implementation of the recommended practices contained in the Clinical Handbook, with a focus on implications for multi-disciplinary teams, service capacity planning considerations and new data collection requirements.

The ministry also asked HQO to make recommendations on performance indicators aligned with the recommended episodes of care, in order to inform the ministry's Quality-Based Procedure (QBP) Integrated Scorecard and to provide guidance on the real-world implementation of the recommended practices contained in the Clinical Handbook. The ministry asked that recommendations focus on implications for multi-disciplinary teams, service capacity planning considerations, and new data collection requirements.

Key Principles

Discussions between HQO, the expert advisory panels, and the ministry established a set of key principles or "ground rules" to guide this evolving work:

- **The handbook analysis does not involve costing or pricing.** All costing and pricing work related to the QBP funding methodology will be completed by the ministry using a

standardized approach, informed by the content produced by HQO. This principle also extends to the deliberations of the expert advisory panels, where discussions are steered away from considering the dollar cost of particular interventions or models of care and instead focused on quality considerations and non-cost measures of utilization, such as length of stay (LOS).

- **The scope of this work includes both hospital care and postacute, community-based care.** Recognizing the importance of this issue, the ministry has communicated that conditions analysed will span all parts of the continuum of care.
- **Recommended practices, supporting evidence, and policy applications will be reviewed and updated at least every 2 years.** The limited 4-month time frame provided for the completion of this work meant that many of the recommended practices in this document could not be assessed with the full rigour and depth of HQO's established evidence-based analysis process. Recognizing this limitation, HQO reserves the right to revisit the recommended practices and supporting evidence at a later date by conducting a full evidence-based analysis or to update this document with relevant newly published research. In cases where the episode-of-care models are updated, any policy applications informed by the models should also be similarly updated.
  Consistent with this principle, the ministry has stated that the QBP models will be reviewed at least every 2 years.
- **Recommended practices should reflect the best patient care possible, regardless of cost or barriers to access.** HQO and the expert advisory panels are instructed to focus on defining best practice for an *ideal* episode of care, regardless of cost implications or potential barriers to access. Hence, the resulting cost implications of the recommended episodes of care are not known. However, all expert advisory panels have discussed a number of barriers that will challenge implementation of their recommendations across the province. These include gaps in measurement capabilities for tracking many of the recommended practices, shortages in health human resources, and limitations in the continuum of care capacity across many parts of the province.

  Some of these barriers and challenges are briefly addressed in the section "Implementation of Best Practices." However, with the limited time available to address these issues, the considerations outlined here should only be viewed as an initial starting point towards a comprehensive analysis of these challenges.

Finally, HQO and the expert advisory panels recognize that, given the limitations of their mandate, the ultimate effect of the analysis and advice in this document will depend on how the ministry incorporates it into the QBP policy and funding methodology. This work will be complex, and it will be imperative to ensure that any new funding mechanisms are well-aligned with the recommendations of the expert advisory panels.

In addition to aiding decisions regarding funding methodology, recommended practices can also provide the basis for broader provincial standards of care for COPD patients. These standards could be linked not only to funding mechanisms, but to other health system change levers such as guidelines and care pathways, performance measurement and reporting, program planning, and quality improvement.

Purpose

Provided by the Ministry of Health and Long-Term Care

This Clinical handbook has been created to serve as a compendium of the evidence-based rationale and clinical consensus driving the development of the policy framework and implementation approach for Chronic Obstructive Pulmonary Disease.

This document has been prepared for informational purposes only. It does not mandate health care providers to provide services in accordance with the recommendations included herein. The recommendations included in this document are not intended to take the place of the professional skill and judgment of health care providers.

Introduction to Quality-Based Procedures

Provided by the Ministry of Health and Long-Term Care

The Ministry of Health and Long-Term Care (ministry) established Health System Funding Reform (HSFR) in Ontario in 2012 with a goal to develop and implement a strategic funding system that promotes the delivery of quality health care services across the continuum of care and is driven by evidence and efficiency. HSFR is based on the key principles of quality, sustainability, access, and integration, and aligns with the four core principles of the *Excellent Care for All Act* (ECFAA):

- Care is organized around the person to support their health;
- Quality and its continuous improvement is a critical goal across the health system;
- Quality of care is supported by the best evidence and standards of care; and
- Payment, policy, and planning support quality and efficient use of resources.

Since its inception in April 2012, the ministry has shifted much of Ontario's health care system funding away from the its current global funding allocation (currently representing a large proportion of funding) toward a funding model that is founded on payments for health care based on best clinical evidence-informed practices. HSFR comprises two key components:

- Organizational-level funding, which will be allocated as base funding using the Health-Based Allocation Model (HBAM); and
- Quality-Based Procedure (QBP) funding, which will be allocated for targeted activities based on a "(price x volume) + quality" approach premised on evidence-based practices and clinical and administrative data.

"Money Follows the Patient"

Prior to the introduction of HSFR, a significant proportion of hospital funding was allocated using a global funding approach, with specific funding for select provincial programs, wait times services, and other targeted activities. However, a global funding approach may not account for complexity in patients, service levels, and costs, and it may reduce incentives to adopt clinical best practices that result in improved patient outcomes in a cost-effective manner. These variations in patient care evident in the global funding approach warranted a move toward a system in which "the money follows the patient."

Under HSFR, provider funding is based on the types and quantities of patients providers treated, the services they delivered, the quality of care delivered, and patient experiences/outcomes. Specifically, QBPs incent give health care providers an incentive to become more efficient and effective in their patient management by accepting and adopting clinical best practices that ensure Ontarians get the right care, at the right time and in the right place.

QBPs were initially implemented in the acute care sector, but as implementation evolves, they are being expanded across the continuum of care, including the community home care sector, to address the varying needs of different patient populations.

Internationally, similar models have been implemented since 1983. Ontario is one of the last leading jurisdictions to move down this path, but this positions the province uniquely to learn from international best practices and pitfalls to create a sustainable, efficient, and effective funding model that is best suited for the province and the people of Ontario.

What Are Quality-Based Procedures?

QBPs are clusters of patients with clinically related diagnoses or treatments who have been identified using an evidence-based framework as providing an opportunity for process improvements, clinical redesign, improved patient outcomes, enhanced patient experience, and potential health system cost savings.

Initially developed in the acute (hospital) sector, QBPs were defined as "procedures." However, implementation has evolved since the introduction of QBPs in 2012, and the approach has as well. Currently, the expanded focus is on care provided in other parts of the health care sector, and on a more functional/programmatic/population-based approach. As a result, the definition of QBPs is expanding to include quality-based procedures, programs, and populations.

QBPs have been selected using an evidence-based framework. The framework uses data from various sources such as, but not limited to: the Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS), adapted by the ministry for its HBAM repository. The HBAM Inpatient Grouper (HIG) groups inpatients based on the diagnosis or treatment responsible for the majority of their patient stay. Additional data have been used from the Ontario Case Costing Initiative (OCCI) and the Ontario Cost Distribution Methodology (OCDM). Evidence published in literature from Canada and international jurisdictions, as well as in World Health Organization reports, has also assisted with the definition of patient clusters and the assessment of potential opportunities (e.g., reducing variation, improving patient outcomes, sustainability).

The evidence-based framework assesses patients using five perspectives, as presented in Figure 1. This evidence-based framework has identified QBPs with the potential to improve quality of care, standardize care delivery across the province, and show increased cost-efficiency.

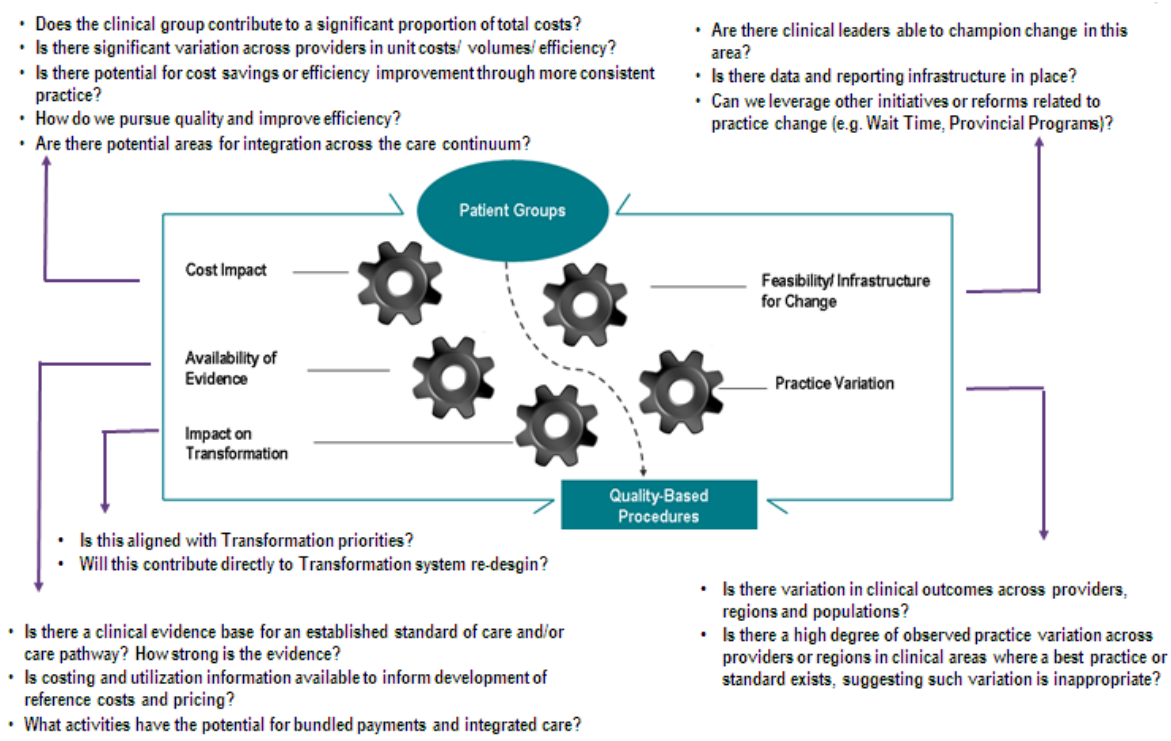


Figure 1: Evidence-Based Framework

Practice Variation

Practice variation is the cornerstone of the QBP evidence-based framework. A demonstrated large practice or outcome variance across providers or regions in clinical areas, where a best practice or standard exists, represents a significant opportunity to improve patient outcomes by focusing on the delivery of standardized, evidence-informed practices. A large number of "beyond expected length of stay" and a large standard deviation for length of stay and costs have been flags to such variation.

Availability of Evidence

A significant amount of research has been conducted and collected, both nationally and internationally, to help develop and guide clinical practice. Working with clinical experts, best practice guidelines and clinical pathways can be developed for QBPs and establish appropriate evidence-informed indicators. These indicators can be used to measure the quality of care and help identify areas for improvement at the provider level, and to monitor and evaluate the impact of QBP implementation.

Feasibility/Infrastructure for Change

Clinical leaders play an integral role in this process. Their knowledge of the identified patient populations and the care currently provided and/or required for these patients represents an invaluable element in the assessment of much needed clinical delivery and clinical process improvements. Many groups of clinicians have already developed care pathways to create evidence-informed practice. There is now an opportunity for this knowledge to be transferred provincially.

Cost Impact

The provincial footprint from a financial perspective also impacts the selection of the QBP. This may include QBPs that are high-volume and low-cost, as well as those that are low-volume and high-cost (i.e., specialized procedures that demonstrate an opportunity for improvement).

A selected QBP should have, as a guide, no fewer than 1,000 cases per year in Ontario and represent at least 1% of the provincial direct cost budget. For patient cohorts that fall below these thresholds, the resource requirements to implement a QBP can be restrictive. Even where the patient cohorts represent an opportunity for improvement, it may not be feasible to create a QBP, even if there are some cost efficiencies.

Impact on Transformation

The *Action Plan for Health Care* was launched in January 2012 and is already making a difference to Ontarians and the Ontario health care system:

- We have bent the cost curve since 2011/2012;
- We are improving the health of Ontarians;
- We are enhancing the experience of Ontarians when they use the health care system; and
- We are working with our health sector partners to improve the quality of health care.

The next phase of transformation will build on and deepen implementation of the action plan. HSFR is a key element of the health system transformation agenda because it ensures sustainability and quality.

Selected QBPs should, where possible, align with the government's transformational priorities. In addition, the impact on the transformation of certain patient populations not previously prioritized by the framework can be included as QBPs. This will ensure that QBPs are wide ranging in their scope (e.g., paediatric patient populations or patients requiring community care). QBPs with a lower cost impact but a higher impact on the provincial health care system may still be a high priority for creation and implementation.

How Will QBPs Encourage the Delivery of High-Quality, Evidence-Based Care and Innovation in Health Care Delivery?

The QBP methodology is driven by clinical evidence and best practice recommendations from expert advisory panels. Expert advisory panels comprise a cross-sectoral, multi-geographic, and multidisciplinary membership, including representation from patients. Members leverage their clinical experience and knowledge to define patient populations and recommend best practices.

Once defined, best practice recommendations are used to understand the required resource utilization for QBPs and will further assist in the development of evidence-informed prices. The development of evidence-informed pricing for the QBPs is intended to give health care providers an incentive to adopt best practices in their care delivery models, maximize their efficiency and effectiveness, and engage in process improvements and/or clinical redesign to improve patient outcomes.

Best practice development for QBPs is intended to promote the standardization of care by reducing inappropriate or unexplained variation and ensuring that patients get the right care at the right place and at the right time. Best practice standards will encourage health service providers to ensure that appropriate resources are focused on the most clinically effective and cost-effective approaches.

QBPs create opportunities for health system transformation where evidence-informed prices can be used as a financial lever to incent providers to:

- adopt best practice standards
- re-engineer their clinical processes to improve patient outcomes
- improve coding and costing practices
- develop innovative care delivery models to enhance the experience of patients

An integral part of the enhanced focus on quality patient care is the development of indicators to allow for the evaluation and monitoring of actual practice and support ongoing quality improvement.

In addition, the introduction of additional QBPs—such as outpatient and community-based QBPs—will further help integrate care across sectors and encourage evidence-based care across the health care continuum.

Methods

Overview of Episode-of-Care Analysis Approach

To produce this work, Health Quality Ontario has developed a novel method known as an *episode-of-care analysis* that draws conceptually and methodologically from several of HQO's core areas of expertise:

- **Evidence-based analyses**: Recommended practices incorporate components of HQO's evidence-based analysis method and draw from the recommendations of the Ontario Health Technology Advisory Committee (OHTAC).
- **Case-mix grouping and funding methodology:** Cohort and patient group definitions use clinical input to adapt and refine case-mix methods from the Canadian Institute for Health Information (CIHI) and the Ontario Health-Based Allocation Model (HBAM).
- **Clinical practice guidelines and pathways:** Recommended practices synthesize guidance from credible national and international bodies, with attention to the strength of evidence supporting each guideline.
- **Analysis of empirical data:** expert advisory panels' recommendations were supposed by descriptive and multivariable analysis of Ontario administrative data (e.g., Discharge Abstract Database and National Ambulatory Care Reporting System) and data from disease-based clinical data sets (e.g., the Ontario Stroke Audit and Enhanced Feedback for Effective Cardiac Treatment databases). Health Quality Ontario works with researchers and ministry analysts to develop analyses for the expert advisory panels' review.
- **Clinical engagement**: All aspects of this work were guided and informed by leading clinicians, scientists, and administrators with a wealth of knowledge and expertise in the clinical area of focus.
- **Performance indicators**: Health Quality Ontario has been asked to leverage its expertise in performance indicators and public reporting to support the development of measurement frameworks to manage and track actual performance against recommended practices in the episodes of care.

Phases of Development

This full continuum of the episode of care was developed in 3 phases:

Phase 1: developed the Acute Episode of Care (1)
Phase 2: developed the Postacute (or "Community") Episode of Care
Phase 3: updated the Acute Episode of Care and integrated with the Postacute Episode of Care for one coherent continuum of care

Each phase had their own unique leadership, expert panel membership (see Acknowledgements), and stakeholders engaged. All individuals involved in all phases were aware of the previous work done and built on prior efforts to ensure consistency and flow between the phases. In 2012, the first expert advisory panel was created to develop the Acute Episode of Care. Stemming from the work of this Acute Episode of Care, another expert advisory panel was convened in fall 2013 to develop a Postacute Episode of Care. Finally, in summer 2014 the Acute Episode of Care was updated and at the same time integrated with the Postacute Episode of Care to create one coherent continuum of care (Update and Integration COPD Expert Advisory Panel).

The development of the episode-of-care analysis involves the following key steps:

1. **Defining the cohort and patient stratification approach**
2. **Defining the scope of the episode of care**
3. **Developing the episode-of-care model**
4. **Identifying recommended practices, including the Rapid Review process**
5. **Supporting the development of performance indicators to measure the episode of care**

The following sections describe each of these steps in further detail.

Defining the Cohort and Patient Stratification Approach

At the outset of this project, the Ministry of Health and Long-Term Care provided HQO with a broad description of each assigned clinical population (e.g., "stroke"), and asked HQO to work with the expert advisory panels to define inclusion and exclusion criteria for the cohort they would examine using data from routinely reported provincial administrative databases. Each of these populations might encompass multiple distinct subpopulations (referred to as "patient groups") with varying clinical characteristics. For example, the congestive heart failure population includes subpopulations with heart failure, myocarditis, and cardiomyopathies. These patient groups have very different levels of severity, different treatments, and different distributions of expected resource use. Consequently, these groups could need different funding policies.

Conceptually, the process employed here for defining cohorts and patient groups shares many similarities with methods used around the world for the development of case-mix methodologies, such as Diagnosis-Related Groups or CIHI's Case Mix Groups. Case-mix methodologies have been used since the late 1970s to classify patients by similarities in clinical characteristics and in resource use for the purposes of payment, budgeting, and performance measurement (1). Typically, these groups are developed using statistical methods such as classification and regression tree analysis to cluster patients with similar diagnoses, procedures, age, and other variables. After the initial statistical criteria have been established, clinicians are often engaged to ensure that the groups are clinically meaningful. Patient groups are merged, split, and otherwise reconfigured until the grouping algorithm reaches a satisfactory compromise between cost prediction, clinical relevance, and usability. Most modern case-mix methodologies and payment systems also include a final layer of patient complexity factors that modify the resource weight (or price) assigned to each group upward or downward. These can include comorbidity, use of selected interventions, long- or short-stay status, and social factors.

In contrast with these established methods for developing case-mix systems, the approach the ministry asked HQO and the expert advisory panels to undertake is unusual in that patient classification *begins* with the input of clinicians rather than with statistical analysis of resource use. The expert advisory panels were explicitly instructed not to focus on cost considerations, but instead to rely on their clinical knowledge of patient characteristics that are commonly associated with differences in indicated treatments and expected resource use. Expert advisory panel discussions were also informed by summaries of relevant literature and descriptive tables containing Ontario administrative data.

On the basis of this information, the expert advisory panels recommended a set of inclusion and exclusion criteria to define each disease cohort. Starting with identifying the *International*

Classification of Diseases, 10th Revision (Canadian Edition) (ICD-10-CA) diagnosis codes included for the population, the expert advisory panels then excluded diagnoses with treatment protocols that would differ substantially from those of the general population, including pediatric cases and patients with very rare disorders. Next, the expert advisory panels recommended definitions for major patient groups within the cohort. Finally, the expert advisory panels identified patient characteristics that they believe would contribute to additional resource use for patients within each group. This process generated a list of factors ranging from commonly occurring comorbidities to social characteristics, such as housing status.

In completing the process described above, the expert advisory panel encountered some noteworthy challenges:

- **Absence of clinical data elements capturing important patient complexity factors:** the expert advisory panels quickly discovered that several important patient-based factors related to the severity of patients' conditions or to expected resource use are not routinely collected in Ontario hospital administrative data. These include both key clinical measures (such as ratio of forced expiratory volume in 1 second to forced vital capacity for chronic obstructive pulmonary disease [COPD] patients and AlphaFIM®[2] scores for stroke patients) and important social characteristics (such as caregiver status).[3] For stroke and congestive heart disease, some of these key clinical variables have been collected in the past through the Ontario Stroke Audit and Enhanced Feedback for Effective Cardiac Treatment data sets, respectively. However, these data sets were limited to a group of participating hospitals and at this time are not funded for future data collection.
- **Limited focus on a single disease or procedure grouping within a broader case-mix system:** while the expert advisory panels were asked to recommend inclusion and exclusion criteria for only specified populations, the patient populations assigned to HQO are a small subset of the many patient groups under consideration for Quality-Based Procedures (QBPs). Defining population cohorts introduced some additional complications; after the expert advisory panels had recommended their initial definitions (based largely on diagnosis), the ministry informed the expert advisory panels that several other patient groups that were planned for future QBP funding efforts overlapped with the cohort definitions.

  For example, while nearly all patients discharged from hospital with a most responsible diagnosis (MRDx) of COPD receive largely ward-based medical care, a few patients diagnosed with COPD receive much more costly interventions, such as lung transplants or resections. On the basis of this substantially different use of resources, the ministry's HBAM algorithm assigns these patients to a group different from the general COPD population. Given this methodologic challenge, the ministry requested that the initial cohorts defined by the expert advisory panels be modified to exclude patients that receive selected major interventions. These patients are likely to be assigned to other QBP patient groups in the future. This document presents both the initial cohort definition defined by the expert advisory panel and the modified definition recommended by the ministry.

[2] The Functional Independence Measure (FIM) is a composite measure consisting of 18 items assessing 6 areas of function. These fall into 2 basic domains; physical (13 items) and cognitive (5 items). Each item is scored on a 7-point Likert scale indicative of the amount of assistance required to perform each item (1 = total assistance, 7 = total independence). A simple summed score of 18–126 is obtained where 18 represents complete dependence / total assistance and 126 represents complete independence.
[3] For a comprehensive discussion of important data elements for capturing various patient risk factors, see Iezzoni LI (Editor. (2)

In short, the final cohorts and patient groups described here should be viewed as a compromise based on currently available data and the parameters of the ministry's HBAM grouping.

Defining the Scope of the Episode of Care

Health Quality Ontario's episode-of-care analysis draws on a conceptual theory from the emerging worldwide use of episode-based approaches for performance measurement and payment. Averill et al (2), Hussey et al (3), and Rosen and Borzecki (4) describe the key parameters required for defining an appropriate episode of care:

- **Index event:** The event or time point triggering the start of the episode. Examples of index events include admission for a particular intervention, presentation at the emergency department (ED), or diagnosis of a particular condition.
- **Endpoint:** The event or time point triggering the end of the episode. Examples of endpoints include death, 30 days after hospital discharge, or a "clean period" with no relevant health care service use for a defined window of time.
- **Scope of services included:** Although an "ideal" episode of care might capture all health and social care interventions received by the patient from index event to endpoint, in reality not all these services may be relevant to the objectives of the analysis. Hence, the episode could exclude some types of services such as prescription drugs or services tied to other unrelated conditions.

Ideally, the parameters of an episode of care are defined on the basis of the nature of the disease or health problem studied and the intended applications of the episode (e.g., performance measurement, planning, or payment). For HQO's initial work here, many key parameters were set in advance by the ministry in the government's QBP policy parameters. For example, in fiscal year 2013/2014 the QBPs will focus on reimbursing acute care and will not include payments for physicians or other non-hospital providers. These policy parameters limited flexibility to examine non-hospital elements, such as community-based care or readmissions.

Developing the Episode-of-Care Pathway Model

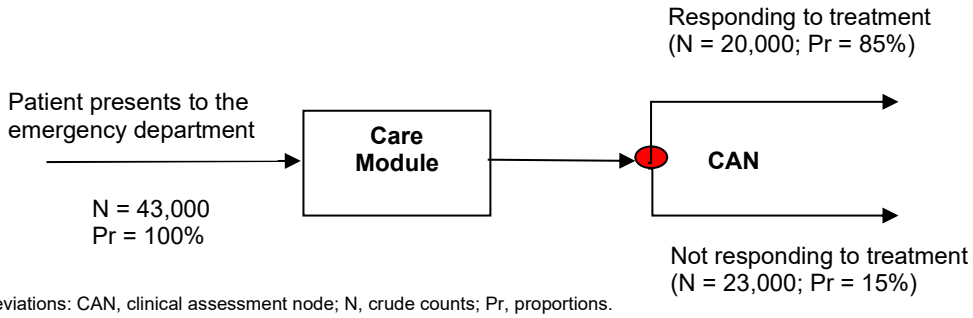
Health Quality Ontario has developed a model that brings together key components of the episode-of-care analysis through an integrated schematic. The model is structured around the parameters defined for the episode of care, including boundaries set by the index event and endpoints, segmentation (or stratification) of patients into the defined patient groups, and relevant services included in the episode. The model describes the pathway of each patient case included in the defined cohort, from initial presentation through segmentation into one of the defined patient groups on the basis of their characteristics, and finally through the subsequent components of care that patients receive across the continuum of care.

Although the model bears some resemblance to a clinical pathway, it is not intended to be used as a traditional operational pathway for implementation in a particular setting. Rather, the model presents the critical decision points (clinical assessment nodes [CANs]) and phases of treatment (care modules) within the episode of care. Clinical assessment nodes provide patient-specific criteria for whether a particular case proceeds down one branch of the pathway or another. Once a particular branch is determined, a set of recommended practices are clustered together as a care module. Care modules represent the major phases of care that patients receive across the continuum of care. The

process for identifying the recommended practices within each CAN and care module is described in the next section.

Drawing from the concepts of decision analytic modelling, the episode-of-care model includes crude counts and proportions of cases proceeding down each branch of the pathway model. For the COPD Clinical Handbook, these counts were determined on the basis of utilization data from administrative databases including the Discharge Abstract Database and NACRS. These counts are based on current Ontario practice and are not intended to represent normative or ideal practice. For some clinical populations, evidence-informed targets have been set at certain CANs for the proportions of cases that should ideally proceed down each branch.

Figure 2 provides an example of a care module and CAN.



Abbreviations: CAN, clinical assessment node; N, crude counts; Pr, proportions.

Figure 2: Episode of Care Model

Identifying Recommended Practices

Consideration of Evidence Sources

Several evidence sources were considered and presented to the expert advisory panel to develop the episode-of-care model and populate individual modules with best practice recommendations. Preference was given to OHTAC recommendations. Where OHTAC recommendations did not exist, additional evidence sources were sought including guidelines from other evidence-based organizations, HQO rapid reviews, empirical analysis of Ontario data, and, where necessary and appropriate, expert consensus.

OHTAC Recommendations

The OHTAC recommendations are considered the criterion standard of evidence for several reasons:

- **Consistency:** While many guidance bodies issue disease-specific recommendations, OHTAC provides a common evidence framework across all the clinical areas analyzed in all disease areas.
- **Economic modelling:** OHTAC recommendations are often supported by economic modelling to determine the cost-effectiveness of an intervention, whereas many guidance bodies assess only effectiveness.
- **Decision-Making Framework:** OHTAC recommendations are guided by a decision determinants framework that considers the clinical benefit offered by a health intervention, in

addition to value for money; societal and ethical considerations; and economic and organizational feasibility.

- **Context:** In contrast with recommendations and analyses from international bodies, OHTAC recommendations are developed specifically for Ontario. This ensures that the evidence is relevant to the Ontario health system.

Clinical Guidelines

Published Canadian and international guidelines that encompass the entirety of the COPD continuum of care were searched with guidance from HQO medical librarians. Additionally, the expert advisory panels were further consulted to ensure all relevant guidelines were identified.

The methodological rigour and transparency of clinical practice guidelines were evaluated by use of the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument. (5) AGREE II comprises 23 items organized into 6 quality domains—scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence. (5) The AGREE II domain scores provide information about the relative quality of the guideline. A score of 1 indicates an absence of information or poor reporting; a score of 7 indicates exceptional reporting that meets all criteria. Guidelines were selected for inclusion on the basis of individual AGREE scores, with an emphasis on the rigour of development score, which reflects the methods used to assess the quality of evidence supporting the recommendations. The final selection of guidelines included a minimum of 1 contextually relevant guideline (i.e., a Canadian guideline) and 3 to 4 highest quality guidelines, when available for each phase of the episode of care.

The contextually relevant, or Canadian, guideline served as the baseline and was directly compared with the other included guidelines. The quality of the evidence supporting each recommendation, as assessed and reported by the published guidelines, was identified, and inconsistencies and gaps between recommendations were noted for further evaluation.

Rapid Reviews

Where there was inconsistency between guidelines, disagreement among expert advisory panel members, or uncertainty about evidence, an HQO evidence review was considered. Recognizing that a full evidence-based analysis would be impractical for all topics, a rapid review of evidence was used to identify the best evidence within the compressed timeframe of developing the entire episode-of-care pathway. Where a rapid review was deemed insufficient or inappropriate to answer the research question, a full evidence-based analysis was considered.

Analysis of Administrative and Clinical Data

In addition to evidence reviews of the published literature, the expert advisory panels also examined the results of descriptive and multivariable regression analysis using Ontario administrative and clinical data sets. Analyses modeling such patient characteristics as age, diagnoses, and procedures were developed for their association with such outcomes of interest as LOS, resource use, and mortality. Dependent (outcome) and independent variables for analysis were identified by expert advisory panel members on the basis of their clinical experience and their review of summaries of the literature evaluating the association between patient characteristics and a range of outcomes. The expert advisory panels also provided advice on the analytical methods used, including data sets included and the most functional forms of the variables.

Other analyses reviewed included studies of current utilization patterns, such as average hospital LOS and regional variation across Ontario in admission practices and hospital discharge settings.

Expert Consensus

The expert advisory panels assessed the best evidence for the Ontario health care system to arrive at the best practice recommendations (see Recommended Practices). Where the available evidence was limited or nonexistent, recommendations were made on the basis of consensus agreement by the expert advisory panels.

Description of Chronic Obstructive Pulmonary Disease

The following is an excerpt from the 2012 Chronic Obstructive Pulmonary Disease (COPD) Evidentiary Framework *by the OHTAC COPD Collaborative. (6)*

Background

COPD is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response by the lungs to noxious particles or gases. The airflow limitation is caused by small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), both of which contribute to the disease to varying degrees, depending on the person. Chronic inflammation causes structural changes in the lungs and narrowing of the small airways. Inflammatory processes also cause destruction of the lung parenchyma, which leads to the loss of alveolar attachments to the small airways and decreases lung elastic recoil. These changes diminish the ability of the airways to remain open during expiration.

The most common symptoms of COPD include chronic and progressive breathlessness, cough, sputum production, wheezing, and chest congestion. In addition to the airflow restriction and changes to the lung, COPD is associated with systemic effects and comorbidities. Systemic effects include weight loss, nutritional abnormalities and malnutrition, and skeletal muscle dysfunction. Common comorbidities are ischemic heart disease, osteoporosis, respiratory infection, bone fractures, depression and anxiety, diabetes, sleep disorders, anemia, glaucoma, cataracts, and cancer.

Natural History of COPD

COPD is a progressive disease. The rate of progression varies and may occur over several years or several decades, depending on factors such as continued exposure to noxious particles (e.g., tobacco smoke). There are several systems for classifying the severity of COPD; one of the most widely used is the Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging criteria, which are based on postbronchodilator spirometry (forced expiratory volume in 1 second [FEV_1]). In the GOLD system there are 4 stages, which range from mild to very severe (Table 1).

Table 1: GOLD Staging Criteria for COPD

Stage	Severity	FEV_1/FVC	FEV_1	Symptoms
I	Mild	< 0.70	≥ 80% predicted	Symptoms may or may not be present Possible symptoms include chronic cough and sputum production
II	Moderate	< 0.70	50%–80% predicted	Shortness of breath on exertion Cough and sputum production are sometimes present
III	Severe	< 0.70	30%–50% predicted	Greater shortness of breath, reduced exercise capacity, fatigue, and repeated exacerbations
IV	Very severe	< 0.70	< 30% predicted	Respiratory failure, which may also lead to cor pulmonale

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease.
Source: Global Initiative for Chronic Obstructive Lung Disease, 2010. (7)

The disease course varies, but typically patients fluctuate between stable disease and acute exacerbations, which become more common as the disease progresses. Acute exacerbations are periods when symptoms worsen. There is debate about the best definition for exacerbations; a consensus definition developed by GOLD defines an acute exacerbation as "an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD." (7) Patients may also experience a variety of other symptoms, such as worsening exercise tolerance, fatigue, malaise, and decreased oxygen saturation. After an acute exacerbation, the individual may not recover to his/her previous level of airflow limitation, and this permanent loss of lung function contributes to the progressive nature of the disease.

Two-thirds of exacerbations are caused by either an infection of the tracheobronchial tree or air pollution, but the cause is unknown in the remaining cases. Risk factors for exacerbations include disease severity, winter months, and a previous exacerbation in the past 8 weeks. The frequency of exacerbations varies by disease severity. Using data from 3 European studies (the Inhaled Steroids in Obstructive Lung Disease in Europe [ISOLDE] study, the European Respiratory Society Study on Chronic Obstructive Pulmonary Disease [EUROSCOP], and the Copenhagen City Lung Study [CCLS]), Donaldson and Wedzicha found that patients with severe disease (GOLD stage III) experienced an average of 3.43 exacerbations per year, while patients with moderate disease (GOLD stage II) experienced an average of 2.68 exacerbations per year. (8)

Epidemiology of COPD

Prevalence

Estimates of COPD prevalence vary depending on the methods and diagnostic criteria used to identify cases. Many of the prevalence estimates are also believed to be underestimates due to underdiagnosis and underrecognition of COPD and to limited diagnoses of mild cases, as individuals often do not require health care services until they reach the moderate to severe stages of the disease.

Based on the Canadian Community Health Survey, in 2007 about 4.4% of Canadians self-reported that they had been diagnosed with COPD by physicians. (9) Based on Ontario administrative data sets, Gershon et al (10) estimated the 2007 age- and sex-standardized prevalence of COPD in Ontario to be 9.5%. (10) The prevalence of COPD has increased over time; Gershon et al (10) found a 23% increase in the prevalence rate between 1996 and 2007 (1996, 7.8%; 2007, 9.5%), (10) and this corresponds to an increase of 64.8% in the number of adults with COPD. The aging population alone does not entirely account for this increase. (10)

Incidence

Based on Ontario administrative data sets, the 2007 age- and sex-standardized incidence of COPD in Ontario was 8.5 cases per 1,000 adults. (10) Gershon et al (10) showed that the incidence rate has been declining since 1996, when it was 11.8 cases per 1,000 adults. (10) The age-standardized incidence rate is higher in males than in females (9.4 cases per 1,000 adults vs. 7.8 cases per 1,000 adults, respectively); however, the incidence rate has been declining faster in males than females (% decline since 1996, 32.3% vs. 24.7%, respectively). (10)

Risk Factors for COPD

The most common risk factor for COPD—and the primary cause of COPD in 80% to 90% of cases—is exposure to tobacco smoke. (9) There are numerous other risk factors, however, including exposure to occupational dusts and chemicals (e.g., vapours, irritants, fumes), indoor air pollution (e.g., from burning biomass fuels for heating and cooking in confined spaces in developing countries), outdoor air pollution, genetics, lung growth and development, oxidative stress, respiratory infections and previous tuberculosis, and asthma. The quality and strength of evidence supporting these risk factors vary, with the strongest evidence being for tobacco smoke, occupational exposures, indoor air pollution, and $alpha_1$-antitrypsin deficiencies.

Diagnosis of COPD

The GOLD guidelines recommend that any individual with breathlessness, chronic cough, or sputum production—especially those with risk factors (such as cigarette smokers)—be evaluated for COPD. Spirometry, the best standardized, objective measurement for airflow limitation, should be used to confirm all COPD diagnoses. Spirometry (a type of pulmonary function test) includes the forced vital capacity (FVC, volume of air forcibly exhaled from the point of maximal inspiration) and the FEV_1 (volume of air exhaled during the first second of the FVC measurement). During a test, patients' reference values are based on age, height, sex, and race; spirometry results are presented as a percentage of the predicted value.

Apart from spirometry, other tests may be conducted to help assess severity of disease and provide additional information necessary for treatment. These tests include bronchodilator reversibility testing, chest x-ray, and arterial blood gas measurements.

Both over- and underdiagnosis of COPD are possible issues. Overdiagnosis can occur when the diagnosis is based solely upon an individual's medical history and physical examination and is not confirmed by spirometry. Underdiagnosis can occur due to underrecognition of COPD by both clinicians and patients.

Management of COPD

COPD management and treatment is a staged process depending on the severity of the disease, with new treatments/management strategies introduced as needed. It begins with avoiding risk factors (e.g., through smoking cessation, vaccinations) and, as the disease progresses, introducing additional treatments and medications (e.g., drug therapy, pulmonary rehabilitation, oxygen therapy).

Impact of COPD

First and foremost, COPD has a considerable impact on the person with the disease. This impact varies and is influenced not just by the degree of airflow limitation, but also by the severity of symptoms, including breathlessness, decreased exercise capacity, systemic effects, and comorbidities. These symptoms can have a substantial impact on people living with the disease: based on the 1998/1999 National Population Health Survey, 51% of Canadians with COPD reported that their disease restricted their activity at home, at work, or in other activities. (11)

In addition, people with moderate to severe COPD typically experience 1 or more acute exacerbations per year. These exacerbations impact health-related quality of life and lung function; may require hospitalization and invasive treatment such as invasive mechanical ventilation; and increase the risk of mortality. COPD is the fourth leading cause of death in Canada and is expected to be the third leading cause of death by 2020. The 2007 age- and sex-standardized mortality rate in Ontario was 4.3%, which translates to 32,156 deaths. (10)

Apart from its impact on individual patients, COPD has a substantial effect on the health system. COPD is a leading cause of health care utilization, both globally and in Canada. In 1997, COPD was the fourth most common cause of hospitalization among Canadian men and the sixth most common among Canadian women. The age- and sex-standardized average hospitalization rate from 1996 to 1999 was 632 hospitalizations per 100,000 adults in Ontario. (11)

Furthermore, acute exacerbations of COPD are a leading cause of emergency department visits and hospitalizations, particularly in the winter. The economic burden of COPD is high. The Canadian component of a large-scale international survey, Confronting COPD in North America and Europe, showed an annual direct cost of almost $2,000 (Cdn) per patient for COPD-related primary and secondary care visits, treatment, and laboratory tests. (12)

Recommended COPD Cohort Definition and Patient Stratification Approach

Notes on Updates to COPD Cohort Definition

In 2013, the initial COPD Episode of Care Expert Advisory Panel recommended a quality-based-procedure (QBP) cohort definition consisting of inclusion and exclusion criteria based on patient characteristics recorded at a patient's initial presentation to hospital. The expert panel recommended that the scope of activity included and funded under the COPD cohort include the emergency department (ED) visit, inpatient admission (if the patient is admitted), and any subsequent postacute care.

The Ministry of Health and Long-Term Care modified the initial panel's COPD cohort definition for use in the QBP funding methodology. The original definition included cases discharged from the emergency department (i.e., without an inpatient admission) and cases assigned a preadmit comorbidity diagnosis of COPD, even if the most responsible diagnosis is not COPD. In contrast, the ministry's QBP funding approach for COPD does not include these cases. The Update and Integration COPD Expert Advisory Panel understands the challenges faced by the ministry in implementing the recommended cohort definition in the context of a case-mix funding system, where there may be overlap with populations funded through other QBPs. However, after considering the cohort definition for this update of the COPD handbook, the panel recommends the ministry address 2 major problem areas associated with the current QBP funding definition:

- **The COPD QBP should include funding for COPD-related emergency department and outpatient activity.**

  The expert panel strongly recommends that the ministry provide QBP funding to hospitals not only for admitted COPD cases but also for cases that can be successfully treated and discharged from the ED. Including only admitted COPD cases under the COPD QBP funding model may financially penalize hospitals able to implement best practices for treating and discharging patients without requiring an inpatient admission.

  Therefore, consistent with the cohort definition recommended in the 2013 Clinical Handbook for COPD, the ministry should amend its QBP funding definition to include ED discharges as part of the COPD cohort criteria. QBP funding should also be expanded to include COPD-related outpatient activity, such as rapid access clinics for COPD, which some hospitals have implemented to prevent admissions, as well as pulmonary rehabilitation clinics, which patients access in the postacute phase of care.

  Virtually no patient-level data on COPD-related outpatient clinic services are currently collected or reported in Ontario. The ministry should adopt this as a priority area for new data collection, starting with the collection of activity data from outpatient pulmonary rehabilitation clinics.

- **The COPD QBP should include funding for cases assigned a most responsible diagnosis of acute respiratory failure if they also have a COPD comorbidity diagnosis (Type 1, W, X or Y).**

While the expert panel understands the challenges, from a case-mix classification perspective, created by this broader recommended cohort definition, the narrower definition adopted by the ministry for QBP funding excludes patients who have underlying COPD but are assigned a most responsible diagnosis of acute respiratory failure (ARF) by the hospital. These are typically patients who present to hospital in severe respiratory distress as a result of their COPD. According to CIHI coding standards, such cases should be assigned a most responsible diagnosis of ARF with a preadmit comorbidity diagnosis of COPD.

The expert panel reviewed data suggesting wide variation among Toronto-area hospitals in the proportion of patients coded to COPD versus ARF diagnoses. The panel noted that hospitals that tend to code a higher proportion of cases as COPD would be financially advantaged, while those that (appropriately) code a higher proportion of cases as ARF would conversely be financially penalized, particularly if their percentage of ARF cases has increased since their original QBP funding "carve-out."[4]

Therefore, the expert panel recommends that the ministry amend its COPD QBP definition to include cases with a most responsible diagnosis of ARF if they also have a COPD comorbidity diagnosis recorded as either a Type 1, W, X or Y diagnosis type.

COPD Cohort Inclusion/Exclusion Criteria

The expert panels recommend the following age range, diagnostic codes, and diagnosis types to define the COPD population for this episode-of-care analysis:

- **Age:** Persons aged 35 years and older.

  *Rationale***:** The 35-year age threshold is used in the COPD cohort definition adopted for use by the Institute for Clinical Evaluative Sciences (ICES) (13) and a wide range of COPD-related studies. COPD is a progressive disease that generally manifests itself after a person is exposed to risks for a number of years. Few people younger than 35 years are diagnosed with COPD (only 67 cases were admitted to acute inpatient care in Ontario in 2010/2011) and their disease most likely results from congenital factors. The care pathways and treatment protocols for these younger patients are likely to be substantially different from the vast majority of COPD patients and are not practical to consider within the same episode-of-care analysis.

- **Diagnosis codes:** ICD-10-CA codes J41-J44, with the exception of panlobular emphysema (J43.1), centrilobular emphysema (J43.2), and Macleod syndrome (J43.0).

  Rationale: The diagnoses included in the ICES COPD cohort (ICD-10-CA codes J41-J44) (13) have been adopted for this handbook, with the exception of 3 very rare, low volume diagnoses (each were the most responsible diagnosis for only 1 inpatient acute admission in Ontario in 2010/2011); these rare diagnoses have significantly different care pathways than the general

[4]Carve-out is the ministry term for the baseline global budget funding reduction that is applied to each hospital when a new QBP funding model is introduced. The funding subtracted from the hospital through the carve-out is based on the estimated costs of historical volumes in that QBP population. The hospital is then reimbursed for that population moving forward using the QBP pricing model.

COPD population, and the expert panel did not consider them as practical to attempt to address them in their work.

It should also be noted that 2 diagnosis codes included in the HIG and Case Mix Groups+ (CMG+) methodologies are not included in this cohort definition: bronchitis, not specified as acute or chronic (J40) and chronic respiratory conditions due to chemicals, gases, fumes, and vapours (J68.4). These diagnoses are seldom found in COPD cohorts in the literature and the expert panel did not regard these cases as part of the general COPD population.

- **Diagnosis types**

Acute inpatient cases: Patients with any of the included diagnosis codes (specified above) present as one of the following diagnosis types:

- **Most responsible diagnosis** (MRDx): The diagnosis determined by the coder as having the greatest contribution to the patient's utilization and/or length of stay. This is most often—but not always—the same as the admitting diagnosis.
- **Admitting diagnosis**: An optional diagnosis type coded in cases where the most responsible diagnosis differs from the original diagnosis the patient was admitted for.
- **Pre-admit comorbidity**: Coded in a case where a patient has multiple recorded diagnoses, where the preadmit comorbidity is seen to have contributed to at least an additional 24 hours of the patient's stay, but not seen to have been the primary contributing diagnosis to a patient's utilization or length of stay.

