Lymphedema, a frequent complication following treatment for breast cancer, is a substantial chronic swelling of the arm, breast and chest wall that occurs on the side where lymph nodes were removed. The aim of this work is to update recommendations on the prevention, diagnosis and management of lymphedema related to breast cancer.

Methods: We present the protocol for an update of the 2001 clinical practice guideline on lymphedema from the Steering Committee for Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. We will use a patient-oriented research approach with a focus on self-management and the positive health model to inform the updated guideline development. The methods proposed will be undertaken with consideration of the standards outlined in the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. The literature will be appraised by evaluating existing guidelines from other countries, the evidence from systematic reviews and meta-analyses and direct evidence from clinical studies. We will manage competing interests according to Guidelines International Network principles. Recommendations will be presented using an actionable statement format and will be linked to the level of evidence along with any relevant considerations used in formulation. A draft of the guideline will be produced by the steering committee then sent out to international experts and stakeholder groups for feedback.

Interpretation: The primary benefit of this clinical guideline will be to improve the quality of care of women with breast cancer-related lymphedema. Findings will be disseminated at national and international conferences and through webinars and educational videos hosted on the websites of the supporting organizations.
management of the lymphedema itself varies across and within provinces and territories; in some regions, services are provided through the public system and in other regions, services are available only through the private sector.11,12

In 2001, an expert panel of clinicians from across Canada published the first Canadian clinical practice guideline for the care and treatment of BCRL.13 The guideline was developed on the basis of evidence from a systematic review of the literature from 1966 to 2000 performed by researchers at the British Columbia Cancer Agency. At the time, there was a lack of high-quality research in the field, namely randomized controlled trials (RCTs), limiting the evidence available to inform the guideline. Over the past 20 years, over 100 RCTs and more than 50 systematic reviews have been published in the area of cancer-related lymphedema.

Given the growing cohort of survivors living with BCRL, new scientific research, improvements in breast cancer surgical and radiotherapy techniques, and new diagnostic and measurement technologies, an update to the Canadian guideline is long overdue. Although several guidelines have been published recently,14–18 a recent review of 5 lymphedema-specific guidelines reported that none could be recommended for clinical practice because of the poor methodologic quality and lack of rigour of development.19

Our updated evidence-based guideline will serve as a tool on best practice and clinical decision-making for the long-term management of BCRL in Canada. Specifically, the objective of the guideline is to provide information and recommendations for patients and their physicians when they are making decisions about diagnosis, prevention and risk reduction practices, and long-term management of the condition. Although the guideline may also provide some direction for other health care professionals and may be useful in the context of patient advice and education, practitioner education and training, and service standards, the main aim of the work is to provide recommendations for clinical practice based on the available evidence. This paper describes the protocol for the development of the guideline.

Methods

The proposed evidence-based guideline development is an initiative of the Canadian Lymphedema Framework in partnership with the Oncology Division of the Physiotherapy Association and Cancer Care Alberta’s Guideline Resource Unit.

Figure 1 illustrates the planned stages and timeline of the guideline development process. Development of the guideline will be undertaken with consideration of the standards outlined in the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument.20–22 Table 1 provides details on the proposed methods as per the AGREE II tool.24

The new guideline will encompass a patient-oriented research approach and focus on the ability of people with breast cancer to adapt to and self-manage their lymphedema. We will follow the principles of patient-oriented research as per Canada’s patient-oriented research strategy; people with BCRL will be involved in all stages of the guideline development.25 We will work collaboratively with patients and stakeholders on the development and implementation of the guideline.

In addition, we will ensure the guideline is responsive to the areas of greatest need; expand on existing knowledge, expertise and excellence in the field; and foster a culture of new ideas and solutions. Inclusivity is an important guideline principle, and decisions will be made through open, collegial and engaging discussion. Thus, the proposed guideline will be developed by an interdisciplinary group with strong user and patient representation.

Self-management is a process through which women with BCRL actively manage their condition in the context of their day-to-day lives, and it is an important strategy to reduce the burden of lymphedema.26–28 For the purposes of the guideline development and recommendations, we will follow the positive health model introduced in the Netherlands in 2011.29 In this model, health is defined as the “ability to adapt and to self-manage, in the face of social, physical and emotional challenges.” This definition of health focuses on the individual’s capacity for resilience and for coping with new situations and chronic health conditions over the lifespan. This model aligns well with our intent to identify, where possible, effective self-management strategies for BCRL.

Composition of participating groups

Before the proposed guideline update was undertaken, a meeting was held in Toronto on Nov. 1, 2019. The meeting was convened at the National Lymphedema Conference, a conference hosted by the Canadian Lymphedema Framework, and included researchers and health care practitioners with expertise in BCRL, as well as patient representatives. The purpose of the meeting was to discuss the need for an updated Canadian guideline and provide attendees with the opportunity to propose topic areas, identify key questions and discuss clinical issues to inform guideline development.

Twenty stakeholders from across Canada, including people with BCRL, took part in the initial meeting. Following the meeting, the Canadian Lymphedema Framework assembled a steering committee to ensure broad stakeholder representation from across Canada, with diversity of experience and perspectives. This included 2 co-chairs (M.L.M., D.K.), the 2001 Canadian guideline chair (S.R.H.), a palliative care physician (A.T.), a breast cancer oncologist (K.K.), a physical medicine and rehabilitation resident (L.C.), a nurse specialist (J.A.R.), a breast cancer rehabilitation researcher (K.L.C.), a representative from the Oncology Division of the Canadian Physiotherapy Association (M.D.) and 3 patient advisors (S.R.H., J.B., A.K.). The steering committee will be responsible for evaluating the evidence at each stage of the review and for directing next steps. The steering committee will meet at approximately 4-month intervals starting in the fall of 2021.

The project will be guided by a knowledge management specialist from Alberta Health Services’ Guideline Resource Unit (X.K.) and a research librarian (L.D.). The management team includes a co-chair (M.L.M.), a funded postdoctoral fellow (N.D.D.), a clinical physical therapist (L.R.) and 2 graduate...
students (M.M.A.O., J.F.P.). The management team will meet regularly. A project platform has been created to identify milestones, organize daily tasks and monitor overall work progress (https://canadalymph.ca/project/research/). Working groups will be established for each category comprising the framework of the guideline (described below). Team members from stakeholder groups may be added to the steering committee, management team or working groups, as needed, as the guideline work progresses.

To facilitate engagement of a larger number of people with BCRL in the guideline development process, we will involve people with BCRL in prioritizing the key questions for the guideline. We will also get feedback from stakeholders and international experts on the draft recommendations.

**Selection of key questions and outcomes**
The steering committee created a framework for the guideline based on 4 main categories as determined at the stakeholder meeting in 2019: diagnosis, prevention and risk reduction, effective management and measurement outcomes. To narrow the focus of the guideline, 4 areas of focus were identified based on areas of contention or where guidance is currently lacking in clinical practice, and metrics were established to aid in interpreting research findings (Table 2). The areas of focus were diagnosis, risk reduction, effective management and measurement outcomes. A full list of key questions identified at the stakeholder meeting in November 2019 can be found in Appendix 1, available at www.cmajopen.ca/content/10/2/E338/suppl/DC1.
Table 1 (part 1 of 2): Clinical practice guideline methodology: AGREE II checklist