Emergency department cases: Included diagnosis codes (described above) present as one of the following diagnosis types:

- **Main problem:** Similar to MRDx for inpatient, the diagnosis determined by the coder to have had the greatest contribution to patient utilization and/or length of stay.
- **Other problem(s):** Similar to preadmit comorbidity, a diagnosis existing in combination with the main problem that is seen to have contributed to utilization and/or length of stay.

Rationale: The expert panel felt that cases where a COPD-related diagnosis was not recorded as MRDx (inpatient acute) or main problem (ED visit) but recorded as admitting diagnosis or preadmit comorbidity (inpatient care), or other problem (ED visit) would still be likely to benefit from at least a subset of the recommended interventions in the COPD pathway. Additionally, due to the uncertainty around COPD diagnosis and coding, it was thought there are likely to be a number of cases where COPD might be considered the true "most responsible" condition or the etiological disease behind a presenting condition such as chronic obstructive pulmonary disease, but was not attributed as MRDx. Narrowing the cohort definition to only include cases with a COPD MRDx excludes more than 50% of the total population of admitted cases coded with COPD diagnoses contributing to their hospital utilization, as illustrated in Table 2 (complete cohort) and Table 3 (MRDx of COPD only). Table 4 shows volumes of ED visit by COPD diagnosis for 2013/2014.

Table 2: COPD Episode-of-Care Cohort – Acute Inpatient Discharges (Ontario, 2012/2013 and 2013/2014)

Admission Fiscal Year		2012/2013				2013/2014			
COPD Diagnosis Code		Cases, n	Avg LOS, days	Med LOS, days	Avg HIG wt	Cases, n	Avg LOS, days	Med LOS, days	Avg HIG wt
J410	Simple chronic bronchitis	6	4.7	4.00	1.10	6	6.0	5.00	2.02
J411	Mucopurulent chronic bronchitis	9	12.6	21.00	1.95	0	N/A	N/A	N/A
J418	Mixed simple and mucopurulent chronic bronchitis	0	N/A	N/A	N/A	1	10.0	10.00	0.45
J42	Unspecified chronic bronchitis	70	7.7	4.00	2.02	62	14.4	7.00	2.59
J438	Other emphysema	10	11.2	4.00	3.31	12	16.5	6.00	5.96
J439	Emphysema unspecified	350	12.0	7.50	3.05	339	11.7	8.00	2.92
J440	COPD with acute lower respiratory infection	15,980	11.5	13.00	2.43	14,877	10.1	12.00	2.21
J441	COPD with acute exacerbation unspecified	17,375	8.1	10.00	1.56	16,470	7.4	8.50	1.53
J448	Other specified COPD	677	11.3	7.00	2.27	730	10.1	8.00	2.05
J449	COPD unspecified	4,245	12.2	8.50	2.35	4,372	10.6	7.00	2.16
	Total cases	**38,716**				**36,863**			

Abbreviations: avg, average; COPD, chronic obstructive pulmonary disease; HIG, health-based allocation model inpatient group; LOS, length of stay; med, median; n, number; N/A, not available; wt, weight.

Data source: Canadian Institute for Health Information, Discharge Abstract Database.

Table 3: COPD Episode-of-Care Cohort – Acute Inpatient Discharges, Using Most Responsible Diagnosis of COPD Only (Ontario, 2012/2013 and 2013/2014)

Admission Fiscal Year		2012/2013				2013/2014			
ICD-10-CA Diagnosis Code (MRDx)		Cases, n	Avg LOS, days	Med LOS, days	Avg HIG wt	Cases, n	Avg LOS, days	Med LOS, days	Avg HIG wt
J411	Mucopurulent chronic bronchitis	4	5.0	4.0	1.12	3	6.7	5.0	1.40
J418	Mixed simple and mucopurulent chronic bronchitis	5	4.0	4.0	0.84	0	N/A	N/A	N/A
J42	Unspecified chronic bronchitis	24	5.7	3.0	1.1	14	4.9	4.0	1.03
J438	Other emphysema	5	8.6	4.0	2.99	5	27.6	7.0	11.74
J439	Emphysema unspecified	103	10.5	6.0	3.91	101	11.2	6.0	3.31
J440	COPD with acute lower respiratory infection	11,146	8.8	6.0	1.78	10,400	8.0	6.0	1.68
J441	COPD with acute exacerbation unspecified	12,998	6.5	4.0	1.26	12,325	6.1	4.0	1.25
J448	Other specified COPD	289	9.0	4.0	1.91	289	6.6	4.0	1.52
J449	COPD unspecified	695	6.8	4.0	1.48	621	6.7	4.0	1.47
	Total cases	**25,269**				**23,758**			

Abbreviations: avg, average; COPD, chronic obstructive pulmonary disease; HIG, health-based allocation model inpatient group; ICD-10-CA, International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada; LOS, length of stay; med, median; MRDx, most responsible diagnosis; n, number, N/A, not available; wt, weight.

Data source: Canadian Institute for Health Information, Discharge Abstract Database.

Table 4: COPD Episode-of-Care Cohort – Emergency Department Visits (Ontario, 2012/2013 and 2013/2014)

All Problem ICD-10-CA		Number of Cases
J410	Simple chronic bronchitis	52
J411	Mucopurulent chronic bronchitis	5
J418	Mix simple and mucopurulent chronic bronchitis	10
J42	Unspecified chronic bronchitis	290
J438	Other emphysema	5
J439	Emphysema unspecified	232
J440	COPD with acute lower respiratory infection	6,894
J441	COPD with acute exacerbation unspecified	28,498
J448	Other specified COPD	1,008
J449	COPD unspecified	10,281
	Total cases	**47,275**

Abbreviations: COPD, chronic obstructive pulmonary disease; ICD-10-CA, International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada.
Data source: Canadian Institute for Health Information, Discharge Abstract Database.

Recommended COPD Patient Stratification Approach: Acute Care Phase

As described in the Methods section, the expert panel was asked to recommend an approach to stratifying patients hospitalized with exacerbations of COPD based on their clinical characteristics and expected resource utilization. The expert panel reviewed the ministry's default HIG grouping logic for COPD and agreed that the 2 HIG groups for the cohort were not clinically meaningful; they appeared to be largely determined based on the coding of a concurrent lower respiratory tract infection in a patient, which would assign the case to HIG 139b (COPD) as opposed to HIG 139a (chronic bronchitis), a group that does not include cases with respiratory infection. Given that a high proportion of COPD admissions have lower respiratory tract infections in combination with COPD, with inconsistent diagnosis and coding, the expert panel agreed that it would be necessary to explore alternative grouping approaches.

Determining an appropriate approach for stratifying COPD patients for this task was challenging given the outcome of interest: resource utilization during the hospitalization episode. While a number of approaches have been developed to classify COPD patients by severity over the course of their disease—such as the GOLD Staging Criteria (Table 1) using FEV_1/FVC and the BODE Index (recommended by NICE, GOLD and CTS)—these are not intended to be applied to the stratification of particular COPD acute exacerbations. With that said, studies have found that COPD patients with lower FEV_1/FVC scores and more severe dyspnea tend to both have more frequent exacerbations and more severe exacerbations, contributing to higher costs. (14, 15) Routine collection of these types of clinical measures may assist the ministry in developing more accurate risk adjustment models for COPD patient groups.

In a review of studies examining the costs of COPD exacerbations, Toy et al (16) found that the majority of articles surveyed used retrospective utilization as a proxy for grouping exacerbations by severity—e.g., seen in primary care (typically classified as a mild exacerbation) versus admitted to hospital (typically a moderate or severe exacerbation).

Consistent with much of the literature, the expert panel recommended that, given the limitations of current administrative data sources, COPD exacerbation hospitalizations be classified into the following 3 groups for the purpose of QBP funding:

- **Mild exacerbation:** Patient is treated in the ED or in outpatient settings and discharged home without requiring an inpatient admission.
- **Moderate exacerbation:** Patient requires admission to inpatient care.
- **Severe exacerbation:** Patient requires ventilation (either noninvasive or invasive ventilation) and/or admission to an intensive care unit.

It is recognized that these 3 patient groups are largely based on disposition (or level of care received) rather than prospective clinical symptoms. While severe exacerbations may be defined by markers of acute respiratory failure or acidosis, the expert panel noted that there are few definitive measures to distinguish between mild and moderate exacerbations; these largely rely on clinical judgment and the availability of hospital resources. For example, it may be possible for the same patient to be treated in and discharged from a well-equipped ED in one hospital, and thus classified as mild, while they might be admitted in another hospital and be classified as moderate. The ministry should exercise extreme caution in designing funding methodologies based on these groups, paying particularly close attention to the possibility of creating perverse incentives for hospitals to admit borderline mild/moderate patients in order to claim a higher payment for the moderate group.

While the COPD care pathway (see Recommended Practices section) includes a list of criteria for consideration in determining whether to admit patients or to treat them in ED/outpatient settings, this there are no objective markers or thresholds defined in this list for a mild versus a moderate exacerbation; this may be a potential future area for research and/or evidence-based analysis.

Using the expert panel's definitions, the ministry subsequently conducted analysis of the costs for the 2 COPD patient groups that require admission for moderate and severe exacerbations. Table 5 presents this analysis and demonstrates that the group definitions are highly predictive of cost: the severe group has a mean total cost nearly 3 times that of the moderate group ($17,791.46 compared with $6,101.81).

Table 5: Costs per Case for Moderate and Severe Exacerbation Groups for Patients With COPD (2010/2011 Acute Inpatient Discharges, Ontario Case Costing Initiative)

Admitted COPD subgroup	Number of cases	Mean total cost, $	Median total cost, $
All admitted cases	17,916	7,569	4,925.4
Moderate	15,668	6,102	4,490.1
Severe	2,248	17,791.46	13,385.11

Abbreviations: COPD, chronic obstructive pulmonary disease.
Source: Ontario Ministry of Health and Long-Term Care.

Factors Contributing to Severity of Acute Exacerbations of COPD

Evidence shows that within the 3 major exacerbation severity groups defined above, there is considerable heterogeneity in patient clinical characteristics, utilization, and cost. The expert panel identified a number of markers that should be considered as potential complexity adjustment factors within the QBP funding model, in terms of their impact on the indicated interventions for a patient

and their expected utilization of health care resources.

The expert panel grouped these complexity factors for consideration into 3 broad categories:

Severity of disease

- O_2 dependence
- respiratory failure
- recent (e.g., within 30 days) discharge from ED/hospital
- frequency of acute exacerbations over previous 6 to 12 months
- oral steroid use/dependence
- functional ability (activity) on the Modified Medical Research Council (MMRC) dyspnea scale
- lung function (FEV_1/FVC)
- failed response to outpatient therapy
- delay in receiving medical attention for an exacerbation

Significant comorbidities

- bronchiectasis
- pneumonia
- co-infections (pseudomonas, mycobacterium, urosepsis)
- mental health (anxiety, depression, dementia, delirium)
- chronic obstructive pulmonary disease
- arrhythmia (including atrial fibrillation)
- diabetes
- tobacco dependence
- benzodiazepine dependence/chronic benzodiazepine use
- immunosuppressant disease
- lung cancer
- renal failure
- osteoporosis
- BMI (overweight or underweight)
- chronic pain
- sleep apnea
- myocardial infarction
- neuromuscular disorder
- gastroesophageal reflux disease
- musculoskeletal disorders
- asthma
- interstitial lung disease

Housing/supports/frailty

- homeless
- lack of support (isolation, lack of transportation)
- continuing care/nursing home
- access to primary care
- functional status (e.g., walking aids)
- drug plan
- access to pulmonary rehabilitation

Many of the factors identified here have also been substantiated in the scientific literature as being associated with higher costs for COPD exacerbations, including lower FEV_1/FVC, more severe dyspnea, underweight BMI, and comorbidity score.

The expert panel requests that the ministry conduct multivariate analysis on the impact of the identified factors above on COPD case cost, recognizing that not all of the factors above will be measurable through current provincial administrative data sets.

Further consideration of comorbidities: There has been some discussion that upon completion of the pathway for the "typical" COPD case, the expert panel may consider the implications of commonly occurring comorbidities such as pneumonia, diabetes and arrhythmia on the COPD pathway. While it is expected that the foundational pathway will remain the same, the inclusion of comorbidities may result in recommending additional interventions in each care module.

Recommended COPD Patient Stratification Approach: Postacute Care Phase

The expert panel noted that the original patient groups defined for the acute care phase COPD QBP—mild, moderate, and severe, based largely on disposition (discharged from ED, admitted to ward, or received ventilation or admitted to intensive care unit)—did not necessarily reflect patients' complexity or risk of adverse outcomes in the postacute setting. A new risk stratification model may be required to assign patients appropriately based on differing levels of risk for the postdischarge period analyzed in this project. The expert panel discussed available approaches for stratifying patients by risk, including COPD-specific methods such as the GOLD COPD staging criteria, the BODE index (a grading system that uses body mass index, airflow obstruction, dyspnea, and exercise capacity) and the CAT index (COPD Assessment Test) as well as generic methods such as the interRAI (Resident Assessment Instrument) suite of tools and the LACE Index (L, length of stay; A, acuity of admission; C comorbidity, as measured by Charlson index; E, emergency department visits in the previous 6 months) (17).

After some discussion, the expert panel proposed the use of the LACE index as a risk stratification tool, as it captures a number of the key risk factors in COPD patients that, based on clinical experience, the panel members deemed important: inpatient length of stay, patients' comorbidity level, and previous emergency hospitalizations (Table 6). Importantly, the LACE index has been adopted by a wide range of providers and is currently in use in many parts of Ontario.

The expert panel recommends that analysis be conducted to examine the utility of the LACE index as a tool for stratifying COPD patients based on their risk of postacute readmission and mortality following discharge from the ED or from inpatient care. The index should also be examined for application to case-mix adjustment for postacute costs.

Table 6: LACE Index Covariates and Weights

Attribute	Value	Points
Length of stay	<1	0
	1	1
	2	2
	3	3
	4–6	4
	7–13	5
	≥ 14	7
Acute (emergent) admission	Yes	3
Comorbidity (Charlson index score)	0	0
	1	1
	2	2
	3	3
	≥ 4	5
Visits to ED during previous 6 months	0	0
	1	1
	2	2
	3	3
	≥ 4	4

Abbreviations: ED, emergency department.
Source: van Walraven et al, 2010. (17)

Additional Considerations Related to the COPD Cohort and Patient Grouping Approach

The expert panel highlighted the following considerations related to the COPD cohort and patient groups:

- **Accuracy and consistency of current practices in COPD diagnosis, charting, and coding:** Expert panel members agreed that the diagnosis, charting, and coding of COPD in Ontario is likely to be inconsistent and unreliable. In many cases, COPD diagnoses are assigned based on symptoms or clinical intuition without objective confirmation through spirometry. The expert panel recommended that, in the future, any charting of a COPD diagnosis should be accompanied by confirmation through spirometry (either during the stay or reported in the patient's history). In the absence of such confirmation, coders should assign a Q prefix (Query) to the COPD diagnosis.

- **Meaningfulness of ICD-10-CA COPD-related diagnosis codes:** The expert panel felt that a number of the ICD-10-CA diagnosis codes for COPD-related conditions were not clinically meaningful. For example, some of the different specificities of bronchitis (e.g., mucopurulent vs. simple and mucopurulent) appeared to be nonexclusive, while, on the other hand, the 2 COPD

diagnosis codes (J44.0 and J44.1) that capture the vast majority of COPD-related cases are not specific enough to be meaningful.

- **Important unmeasured clinical variables:** There are a number of patient characteristics and clinical measures, such as FEV_1/FVC and MMRC, that studies have shown are associated with the severity and cost of COPD exacerbations but that are not captured in routine administrative data in Ontario. These variables may be important for adequately adjusting the COPD patient groupings for variation in patient complexity. The collection of these measures might be facilitated through creation of a COPD registry or piloted through chart review in a small number of hospitals.

- **Completeness of coding for COPD-related procedure codes:** Some interventions that play an important role within the COPD pathway are not routinely recorded in hospital data. For example, only 33 instances of spirometry testing were recorded in Ontario acute inpatient records in 2010/2011, while use of bronchodilators is not captured at all. The coding of other interventions, such as different modalities of ventilation, may also be inconsistent. Given that such missing data elements would invalidate attempts to estimate the costs of all interventions for these cases, the ministry should consider chart reviews of a COPD case sample to assess current hospital coding practices.

- **Consistency of diagnosis coding across ED and inpatient settings:** Given the importance of capturing both ED visits and inpatient admissions for COPD, the expert panel drew the scope of the COPD "bundle" to include both the ED visit and inpatient acute stay for admitted cases. From a payment perspective, COPD patients admitted to hospital under this model would be funded at a rate including both the ED visit and the inpatient hospitalization. The expert panel saw a challenge related to administrative data in this area: in 2010/2011, about 23% of inpatients with a COPD-related MRDx assigned for their inpatient stay were previously assigned a non-COPD–related MRDx for their ED visit. It can be assumed that the MRDx assigned based on the inpatient stay is likely the more accurate of the 2 diagnoses, given the greater amount of time and resources available to record this.

  These data raise 2 considerations: 1) The bundled rate for the inpatient stay and ED visit would likely need to be grouped based on the inpatient MRDx and then linked backwards to the preceding ED visit. 2) If a similar proportion of "misdiagnosis" can be assumed for COPD cases discharged from the ED, then a substantial portion of COPD cases would not receive COPD QBP funding.

Continuum-of-Care Model

Health Quality Ontario developed the COPD continuum-of-care model in Figure 5 based on the previous work of the expert advisory panels. It has served as a working model as the components of this clinical handbook were developed. Beginning as a simplified sketch of key phases in the episode of care, the model has been modified to reflect the full range of elements of the episode-of-care pathway as determined by the expert advisory panels.

The following sections lay out the recommended practices for the modules in Figure 3 and divide the continuum into 2 episodes of care: acute care (Figure 4) and postacute community care (Figure 5).

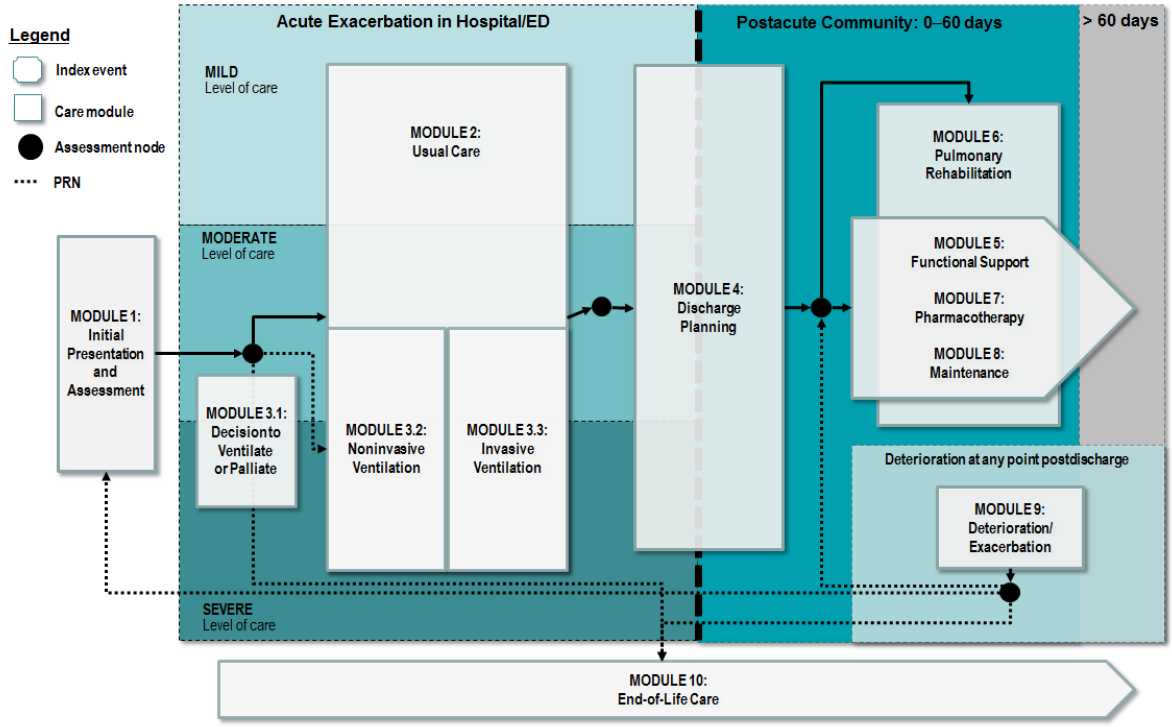


Figure 3: Continuum-of-Care Model for COPD

Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; PRN, as needed.

Recommended Practices for Chronic Obstructive Pulmonary Disease

Sources Used to Develop Recommended Practices

OHTAC Recommendations

Acute Episode of Care

Several evidence-based analyses by Health Quality Ontario and the corresponding OHTAC recommendations were contributing sources for recommended practices in the acute episode of care:

- Noninvasive Positive Pressure Ventilation for Acute Respiratory Failure Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (18)
- Preference for Ventilation among COPD Patients[5] (19)
- Influenza and Pneumococcal Vaccinations for Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (20)
- Pulmonary Rehabilitation for Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (21)
- Experiences of Living and Dying With COPD: A Systematic Review and Synthesis of the Qualitative Empirical Literature[5] (22)
- Discharge Planning in Chronic Conditions: An Evidence-Based Analysis[6] (23)

Postacute Episode of Care

Several evidence-based analyses by Health Quality Ontario and the corresponding OHTAC recommendations were contributing sources for recommended practices in the postacute episode of care:

- Pulmonary Rehabilitation in Ontario: A Cross-Sectional Survey (24)
- Pulmonary Rehabilitation for Postacute Exacerbations of Chronic Obstructive Pulmonary Disease (COPD): A Cost-Effectiveness and Budget Impact Analysis (25)
- Community-Based Multidisciplinary Care for Patients with Stable Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (26)
- Smoking Cessation for Patients With Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (27)
- Influenza and Pneumococcal Vaccinations for Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (20)
- Pulmonary Rehabilitation for Patients with Chronic Obstructive Pulmonary Disease (COPD): An Evidence-Based Analysis[5] (21)

[5] From the HQO mega-analysis on chronic obstructive pulmonary disease (2012). Available from: http://www.hqontario.ca/en/mas/tech/pdfs/2012/rev_COPD_compendium_March2012.pdf

[6] From Optimizing Chronic Disease Management in the Community (Outpatient) Setting: An Evidentiary Framework (2013). Available from: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series/optimizing-cdm-in-the-community-setting

- Screening and Management of Depression for Adults With Chronic Diseases: An Evidence-Based Analysis[6] (28)
- Experiences of Living and Dying With COPD: A Systematic Review and Synthesis of the Qualitative Empirical Literature[5] (22)
- Health Care for People Approaching the End of Life: An Evidentiary Framework (29)

Clinical Handbooks

Acute Episode of Care

The previous HQO clinical handbook on COPD, published in 2013, was used as the primary source for the update to the acute episode of care:

- Quality-Based Procedures: Clinical Handbook for Chronic Obstructive Pulmonary Disease (1)

Postacute Episode of Care

Three HQO clinical handbooks containing recommendations relevant to the postacute, community-based episode of care for COPD were incorporated as sources of evidence:

- Quality-Based Procedures: Clinical Handbook for Chronic Obstructive Pulmonary Disease (1)
- Quality-Based Procedures: Community Home Care Handbook for Postacute Medical Discharge Short-Stay Populations (30)
- Quality-Based Procedures: Clinical Handbook for Heart Failure (Acute and Postacute) (31)

HQO Rapid Reviews

Rapid reviews were conducted on specific topics where gaps or inconsistencies in the evidence were identified or as requested by the COPD expert advisory panels.

Acute Episode of Care

Two rapid reviews were conducted during the initial drafting of the acute episode of care, and 1 new rapid review (prophylactic antibiotics) was added for this update

1. Inhospital Physiotherapy for Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD): A Rapid Review
2. Action Plans for Individuals with Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
3. Prophylactic Antibiotics for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

Postacute Episode of Care

In addition to informing the recommended practices for COPD, some of the following rapid reviews were also incorporated into the Community Home Care Handbook for Postacute Medical Discharge Short-Stay Populations (30):

1. Pulmonary Rehabilitation in the Home Versus Other Settings for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
2. Pulmonary Rehabilitation Setting for Individuals with Chronic Obstructive Pulmonary Disease (COPD): An Economic Rapid Review
3. Exercise Programs After Pulmonary Rehabilitation for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

4. Respiratory Therapy Services in Home Care for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
5. Airway Clearance Techniques for Individuals With Stable Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
6. Cognitive-Behavioural Therapy for Anxiety and Depression in Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

The complete rapid reviews are available online and their conclusions are included within each of the modules. The GRADE quality scores in the modules can be interpreted using the following definitions established by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group (19):

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Clinical Guidelines

Acute Episode of Care

The Canadian guideline used during the development of the original HQO clinical handbook on COPD was used as the reference standard due to its relevance and local context:

- Canadian Thoracic Society (CTS) 2007 Update (CA) (32)

Two additional international clinical guidelines encompassing the acute episode of care were identified and used for this update:

- National Institute for Health and Clinical Excellence (NICE) 2010 Update (UK) (33)
- Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2014 Update (International) (34)

Postacute Episode of Care

The guideline review process identified 1 Canadian guideline, and it was used as the reference standard due to its relevance and local context:

- Canadian Thoracic Society (CTS) 2007 Update (CA) (32)

Four additional international clinical guidelines encompassing the postacute episode of care were included:

- Department of Veterans Affairs (VA) and Department of Defense (DoD) 2007 (United States) (35)
- National Institute for Health and Clinical Excellence (NICE) 2010 Update (United Kingdom) (33)
- American College of Physicians (ACP)/American College of Chest Physicians (ACCP)/American Thoracic Society (ATS)/European Respiratory Society (ERS) 2011 Update (International) (36)
- Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2013 Update (International) (37)

Quality Assessment for Guidelines

Quality assessment using the AGREE II (5) domain scores for each of the included guidelines are presented in Table 6. Given the limited number of guidelines identified for each cohort, the expert advisory panel considered all the guideline recommendations.

Table 6: AGREE II Domain Scores for COPD Guidelines

Guideline, Year	AGREE II Domain					
	Scope & Purpose	Stakeholder Involvement	Rigour of Development	Clarity of Presentation	Applicability	Editorial Independence
Acute Period						
CTS, 2007 (32)	44%	25%	30%	89%	25%	88%
NICE, 2010 (33)	86%	81%	79%	83%	71%	38%
GOLD, 2014 (34)	44%	36%	61%	64%	13%	50%
Postacute Period						
CTS, 2007 (32)	44%	25%	30%	89%	25%	88%
VA/DoD, 2007 (35)	86%	50%	66%	78%	40%	4%
NICE, 2010 (33)	86%	81%	79%	83%	71%	38%
ACP/ACCP/ ATS/ERS, 2011 (36)	86%	44%	64%	75%	10%	71%
GOLD, 2013 (37)	42%	33%	61%	58%	13%	50%

Abbreviations: ACP, American College of Physicians; ACCP, American College of Chest Physicians; ATS, American Thoracic Society; CTS, Canadian Thoracic Society; DoD, Department of Defense; ERS, European Respiratory Society; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NICE, National Institute of Health and Clinical Excellence; VA, Department of Veterans Affairs.

The guidelines supporting the expert panels' recommendations were summarized, along with the quality of evidence supporting individual guideline recommendations. The quality assessment tools used by each guideline are summarized in Table 7.

Table 7: Summary of Evidence Assessments Used by Included Guidelines

Organization	Grade of Recommendation/Level of Evidence
Acute Period	
CTS, 2007 (CA)	**1:** Evidence from 1 or more RCTs or MAs **2:** Evidence from 1 or more well-designed cohort or case-control studies **3:** Consensus from expert groups based on clinical experience **A:** Good evidence to support a recommendation for use **B:** Moderate evidence to support a recommendation for use **C:** Poor evidence to support a recommendation for use **D:** Moderate evidence to support a recommendation against use **E:** Good evidence to support a recommendation against use
NICE, 2010 (UK)	**A:** Based on evidence from SRs or MAs of RCTs **or** evidence from at least 1 RCT **B:** Based on evidence from at least 1 controlled study without randomization **or** evidence from at least 1 other type of quasi-experimental study **C:** Based on evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies **D:** Directly based on evidence from expert committee reports or opinions and/or clinical experience of respected authorities
GOLD, 2014 (International)	**A:** RCTs, rich body of data **B:** RCTs, limited body of data **C:** Nonrandomized trials, observational studies **D:** Panel consensus judgment
Postacute Period	
CTS, 2007 (CA)	**1:** Evidence from 1 or more RCTs or MAs **2:** Evidence from 1 or more well-designed cohort or case-control studies **3:** Consensus from expert groups based on clinical experience **A:** Good evidence to support a recommendation for use **B:** Moderate evidence to support a recommendation for use **C:** Poor evidence to support a recommendation for use **D:** Moderate evidence to support a recommendation against use **E:** Good evidence to support a recommendation against use
VA/DoD, 2007 (US)	**A:** A strong recommendation that clinicians provide the intervention to eligible patients (Good evidence that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.) **B:** A recommendation that clinicians provide (the service) to eligible patients (At least fair evidence that the intervention improves important health outcomes and concludes that benefits outweigh harm.) **C:** No recommendation for or against the routine provision of the intervention is made (At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.) **D:** Recommendation is made against routinely providing the intervention to asymptomatic patients (At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.)

Organization	Grade of Recommendation/Level of Evidence
	I: The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention (Evidence that the intervention is effective is lacking or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.)
NICE, 2010 (UK)	**A:** Based on evidence from SRs or MAs of RCTs **or** evidence from at least 1 RCT **B:** Based on evidence from at least 1 controlled study without randomization **or** evidence from at least 1 other type of quasi-experimental study **C:** Based on evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies **D:** Directly based on evidence from expert committee reports or opinions and/or clinical experience of respected authorities
ACP/ACCP/ATS/ ERS, 2011 (International)	**Strong:** Benefits clearly outweigh risks and burden or risks and burden clearly outweigh benefit **Weak:** Benefits finely balanced with risk and burden **High:** Very confident that the true effect lies close to that of the estimate of the effect **Moderate:** Moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low:** Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect
GOLD, 2013 (International)	**A:** RCTs, rich body of data **B:** RCTs, limited body of data **C:** Nonrandomized trials, observational studies **D:** Panel consensus judgment

Abbreviations: ACP, American College of Physicians; ACCP, American College of Chest Physicians; ATS, American Thoracic Society; CA, Canada; CTS, Canadian Thoracic Society; DoD, Department of Defense (US); ERS, European Respiratory Society; GOLD, Global Initiative for Chronic Obstructive Lung Disease; MA, meta-analysis; NICE, National Institute of Health and Clinical Excellence; RCT, randomized controlled trial; SR, systematic review; US, United States; VA, Department of Veterans Affairs.

Other Contributing Sources

In addition to the evidence provided through OHTAC recommendations, HQO clinical handbooks, rapid evidence reviews, and international guidelines, the following sources of evidence were used to develop the practice recommendations for COPD.

Acute Episode of Care

- **Related reports and updates:** Important scientific reports identified by the expert advisory panel were incorporated into relevant recommendations, particularly if the evidence contextualized the recommendation for Ontario.
  - **Canadian Thoracic Society/American College of Chest Physicians:** Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease (updated guideline) (38)

    At the time the acute episode of care was updated, this new guideline was anticipated but not yet published. Information from experts involved in the guideline update suggested general alignment with the recommendations in this clinical handbook. However, HQO may revise the handbook in the event that there are major discrepancies.
  - **Canadian Thoracic Society:** Alpha-1 Antitrypsin Deficiency Targeted Testing and Augmentation Therapy (2012)

    (Available from: http://www.respiratoryguidelines.ca/sites/all/files/2012_CTS_Guidline_Alpha-1.pdf)

- **Ontario Drug Policy Research Network:** Drug Class Review Inhaled Corticosteroids (ICS) + Long-acting Beta2-agonists (LABA) for Treatment of Chronic Obstructive Pulmonary Disease (COPD) Consolidated Final Report (2014)

  (Available from: http://www.odprn.ca/wp-content/uploads/2014/05/ICS-LABA-consolidated-report-may-9-final1.pdf)
- **Expert consensus:** Where other forms of evidence were lacking, expert panel opinion and consensus were incorporated.

Postacute Episode of Care

- **Health Links:** Adopting a Common Approach to Transitional Care Planning: Helping Health Links Improve Transitions and Coordination of Care

  (Available from: http://www.hqontario.ca/Portals/0/Documents/bp/bp-traditional-care-planning-1404-en.pdf)
- **Ministry of Health and Long-Term Care:** Assistive Device Program Home Oxygen Therapy Policy and Administration Manual (2014)

  (Available from: http://www.health.gov.on.ca/en/pro/programs/adp/information_technology/docs/home_oxygen_manual.pdf)
- **Related reports and updates**: Important scientific reports identified by the expert advisory panel were incorporated into relevant recommendations, particularly if the evidence contextualized the recommendation for Ontario.
  - **Canadian Thoracic Society:** 2013 CTS COPD Action Plan

    (Available from: http://www.respiratoryguidelines.ca/updated-cts-copd-action-plan)
  - **Canadian Thoracic Society/American College of Chest Physicians:** Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease (updated guideline) (38)

    At the time the postacute episode of care was undertaken, this new guideline was anticipated but not yet published. Information from experts involved in the guideline update suggested general alignment with the recommendations in this clinical handbook. However, HQO may revise the handbook in the event that there are major discrepancies.
- **Expert consensus:** Where other forms of evidence were lacking, expert panel opinion and consensus were incorporated.

Language Used to Reference Contributing Sources of Evidence

For clarity and transparency, the following terms were consistently applied to describe how the expert advisory panel used various evidence sources to develop episode-of-care best practice recommendations:

Taken from	Recommendation was taken directly from another source
Modified	Minor modifications from the source materials were made to the recommendation
Consistent with	Recommendation was developed by the expert panel and was consistent with other sources
Based on expert advisory panel consensus	Recommendation was largely derived through expert panel consensus

What's New?

During Phase 3 (this update and integration to include the postacute episode of care), recommended practices may have been added, amended (e.g., because modules have been reorganized or new evidence has changed an original recommendation), and/or deleted. Below is a summary of these changes, numbered according to the modules that follow.

Additions

- Recommendation E: diagnosis of COPD
- Recommendation 4a.3.5: transition to community-based care
- Modules 4b to 10: postacute, community-based episode of care

Amendments

- Recommendation D: diagnosis of COPD
- Recommendations 1.1.2, 1.1.5, 1.1.6, 1.1.7, 1.1.9, 1.1.10, and 1.1.13: patient presents with suspected COPD exacerbation
- Recommendation 1.2.1: assess level of care required
- Recommendations 2.1, 2.2, 2.3, and 2.6: usual medical care
- Recommendations 4a.2.3, 4a.2.5, 4a.2.7, 4a.2.8, and 4a.2.9: preparation for discharge
- Recommendations 4a.3.2, 4a.3.6, and 4a.3.7: transition to community-based care

Recommended Practices

While recommendations are presented within their respective modules according to the continuum-of-care model for COPD (Figure 5), they are not necessarily in the order in which they should be conducted. It is therefore important for readers to review the entire set of recommendations for COPD care and not isolated sections. The recommended practices for COPD diagnosis and the definition of an acute exacerbation of COPD applies to the full continuum of care.

Diagnosis Recommended Practices	Contributing Sources of Evidence
Diagnosis of COPD	
A. Consider clinical diagnosis of COPD in any patient who has dyspnea, chronic cough, or sputum production, and/or a history of exposure to risk factors for the disease.	Taken from GOLD; consistent with CTS and NICE (level D evidence)
B. Spirometry is required to make clinical diagnosis: post-bronchodilator $FEV_1/FVC < 0.70$ confirms COPD.	Taken from GOLD; consistent with CTS (level 3A evidence) and NICE (level D evidence)
C. Spirometry need not be performed during the initial phase of an exacerbation when the patient is unstable, but should be performed once the patient has stabilized.	Based on CTS (level 3C evidence); modified by the expert advisory panel; consistent with GOLD and NICE (level D evidence)
D. Spirometry should be performed if the patient has no recent, reliable, objective documentation of COPD by spirometry.	Based on CTS (level 3C evidence); modified by the expert advisory panel
E. To ensure accurate diagnosis and optimal treatment, it is recommended that a case-finding strategy to identify $alpha_1$-antitrypsin deficiency; follow the Canadian Thoracic Society guidance on targeted testing.	Based on CTS clinical practice guideline on $alpha_1$-antitrypsin deficiency targeted testing and augmentation therapy[7] (level 2C evidence)
Acute Exacerbation	
F. An exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms (baseline dyspnea, cough, and/or sputum production) that is beyond normal day-to-day variations and leads to a change in medication.	Taken from GOLD; consistent with CTS and NICE

Abbreviations: COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NICE, National Institute for Health and Clinical Excellence.

[7]Canadian Thoracic Society. Available from: http://www.respiratoryguidelines.ca/sites/all/files/2012_CTS_Guidline_Alpha-1.pdf

Acute Episode of Care

The diagram in Figure 4 has been adopted by the expert panel as a high-level functional model of the COPD acute exacerbation episode of care. The model framework was developed by Health Quality Ontario to structure its episode-of-care analyses in selected clinical areas. It includes 2 key components: *care modules* cluster recommended practices and interventions at each stage of the patient pathway, while *assessment nodes* provide patient-based criteria for a particular case proceeding down one branch of the pathway or another.

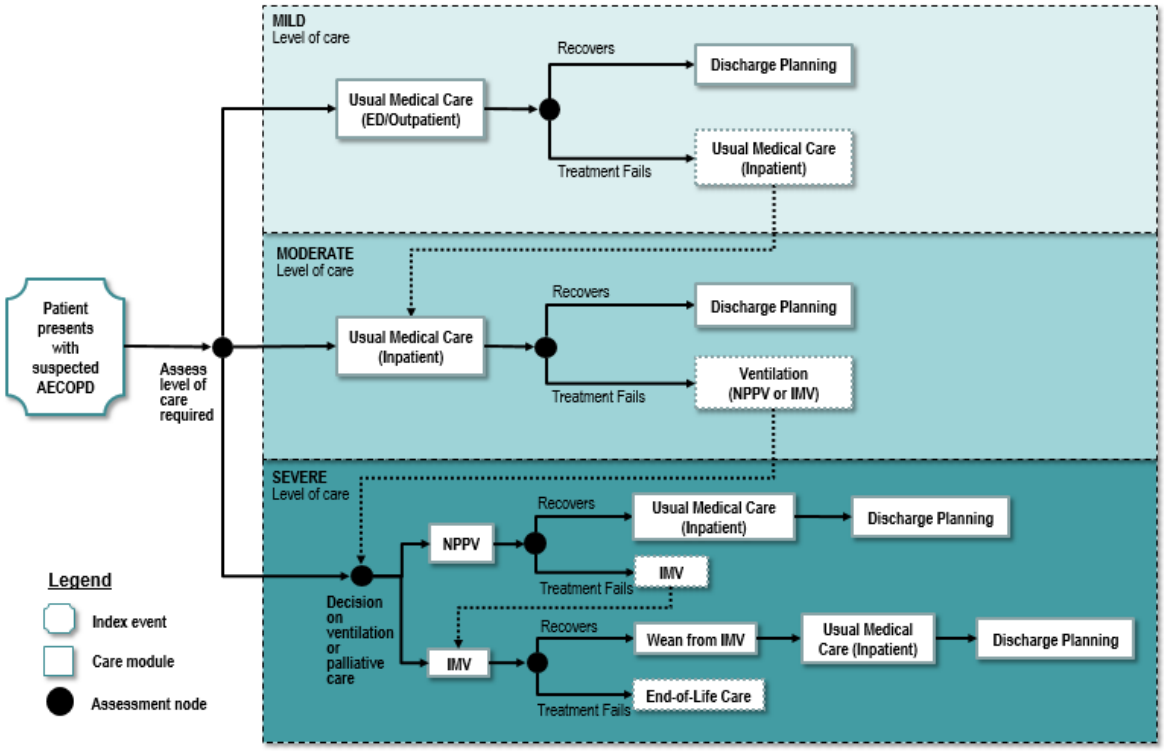


Figure 4: Episode-of-Care Model for Acute COPD

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ED, emergency department; IMV, mechanical ventilation; NPPV, noninvasive positive pressure ventilation.

In the recommendations that follow, please refer to Figure 3, page 37, to locate the module numbers within the continuum-of-care model for COPD.

Module 1: Initial Presentation and Assessment

Recommendations for Modules 1 through 4 were originally developed by the Acute COPD Expert Advisory Panel in 2013 and have been updated in this clinical handbook by the Update and Integration COPD Expert Advisory Panel.

This module identifies recommended practices for patients presenting with suspected COPD to the ED or outpatient clinic or for patients who are admitted directly. This module also identifies recommended practices for assessing the level of care required. Many patients with COPD exacerbations do not present to the ED as patients with well-characterized COPD but as undifferentiated patients who could potentially be suffering from a variety of conditions (e.g., COPD, acute myocardial infarction or other cardiac conditions, pulmonary embolus, pneumonia, asthma, acute bronchitis). As the recommendations presented here focus on defining a COPD-specific care pathway, it is expected that additional diagnostic interventions not included here may be required based on clinical assessment. The type of tests performed may depend on the individual hospital's standard ED processes rather than COPD-specific guidelines.

Module 1 Recommended Practices	Contributing Sources of Evidence
1.1 Patient Presents With Suspected COPD Exacerbation	
1.1.1 Check vital signs, including: • Assess for hypoventilation • Check level of consciousness/cognition • Check blood-oxygen saturation level via pulse oximetry • Assess whether patient has purulent sputum	Based on CTS, GOLD and NICE (level D evidence); modified by the expert advisory panel
1.1.2 Perform a physical examination.	Based on CTS, GOLD and NICE; modified by the expert advisory panel
1.1.3 Check patient history.	Based on CTS, GOLD and NICE; modified by the expert advisory panel
1.1.4 Document and reconcile medications currently used by patient.	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
1.1.5 Perform a chest x-ray: • posteroanterior and lateral • portable x-ray for patients who are too unwell to leave emergency department • expiratory view when concerned with pneumothorax	Based on CTS (level 2B evidence) and NICE (level D evidence); modified by the expert advisory panel; consistent with GOLD
1.1.6 Conduct baseline blood work: • complete blood count • electrolytes • creatinine • blood urea nitrogen (if available)	Based on GOLD and NICE; modified by the expert advisory panel
1.1.7 Perform an electrocardiogram to check for arrhythmias, myocardial ischemia, right ventricular strain, etc.	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
1.1.8 If low oxygen saturation on oximetry and/or acute respiratory failure is suspected, check arterial blood gases where appropriate.	Based on CTS, GOLD and NICE (level D evidence); modified by the expert advisory panel

Module 1 Recommended Practices	Contributing Sources of Evidence
1.1.9 If pneumonia or suspected sepsis, draw blood cultures.	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
1.1.10 Examine cardiac markers for suspected cardiac disorders, if appropriate.	Based on GOLD; modified by the expert advisory panel
1.1.11 Identify patient wishes with respect to goals of care and/or limitations of treatment (i.e., code status).	Based on expert advisory panel consensus
1.1.12 Spirometry need not be performed during the initial assessment of an exacerbation, but should be performed once the patient has stabilized, if patient has no prior objective documentation of COPD through spirometry.	Based on CTS (level 3C evidence); modified by the expert advisory panel; consistent with GOLD and NICE (level D evidence)
1.1.13 Perform other diagnostic interventions as appropriate to identify and/or rule out other suspected diagnoses or comorbidities.	Based on GOLD; modified by the expert advisory panel
1.2 Assess Level of Care Required	
1.2.1 The decision to admit relies largely on clinical judgment and availability of local resources. Use the NICE and/or GOLD criteria below as a guide: • failure of an exacerbation to respond to initial medical management • insufficient home support; inability to cope at home • breathlessness or marked increase in intensity of symptoms, such as development of resting dyspnea • general condition and severe underlying COPD • decreased level of activity • cyanosis • worsening peripheral edema or onset of new physical signs (e.g., cyanosis, fatigue, inability to stand) • decreased level of consciousness • already receiving long-term oxygen therapy • social circumstances, older age • acute confusion • rapid rate of onset or frequent exacerbations • significant comorbidity (e.g., heart failure, newly occurring arrhythmias) • arterial oxygen saturation (SaO_2) < 90%, pH level, and partial pressure of oxygen (PaO_2) • changes on chest x-ray	Based on GOLD and NICE (level D evidence); modified by expert advisory panel
1.2.2 Trial immediate resuscitation on initial presentation at the ED; follow up with re-evaluation for admission.	Based on expert advisory panel consensus

Abbreviations: COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NICE, National Institute for Health and Clinical Excellence.