| AGREE II checklist item | Reporting criteria | Planned guideline protocol |
|------------------------|--------------------|---------------------------|
| **Domain 1: Scope and purpose** | | |
| 1. Guideline objectives | Health intent, expected benefit, targets | • To provide information and recommendations for women and their physicians when making decisions about diagnosis, prevention and risk reduction, management and outcomes related to BCRL |
| 2. Questions | Target population; Interventions or exposures; Outcomes; Context | • Women with breast cancer with or at risk of developing lymphedema  
• Diagnosis, risk reduction, management and outcomes  
• Improve the care of women with BCRL; focus on self-management  
• Canadian health care system |
| 3. Population | Target population; Clinical condition; Severity of disease | • Adult women with breast cancer*  
• Breast cancer — from diagnosis to palliative stages  
• Lymphedema — all stages and severity of the condition |
| **Domain 2: Stakeholder involvement** | | |
| 4. Group membership | Participants; Membership expertise; Institutions and organizations; Geographic location; Members’ roles | • Steering committee, management team and working groups: researchers, clinicians, specialist and patient representatives from across Canada  
• Partners: Canadian Physiotherapy Association Oncology Division, CancerControl Alberta’s Guideline Resource Unit and the Canadian Lymphedema Framework  
• Member roles will be defined and shared |
| 5. Target population preferences and views | Patients’ views and preferences | • Patient representatives will be involved at all stages of guideline development  
• Literature review of patients’ values and preferences  
• Survey, focus groups and consultation with patient groups |
| 6. Target users | Intended audience; Use of guideline | • Physicians as well as women with and at risk of BCRL  
• Inform clinical decisions and standards of care |
| **Domain 3: Rigour of development** | | |
| 7. Search methods | Electronic databases; Time periods of searches; Search strategy | • MEDLINE, Embase, Scopus, CINAHL, Proquest Dissertations and Theses Global, PEDro, Cochrane Library, Trip Pro, Agency for Healthcare Research and Quality’s National Guideline Clearinghouse  
• Guidelines and systematic reviews: Mar. 1, 2014, to Oct. 31, 2021; RCTs: Mar. 1, 2014, to Oct. 31, 2021  
• Further details on the search terms and strategy are provided in Appendix 1 (available at www.cmajopen.ca/content/10/2/E338/suppl/DC1) |
| 8. Evidence selection criteria | Target population; Study design; Outcomes; Languages | • Women with BCRL  
• CPGs; systematic reviews; cross-sectional studies (diagnosis); cohort studies (prognosis); RCTs (treatment and management)  
• Diagnosis and assessment; risk reduction and prevention; management and treatment; outcomes and surveillance  
• No language restrictions |
| 9. Strengths and limitations of evidence | Study methodology to evaluate quality | • CPGs: AGREE II appraisal; systematic reviews: AMSTAR; cross-sectional studies: AXIS; cohort studies: Newcastle–Ottawa Scale; RCTs: Cochrane risk-of-bias tool  
• Rating of evidence: tables reflecting GRADE and detailing the level of evidence, consistency of results, direction of results, magnitude of benefit (versus harm) and applicability to practice context in Canada will be developed |
| 10. Formulation of recommendations | Recommendation development process | • ADAPTE will be used to incorporate recommendations from existing guidelines  
• Noncontentious findings: steering committee will vote in situations where the level of evidence and the balance between benefits and harms is established, findings are consistent across studies and the recommendation is applicable to the Canadian context  
• Contentious findings or in cases in which there is no evidence: stakeholder consensus on recommendation (best practice statement) or explanation of reasons if consensus cannot be reached |
### Table 1 (part 2 of 2): Clinical practice guideline methodology: AGREE II checklist\(^{21,23,24}\)

| AGREE II checklist item | Reporting criteria | Planned guideline protocol |
|-------------------------|--------------------|----------------------------|
| 11. Consideration of health benefits, side effects and risks | Data supporting benefits, harms and side effects, and balance of benefits and harms | • Tables will be developed to outline the benefits and risks  
• Recommendations will consider the balance between benefits and risks as appropriate |
| 12. Link between recommendations and evidence | Link between evidence and recommendations is explicit | • The recommendations will be supported by the level of evidence, the extent of the evidence (total number of studies and total number of subjects), the direction of effect and the magnitude of effect and, where possible, consideration will be given to the stage and severity of lymphedema |
| 13. External review | Participants, purpose and intent of external review | • Feedback from external experts and stakeholder groups will be solicited to improve the CPG quality and to obtain feedback on the draft recommendations |
| 14. Updating procedure | Statement on when the guideline will be updated | • The steering committee will determine the timeline and outline criteria for future updates |

**Domain 4: Clarity of presentation**

| AGREE II checklist item | Reporting criteria | Planned guideline protocol |
|-------------------------|--------------------|----------------------------|
| 15. Specific and unambiguous recommendations | Recommendations are specific with circumstances and relevant populations identified | • Recommendations will be presented with a clear purpose and in an actionable statement format  
• Areas of uncertainty and those requiring further research will be identified  
• A lay summary of the findings will be shared with stakeholder groups |
| 16. Management options | Possible management options are clearly described | • Management options will be articulated given the Canadian health care context, and the focus on self-management of lymphedema |
| 17. Identifiable key recommendations | Key recommendations are easily identifiable | • Key recommendations will be highlighted in an executive summary  
• Algorithms and flow charts will be created to highlight findings |

**Domain 5: Applicability**

| AGREE II checklist item | Reporting criteria | Planned guideline protocol |
|-------------------------|--------------------|----------------------------|
| 18. Facilitators and barriers to application | Facilitators and barriers to the guideline's application are described | • Information on barriers and facilitators to the CPG will be sought at the draft CPG stage  
• The CPG will be evaluated in Alberta, Canada, before national implementation |
| 19. Implementation advice and tools | Tools to support application of the guideline | • Materials will be created to support CPG implementation  
• Short videos will be created for health care professionals and patients; videos will be housed on the Oncology Division of the Canadian Physiotherapy Association and Canadian Lymphedema Framework websites |
| 20. Resource implications | Potential resource implications of recommendations | • Where possible, costs related to diagnosis and management will be collected  
• Costs will be considered within the Canadian context |
| 21. Monitoring and auditing criteria | Provide auditing criteria | • Operational definitions will be determined to inform auditing and measurement of impact |

**Domain 6: Editorial independence**

| AGREE II checklist item | Reporting criteria | Planned guideline protocol |
|-------------------------|--------------------|----------------------------|
| 22. Funding body | Influence of funding body on guideline recommendations | • Initial funding for the stakeholders meeting was received from the Oncology Division of the Canadian Physiotherapy Association  
• The CPG will be completed without influence from any funding body |
| 23. Competing interests | All group members must declare competing interests | • All CPG steering committee, management team and working group members will be required to provide written documentation declaring any competing interests  
• People associated with industry or private businesses or who declare other competing interests that could influence the guideline process or development will not be eligible to participate |

Note: AGREE II = Appraisal of Guidelines for Research and Evaluation II, AMSTAR = A Measurement Tool to Assess Systematic Reviews, AXIS = Appraisal Tool for Cross-Sectional Studies, BCRL = breast cancer–related lymphedema, CPG = clinical practice guideline, GRADE = Grading of Recommendations Assessment, Development and Evaluation, RCT = randomized controlled trial.  
*Physicians are the target users in this domain.
Table 2: Guideline key questions and outcomes by category

| Relevant guideline category | Primary area of focus                                                                 | Rationale                                                                                           | Primary outcome of interest and rationale |
|----------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|-----------------------------------------|
| Diagnosis                 | What valid and reliable tests can assist with a clinical diagnosis of BCRL?          | Guidance is lacking on best methods for early identification of BCRL                                  | Sensitivity and specificity<sup>30</sup>  |
| Prevention and risk reduction | What is the evidence supporting the benefit of prevention and risk reduction strategies? | Controversies exist over many of the recommended prevention and risk reduction strategies           | Incidence rates: presented as percentages, fractions or simple frequencies<sup>31</sup> |
| Effective management      | What is the state of the evidence supporting conservative, pharmacologic and surgical management of BCRL? | Inconsistencies are found across guideline recommendations and grades of evidence for best-practice management of BCRL | Arm lymphedema volume was chosen as this metric is used clinically for decisions related to treatment<sup>32</sup> |
| Measurement outcomes     | What metrics need to be captured to inform ongoing care of BCRL over the longer term? | Guidance is lacking on best practices related to follow-up and surveillance of chronic BCRL          | Valid, reliable and sensitive methods<sup>33</sup> |

Note: BCRL = breast cancer–related lymphedema.

To establish consensus on the top 4–6 questions from the perspective of people with and at risk of BCRL, we will conduct a series of surveys (using a modified Delphi approach) and focus group sessions.<sup>35,36</sup> This process will also help to identify any additional barriers and facilitators to seeking lymphedema care that may have been missed at the original stakeholders meeting.

An initial survey will be created using the secure REDCap Web platform for managing online databases and surveys, supported by the Women and Children’s Health Research Institute and housed in the Faculty of Medicine and Dentistry at the University of Alberta. The survey was developed on the basis of prior work by our group in cancer and lymphedema.<sup>37,38</sup> The survey will be pilot tested with 5 patient volunteers before it is sent out more broadly. Potential participants for both the survey and focus groups will be identified through recruitment emails sent by the Canadian Lymphedema Framework and the Canadian provincial lymphedema associations.