Module 1 Implementation Considerations
• On a quarterly basis, hospital administration and admitting clinicians should be made aware of COPD admission rates benchmarked against similar hospitals in the province. • Emergency room staff should use a checklist for admission to hospital. In addition to the practices in the Module 1 table, the checklist should at a minimum include non-COPD concerns such as pain, anxiety, and comorbidities.

Abbreviations: COPD, chronic obstructive pulmonary disease.

Module 2: Usual Medical Care

Module 2 Recommended Practices	Contributing Sources of Evidence
2.1 Short-acting bronchodilators are effective for treating a COPD exacerbation.	Based on CTS (level 2A evidence), GOLD (level C evidence) and NICE (level B evidence); modified by the expert advisory panel
• Beta-2 agonists with or without short-acting anticholinergics are recommended.	Based on CTS (level 3C evidence) and GOLD (level C evidence); modified by the expert advisory panel
• If patient is already on long-acting anticholinergics, continue to administer in combination with beta-2 agonists.	Based on CTS (level 3C evidence) and GOLD; modified by the expert advisory panel
• There is insufficient evidence to support the benefits of adding short-acting anticholinergics to long-acting anticholinergics.	Based on expert advisory panel consensus
• Metered dose inhalers with spacers are the preferred delivery vehicle; if metered dose inhalers are not appropriate and/or cannot be used, nebulizers should be considered second-line treatment, due to infection risk.	Based on expert advisory panel consensus; consistent with GOLD and NICE (level D evidence)
• Ensure continuous supervision of the patient during drug delivery, whether by metered dose inhaler or nebuliser, to ensure drugs are taken successfully.	Based on expert advisory panel consensus
2.2 Corticosteroids are effective except for only very mild exacerbations, or if contraindicated.	Based on CTS (level 1A evidence); modified by the expert advisory panel; consistent with GOLD (level A evidence) and NICE (level A evidence)
• Oral corticosteroids are preferred over intravenous corticosteroids.	Based on CTS (level 2B evidence), GOLD and NICE (level D evidence); modified by the expert advisory panel
• Manage corticosteroid-induced side-effects.	Based on expert advisory panel consensus
• Use a 10- to 14-day course of therapy	Based on CTS (level 1A evidence) and NICE (level D evidence); modified by the expert advisory panel
• Specific cautions and/or contraindications include: – frequency of use (dependence or chronic use) – chronic obstructive pulmonary disease – diabetes – osteoporosis – avascular necrosis	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
2.3 Antibiotics should be used for indications of infection (e.g., purulent or high-volume sputum)	Based on CTS (level 1A evidence), GOLD (level B evidence) and NICE (level A evidence); modified by the expert advisory panel
• Refer to Canadian Thoracic Society recommendations on antibiotic treatment (Table 8).	Taken from CTS
• Refer to institution-specific antimicrobial stewardship policies.	Based on GOLD; modified by the expert advisory panel
• Oral antibiotics are preferred.	Based on GOLD; modified by the expert advisory panel
• Intravenous antibiotics should be considered second-line therapy, used only when oral antibiotics are contraindicated or inappropriate (e.g., gastrointestinal issues).	Based on GOLD; modified by the expert advisory panel
2.4 Theophylline is not recommended unless the patient is already receiving it; if so, check levels.	Based on GOLD (level B evidence) and NICE (level D evidence); modified by the expert advisory panel

Module 2 Recommended Practices	Contributing Sources of Evidence
2.6 If necessary, deliver oxygen to maintain target oxygen saturation of ~ 90%. Assess risk of hypercarbia.	Based on GOLD; modified by the expert advisory panel
2.7 Where appropriate, initiate bronchopulmonary (lung) hygiene physical therapy to clear mucus and secretion from the airway.	Based on Inhospital Physiotherapy for Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) (low GRADE quality of evidence): There is low-quality evidence that certain airway clearance techniques have beneficial impacts on some outcomes; modified by expert advisory panel; consistent with NICE (level B evidence)
2.8 If patient is admitted, use early ambulation therapy.	Based on Inhospital Physiotherapy for Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) (poor quality of evidence): 1 small RCT found statistically significant improvements for a number of patient outcomes, including exercise capacity and lung function, for the walking program compared to standard care, but the quality of evidence is poor and not generalizable to the Ontario context; modified by expert advisory panel; consistent with GOLD
2.9 Begin discharge planning, including referral to pulmonary rehabilitation.	Based on expert advisory panel consensus

Abbreviations: COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; HQO, Health Quality Ontario; NICE, National Institute for Health and Clinical Excellence; RCT, randomized controlled trial.

Table 8: Canadian Thoracic Society Antibiotic Treatment Recommendations for Purulent Exacerbations of COPD

Group	Basic Clinical State	Symptoms and Risk Factors	Probable Pathogens	First Choice
Simple	COPD without risk factors	Increased cough and sputum, sputum purulence, and increased dyspnea	*Haemophilus influenzae, Haemophilus* species, *Moraxella catarrhalis, Streptococcus pneumoniae*	Amoxicillin, doxycycline, trimethoprim/sulfamethoxazole, second- or third-generation cephalosporins, extended-spectrum macrolides
Complicated	COPD with risk factors	As in simple plus at least 1 of: • FEV_1 < 50% predicted • ≥ 4 exacerbations per year • ischemic heart disease • use of home oxygen • chronic oral corticosteroid use • antibiotic use in the past 3 months	As in simple, plus: *Klebsiella* species and other gram-negatives Increased probability of beta-lactam resistance	Beta-lactam/beta-lactamase inhibitor; fluoroquinolone (antibiotics for uncomplicated patients when combined with oral steroids may suffice)

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.

Module 2 Implementation Considerations
• Daily physical inactivity is evident across the spectrum of COPD disease stages but particularly after acute exacerbations of the disease. Facilitating early ambulation contributes to improving long-term outcomes in COPD patients. – Standardized ambulation interprofessional team care pathway should be in place at all hospitals. – Early ambulation requires physiotherapy or nursing and/or nursing assistants available 7 days per week to accomplish early ambulation. – Anticipated numbers of patients should be determined for assessment, treatment, care coordination or case management, and home care and/or end-of-life care, accounting for the possibility of increased numbers of patients moving through the system during specific time periods (e.g., seasons). • Documentation of ambulation should be readily accessible to other providers who need to know this information. • Appropriate use of medication can diminish the frequency and effect of COPD exacerbations. Oral antibiotics encourage early ambulation. Hospitals should have a hospital-wide (including ED) drug therapy protocol that supports and details the clinical use, administration, and supply of the scheduled drugs. If not, it is recommended that the relevant interprofessional team be assembled to develop standardized drug therapy protocols to serve the hospitals' professional practices. – Printed or computerized order sheets should prioritize oral over IV antibiotics. – It is important to consider the potential implications on hospitals' antimicrobial stewardship policies. – Practitioners should know the contraindications, known side-effects, and drug interactions of each drug and advise patients accordingly. – Patients' drug allergies should be entered in the hospital's EHR. – Practitioners and patients should understand when to discontinue the use of oral corticosteroids (10–14 days). – Prior to patients' discharge from hospital, staff should ask the patient how they will pay for medications. Patients without insurance coverage for drugs may be at risk of non-compliance if they have difficulty affording their medications. • Patient comorbidities can be a barrier to implementation. • Depending on the clinical condition of the patient, an appropriate fluid balance with special attention to the administration of diuretics, anticoagulants, treatment of comorbidities, and nutritional aspects should be considered. (34) • Pulmonary rehabilitation helps to decrease symptoms and improve the patient's quality of life, daily functioning, and ability to exercise. – Pulmonary rehabilitation must be accessible to all relevant individuals with COPD, including those who have had a recent hospitalization for an acute COPD exacerbation. – Criteria for referral to pulmonary rehabilitation should be developed if not already in place. – Hospitals should inform their LHINs about the pulmonary rehabilitation services they offer so that the LHINs know what services exist in their areas. – Hospitals should consider accessibility of pulmonary rehabilitation when referring COPD patients to other services, to reduce potential hospital admissions and length of hospital stay. – The Ministry of Health and Long-Term Care should accept and fund HQO's provincial implementation plan for pulmonary rehabilitation, submitted in September 2014.

Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; EHR, electronic health record; HQO; Health Quality Ontario; IV, intravenous; LHIN, local health integration network.

Module 3: Ventilation and Palliative Care

Module 3 Recommended Practices	Contributing Sources of Evidence
3.1 Decision on Ventilation or Palliative Care	
3.1.1 If possible, seek patient preferences for ventilation therapy before proceeding to ventilation interventions, consistent with OHTAC's recommendation:	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
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.	Taken from OHTAC for HQO EBA, Preference for Ventilation Among COPD Patients
3.1.2 If ventilation is not desired, proceed to palliative care management of the patient, consistent with OHTAC's recommendation:	Based on expert advisory panel; consistent with OHTAC for HQO synthesis of the qualitative empirical literature on palliative care for COPD and with GOLD
In making palliative care services available, the fluctuating physical, psychosocial, spiritual, and information needs should be considered, without necessarily forgoing acute care or hope of improvement during and following severe exacerbations.	Taken from OHTAC for HQO synthesis of the qualitative empirical literature on palliative care for COPD
3.1.3 Noninvasive positive pressure ventilation (NPPV) should be considered as part of first-line treatment for patients with acute respiratory failure and pH < 7.35, consistent with OHTAC's recommendation:	Based on GOLD; modified by the expert advisory panel; consistent with NICE (level A evidence)
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 invasive mechanical ventilation (IMV).	Taken from OHTAC for HQO EBA on NPPV for acute respiratory failure (low to moderate GRADE quality of evidence)
3.1.4 NPPV should be trialed before proceeding to IMV for all patients with indications for ventilation, including severe patients (pH < 7.20), unless contraindications are present (including respiratory or cardiac arrest, loss of consciousness, craniofacial trauma, hemodynamic instability, impaired mental status).	Based on CTS (level 1A evidence); modified by the expert advisory panel; consistent with GOLD and NICE (level A evidence)
3.1.5 Where patients have expressed preferences against intubation, NPPV can still be considered but ensure that therapy does not progress to IMV in the case of failure to respond to NPPV.	Based on NICE (level D evidence); modified by the expert advisory panel; consistent with GOLD
3.2 Noninvasive Ventilation	
3.2.1 Ensure continuous monitoring of patients receiving NPPV.	Based on CTS (level 1A evidence); modified by the expert advisory panel
3.2.2 Specialized respiratory teams and/or units are likely to be more effective in delivering NPPV, consistent with OHTAC's recommendation:	Based on CTS (level 1A evidence), GOLD and NICE (level D evidence); modified by the expert advisory panel
NPPV should be made widely available, with appropriate support systems and human resources for this indication.	Taken from OHTAC for HQO EBA on NPPV for acute respiratory failure (low to moderate GRADE quality of evidence)
3.3 Invasive Ventilation/Weaning from Invasive Ventilation	
3.3.1 Use NPPV to help wean patients from IMV when they fail spontaneous breathing tests. This is consistent with OHTAC's recommendation:	Based on GOLD; modified by the expert advisory panel
OHTAC recommends the use of NPPV to wean COPD patients who have failed spontaneous breathing tests following IMV.	Taken from OHTAC for HQO EBA on NPPV for acute respiratory failure (low to moderate GRADE quality of evidence)

Module 3 Recommended Practices	Contributing Sources of Evidence
3.3.2 A volume-outcome relationship at the hospital level associated with effectiveness of IMV should be considered.	Based on expert advisory panel consensus

Abbreviations: COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; EBA, evidence-based analysis; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; HQO, Health Quality Ontario; IMV, invasive mechanical ventilation; NICE, National Institute for Health and Clinical Excellence; NPPV, noninvasive positive pressure ventilation; OHTAC, Ontario Health Technology Advisory Committee.

Module 3 Implementation Considerations

NPPV has demonstrated benefits on mortality and intubation rates in patients with acute COPD exacerbations and may shorten hospital stay, in turn reducing costs.

- Hospitals should have a process for getting an advanced directive either from the patients' PCP or through the hospital regarding patient preferences for ventilation therapy.
- Hospitals should have standardized practices and protocols in place for the use of NPPV. These practices and protocols should be standardized and available throughout the hospital.
- NPPV should be used as the preferred treatment during COPD exacerbations resistant to medical therapy. NPPV should be provided by staff who are trained, experienced, and familiar with its limitations.
- Hospitals should carefully identify COPD patients for NPPV according to indications and contraindications.
- Using NPPV to wean COPD patients with acute respiratory failure who have failed spontaneous breathing tests from invasive mechanical ventilation should be the standard of care in hospitals. Hospitals should invest in the required equipment and human resources (e.g., registered respiratory therapists) to make this possible.
- The use of NPPV for chronic respiratory failure in stable COPD patients is not recommended due to its lack of clinical effectiveness.
- Hospitals should be appropriately resourced to offer NPPV not only in the intensive care unit but also in hospital wards.
- To ensure patients' wishes are followed, advance care planning discussions should take place at each transition point in the continuum of health care service provision.

Abbreviations: COPD, chronic obstructive pulmonary disease; NPPV, noninvasive positive pressure ventilation; PCP, primary care provider.

Module 4: Discharge Planning

This module contains recommendations for the preparation for discharge and transition from hospital to the community. As a result, there is overlap with recommendations in Module 4b in the postacute episode of care, which also supports a smooth transition and continuity of care.

Module 4a Recommended Practices	Contributing Sources of Evidence
4a.1 Clinical Assessment of Stabilized Patient	
4a.1.1 Where a patient has no prior objective documentation of spirometry assessment, spirometry should be performed on the stabilized patient before discharge (as time and patient's condition allow) or arranged for following discharge.	Based on CTS (level 3C evidence) and NICE (level D evidence); modified by the expert advisory panel; consistent with GOLD
4a.1.2 In addition to classification of airflow limitation, patients should also be assessed for the severity of their symptoms and other risk factors (e.g., comorbidities), considering tools such as the MRC dyspnea scale and the CAT, BODE, and LACE indices.	Based on CTS (level 3A evidence), GOLD and NICE (level D evidence); modified by the expert advisory panel
4a.1.3 Perform a full clinical assessment on suspected COPD patients once their condition stabilizes, before they are discharged.	Based on GOLD; modified by the expert advisory panel; consistent with NICE
4a.2 Preparation for Discharge	
4a.2.1 Patients should leave the hospital with an individualized discharge plan, consistent with OHTAC's recommendation:	Based on GOLD and NICE; modified by the expert advisory panel
OHTAC recommends the implementation of individualized predischarge planning[8] for chronic disease patients admitted to hospital, the primary responsibility for which resides with the hospital. OHTAC strongly recommends that the discharge plan be communicated and coordinated across relevant health care providers.	Taken from OHTAC for HQO EBA, Discharge Planning in Chronic Conditions (moderate GRADE quality of evidence)
4a.2.2 (Re-)establish patients on long-term COPD maintenance bronchodilator therapy before discharge, including continuing or resuming use of hand-held inhalers.	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
4a.2.3 As should be done at every transition, review and reconcile patients' full range of medications before discharge. Ensure that patients understand their medication therapy, including when to stop corticosteroids if prescribed.	Based on GOLD and NICE (level D evidence); modified by the expert advisory panel
4a.2.4 Assess the patient's inhaler technique before discharge.	Based on GOLD; modified by the expert advisory panel
4a.2.5 Provide a comprehensive self-management plan for patients, including education and case management,[9] with or without a written action plan. Action plans[10] in isolation cannot	Based on Action Plans for Individuals with Chronic Obstructive Pulmonary Disease (COPD) (moderate GRADE quality of evidence); modified by expert advisory panel

[8]Based on the included studies, individualized predischarge planning should be a multicomponent intervention, including some combination of the following: discharge assessment and planning (that commences as early during the admission as possible); patient education component; patient-centred discharge instructions; and coordination/communication with family physicians and other appropriate community-based services.
[9]*Case management* refers to structured follow-up and/or communication with health care professionals with a particular focus on changes to the patient's signs and symptoms, advising on appropriate interventions, referring to physicians and recommending the initiation of therapy to reduce or prevent the risk of serious acute exacerbations of COPD. Communication can be in person, telephone, or other technology not including biomonitoring or teletechnology.
[10]A written communication tool "to help those with COPD prevent and manage exacerbations in conjunction with the healthcare professional team (the physician, the certified respiratory educator and the pharmacist)." (Canadian Thoracic Society, 2013 COPD Action Plan)

Module 4a Recommended Practices	Contributing Sources of Evidence
be recommended at this time due to inconsistency in the evidence of safety and effectiveness. If used, action plans should be developed according to the Canadian Thoracic Society guidelines, with special attention to the cautions and warnings.	Based on CTS 2013 COPD Action Plan
4a.2.6 COPD patients with functional disabilities (e.g., shortness of breath when walking) should begin therapy in an evidence-based pulmonary rehabilitation program within 1 month following hospital discharge for an acute exacerbation of COPD, consistent with OHTAC's recommendations:	Based on OHTAC for HQO EBA on pulmonary rehabilitation for COPD; consistent with CTS (level 1A evidence), GOLD and NICE
OHTAC recommends the use of pulmonary rehabilitation in patients following an acute exacerbation (within 1 month of hospital discharge).	Taken from OHTAC for HQO EBA on pulmonary rehabilitation for COPD (moderate GRADE quality of evidence)
4a.2.7 COPD patients who smoke should receive smoking cessation counselling while in hospital, with the goal of referral to longer-term, intensive smoking cessation counselling (including appropriate pharmacotherapy) in the outpatient setting. This may include providing information to patients with contact information/instructions for resources or other guidance. This is consistent with OHTAC's recommendation:	Based on CTS (level 1A evidence), GOLD (level A evidence), and NICE (level A evidence); modified by the expert advisory panel
OHTAC strongly endorses evidence-based strategies aimed at encouraging smoking cessation in patients with COPD. Intensive counselling (≥ 90 minutes) is the most effective and cost-effective strategy, and should continue to be encouraged.	Taken from OHTAC for HQO EBA on smoking cessation for COPD patients
4a.2.8 If the patient does not have a regular PCP, ensure they are connected with one before discharge. If no PCP is available in the community, the patient may need support from hospitalists, specialists, or home care providers.[11]	Based on expert advisory panel consensus
4a.2.9 Patients without up-to-date influenza (annual) or pneumococcal vaccinations should either be vaccinated before discharge or referred for vaccination following discharge, unless contraindications are present. This is consistent with OHTAC's recommendation:	Based on GOLD, CTS, and NICE; modified by the expert advisory panel
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.	Taken from OHTAC for HQO EBA on vaccination for COPD patients (high GRADE quality of evidence: influenza-related respiratory illness and incidence of pneumococcal pneumonia; low GRADE quality of evidence: hospitalizations, length of stay, need for ventilation, adverse reactions)
• Annual influenza vaccination should be offered to all patients unless contraindicated.	Based on expert advisory panel; consistent with OHTAC for HQO EBA on vaccination for COPD patients, CTS (level 2A evidence), GOLD (level A evidence), and NICE
• A pneumococcal vaccine may be considered for all patients with COPD.	Based on expert advisory panel; consistent with OHTAC for HQO EBA on vaccination for COPD patients, CTS (level 3C evidence), GOLD (level B evidence), and NICE
4a.3 Transition to Community-Based Care	
4a.3.1 All patients who qualify for home oxygen should be discharged on home oxygen.	Based on expert advisory panel consensus

[11] *Home care provider* includes both community care access centres and independent home care agencies.

Module 4a Recommended Practices	Contributing Sources of Evidence
4a.3.2 Ensure that patients are supported by home care providers[11] with appropriate home care services in the community after discharge.	Based on expert advisory panel consensus; consistent with GOLD and NICE (level D evidence)
4a.3.3 Where appropriate, arrange for an assessment of the patient's home or living situation by an occupational therapist following discharge.	Based on expert advisory panel consensus
4a.3.4 Ensure patients have a follow-up appointment with a PCP, respirologist, or internist within 1 to 2 weeks of discharge.	Based on expert advisory panel consensus
4a.3.5 If prophylactic antibiotics are appropriate for a moderate-severe COPD patient who is at increased risk for future exacerbation despite optimal treatment, the potential benefit (for exacerbation rate and duration) and potential risks (gastrointestinal side effects, hearing impairment, and antibiotic resistance associated with a course of prophylactic azithromycin) should be discussed.	Based on Prophylactic Antibiotics for Individuals With Chronic Obstructive Pulmonary Disease (COPD) (very low to moderate GRADE quality of evidence): The evidence highlighted a general trend of beneficial effect on patients' COPD exacerbation rate and yielded uncertainty around risk of adverse events and antibiotic resistance associated with prophylactic azithromycin therapy.
• In the event of bacterial infection in a patient on prophylactic azithromycin, assume that the bacteria will be resistant to all macrolides.	Based on expert advisory panel consensus
4a.3.6 Ensure the patient's circle of care including PCP, home care providers[11] and pharmacist receive a copy of the care plan.[12]	Based on expert advisory panel consensus
4a.3.7 In some cases, direct communication between hospital staff and the PCP and/or home care coordinator[13] is recommended.	Based on expert advisory panel consensus

Abbreviations: BODE, body mass index, obstruction, dyspnea, exercise capacity; CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; EBA, evidence-based analysis; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; HQO, Health Quality Ontario; LACE, length of stay in hospital, acuity of admission, comorbidities, emergency department visits during previous 6 months; MRC, Medical Research Council; NICE, National Institute for Health and Clinical Excellence; OHTAC, Ontario Health Technology Advisory Committee; PCP, primary care provider.

[12] *Discharge plan* refers to the official hospital documentation including the dictated details of the hospital episode and full care plan. *Care plan* refers to a package of information on the patient's condition and hospital episode including issues identified, medications related and unrelated to COPD, and all planned follow-up appointments and referrals.

[13] *Home care coordinator* refers to the person responsible for coordinating home care services through home care agencies.

Module 4a Implementation Considerations
• Encouraging patients to stop smoking should be one of the priorities of COPD management. • Core hospital services should include smoking cessation counselling while patients are in the hospital. • At admission, discussions with patients and caregivers regarding entry to the CAMH STOP smoking cessation program should be undertaken; the program provides smoking cessation counselling, drug therapy, and/or nicotine replacement therapy free of charge. • Where a CAMH STOP smoking cessation program is not available, patients should be referred to a smoking program in a local community. • To reduce ED visits and inpatient readmissions, hospitals should have a patient education and patient-centred health literacy program which includes, in plain language, how to live with COPD and smoking cessation. • Education materials for patients and caregivers should be similar to the materials distributed in the community. • Prior to patients' discharge from hospital, staff should ask the patient how they will pay for medications. Patients without insurance coverage for drugs may be at risk of noncompliance if they have difficulty affording their medications. • Discharge planning aims to build a link between hospital and community care, with the potential to reduce hospital length of stay and unplanned readmissions. Service providers should do the following when undertaking discharge planning: – Confirm the preferred maintenance therapy and gauge patients' daily care practices and assess patients' knowledge of proper inhaler technique. – Arrange follow-up and home care. – Provide clear instructions about appropriate medication usage (including patients' knowledge of proper inhaler technique) and potential adverse effects. – Formally assess activities of daily living if concerns remain about how the individual will cope at home. – Ensure that hospitals identify or establish services to review people admitted to hospital with a COPD exacerbation within 1 to 2 weeks following discharge. – Ensure that discharge plans identify the cause of admission and treatment provided so that the PCP can assist in ensuring the appropriate community-based service. • Medication reconciliation should take place on discharge. A copy of medications should be provided to patients and caregivers, sent to PCPs, and where known, to the community pharmacist.

Abbreviations: CAMH, Centre for Addiction and Mental Health; COPD, chronic obstructive pulmonary disease; ED, emergency department; PCP, primary care provider; STOP, Smoking Treatment for Ontario Patients.

Postacute, Community-Based Episode of Care

The model of the postacute, community-based episode of care for COPD in Figure 5 was developed by the Postacute, Community-Based COPD Expert Advisory Panel and served as a working model as the components of this episode of care were delineated. Beginning as a simplified sketch of key phases in the community-based COPD episode of care (e.g., discharge, follow-up, pulmonary rehabilitation, deterioration, maintenance), the model has been modified to reflect the elements of the pathway determined by the panel.

The Postacute, Community-Based COPD Expert Advisory Panel emphasized that it is essential that all members in the circle of care function in a holistic, integrated fashion. Community-based COPD care involves many providers and the goal is to provide multidisciplinary care. The expert advisory panel encourages providers to function as an interdisciplinary team with coordinated provision and integration of care and full communication across providers. The panel was challenged by separating the assignment of responsibility (e.g., registered respiratory therapist) from the settings where care activities take place (e.g., in a specialized COPD clinic). Given the complexity of care in the community, the expert advisory panel emphasized the required standard care activities, recognizing that they may be provided by various qualified professionals in a number of appropriate locations based on geography and resource availability.

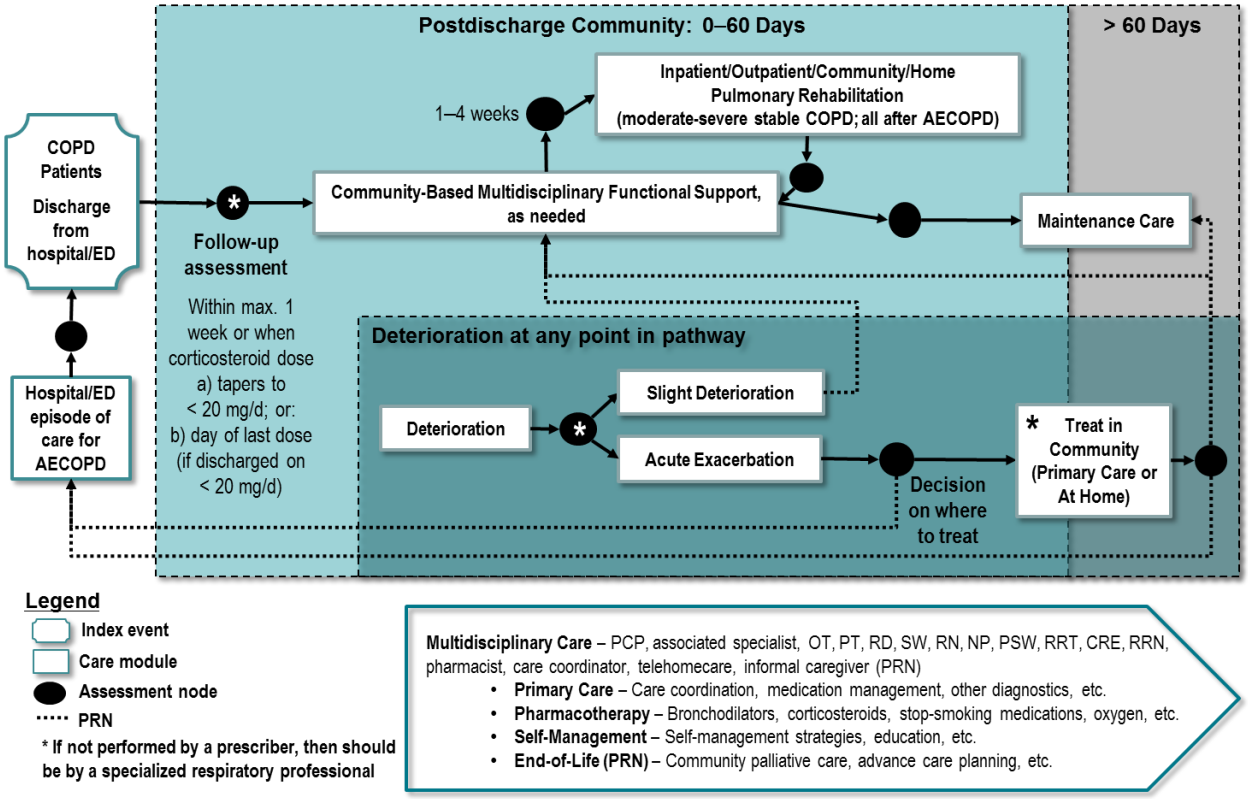


Figure 5: Episode-of-Care Model for Postacute, Community-Based COPD

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; CRE, certified respiratory educator; ED, emergency department; NP, nurse practitioner; OT, occupational therapist; PCP, primary care provider; PT, physiotherapist; PRN, as needed; PSW, personal support worker; RD, registered dietitian; RN, registered nurse; RRN, rapid response nurse; RRT, registered respiratory therapist; SW, social worker.

In the recommendations that follow, please refer to Figure 3, page 37, for the module numbers within the continuum of care for COPD.

Module 4b. Transition to Postacute, Community-Based Care

As noted in Module 4a, there is overlap among the recommendations in Module 4 because 4a (Predischarge Planning) was used as basis for the development of the postacute COPD episode of care by the Postacute, Community-Based COPD Expert Advisory Panel. This module identifies recommended practices for the transition from hospital to community. The recommendations emphasize adhering to standard practices of transitional care planning to ensure patients are properly supported and followed after discharge.

Module 4b Recommended Practices	Contributing Sources of Evidence
4b.1 Predischarge	
4b.1.1 Predischarge activities should include a full clinical assessment and individualized discharge plan[14] and should prepare patients with all appropriate skills and follow-up referrals in the community.	Taken from HQO Clinical Handbook for COPD (2013), Module 6
4b.2 Transitional Care Planning	
4b.2.1 Transitional care plans are developed using a standardized approach. The plan: • includes essential education on health conditions, medications, and instructions to the patient • is easy to read (i.e., uses plain language and is available in multiple languages) • involves patients and families/caregivers in the development of the plan • includes a home care referral as appropriate	Based on Health Links; modified by the expert advisory panel
4b.2.2 Standardized risk assessment tools should be used to assess and stratify complex patients.	Taken from Health Links
4b.2.3 Each health care organization should put in place standardized processes to ensure that, prior to transition, a post-transition follow-up appointment(s) is scheduled for patients with their primary care provider accompanied by discharge communication.	Based on Health Links; modified by the expert advisory panel

Abbreviations: COPD, chronic obstructive pulmonary disease; HQO, Health Quality Ontario.

[14] *Discharge plan* refers to the official hospital documentation including the dictated details of the hospital episode and full care plan. *Care plan* refers to a package of information on the patient's condition and hospital episode including issues identified, medications related and unrelated to COPD, and all planned follow-up appointments and referrals.

Module 4b Implementation Considerations
• Predischarge planning should commence shortly after admission to hospital. • Assessment for community-based home care, rapid assessment clinic, and rehabilitation services should commence while the patient is still in hospital. For patients who require home care services, early referral to a care coordinator through home care is essential. • Follow-up care should ideally be with a prescriber or a health care provider who has expertise in COPD management or respiratory training. • Assessment and referral to appropriate pulmonary rehabilitation services should be made (inpatient, outpatient, community-based, or home-based). • A risk assessment should be performed and steps taken to reduce the risk of readmission or presentation to the ED. • Ensure that the discharge plan identifies the cause for admission and treatment provided so that the PCP can assist in providing the appropriate community-based services.

Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; PCP, primary care provider.

Module 5: Functional Support

This module identifies recommended practices for follow-up and functional support of community-dwelling COPD patients after discharge from hospital. The recommendations emphasize connecting patients with appropriate community resources and follow-up to maximize functional independence.

Module 5 Recommended Practices	Contributing Sources of Evidence
5.1 Postdischarge Follow-Up	
5.1.1 Patients should leave the hospital with an individualized care plan,[15] and a copy should be faxed to the patient's pharmacy of choice.	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
5.1.2 Ensure patients have a follow-up appointment with a prescriber or specialized respiratory professional within maximum 1 week of discharge, or a) when steroid dose tapers to < 20 mg/day or b) on day of last steroid dose (if discharged on < 20 mg/day); and complex patients receive a phone call within 48 hours. Both the arrangement of the follow-up appointment and care plan sent to next care provider should be done at time of discharge.	Based on HQO Clinical Handbook for COPD (2013) and Health Links; modified by expert advisory panel
5.1.3 Ensure the patient, patient's PCP, associated specialist, and home care providers receive a care plan from the hospital at discharge, including full clinical assessment of the patient.	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
5.1.4 In some cases, additional direct communication between hospital staff, associated specialist, and the PCP and/or home care coordinator is recommended.	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
5.1.5 Follow-up appointment may include the following if not done in hospital before discharge: - smoking cessation counselling/pharmacotherapy (see Recommendation 5.3) - vaccination (see Recommendation 5.4)	Taken from HQO Clinical Handbook for COPD (2013)
5.1.6 Review and reconcile patients' full range of medications before discharge. Ensure that patients understand their medication therapy, including the continuation of corticosteroids and antibiotics.	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
5.1.7 Medication management including assessment of patient and medications should occur to ensure: - optimization of evidence-based/guideline-recommended medications - use of appropriate symptom-relief medications - adherence assessment (e.g., MMAS-4) - potential medication errors/misadventures	Based on expert advisory panel consensus; consistent with the HQO Clinical Handbook for Congestive Heart Failure (2014 Update) based on OHTAC heart failure clinic standards and the Canadian Cardiovascular Society guidelines
5.1.8 Medication reconciliation should be performed at all transition points in care (e.g. referrals, consults) and is recommended to occur in accordance with the HQO community home care handbook.	Based on expert advisory panel consensus and HQO Community Home Care Handbook for Postacute Medical Discharge Short-Stay Populations

[15] *Discharge plan* refers to the official hospital documentation including the dictated details of the hospital episode and full care plan. *Care plan* refers to a package of information on the patient's condition and hospital episode including issues identified, medications related and unrelated to COPD, and all planned follow-up appointments and referrals.

Module 5 Recommended Practices	Contributing Sources of Evidence
5.2 Referrals, Multidisciplinary Care, and Home Care	
5.2.1 The expert advisory panel recommends multidisciplinary care for COPD patients, consistent with OHTAC's recommendation:	Based on expert advisory panel consensus
OHTAC recommends ongoing access to existing community-based multidisciplinary care for the management of moderate to severe stable COPD.	Consistent with OHTAC for HQO EBA on community-based multidisciplinary care for COPD (moderate to very low GRADE quality of evidence)
5.2.2 A care coordinator must ensure that the right services are provided to the right clients at the right time, working with relevant health care providers to deliver comprehensive care that addresses as many of the patient's health care and psychosocial needs as possible. The multidisciplinary team: - may include (as needed) PCP, associated respiratory specialist or internist, occupation therapist, physiotherapist, registered dietitian, social worker, registered nurse, nurse practitioner, personal support worker, registered respiratory therapist, certified respiratory educator, rapid response nurse, pharmacist, care coordinator, telehomecare provider, and/or informal caregiver - should be responsible for assessment, care planning and treatment, advising on self-management, education, monitoring, and identifying high risk patients	Taken from HQO Community Home Care Handbook for Postacute Medical Discharge Short-Stay Populations and from HQO EBA on community-based multidisciplinary care for COPD (moderate to very low GRADE quality of evidence) Based on expert advisory panel consensus
5.2.3 Refer patient/caregiver for consultation/social services as appropriate.	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel; consistent with NICE (level D evidence) and VA/DoD (level I evidence)
5.2.4 Care coordination is recommended in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
5.2.5 Nursing assessment and monitoring, wound care, intravenous therapy, incontinence, medication reconciliation, and nonpalliative pain management are recommended to occur in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
5.2.6 Physiotherapy services are recommended to be provided in accordance with HQO community home care handbook. (See also Module 6, Pulmonary Rehabilitation.)	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
• There is insufficient evidence to recommend for or against airway clearance techniques to clear mucus and secretion in stable COPD patients.	Based on Airway Clearance Techniques for Individuals With Stable Chronic Obstructive Pulmonary Disease (COPD) (low quality of evidence): 13 of the 19 studies showed improvement through the use of airway clearance techniques for patients with stable COPD (for exacerbations, hospitalizations, health-related quality of life, pulmonary function, gas exchange, symptoms, sputum clearance, exercise tolerance, or antibiotic use), but with considerable study limitations and differences in techniques examined and of generally low quality; modified by expert advisory panel
5.2.7 Home safety support services are recommended to be provided in accordance with the HQO community home care handbook. (See also Module 6, Pulmonary Rehabilitation.)	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
5.2.8 Respiratory therapy services are recommended to be made accessible and be provided in accordance with HQO community home care handbook. (See also Module 6, Pulmonary Rehabilitation.)	Based on Respiratory Therapy Services in Home Care for Individuals With Chronic Obstructive Pulmonary Disease (COPD) (moderate-serious risk of bias) COPD educational strategies did not have an effect on HRQOL, compared with usual care, whereas a community-based COPD-specific disease management program led by an RT reduced ED visits and hospitalizations and led to a smaller decline in HRQOL over a 1-year period, compared with usual care; consistent with HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations

Module 5 Recommended Practices	Contributing Sources of Evidence
5.2.9 Caregiver and family support interventions are recommended to be provided in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
5.2.10 Mental health support services are recommended to be provided in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Short-Stay Post-Acute Medical Discharge Populations
5.2.11 Personal support services are recommended to be provided in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Short-Stay Post-Acute Medical Discharge Populations
5.3 Smoking Cessation	
5.3.1 While in hospital, COPD patients who smoke should receive smoking cessation counselling and be considered for initiation of appropriate pharmacotherapy, with the goal of referral to longer-term, intensive smoking cessation counselling (including continuation of appropriate pharmacotherapy) in the outpatient setting. This must include providing information to patients with contact information/instructions for resources or other guidance. This is consistent with OHTAC's recommendation:	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
OHTAC strongly endorses evidence-based strategies aimed at encouraging smoking cessation in patients with COPD. Intensive counselling (≥ 90 minutes) is most effective and cost-effective strategy, and should continue to be encouraged.	Taken from OHTAC for HQO EBA on smoking cessation for COPD patients (moderate GRADE quality of evidence)
5.3.2 Smoking cessation counselling by physicians and other health professionals is recommended for all COPD patients. Even brief interventions (e.g., 3 minutes) should be offered at every opportunity.	Based on CTS (level 1A evidence), NICE (level A evidence), and GOLD (level A evidence); modified by expert advisory panel
5.3.3 All smokers should be considered for cessation medications (e.g., nicotine replacement therapy, buproprion, varenicline, as appropriate) to aid in maximizing quit rates, unless contraindicated, building on OHTAC's recommendation:	Based on VA/DoD (level A evidence) and NICE (level B evidence); modified by expert advisory panel
OHTAC recommends buproprion or nicotine replacement therapies for smoking cessation.	Taken from OHTAC for HQO EBA on smoking cessation for COPD patients (low GRADE quality of evidence)
5.3.4 All patients should be counselled not to smoke and to avoid second-hand smoke.	Based on VA/DoD (level A evidence); modified by expert advisory panel
5.3.5 Smokers should be assessed for willingness to quit at every health care encounter and then referred to formalized smoking cessation programs including programs that offer nicotine replacement therapy, when appropriate (i.e., contemplative and preparation stages).	Based on VA/DoD (level C evidence); modified by expert advisory panel
5.4 Vaccination	
5.4.1 Patients without up-to-date annual influenza or pneumococcal vaccinations should either be vaccinated before discharge or referred for vaccination following discharge, unless contraindications are present. This is consistent with OHTAC's recommendation:	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
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.	Taken from OHTAC for HQO EBA on vaccination for COPD patients (high GRADE quality of evidence: influenza-related respiratory illness and incidence of pneumococcal pneumonia; low GRADE quality of evidence: hospitalizations, length of stay, need for ventilation, adverse reactions)

Module 5 Recommended Practices	Contributing Sources of Evidence
• Annual influenza vaccination should be offered to all patients unless contraindicated.	Based on expert advisory panel; consistent with OHTAC for HQO EBA on vaccination for COPD patients, CTS (level 2A evidence), VA/DoD (level A evidence), and GOLD (level A evidence)
– Inactivated influenza vaccines should be used	Taken from VA/DoD (level A evidence)
– Optimal vaccination time is October–November.	Taken from VA/DoD (level A evidence)
• A pneumococcal vaccine may be considered for all patients with COPD.	Based on expert advisory panel; consistent with OHTAC for HQO EBA on vaccination for COPD patients and CTS (level 3C evidence)
5.5 Management of Comorbidities	
• **5.5.1** Comorbidities are common in COPD and may affect function and should be treated appropriately. The presence of comorbidities should trigger a referral to a specialist.	Based on expert advisory panel consensus
5.5.2 Treat the following according to usual guidelines, unless contraindicated: • cor pulmonale • ischemic heart disease, heart failure, and atrial fibrillation • hypertension • osteoporosis • lung cancer • infections • metabolic syndrome/diabetes	Taken from GOLD (level D evidence)
5.5.3 Further investigation into the role of cognitive-behavioural therapy among treatment options for anxiety and depression in COPD is needed. Health care providers should be aware of the high risk of these disorders in COPD patients and should follow OHTAC's recommendation:	Cognitive-Behavioural Therapy for Anxiety and Depression in Individuals With Chronic Obstructive Pulmonary Disease (COPD): • Cognitive-behavioural therapy did not significantly reduce symptoms of anxiety or depression in patients with mild to severe COPD, compared with usual care or education. (GRADE: Low) • Based on 4 randomized controlled trials with considerable limitations due to risk of bias, cognitive-behavioural therapy had mixed effectiveness on improving the quality of life of patients with moderate to severe COPD, compared with usual care, wait list controls, or education.
OHTAC does not recommend routine screening[16,17] for depression among adults with chronic disease. Health care providers should be aware of the increased rates of depression in this population and should use a higher index of suspicion when assessing these patients.	Taken from OHTAC for HQO EBA on screening and management of depression for adults with chronic diseases
5.6 Self-Management and Education	
5.6.1 Action plans[18] in isolation cannot be recommended at this time due to inconsistency in the evidence of safety and effectiveness. This may be an area warranting reconsideration should new evidence become available. If used, action plans should be developed according to the Canadian Thoracic	Action Plans for Individuals with Chronic Obstructive Pulmonary Disease (COPD) (moderate GRADE quality of evidence); modified by expert advisory panel

[16]OHTAC recognizes the significant burden that depression places on affected individuals and the importance of treating this condition. OHTAC also recognizes the increased prevalence of depression among individuals with chronic diseases, such as heart disease, diabetes, chronic obstructive pulmonary disease, and stroke.
[17]Routine screening occurs at a specific frequency (e.g., annually).
[18]A written communication tool "to help those with COPD prevent and manage exacerbations in conjunction with the healthcare professional team (the physician, the certified respiratory educator and the pharmacist)." (Canadian Thoracic Society, 2013 COPD Action Plan)

Module 5 Recommended Practices	Contributing Sources of Evidence
Society guidelines, with special attention to the cautions and warnings.	Based on CTS 2013 COPD Action Plan
5.6.2 Self-management and education packages separate from pulmonary rehabilitation need to be provided at discharge or by the health care worker who sees them within 1 week and be disease-specific, including:	Based on expert advisory panel consensus
• skills training (e.g., breathing techniques)	Taken from CTS (level 1A evidence); consistent with NICE (level A evidence)
• education on medications, devices, and triggers	Taken from VA/DoD (level I evidence)
• how to deal with acute exacerbations as well as other aspects of managing the disease	Taken from NICE (level B evidence) and VA/DoD (level I evidence)
• how to cope with comorbidities	Based on expert advisory panel consensus
5.6.3 Relevant components of self-management and patient education should be provided in accordance with the HQO community home care handbook.	Based on HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations; modified by expert advisory panel
5.7 Nutrition, Weight Monitoring, and Lifestyle	
5.7.1 Body mass index (BMI) needs to be monitored to determine if it is in the normal range (ideal range, 20–25). Large fluctuations in weight (e.g., 10% of body weight or 2.5 kg) should be investigated for alternative causes and referred to a registered dietitian for dietary evaluation and consultation if no other clear cause is found.	Based on VA/DoD (level B evidence) and NICE (level D evidence); modified by expert advisory panel
5.7.2 Nutrition support and dietitian services are recommended to be provided in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
5.7.3 Healthy lifestyle should be encouraged and all patients should be provided with strategies to optimize exercise capacity.	Based on CTS (level 3A evidence); modified by expert advisory panel
5.7.4 All stable COPD patients, regardless of severity of disease, should be physically active or engage in regular exercise.	Based on expert advisory panel consensus; consistent with HQO Clinical Handbook for Congestive Heart Failure (2013) (low GRADE quality of evidence)
5.7.5 Physical activity counselling is recommended to be provided in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations
5.7.6 Lifestyle modifications for primary and secondary prevention are recommended to be implemented in accordance with the HQO community home care handbook.	Taken from HQO Community Home Care Handbook for Postacute Short-Stay Medical Discharge Populations

Abbreviations: CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; EBA, evidence-based analysis; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HQO, Health Quality Ontario; MMAS-4, Morisky Medication-Taking Adherence Scale, 4-item; NICE, National Institute for Health and Clinical Excellence; OHTAC, Ontario Health Technology Advisory Committee; PCP, primary care provider; VA/DoD, Department of Veterans Affairs/Department of Defense.