The primary outcomes considered for each of the 4 proposed categories of this guideline are as follows: sensitivity and specificity (for the diagnosis category), incidence rates related to risk reduction strategies and practices (for the prevention and risk reduction category), limb volume (for the effective management category) and valid, reliable and sensitive methods to detect and monitor lymphedema, and surveillance timelines (for the measurement outcomes category).

We will also consider outcomes related to lymphedema in the breast, chest wall and trunk given that involvement of these areas is common but less explored than lymphedema in the arm.<sup>19,40</sup> Secondary outcomes will include upper limb function, lymphedema-related symptoms and quality of life, and consideration will also be given to the cost associated with a given recommendation.

**Summarizing the evidence**

The management team, under the direction of the research librarian (L.D.), will conduct a search of the following electronic databases: MEDLINE, Embase, Scopus, CINAHL, Proquest Dissertations and Theses Global, PEDro, Cochrane Library (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews), Trip Pro, Agency for Healthcare Research and Quality’s National Guideline Clearinghouse. Published and unpublished studies from Mar. 1, 2014, to Oct. 31, 2021, are eligible for inclusion, with no language restrictions.

We will consider clinical practice guidelines, systematic reviews, cohort studies, cross-sectional studies and randomized controlled trials published since 2015 describing diagnosis, risk reduction, management and measurement outcomes involving people with breast cancer of any age who have or are at risk of developing lymphedema. To locate unpublished research, we will review proceedings from lymphedema conferences and search websites housing clinical trial details, theses or dissertations. In addition, we will hand search the reference lists of all potentially relevant studies and contact experts to identify relevant articles.

To start, we will review existing clinical practice guidelines, published since 2015, from within and outside of Canada: the quality of existing guidelines will be assessed by 4 appraisers using the AGREE II instrument, and domains will be scored.<sup>20,21</sup> The objective of this stage is to determine the quality of the guideline and its relevance to the Canadian context and appropriateness for use in that context and to identify any gaps requiring further research evidence. To ensure confidence in recommendations adapted from existing guidelines and to ensure transparency in decision-making, a priori, we have chosen to prioritize the domain of rigour of development with a threshold score of 70%,<sup>21,41</sup> Thresholds for other domains were set at 60% for stakeholder involvement and editorial independence (to set a standard for stakeholder representativeness and avoidance of bias in recommendations) and at 50% for all other domains.<sup>21</sup>

We will use [The ADAPTE Process: Resource Toolkit for Guideline Adaptation](#) for amalgamating and incorporating recommendations from existing guidelines into a new guideline.<sup>42</sup> The ADAPTE process has 3 phases: set-up, adaptation
and finalization. The ADAPTE process will be used in specifying clinical questions, organizing and analyzing available guidelines together with the AGREE II tool, and incorporating information that meets the criteria of both the AGREE II tool review and the ADAPTE process into the current proposed guideline. The recommendations of existing guidelines will be mapped to the relevant category along with information on AGREE II scores.

The literature will then be appraised to address specific categories or gaps in recommendations by evaluating the evidence from systematic reviews and meta-analyses, and direct evidence from clinical studies. Existing systematic reviews and clinical trials will be evaluated using relevant quality evaluation tools (e.g., Measurement Tool to Assess Systematic Reviews [AMSTAR], AXIS tool for cross-sectional studies, Newcastle–Ottawa Scale for cohort studies, Cochrane risk-of-bias tool for RCTs). At each stage of the review, findings will be presented to the steering committee for feedback and approval. If the steering committee identifies the need for a new or updated systematic review, the proposed review protocol will be registered in PROSPERO (www.crd.york.ac.uk/PROSPERO). We will strive for a balance between rigour and pragmatism to maintain efficiency.

The management team will produce a final synthesis of the evidence with consideration given to the Canadian health care context (e.g., where provincial and territorial or national data are available to estimate the cost and availability of diagnostic test or service across provinces and territories) as well as the alignment of the guideline with a self-management focus where appropriate.

Development of recommendations

We will use the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach to develop and present the summaries of evidence. We will develop a GRADE summary of findings table for each question. When the level of evidence is strong, benefit and harm are clearly established, and findings are consistent across studies and appropriate to the Canadian context, the management team will formulate a recommendation including the determined strength and level of certainty, as per GRADE. (We will also create a subsection in the guideline that provides a table showing the main differences between our recommendations and those found in other guidelines.)

The steering committee will vote on each recommendation, with greater than 75% agreement required for the recommendation to be included in the guideline. As necessary, where there is little evidence to guide the answers or when findings are contentious, we will aim to establish expert consensus on recommended diagnostic and risk reduction practices, treatment and long-term management strategies. These recommendations will be identified as best practice statements. Seventy-five percent agreement on a statement will be required to reach consensus. If consensus is not reached, no recommendation will be provided and the reasons for the divergent views will be outlined to provide clarity on the lack of consensus.

Recommendations will be presented, where applicable, using algorithm maps and summary tables, and as actionable statements to guide users on what to do, when and under what specific circumstances. Each recommendation statement will be linked to the formulated GRADE certainty of evidence along with any relevant discussion or considerations used in developing the recommendation.

External review process

A draft of the guideline will be produced by the steering committee then sent out to international experts and stakeholder groups (Table 3) for feedback. The Steering Committee will collect and record the feedback from the external review process, including how the committee addressed the feedback.

Following expert and stakeholder external review, the steering committee will make recommendations available for a 3-week period for public comment and review, before finalizing them. Records and documents related to the external review process will be made available to the public and the broader stakeholder group through the Canadian Lymphedema Framework website.

Management of competing interests

We will follow the Guidelines International Network principles for disclosures of interests and management of competing interests. All steering committee members, management team members and working group members will be asked to update their disclosures regularly throughout the guideline development process. Cancer Care Alberta’s Guideline Resource Unit will be responsible for evaluating and adjudicating competing interests, led by the knowledge management expert (X.K.). These disclosures will be available on the project platform and disclosed in any publications related to the guideline work. External stakeholders involved in any aspects of the guideline process will also disclose relevant interests at the outset of their participation and annually thereafter. To date, no disclosures have been found to represent competing interests that preclude an individual’s participation as a clinical or content expert.

The Oncology Division of the Canadian Physiotherapy Association funded the initial meeting held in Toronto. A Mitacs Accelerate postdoctoral fellowship (N.D.D.) was received through a partnership between the Canadian Lymphedema Framework and the University of Alberta. Cancer Care Alberta’s Guideline Resource Unit will provide in-kind support, and we have engaged expert and non-expert professionals and patients in the process. All steering committee, management team and working group members are volunteers and will not be remunerated for their services.

Ethics approval

Ethics approval will be sought from the Health Research Ethics Board of Alberta Cancer Committee for participants involved in the survey and focus group work. All participants will be required to provide informed consent.
This paper describes the protocol for how the proposed BCRL guideline will be developed. As part of the dissemination and implementation of the guideline, steering committee members will share the findings at both national and international conferences. A webinar will be hosted by the Canadian Lymphedema Framework for both patient and health care professional groups. In addition, we will apply for funding to support the creation of videos to disseminate our key findings to the targeted users of the guideline: people with BCRL, physicians and other health care professionals. To increase the reach of the guideline, the professional and patient series of videos will be hosted on the websites of the Oncology Division of the Canadian Physiotherapy Association and the Canadian Lymphedema Framework in both official languages.

### Limitations

There are a number of potential limitations to the proposed guideline protocol. First, the development of comprehensive recommendations may be limited by the availability of high-quality research evidence, affecting some or all categories. Second, even in the case where data are strong, evidence in support of or against a specific recommendation will involve subjective value judgments; to address this issue we have established objective cut points for decision-making. Third, recommendations may be influenced by the opinions, time availability and clinical experience of the steering committee, management team and working groups. To minimize any potential bias, Cancer Care Alberta’s Guideline Resource Unit will oversee and guide processes, and we will involve patients as partners in the process and solicit feedback from known experts and external stakeholders.

### Conclusion

This protocol describes the process that will be used to develop an updated guideline for people with or at risk of BCRL and their physicians in Canada. Our goal is to improve consistency in care for women with BCRL regardless of where they live in Canada or by whom they are treated. In this way, we hope to support better management of BCRL and improve health outcomes for this condition.

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Data sharing: Raw data will be available through the University of Alberta Libraries’ Dataverse network.

Supplemental information: For reviewer comments and the original submission of this manuscript, please see www.cmajopen.ca/content/10/2/E338/suppl/DC1.