Module 5 Implementation Considerations
Follow-Up Care • Hospital-based staff should make follow-up contact with the patient within 48 hours of discharge. • For patients without a PCP, consider referral to Health Care Connect prior to discharge to reduce postdischarge wait times. Where a patient's PCP is not known, follow-up should be expedited by referral, based on local resources, to a respirologist, walk-in clinic, new PCP for chronic care, or a nurse practitioner. • If a home care nurse practitioner is available, a connection should be considered as a temporary measure, but only after patients have a referral to Health Care Connect and if they do not have access to a local walk-in clinic for follow-up. • Medication reconciliation should be completed by the PCP and where possible by the appropriate home care provider in a patient's home. Results of the medication reconciliation should be shared between home care and PCP. In order to increase adherence to medication management, pharmacists should consider blister-packing medications and providing patient and caregiver importance of medication compliance education. • The postdischarge care plan should include management of comorbidities. The care plan should be reviewed and updated by the patient's PCP. The Toronto Health Economic and Technology Assessment (THETA) Collaborative evaluation of telehomecare will be reviewed after its completion, with recommendations to follow
Smoking Cessation • Smoking cessation strategies specifically for patients with COPD should be developed and implemented. Targeted materials and messaging on smoking cessation should be stressed with all COPD patients who are current smokers, as smoking cessation has been shown to have a significantly positive and immediate clinical impact for these patients. • Patients and caregivers should be informed about the effects of second-hand smoke on the patient's health. • NRT should become a free benefit to any Ontario resident with an OHIP card. • Public health departments should provide free NRT under the STOP program; pharmacies should be permitted to do the same after screening patients. • Drug therapy for smoking cessation should be made available at no cost to all Ontarians with a prescription by a physician. • Patients covered by the Ontario Drug Benefit should be informed at discharge that they are entitled to a series of face-to-face smoking cessation sessions. (Smoking Cessation Task Force).
Screening and Education, Self-Management, and Lifestyle • Standardized self-management education materials should be available and used both in the hospital and community to ensure consistent messages to patients and caregivers. At a minimum, patient education materials should include skills training (e.g., breathing techniques), education on medication, how to deal with acute exacerbations, and how to access care when intervention is required. • The CAMH behaviour modification program, which targets the "universal 6 pack" (smoking, diet, sleep, exercise, stress, and alcohol), should be explored for province-wide implementation. • The Ministry of Health and Long-Term Care and Public Health Ontario should widen public awareness programs on vaccination to increase immunization rates.

Abbreviations: CAMH, Centre for Addiction and Mental Health; COPD, chronic obstructive pulmonary disease; NRT, nicotine replacement therapy; OHIP, Ontario Health Insurance Plan; PCP, primary care provider; STOP, Smoking Treatment for Ontario Patients.

Module 6: Pulmonary Rehabilitation

This module identifies recommended practices for pulmonary rehabilitation (PR) programs for COPD patients. The recommendations emphasize access to a PR program, its components, and enabling patients to maintain the benefits over time.

Module 6 Recommended Practices	Contributing Sources of Evidence
6.1 Target Population	
6.1.1 The expert advisory panel agrees with OHTAC's recent recommendations on pulmonary rehabilitation:	Based on expert advisory panel consensus
OHTAC reaffirms the recommendations it made in 2012, namely: • ongoing access to existing pulmonary rehabilitation for the management of moderate to severe chronic obstructive pulmonary disease (COPD) in stable patients, and • the use of pulmonary rehabilitation in patients following an acute exacerbation (within 1 month of hospital discharge).	Taken from OHTAC for HQO EBA on pulmonary rehabilitation for COPD (moderate GRADE quality of evidence)
Further, based on a field evaluation study, OHTAC recommends increased availability of resources for pulmonary rehabilitation following discharge for patients who have had an acute exacerbation of COPD.	Taken from OHTAC for HQO Pulmonary Rehabilitation in Ontario: A Cross-Sectional Survey
6.1.2 Access needs be improved for all appropriate patients including:	Taken from CTS (level 2A evidence)
• all patients with moderate to severe COPD	Taken from GOLD (level A evidence); consistent with VA/DoD (level A evidence)
• stable patients with dyspnea exercise limitation, fatigue, or functional disability	Taken from CTS (level 1A evidence); consistent with VA/DoD (level A and B evidence) and ACP (moderate quality of evidence)
• patients with recent acute exacerbation (PR should begin, within 1 to 4 weeks of discharge)	Based on OHTAC for HQO EBA on pulmonary rehabilitation for COPD (moderate GRADE quality of evidence); modified by the expert advisory panel
6.1.3 Contraindications for pulmonary rehabilitation may include inability to walk, unstable angina, recent myocardial infarction, and reduced cognition.	Based on NICE (level D evidence); modified by the expert advisory panel
6.2 Pulmonary Rehabilitation Program	
6.2.1 Pulmonary rehabilitation is recommended for COPD patients at an accessible and clinically appropriate location (inpatient, outpatient, community, or home).	Based on Pulmonary Rehabilitation in the Home Versus Other Settings for Individuals With Chronic Obstructive Pulmonary Disease (COPD) (very low GRADE quality of evidence): There were no significant differences between home versus outpatient pulmonary rehabilitation for the outcomes of exercise capacity and health-related quality of life for COPD; and only one published study compared the costs and quality-adjusted life years (QALYs) of pulmonary rehabilitation across different settings and showed that hospital-based pulmonary rehabilitation is more costly and more effective than community-based pulmonary rehabilitation (no reason for the difference in QALYs was proposed); consistent with HQO Clinical Handbook for COPD (2013)

Module 6 Recommended Practices	Contributing Sources of Evidence
Centre-based pulmonary rehabilitation is preferred for access to exercise equipment and additional psychosocial support provided in a group setting. Outpatient or community-based pulmonary rehabilitation is more cost-effective than home-based programs. Home-based pulmonary rehabilitation may be recommended for those with barriers to participation in centre-based programs, and the services can be consolidated under the role of a single health care professional with expertise in pulmonary rehabilitation. The components at a centre can be delivered by health care professionals trained in exercise and specialized in respiratory care.	Based on Pulmonary Rehabilitation for Postacute Exacerbations of Chronic Obstructive Pulmonary Disease: A Cost-Effectiveness and Budget Impact Analysis[19]
According to evidence-based COPD guidelines, components of pulmonary rehabilitation include supervised aerobic and resistance and strength training to increase exercise capacity and functional status; education and self-management components; nutrition, psychological, and behavioural interventions; and should be delivered in a multicomponent, multidisciplinary, and individualized program of at least 6 to 8 weeks in duration.	Based on NICE (level A) and Va/DoD (level A and B evidence); modified by expert advisory panel
A standardized pulmonary rehabilitation program is about 40 hours in total, with 3 sessions per week at 1.5 to 2 hours per session.	Based on expert advisory panel consensus
Optimal treatment improves the effectiveness of pulmonary rehabilitation, and maintenance of gains requires subsequent exercise training.	Based on GOLD (level B evidence) and VA/DoD (level B evidence); modified by expert advisory panel
6.2.2 The expert advisory panel recognizes uncertainty in the evidence and agrees with OHTAC's recommendation that:	Taken from OHTAC for HQO EBA on pulmonary rehabilitation for COPD (low GRADE quality of evidence)
There is insufficient evidence for maintenance pulmonary rehabilitation programs. Due to substantial uncertainty arising from low/very low quality of evidence of effectiveness and cost-effectiveness, but the potential for important health system and/or patient/clinical benefits, OHTAC recommends a field evaluation for pulmonary rehabilitation maintenance.	
6.2.3 COPD patients who have completed pulmonary rehabilitation are recommended to transition to an exercise program to support the maintenance of functional gains, but parameters of delivery still need to be decided.	Based on Exercise Programs After Pulmonary Rehabilitation for Individuals With Chronic Obstructive Pulmonary Disease (COPD) (low to very low GRADE quality of evidence): There was a significant benefit to exercise capacity for those enrolled in a maintenance exercise program compared to those in usual care at 6 months but not 12 months of follow-up. There was no difference in health-related quality of life at 6 months of follow-up or 12 months of follow-up.

Abbreviations: ACP, American College of Physicians; COPD, chronic obstructive pulmonary disease; CTS, Canadian Thoracic Society; EBA, evidence-based analysis; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HQO, Health Quality Ontario; NICE, National Institute for Health and Clinical Excellence; OHTAC, Ontario Health Technology Advisory Committee; PR, pulmonary rehabilitation; VA/DoD, Department of Veterans Affairs/Department of Defense.

[19]Xie X, Wang M, Schaink A, Krahn M. Pulmonary rehabilitation for postacute exacerbations of chronic obstructive pulmonary disease (COPD): a cost-effectiveness and budget impact analysis. Toronto: Health Quality Ontario. In press.

Module 6 Implementation Considerations
• Pulmonary rehabilitation must be accessible to all appropriate individuals with COPD, including those who have had a recent hospitalization for an acute COPD exacerbation. A centre-based PR program is considered to be more efficient than home-based rehabilitation. • Provincially standardized criteria for referral to pulmonary rehabilitation should be in place or developed. • A provincial intensity or stratification tool for pulmonary rehabilitation should be developed (inpatient, outpatient, community, or home-based). • Home-based pulmonary rehabilitation for COPD, when taught by a health care professional and properly conducted may be offered as an alternative to outpatient-based pulmonary rehabilitation to improve access in situations of limited resources and availability. All patients receiving home-based pulmonary rehabilitation should have a formal program of home exercise developed. • Key components of pulmonary rehabilitation programs should be implemented province-wide and should, at a minimum, include aerobic and resistance training to increase exercise capacity and functional status, education and self-management components, nutrition, and psychological and behavioural interventions, and should be delivered in a multicomponent, multidisciplinary, and individualized program of at least 6 to 8 weeks duration. • Consideration should be given to expanding existing volunteer driver programs to assist patients in travelling to a centralized rehabilitation program. • All health care providers involved in the delivery of pulmonary rehabilitation programs should complete a certification course to ensure training in core competencies. • The Ministry of Health and Long-Term Care should fund Health Quality Ontario's pulmonary rehabilitation implementation plan, submitted in September 2014.

Abbreviations: COPD, chronic obstructive pulmonary disease; PR, pulmonary rehabilitation.

Module 7: Pharmacotherapy

This module identifies recommended practices for the use of drugs in the treatment of COPD patients in the community. The recommendations emphasize optimizing pharmacotherapy treatment.

Module 7 Recommended Practices	Contributing Sources of Evidence
7.1 Inhaled Pharmacotherapy Delivery System	
7.1.1 Treatment can be optimized with bronchodilation therapy, inhaled steroids, and/or oral steroids.	Based on expert advisory panel consensus
7.1.2 (Re-)establish patients on their long-term COPD maintenance bronchodilator therapy before discharge, including continuing or resuming use of hand-held inhalers (metered dose inhalers or dry powder inhalers).	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
7.1.3 A dedicated person such as a registered respiratory therapist or nurse or pharmacist should assess the patient's inhaler technique and ensure they can demonstrate proficiency before discharge.	Based on HQO Clinical Handbook for COPD (2013); modified by expert advisory panel
7.1.4 Metered dose inhalers with spacers and/or dry powder inhalers are the preferred delivery systems; nebulisers should be considered second-line treatment.	Taken from HQO Clinical Handbook for COPD (2013) (expert opinion)
7.1.5 The delivery method of inhaled therapy should be tailored to the patient's or caregiver's ability to use the inhaler. Provide necessary equipment, servicing (e.g., nebuliser, spacer cleaning monthly), advice, and support.	Taken from NICE (level D evidence)
7.1.6 Inhalers • Preferred delivery of bronchodilator therapy is by hand-held inhaler, with or without a compatible spacer as appropriate for each patient and dose of medication; patients should be trained on the specific device and assessed for proper technique.	Taken from NICE (level D evidence)
• Patients should be changed to hand-held inhaler as soon as they are stabilized after acute exacerbations.	Taken from NICE (level D evidence)
• Ensure continued supervision of the patient during delivery of the medication.	Taken from HQO Clinical Handbook for COPD (2013) (expert opinion)
7.1.7 Both inhalers and, secondarily, nebulisers can be used to deliver inhaled therapy during acute exacerbations.	Taken from NICE (level A evidence)
7.2 Pharmacotherapy Regimens	
7.2.1 Patients should be treated with bronchodilators, corticosteroids, methylxanthines, antibiotics, phosphodiesterase-4 inhibitors and/or other necessary pharmacotherapy according to the Canadian Thoracic Society recommendations, as applicable.	Based on expert advisory panel consensus

Abbreviations: COPD, chronic obstructive pulmonary disease; HQO, Health Quality Ontario; NICE, National Institute for Health and Clinical Excellence.

Module 8: Maintenance

This module identifies recommended practices for ongoing support and follow-up of patients after they have transitioned into the community. The recommendations emphasize reassessing patients to respond to any ongoing treatment needs and to monitor their overall status.

Module 8 Recommended Practices	Contributing Sources of Evidence
8.1 Ongoing Follow-Up	
8.1.1 Treatment decisions should be individualized and guided by symptom severity and updated at follow-up.	Based on CTS (level 3A evidence); modified by the expert advisory panel
8.1.2 Periodic follow-up should be conducted 1 to 2 times per year or more frequently if needed.	Taken from NICE (level D evidence); consistent with VA/DoD (level I evidence)
8.1.3 Assessment components include symptoms, treatment (including proper inhaler technique), spirometry, smoking cessation, inquiring about ability to carry out ADLs and IADLs, assessing the need for occupational therapy (validated tools), and inquiring about the ability for patients to recognize the signs and symptoms of a flare-up or deterioration in condition.	Based on NICE (level D evidence); modified by expert advisory panel; consistent with VA/DoD (level I evidence)
8.2 Oxygen Therapy	
8.2.1 Patients who may need home oxygen should be tested to determine if it is required. All patients who have a clinical need should be discharged on home oxygen and be reassessed at a later date when clinically stable.	Based on expert advisory panel consensus
• Assistive Device Program Medical Eligibility Criteria for home oxygen therapy include hypoxemia at rest, hypoxemia at exertion, bronchopulmonary dysplasia, and palliative care.	Taken from Ministry of Health and Long-Term Care, Home Oxygen Therapy Policy and Administration Manual (2014)
8.2.2 Patients on oxygen therapy should be reassessed for ongoing need after 90 days.	Based on expert advisory panel consensus
8.2.3 Patients should be treated with oxygen therapy according to the Canadian Thoracic Society recommendations, as applicable.	Based on expert advisory panel consensus
8.3 Surgery and Transplantation	
8.3.1 Patients with severe to very severe airway obstruction, as measured by $FEV_{1,}$ who meet other clinical eligibility criteria should be referred to a specialist for surgical or transplant consultation.	Based on expert advisory panel consensus

Abbreviations: ADL, activity of daily living; CTS, Canadian Thoracic Society; FEV_1, forced expiratory volume in 1 second; IADL, instrumental activity of daily living; NICE, National Institute for Health and Clinical Excellence; VA/DoD, Department of Veterans Affairs/Department of Defense.

Module 9: Deterioration/Exacerbation

This module identifies recommended practices for the decisions surrounding treatment of community-dwelling patients who experience a deterioration or an acute exacerbation of their condition. The recommendations emphasize assessing the patient and their circumstances to inform clinical decision-making on the most appropriate treatment trajectory.

Module 9 Recommended Practices	Contributing Sources of Evidence
9.1 Decision on Where to Treat	
9.1.1 The decision to admit relies largely on clinical judgment and availability of local resources. Use the NICE and/or GOLD criteria below as a guide: • failure of an exacerbation to respond to initial medical management • insufficient home support, inability to cope at home • breathlessness or marked increase in intensity of symptoms, such as development of resting dyspnea • general condition and severe underlying COPD • decreased level of activity • cyanosis • worsening peripheral edema or onset of new physical signs (e.g., cyanosis, fatigue, inability to stand) • decreased level of consciousness • already receiving long-term oxygen therapy • social circumstances, older age • acute confusion • rapid rate of onset or frequent exacerbations • significant comorbidity (e.g., heart failure, newly occurring arrhythmias) • arterial oxygen saturation (SaO_2) < 90%, pH level, and partial pressure of oxygen (PaO_2) • changes on chest x-ray	Taken from HQO Clinical Handbook for COPD (2013) (expert opinion)
9.2 At-Home Management	
9.2.1 Treatment approach and considerations are the same as for treatment in hospital.	Taken from NICE (level D evidence)
9.2.2 For guidance on self-management and action plans, refer to Module 5.6.	Based on expert advisory panel consensus

Abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HQO, Health Quality Ontario; NICE, National Institute for Health and Clinical Excellence.

Module 9 Implementation Considerations
• As part of discharge education, patients and caregivers should be instructed on how to access care when required and where to present when experiencing symptoms of an acute exacerbation.

Module 10: End-of-Life Care

This module identifies recommended practices for end-stage COPD and palliative care. The recommendations emphasize advance care planning and comfort measures to support patients and informal caregivers.

Module 10 Recommended Practices	Contributing Sources of Evidence
The expert advisory panel supports OHTAC's recommendations:	Taken from OHTAC for HQO Health Care for People Approaching the End of Life: An Evidentiary Framework
10.1 OHTAC recommends that all palliative care patients have access to interprofessional, team-based, integrated, and patient-centred care at the end of life, provided directly to them across multiple venues. Optimally and where feasible, OHTAC recommends that this care be provided by the same team. Specifically, OHTAC recommends that: • Patient care planning, including advance care planning and goals of care, be discussed with patients and their informal caregivers early, frequently, and as circumstances change; • Evidence about the determinants of place of death be used to inform discussions among patients, informal caregivers, and health care providers regarding the feasibility of patients dying in their preferred location; • Patients and informal caregivers be provided education about symptom management and coping strategies, respectively; and • Education in EOL care for health care professionals be provided pre- and post-licensure, and include training on providing supportive care to informal caregivers. **10.2** OHTAC recommends that cardiopulmonary resuscitation (CPR) not be the default intervention for adults designated as palliative and for whom death is anticipated. **10.3** OHTAC calls for public debate on the normalization and demedicalization of death and dying.	
10.4 Symptom management with opioids, benzodiazepines, antidepressants, major tranquilizers, other non-opioid therapies, and oxygen when appropriate for breathlessness is recommended when patients are unresponsive to other therapies.	Based on NICE (level D evidence); modified by the expert advisory panel
10.5 If ventilation is not desired, proceed to palliative care management of the patient, consistent with OHTAC's recommendation:	Taken from HQO Clinical Handbook for COPD (2013) (expert opinion)
In making palliative care services available, the fluctuating physical, psychosocial, spiritual, and information needs should be considered, without necessarily forgoing acute care or hope of improvement during and following severe exacerbations.	Taken from OHTAC for HQO synthesis of the qualitative empirical literature on palliative care for COPD

Abbreviations: COPD, chronic obstructive pulmonary disease; EOL, end of life; HQO, Health Quality Ontario; OHTAC, Ontario Health Technology Advisory Committee; NICE, National Institute for Health and Clinical Excellence.

Module 10 Implementation Considerations
• The expert advisory panel fully endorses the OHTAC recommendations on end-of-life recommendations (June 2014) and encourages HQO to work with health system partners to develop a roll-out strategy for the OHTAC recommendations. • Once completed, the Health Links Care Coordination Tool should be fully implemented. The HQO/Ministry of Health Transformation Secretariat care coordination initiative includes a section on advance care planning and advance directives. • The Ministry of Health and Long-Term Care should fund expansion of an interdisciplinary, team-based approach to provision of end-of-life care. • Standardized education materials on end-of-life care should be developed and used in hospitals, long-term care facilities, and home care. • All health care professionals involved in the provision of end-of-life services should be appropriately trained and skill levels should be continually updated.

Abbreviations: HQO, Health Quality Ontario; OHTAC, Ontario Health Technology Advisory Committee.

System-Level Considerations

The 2 expert advisory panels on chronic obstructive pulmonary disease (COPD) agreed on the following sets of recommendations in 2 key areas: the need to expand pulmonary rehabilitation services in Ontario and the need to establish a provincial COPD network. Both are aimed at improving outcomes for patients with COPD and reducing the burden of this disease on provincial health care services.

Pulmonary Rehabilitation

Pulmonary rehabilitation (PR) refers to a multidisciplinary program of care that is designed and individually tailored to optimize physical and social performance and autonomy for patients with chronic respiratory impairment. Pulmonary rehabilitation is recommended as the standard of care in the treatment and rehabilitation of patients with COPD who remain symptomatic despite treatment with bronchodilators.

The current capacity of PR in Ontario can serve less than 2% of all COPD patients (including those classified as stable, moderate-to-severe, or post-exacerbation) who require such a program. (24) Pulmonary rehabilitation should be made available to all patients following an acute exacerbation (within 1 to 4 weeks of discharge from hospital). Patients should access the service once per year following an acute exacerbation, if needed. Focusing only on post-exacerbation patients, the expert advisory panel estimated that approximately 65% of postdischarge patients are eligible for PR. Standardized provincial criteria for referral to rehabilitation need to be developed and monitored.

Key components of a rehabilitation program should be standardized so that all patients receive access to high-quality rehabilitation regardless of the setting for delivery: in the patient's home, in an inpatient setting, or in an outpatient or community rehabilitation centre. Key components of pulmonary rehabilitation include supervised aerobic and strength training to increase exercise capacity and functional independence; education and self-management components; and nutrition, psychosocial support and behavioural interventions. They should be delivered in a multicomponent, multidisciplinary, and individualized program of at least 6 to 8 weeks in duration, with 2 to 3 sessions per week.

Program components at a centre can be delivered by health care professionals with certified expertise in the development of exercise programs and respiratory care. Consideration should be given to enhancing the existing Certified Respiratory Educator (CRE) to provide training in core competencies for all health care professionals involved in pulmonary rehabilitation. Certified health care providers can have interchangeable functional roles in the delivery of PR, except where there is a specific indication for particular expertise (e.g., respirologist).

An economic analysis of a standardized PR program may include the following main assumptions:

- The intensity and duration of PR programs are similar across outpatient hospital and community settings. Except for setting, outpatient hospital and community PR are equivalent.
- Home-based PR can be provided for select patients who cannot access centre-based PR programs due to potential barriers (e.g., accessibility, cognitive impairment, language). Home-based PR services can be consolidated under the role of a single health care professional with certified expertise in PR.

- For outpatient or community PR, exercise training and education are in group format.
- For their safety, patients are supervised for the entire PR program (i.e., no unsupervised components).
- Some core health care professionals involved in PR delivery have interchangeable functional roles (e.g., recreational therapist, physiotherapist, or kinesiologist for exercise, registered respiratory therapist or nurse/CRE for education components).

A centralized outpatient pulmonary rehabilitation clinic is preferred over home-based pulmonary rehabilitation for 2 reasons: a centralized clinic would have a multidisciplinary team and specialist access with in-depth knowledge of pulmonary rehabilitation, and program delivery in that setting has a lower cost compared to home-based pulmonary rehabilitation. (25) Transportation supports will need to be in place to support access to rehabilitation services, particularly when an outpatient or community-based rehabilitation program is the optimal model.

The expert advisory panel was in full support of OHTAC's updated (2014) recommendations on pulmonary rehabilitation:

- OHTAC reaffirms the recommendations it made in 2012, namely:
  - ongoing access to existing pulmonary rehabilitation for the management of moderate to severe COPD in stable patients, and
  - the use of pulmonary rehabilitation in patients following an acute exacerbation (within 1 month of hospital discharge).
- Further, based on a field evaluation study, OHTAC recommends increased availability of resources for pulmonary rehabilitation following discharge for patients who have had an acute exacerbation of COPD.

The pulmonary rehabilitation implementation plan that Health Quality Ontario submitted to the Ministry of Health and Long-Term Care in September 2014 should be fully funded and executed in 2015/2016.

COPD Network

The expert advisory panel strongly recommends the development of a provincial network on COPD (or, more broadly, lung health) that would be charged with improving patient outcomes and reducing the burden of COPD on provincial health care services. The newly established COPD network would provide clinical leadership, coordination, and support for provincial efforts including:

- COPD performance measurement and reporting, including the development of new indicators and data sources
- quality improvement efforts, supported by clinical leadership
- provincial expansion of pulmonary rehabilitation clinics, including data and reporting requirements
- development of patient and caregiver education materials for consistent use in all health care settings
- development of health professional education tools
- assessment in each local health integration unit (LHIN) of COPD needs and capacity building
- development of novel knowledge translation interventions to optimize inpatient, emergency department, and postacute care, with objective evaluation of their effectiveness

The Ontario Ministry of Health and Long-Term Care should provide funding for the establishment and ongoing operations of the network. Where feasible and appropriate, the network could be built on existing provincial infrastructure.

System-Level Considerations for the Acute Episode of Care

After formulating the majority of their recommendations, the expert advisory panel was asked by the ministry to provide high-level advice around implementation, including specific recommendations focused on the following areas:

- aligning the expert panel's recommendations with the quality-based procedure (QBP) funding methodology
- implementation of recommended practice
- impact on multidisciplinary teams
- system program and capacity planning required
- change management and support for change required

Aligning Recommendations to Funding

Importance of a well-designed funding policy framework and methodology: Health Quality Ontario and the expert panel recognize that their mandate in developing this work was to provide evidence, analysis, and recommendations that would inform a separate process of costing, pricing, and payment methodology design to be led by the ministry. However, the expert panel continually emphasized that these recommendations will be inconsequential if they are not supported by a well-designed quality-based procedure funding system that takes into consideration issues such as the complexity and heterogeneity of the COPD patient population, avoids creating inappropriate incentives, and enables the extension of the funded episode into postacute and community care.

Consideration of patient heterogeneity and complexity: COPD patients are a very heterogeneous population characterized by varying levels of severity in their underlying COPD, high prevalence of comorbidities, and frequent presence of social issues and other factors that contribute to complexity. Ontario currently only captures a subset of the relevant variables necessary to account for COPD patient complexity in routine administrative data. Moving forward, effectively risk-adjusting QBP prices for justifiable cost variation across COPD patients will require collecting some of these variables and incorporating these into a costing analysis.

Variation in costs for COPD patients: While the recommended practices in this clinical handbook provide a core set of interventions that should be performed in the treatment of COPD patients, a large proportion of utilization and costs for these patients will also be attributable to other factors, such as the severity of their disease and the number of recent exacerbations, comorbidities, and tests performed to confirm their diagnosis. These factors contribute to variations in both cost and length of stay. As a result, it should be recognized that the recommended practices in this handbook capture only a fraction of the total costs of COPD patients. Design of the funding methodology should take this into consideration and incorporate suitable adjustments for cost variation and long-stay outliers.

Implications of COPD diagnosis issues on the ministry "carve-out" approach: The expert panel reinforced that the issues observed in current diagnosis and coding of COPD would have

profound implications on the ministry funding methodology if the same carve-out approach used for funding the 2012/2013 QBPs was applied for 2014/2015. While the carve-out is based on historical activity (2011/2012 activity for 2013/2014 carve-out), the expert panel will be making recommendations around standards for future COPD diagnosis and coding. Thus, the activity coded as COPD-related care in 2011/2012 may not align with what will be coded as COPD-related activity in 2014/2015 moving forward. This may also create considerable variability in an individual hospital's recorded COPD case mix from year to year.

Incentives for inappropriate utilization: The expert panel recognized that in defining COPD patient groups largely based on utilization and disposition (see Recommended COPD Cohort Definition and Patient Stratification Approach), there is the potential for perverse incentives to be created when these groups are assigned "prices" in a funding methodology. The cost of an average admitted COPD patient is often more than 10 times the cost of treating and discharging a COPD patient in the ED, while the cost of treating a COPD patient with ventilation is similarly much higher than treating them with usual medical care. If prices for the QBP funding system reflect these costs, care must be taken to ensure hospitals are not incentivized to admit greater proportions of patients for a higher payment or to make inappropriate use of ventilation. The QBP funding system can potentially mitigate these risks by bundling payment across the ED and inpatient settings and setting policies around appropriateness. In the longer term, the collection of new data elements capturing important patient complexity factors may allow for these groups to be redefined based on patient characteristics rather than utilization.

Opportunity areas for funding: Notwithstanding these challenges, the expert panel also discussed some of the key areas of opportunity for funding mechanisms to drive high-quality COPD care:

- supporting increased access to, and use of, pulmonary rehabilitation following an acute exacerbation by bundling rehabilitation into the hospital payment
- supporting improvements in objective diagnosis of COPD through spirometry by requiring confirmation of diagnosis as a condition of funding
- supporting more effective and efficient use of noninvasive ventilation, both in relation to its increased use where it is shown to be effective (i.e., in addition to usual medical care and as a first-line treatment before progressing to invasive ventilation) and its provision in more cost-effective settings (i.e., in respiratory wards instead of only in intensive care units)

Implementation of Recommended Practices

Provincial versus local care pathways: It should be recognized that the practices recommended in this clinical handbook have been defined at an aspirational level to guide all hospitals across the province. The handbook is not intended to be an operational care pathway; individual providers will have to implement these best practices based on their own local circumstances and available capacities. In many cases, the implementation of these recommendations will be challenged by local arrangements or the availability of services. For example, the expert panel discussed variation across the province in the provision of ventilation (while some hospitals provide noninvasive ventilation in a dedicated respiratory or general medical ward, others only provide it in intensive care units) as well as access to pulmonary rehabilitation, which is not available in many communities.

Adapting recommended practices to the local level: Implementing recommended services will require customization at the local level. For example, it was discussed that many communities should look at the possibility of delivering pulmonary rehabilitation out of local community centre gyms or YMCAs, given the lack of hospital outpatient capacity in many areas. Similarly, follow-up care for a

COPD patient after discharge may take place with a variety of different primary care providers or a respirologist, depending on local availability of services.

Implementation as a program of care: Many of these considerations speak to the need to approach the implementation of the recommended practices not simply at the level of individual patients and clinicians, but within a program of care that requires organization-level planning, resourcing, and the involvement of administrators. Program design should also involve a measurement system for tracking performance, supporting quality improvement, and it should include the consideration of other non-COPD respiratory patient groups, such as asthma and other lung disorders, which may be managed with the same types of resources. The program should also span the improvement of COPD care across care settings, including the community, recognizing that hospitalization is only one part of the COPD continuum of care.

Tracking current practice against recommended practices: Many of the practices recommended by the expert panel are not currently tracked in any consistent way at either the local or provincial level. Thus, it is difficult to know what the gap is between current and ideal COPD practice and how much this gap varies across different organizations and parts of the province. A key objective of developing a COPD performance measurement strategy should be to enable organizations to track, audit, and evaluate the implementation of care pathways and recommended practices at the organization level. Through such monitoring, variances can be identified, progress monitored, and the pathway can be refined over time.

Roles of Multidisciplinary Teams

One of the important issues in COPD care discussed by the expert panel is the lack of dedicated teams and resources in Ontario for COPD. In stroke care, for example, the Ontario Stroke Strategy has led to the widespread use of dedicated stroke units and interdisciplinary stroke teams. Such dedicated units and teams are much less common for COPD and respiratory diseases. The expert panel discussed a promising area for further research in evaluating the difference in outcomes between COPD patients cared for in nonspecialized teams and/or units with those cared for by specialized respiratory teams and/or units. Further work is required to define what constitutes a specialized respiratory team and to assess the feasibility of establishing these teams in hospitals of different sizes across the province.

Service Capacity Planning

The ministry was interested in advice from the expert panel around capacity planning and shifts across care settings for COPD. The most important issue in this respect identified by the expert panel is the inconsistent capacity in, and access to, pulmonary rehabilitation across the province. This is a major opportunity area for the ministry, LHINs, hospitals, home care providers, and other providers to work together to improve outcomes for COPD patients and to also impact rates of unplanned readmissions. Current OHTAC-commissioned field evaluation work in this area, as well as the work of the OHTAC Implementation Subcommittee and Health Quality Ontario staff focusing on implementation of the OHTAC COPD recommendations, can support this area of focus.

System-Level Considerations for the Postacute Episode of Care

The Postacute, Community-Based COPD Expert Advisory Panel believes that implementation of best practices related to community-based COPD care will require significant investment. The following points highlight some of the key issues for and barriers towards the successful implementation of the community-based COPD QBP best practices discussed:

1. A transitional approach to funding is recommended so as to enable the building of capacity in the community and to avoid the consequences of patients receiving no service.

2. It will not be possible to promote the movement of appropriate patients to community or ambulatory care and achieve the associated cost efficiencies without addressing best practices for capacity and access issues, whether there is adequate outpatient pulmonary rehabilitation services post-discharge, and the best possible environment for providing rehabilitation to the patient.

3. Patient education materials should be standardized and available in multiple languages. Education materials for patients and caregivers at discharge should be used and reinforced by the home care team. Patients have concerns that new educational materials distributed by home care service providers conflict with materials provided on discharge or are confusing. Caregivers should be conscious of patients' and caregivers' health literacy when distributing educational materials.

4. Pathways to the evidence-based recommendations made in this report should be adopted by all providers. Provincial guidelines and pathways should be available in electronic format for primary care providers.

5. All hospitals should adopt the forthcoming health transformation discharge planning standards.

6. Smoking cessation counselling should be made readily available at no cost to all patients and caregivers.

7. Barriers to accessing nicotine replacement therapy should be removed.

8. Barriers to accessing smoking cessation drug therapy should be removed.

9. Patient self-management programs should be developed and incorporated into the care plans. Monitoring of the self-management care plans is the responsibility of all health care providers. Barriers to communication that hinder multidisciplinary care provision should be removed.

10. The Health Quality Ontario/Health Links care coordination tool should be adopted by all primary care providers to facilitate greater coordination with community health services.

11. Once finalized, the Health Quality Ontario/Health Links care coordination tool's e-chart should be adopted by all primary care providers, home care providers, and their contracted service providers to improve communication on patient care.

12. Where appropriate, post-acute medical discharge care should be coordinated in the patient's home with a multidisciplinary team.

13. All home care contracted service providers should work to integrate care to drive performance and improve communication to ensure common care plan are followed, and to report health changes and changes related to self-management plans along with home care coordinator.

14. The challenge of shortages in human resources on the implementation of community care for post-discharge populations in some regions of the province should be considered. In regions where human resources are in shortage, the LHINs should be involved to grow capacity.

15. The impact of this QBP should be analyzed on a regular basis and updated where required.

16. Physicians and health care leaders should be engaged early in the development of funding programs and quality-based measures to promote understanding and acceptance and ensure successful uptake of the QBP recommendations.

17. Health care leaders should be involved in the development of implementation materials.

18. Primary care providers should have adequate decision support to respond to the increasing demand for data.

19. Once developed, implementation of this QBP should use evidence-based Knowledge Translation and Exchange (KTE) strategies to increase the uptake of recommendations.

20. Once completed, OHTAC recommendations on end-of-life care and planning should be implemented.

Expert Advisory Panel Membership

Health Quality Ontario's Expert Advisory Panel on Episodes of Care for Acute COPD

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Health Quality Ontario's Expert Advisory Panel on Episodes of Care for Post-Acute Community-Based Care for COPD Patients

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Appendix 1: Rapid Reviews

Acute Episode of Care

1. Inhospital Physiotherapy for Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD): A Rapid Review
2. Action Plans for Individuals with Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
3. Prophylactic Antibiotics for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

Postacute Episode of Care

4. Pulmonary Rehabilitation in the Home Versus Other Settings for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
5. Pulmonary Rehabilitation Setting for Individuals with Chronic Obstructive Pulmonary Disease (COPD): An Economic Rapid Review
6. Exercise Programs After Pulmonary Rehabilitation for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
7. Respiratory Therapy Services in Home Care for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
8. Airway Clearance Techniques for Individuals With Stable Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review
9. Cognitive-Behavioural Therapy for Anxiety and Depression in Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

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Inhospital Physiotherapy for Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD): A Rapid Review

BR McCurdy

January 2013

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Conflict of Interest Statement

All reports prepared by the Division of Evidence Development and Standards at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Division of Evidence Development and Standards at Health Quality Ontario in consultation with experts, end-users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials (RCTs), and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies included in the systematic review are retrieved and a maximum of two outcomes are graded. If no well-conducted systematic reviews are available, RCTs and/or guidelines are evaluated. Because rapid reviews are completed in very short timeframes, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

Disclaimer

This rapid review is the work of the Division of Evidence Development and Standards at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current to the date of the literature search specified in the Research Methods section, as appropriate. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

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Health Quality Ontario 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.

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Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
COPD	Chronic obstructive pulmonary disease
CI	Confidence interval(s)
FEV_1	Forced expiratory volume in 1 section
HQO	Health Quality Ontario
HRQOL	Health-related quality of life
MD	Mean difference
n	Sample size
NPPV	Noninvasive positive pressure ventilation
OR	Odds ratio
OHTAC	Ontario Health Technology Advisory Committee
PEP	Positive expiratory pressure
RCT	Randomized controlled trial
RR	Relative risk

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this rapid review is to evaluate the effectiveness and safety of inhospital physiotherapy for individuals with acute exacerbations of chronic obstructive pulmonary disease (COPD).

Clinical Need and Target Population

Chronic obstructive pulmonary disease is a disease state that is characterized by a limitation in airflow that is not fully reversible. This airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. (1) The natural history of COPD involves periods of worsening symptoms known as acute exacerbations. There is some debate about the best definition for 'exacerbations.' A consensus definition developed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines an acute exacerbation as "an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication." (2) Patients may also experience a variety of other symptoms such as worsening exercise tolerance, fatigue, malaise, and decreased oxygen saturation. (3)

Two-thirds of COPD exacerbations are caused by an infection of the tracheobronchial tree or by air pollution. The cause is unknown in the remaining cases. (2;4) Risk factors for exacerbations include disease severity, winter months, and a previous exacerbation over the past 8 weeks. (3;5) The frequency of exacerbations seems to vary with disease severity. Using data from the Inhaled Steroids in Obstructive Lung Disease Study (ISOLDE Study), the European Respiratory Society Study on COPD, and the Copenhagen City Lung Study, Donaldson et al (3) found that patients with severe disease (GOLD category III) experienced an average of 3.43 exacerbations per year, whereas patients with moderate disease (GOLD category II) experienced an average of 2.68 exacerbations per year. (3)

Exacerbations have an important impact on patients and on the health care system. For patients, exacerbations result in decreased quality of life, potential permanent loss in lung function, and increased risk of mortality. For patients with severe exacerbations that require hospitalization, estimates of inpatient mortality range from 4% to 30%. Higher hospital mortality rates are observed for patients admitted with respiratory failure. Mortality following discharge is also high. Data from the United Kingdom shows a 14% mortality rate within 3 months of readmission, and data from the United States shows a 43% mortality rate after 12 months. (3) In addition, exacerbations of COPD are a leading cause of emergency

department visits and hospitalizations, particularly in winter. The health care burden associated with exacerbations is high—inpatient costs have been estimated to account for 70% of total health care costs for COPD treatment. (6;7)

Inhospital Physiotherapy

Individuals hospitalized with acute exacerbations of COPD may receive physiotherapy during their hospital stay. Physiotherapists may utilize a number of chest physiotherapy techniques for COPD patients aimed at improving lung function or facilitating the removal of airway secretions. (8)

Airway Clearance Techniques

Airway clearance techniques involve the application of external forces to enhance the removal of sputum (mucous secretions from the lungs) from the airway. (9;10) There are numerous airway clearance techniques, including conventional/traditional chest physiotherapy methods (e.g., postural drainage, percussion, and vibration), breathing exercises (e.g., the active cycle of breathing technique and autogenic drainage), hand-held positive expiratory pressure (PEP) devices (e.g., mask, mouthpiece or oscillatory PEP devices), and mechanical devices that are applied externally to the chest wall (e.g., high-frequency chest wall oscillation). (10-12)

Early Mobilization Programs

Acute exacerbations of COPD have a substantial impact on the individual. Studies have shown acute exacerbations negatively impact health-related quality of life (HRQOL), pulmonary function, and survival. (13) Studies have also shown decreased skeletal muscle strength and quadriceps muscle strength in those individuals hospitalized for an acute exacerbation. (13) A number of factors contribute to these findings, one of which is inactivity during the hospital stay, which may lead to muscle atrophy. (13;14) In addition, the reduced activity level and muscle strength may continue beyond discharge from hospital. (13) Pitta et al (13) showed that individuals with reduced activity levels 1 month after a hospital discharge for an acute exacerbation of COPD were more likely to be readmitted the following year, although this was a small, observational study. Therefore, early mobilization of individuals during their hospitalization has been proposed to help prevent the decline in muscle performance and activity levels.

Ontario Context

Harth et al (15) conducted a survey of physiotherapists at Canadian acute care hospitals with more than 250 beds to determine the current practice patterns of physiotherapists in the management of individuals hospitalized with acute exacerbations of COPD. Thirty-six Ontario hospitals responded (66.6% response rate), but as the paper does not provide the results by province, the aggregate results are presented here.

For those patients being treated in a hospital ward, more than 70% of respondents reported using the following treatment methods ‘always or frequently’ (defined as use 61% to 100% of the time): pursed lip breathing (72%), walking (78%), transfer training (75%), and bed mobility exercises (78%). Fifty-seven percent and 42% of respondents used lower and upper limb resistance exercises ‘always or frequently,’ respectively, while fewer than 50% of respondents used airway clearance techniques ‘always or frequently.’ (15)

In the intensive care setting, bed mobility and transfer training were used most commonly (68% and 57% of respondents used these techniques ‘always or frequently’), while less than 50% of respondents used airway clearance techniques ‘always or frequently’. (15) Of those using airway clearance techniques, vibration and facilitated coughing were used most frequently. (15)

Physiotherapists may include education as a part of the treatment they provide. The survey found that, among other topics, physiotherapists often provide education on breathing exercises, airway clearance techniques, and whole-body exercise. (15)

Rapid Review

Research Question

What is the effectiveness and safety of inhospital rehabilitation for individuals with acute exacerbations of COPD?

Research Methods

Literature Search

A literature search was performed on October 12, 2012, using 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, for studies published from January 1, 2006, until October 12, 2012. Titles and abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-reports
- published between January 1, 2006, and October 12, 2012
- systematic reviews, health technology assessments, and meta-analyses
- analyses that compare the intervention with control group (no intervention or sham intervention)

Exclusion Criteria

- Analyses in which discrete results on individuals with acute exacerbations of COPD cannot be abstracted
- abstracts and conference proceedings
- duplicate publications (publications that have been superseded by newer analyses on the same topic or studies that report the same outcomes for the study population)
- analyses that compared different methods of inhospital physiotherapy
- studies examining pulmonary rehabilitation

Outcomes of Interest

- Hospital or intensive care unit length of stay
- Need for ventilation (invasive or noninvasive ventilation)
- Hospital readmissions
- Mortality
- HRQOL
- Lung function

- Gas exchange
- Symptoms
- Sputum clearance
- Functional capacity

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (16)

The quality of the body of evidence for each outcome was examined according to the GRADE Working Group criteria. (17) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

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. (17) For more detailed information, please refer to the latest series of GRADE articles. (17)

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

High	Very confident that the true effect lies close to the estimate of the effect
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Literature Search

The database search yielded 255 citations published between January 1, 2006, and October 12, 2012 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded from the analysis.

Six studies (5 systematic reviews and one systematic review of reviews) met the inclusion criteria. The reference lists of the included studies and health technology assessment websites were hand searched to identify any additional potentially relevant studies, and no additional citations were identified.

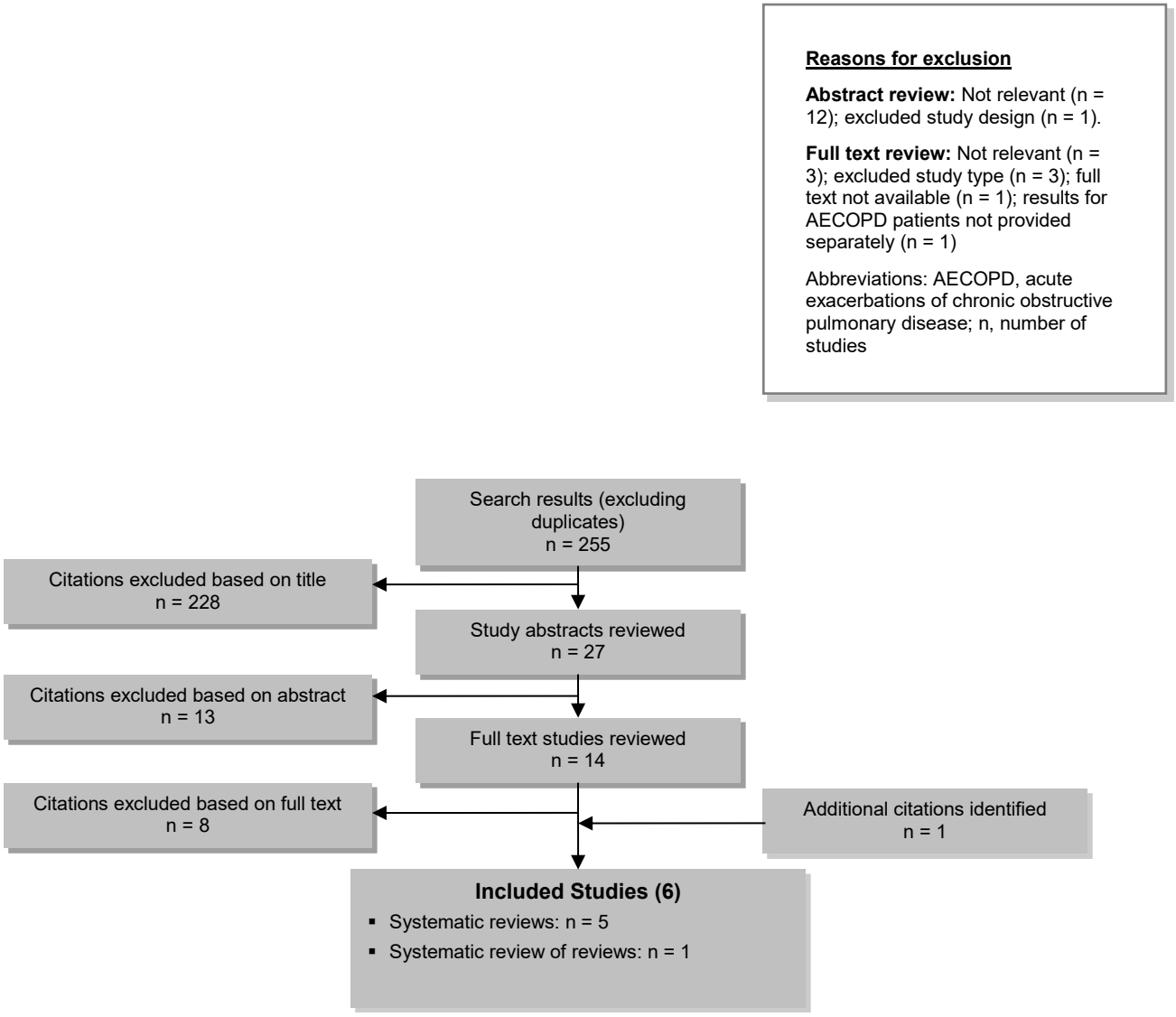

Figure 1: Citation Flow Chart

Nowobilski et al (18) conducted a systematic review of systematic reviews, narrative reviews, and clinical practice guidelines published between January 1, 2000, and July 1, 2010. Seven systematic reviews, 4 narrative reviews, and 4 clinical practice guidelines were included, as well as the direct examination of primary literature in this area. The summary of the evidence provided by Nowobilski et al (18) does not always clearly identify whether the population of interest is stable or acute exacerbations of COPD so it is challenging to extract meaningful conclusions on the acute exacerbation population of interest. Overall, Nowobilski et al (18) concludes that there is limited evidence to support the use of airway clearance techniques in individuals with COPD because the majority of the studies have serious methodological limitations and do not evaluate important outcomes such as hospital length of stay, health-related quality of life, and exercise capacity. (18)

Three of the systematic reviews identified focus specifically on inhospital physiotherapy for individuals with acute exacerbations of COPD, although the Cochrane Collaboration systematic review by Osadnik et al (10) also includes a separate analysis on the stable COPD population. (8;10;11) The systematic reviews

by Osadnik et al (10) and Hill et al (11) evaluate airway clearance techniques while the systematic review by Tang et al (8) evaluates both airway clearance techniques and early mobilization programs.

Osadenik et al (10) included 9 studies: 7 randomized controlled trials (RCTs) and 2 randomized cross-over trials. There was substantial clinical heterogeneity across trials, including different methods of physiotherapy, use of cointerventions, different types of care provided to the control groups, different study designs (RCT versus cross-over), and different outcomes. However, whenever possible, the authors conducted meta-analyses. In addition to the pooled results, the authors also reported subgroups for those studies using positive expiratory pressure (PEP) airway clearance methods and those that used non-PEP methods. (10) Using the AMSTAR measurement tool to assess the methodological quality of the systematic review, Osadenik et al (19) had an overall score of 8 out of 11 (refer to Table A1 in Appendix 2 for more details).

Hill et al (11) included 5 studies: 3 RCTs and 2 randomized cross-over trials. There was substantial heterogeneity across these 5 trials in terms of the included population (where patients were recruited from and whether hypersecretive patients were targeted), outcomes assessed, and physiotherapy techniques used. As a result, Hill et al (11) did not pool the results of the studies, and presented by the type of physiotherapy technique. Using the AMSTAR measurement tool to assess the methodological quality of the systematic review, Hill et al (11) had an overall score of 4 out of 10[20] (refer to Table A1 in Appendix 2 for more details).

Tang et al (8) included 13 trials: 5 RCTs, 1 randomized parallel groups trial, 2 non-randomized clinical controlled trials, and 5 single group pre-post trials. Given the heterogeneity across studies in terms of physiotherapy techniques, Tang et al (8) reported the results by type of technique. Using the AMSTAR measurement tool to assess the methodological quality of the systematic review, Tang et al (8) had an overall score of 4 out of 10[1] (refer to Table A1 in Appendix 2 for more details).

If an included systematic review did not use GRADE to assess the quality of the body of evidence, the intention was to re-evaluate the quality of the primary literature using GRADE. Each of the 3 systematic reviews assessed the quality of evidence, however, only the review by Osadenik et al (10) used GRADE. Since it was not feasible to obtain the full text of all of the primary literature during the timelines of the rapid review, the evidence from Hill et al (11) and Tang et al (8) was not reassessed using GRADE. Instead, the authors' assessment of the evidence is provided.

Airway Clearance Techniques

Hospital Length of Stay

Osadenik et al (10) identified 3 studies that reported on hospital length of stay and found a statistically significant reduction in favour of physiotherapy when the 3 trials were pooled (mean difference [MD], −0.75 days; 95% confidence interval [CI], −1.38 to −0.11). However, this significant reduction was driven by the significant reduction (MD, −1.10 days; 95% CI, −1.89 to −0.31) found in 1 study in the PEP-subgroup which compared intrapulmonary percussive ventilation[21] used 3 times per day with a control group in acute exacerbation patients with mild respiratory acidosis.

Using GRADE to assess the quality of evidence, Osadenik et al (10) found the overall quality of evidence on hospital length of stay to be low quality.

[20] Maximum possible score was reduced to 10 because the question regarding the appropriateness of the methods used to combine the findings was not applicable to this systematic review as the studies were not pooled due to clinical heterogeneity across studies.
[21] Intrapulmonary percussive ventilation devices deliver high frequency short bursts of air through a face mask or mouthpiece to create an internal vibration within the patients' airways that helps to clear sputum. (11)

Need for and Duration of Ventilatory Assistance
Osadenik et al (10) identified 4 studies that reported on the need for invasive or noninvasive ventilatory assistance. The results of the pooled analysis found a significant reduction in the need for increased ventilatory assistance (n, 171; odds ratio [OR], 0.21; 95% CI, 0.05–0.85). (10) However, the statistical significance of this reduction is only maintained in the PEP subgroup (PEP: OR, 0.11; 95% CI, 0.01–0.87; non-PEP: OR, 0.47; 95% CI, 0.07–3.36; test for subgroup difference, $P = 0.31$; $I^2 = 4.1\%$). (10) Hill et al (11) also identified the significant reduction in the need for increased ventilatory assistance based on 1 study, the larger of the 2 trials in the PEP subgroup. Of note, this trial was conducted in patients with mild respiratory acidosis. (11) Using GRADE to assess the quality of evidence, Osadenik et al (10) found the overall quality of evidence on the need for ventilator assistance to be low quality.

Similarly, Osadenik et al (10) identified 2 studies that examined the duration of use of noninvasive positive pressure ventilation (NPPV) and found a significant reduction in favour of the physiotherapy group (n = 54; MD, −2.05 days; 95% CI, −2.60 to −1.51). (10) This significant reduction was driven by 1 study in the PEP subgroup that compared positive expiratory pressure treatment delivered by mask plus assisted coughing with coughing alone in patients with copious secretions and hypercapnic respiratory failure, which was also reported by Hill et al (11). Using GRADE to assess the quality of evidence, Osadenik et al (10) found the overall quality of evidence on the duration of ventilator assistance to be of low quality.

Health-Related Quality of Life
Conflicting results were observed for HRQOL. Both Tang et al (8) and Osadenik et al (10) included 1 study that assessed HRQOL using the St. George's Respiratory Questionnaire. However, while Osadenik et al (10) reported no difference at discharge or 1-month follow-up, Tang et al (8) found a significant improvement in HRQOL when comparing incentive spirometry with usual care.

Lung Function
Percussion airway clearance techniques may have a short-term adverse effect on lung function measured by forced expiratory volume in 1 second (FEV_1). Tang et al (8) identified 2 studies which evaluated percussion methods which both reported statistically significantly short-term reductions in lung function measured by FEV_1 in the percussion group. (8) While Hill et al (11) also reported the results of 1 of these 2 studies, the authors noted that the method for administration of percussion was outdated and more current methods (short periods of percussion interspersed with periods of controlled/relaxed breathing) may prevent the decline in FEV_1. (11)

The impact of other airway clearance techniques on lung function reported by Hill et al (11) and Osadenik et al (10) were conflicting and varied by technique. Overall conclusions on this topic were not possible based on the information provided in the systematic reviews.

Sputum Clearance
Overall, the results on sputum clearance were mixed. Osadenik et al (10), Hill et al (11), and Tang et al (8) found that chest wall vibration and PEP-mask therapy were found to temporarily (for up to 1 hour) increase sputum expectoration in patients with copious secretions. However, in these 2 studies, the expectoration was assessed using the wet weight of sputum—a measure that is often inaccurate due to contamination by saliva—so it is difficult to conclude whether these results are meaningful. Both reviews also reported the results of studies (1 study in Hill et al (11) and 2 studies in Osadenik et al (10)) that measured sputum clearance using clearance of inhaled radiolabeled particles which did not find a significant difference in sputum clearance between the airway clearance and control groups. Osadenik et al (10) also reported no significant different in sputum volume between the groups in the 2 other studies that looked at short-term (24 hour) results.

Gas Exchange
Overall, the results on sputum clearance were mixed. While Osadenik et al (10) primarily reported negative findings, Hill et al (11) and Tang et al (8) both reported mixed results with no consistent impacts on gas exchange outcomes.

Breathlessness
Conflicting results were observed regarding breathlessness, but different methods of airway clearance were used in the 2 studies. Osadenik et al (10) identified a study that compared expiration with glottis open in lateral position with the control group that reported statistically and clinically significantly greater improvement in self-reported breathlessness using the Borg scale in the airway clearance group. Tang et al (8) identified a before-after study which found a significant worsening of breathlessness associated with deep diaphragmatic breathing.

Other Outcomes
Osadenik et al (10) reported a number of additional outcomes that were not included in the other systematic reviews. Overall, no statistically significant differences were observed between the airway clearance techniques and the control groups for the following outcomes:

- Future exacerbations (2 studies, n = 155)
- Need for hospitalizations due to respiratory causes (2 studies, n = 155)
- Time to exacerbation (1 study, n = 59)
- Time to hospitalization (1 study, n = 59)
- ICU length of stay (1 study, n = 35; MD, 0.64 days; 95% CI, −3.16 to 4.44)
- Short-term mortality (4 studies, n = 161; OR, 0.72; 95% CI, 0.14–3.80) (10)
- Long-term mortality (2 studies, n = 107; OR, 0.82; 95% CI, 0.26–2.63) (10)

Early Mobilization Programs
Tang et al (8) was the only systematic review that included an evaluation of early mobilization methods. One RCT and 1 randomized parallel groups trial were identified; however, the randomized parallel groups trial compared different walking programs using 2 different walking aids (gutter frame and rollator), rather than comparing a walking program with a control group. Based on the 1 RCT with 29 participants, compared with standard care, walking programs:

- Statistically significantly improved arterial blood gases
- Statistically significantly improved lung function measured by minute ventilation
- Statistically significantly reduced breathlessness measured by the Borg scale after exercise
- Statistically significantly improved exercise capacity measured by walking distance, lactic acid concentration, and oxygen uptake per body weight

Tang et al (8) evaluated the quality of evidence using the Physiotherapy Evidence Database (PEDro) scale which has a maximum of 10 possible points. The walking program RCT scored 5 out of 10, which exceeded Tang et al's (8) cut off of 4 to identify lower quality studies. However, according to their quality evaluation, the RCT had serious methodological limitations, including lack of allocation concealment, lack of blinding of subjects, therapists, or assessors, and not including all subjects in the analysis. (8) While some of these outcomes are objective, making lack of blinding less of a problem, these are still important methodological concerns. In addition, patients were enrolled in the study 6 to 8 days after

admission to the hospital, once their exacerbation had stabilized, and then they were enrolled in a 10-day program. A 2008 Canadian study estimated that the average hospital length of stay for a severe exacerbation was 10 days. (20) Therefore, the generalizability of this intervention to the Ontario context is limited.

The remaining 2 systematic reviews examined airway clearance techniques for individuals with both stable and acute chronic obstructive pulmonary disease. (21;22) These reviews provide some limited results and conclusions for the acute exacerbation population. Given the limited focus on the population of interest, the quality of these 2 systematic reviews was not assessed using AMSTAR.

The systematic review by Ides et al (22) provides a summary of the results of 1 study comparing intrapulmonary percussive ventilation with a standard treatment control group in individuals with acute exacerbations of COPD and mild respiratory acidosis. The study found a significant decline in the number of exacerbations that worsened in the physiotherapy group compared with the control group, and a corresponding significantly reduced hospital length of stay. (22) In addition, the study found significant improvements in gas exchange (increase in the partial pressure of oxygen in the arterial blood and decrease in the partial pressure of carbon dioxide in the arterial blood). (22) As a result, the study authors concluded that intrapulmonary percussive ventilation is safe for use in individuals with acute exacerbations of COPD. (22) This study was included in 3 systematic reviews reported above.

The systematic review by Langer et al (21) reported on 1 study that evaluated the effectiveness of daily resistance training in hospitalized patients with acute exacerbations of COPD. This study found that the training counteracted the decline in leg muscle force and did not cause any adverse effects. As a result of this study and other evidence which is not fully described, Langer et al (21) recommends that patients receive training strategies during an acute exacerbation hospitalization, so as to enable the patient to return to pulmonary rehabilitation as soon as possible. Resistance training, transcutaneous electrical neuromuscular stimulation, and interval training are identified by Langer et al (21) to be most appropriate for these patients. However, the evidence supporting these methods over others is not presented.

Conclusions

Airway clearance techniques

There is low quality evidence that certain airway clearance techniques have beneficial impacts on some outcomes, as described below:

- Airway clearance techniques that apply a positive pressure to the airways, such as intrapulmonary percussive ventilation and positive expiratory pressure (PEP), reduce the need for, and duration of, ventilation.
- Intrapulmonary percussive ventilation reduces the hospital length of stay in COPD patients with acute exacerbations of COPD and mild respiratory acidosis.
- Some airway clearance techniques may increase sputum expectoration, but the results of the supporting studies may be inaccurate given the method of measurement used.

Given the low quality of evidence, further research may change the estimate of effect.

Early mobilization programs

One systematic review identified 1 small RCT that assessed the effectiveness of walking programs compared to standard care. Although the study found statistically significant improvements for a number of patient outcomes, including exercise capacity and lung function for the walking program compared to standard care, the quality of evidence is poor and not generalizable to the Ontario context. However, the positive outcomes observed indicate that this may be a good area for future high-quality research.

Acknowledgements

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Appendices

Appendix 1: Literature Search Strategies

Search date: October 12, 2012
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; CRD; CINAHL

Q: Effectiveness and safety of physiotherapy for patients admitted to hospital for an acute exacerbation of COPD
Limits: 2006-current; English
Filters: health technology assessments, systematic reviews, and meta-analyses

Database: Ovid MEDLINE(R) <1946 to October Week 1 2012>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <October 10, 2012>, Embase <1980 to 2012 Week 40>

Search Strategy:

#	Searches	Results
1	exp Pulmonary Disease, Chronic Obstructive/ use mesz	19331
2	Chronic Obstructive Lung Disease/ use emez	61150
3	Chronic Bronchitis/ use emez	7321
4	(chronic adj2 obstructive adj2 (lung* or pulmonary or airway* or airflow or respiratory) adj (disease* or disorder*)).ti,ab.	61579
5	(copd or coad).ti,ab.	53256
6	chronic airflow obstruction.ti,ab.	1094
7	exp Emphysema/	39935
8	((chronic adj2 bronchitis) or emphysema).ti,ab.	53951
9	or/1-8	174206
10	Physical Therapy Modalities/ use mesz	26466
11	physiotherapy/ use emez	45913
12	physical medicine/	6076
13	exp kinesiotherapy/ use emez	41108
14	(physiotherap* adj2 chest).mp.	1481
15	exp Exercise Therapy/ use mesz	26442
16	Occupational Therapy/	28038
17	respiratory therapy/ use mesz	5511
18	Breathing Exercises/ use mesz or breathing exercise/ use emez	6402
19	Drainage, Postural/ use mesz or Postural Drainage/ use emez	670
20	Percussion/	2415
21	exp Vibration/	60103
22	Intermittent Positive-Pressure Ventilation/	4345
23	Early Ambulation/ use mesz	1796
24	mobilization/ use emez	14664
25	(active cycle adj2 breath*).mp.	100
26	((lung or pulmonary) adj2 hygien*).mp.	163

27	autogenic drainage*.mp.	88
28	incentive spirometr*.mp.	409
29	acapella*.mp.	51
30	((airway or secretion or sputum) adj clearance technique*).mp.	234
31	(sputum adj2 (clear* or mobili*)).mp.	297
32	airway clearance*.mp. use emez	669
33	((continuous or oscillating) adj2 positive expiratory pressure*).mp.	44
34	thoracic expansion exercise*.mp.	17
35	((physio* or therap*) adj2 (percussion or humidification)).mp.	365
36	(walk* adj2 (therap* or program*)).mp.	2964
37	((accelerat* or earl*) adj (ambulation or mobilisation or mobilization or recover*)).mp.	15136
38	((physical or respiratory) adj (therap* or physiotherap*)).mp.	60662
39	((physical* adj (therap* or train*)) or (train* adj (aerobic* or resistance or strength*)) or exercise* or kinesiotherap* or physiotherap* or physio-therap*).ti,ab.	447901
40	or/10-39	648081
41	9 and 40	13759
42	Meta Analysis.pt.	36957
43	Meta Analysis/ use emez	66280
44	Systematic Review/ use emez	53571
45	exp Technology Assessment, Biomedical/ use mesz	8872
46	Biomedical Technology Assessment/ use emez	11395
47	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	292262
48	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	3668
49	or/42-48	352098
50	41 and 49	489
51	limit 50 to english language	454
52	limit 51 to yr="2006 -Current"	285
53	remove duplicates from 52	185
54	from 53 keep 1-185	185

Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	1838
#2	chronic near/2 obstructive near/2 (lung* or pulmonary or airway* or airflow or respiratory) next (disease* or disorder*):ti,ab,kw OR copd or coad:ti,ab,kw OR chronic airflow obstruction:ti,ab,kw	7234
#3	MeSH descriptor: [Emphysema] explode all trees	92
#4	(chronic near/2 bronchitis) or emphysema:ti,ab,kw	1932
#5	#1 or #2 or #3 or #4	8822
#6	MeSH descriptor: [Physical Therapy Modalities] this term only	2216
#7	MeSH descriptor: [Drainage, Postural] this term only	52
#8	MeSH descriptor: [Exercise Therapy] explode all trees	5384
#9	MeSH descriptor: [Percussion] this term only	47
#10	MeSH descriptor: [Vibration] this term only	559
#11	MeSH descriptor: [Intermittent Positive-Pressure Ventilation] this term only	178
#12	MeSH descriptor: [Breathing Exercises] this term only	444
#13	MeSH descriptor: [Occupational Therapy] this term only	452
#14	MeSH descriptor: [Respiratory Therapy] this term only	447
#15	MeSH descriptor: [Physical Medicine] this term only	15
#16	MeSH descriptor: [Early Ambulation] this term only	258
#17	(physiotherap* near/2 chest) or (active cycle near/2 breath*) or ((lung or pulmonary) near/2 hygien*) or autogenic drainage* or incentive spirometr* or acapella* or ((airway or secretion or sputum) adj clearance technique*) or (sputum near/2 (clear* or mobili*)) or ((continuous or oscillating) near/2 positive expiratory pressure*) or thoracic expansion exercise* or ((physio* or therap*) near/2 (percussion or humidification)) or (walk* near/2 (therap* or program*)) or ((accelerat* or earl*) near (ambulation or mobilisation or mobilization or recover*)) or ((physical or respiratory) near (therap* or physiotherap*)) or ((physical* near (therap* or train*)) or (train* near (aerobic* or resistance or strength*)) or exercise* or kinesiotherap* or physiotherap* or physio-therap*):ti	32046
#18	#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17	34682
#19	#5 and #18 from 2006 to 2012	665
#20	MeSH descriptor: [Meta-Analysis] explode all trees	75
#21	MeSH descriptor: [Technology Assessment, Biomedical] explode all trees	523
#22	meta analysis:pt	477
#23	(meta analy* or metaanaly* or pooled analysis or (systematic* near/2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane):ti,ab	34059
#24	((health technolog* or biomedical technolog*) near/2 assess*):ti,ab	638
#25	#20 or #21 or #22 or #23 or #24	34960
#26	#19 and #25	67

CRD

Line	Search	Hits
1	MeSH DESCRIPTOR Pulmonary Disease, Chronic Obstructive EXPLODE ALL TREES	298
2	(chronic adj2 obstructive adj2 (lung* OR pulmonary OR airway* OR airflow OR respiratory) adj (disease* OR disorder*)):TI OR (copd OR coad):TI OR (chronic airflow obstruction):TI	249
3	MeSH DESCRIPTOR Emphysema EXPLODE ALL TREES	19
4	((chronic adj2 bronchitis) OR emphysema):TI	51
5	#1 OR #2 OR #3 OR #4	386
6	MeSH DESCRIPTOR physical therapy modalities	365
7	MeSH DESCRIPTOR drainage, postural	3
8	MeSH DESCRIPTOR exercise therapy EXPLODE ALL TREES	613
9	MeSH DESCRIPTOR percussion	1
10	MeSH DESCRIPTOR vibration	18
11	MeSH DESCRIPTOR intermittent positive-pressure ventilation	4
12	MeSH DESCRIPTOR breathing exercises	43
13	MeSH DESCRIPTOR occupational therapy	67
14	MeSH DESCRIPTOR respiratory therapy	38
15	MeSH DESCRIPTOR physical medicine	3
16	MeSH DESCRIPTOR early ambulation	22
17	((physiotherap* near2 chest) or (active cycle near2 breath*) or ((lung or pulmonary) near2 hygien*) or autogenic drainage* or incentive spirometr* or acapella* or ((airway or secretion or sputum) adj clearance technique*) or (sputum near2 (clear* or mobili*)) or ((continuous or oscillating) near2 positive expiratory pressure*) or thoracic expansion exercise* or ((physio* or therap*) near2 (percussion or humidification)) or (walk* near2 (therap* or program*)) or ((accelerat* or earl*) near (ambulation or mobilisation or mobilization or recover*)) or ((physical or respiratory) near (therap* or physiotherap*)) or ((physical* near (therap* or train*)) or (train* near (aerobic* or resistance or strength*)) or exercise* or kinesiotherap* or physiotherap* or physio-therap*)):TI	862
18	#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17	1438
19	#5 AND #18	44
20	(#19):TI FROM 2006 TO 2012	30

CINAHL

#	Query	Limiters/Expanders	Results
S41	S36 and S39	Limiters - Published Date from: 20060101-20131231; English Language Search modes - Boolean/Phrase	69
S40	S36 and S39	Search modes - Boolean/Phrase	122
S39	S37 or S38	Search modes - Boolean/Phrase	48114

S38	(health technology N2 assess*) or meta analy* or metaanaly* or pooled analysis or (systematic* N2 review*) or published studies or medline or embase or data synthesis or data extraction or cochrane	Search modes - Boolean/Phrase	48114
S37	(MH "Meta Analysis") or (MH "Systematic Review")	Search modes - Boolean/Phrase	21033
S36	S6 and S35	Search modes - Boolean/Phrase	1859
S35	S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34	Search modes - Boolean/Phrase	144578
S34	(physical* N1 (therap* or train*)) or (train* N1 (aerobic* or resistance or strength*)) or exercise* or kinesiotherap* or physio-therap*	Search modes - Boolean/Phrase	104370
S33	(physical or respiratory) N1 (therap* or physiotherap*)	Search modes - Boolean/Phrase	41254
S32	(accelerat* or earl*) N1 (ambulation or mobilisation or mobilization or recover*)	Search modes - Boolean/Phrase	1277
S31	walk* N2 (therap* OR program*)	Search modes - Boolean/Phrase	492
S30	(physio* or therap*) N2 (percussion or humidification)	Search modes - Boolean/Phrase	26
S29	thoracic expansion exercise*	Search modes - Boolean/Phrase	10
S28	((continuous or oscillating) N2 positive expiratory pressure*)	Search modes - Boolean/Phrase	7
S27	airway clearance*	Search modes - Boolean/Phrase	272
S26	sputum N2 (clear* or mobili*)	Search modes - Boolean/Phrase	28
S25	(active cycle N2 breath*)	Search modes - Boolean/Phrase	26
S24	((airway OR secretion OR sputum) N clearance technique*)	Search modes - SmartText Searching	557
S23	acapella*	Search modes - Boolean/Phrase	9
S22	incentive spirometr*	Search modes - Boolean/Phrase	79
S21	autogenic drainage*	Search modes - Boolean/Phrase	13
S20	pulmonary hygiene	Search modes - Boolean/Phrase	14
S19	lung hygiene	Search modes - SmartText Searching	73
S18	(MH "Early Ambulation")	Search modes - Boolean/Phrase	281
S17	(MH "Intermittent Positive Pressure Ventilation")	Search modes - Boolean/Phrase	272
S16	(MH "Vibration")	Search modes - Boolean/Phrase	1373
S15	(MH "Percussion")	Search modes - Boolean/Phrase	188
S14	(MH "Drainage, Postural")	Search modes - Boolean/Phrase	90
S13	(MH "Breathing Exercises+")	Search modes - Boolean/Phrase	958
S12	(MH "Respiratory Therapy")	Search modes - Boolean/Phrase	2444
S11	(MH "Occupational Therapy")	Search modes - Boolean/Phrase	10349
S10	(MH "Therapeutic Exercise+")	Search modes - Boolean/Phrase	24536
S9	(MH "Physical Medicine")	Search modes - Boolean/Phrase	802
S8	(MH "Chest Physical Therapy+")	Search modes - Boolean/Phrase	483
S7	(MH "Physical Therapy+")	Search modes - Boolean/Phrase	60743

S6	S1 or S2 or S3 or S5	Search modes - Boolean/Phrase	9484
S5	chronic bronchitis or emphysema	Search modes - Boolean/Phrase	1880
S4	(MH "Emphysema+")	Search modes - Boolean/Phrase	1189
S3	copd or coad	Search modes - Boolean/Phrase	5022
S2	(chronic obstructive and (lung* or pulmonary or airway* or airflow or respiratory) and (disease* or disorder*))	Search modes - Boolean/Phrase	7495
S1	(MH "Pulmonary Disease, Chronic Obstructive+")	Search modes - Boolean/Phrase	6022

Appendix 2: AMSTAR Checklist

Table A1: Results of Assessment of Systematic Review Quality Using AMSTAR

Question	Score and Details		
	Hill et al (11)	Osadenik et al (10)	Tang et al (8)
1. Was an a priori design provided?	1 (yes)	1 (yes)	1 (yes)
2. Was there duplicate study selection and data extraction?	0 (no): duplicate data extraction was conducted, but not for study selection	1 (yes)	0 (no): duplicate study extraction was conducted, but it is not specified whether duplicate study selection was utilized
3. Was a comprehensive literature search performed?	0 (no): literature search was not supplemented by grey literature and contacting experts	1 (yes)	0 (no): literature search was not supplemented by grey literature and contacting experts
4. Was the status of publication (i.e., grey literature) used as an inclusion criteria?	1 (yes)	1 (yes)	0 (can't answer): no information was provided in the publication regarding any restrictions on language, grey literature, etc
5. Was a list of the studies (included and excluded) provided?	0 (no): a list of excluded studies was not included	1 (yes)	0 (no): a list of excluded studies was not included
6. Were the characteristics of the included studies provided?	1 (yes)	1 (yes)	1 (yes)
7. Was the scientific quality of the included studies assessed and documented?	1 (yes)	1 (yes)	1 (yes)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	1 (yes)	1 (yes): quality of evidence was considered in sensitivity analyses	1 (yes)
9. Were the methods used to combine the findings of the studies appropriate?	n/a: studies were not combined due to clinical heterogeneity	0 (no): there is substantial clinical heterogeneity across trials, particularly relating to the type of intervention used, so it is difficult to draw conclusions from the results. Often, 1 study drove significant results	n/a: studies were not combined due to clinical heterogeneity

10. Was the likelihood of publication bias assessed?	0 (no): assessment of publication bias was not reported	0 (no): while the methods included assessment of publication bias, the authors noted that this was not possible due to the small number of studies	0 (no): assessment of publication bias was not reported
11. Was the conflict of interest stated?	0 (no): conflict of interest statements were included for the authors of the systematic review but not for the authors of the individual studies included in the review	0 (no): conflict of interest statements were included for the authors of the systematic review but not for the authors of the individual studies included in the review	0 (no): conflict of interest statements were included for the authors of the systematic review but not for the authors of the individual studies included in the review
TOTAL SCORE	**4 out of 10[a]**	**8 out of 11**	**4 out of 10[a]**

[a]Maximum possible score was reduced to 10 because the question regarding the appropriateness of the methods used to combine the findings was not applicable to this systematic review as the studies were not pooled due to clinical heterogeneity across studies.

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Action Plans for Individuals with Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

BR McCurdy

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Conflict of Interest Statement

All reports prepared by the Division of Evidence Development and Standards at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Division of Evidence Development and Standards at Health Quality Ontario in consultation with experts, end-users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials (RCTs), and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies included in the systematic review are retrieved and a maximum of two outcomes are graded. If no well-conducted systematic reviews are available, RCTs and/or guidelines are evaluated. Because rapid reviews are completed in very short timeframes, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

Disclaimer

This rapid review is the work of the Division of Evidence Development and Standards at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current to the date of the literature search specified in the Research Methods section, as appropriate. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. Health Quality Ontario 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 Health Quality Ontario and its partners, the Ontario Health Technology Advisory Committee (OHTAC)—a standing advisory subcommittee of the Health Quality Ontario 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.

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In addition, Health Quality Ontario 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 can 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

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Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
COPD	Chronic obstructive pulmonary disease
CI	Confidence interval(s)
ED	Emergency department
GP	General practitioner
HQO	Health Quality Ontario
HRQOL	Health-related quality of life
MD	Mean difference
n	Sample size
OR	Odds ratio
RCT	Randomized controlled trial

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this rapid review is to determine the effectiveness of action plans for individuals with chronic obstructive pulmonary disease (COPD). This review focuses on action plans themselves and excludes broader, more comprehensive self-management programs.

Clinical Need and Target Population

Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease is a disease state that is characterized by a limitation in airflow that is not fully reversible. This airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. (1) The natural history of COPD involves periods of worsening symptoms known as acute exacerbations. There is some debate about the best definition for 'exacerbations.' A consensus definition developed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines an acute exacerbation as "an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication." (2) Patients may also experience a variety of other symptoms such as worsening exercise tolerance, fatigue, malaise, and decreased oxygen saturation. (3)

Two-thirds of COPD exacerbations are caused by an infection of the tracheobronchial tree or by air pollution. The cause is unknown in the remaining cases. (2;4) Risk factors for exacerbations include disease severity, winter months, and a previous exacerbation over the past 8 weeks. (3;5) The frequency of exacerbations seems to vary with disease severity. Using data from the Inhaled Steroids in Obstructive Lung Disease Study (ISOLDE Study), the European Respiratory Society Study on COPD, and the Copenhagen City Lung Study, Donaldson et al (3) found that patients with severe disease (GOLD category III) experienced an average of 3.43 exacerbations per year, whereas patients with moderate disease (GOLD category II) experienced an average of 2.68 exacerbations per year. (3)

Exacerbations have an important impact on patients and on the health care system. For patients, exacerbations result in decreased quality of life, potential permanent loss in lung function, and increased risk of mortality. For patients with severe exacerbations that require hospitalization, estimates of inpatient mortality range from 4% to 30%. Higher hospital mortality rates are observed for patients admitted with

respiratory failure. Mortality following discharge is also high. Data from the United Kingdom show a 14% mortality rate within 3 months of readmission, and data from the United States show a 43% mortality rate after 12 months. (3;5) In addition, exacerbations of COPD are a leading cause of ED visits and hospitalizations, particularly in winter. The health care burden associated with exacerbations is high—inpatient costs have been estimated to account for 70% of total health care costs for COPD treatment. (6;7)

Ontario Context

In collaboration with the Family Physician Airways Group of Canada and Living Well with COPD, the Canadian Thoracic Society has developed a standardized action plan for individuals with COPD. It is available online at http://www.respiratoryguidelines.ca/COPD-actionplan.

Action Plans

Action plans are written instructions to help an individual with COPD identify an acute exacerbation and understand the steps that should be taken to treat it (e.g., changing medication, initiating antibiotics, or visiting a health care provider). (8;9) Action plans were developed to help patients initiate treatment quickly, since prompt treatment of acute exacerbations of COPD has been shown to result in faster recovery and a better quality of life compared to those individuals who neglect treatment for their exacerbations. (8) Action plans have been shown to be effective in the treatment of asthma. (8)

Action plans are one of many tools that can be used to promote self management in COPD. A 2009 systematic review by the Cochrane Collaboration defined self management as "educational programs aimed at teaching skills needed to carry out medical regimens specific to the disease, guide behaviour change, and provide emotional support for patients to control their disease and live functional lives." (10)

Rapid Review

Research Questions

What is the effectiveness of action plans for individuals with chronic obstructive pulmonary disease (COPD)?

Research Methods

Literature Search

A literature search was performed on September 15, 2012, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until September 15, 2012. Titles and abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-reports
- published between January 1, 2008, and September 15, 2012
- systematic reviews, meta-analyses, and health technology assessments
- analyses in which action plans are the primary intervention evaluated in the included studies

Exclusion Criteria

- analyses in which discrete results on COPD cannot be abstracted
- analyses that include studies evaluating comprehensive self-management programs in which the action plan component is not isolated

Outcomes of Interest

Clinical Outcomes

- Use of medications (steroids and antibiotics)
- Health-related quality of life (HRQOL)
- Mortality
- Lung function
- Functional capacity
- Symptoms

Health System Outcomes

- Emergency department (ED) visits
- Family physician or clinic visits

- Hospital admissions
- Hospital length of stay

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (11)

Within the systematic review, the quality of the body of evidence for each outcome was examined according to the GRADE Working Group criteria. (12) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

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. (12) For more detailed information, please refer to the latest series of GRADE articles. (12)

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

High	Very confident that the true effect lies close to the estimate of the effect
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Literature Search

The database search yielded 50 citations published between January 1, 2008, and September 15, 2012 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded in the analysis.

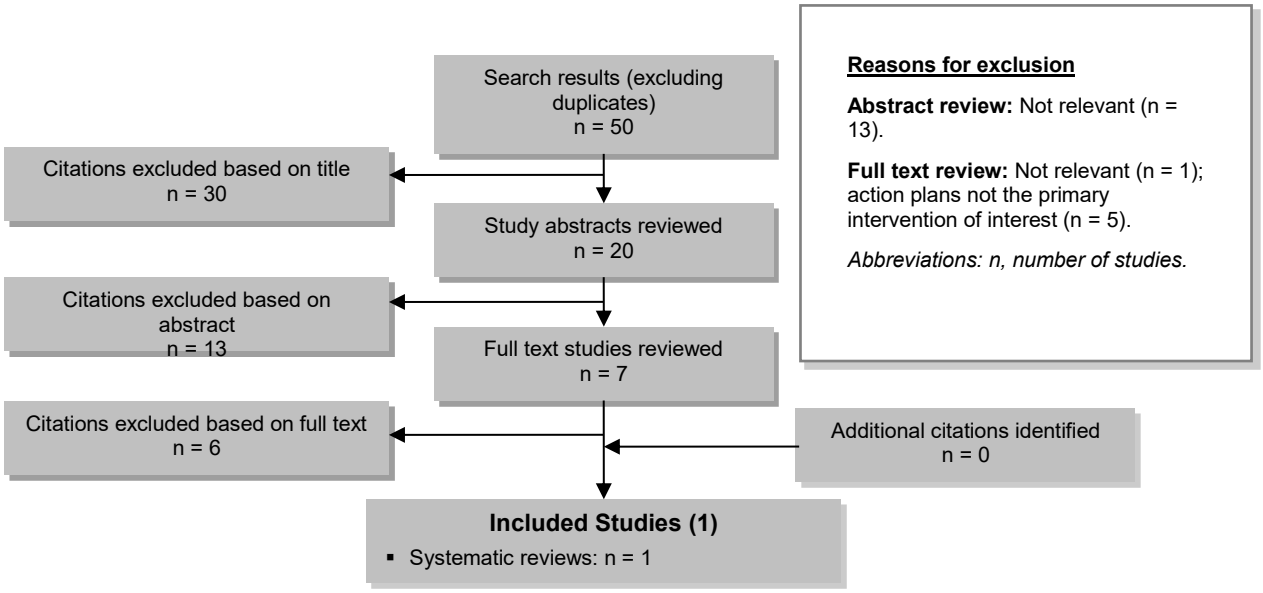

Figure 1: Citation Flow Chart

One study, a Cochrane Collaboration systematic review conducted by Walters et al, (8) met the inclusion criteria. Walters et al (8) defined action plans as "guidelines detailing self-initiated interventions (such as changing medication regime or visiting a [general practitioner] or hospital) which were undertaken in response to alternations in the state of the patients' COPD (e.g., increase in breathlessness, increased amount or purulence of sputum), i.e., changes that would suggest the commencement of an exacerbation." In addition to the action plan, the study's intervention could include a short education component (≤ 1 hour in length). Studies that examined comprehensive self-management programs in which the action plan component could not be isolated were excluded.

Walters et al (8) included 5 randomized controlled trials (RCTs) with 574 individuals with COPD who were followed for 6 to 12 months. The interventions varied: 2 studies used individualized action plans, 2 studies used standardized action plans, and 1 study provided individuals with instructions on what to do in an exacerbation. (8) The action plans were supplemented with prescriptions for antibiotics and corticosteroids in 4 of the studies, although not all patients received the prescriptions in 2 of the 4 studies. (8) Four of the studies provided individuals in the intervention group with additional education, including informational booklets (including information on smoking cessation, controlling breathlessness, nutrition, medications, etc.) and up to 1 hour of specific educational instruction. In the usual care groups, the individuals did not receive action plans. However, individuals did receive some education in 2 of the studies. (8)

Using the AMSTAR measurement tool to assess the methodological quality of the systematic review, Walters et al (8) had an overall score of 7 out of 11 (refer to Table A1 in Appendix 2 for more details). Walters et al (8) used GRADE to evaluate the overall body of evidence for several of the primary outcomes. The GRADE scores are discussed below.

Primary Outcomes

Health Care Utilization

For the majority of health care utilization outcomes examined, no statistically significant differences were observed in the action plan group compared with the usual care group. A summary of the pooled results are shown in Table 1 for hospital admissions, ED visits, and GP visits/phone calls.

Table 1: Meta-Analysis Results for Health Care Utilization Outcomes

Outcome	No. of Studies	No. of Participants	Mean Difference (95% CI)	GRADE Quality of Evidence
Hospital admission (12 m)	2	205	0.23 (−0.03 to 0.49)[a]	Moderate[b]
ED visits for COPD (12 m)	2	201	0.37 (−0.50 to 1.24)[c]	Moderate[b]
COPD-related GP visits / phone calls	3	256	0.53 (−0.45 to 1.50)[a]	Moderate[a]
Non-COPD GP visits / phone calls	2	200	1.25 (−1.54 to 4.03)[a]	NR

Abbreviations: CI, confidence intervals; ED, emergency department; GP, general practitioner; m, months; No, number; IV, inverse-variance; Not reported.

[a]Fixed effects model

[b]GRADE score was not downgraded due to important concerns regarding the potential risk of bias in the studies.

[c]Random effects model

Source: Walters JAE, Turnock AC, Walters EH, Wood-Baker R. Action plans with limited patient education only for exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2010, Issue 5. Art. No.: CD005074. DOI: 10.1002/14561858.CD005074.pub3.

In the systematic review, the assessment of the quality of the evidence for hospital admissions, COPD-related ED visits, and COPD-related GP visits/phone calls was downgraded to moderate quality of evidence because the estimate of effect includes both benefit and harm associated with action plans (imprecision/sparse evidence). (8) The authors did not downgrade the studies based on risk of bias; however, the review identifies a number of important concerns regarding the methodological quality of the studies included in these outcomes. For example, there was inadequate information in the published report of 1 of the 2 studies used in the pooled results for hospital admission and ED visits for COPD on randomization methods, allocation concealment, blinding of participants, outcome assessors, and personnel recruiting participants, how incomplete quality of life data were addressed, and whether the study is free of selective reporting and other biases. The second study also did not report adequate information on randomization methods and blinding of participants and outcome assessors. (8) Given that these are important methodological considerations, the GRADE scores could be downgraded to low quality. Therefore, the moderate GRADE level may overestimate the certainty in the estimate of effect.

One study (sample size [n], 89) did show a significant increase in the total number of ambulance calls in the action plan group compared with the usual care group (mean difference [MD], 1.70; 95% confidence interval [CI], 0.17–3.23). (8)

Use of Medications

Four studies reported information on the use of corticosteroids during the follow-up period. Although the study did not present the raw data, 1 study found that individuals in the action plan group were statistically significantly more likely to be treated with oral corticosteroids for an acute exacerbation over 12-months follow-up ($P < 0.001$). (8) Two studies showed a statistically significant increase in the number of courses of oral corticosteroids over 12 months of follow-up (n, 200; MD, 0.74; 95% CI, 0.12–1.35) (GRADE = moderate); however, the other 2 studies showed no statistically significant difference in the odds of being treated with at least 1 course of oral corticosteroids for an acute exacerbation (n, 200; odds ratio [OR], 2.60; 95% CI, 0.98–6.90) (GRADE = not reported). (8) Of note, as discussed above, the GRADE score does not

take into consideration potentially important concerns regarding the methodological quality of the studies. Therefore, the moderate GRADE level may overestimate the certainty in the estimate of effect.

In contrast, the pooled odds of being treated with at least 1 course of antibiotics for an acute exacerbation of COPD were statistically significantly higher (n, 349; OR, 2.02; 95% CI, 1.29–3.17), but there was no statistically significant difference in the number of courses of antibiotics (n, 200; MD, 0.78[1]; 95% CI, −0.24 to 1.79). (8) A statistically significant increase in the number of days on antibiotics was observed for the action plan group in 1 study (n, 56; MD, 6.00; 95% CI, 1.40 to 10.60). (8) While a similar trend in increased days on corticosteroids in the action plan group was also observed, this difference was not statistically significant (n, 56; MD, 6.00; 95% CI, −5.53 to 17.53). (8)

Secondary Outcomes

COPD Self-Management Knowledge and Actions

One study (n, 154) evaluated COPD self-management knowledge and actions using a validated standardized COPD self-management questionnaire. Overall, the study found that individuals in the action plan group had statistically significant higher scores for knowledge outcomes and for actions that participants would take when experiencing an acute exacerbation compared with the usual care group. The knowledge outcomes examined were recognition of respiratory health stability (MD, 1.10; 95% CI, 0.46–1.74), recognition of an early exacerbation (MD, 1.80; 95% CI, 0.75–2.85), and recognition of a severe exacerbation (MD, 2.50; 95% CI, 1.04–3.96). (8) Individuals in the action plan group also had statistically significantly higher scores for actions taken in an early exacerbation (MD, 2.30; 95% CI, 0.96–3.64) and actions in a severe exacerbation (MD, 1.50; 95% CI, 0.62–2.38) compared with the control group. (8)

A second study (n, 111) also evaluated COPD knowledge and found no significant differences between the action plan and control groups for knowledge or actions to be taken for an acute exacerbation. However, the questionnaire used to assess these outcomes is not validated. (8)

Other Outcomes

No statistically significant differences were observed for the other reported secondary outcomes of anxiety, depression, mortality, symptoms, functional capacity, or lung function. (8)

Walters et al (8) found that adverse effects were not well reported in the included studies, but references other literature which highlights potential concerns associated with increased adverse drug reactions due to increased oral corticosteroid use because of the use of action plans.

Summary of the Evidence

Overall, Walters et al (8) concluded that "the practice of giving patients an action plan and limited self management education for the management of COPD exacerbations, without a multi-faceted self management program or ongoing case management, cannot be recommended as the standard of care in COPD." This conclusion is based on evidence from other systematic reviews that have looked at more comprehensive self-management programs—in which action plans may be 1 component of the intervention—that have shown benefits for individuals with COPD. For example, a 2009 Cochrane Collaboration systematic review that evaluated COPD self-management education programs concluded that self-management education is associated with a reduction in hospital admissions. (10) Similarly, a systematic review by Peytremann-Bridevaux et al (13) concluded that COPD-disease management programs improved exercise capacity, health-related quality of life, and hospital admissions.

[1] The text of the review reports the mean differences as 0.79, but the forest plot and summary data table (Comparison 1. action plan versus usual care) report the mean difference as 0.78. (8)

Conclusions

Based on 1 systematic review that evaluated the effectiveness of action plans with or without limited education (education sessions up to 1 hour in length) compared with usual care, the following conclusions were reached:

- Action plans significantly increase antibiotic and corticosteroid use during an acute exacerbation.
- Action plans significantly increase patient knowledge about COPD and what actions to take during an exacerbation.
- Action plans do not impact health care utilization or other clinical outcomes including health-related quality of life, mortality, lung function, functional capacity, symptoms, anxiety, or depression.

Acknowledgements

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Appendices

Appendix 1: Literature Search Strategies

Search date: September 15, 2012
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; CRD

Q: COPD action plans
Limits: 2008-current; English
Filters: health technology assessments, systematic reviews, and meta-analyses

Database: Ovid MEDLINE(R) <1946 to September Week 1 2012>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <September 14, 2012>, Embase <1980 to 2012 Week 37>
Search Strategy:

#	Searches	Results
1	exp Pulmonary Disease, Chronic Obstructive/ use mesz	19095
2	Chronic Obstructive Lung Disease/ use emez	60772
3	Chronic Bronchitis/ use emez	7298
4	(chronic adj2 obstructive adj2 (lung* or pulmonary or airway* or airflow or respiratory) adj (disease* or disorder*)).ti,ab.	61114
5	(copd or coad).ti,ab.	52753
6	chronic airflow obstruction.ti,ab.	1094
7	exp Emphysema/	39763
8	((chronic adj2 bronchitis) or emphysema).ti,ab.	53761
9	or/1-8	173230
10	Self Care/	46311
11	Patient Care Planning/	57345
12	Health Plan Implementation/ use mesz	3252
13	Health Care Planning/ use emez	71752
14	Treatment Planning/ use emez	85608
15	(action adj2 plan*).mp.	10482
16	((self adj (care or manag* or treat*)) or self-care or self-manag* or self-treat*).ti.	11431
17	((care or disease) adj manag*).ti.	8602
18	((care or disease or health or patient*) adj2 plan*).ti.	18638
19	Patient Care/	176297
20	*Patients/ use mesz	9149
21	*Patient/ use emez	133261
22	*Chronic Patient/ use emez	426
23	or/19-22	317588

24	Health Planning/ use mesz	20354
25	Planning/ use emez	15783
26	or/24-25	36137
27	23 and 26	1634
28	or/10-18,27	294968
29	Meta Analysis.pt.	36232
30	Meta Analysis/ use emez	65756
31	Systematic Review/ use emez	52961
32	exp Technology Assessment, Biomedical/ use mesz	8833
33	Biomedical Technology Assessment/ use emez	11371
34	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	288884
35	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	3611
36	or/29-35	348468
37	9 and 28 and 36	112
38	limit 37 to english language	101
39	limit 38 to yr="2008 -Current"	51
40	remove duplicates from 39	42

Cochrane Library

MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees 1838
chronic near/2 obstructive near/2 (lung* or pulmonary or airway* or airflow or respiratory) next (disease* or disorder*):ti,ab,kw OR copd or coad:ti,ab,kw OR chronic airflow obstruction:ti,ab,kw 7234
MeSH descriptor: [Emphysema] explode all trees 92
(chronic near/2 bronchitis) or emphysema:ti,ab,kw 1932
#1 or #2 or #3 or #4 8822
MeSH descriptor: [Self Care] this term only 2158
MeSH descriptor: [Patient Care Planning] this term only 386
MeSH descriptor: [Health Plan Implementation] this term only 63
action near/2 plan* or (self next (care or manag* or treat*)) or self-care or self-manag* or self-treat*:ti or (care or disease) next manag*:ti or (care or disease or health or patient*) near/2 plan*:ti 1854
#6 or #7 or #8 or #9 3759
MeSH descriptor: [Patient Care] this term only 91
MeSH descriptor: [Patients] this term only 219
#11 or #12 310
MeSH descriptor: [Health Planning] this term only 58
#13 and #14 0
#5 and #10 76

CDSR=8
DARE=2
HTA=1

CRD

Line	Search	Hits
1	MeSH DESCRIPTOR Pulmonary Disease, Chronic Obstructive EXPLODE ALL TREES	298
2	(chronic adj2 obstructive adj2 (lung* OR pulmonary OR airway* OR airflow OR respiratory) adj (disease* OR disorder*)):TI OR (copd OR coad):TI OR (chronic airflow obstruction):TI	236
3	MeSH DESCRIPTOR Emphysema EXPLODE ALL TREES	19
4	((chronic adj2 bronchitis) OR emphysema):TI	50
5	#1 OR #2 OR #3 OR #4	372
6	MeSH DESCRIPTOR Self Care	282
7	MeSH DESCRIPTOR Patient Care Planning	62
8	MeSH DESCRIPTOR Health Plan Implementation	13
9	(action ADJ2 plan*) OR ((self ADJ (care OR manag* OR treat*)) OR self-care OR self-manag* OR self-treat*):TI OR ((care OR disease) ADJ manag*):TI OR ((care OR disease OR health OR patient*) ADJ2 plan*):TI	325
10	#6 OR #7 OR #8 OR #9	574
11	MeSH DESCRIPTOR Patient Care	26
12	MeSH DESCRIPTOR Patients	22
13	MeSH DESCRIPTOR Health Planning	32
14	#11 OR #12	48
15	#13 AND #14	0
16	#5 AND #10	25

Appendix 2: AMSTAR Checklist

Table A1: Results of Assessment of Systematic Review Quality Using AMSTAR

Question	Score and Details
1. Was an a priori design provided?	1 (yes): research question and inclusion criteria were clearly stated
2. Was there duplicate study selection and data extraction?	1 (yes): duplicate study selection and data extraction was used and there was a process in place to deal with disagreements
3. Was a comprehensive literature search performed?	1 (yes): > 2 electronic databases were searched, key words and MESH terms were stated
4. Was the status of publication (i.e., grey literature) used as an inclusion criteria?	0 (can't answer): this information was not provided in the review
5. Was a list of the studies (included and excluded) provided?	1 (yes): both included and excluded studies were listed
6. Were the characteristics of the included studies provided?	1 (yes): data from the original studies including characteristics of the participants, interventions, and outcomes were provided
7. Was the scientific quality of the included studies assessed and documented?	1 (yes): the Cochrane Collaboration risk of bias tool was used to assess the quality of the studies, and the overall quality of the evidence was assessed using GRADE
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	0 (no): while the quality of the studies was assessed and discussed, the quality of the evidence was not explicitly stated in the recommendations or in the conclusions
9. Were the methods used to combine the findings of the studies appropriate?	0 (no): for some outcomes (COPD GP visits/phone calls, non-COPD GP visits/phone calls, at least 1 course of antibiotics, at least 1 course of corticosteroids) there was substantial heterogeneity (I^2 > 50%), but the fixed effects model was still used
10. Was the likelihood of publication bias assessed?	1 (yes): the methods state that funnel plots were used to assess publication bias; however, the results of the funnel plot are not reported
11. Was the conflict of interest stated?	0 (no): while sources of support were listed for the systematic review authors, sources of support for the authors of the included studies were not reported
TOTAL SCORE	**7 out of 11**

Abbreviations: COPD, chronic obstructive pulmonary disease; GP, general practitioner; MESH, medical subject headings.

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Prophylactic Antibiotics for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

Health Quality Ontario

February 2015

Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario 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. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario 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.

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To conduct its rapid reviews, the Evidence Development and Standards branch and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
AZM	Azithromycin
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
FEV_1	Forced expiratory volume in 1 second
GI	Gastrointestinal
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
MD	Median days
NNT	Number needed to treat
NNH	Number needed to harm
OR	Odds ratio
OHTAC	Ontario Health Technology Advisory Committee
QBP	Quality-Based Procedure
RCT	Randomized controlled trial
RR	Relative risk
SR	Systematic review

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to assess the effectiveness and safety of the prophylactic use of the antibiotic azithromycin (AZM) for COPD patients who are at increased risk of future exacerbations.

Clinical Need and Target Population

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition of irreversible airflow limitation. (1) An inflammatory disease, it fluctuates from periods of stability to periods of acute worsening (exacerbation) where interventions and hospitalization may be required to improve airflow. (1) Antibiotics are one intervention with demonstrated effectiveness for treating COPD exacerbations where there is evidence of infection (e.g., purulent sputum). (2) However, their role in preventing exacerbations, especially among patients who have frequent exacerbations despite optimal therapy, is poorly understood.

Technology/Technique

There are many classes of antibiotics, including beta-lactams (e.g., penicillin), tetracyclines (e.g., doxycycline), quinolones (e.g., moxifloxacin), and macrolides (e.g., azithromycin [AZM]). (3) The latter type have demonstrated antimicrobial effectiveness for the treatment of respiratory infections, (4) and also exert immunoregulatory actions that restrict the destruction of lung tissue by key immune-system cells. (2)

Macrolide maintenance therapy became standard care for patients with diffuse panbronchiolitis (a severe progressive inflammatory lung disease affecting small air passages) in the late 1980s. This was prompted after it was observed to result in a dramatic decrease in symptoms and increase in survival (i.e., a 60% to 70% increase in 10-year survival). (2) Randomized controlled trials (RCTs) investigating macrolide maintenance therapy with AZM to treat cystic fibrosis (another chronic inflammatory respiratory disease) have shown significant improvements in lung function, physical condition, and weight gain, and decreases in the frequency of infectious exacerbations. (5) Maintenance (i.e., prophylactic) doses of antibiotics tend to be lower than the doses needed to treat an acute infection, but adverse effects of prolonged antibiotic therapy are of great concern. This is true at both the patient level (e.g., AZM-associated hearing impairment) and at the societal level, with concerns about antibiotic resistance. The evidence for the effectiveness and safety of the prophylactic use of macrolides in COPD has been mixed. (5) To our knowledge, a systematic evidence review synthesizing studies on AZM alone has yet to be undertaken.

Rapid Review

Research Question

What is the effectiveness and safety of the prophylactic use of the antibiotic azithromycin (AZM) for COPD patients who are at increased risk of future exacerbations?

Research Methods

Literature Search

Search Strategy

A literature search was performed on July 4, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, and EBM Reviews, for studies published from January 1, 2009, to July 4, 2014. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2009, and July 4, 2014
- health technology assessments, systematic reviews (SRs), and meta-analyses
- studies evaluating prophylactic use of antibiotics
- studies on adult, stabilized COPD patients
- azithromycin (AZM) results reported separately

Exclusion Criteria

- RCTs, observational studies, case series, editorials, conference abstracts
- studies on populations other than COPD (e.g., tracheostomy, cystic fibrosis)
- studies evaluating antibiotic treatment during an acute exacerbation of COPD
- studies reporting only on classes of antibiotics or all antibiotics in aggregate

Outcomes of Interest

- effect on exacerbations
- adverse events (i.e., gastrointestinal side effects, hearing, and antibiotic resistance)

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (6)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (7) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) 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. Any limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: the large magnitude of effect, the dose response gradient, and any residual confounding factors. (7) For more detailed information, please refer to the latest series of GRADE articles. (7)

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

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect.
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different.
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect.
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of the effect.

Results of Rapid Review

The database search yielded 262 citations published between January 1, 2009, and July 4, 2014 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Four systematic reviews (SRs) met the inclusion criteria (8-11) and received AMSTAR scores of 10, 8, 8, and 7, respectively. We selected the SR by Herath and Poole for inclusion in this rapid review because of its superior quality as assessed by AMSTAR, and because it had the most comprehensive search. It captured the same RCTs on AZM in COPD populations as were captured in the other 3 SRs, as well as

recent literature, both published and unpublished. The reference list of the included SR and health technology assessment websites were hand-searched to identify other relevant studies, and no additional citations were identified.

The SR by Herath and Poole (8) is an update to another Cochrane review, done in 2003, on chronic bronchitis. Herath and Poole aimed to a) focus exclusively on COPD patients, and b) update the evidence of the effect on exacerbations, quality of life, and, secondarily, possible harms. Their search for eligible RCTs included literature up to August 2013. Although their review examined all classes of oral antibiotics, AZM was analyzed and results were reported separately, as available. Table 1 provides an overview of the AZM trials included in the review.

Table 1: Prophylactic Azithromycin Trials on COPD Patients Included in Systematic Review

Author, Year	Country	Intervention (n) Comparator (n)	Follow-up Period	Outcomes Reported
Albert et al, 2011 (12)	United States	AZM 250mg daily for 1 year (570) Placebo (572)	1 year	Time to first AE Frequency of AEs QOL Hearing impairment
Mygind et al, 2010 (13)[a]	Denmark	AZM 500mg 3 days every month for 36 months (287) Placebo (288)	3 years	Change in pulmonary function AE duration and frequency Hospital admissions QOL Mortality

Abbreviations: AE, acute exacerbation of COPD; AZM, azithromycin; COPD, chronic obstructive pulmonary disease; n, number; QOL, quality of life.
[a]Trial information included in the review is based on unpublished data presented at a conference.
Source: Herath and Poole, 2013. (8)

The 2 AZM trials were conducted on moderate to severe COPD patients (i.e., with forced expiratory volume in 1 second [FEV_1] < 70%), who, within the previous year, had at least 1 documented exacerbation OR emergency-department visit or hospitalization for exacerbation, OR used systemic corticosteroids, OR had continuous oxygen supplementation. Mygind and colleagues excluded patients whose life expectancy was shorter than the study duration, (13) both studies excluded patients with other significant respiratory conditions, and Albert and colleagues also excluded those at risk for cardiac conditions (e.g., with resting heart rate above 100 beats per minute). (12) In the study by Albert and colleagues, (12) about 80% of participants took AZM as an adjunct to inhaled therapy of glucocorticoids, a long-acting beta2-agonist, a long-acting muscarinic agent, or any combination of the above. In both studies, all participants were 40 years of age or older.

Effect on Exacerbations

As seen in Table 1, the 2 RCTs reported the effect of AZM on COPD exacerbations via slightly different outcomes. Thus, in the SR, outcome was reported separately for each RCT. The primary outcome for Albert and colleagues (12) was time to first exacerbation (median days [MD]), which was significantly longer for patients in the AZM group (266 days; 95% confidence interval [CI], 227–313) than for those who received a placebo (174 days; 95% CI, 143–215, $P < 0.001$). The rate of exacerbations per patient-year was also significantly lower in the AZM group (1.48) compared with 1.83 in the placebo group (rate ratio, 0.83; 95% CI, 0.72–0.95, $P = 0.01$). The number of patients who would need to be treated (NNT) to prevent one exacerbation was 2.86. Reporting on the RCT by Albert and colleagues, SR authors Herath and Poole present the rate ratios of exacerbations, stratified by COPD severity, for patients at stage 2, 3,

and 4 per the Global Initiative for Chronic Obstructive Lung Disease (GOLD). The rates are 0.77, 0.89, and 0.72 per patient-year, respectively. The SR states that the data were inadequate to determine statistical significance for the rate ratios. (8)

The trial by Mygind and colleagues (13) analyzed duration of exacerbations and found that the number of days of exacerbation was significantly lower in the AZM group than in the placebo group (MD 93 versus MD 111, $P = 0.04$). They broke it down further, looking separately at home- and hospital-managed exacerbations, and also found a statistically significant reduction in days of severe exacerbation managed at home (MD 31 in the AZM group versus MD 42.5 in the placebo group, $P = 0.01$). A similarly shortened duration was found for hospital-managed exacerbations (a median hospital stay of 15.5 days for the AZM group versus 18 days for the placebo group). In this case, however, the authors did not provide a *P* value, so statistical significance cannot be determined.

Adverse Events

Overall, serious adverse events are poorly explained in this body of literature. Albert and colleagues (12) did not find any difference in the risk of gastrointestinal (GI) disorders between AZM and placebo groups (odds ratio [OR], 0.71; 95% CI, 0.36–1.39), though the overall event rate was low (AZM: 15 events, placebo: 21 events, $P = 0.38$). In contrast, Mygind and colleagues reported significantly more adverse lower-GI effects in the AZM group (513 versus 185 events, $P = 0.006$), with no difference in the number of upper-GI adverse effects or infections. (13)

Albert and colleagues found a significant increase in the risk of hearing impairment in the AZM group compared with the placebo group (OR, 1.39; 95% CI, 1.05–1.85), and reported that this, in the majority of cases, was the cause of the drug being discontinued. (12) Based on this study, the number of patients who would need to be treated to cause harm to one patient (NNH) was 18 (95% CI, 128–9). The study reported that hearing returned to baseline level in 25% to 38% of the participants in both study groups (see (12) for details). The authors speculate that their study overestimated the incidence of hearing decrements because of overly stringent eligibility criteria and audiometry measurement error.

The same study (12) included antibiotic resistance as a secondary outcome. Specifically, Albert and colleagues measured colonization at baseline (see Table 2) and again at follow-up, to see if more patients in the AZM group were colonized by macrolide-resistant organisms. If so, this could contribute to a macrolide-resistance problem. When organisms develop resistance to the antimicrobial effects of AZM and other macrolides, these drugs are no longer effective for preventing or treating infections. As therapy options become fewer, individual clinical outcomes are poorer, the infective phase can be prolonged, and resistant bacteria are allowed to spread across patients and populations. (14) The researchers used sputum organism analysis to evaluate the rates of bacterial colonization for the 2 groups, identifying the most common organisms via expectorated sputum when possible (in 15% of participants) and via nasopharyngeal swab in the remaining 85%. The results of evaluation at baseline are shown in Table 2.

Table 2: Most Common Organisms Identified at Baseline in Study Participants

Organisms	Number of Patients per Group		Number of Patients Colonized (%)	
	Intervention	Control	Intervention	Control
S. aureus	570	572	60 (10.7)	71 (12.7)
Moraxella spp.			13 (2.3)	6 (1.1)
S. pneumoniae			6 (1.1)	6 (1.1)

Abbreviations: *Moraxella* spp., *Moraxella* species; *S. aureus, Staphylococcus aureus*; *S. pneumoniae, Streptococcus pneumonia.*
Source: Albert et al, 2011. (12)

The authors speculated that the predominance of *S. aureus* in their study sample may be confounded by the use of nasopharyngeal sampling of patients in the 85% who could not expectorate sputum at the end of the treatment period.

The next finding—the results at follow-up—concerned patients who did not have existing bacterial colonization at baseline (i.e., those patients *not* in Table 2). Of these, the placebo group (n = 172) had a higher incidence rate of colonization by respiratory pathogens (i.e., rate of new colonization) at follow-up than did the AZM group (n = 66; $P < 0.001$). This statistically significant finding refers to colonization by any organism—macrolide-resistant or not—during the study period, and would generally be expected provided AZM is effective at killing bacteria. However, while less likely to have new colonization overall, those in the AZM group were more likely to have new colonization by macrolide-resistant organisms. This is also to be expected, given the natural history of how pathogens mutate and therefore develop resistance. In a both statistically and clinically significant finding, the incidence of macrolide resistance was significantly higher in the newly colonized AZM group than in the corresponding placebo group (81% versus 41%, $P < 0.001$).

Limitations

The body of evidence on the effectiveness and safety of AZM as a prophylactic intervention for COPD has limitations. The number of studies is small, with significant heterogeneity across studies. The RCT by Albert and colleagues (12) is cited as groundbreaking in this field due to its large size and resulting statistical power. However, 22 *a priori* subgroup analyses were conducted as part of that RCT, thus decreasing its statistical power to about 62%, as they were performed without statistical adjustment for multiple comparisons (resulting in a high risk of false positives). The results of the trial by Mygind and colleagues (13) were extracted by the SR authors from the abstract of a conference presentation of unpublished data which does not appear to have since been published. Herath and Poole report that their attempts to contact the authors were unsuccessful. Therefore, some important details of methodology (i.e., randomization) execution, and results are missing. Albert and colleagues, in their article, briefly discuss a case series on the topic of prophylactic AZM for COPD. However, this rapid review has been conducted without knowledge of other published observational or case-based literature, if any, which may exist. A full systematic review of primary studies is needed, to rigorously analyze and evaluate the entire body of contemporary evidence.

The GRADE quality assessment of the body of evidence on the effectiveness and safety of AZM for COPD exacerbation prophylaxis, based on the SR by Herath and Poole, can be found in Table A2 (Appendix 2).

Addendum to Rapid Review of Systematic Reviews

Herath and Poole (8) identified an RCT that was ongoing at the time of their review, which has since been published. (15) Given the knowledge of at least one trial and potentially others published since the SR, and given the gravity of the potential benefits and implications of long-term antibiotic therapy, it was determined that a supplemental search was warranted. A unique literature search was performed for published single RCTs comparing AZM with placebo in COPD patients in Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Embase, and EBM Reviews between January 1, 2013 and July 17, 2014 (see Appendix 1b). The 91 resulting citations were reviewed by a single author, who screened for RCTs but otherwise used identical inclusion and exclusion criteria as detailed on page 8.

Two single RCTs, both conducted in the Netherlands, met the inclusion criteria. (15, 16) Uzun and colleagues' study, the study identified as ongoing in the Herath and Poole SR, evaluated 500mg of AZM,

3 times per week for 1 year, in patients 18 years or older who had 3 or more exacerbations in the previous year. (15) In this study, 92 patients at a single centre were randomized to AZM (n = 47) or placebo (n = 45) in order to assess the rate of exacerbations over 12 months (per patient-year) and, secondarily, to assess the rate of adverse events, side effects, and macrolide resistance. The results of these outcomes are in Table 3.

Table 3: Prophylactic AZM Versus Placebo for COPD Patients—Results on Primary and Secondary Outcomes of Interest from an RCT

Outcome	Measurement Reported	Azithromycin	Placebo	*P* Value
Exacerbation rate (unadjusted)	rate ratio per patient-year	0.60 (95% CI: 0.43–0.84)		0.003
Exacerbation rate (adjusted[a])	rate ratio per patient-year	0.58 (95% CI: 0.42–0.79)		0.001
Time to first exacerbation	median days	130 (95% CI: 28–323)	59 (95% CI: 31–87)	0.001
Gastrointestinal adverse events	n (%)	16	10	NR
Diarrhoea		9 (19%)	1 (2%)	0.015
Nausea or vomiting		3 (6%)	2 (4%)	NR
Other		4 (9%)	7 (16%)	NR
Acquisition of macrolide-resistant bacteria[b]	n (%)	3 (6%)	11 (24%)	0.036

Abbreviations: AZM, azithromycin; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; n, number of patients; NR, not reported; RCT, randomized controlled trial.

[a]Covariates adjusted for: use of low-dose long-term prednisolone, number of exacerbations in previous year, age, sex, smoking, and FEV_1.

[b]Sputum samples were obtained and analyzed from only a subset of 42 participants.

Source: Uzun et al, 2014. (15)

The exacerbation rate over 12 months was significantly lower in the AZM group compared with the placebo group, and was nearly identical after adjusting for relevant covariates. In terms of adverse events, diarrhoea was significantly more common in the AZM group. Interestingly, more patients taking placebo acquired macrolide-resistant bacteria, compared with those taking AZM. (15) This finding could not be explained by the authors and, in contrast to the macrolide-resistance finding by Albert and colleagues, it is the opposite of what would be expected. No audiometry was performed, and no formal results presented regarding hearing impairment. However, the authors stated that 1 participant receiving placebo reported hearing loss at the end of the study. (15) The authors highlight important differences between their study and the one conducted by Albert and colleagues in terms of methodology, inclusion criteria, participant characteristics, and drug regimen; they caution against direct comparison of the 2 studies. Uzun and colleagues' study population had a larger representation of females, and stricter exclusion of participants with bronchiectasis, a condition for which AZM is known to be effective, and whose inclusion may, therefore, confound the results.

In the second RCT that met our inclusion criteria, Berkhof and colleagues had a primary focus on cough-specific quality of life in COPD patients at GOLD stage 2 or higher, aged 40 years and older, with chronic productive cough. (16) Participants (n = 84) were randomized to receive a placebo or 250mg of AZM 3 times per week for 12 weeks, with follow-up extending to 18 weeks. (16) As secondary outcomes, time to first exacerbation, adverse events, and global measurement of colonization with respiratory pathogens were reported (see Table 4 for results).

Table 4: Prophylactic AZM Versus Placebo for COPD Patients—Results on Secondary Outcomes of Interest From an RCT

Outcome	Measurement Reported	Azithromycin	Placebo	*P* Value
Time to first exacerbation	20th percentile, days[a]	105 (SD = 30)	66 (SD = 21)	0.13
Gastrointestinal adverse events	n (%)	5 (11.9%)	6 (14.3%)	0.75
Colonization with respiratory pathogens at 12 weeks (all)	n (Δ from baseline)	5[b] (-13)	18[c] (0)	NR

Abbreviations: AZM, azithromycin; COPD, chronic obstructive pulmonary disease; n, number of patients; NR, not reported; RCT, randomized controlled trial; SD, standard deviation.
[a]Percentile time calculated because less than 25% of the patients in the azithromycin group had an exacerbation during the 18-week follow-up period.
[b]One participant developed colonization by azithromycin-resistant *Haemophilus influenzae* bacteria at 12 weeks.
[c]One participant had colonization with azithromycin-resistant *Staphylococcus aureus* bacteria at baseline, but not at 12 weeks.
Source: Berkhof et al, 2013. (16)

Berkhof and colleagues found no difference in time to first exacerbation—a finding which must be considered in the context that a very small number of events occurred over the potentially too-short follow-up period (Table 4, footnote a). Similar to Mygind and colleagues, they found no difference in adverse events between groups; and their study, in line with the others identified in this review, observed a reduction in respiratory pathogen colonization among participants taking AZM. (16)

The findings from the SR by Herath and Poole (8) and from the 2 RCTs in this addendum (15, 16) are limited in comparability in terms of:

- AZM administration: 4 different regimens and treatment periods. The Expert Panel advised that, while 3 dosages per week will unlikely differ significantly from daily administration (due to the long half-life of AZM), a drug regimen of 3 days per month (Mygind et al (13)) is clinically different and, moreover, unlikely to be sufficient for effectiveness.
- Follow-up time: This ranged from as short as 18 weeks to 3 years (median: 12 months), leaving long-term effects unknown.
- Clinical characteristics: To combine the 4 study populations would be challenging. The Expert Panel advised that 1 or more exacerbations in a year would capture the vast majority of patients, but those with 3 or more exacerbations in a year, and those with chronic productive cough, are distinct subsets of COPD patients.
- Sample size: Most of the studies were adequately powered for primary outcomes. However, they likely lack sufficient group sizes and/or event rates for statistical comparison of subgroup or secondary analyses, especially of adverse events.
- Outcomes of interest: These were measured using different units of analysis, thus precluding statistical synthesis.
- Antibiotic-resistance measurement: Sputum analysis was conducted on a subset of the study populations, and acquired via different methods (i.e., expectorated sputum versus nasopharyngeal swab).

In light of heterogeneity in study populations and outcome measures, the Health Quality Ontario Rapid Review methodology for primary studies includes a risk of bias assessment based on GRADE Working Group criteria (7) to assess quality of evidence. Risk of bias is evaluated based on consideration of allocation concealment, blinding, complete accounting of patients and outcome events, selective reporting bias, and other limitations. Risk of Bias for the Uzun (15) and Berkhof (16) RCTs can be found in Table A4 (Appendix 3).

Conclusions

The evidence yielded mixed results on the effectiveness and safety of the prophylactic use of the antibiotic azithromycin (AZM) for COPD patients.

From the examination of 1 systematic review of RCTs (in Rapid Review, proper):

- Compared with placebo, prophylactic treatment with AZM in moderate to severe COPD patients at increased risk of future exacerbations significantly:
    - increased time to first exacerbation (GRADE quality of evidence: Moderate)
    - decreased the frequency of exacerbations (GRADE: Moderate)
    - shortened the duration of exacerbations (GRADE: Low)
- Compared with placebo, prophylactic treatment with AZM in moderate to severe COPD patients at increased risk of future exacerbations was associated with significant occurrence of adverse events, including:
    - GI adverse events (GRADE: Very low)
    - hearing impairment (GRADE: Moderate)
    - increased likelihood of colonization with macrolide-resistant organisms (i.e., increased risk of macrolide resistance) (GRADE: Moderate)

From the examination of 2RCTs (in addendum to Rapid Review):

- Based on a single RCT conducted on COPD patients who had experienced 3 or more exacerbations in the previous year, prophylactic AZM therapy compared with placebo:
    - increased the time to first exacerbation
    - reduced the frequency of exacerbations
    - increased the likelihood of diarrhoea
    - *reduced* the likelihood of colonization with macrolide-resistant organisms (i.e., reduced risk of macrolide resistance), for which no explanation was provided
- Based on a single RCT conducted on COPD patients with chronic productive cough, no difference was found between the AZM and placebo groups in
    - effect on exacerbations
    - GI adverse events

The evidence showed both a general trend of beneficial effect on patients' COPD exacerbation rates and uncertainty around the risk of adverse events and antibiotic resistance associated with prophylactic AZM therapy.

Acknowledgements

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*Member actively participated in the Update and Integration COPD Expert Advisory Panel in Phase 3, which involved updating the acute episode of care and integrating it with the post-acute episode of care.

Health Quality Ontario's Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients

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Cardiovascular Services		
Kori Kingsbury	Cardiac Care Network	Chief Executive Officer

Appendices

Appendix 1a: Literature Search Strategy for Rapid Review

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 2014>, EBM Reviews - ACP Journal Club <1991 to June 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <2nd Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <May 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <2nd Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <2nd Quarter 2014>, Ovid MEDLINE(R) <1946 to June Week 4 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 03, 2014>
Search Strategy:

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1 exp Patient Discharge/ (20028)
2 exp Aftercare/ or exp Convalescence/ (10216)
3 "Continuity of Patient Care"/ or exp "Recovery of Function"/ (49265)
4 ((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab. (38163)
5 exp Stroke/ (90485)
6 exp brain ischemia/ or exp intracranial hemorrhages/ (132869)
7 (stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*)).ti,ab. (204881)
8 exp Heart Failure/ (92463)
9 (((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab. (135313)
10 exp Pulmonary Disease, Chronic Obstructive/ (38585)
11 exp Emphysema/ (10912)
12 (copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab. (58516)
13 (chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab. (36565)
14 exp Pneumonia/ (76229)
15 (pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab. (141791)
16 or/1-15 (781419)
17 exp Anti-Bacterial Agents/ (549766)
18 Antibiotic Prophylaxis/ (9748)
19 exp Macrolides/ (92986)
20 ((antibiotic* adj2 (prophylaxis or prophylactic or preemptive or pre-emptive)) or macrolide* or erythromycin or azithromycin or clarithromycin or azasite or azenil or azibiot or azin or azithrocin or azitromax or aztrin or hemomycin or misultina or sumamed or vinzam or zifin or zithromax or zitrocin or zitrotek or zmax).ti,ab. (51341)
21 or/17-20 (590273)
22 16 and 21 (38799)
23 Meta Analysis.pt. (50072)
24 Meta-Analysis/ or Meta-Analysis as Topic/ or exp Technology Assessment, Biomedical/ (72206)
25 (((systematic* or methodologic*) adj3 (review* or overview*)) or pooled analysis or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab. (183814)
26 (meta analy* or metaanaly* or health technolog* assess*).mp. (133214)
27 or/23-26 (263807)
28 22 and 27 (717)
29 limit 28 to (english language and yr="2009 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CLCMR; records were retained] (282)
30 remove duplicates from 29 (262)

Appendix 1b: Literature Search Strategy for Addendum

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 2014>, EBM Reviews - ACP Journal Club <1991 to June 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <2nd Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <June 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <2nd Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <2nd Quarter 2014>, Embase <1980 to 2014 Week 28>, Ovid MEDLINE(R) <1946 to July Week 2 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 16, 2014>
Search Strategy:

1	exp Pulmonary Disease, Chronic Obstructive/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	38683
2	Chronic Obstructive Lung Disease/ use emez	70346
3	exp Emphysema/	42760
4	(copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab.	124284
5	(chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab.	76614
6	or/1-5	207582
7	exp azithromycin/	26824
8	exp Macrolides/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	93105
9	exp macrolide/ use emez	125894
10	Antibiotic Prophylaxis/	30758
11	((antibiotic* adj2 (prophylaxis or prophylactic or preemptive or pre-emptive)) or macrolide* or erythromycin or azithromycin or clarithromycin or azasite or azenil or azibiot or azin or azithrocin or azitromax or aztrin or hemomycin or misultina or sumamed or vinzam or zifin or zithromax or zitrocin or zitrotek or zmax).ti,ab.	106776
12	or/7-11	285604
13	(Meta Analysis or Controlled Clinical Trial).pt.	223587
14	Meta-Analysis/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Meta-Analysis as Topic/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Technology Assessment, Biomedical/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	72466
15	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	104349
16	(((systematic* or methodologic*) adj3 (review* or overview*)) or pooled analysis or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	372138
17	(meta analy* or metaanaly* or health technolog* assess*).mp.	260538
18	exp Randomized Controlled Trial/	724584
19	exp Random Allocation/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Double-Blind Method/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Control Groups/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Placebos/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	349383
20	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	428335
21	(random* or RCT or RCTs or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2315015

22	or/13-21	3201712
23	6 and 12 and 22	1089
24	limit 23 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CLCMR; records were retained]	985
25	limit 24 to yr="2013 -Current" [Limit not valid in DARE; records were retained]	111
26	remove duplicates from 25	96

Appendix 2: Evidence Quality Assessment for Rapid Review

Table A1: AMSTAR Scores of Systematic Reviews That Met the Inclusion Criteria

Author, Year	AMSTAR Score[a]	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Herath and Poole, 2013 (8)	10	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
Yao et al, 2013 (9)	8	✓	✓		✓		✓	✓		✓	✓	✓
Donath et al, 2013 (10)	8	✓	✓	✓	✓		✓	✓		✓		✓
Simoens et al, 2013 (11)	7	✓		✓	✓		✓	✓		✓		✓

Abbreviation: AMSTAR, Assessment of Multiple Systematic Reviews.

[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al. (6)

Table A2: GRADE Evidence Profile for RCTs Comparing Prophylactic AZM With Placebo in COPD

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Time to first exacerbation							
1 (RCT)	No serious limitations[a]	No serious limitations	No serious limitations	Serious limitations (–1)[b]	Undetected	None	⊕⊕⊕ Moderate
Frequency of exacerbations							
1 (RCT)	No serious limitations[a]	No serious limitations	No serious limitations	Serious limitations (–1)[b]	Undetected	None	⊕⊕⊕ Moderate
Duration of exacerbations							
1 (RCT)	Serious limitations (–1)[a]	No serious limitations	No serious limitations	Serious limitations (–1)[b]	Undetected	None	⊕⊕ Low
Gastrointestinal adverse effects							
2 (RCT)	Serious limitations (–1)[a]	Serious limitations (–1)[c]	No serious limitations	Serious limitations (–1)[d]	Undetected	None	⊕ Very low
Hearing impairment							
1 (RCT)	No serious limitations[a]	No serious limitations	No serious limitations	Serious limitations (–1)[d]	Undetected	None	⊕⊕⊕ Moderate
Antibiotic resistance							
1 (RCT)	No serious limitations[a]	No serious limitations	No serious limitations	Serious limitations (–1)[d]	Undetected	None	⊕⊕⊕ Moderate

Abbreviations: AZM, azithromycin; COPD, chronic obstructive pulmonary disease; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial.
[a]For details on risk of bias, see Table A3.
[b]The following were not identified: minimal clinically important reduction in time to, rate of, or duration of exacerbations. Therefore, the relative clinical importance of these findings is poorly understood.
[c]Gastrointestinal adverse effects were scantily reported in both studies, with one finding a significant increase in the treatment arm (13) and the other finding no difference. (12)
[d]Adverse event results are poorly reported and are based on subgroup analysis and may lack adequate power to detect important differences (i.e., the Optimal Information Size criteria is not met).

Table A3: Risk of Bias Among RCTs Comparing Prophylactic AZM With Placebo in COPD

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Albert et al, 2011 (12)	No limitations	No limitations	No limitations	No limitations	No limitations
Mygind et al, 2010 (13)	Limitations[a]	No limitations	Limitations[b]	No limitations	No limitations

Abbreviations: AZM, azithromycin; COPD, chronic obstructive pulmonary disease; RCT, randomized controlled trial.
[a]Random sequence generation and allocation concealment were not well described, as only an abstract was available and attempts to contact authors were unsuccessful.
[b]Limited information on which to judge attrition bias; withdrawal rates were over 40%.
Note: Risk of bias assessment taken from Herath and Poole. (8)

Appendix 3: Evidence Quality Assessment for Addendum

Table A4: Risk of Bias Among RCTs Comparing Prophylactic AZM with Placebo in COPD, Published Between January 1, 2013 and July 17, 2014

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Uzun et al, 2014 (15)	No limitations[a]	No limitations[b]	No limitations[c]	No limitations[d]	No limitations
Berkhof et al, 2010 (16)	No limitations[e]	No limitations[b]	No limitations[f]	No limitations[d]	No limitations

Abbreviations: AZM, azithromycin; COPD, chronic obstructive pulmonary disease; RCT, randomized controlled trial.

[a]Adequate randomization and allocation concealment via computer allocation program with a 1:1 ratio and permutated block size of 10, stratified by use of low-dose long-term prednisolone. (15)

[b]Double-blind study, researchers and participants masked until completion of analysis.

[c]Intention-to-treat analysis was conducted on all randomized participants and also per protocol analysis (80% completion in placebo group, 87% in treatment group) for primary outcome.

[d]All pre-specified outcomes are reported.

[e]Adequate randomization and allocation concealment via computer allocation program with a 1:1 ratio and permutated block size of 4. (16)

[f]Primary and secondary analysis conducted using intention-to-treat principle (95% completion in placebo group, 90% in treatment group). (16)

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(13) Mygind LH, Pedersen C, Vestbo J, Christensen JJ, Frimodt-Moller N, Kristiansen IS, et al., editors. A randomised, placebo-controlled 3 years study of prophylactic azithromycin in 575 patients with chronic obstructive pulmonary disease. ERS Congress; 2010 Sep 18-22; Barcelona, Spain.

(14) World Health Organization. Fact sheet no. 194: Antimicrobial resistance 2014 [updated April 2014]. Available from: http://www.who.int/mediacentre/factsheets/fs194/en/.

(15) Uzun S, Djamin RS, Kluytmans JA, Mulder PG, van't Veer NE, Ermens AA, et al. Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial. Lancet Respir Med. 2014;2(5):361-8.

(16) Berkhof FF, Doornewaard-ten Hertog NE, Uil SM, Kerstjens HA, van den Berg JW. Azithromycin and cough-specific health status in patients with chronic obstructive pulmonary disease and chronic cough: a randomised controlled trial. Respir Res. 2013;14:125.

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Pulmonary Rehabilitation in the Home Versus Other Settings for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews are completed in 2–4-week time frames. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario 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. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario 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.

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In addition, Evidence Development and Standards 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
COPD	Chronic obstructive pulmonary disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HRQOL	Health-related quality of life
PR	Pulmonary rehabilitation
RCT	Randomized controlled trial
SR	Systematic review

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective is to determine the effectiveness of home-based pulmonary rehabilitation compared to pulmonary rehabilitation in other settings for patients with chronic obstructive pulmonary disease (COPD).

Clinical Need and Target Population

Chronic obstructive pulmonary disease encompasses a group of conditions which are all characterized by irreversible airflow limitation from lung tissue damage. COPD affects more than 1.5 million Canadians (1) and is a major cause of both morbidity and mortality, with patients often experiencing shortness of breath (dyspnea), decreased exercise capacity and impaired quality of life. Sudden worsening of COPD is characterized by exacerbations, which often lead to hospitalizations and therefore increased health care costs. Due to the long-term effects of the condition, therapeutic interventions are aimed at preventing disease progression and exacerbations, relieving symptoms, increasing exercise tolerance, and reducing mortality.

Technology/Technique

Pulmonary rehabilitation (PR) is considered one of the most important interventions for COPD patients and has been shown to control and alleviate symptoms of COPD through improvements in dyspnea, exercise capacity, functional status, and health-related quality of life. (2) Programs vary in duration and may be broad in nature, usually combining exercise or endurance training with other components such as nutrition counselling, patient self-management and education, breathing and energy-conserving strategies, and/or psychosocial support. By focusing on multiple patient needs, PR functions to address the chronic and disabling aspect of COPD.

Despite the recognized benefits of PR, it is underutilized, with an estimated less than 2% of Ontarians having access. (3) To date, most PR programs are multidisciplinary and have been performed in a hospital or physical therapy facility; however, they are costly even in an outpatient setting and are limited in availability. Recently, home-based PR programs have emerged as an alternative due to their potential for fewer resources and increased patient accessibility based on their location. However, the effectiveness of these PR programs compared to other settings is unclear.

Rapid Review

Research Question

What is the effectiveness of home-based pulmonary rehabilitation compared to pulmonary rehabilitation in other settings?

Research Methods

Literature Search

Search Strategy

A literature search was performed on December 10, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews for studies published from January 1, 2008, to December 10, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2008, and December 10, 2013
- systematic reviews (SRs) and meta-analyses comparing home-based pulmonary rehabilitation with pulmonary rehabilitation in settings other than the home for COPD and pneumonia patients

Exclusion Criteria

- randomized controlled trials (RCTs), editorials, case studies, observational studies, or commentaries
- home-based pulmonary rehabilitation indicated for maintaining the effects of inpatient/outpatient programs, where training was completed in locations other than at home, or programs requiring regular visits to a rehabilitation centre
- comparison of home-based pulmonary rehabilitation program to standard or usual care (i.e., no pulmonary rehabilitation)
- studies where outcomes of interest cannot be abstracted

Outcomes of Interest

- exercise capacity
- health-related quality of life (HRQOL)

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute, Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community-based care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (4)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (5) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) 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. (5) For more detailed information, please refer to the latest series of GRADE articles. (5)

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

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect.
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different.
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect.
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect.

Results of Rapid Review

The database search yielded 613 citations published between January 1, 2008, and December 10, 2013, (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One systematic review by Vieira et al (6) published in 2010 met the inclusion criteria, which examined the effectiveness of home-based PR and included 12 studies in total, 4 of which were relevant comparing home-based PR to PR in another setting (Table 1). No systematic reviews or meta-analyses pertaining to a pneumonia population were found for the research question. A hand search of the reference list did not identify any other relevant studies. The included systematic review by Vieira et al (6) was of mediocre quality, with an AMSTAR rating of 6 (see Appendix 2, Table A1 for AMSTAR evaluation).

Table 1: Summary of Included Systematic Review by Vieira et al (2010)

Inclusion Criteria	# of RCTs	Comparison
COPD (by any definition) patients, ≥40 years old.	8	Home PR vs. standard care (i.e., no PR)
Home-based PR ≥4 weeks in duration or 12 sessions with lower limb endurance exercise training.	3	Home PR vs. outpatient PR
	1	Home PR vs. standard care vs. outpatient PR

Abbreviations: COPD; chronic obstructive pulmonary disease; PR, pulmonary rehabilitation; RCT, randomized controlled trial.

As pulmonary rehabilitation has already been shown to be effective in improving outcomes such as health-related quality of life and exercise capacity, (2) the focus was on the 4 studies comparing the location of PR (see Appendix 3, Table A4 for characteristics of the 4 included studies). Of the included studies, by far the largest in size was by Maltais et al involving 252 total COPD patients, while the other 3 studies were of smaller sample size, ranging from 41 to 57, and underpowered for the study outcomes measured (6). Maltais et al was also the most rigorously designed study in considering noninferiority and intention-to-treat, which were not mentioned in the other studies (6). The comparison was of home PR to PR in another setting and blinding was not possible as the setting was apparent to both the patients and therapists; however, two of the studies blinded the assessor in measuring outcomes. (7;8) The patient population for all was stable patients with moderate to very severe COPD. Although all settings were considered for the research question, the only comparisons found were between the home and outpatient setting. In addition, due to the self-monitored nature of PR along with necessary adherence, there were high drop-out rates between both groups of patients, although studies reported no difference between the dropout patients among the groups. Adverse events were reported in only one study (7) (see Appendix 2, Table A3 for risk of bias).

The studies could not be combined for meta-analysis due to differences in study duration (8 to 12 weeks), follow-up (6 to 18 months), PR components offered, and measures and values of the study outcomes for exercise capacity and HRQOL (see Appendix 2, Table A2 for GRADE of the outcome measures). Additional PR components included patient self-management information and education, which when included were offered to both groups. Thus, the studies were summarized in tabular format for the individual study results based on the outcomes of interest: HRQOL and exercise capacity (Tables 2 and 3, respectively). Health-related quality of life was measured using the COPD-specific Chronic Respiratory Questionnaire (domains of dyspnea, mastery, fatigue, and emotion) in 3 studies (7-9), with one study using the Borg scale for dyspnea (10) and another also including the St. George's Respiratory Questionnaire (SGRQ) (7). Exercise capacity was measured either through the 4- or 6-minute walk test, the constant work rate test, peak maximum oxygen consumption, and/or maximum work load.

Table 2: Health-related Quality of Life for Home-based Versus Other Setting Pulmonary Rehabilitation

		Within group difference from baseline		Between group difference
HRQOL Test	**Study**	**Home PR**	**Other PR**	**Home PR – Other PR**
CRQ Dyspnea	Güell et al (8)	0.56[a]	0.87[a]	−0.21 (NS)
	Maltais et al (7)	0.82[a]	0.78[a]	0.05 (NS)
	Puente-Maestu et al (9)	0.8[a]	0.72[a]	(NS)
CRQ Mastery	Güell et al (8)	NS	0.6[a]	−0.42 (NS)
	Maltais et al (7)	0.49[a]	0.51[a]	−0.02 (NS)
	Puente-Maestu et al (9)	1.35[a]	0.75[a]	(NS)
CRQ Fatigue	Güell et al (8)	NS	0.56[a]	−0.19 (NS)
	Maltais et al (7)	0.36[a]	0.46[a]	−0.10 (NS)
	Puente-Maestu et al (9)	0.7[a]	0.82[a]	(NS)
CRQ Emotion	Güell et al (8)	NS	0.76[a]	−0.58[b]
	Maltais et al (7)	0.35[a]	0.38[a]	−0.03 (NS)
	Puente-Maestu et al (9)	0.67[a]	0.43[a]	(NS)
SGRQ	Maltais et al (7)	-7.7[b]	-6.3[b]	−1.4 (NS)
Total		-9.2[b]	-3.1 (NS)	−6.1[b]
Symptom		-5.9[b]	-5.7[b]	−0.2 (NS)
Activity Impact		-8.1[b]	-7.9[b]	−0.2 (NS)
Borg Dyspnea	Strijbos et al (10)	-0.4[c]	-0.3[c]	(NS)

Abbreviations: CRQ, Chronic Respiratory Questionnaire; HRQOL, health-related quality of life; NS, not significant; PR, pulmonary rehabilitation; SGRQ, St. George's Respiratory Questionnaire.

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] $P < 0.005$.

Table 3: Exercise capacity for home-based versus other setting pulmonary rehabilitation

Exercise Capacity Test	Study	Within group difference from baseline		Between group difference
		Home PR	Other PR	Home PR – Other PR
4-minute walk test (metres)	Strijbos et al (10)	Difference NA[a]	Difference NA[a]	NS
6-minute walk test (minutes)	Guëll et al (8)	Difference NA[b]	Difference NA[b]	8.69 (NS)
	Maltais et al (7)	8 (NS)	11[b]	-3 (NS)
Constant work rate test (minutes)	Maltais et al (7)	4.1[c]	3.95[c]	0.15 (NS)
	Puente-Maestu et al (9)	3.9[c]	8[c]	NS
Peak VO_2 max (mL/min)	Puente-Maestu et al (9)	5 (NS)	110[c]	Difference NA[b]
Borg scale for leg effort	Strijbos et al (10)	-2.4[a]	-1.0[a]	NS
Maximum workload (Watts)	Strijbos et al (10)	Difference NA[b]	Difference NA[a]	NS

Abbreviations: NA, data not available; NS, not significant; PR, pulmonary rehabilitation; VO_2 max, maximum oxygen consumption.
[a] $P < 0.005$.
[b] $P < 0.05$.
[c] $P < 0.01$.

In general across the studies, there was no difference in improvement between home PR and outpatient PR for exercise capacity or health-related quality of life, suggesting benefit for both types of PR regardless of location. However, Puente-Maestu et al (9) found significant changes in physiological improvements which were not present in the home PR group, which may be due to the study specifically examining the effects of supervised versus self-monitored PR. As such, there was minimal involvement on the part of the home PR therapists compared to other home-based PR programs, which attempted to be more consistent with the corresponding components offered in outpatient PR. In addition, Guëll et al (8) found a significant difference between home and outpatient PR for the Chronic Respiratory Questionnaire (CRQ) domain of emotion only, which the authors hypothesized may be related to the presence of psychological support, which was unique to the outpatient PR program. Exercise capacity values were reported more variously, with some studies noting a significant difference within each of the home and outpatient PR groups without presenting the exact values. The overall outcome was not significant in exercise capacity regardless of the method of measure when comparing home and outpatient PR programs.

From the Vieira et al (6) systematic review, there are few studies comparing home-based PR, with very low quality evaluation of the outcomes of exercise capacity and health-related quality of life. In general, the conclusions of the studies were that home PR and hospital outpatient PR resulted in similar improvements in exercise capacity and HRQOL if properly adhered to. As home-based PR can also be tailored to patients and allow for greater accessibility, they may be an alternative to outpatient PR.

Conclusions

- One relevant systematic review by Vieira et al 2010 (6) was identified and within the review 4 relevant RCTs compared home-based pulmonary rehabilitation with outpatient-based pulmonary rehabilitation.
- Statistically or clinically significant differences were in general not found for the outcomes of exercise capacity or health-related quality of life between home-based versus outpatient-based pulmonary rehabilitation (GRADE quality: very low).

Acknowledgements

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Health Quality Ontario's Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients

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Lisa Droppo	Ontario Association of Community Care Access Centers (OACCAC)	Chief Care Innovations Officer
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Panel Members	Affiliation(s)	Appointment(s)
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Suzy Young	St. Mary's General Hospital	Nurse Practitioner Primary Health Care SWCCAC Intensive Health Care Team Certified Respirator Educator

Appendices

Appendix 1: Literature Search Strategies

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to October 2013>, EBM Reviews - ACP Journal Club <1991 to November 2013>, EBM Reviews - Database of Abstracts of Reviews of Effects <4th Quarter 2013>, EBM Reviews - Cochrane Central Register of Controlled Trials <November 2013>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <4th Quarter 2013>, EBM Reviews - NHS Economic Evaluation Database <4th Quarter 2013>, Ovid MEDLINE(R) <1946 to November Week 3 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <December 09, 2013>
Search Strategy:

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1 exp Patient Discharge/ (19905)
2 exp Aftercare/ or exp Convalescence/ (10298)
3 "Continuity of Patient Care"/ or exp "Recovery of Function"/ (49411)
4 ((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab. (37891)
5 exp Heart Failure/ (93131)
6 (((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab. (135925)
7 exp Pulmonary Disease, Chronic Obstructive/ (26667)
8 exp Emphysema/ (11099)
9 (copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab. (60068)
10 (chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab. (37815)
11 exp Pneumonia/ (78260)
12 (pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab. (147382)
13 or/1-12 (513261)
14 exp Exercise Tolerance/ (9966)
15 exp Exercise/ (127308)
16 exp Rehabilitation/ (162816)
17 exp Rehabilitation Nursing/ (1136)
18 exp "Physical and Rehabilitation Medicine"/ (19975)
19 exp Rehabilitation Centers/ (12881)
20 exp Physical Therapy Modalities/ (136983)
21 (rehabilitat* or (physical* adj (fit* or train* or therap* or activit*)) or ((exercise* or fitness) adj3 (treatment or intervent* or program*)) or (train* adj (strength* or aerobic or exercise*)) or wellness program* or ((pulmonary or lung* or respirat* or cardiac) adj2 (physiotherap* or therap* or rehabilitat*)) or angina plan* or heart manual*).ti,ab. (235554)
22 or/14-21 (536336)
23 Meta Analysis.pt. (52738)
24 Meta-Analysis/ use mesz or exp Technology Assessment, Biomedical/ use mesz (61456)
25 (meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (211340)
26 ((health technolog* or biomedical technolog*) adj2 assess*).ti,ab. (2746)
27 or/23-26 (227857)

28 13 and 22 and 27 (1230)
29 limit 28 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained] (773)
30 remove duplicates from 29 (613)

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Score of Included Systematic Review

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Vieira et al, 2010 (6)	6	✓		✓			✓	✓	✓			✓

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews.

[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al (4)

Table A2: GRADE Evidence Profile for Exercise Capacity and Health-Related Quality of Life Outcomes

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Exercise capacity							
4 (RCTs)	Serious limitations (–1)[a]	No serious limitations	Serious limitations (–1)[b]	Serious limitations (–1)[c]	Undetected		⊕ Very Low
Health-related quality of life							
4 (RCTs)	Serious limitations (–1)[a]	No serious limitations	Serious limitations (–1)[b]	Serious limitations (–1)[c]	Undetected		⊕ Very Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial.

[a]Method of randomization was not specified in two studies although it was noted they were RCTs (9;10). Lack of blinding for all studies for patient and therapists due to home-based versus other setting pulmonary rehabilitation; however, in 2 studies, the assessors were blinded. (9;10) Only 1 study followed the intention-to-treat principle and was designed as a noninferiority trial. (7) There were high losses of follow-up and lack of adherence, but it was explicitly stated in studies that there was not an imbalance between rates in the home versus outpatient groups. One study reported only pre- and post- pulmonary rehabilitation measures and did not contain follow-up reporting. (9) Adverse events were only reported in one study. (7)

[b]The types of pulmonary rehabilitation programs varied in terms of study duration (8-12 weeks) and components (e.g., endurance training, informative sessions, physical therapy). One study's objective was to compare two types of rehabilitation programs, one which was self-monitored with minimal therapist involvement (analogous to a home-based PR program) versus a stricter supervised program involving hospital workers. (9) Reported outcome measures differed between the studies for health-related quality of life (St. George's Respiratory Questionnaire, Chronic Respiratory Questionnaire, Borg scale for dyspnea) as well as for exercise capacity (4-minute walk test, 6-minute walk test, maximum work level, maximum oxygen consumption). Follow-up reporting also varied from 6 to 18 months, except for one study where there was no period of follow-up. (9)

[c]All studies had low sample sizes (30-57 for the home-based versus outpatient-based arms of the study) and were underpowered, except for the study which had the largest number of participants (N=252) and was adequately powered for noninferiority. (7) However, this study's primary outcome was only dyspnea, with secondary outcomes of other domains of health-related quality of life and exercise capacity. (7)

Table A3: Risk of Bias Among Randomized Controlled Trials for Pulmonary Rehabilitation at Home Versus in Another Setting for COPD

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Güell et al, 2008 (8)	Limitations[a]	Limitations[b]	No limitations	No limitations	Limitations[c]
Maltais et al, 2008 (7)	No limitations	Limitations[b]	No limitations	No limitations	No limitations
Puente-Maestu et al, 2000 (9)	Limitations[d]	Limitations[e]	Limitations[f]	No limitations	Limitations[c]
Strijbos et al, 1996 (10)	Limtations[a]	Limitations[e]	No limitations	No limitations	Limitations[c]

[a]Specific method of randomization was not specified; however, the study was identified as a RCT.
[c]No mention of noninferiority study design or intention-to-treat principle.
[b]Patients and therapists could not be blinded due to study design; however, assessors were blinded.
[d]Allocation to pulmonary rehabilitation program was determined by the patients' referring pneumologist.
[e]Patients, therapists, and assessors could not be blinded due to the supervised nature of the comparator pulmonary rehabilitation program.
[f]Unlike the other two studies, Puente-Maestu et al (9) did not have a follow-up period and the only analyses performed were for pre- and post-training. Most of the patients in the self-monitoring (home-based) group walked more than the time requested by the study. More than half the patients missed at least one visit.

Appendix 3: Randomized Controlled Trials Included in Vieira et al 2010 Systematic Review

Table A4: Characteristics of Included Studies for Home Versus Other Setting Pulmonary Rehabilitation for COPD

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Population	Home-Based PR	PR in Other Setting	Study Outcomes	Length of Follow-Up
Güell et al, 2008 (8)	Total: 51 Home PR: 23 Other PR: 28	Home PR: 66 (6) Other PR: 63 (7)	Stable severe to very severe COPD, 50-75 years old Former smokers or current smokers intending to quit FEV_1 30%-50% predicted Exclusion: significant response to bronchodilator, severe hypoxemia, asthma, severe coronary artery disease, orthopedic disease limiting mobility	9 weeks, 3x/week Respiratory muscle training in two 15-min sessions using threshold device at 40% maximum inspiratory pressure 30 min arm training lifting weights Unsupervised walking daily at 4 km/h for: 15 min (week 1); 30 min (week 2-4); 45 min (weeks 5-9); and stepping up and down stairs for 5 min before and after each walk Attended 2 sessions about COPD education, self-management and respiratory and exercise therapies in week 1	Hospital outpatient PR: 9 weeks, 3x/week Respiratory muscle training in two 15-min sessions using threshold device at 40% maximum inspiratory pressure 30 min arm training lifting weights 30 min leg training cycling at 60% of peak work rate Attended 2 sessions about COPD education, self-management and respiratory and exercise therapies in week 1	HRQOL (CRQ) Exercise capacity (6 minute walk test, muscle strength of upper limb) Pulmonary function	6 months
Maltais et al, 2008 (7)	Total: 252 Home PR: 126 Other PR: 126	Home PR: 66 (9) Other PR: 66 (9)	Stable moderate-severe COPD, ≥40 years old Current or former smokers of ≥ 10 pack-years FEV_1 <70% predicted, FEV_1/FVC <0.70, MRC dyspnea score ≥2 Exclusion: previous diagnosis of asthma, congestive heart failure,	Aerobic and strength exercise 8 weeks, 3x/week Self, monitored with weekly telephone calls for reinforcement and problem detection Endurance cycling at 60% peak work rate for 40 min/day	Hospital outpatient PR: 8 weeks, 3x/week Endurance cycling at 80% of peak work rate for 25-30 min Strength training exercises for 30 min	Primary: HRQOL (dyspnea domain of CRQ) Secondary: HRQOL (other domains of CRQ, and SGRQ)	12 months

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Population	Home-Based PR	PR in Other Setting	Study Outcomes	Length of Follow-Up
			terminal disease, dementia, uncontrolled psychiatric illness	Strength training exercises for 30 min Diary of each completed training session		Exercise capacity (6-min walk test, CPET) Pulmonary function Adverse events	
Puente-Maestu et al, 2000 (9)	Total: 41 Home PR: 20 Other PR: 21	Home PR: 66 (5) Other PR: 63 (4)	Stable severe COPD, <75 years old Former smokers of ≥10 pack-years FEV_1 <50% predicted, FEV_1/FVC <0.70, arterial blood carboxyhemoglobin <3%, mMRC dyspnea score ≥2 Exclusion: asthma, bronchiectasis, obliterating bronchiolitis, scarring affecting >20% of one hemithorax, thoracic deformities, fibrothorax, cardiomyopathies, severe arrhythmia, type 1 diabetes, neuromuscular disorders, severe hepatic or renal diseases, physical or psychological impairment impeding exercise	8 weeks, 4x/week Self-monitored endurance walking 3-4 km in 1 hour Visit 1x/week in clinic to check record log and encouraged to continue with training	8 weeks, 4x/week Hospital outpatient PR: supervised endurance walking on treadmill for 1 hour at 3km/h and slope 25% of peak VO_2	HRQOL: CRQ Exercise capacity: CPET and constant work rate on treadmill Pulmonary function	None

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Population	Home-Based PR	PR in Other Setting	Study Outcomes	Length of Follow-Up
Strijbos et al, 1996 (10)	Total: 45 Home PR: 15 Other PR: 15 Control: 15	Home PR: 61 (6) Other PR: 60 (8) Control: 63 (5)	Stable COPD Dyspnea on exertion, limiting activities of daily living $PaCO_2$ <6.5 kPa at rest, PaO_2 >7.5 kPa at rest, FEV_1 postbronchodilation between 600 and 1800 mL, FEV_1 <65% predicted Exclusion: ischemic heart disease, musculoskeletal disorders, disabling diseases restricting rehabilitation therapy	12 weeks, 24 sessions x 30 min of individualized exercise by physiotherapist Instructed to exercise individually ≥30 min on exercise days, ≥15 min other days Local homecare nurse visit 3x for medication check, daily peak flow values, motivation to continue exercises at home All patients visited their general practitioner 3x Patient education for correct medication use, disease course, and when to seek help Taught breathing and relaxation exercises and bronchial hygiene	Hospital outpatient PR: 12 weeks, 2x/week 1 hour individualized rehabilitation exercises by PT Instructed to practice daily exercises individually for ≥15 min Patient education 3x by respiratory nurse, 1 hour per visit All patients visited supervising physician 3x Patient education for correct medication use, disease course, and when to seek help Taught breathing and relaxation exercises and bronchial hygiene	HRQOL: Borg scale for dyspnea Exercise capacity: Borg scale for leg effort, 4-min walk test, maximum workload	18 months

Abbreviations: COPD, chronic obstructive pulmonary disease; CPET, cardiopulmonary exercise testing; CRQ, Chronic Respiratory Questionnaire; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; HRQOL, health-related quality of life; MRC, Medical Research Council; mMRC, modified Medical Research Council; PR, pulmonary rehabilitation; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire; VO2, oxygen consumption.

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Exercise Programs After Pulmonary Rehabilitation for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

Health Quality Ontario

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario 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. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario 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.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

COPD	Chronic Obstructive Pulmonary Disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HRQOL	Health-related quality of life
PR	Pulmonary rehabilitation
RCT	Randomized controlled trial

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to determine the effectiveness of exercise programs in maintaining the gains brought about by pulmonary rehabilitation in patients with chronic obstructive pulmonary disease (COPD) or pneumonia.

Clinical Need and Target Population

Description of Disease/Condition

Respiratory diseases and infections have pervasive implications for patients. COPD is characterized by progressive airflow obstruction that cannot be fully reversed with bronchodilator medication. (1) Patients are often limited in their physical activity as a result, or they may self-limit their physical activity to reduce dyspnea (2), though doing so is associated with poorer health-related quality of life (HRQOL), reduced survival, and increased health service use. (3-6)

Technology/Technique

Pulmonary rehabilitation (PR) is a therapeutic intervention that has been shown to improve the poor outcomes associated with COPD, especially immediately following completion of the rehabilitation program. (7-9) The longevity of the gains from PR are known to diminish over the subsequent year (10). What remains uncertain is the effectiveness of exercise programs in maintaining the benefits of PR.

Rapid Review

Research Question

What is the effectiveness of exercise programs for COPD or pneumonia patients following pulmonary rehabilitation on improving exercise capacity and quality of life?

Research Methods

Literature Search

Search Strategy

A literature search was performed on December 10, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, and EBM Reviews for studies published from January 1, 2008, to December 10, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2008, and December 10, 2013
- systematic reviews, meta-analyses, and health technology assessments
- adult patients with chronic obstructive pulmonary disease (COPD) or pneumonia, who were living in the community
- exercise programs for maintenance or wellness following PR
- reporting 1 or more outcomes of interest

Exclusion Criteria

- studies comparing the effectiveness of types or intensities of exercise
- exercise programs in lieu of PR, or programs not temporally following PR
- COPD patients in institutional or residential settings
- Randomized controlled trials (RCTs), observational studies, case reports, conference abstracts, narrative reviews, clinical practice guidelines

Outcomes of Interest

- exercise capacity
- health-related quality of life (HRQOL)

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (11)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (12) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that RCTs 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. (12) For more detailed information, please refer to the latest series of GRADE articles. (12)

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

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 613 citations published between January 1, 2008, and December 10, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

No relevant articles on pneumonia were identified. One systematic review on COPD patients met the inclusion criteria. The reference list of the included study and health technology assessment websites were hand-searched for other relevant studies, and no additional citations were identified.

A systematic review by Beauchamp and colleagues (13) evaluated the effectiveness of post-PR supervised exercise programs compared with usual community-based care at 6 and 12 months. The PR programs that preceded the maintenance programs ranged from 7 to 12 weeks in duration. The primary outcomes were exercise capacity and HRQOL. Table 1 shows an overview of the 7 included studies reporting on 6 RCTs pooled in the review.

Table 1: Pooled Analysis of RCTs on Post-PR Supervised Exercise Programs

Number of RCTs	Number Randomized	Mean Age, years	COPD Severity (FEV_1 predicted)	Range of Exercise Program Duration, months
6	619	67	32%–59%	9–15

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume; PR, pulmonary rehabilitation; RCT, randomized controlled trial.
Source: Beauchamp et al, 2013 (13)

One study administered the maintenance exercise program by integrating patients into local physiotherapy groups in the community (14) whereas all other programs were delivered in hospital-based outpatient settings. The frequency of exercise sessions ranged from once per month to 3 sessions per week. All maintenance exercise interventions included aerobic exercise, and 4 also included strength training of upper and/or lower extremities (14-17). Participants in all the studies were encouraged to also exercise at home.

Loss to follow-up was an issue in all of the studies, so much so that Elliot et al (14) could not analyze the results of the exercise program in their study and the results could not be subsequently included in the meta-analysis. The summary of the effects of the programs at 6 and 12 months follow-up are in Table 2.

Table 2: Exercise Capacity and Health-Related Quality of Life Following Maintenance Exercise Interventions Post-Pulmonary Rehabilitation at 6 and 12 Months

	6 months			12 months		
Outcome	**SMD (Number Pooled, n)**	**95% CI**	***P* value**	**SMD (Number Pooled, n)**	**95% CI**	***P* value**
Exercise Capacity[a]	−0.20 (433[b])	−0.39 to −0.01	0.04*	−0.09 (385[b])	−0.29 to 0.11	0.37
HRQOL[c]	−0.07 (336[b])	−0.29 to 0.14	0.50	−0.15 (416 [b])	−0.42 to 0.13	0.30

Abbreviations: CI, confidence intervals; HRQOL, health-related quality of life; RCT, randomized controlled trial; SMD, standard mean difference.
[a]Measured by the 6-minute walk test in 5 trials (14-18) and endurance shuttle walk test in 2 trials (17;19)
[b]Data from one trial (14) not included in meta-analysis due to high attrition.
[c]Measured by the Chronic Respiratory Questionnaire in 4 trials (16-18;20) and St. George's Respiratory Questionnaire in 2 trials (18;19)
*Statistical significance at $P < 0.05$.
Source: Beauchamp et al, 2013 (13)

The meta-analysis found a significant benefit to supervised exercise programs post-PR compared with usual care only for exercise capacity at 6 months. Although there was no significant statistical heterogeneity in any of the pooled analyses, there were differences in frequency of follow-up, outcome measurement, and interventions in terms of exercise composition and intensity, frequency of sessions, and inclusion of non-exercise components in the program. The authors comment that the absence of the latter program components may have contributed to the lack of effect of such programs on HRQOL. The raw data were not available and thus sub-grouped meta-analysis could not be run. It remains unknown if or to what extent excluding trials that did not adhere to the intention-to-treat principle would influence the overall effect given the high rate of drop-outs from the programs. Similarly, it is unclear if the duration or components of the PR program preceding the exercise program would influence the outcomes.

Conclusions

There was no evidence found on exercise programs for pneumonia patients.

Despite some methodological flaws, based on 1 meta-analysis of 6 randomized controlled trials (RCTs) on COPD patients that evaluated a variety of types of exercise programs following PR:

- There was a significant benefit to exercise capacity for those enrolled in a maintenance exercise program compared to those in usual care at 6 months follow-up (GRADE: Low) but not 12 months follow-up. (GRADE: Low).
- There was no difference in HRQOL between those enrolled in a maintenance exercise program compared to those in usual care at 6 months follow-up (GRADE: Low) or 12 months follow-up. (GRADE: Very low).

Acknowledgements

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Health Quality Ontario's Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients

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Mary-Jane Herlihey	ParaMed Home Health Care Ottawa	Clinical Consultant
Suzy Young	St. Mary's General Hospital	Nurse Practitioner Primary Health Care SWCCAC Intensive Health Care Team Certified Respirator Educator

Appendices

Appendix 1: Literature Search Strategies

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to October 2013>, EBM Reviews - ACP Journal Club <1991 to November 2013>, EBM Reviews - Database of Abstracts of Reviews of Effects <4th Quarter 2013>, EBM Reviews - Cochrane Central Register of Controlled Trials <November 2013>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <4th Quarter 2013>, EBM Reviews - NHS Economic Evaluation Database <4th Quarter 2013>, Ovid MEDLINE(R) <1946 to November Week 3 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <December 09, 2013>

Search Strategy:

#	Searches	Results
1	exp Patient Discharge/	19905
2	exp Aftercare/ or exp Convalescence/	10298
3	"Continuity of Patient Care"/ or exp "Recovery of Function"/	49411
4	((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab.	37891
5	exp Heart Failure/	93131
6	(((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab.	135925
7	exp Pulmonary Disease, Chronic Obstructive/	26667
8	exp Emphysema/	11099
9	(copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab.	60068
10	(chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab.	37815
11	exp Pneumonia/	78260
12	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab.	147382
13	or/1-12	513261
14	exp Exercise Tolerance/	9966
15	exp Exercise/	127308
16	exp Rehabilitation/	162816
17	exp Rehabilitation Nursing/	1136
18	exp "Physical and Rehabilitation Medicine"/	19975
19	exp Rehabilitation Centers/	12881
20	exp Physical Therapy Modalities/	136983
21	(rehabilitat* or (physical* adj (fit* or train* or therap* or activit*)) or ((exercise* or fitness) adj3 (treatment or intervent* or program*)) or (train* adj (strength* or aerobic or exercise*)) or wellness program* or ((pulmonary or lung* or respirat* or cardiac) adj2 (physiotherap* or therap* or rehabilitat*)) or angina plan* or heart manual*).ti,ab.	235554
22	or/14-21	536336
23	Meta Analysis.pt.	52738
24	Meta-Analysis/ use mesz or exp Technology Assessment, Biomedical/ use mesz	61456

25	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	211340
26	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	2746
27	or/23-26	227857
28	13 and 22 and 27	1230
29	limit 28 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	773
30	remove duplicates from 29	613

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Score of Included Systematic Review

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Beauchamp et al, 2013 (13)	8	✓	✓	✓			✓	✓	✓	✓		✓

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; RCT, randomized controlled trial.
[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al. (11)

Table A2: GRADE Evidence Profile for Comparison of Supervised Exercise Programs Following Pulmonary Rehabilitation and Usual Care

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Exercise Capacity at 6 months follow-up							
5 (RCTs)	Serious limitations (–1)[a]	No serious limitations	No serious limitations	Serious limitations (–1)[b]	No serious limitations	None	⊕⊕ Low
Exercise Capacity at 12 months follow-up							
5 (RCTs)	Serious limitations (–1)[a]	No serious limitations	No serious limitations	Serious limitations (–1)[c]	No serious limitations	None	⊕⊕ Low
HRQOL at 6 months follow-up							
4 (RCTs)	Serious limitations (–1)[a]	No serious limitations	No serious limitations	Serious limitations (–1)[c]	No serious limitations	None	⊕⊕ Low
HRQOL at 12 months follow-up							
5 (RCTs)	Serious limitations (–1)[a]	Serious limitations (–1)[d]	No serious limitations	Serious limitations (–1)[b]	No serious limitations	None	⊕ Very Low

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HRQOL, health-related quality of life; RCT, randomized controlled trial.
[a]RCT evidence starts as high quality. However, adequate allocation concealment was a concern in all trials except 2 (16;17). Due to the nature of the intervention no studies blinded participants, and drop-outs were an issue across trials.
[b]The pooled sample size is relatively small for detecting even small effect sizes, the 95% CIs span both benefit and harm, and all CIs cross 0 except for one study (18).
[c]The pooled sample size is relatively small for detecting even small effect sizes, the 95% CIs span both benefit and harm, and all CIs cross 0.
[d]Although there was no statistically significant heterogeneity, the 5 point estimates differed considerably with 2 trials favouring exercise programs (18;20), 2 favouring usual care (17;19), and 1 finding no effect (16).

Table A3: Risk of Bias Among Randomized Controlled Trials for the Comparison of Supervised Exercise Programs Following Pulmonary Rehabilitation and Usual Care

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Foy et al., 2001 (20) and Berry et al., 2003 (15)	Serious Limitations[a]	No Limitations[b]	No Limitations[c]	No limitations	No limitations
Brooks et al., 2002 (18)	Serious Limitations[a]	No Limitations[b]	No Limitations[c]	No limitations	No limitations
Ries et al., 2003 (16)	No Limitations	No Limitations[b]	Serious Limitations[d]	No limitations	No limitations
Elliott et al., 2004 (14)	Serious Limitations[a]	Serious Limitations[e]	Serious Limitations[d]	No limitations	No limitations
Ringbaek et al., 2010 (19)	Serious Limitations[a]	Serious Limitations[e]	Serious Limitations[d]	No limitations	No limitations
Spencer et al., 2010 (17)	No Limitations	Serious Limitations[e]	No Limitations[c]	No limitations	No limitations

Abbreviations: RCT, randomized controlled trial.
[a]Unclear use or method of allocation concealment.
[b]Outcome assessors and/or clinical staff blinded to participant treatment group. Infeasible to blind participants due to nature of the intervention.
[c]Loss to follow-up was not significantly different between groups and was in the order of 15%–30% however, intention-to-treat analysis was used.
[d]Loss to follow-up was not significantly different between groups and was in the order of 18%–30% and it was unclear if intention-to-treat principle was adhered to in the analysis.
[e]Extent or use of blinding unclear.

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Respiratory Therapy Services in Home Care for Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

Health Quality Ontario

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews are completed in 2-4–week time frames. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario 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. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario 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.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

CCAC	Community Care Access Centre
COPD	Chronic obstructive pulmonary disease
CP	Cardiopulmonary
CRE	Certified respiratory educator
ED	Emergency department
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HQO	Health Quality Ontario
HRQOL	Health-related quality of life
OHTAC	Ontario Health Technology Advisory Committee
PR	Pulmonary rehabilitation
RCT	Randomized controlled trial
RT	Respiratory therapist
SGRQ	St. George's Respiratory Questionnaire
SR	Systematic review

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to determine the effectiveness of respiratory services provided in the home or community by respiratory therapists (RTs) in reducing health care utilization and improving patient outcomes.

Clinical Need and Target Population

Respiratory therapy services comprise a variety of interventions that are related to airway management and maintenance of lung health. These include oxygen therapy, ventilation, tracheostomy care, medication management, and teaching and support of inhaler-use technique. An RT's scope of practice covers caring for cardiopulmonary (CP) conditions and making use of the advanced technology that may be required as part of CP care. (1) RTs provide rehabilitation services, administer inhaled medications, teach patients how to manage their illness, and educate patients and professionals on critical topics such as smoking cessation. (1) They can perform spirometry testing in pulmonary rehabilitation programs, arterial blood gas procurement, and oxygen management—core competencies and skills that are specific to the RT profession. (Personal communication, Expert Consultation, March 10, 2014)

In Ontario, RTs work predominantly in hospitals, especially in high-intensity areas such as intensive care units, emergency departments (EDs), and operating rooms. (1) However, RTs also work in clinic or outpatient settings, for instance in pulmonary rehabilitation programs, and even in patients' homes. In 2009, respiratory therapy was added as a specialized professional service that could be provided through Community Care Access Centres (CCACs) to eligible patients in the home, group settings, or long-term care facilities. (2) Through the Ministry of Health and Long-Term Care's Home Oxygen Program, eligible patients can be funded fully or partially to receive RT home visits for home oxygen, which is usually indicated during end-stage disease. (3) At present, only a few CCACs include RTs within their scope of home care services, outside of home oxygen support.

Rapid Review

Research Questions

What is the effectiveness of respiratory services in the home and/or community provided by respiratory therapists post-discharge, especially for those with respiratory disease?

Research Methods

Literature Search

Search Strategy

A literature search was performed on February 14, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews, for studies published from January 1, 2009, to February 14, 2014. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2009, and February 14, 2014
- observational studies, randomized controlled trials (RCTs), systematic reviews, and meta-analyses
- reporting on services provided in the home or community setting by an RT

Exclusion Criteria

- reporting on the effectiveness of specific respiratory interventions (e.g., long-term oxygen therapy, ventilator management, artificial respiration)
- reporting on respiratory services provided by any other health care provider (e.g., nurse, physiotherapist, occupational therapist)
- case reports, editorials, commentaries, conference abstracts, guidelines

Outcomes of Interest

- ED visits, hospital admissions or readmissions
- health-related quality of life (HRQOL)
- intervals between exacerbations

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The methodology for a rapid review of primary studies includes a risk of bias assessment based on GRADE Working Group criteria (4) to assess quality of evidence. Risk of bias is evaluated based on consideration of allocation concealment, blinding, accounting of patients and outcome events, selective reporting bias, and other limitations.

Results of Rapid Review

The database search yielded 1,465 citations published between January 1, 2009, and February 14, 2014 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One study (5) met the inclusion criteria. The reference list of the included study and health technology assessment websites were hand-searched to identify other relevant studies, and 1 additional citation (6) was found, for a total of 2. Both included studies were randomized controlled trials (RCTs) conducted in the United States.

The 2010 study by Gilmore and colleagues (5) evaluated the effect of educational support on health-related quality of life (HRQOL) for community-dwelling patients with a physician-diagnosis of moderate to severe chronic obstructive pulmonary disease (COPD). In this study, 37 patients were randomized via letter cards in blocks of 4 to one of the following interventions: standard care, a COPD educational guide (booklet and video); a home visit by an RT; both the guide and RT home visit. The time period of follow-up of the study was unclear. Intervention details are shown in Table 1. Health-related quality of life (HRQOL) was measured using a modified version of St. George's Respiratory Questionnaire (SGRQ). (5)

Table 1: Study Design of RCT Evaluating Educational Strategies for Community-Dwelling Patients With Moderate to Severe COPD

Study Group	Description of Intervention
Standard Care *(Group D)*	Information on newly prescribed medication use and reinforcement education at physician's request (e.g., review of inhaler techniques, indications for medications)
COPD Educational Guide *(Group B)*	Educational booklet with chapters on living well, optimizing medication, breathing exercises and techniques, active lifestyle, planning for symptom worsening, and smoking cessation to teach patients and families about COPD and how to better self-manage it; 7-minute video on inhaler technique instruction
RT Home Visit *(Group C)*	Structured visit to reinforce disease-management education and perform a standardized home evaluation of subject's general health environment, ability to move around the home, layout of movable objects, and access to oxygen and local caregiver assistance resources
COPD Educational Guide + RT Home Visit *(Group A)*	Interventions of both Groups B and C (see above for details)

Abbreviations: COPD, chronic obstructive pulmonary disease; RCT, randomized controlled trial; RT, respiratory therapist.
Source: Gilmore et al. (5)

Attrition was high in this study, with 10 of the 37 subjects (27%) lost to follow-up. Thus, results pertain to only the 27 who completed the study. There were no statistically significant differences between any of the groups in HRQOL, although the RT Home Visit group (Group C) observed a minimal improvement that approached statistical significance ($P < 0.10$) in the activity and symptom domains of the 4-domain SGRQ. Given the small sample size, with group sizes ranging from 10 to 17 patients prior to any loss to follow-up, the study was clearly underpowered to detect differences between groups.

The RCT by Rice and colleagues (6), also published in 2010, assessed the effectiveness of a simple disease-management program led by an RT, compared with usual care. In this RCT, 743 eligible patients at high risk of exacerbation were randomized and completed the study. The effect of this intervention on HRQOL and on the number of all-cause and disease-specific hospital or ED visits was assessed via SGRQ over a 12-month follow-up period. The description of the interventions and results of the study for these outcomes are in Table 2.

Table 2: Summary of RCT Evaluating Disease-Management Program for Community-Dwelling COPD Patients at High Risk for Hospitalization

Study Group	Number	Description of Intervention	Proportion of Patients with ≥1 ED Visit or Hospital Admission Within 1 Year (rate)	HRQOL After 1 Year
Usual Care	371	Handout containing principles of COPD care and a 24-hour nursing helpline phone number	39.1% (82.2 per 100,000 patient-years)	Worsened (6.4 points)
Disease Management	372	Single 1- to 1.5-hour group education session with an RT-case manager,[a] action plan including medications and refill prescriptions, RT-case manager contact information and 24-hour helpline phone number, and monthly phone calls from RT to see if action plan medications taken or if patient has questions	27.4%* (48.4 per 100,000 patient-years)	Worsened (1.3 points*)

Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; HRQOL, health-related quality of life; RCT, randomized controlled trial; RT, respiratory therapist.
[a]Education session consisted of COPD information, inhaler technique and medication review and adjustment, smoking cessation, vaccination counselling, exercise encouragement, and hand hygiene instruction.
*Statistically significant difference between groups ($P < 0.001$).
Source: Rice et al. (6)

Over 1 year, a significantly lower proportion of patients in the disease management group had 1 or more ED visit or hospitalization (difference 0.34; 95% confidence interval [CI], 0.15–0.52). There was a statistically significant 41% reduction in the composite ED/hospitalization outcome in the disease management group (rate ratio [RR], 0.59; 95% CI, 0.44–0.75; $P < 0.001$). When separating the subcomponents of the primary outcome, disease management patients had 30% fewer hospitalizations ($P = 0.03$) and 50% fewer ED visits ($P = 0.001$). As seen in Table 2, HRQOL worsened significantly more in the usual care group, a decrease in points on the SGRQ that is considered clinically significant. (7) The authors remark that further study is needed to determine the effect of disease management in conjunction with pulmonary rehabilitation (PR), as the intervention was entirely separate though potentially complementary to PR.

Limitations

The risk of bias assessment for the studies included in this rapid review can be found in Appendix 2. Specific limitations include high attrition in the study by Gilmore and colleagues (5); and both studies lacked blinding due to the nature of the intervention and had incomplete outcome reporting. In addition, the Gilmore et al study had a very small sample size and was inadequately powered to detect a clinically significant change in HRQOL. Based on an *a priori* power calculation, 18 subjects per group would be required to detect a "very efficacious" effect size with 80% power or a "moderately efficacious" effect size with 50% power. (5)

Neither study reported on the outcome of time interval between exacerbations; the potential impact that the educational strategies investigated by Gilmore and colleagues (5) or the disease-management program tested by Rice and colleagues (6) might have on this remains unknown.

In addition, some characteristics of the studies' samples influence the generalizability of the findings. Rice and colleagues (6) conducted their study at 5 Veterans Affairs medical centres. Therefore, an overwhelming number of participants were male (97.6 to 98.4%). Furthermore, the usual care group was slightly older with superior lung function, though these latter between-group differences were not statistically significant. In the Gilmore et al study (5), participants assigned to the educational guide group had a longer smoking history, and were more likely to be female and less likely to be insured. For generalizability, attention needs to be paid to how representative the study participants are of COPD patients in the community.

Conclusions

- There were no studies that reported the effect of RT services on the time interval between acute exacerbations.
- Based on the results of a very small RCT with serious limitations due to risk of bias, COPD educational strategies involving an educational guide, RT home visit, or a combination did not have an effect on HRQOL, compared with usual care.
- Based on a large RCT with some limitations due to risk of bias, a community-based COPD-specific disease management program led by an RT reduced ED visits and hospitalizations and led to a smaller decline in HRQOL over a 1-year period, compared with usual care.

Expert Consultation

In addition to the Expert Advisory Panel, a group of experts comprised of RTs and representatives from the Ontario Lung Association was convened to add professional-practice context to the evidence.

The expert consultation identified "specialized respiratory nurses" in the United Kingdom's National Health Service, a designation approximately equivalent to the RT designation that exists in North America. In light of this, the database was re-screened and a meta-analysis of respiratory nurse-led home-based interventions for COPD patients in the community was identified. (8) The analysis included studies from 1987 to 2006 and found benefit for HRQOL and mixed results for hospitalizations, with significant heterogeneity in the latter. Upon examination of the 9 RCTs included in the analysis, only 2 were conducted in the United Kingdom; the others were mostly from the United States, where RT is a distinct professional discipline. Furthermore, in those studies which described the credentials of those providing the intervention, the reported respiratory specialization of the providers varied from 8 hours of training to having attended weekly rounds for 3 months. (8) Based on the information reported in the primary studies and meta-analysis, there was no conclusive evidence that the providers were specialized respiratory nurses nor that they had a comparable skill set to RTs'. Thus, this study was excluded.

In the consultation, the experts emphasized that a specialized respiratory skill set is essential in order to appropriately support COPD patients across the continuum of care. They emphasized that an ongoing relationship with a dedicated health care provider—one who serves as the patient's main contact—is a key component of management for COPD patients. In the post-acute period (e.g., during PR), a high degree of respiratory clinical expertise is essential, such as the expertise developed through an RT's focused training in respiratory disease management and care. This is less essential for longer-term maintenance support. A holistic approach was cited as key throughout the care continuum, including education, self-management support, and psychosocial support. The experts stated that disease management can be appropriately delivered by an RT or by other health professionals provided they are certified in respiratory core competencies—for example, by a certified respiratory educator (CRE). There was agreement among the experts that consideration should be given to enhancing the CRE certification to provide standardized training for all health care professionals involved in pulmonary rehabilitation.

Acknowledgements

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Health Quality Ontario's Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients

Panel Members	Affiliation(s)	Appointment(s)
Co-Chairs		
Dr Chaim Bell	Mount Sinai Hospital University of Toronto	Clinician Scientist Associate Professor
Lisa Droppo	Ontario Association of Community Care Access Centers (OACCAC)	Chief Care Innovations Officer
Primary Care		
Dr Kenneth Hook	Ontario College of Family Physicians STAR Family Health Team	Past-President Senior Physician
Dr Alan Kaplan	Family Physicians Airway Group of Canada	Chair, Family Physicians Airway Group of Canada
Dr Peter Selby	Department of Family and Community Medicine & Psychiatry and Dalla Lana School of Public Health University of Toronto Ontario Tobacco Research Unit	Associate Professor Principal Investigator
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Dr Roger Goldstein	West Park Health Centre Toronto Rehabilitation Institute	Respiratory Division Head Associate Medical Staff Professor of Medicine
Respiratory Therapy		
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Miriam Turnbull	ProResp Inc	General Manager
Madonna Ferrone	Erie St. Clair LHIN	Project Manager ARGI, Lung Health Collaboratist
Nursing		

Panel Members	Affiliation(s)	Appointment(s)
Cheryl Lennox	South West Community CCAC, Intensive Home Care Team	Nurse Practitioner-Primary Health Care Certified Respiratory Educator
Andrea Roberts	Toronto Central CCAC	Rapid Response Transition Nurse
Mary-Jane Herlihey	ParaMed Home Health Care Ottawa	Clinical Consultant
Suzy Young	St. Mary's General Hospital	Nurse Practitioner Primary Health Care SWCCAC Intensive Health Care Team Certified Respirator Educator

Appendices

Appendix 1: Literature Search Strategies

Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, All EBM Databases (see below), CINAHL
Limits: 2009-current; English
Filters: Removal of case reports, comments, editorials, letters, conference proceedings

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to December 2013>, EBM Reviews - ACP Journal Club <1991 to January 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <January 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <1st Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2014>, Ovid MEDLINE(R) <1946 to February Week 1 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <February 13, 2014>
Search Strategy:

#	Searches	Results
1	exp Patient Discharge/	19216
2	exp Aftercare/ or exp Convalescence/	10054
3	"Continuity of Patient Care"/ or exp "Recovery of Function"/	46227
4	((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab.	36811
5	exp Stroke/	85027
6	exp brain ischemia/ or exp intracranial hemorrhages/	129002
7	(stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*)).ti,ab.	194865
8	exp Heart Failure/	89257
9	(((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab.	130071
10	exp Pulmonary Disease, Chronic Obstructive/	36493
11	exp Emphysema/	10699
12	(copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab.	56196
13	(chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab.	34617
14	exp Pneumonia/	74413
15	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab.	137241
16	or/1-15	752281
17	*Respiratory Therapy/	3387
18	(((respirat* or inhalation or oxygen) adj2 therap*) or (respirat* adj2 (home or service* or outreach or educator*))).ti,ab.	13646
19	17 or 18	16157
20	16 and 19	3470
21	Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt. or Congresses.pt.	2852586
22	20 not 21	3087

23	limit 22 to yr="2009 -Current" [Limit not valid in DARE; records were retained]	703
24	remove duplicates from 23	639

CINAHL

#	Query	Results
S1	(MH "Patient Discharge+") or (MH "After Care") or (MH "Recovery") or (MH "Continuity of Patient Care+")	45,168
S2	((patient* N2 discharge*) or aftercare or after care or post medical discharge* or postdischarge* or post discharge* or convalescen*)	29,321
S3	(MH "Stroke+") or (MH "Cerebral Ischemia+") or (MH "Intracranial Hemorrhage+") or (MH "Stroke Patients")	49,394
S4	(stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) N1 (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or ((brain or cerebral) N2 (ischemia or ischaemia)) or ((intracranial or brain) N2 (hemorrhag* or haemorrhag*)))	61,592
S5	(MH "Heart Failure+")	22,458
S6	((cardia* or heart) N1 (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) N1 (failure or insufficiency))	29,048
S7	(MH "Pulmonary Disease, Chronic Obstructive+") or (MH "Emphysema+")	11,502
S8	((chronic obstructive N2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) N1 (disease* or disorder*)) or (copd or coad or chronic airflow obstruction* or (chronic N2 bronchitis) or emphysema))	14,648
S9	(MH "Pneumonia+")	12,449
S10	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) N1 inflammation*))	19,458
S11	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10	174,707
S12	((respirat* or inhalation or oxygen) N2 therap*) or (respirat* N2 (home or service* or outreach or educator*))	17,581
S13	(MM "Respiratory Therapy") OR (MH "Respiratory Therapy Service") OR (MH "Respiratory Therapists")	5,370
S14	S12 OR S13	17,581
S15	S11 AND S14	2,495
S16	S11 AND S14 Limiters - Published Date: 20090101-20141231	1,000

Appendix 2: Evidence Quality Assessment

Table A1: Risk of Bias Among RCTs for the Comparison of Respiratory Therapist Interventions Versus Usual Care

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Gilmore et al, 2010 (5)	No Limitations	Serious Limitations[a]	Limitations[b]	No limitations	No limitations
Rice et al, 2010 (6)	No limitations	Limitations[a]	Limitations[c]	No limitations	No limitations

[a]No indication of, or only minimal use of, blinding (chart review for primary outcome assessment in Rice et al), although blinding is challenging given the nature of the interventions. Non-blinded participants are of greatest concern for the assessment of health-related quality of life (HRQOL), which is self-reported and is the primary outcome in Gilmore et al (5) and secondary outcome in Rice et al (6).
[b]Loss to follow-up was approximately 27% of those enrolled and randomized, and intention-to-treat principle was not adhered to. It is unclear if attrition differed between study groups.
[c]Response rate for self-reported HRQOL did not differ between groups and was 55% for the usual care group and 60% for the intervention group, resulting in lack of power to draw definitive conclusions.

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Airway Clearance Techniques for Individuals With Stable Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario 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.

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In addition, Evidence Development and Standards 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
ACT	Airway clearance technique
COPD	Chronic obstructive pulmonary disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to determine the effectiveness of airway clearance techniques (ACT) for patients with stable chronic obstructive pulmonary disease (COPD) in the community or home setting.

Clinical Need and Target Population

Chronic obstructive pulmonary disease encompasses a group of conditions characterized by irreversible airflow limitation from lung tissue damage. These conditions affect more than 1.5 million Canadians (1) and are a major cause of both morbidity and mortality, with patients often experiencing shortness of breath (dyspnea), decreased exercise capacity, and impaired quality of life. One of the symptoms of COPD is increased sputum production, which over time can obstruct the airways and has been shown to be associated with increased risk of hospitalization and infections of the lower respiratory tract. (2-4) Thus, removing mucus from the airway may be an important target for COPD therapy.

Technology/Technique

Airway clearance techniques promote the removal of pulmonary secretions and are usually performed by patients themselves. A wide array of techniques are used, including manual therapies and mechanical interventions.

Manual therapies are based on the assumption that applying external force to the chest can loosen mucus, or that using effective and productive coughing or breathing methods along with proper gravitational positioning can aid in airway mobilization and clearance. Specific techniques in this group include postural drainage, autogenic drainage, percussion, vibration, shaking, deep breathing, directed coughing, active breathing techniques, and forced expiratory technique. Mechanical interventions involve the use of additional devices to open the airways and loosening of the remaining trapped mucus higher, or to produce turbulence in the airways to enable mucus to separate from the airway walls to aid in its removal. Devices and techniques include positive expiratory pressure mask, oscillating positive expiratory pressure, high-frequency chest wall oscillation, and intrapulmonary percussive ventilation.

A previous rapid review by Health Quality Ontario found limited evidence of benefit from ACTs for patients with acute exacerbations of COPD. (5) While patients often perform or receive ACTs, the benefits of these techniques are unclear, especially in a population with stable COPD.

Rapid Review

Research Question

What is the effectiveness of airway clearance techniques for patients with stable COPD in the community or home?

Research Methods

Literature Search

Search Strategy

A literature search was performed on April 8, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations and EBM Reviews, for studies published from January 1, 2009, to April 8, 2014. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2009, and April 8, 2014
- systematic reviews and meta-analyses on airway clearance techniques for stable (non-hospitalized) COPD patients

Exclusion Criteria

- randomized controlled trials, editorials, case studies, observational studies, or commentaries
- comparison of different methods of airway clearance techniques

Outcomes of Interest

- COPD exacerbations
- hospitalizations
- health-related quality of life

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the

methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (6)

Rapid reviews of systematic reviews normally examine the quality of the body of evidence for each outcome using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (7) Where this is not possible due to the limited number of studies available for the outcomes of interest, we assess the quality of the evidence using a risk of bias assessment of the individual studies in a systematic review, including allocation concealment, blinding, accounting of patients and outcome events, selective reporting bias, and other limitations. (8)

Results of Rapid Review

The database search yielded 396 citations published between January 1, 2009, and April 8, 2014 (duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Five systematic reviews examining airway clearance techniques for non-acute exacerbations of COPD were identified (Table 1). (9-13) The reference lists of the included studies were hand-searched to identify other relevant studies but none were found. Only the systematic review by Osadnik et al (13) separated acute exacerbations of COPD from the stable COPD population. Based on its relevant focus and high quality (AMSTAR rating of 11; Appendix 2, Table A1), it was chosen for this analysis.

Table 1: Systematic Reviews of Airway Clearance Techniques for COPD

Author, Year	Description of Systematic Review
Ides et al, 2011 (9)	Systematic review of airway clearance techniques for COPD
Langer et al, 2009 (10)	Clinical practice guideline for the physiotherapy management of COPD based on systematic review of the evidence, which includes improving airway mucus clearance
Nowobilski et al, 2010 (11)	Systematic review of systematic reviews, narrative reviews, clinical practice guidelines, and secondarily, primary studies on chest physical therapy for COPD
Fagevik Olsén and Westerdahl, 2009 (12)	Systematic review of chest physiotherapy techniques with positive expiratory pressure for COPD
Osadnik et al, 2012 (13)	Systematic review for AECOPD and stable COPD

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease.

The systematic review included 19 studies of airway clearance techniques for stable COPD (see Appendix 3 for study characteristics), 6 of which were randomized controlled trials and the remaining being randomized cross-over trials. (13) We could not perform the typical analysis using GRADE to assess the quality of evidence for each outcome of interest as only a few studies analyzed the specified outcomes. None of the studies were done in a home setting, and other study settings were identified as either hospital, outpatient clinic or research institute. Since it was not always clear if the hospital setting was outpatient-based, the results of this rapid review focused on the patient population of stable COPD regardless of setting.

Two studies examined subsequent exacerbations (both with nonsignificant findings), 2 studies examined hospitalization (with inconsistent findings), and only 1 study looked at health-related quality of life (with a finding of improvement). (13) Table 2 summarizes the heterogeneity in airway clearance techniques examined in these studies and the significance of results for the 9 outcomes examined by Osadnik et al. (13)

The included studies were in general of low quality with small numbers of study participants, inadequate or no mention of randomization/allocation and blinding, and short length of follow-up (Appendix 2, Table A2). Most studies involved comparison with usual care; a few examined comparisons with sham therapy. A variety of techniques were examined (positive expiratory pressure mask, forced expiratory technique, vibration, postural drainage, breathing techniques, percussion, directed coughing) with co-interventions such as standard COPD bronchodilator therapy. For 4 studies, only the abstract was available and additional details of the results could not be extracted by the authors, and 2 studies were noted to be without full English translation.

Due to study heterogeneity and differences in reporting study outcomes, the data could not be meta-analyzed for a summary effect measure for specific outcomes, nor could data be subgrouped by technique. In addition, 11 of the 19 studies were published before 2000, potentially limiting the ability to generalize their findings for current techniques, particularly recent advancements in mechanical airway clearance techniques. Although the remaining 8 studies were more recent, no study published within the last 5 years examined a population with stable COPD.

Findings for the secondary outcomes in the systematic review (pulmonary function, gas exchange, symptoms, sputum clearance, exercise tolerance, antibiotic use) were also inconsistent among studies. For pulmonary function, only 4 of 13 studies reported significant improvement. No studies (0 of 7) found an improvement in gas exchange. Airway clearance techniques showed potential benefit for exercise tolerance and sputum clearance (3 of 3 studies and 6 of 8 studies, respectively). Finally, 1 of 3 studies examining antibiotic use found a significant reduction, and 4 of 7 studies found improved symptoms. In total, considering all the included studies for any type of airway clearance technique for stable COPD patients, 13 of the 19 studies reported an improvement in at least 1 of the 9 study outcomes examined.

From the current evidence, uncertainty still exists about the clinical effectiveness of airway clearance techniques for patients with stable COPD; however, they may be clinically beneficial based on low quality studies.

Table 2: Summary of Airway Clearance Techniques for Stable COPD and Reported Outcomes in Included Systematic Review

Author, Year	Intervention	Primary Outcomes of Interest			Secondary Outcomes					
		Exacerbations	Hospitalization	HRQOL	Pulmonary Function	Gas Exchange	Symptoms	Sputum Clearance	Exercise Tolerance	Antibiotic Use
Cegla et al, 1997	PEP (Cornet, Flutter)				NS	NS				
Cegla et al, 2001	PEP (Cornet)				✓					
Cegla et al, 2002	PEP (Cornet)		✓		✓					✓
Christensen et al, 1990	PEP (mask with PEEP valve)	NS	NS		NS	NS	NS			NS
Christensen and Dahl, 1991	PEP mask	NS			NS		✓			NS
Christensen et al, 1991a	PEP mask				NS		✓			
Martins et al, 2006	ELTGOL							✓		
Martins et al, 2007	ELTGOL							✓		
May and Munt, 1979	CCPT				NS	NS		✓		
Morsch et al, 2008	PEP (Flutter +/- FET)							NS		
Oldenburg et al, 1979	CCPT; physical exercise				NS			✓		
Pavia et al, 1976	mechanical vibration						NS	NS		
Rasmussen and Juul, 2001	PEP valve							✓		
Rivington-Law et al, 1984	breathing; breathing + CPPT				NS	NS				
van Hengstum et al, 1988	PEP mask; breathing + CPPT				NS			✓		
Weiner et al, 1996	PEP (Flutter)				NS	NS	✓		✓	
Wolkove et al, 2002	PEP (Flutter)				✓	NS	✓		✓	
Wolkove et al, 2004	PEP (Flutter)			✓	✓	NS	NS		✓	

Abbreviations: CCPT, conventional chest physiotherapy; COPD, chronic obstructive pulmonary disease; ELTGOL, slow expiration with glottis open in the lateral position; FET, forced expiratory technique; HRQOL, health-related quality of life; NS, not significant; PEEP, positive end-expiratory pressure; PEP, positive expiratory pressure.
Note: Check mark denotes significant finding(s), and where described by the systematic review, those that are clinically meaningful. The results of the Hasani et al study (abstract only) were not explicitly mentioned in the included systematic review.
Source: Osadnik et al, 2012. (13)

Conclusions

- One systematic review was included that examined airway clearance techniques for patients with stable COPD.
- The 19 studies (4 of which were only available as abstracts) were generally of low quality, based on risk of bias assessment; due to the heterogeneity in study design, interventions, and reporting, the evidence could not be analyzed using GRADE for our specific outcomes of interest.
- Thirteen of the 19 studies showed potential improvement through the use of airway clearance techniques for patients with stable COPD for the following outcomes: exacerbations, hospitalizations, health-related quality of life, pulmonary function, gas exchange, symptoms, sputum clearance, exercise tolerance, or antibiotic use; but there were considerable study limitations and differences in techniques examined.
- Further well-designed studies are required to determine with certainty the effectiveness of airway clearance techniques for patients with stable COPD.

Acknowledgements

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Appendices

Appendix 1: Literature Search Strategy

Databases: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to February 2014>, EBM Reviews - ACP Journal Club <1991 to March 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <January 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <1st Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2014>, Ovid MEDLINE(R) <1946 to March Week 4 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <April 08, 2014>

Search Strategy:

#	Searches	Results
1	exp Patient Discharge/	19503
2	exp Aftercare/ or exp Convalescence/	10124
3	"Continuity of Patient Care"/ or exp "Recovery of Function"/	47225
4	((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab.	37339
5	exp Stroke/	87237
6	exp brain ischemia/ or exp intracranial hemorrhages/	130703
7	(stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*)).ti,ab.	199089
8	exp Heart Failure/	90534
9	(((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab.	132170
10	exp Pulmonary Disease, Chronic Obstructive/	37292
11	exp Emphysema/	10805
12	(copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab.	57323
13	(chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab.	35566
14	exp Pneumonia/	75197
15	(pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab.	139396
16	or/1-15	764570
17	exp Physical Therapy Modalities/	134218
18	exp "Physical and Rehabilitation Medicine"/	19795
19	exp Respiratory Therapy/	92927
20	exp Breathing Exercises/ or Percussion/ or Intermittent Positive-Pressure Ventilation/ or Vibration/	26337
21	(((physiotherap* or physio-therap* or physical ther* or kinesiotherap*) adj2 (respirat* or chest* or lung* or pulmonar* or percussion* or humidification or breath* or COPD or airway* or thora*)) or (active cycle adj2 breath*) or ((lung or pulmonary) adj2 hygien*) or incentive spirometr* or acapella* or ((airway or secretion* or sputum or bronchopulmonar* or	31480

	tracheobronch* or mucus or chest*) adj2 clear*) or (sputum adj2 (clear* or mobili*)) or ((postural or autogenic or gravity assist*) adj2 drainage*) or positive expiratory pressure* or thoracic expansion exercise* or chest percussi* or percussive ventilat* or forced expir* technique* or chest wall oscillat* or draining technique* or clapping or vibration or flutter*).ti,ab.	
22	or/17-21	283800
23	16 and 22	30512
24	Meta Analysis.pt.	47150
25	Meta-Analysis/ or exp Technology Assessment, Biomedical/	56209
26	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	201233
27	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	2762
28	or/24-27	217647
29	23 and 28	920
30	limit 29 to (english language and yr="2009 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	463
31	case reports/ or comment.pt. or editorial.pt. or letter.pt. or congresses.pt.	2882301
32	30 not 31	450
33	remove duplicates from 32	396

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Scores of Included Systematic Review

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Osadnik et al, 2011 (13)	11	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al, 2007. (6)

Table A2: Risk of Bias Among Randomized Controlled Trials for Airway Clearance Techniques for Stable COPD Patients

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Cegla et al, 1997	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[d]
Cegla et al, 2001	Limitations[e]	Limitations[b]	No limitations	No limitations	No limitations
Cegla et al, 2002	Limitations[e]	Limitations[b]	No limitations	Limitations[c]	Limitations[f]
Christensen et al, 1990	Limitations[a]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
Christensen and Dahl, 1991	Limitations[a]	Limitations[b]	Limitations[g]	No limitations	No limitations
Christensen et al, 1991a	Limitations[e]	Limitations[b]	No limitations	No limitations	Limitations[h]
Hasani et al, 1995	Limitations[e]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
Martins et al, 2006	Limitations[i]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
Martins et al, 2007	Limitations[i]	Limitations[b]	Limitations[g]	Limitations[c]	No limitations
May and Munt, 1979	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[j]
Morsch et al, 2008	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Oldenburg et al, 1979	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Pavia et al, 1976	Limitations[i]	Limitations[b]	No limitations	No limitations	No limitations
Rasmussen and Juul, 2001	Limitations[e]	Limitations[b]	Limitations[g]	Limitations[c]	Limitations[h]
Rivington-Law et al, 1984	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[k]
van Hengstum et al, 1988	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Weiner et al, 1996	Limitations[a]	Limitations[b]	No limitations	Limitations[c]	Limitations[d]
Wolkove et al, 2002	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Wolkove et al, 2004	Limitations[l]	Limitations[b]	No limitations	No limitations	No limitations

[a]Randomization said to be done, but method was not described. No information on allocation concealment.
[b]No information or insufficient information provided; study not likely to have been adequately blinded.
[c]Data not available for some patients or outcomes.
[d]Full English translation not available.
[e]No information or insufficient information provided for random sequence generation and allocation concealment methods.
[f]Unclear why participants were randomly excluded.
[g]Incomplete or inadequate data for patients or outcomes.
[h]Washout period unclear.
[i]Random sequence generation mentioned, but no mention of allocation concealment.
[j]Unclear why some participants received the intervention while others did not.
[k]Unclear which group excluded patients were from.
[l]Random sequence generation methods not mentioned, but study had adequate allocation concealment.
Source: Osadnik et al, 2012. (13)

Appendix 3: Randomized Controlled Trials for Stable COPD in the Included Systematic Review

Table A3: Characteristics of Included Studies for Airway Clearance Techniques in Stable COPD

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Cegla et al, 1997	90	56.0 (10.4)	RCT	Outpatient pulmonary clinic	Presumed stable COPD Tracheobronchial instability Productive sputum < 65 years of age	COPD pharmacotherapy and oxygen	1) Same as control + Cornet (5 min, 4x/day for 7 days) 2) Same as control + Flutter (5 min, 4x/day for 7 days)	7 days
Cegla et al, 2001	35	65.0 (10.0)	RXT	Pulmonary research institute	Stable COPD Tracheobronchial instability Non-smoker in last 5 years	COPD pharmacotherapy	Same as control, but exhalation via Cornet	2 days
Cegla et al, 2002	81	63.4 (9.2)	RCT	Pulmonary research institute	Stable severe COPD Tracheobronchial instability	COPD pharmacotherapy	Same as control + Cornet (≥ 5 min, 3x/day whenever dyspnea or mucus was noticed)	2 years
Christensen et al, 1990	60	65 (median)	RCT	Outpatient chest clinic	Stable severe COPD Chronic mucus hypersecretion	PEP mask, with PEEP valve at 0 cm H_2O (≥ 15 min, 3x/day)	Same as control, but PEP mask, with PEEP valve at 10 cm H_2O	6 months
Christensen and Dahl, 1991	30	64	RCT	Hospital	Stable COPD Any smoking status	COPD pharmacotherapy via spacer connected to PEP mask at 0 cm H_2O (10 tidal breaths, 2x/day)	Same as control, but PEP of 10–20 cm H_2O	4 weeks
Christensen et al, 1991a	10	54.4 (16.6)	RXT	Outpatient clinic	Stable COPD Daily cough, expectoration, and dyspnea, requiring daily COPD pharmacotherapy	COPD pharmacotherapy with PEP mask at 0 cm H_2O (3x/day for 2 weeks)	1) Same as control, except 10–15 cm H_2O 2) Same as control, except 1 placebo medication	3 x 2 weeks

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Hasani et al, 1995 (Abstract only)	24	69 (8.5)	RXT	Thoracic medicine department	Asthma, bronchiectasis, stable COPD	Resting	1) 6 coughs/min x 5 cycles with 1 min rest in between 2) 6 forced expiratory techniques/min x 5 cycles with 1 min rest in between	1 day
Martins et al, 2006 (Abstract only)	5	N/A	RXT	Physiotherapy/nuclear medicine department	Mild-moderate COPD Daily excessive sputum expectoration	Rest for 20 min Only spontaneous coughing allowed	Expiration with glottis open in lateral posture for 20 min (10x slow and deep expirations followed by 2 min rest x 3 sets in right lateral position	1 week
Martins et al, 2007 (Abstract only)	12	45–75 (Range)	RXT	Physiotherapy/nuclear medicine department	Mild-moderate stable COPD Daily excessive sputum expectoration	Rest for 20 min Only spontaneous coughing allowed	Expiration with glottis open in lateral posture for 20 min (10x slow and deep expirations followed by 2 min rest x 3 sets in right lateral position	1 week
May and Munt, 1979	35	59	RXT	Hospital	Stable COPD History of productive cough and obstructive defect on spirometry	30 min chest heat lamp therapy (10 min heat in side-lying, 10 min rest supine no heat, 10 min heat side-lying alternate side)	1) 90 sec manual percussion followed by vibrations, assisted coughing and brief rest in 7 different postural drainage positions 2) Directed, unassisted coughing every 5 min x 30 min	2 days
Morsch et al, 2008	20	64.9 (6.8)	RCT	Outpatient pulmonology clinic	Stable stage III COPD	7 min induced sputum via ultrasonic nebulizer	Same as control + Flutter (5 min calm, prolonged exhalations through Flutter followed by vigorous coughing)	1 day
Oldenburg et al, 1979	8	62.1 (4.4)	RXT	Hospital clinic	Stable, simple and obstructive COPD	Upright resting	1) 5 x 4 min cycle ergometry, with 4 min rest 2) 5 x 6 min postural drainage, with 1 min rest 3) Coughing once/min x 5 min, with 3 min rest	5–10 days

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Pavia et al, 1976	10	65.3 (5.9)	RXT	Hospital chest clinic	Stable COPD Productive cough, shortness of breath, difficulty expectorating phlegm	1 hour rest in reclined position Inactive vibration pad	Same as control + active vibration	N/A
Rasmussen and Juul, 2001	25	66.6	RXT	Hospital	Stable COPD	Self-administered PEP valve therapy at 0 cm H_2O, 2x/day for 4 days	1) Same as control, but PEP at 5 cm H_2O 2) Same as control, but PEP at 12.5 cm H_2O 3) Same as control, but PEP at 20 cm H_2O	4 x 4 days
Rivington-Law et al, 1984	14	66	RXT	N/A	Stable COPD Crackles on auscultation	15 min rest with hands on chest	1) Same as control, except followed by 15 min deep breathing 2) Same as control, except followed by 15 min deep breathing + manual chest wall vibrations	3 days
van Hengstum et al, 1988	8	63	RXT	Hospital	Presumed stable COPD	Rest with spontaneous coughing only	1) PEP mask in forward leaning sitting position (10–15 cm H_2O for 2 min, followed by abdominal breathing and 2 maximal huffs and coughs x 5 cycles 2) 6 positions of postural drainage with diaphragmatic breathing, thoracic expansion exercises, diaphragmatic breathing, 2 huffs interspersed with relaxed diaphragmatic breathing and coughs	≥ 12 days

Author, Year	Sample Size, n	Mean Age, Years (SD)	Study Design	Study Setting	Study Population	Control	Intervention	Duration
Weiner et al, 1996	20	63.3 (9.5)	RCT	Medical centre	Stable COPD Bronchial hypersecretion	Flutter (with steel ball removed) x 10 breaths followed by 30 sec rest x 4–8 sets, daily for 3 months	Same as control, but with steel ball	3 months
Wolkove et al, 2002	23	71.7 (6.3)	RXT	Hospital	Stable severe COPD	Flutter for 10 min (steel ball removed), followed by COPD pharmacotherapy	Same as control, but with steel ball	3 days
Wolkove et al, 2004 (Abstract only)	15	71 (10)	RXT	Outpatient clinic	Stable COPD ≥ 10 pack-year smoking history	Flutter for 10 min (steel ball removed), 4x/day prior to usual COPD pharmacotherapy for 1 week	Same as control, but with steel ball	22 days

Abbreviations: COPD, chronic obstructive pulmonary disease; MRC, Medical Research Council; min, minute(s); N/A, not available; PEEP, positive end-expiratory pressure; PEP, positive expiratory pressure; RCT, randomized controlled trial; RXT, randomized cross-over trial.

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Cognitive-Behavioural Therapy for Anxiety and Depression in Individuals With Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review

Health Quality Ontario

February 2015

Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews must be completed in a 2- to 4-week time frame. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario 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. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario 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.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards 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 may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

CBT	Cognitive-behavioural therapy
COPD	Chronic obstructive pulmonary disease
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
QoL	Quality of life
RCT	Randomized controlled trial

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Rapid Review

The objective of this analysis was to determine the effectiveness of cognitive-behavioural therapy (CBT) for treating anxiety and depression in patients with chronic obstructive pulmonary disease (COPD).

Clinical Need and Target Population

Chronic obstructive pulmonary disease is characterized by progressive airflow limitation that cannot be completely reversed. The hallmark symptoms of shortness of breath (dyspnea), limitation in exercise capacity, and fatigue take a psychological toll as well as a physical one. Although prevalence estimates range substantially with differing assessment tools and definitions, (1) depression affects an estimated 7% to 42% of COPD patients and anxiety up to 96%. (2-5) Both subclinical and diagnosed mood disorders are associated with negative outcomes for COPD patients including poorer health-related quality of life, (6) more frequent hospitalization for COPD exacerbations among patients with anxiety, (7) longer lengths of stay, (8) self-reported physical disability, (9;10) and reduced engagement in (11) and likelihood of completion of (12) pulmonary rehabilitation.

Technology/Technique

A number of options to treat symptoms of or clinically diagnosed mood disorders are available, including exercise (e.g., pulmonary rehabilitation), medications, and psychological treatments. The latter includes psychotherapy, cognitive-behavioural therapy, and other techniques to minimize the catastrophic thought patterns between anxiety, depression, and dyspnea. (1) CBT aims to interrupt the cycle of breathlessness leading to anxiety and anxiety leading to further breathlessness, potentially decreasing anxiety and depression overall. (1) The extent to which CBT is effective for the treatment of anxiety and depression in COPD patients is in need of clarification.

Rapid Review

Research Question

What is the clinical effectiveness of cognitive-behavioural therapy (CBT) for patients with chronic obstructive pulmonary disease (COPD) and coexisting anxiety or depression?

Research Methods

Literature Search

Search Strategy

A literature search was performed on April 25, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, and EBM Reviews, for studies published from January 1, 2008, to April 15, 2014. (Appendix 1 provides details of the search strategy.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2008, and April 25, 2014
- systematic reviews, meta-analyses, and health technology assessments
- adults with COPD with clinical or subclinical anxiety or depression
- assessing effectiveness of CBT
- control groups of usual care, education, inactive controls, or active controls

Exclusion Criteria

- randomized controlled trials (RCT), observational studies, case reports, editorials, conference abstracts
- studies in other populations (e.g., elderly, general population)
- studies of the effectiveness of pharmacologic or other treatments, or comparative effectiveness of treatments

Outcomes of Interest

- change in symptoms of anxiety and/or depression
- quality of life

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a

care pathway model. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (13)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (14) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that RCTs 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. (14) For more detailed information, please refer to the latest series of GRADE articles. (14)

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

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 129 citations published between January 1, 2008, and April 25, 2014 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

The literature search identified 3 systematic reviews (15-17) and they received AMSTAR scores of 6, 7, and 9 out of 11, respectively (Appendix 2, Table A1). The 2013 systematic review by Coventry et al (17) was the highest quality as assessed by AMSTAR, included the most RCTs on CBT, and was the most recent; therefore, it was selected as the basis for the results related to change in symptoms of anxiety and depression. Only one review measured quality of life (QoL) and was therefore the basis of the findings for that outcome. (15) The reference lists of included studies and health technology assessment websites were hand-searched for other eligible reviews, and no additional citations were identified.

Symptom Improvement

A systematic review by Coventry et al (17) published in 2013 evaluated the effectiveness of complex interventions compared with usual care, wait list controls, or active controls for patients with COPD and coexisting anxiety or depression. Included in this review was a preplanned subgroup analysis examining CBT interventions specifically, compared to usual care or education (Table 1).

Table 1: Subgroup Analysis of RCTs of Cognitive-Behavioural Therapy for Patients with COPD

Number of RCTs (n range)	Range of Follow-Up, Weeks	Range of Mean Ages, Years	Range of COPD Severity	Professionals Delivering Interventions	Types of CBT Intervention
7 (23–238)	4–12	50–73	Mild–severe	Clinical psychologist, psychology student, social worker, nurse specialist, gero-psychiatrist, primary care nurses	30–120 minutes x 4–12 sessions Group or individual Face-to-face or remote

Abbreviations: CBT, cognitive-behavioural therapy; COPD, chronic obstructive pulmonary disease; n, number of patients; RCT, randomized controlled trial.
Source: Coventry et al, 2013. (17)

Change in symptoms was analyzed via standardized mean difference as the tools used to measure mood disorder symptoms varied. To assess depression, 4 studies used a version of the Beck Depression Inventory, (18-21) 1 used the Geriatric Depression Scale, (22) and 1 used the Profile of Mood States Depression tool. (23) To quantify anxiety, 3 studies used the Beck Anxiety Inventory, (19;20;22) 1 used the State Trait Anxiety Inventory (18), 1 used the Symptom Checklist-90, (21) and 1 used the Profile of Mood States Anxiety tool. (23) One study used the Hospital Anxiety and Depression Scale for assessment of both anxiety and depression. (24) Follow-up ranged from 4 to 12 weeks; however, for studies with multiple time points, the time period closest to end of treatment was included in the analysis. A random effects model was used for meta-analysis; Table 2 shows results for the effect of CBT interventions on anxiety and depression.

Table 2: Change in Anxiety and Depression after Cognitive-Behavioural Therapy Interventions for Patients with COPD

Outcome	Anxiety			Depression		
	Pooled SMD	95% CI	I^2 (*P* value)	Pooled SMD	95% CI	I^2 (*P* value)
Change in symptoms	-0.12	-0.34 to 0.11	34.5% (0.164)	-0.17	-0.35 to 0.01	10.1% (0.352)

Abbreviations: CI, confidence intervals; COPD, chronic obstructive pulmonary disease; SMD, standardized mean difference.
Source: Coventry et al, 2013. (17)

The meta-analysis revealed a small beneficial effect of CBT on both anxiety and depression, neither of which was statistically significant. There was no significant heterogeneity in the pooled analysis; but, there were differences in frequency of follow-up, outcome measurement, and interventions (duration, modality, frequency, and type of sessions [group or individual]). The authors discuss the potential role of methodological differences and the reality that the cognitive demands required to participate in, and therefore benefit from, CBT may be too high for the COPD population. They also discuss the age trends in COPD and the potential presence of cognitive impairments (both hypoxic and non-hypoxic) secondary to COPD as potential contributors to the observed lack of effectiveness. (17) Appendix 2, Table A2 provides the GRADE evidence profile for these results.

Quality of Life

The efficacy of psychological interventions for anxiety and depression in COPD was assessed in a systematic review by Baraniak and Sheffield. (15) This review included studies of interventions aimed at reducing symptoms and improving quality of life. Six studies evaluating CBT interventions were identified; however, only 4 assessed QoL compared with usual care, wait list controls, or education. (20;22;25;26) Three of the studies assessing CBT measured generic QoL (22;25;26) and 1 assessed both generic and disease-specific QoL. (20) Similar to the review by Coventry et al, (17) there was a wide range in the facilitators, intensity, frequency, and duration of the CBT interventions (Table 3).

Table 3: Overview of RCTs Examining Cognitive-Behavioural Therapy and Quality of Life

Number of RCTs (n range)	Range of Mean Ages, years	Range of COPD Severity	Professionals Delivering Interventions	Description of CBT Intervention Types
4 (48–238)	66–72	Moderate–severe	Psychiatrist, psychology intern/post-doctoral fellow, gero-psychiatrist, researcher	60–120 minutes 4–12 sessions or 10 weeks Group-based, face-to-face

Abbreviations: CBT, cognitive-behavioural therapy; COPD, chronic obstructive pulmonary disease; n, number of patients; RCT, randomized controlled trial.

Source: Baraniak and Sheffield, 2011 (15)

The Baraniak and Sheffield review (15) summarized the results from individual studies narratively; without a quantitative synthesis, we were not able to GRADE the results for QoL based on data reported in the review. We therefore assessed risk of bias for each study that measured QoL, using information from the quality assessment in the systematic review (Appendix 2, Table A3).

The narrative summary reported mixed results. Two studies reported some improvement in both health-related (20) and generic QoL score (mental health subscale) (20;22), though no differences were found between study groups. Between-groups findings were not reported from the other 2 studies, and no change was found in generic QoL within subjects in each group after the CBT intervention. (25;26)

Overall, the studies had small sample sizes and were likely underpowered to assess QoL; the authors indicate it was a secondary outcome for most of the studies. The authors also cited challenges in the synthesis of findings including unclear measurement and vague reporting of analysis. (15) One study reported significantly higher anxiety in the CBT group at baseline despite randomization (25) and it is unclear if the analysis accounted for the potential confounding from this difference. Although they did not statistically synthesize the QoL results, Baraniak and Sheffield (15) comment on a heterogeneity problem and say they detected some publication bias, but it is unclear which studies or outcomes their statements pertain to. The authors discuss the potential for CBT and other interventions to be ineffective for patients with COPD, despite demonstrated effectiveness in other populations.

Both systematic reviews cite the overlap in symptoms between COPD and these mood disorders as potential contributors to the lack of effectiveness observed.

Conclusions

- Cognitive-behavioural therapy did not significantly reduce symptoms of anxiety or depression in patients with mild to severe chronic obstructive pulmonary disease (COPD), compared with usual care or education. (GRADE: Low)

- Based on 4 randomized controlled trials with considerable limitations due to risk of bias, cognitive-behavioural therapy had mixed effectiveness on improving the quality of life of patients with moderate to severe COPD, compared with usual care, wait list controls, or education.

Acknowledgements

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Suzy Young	St. Mary's General Hospital	Nurse Practitioner Primary Health Care SWCCAC Intensive Health Care Team Certified Respirator Educator

Appendices

Appendix 1: Literature Search Strategies

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to March 2014>, EBM Reviews - ACP Journal Club <1991 to April 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <January 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <1st Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2014>, All Ovid MEDLINE(R) <1946 to Present>

Search Strategy: Community QBP COPD - Anxiety and Depression

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1 exp Patient Discharge/ (19612)
2 exp Aftercare/ or exp Convalescence/ (10162)
3 "Continuity of Patient Care"/ or exp "Recovery of Function"/ (47562)
4 ((patient* adj2 discharge*) or after?care or post medical discharge* or post?discharge* or convalescen*).ti,ab. (37579)
5 exp Stroke/ (87910)
6 exp brain ischemia/ or exp intracranial hemorrhages/ (131389)
7 (stroke or poststroke or tia or transient ischemic attack or ((cerebral vascular or cerebrovascular) adj (accident* or infarct*)) or CVA or cerebrovascular apoplexy or brain infarct* or (brain adj2 isch?emia) or (cerebral adj2 isch?emia) or (intracranial adj2 h?emorrhag*) or (brain adj2 h?emorrhag*)).ti,ab. (199959)
8 exp Heart Failure/ (91111)
9 (((cardia? or heart) adj (decompensation or failure or incompetence or insufficiency)) or cardiac stand still or ((coronary or myocardial) adj (failure or insufficiency))).ti,ab. (133265)
10 exp Pulmonary Disease, Chronic Obstructive/ (37678)
11 exp Emphysema/ (10911)
12 (copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema).ti,ab. (57781)
13 (chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*)).ti,ab. (35676)
14 exp Pneumonia/ (75675)
15 (pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab. (140837)
16 or/1-15 (769935)
17 exp Psychotherapy/ (162316)
18 exp Adaptation, Psychological/ (104886)
19 px.fs. (776125)
20 CBT.ti,ab. (6782)
21 ((cognition* or cognitive*) adj2 (behaviour* or behavior* or therap*)).ti,ab. (33006)
22 (mindfulness* or mindful-ness*).ti,ab. (2306)
23 (psychoanaly* or psycho-analy* or psychological* or psychosocial* or psycho-social* or psychotherap* or psycho-therap*).ti,ab. (237711)
24 or/17-23 (1030059)
25 Anxiety/ (56691)
26 Anxiety Disorders/ (24342)
27 Depression/ (79564)
28 exp Depressive Disorder/ (86432)
29 Panic/ (2661)
30 Panic Disorder/ (6604)
31 (anxiet* or anxious* or depress*).ti,ab. (421536)

32 ((emotional* adj distress*) or panic*).ti,ab. (20386)
33 or/25-32 (484700)
34 16 and 24 and 33 (6399)
35 limit 34 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained] (2683)
36 Meta Analysis.pt. (47780)
37 Meta-Analysis/ or exp Technology Assessment, Biomedical/ (56855)
38 (meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (202542)
39 ((health technolog* or biomedical technolog*) adj2 assess*).ti,ab. (2773)
40 or/36-39 (219010)
41 16 and 24 and 33 and 40 (238)
42 limit 41 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained] (141)
43 from 42 keep 13-141 (129)
44 remove duplicates from 43 (115)
45 from 35 keep 1-13,227 (14)
46 44 or 45 (129)

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Score of Included Systematic Reviews

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Coventry et al, 2013 (17)	9	✓	✓	✓	✓		✓	✓	✓	✓	✓	
Baraniak and Sheffield, 2011 (15)	6	✓		✓	✓		✓	✓	✓			
Coventry and Gellatly, 2008 (16)	7	✓		✓	✓		✓	✓	✓	✓		

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews.

[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al. (13)

Table A2: GRADE Evidence Profile for Comparison of Cognitive-Behavioural Therapy and Usual Care

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Anxiety Symptoms (Standardized Mean Difference)							
7 (RCTs)	Serious limitations (–1)[a]	Serious limitations (–1)[b]	No serious limitations	Serious limitations (–1)[c]	No serious limitations	None	⊕⊕ Low
Depression Symptoms (Standardized Mean Difference)							
7 (RCTs)	Serious limitations (–1)[a]	Serious limitations (–1)[d]	No serious limitations	Serious limitations (–1)[c]	No serious limitations	None	⊕⊕ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.
[a]Risk of bias assessment taken from Coventry et al, 2013. (17)
[b]The range of point estimates (-0.71 to 0.36) includes large benefit to moderate favour of the control. (27)
[c]Power cannot be assessed as pooled sample size is not reported, sample sizes range from 23 to 238 participates, and the 95% confidence interval includes 0, as well as appreciable benefit or harm.
[d]The range of point estimates (-0.63 to 0.10) includes large benefit, no effect, and slight favouring of the control. (27)

Table A3: Risk of Bias Among Randomized Controlled Trials for the Comparison of Cognitive-Behavioural Therapy and Controls for Studies Assessing Quality of Life

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Kunik et al, 2001 (22)	Serious limitations[a]	Serious limitations[b]	Serious limitations[c]	No limitations	No limitations
Kunik et al, 2008 (20)	Serious limitations[a]	Serious limitations[b]	No limitations[d]	No limitations	No limitations
Emery et al, 1998 (26)	No limitations	No limitations[e]	No limitations[d]	No limitations	No limitations
Eiser et al, 1997 (25)	Serious limitations[a,f]	Serious limitations[b]	Serious limitations[c]	No limitations	No limitations

[a]Inadequate allocation concealment method.
[b]Only participants were blinded to treatment group. Infeasible to blind interventionists due to nature of the intervention.
[c]Loss to follow-up was partially reported and differences in attrition between groups was not analyzed.
[d]Loss to follow-up was fully reported and considered in the analysis, although intention-to-treat principle was not adhered to.
[e]Outcome assessors and participants were blinded to treatment group. Infeasible to blind interventionists due to nature of the intervention.
[f]Randomization unclear and suspected to be inadequate as intervention group had significantly higher prevalence of anxiety than control group at baseline.
Source: Baraniak and Sheffield, 2011. (15)

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