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Guidelines for Testing & Treating Long COVID

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May 1st, 2025

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Disclosures

This project was made possible through a financial contribution from the Public Health Agency of Canada.

- **E. Falcone:**
  - Grants/Research Support: CIHR, FRQS, MSSS, MEIE, J.-Louis Lévesque Foundation, Mirella and Lino Saputo Foundation
  - Other: Collaboration with Bruker and Laurent Pharma

- **K. Quinn:**
  - Grants: CIHR, Long COVID Web
  - Other: Previously owned stock in manufacturers of COVID-19 antivirals.

Financial contribution:

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Land Acknowledgement

The work of CAN-PCC has taken place in Canada - the traditional, ancestral, and unceded territory of many Indigenous nations.

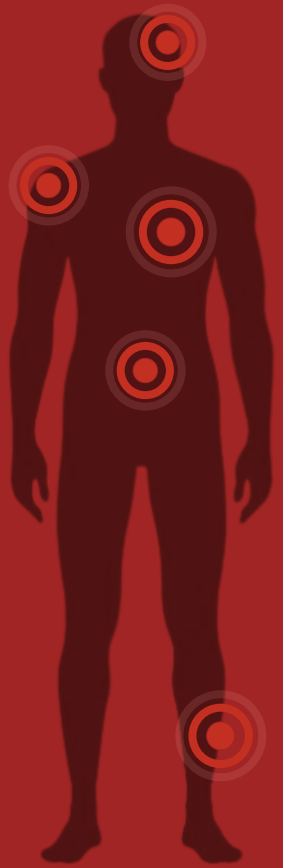
We honour the rich cultural and traditional practices, languages, and histories of Indigenous communities across Turtle Island. We pay our respect to the First Nations, Inuit, and Métis peoples of this place who have stewarded this land for millennia.

Objectives

By the end of this session, participants will be able to:

1. Describe the impact of Post COVID-19 Condition (PCC) and the methods used to develop the guidelines.
2. Describe the recommendations for testing, identification, diagnosis, and clinical interventions for PCC.
3. Discuss how the recommendations can be integrated into practice.
4. Identify key resources for dissemination and strategies for implementing PCC recommendations.

Post COVID-19 Condition (PCC), or long COVID, is a relatively **new** and **complex** condition affecting different parts of the body.



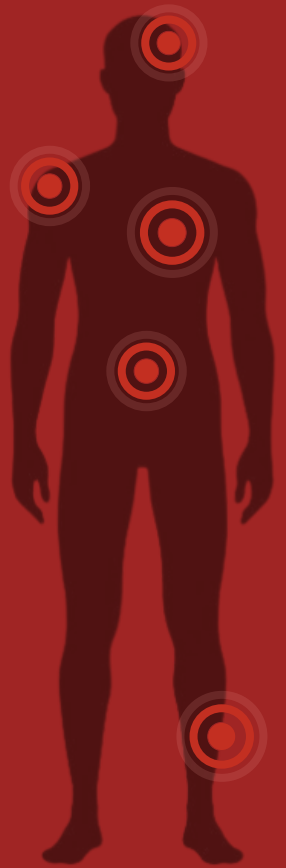
Source: FreePik

What is Post COVID -19 Condition (Long COVID)?

Post COVID-19 Condition (PCC), or Long COVID, usually appears **within three months from the acute COVID-19 infection and lasts at least two months**.

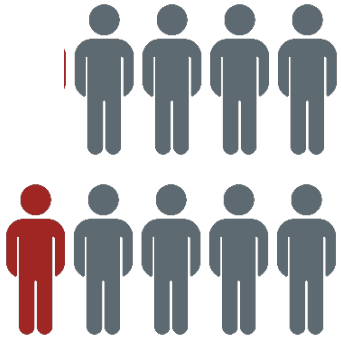
Symptoms vary, and can change or worsen over time, and significantly impact daily life.[1]

Around **400 million** are estimated to have had PCC globally. [2,3]



Source: FreePik

Impact on People in Canada



In Canada, **1 in 9 adults (18+),** or 3.5 million Canadian adults, have experienced **long-term symptoms** after a COVID-19 infection.[4]

600,000 Canadian adults with long-term symptoms missed days of work or school.[4]

Over 200+ symptoms exist, the most common including[5,7]:

Fatigue

Pain

Shortness of breath

Brain fog

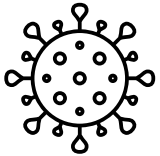
Sleep problems

Post exertional malaise[6]

Source: Mcrosoft Powerpoint

Only **1 in 8** adults in Canada who sought support for their symptoms felt they **received appropriate care**[4]

Cochrane Canada | McMaster University | GRADE Centre



For health professionals, what proportion of your clients experience PCC (or long COVID)?

While scientific studies are undertaken and the evidence-base grows to fill knowledge gaps and inform practice, **individuals living with PCC require care, support, and treatment now**.[8]

– ***Dr. Mona Nemer***
Chief Science Advisor

Cochrane Canada | McMaster University | GRADE Centre

CAN-PCC

CANADIAN GUIDELINES FOR
POST COVID-19 CONDITION

canpcc.ca

Working together to improve care for Post COVID-19 Condition.

Cochrane Canada

McMaster University

Grade Centre

Financial contribution:

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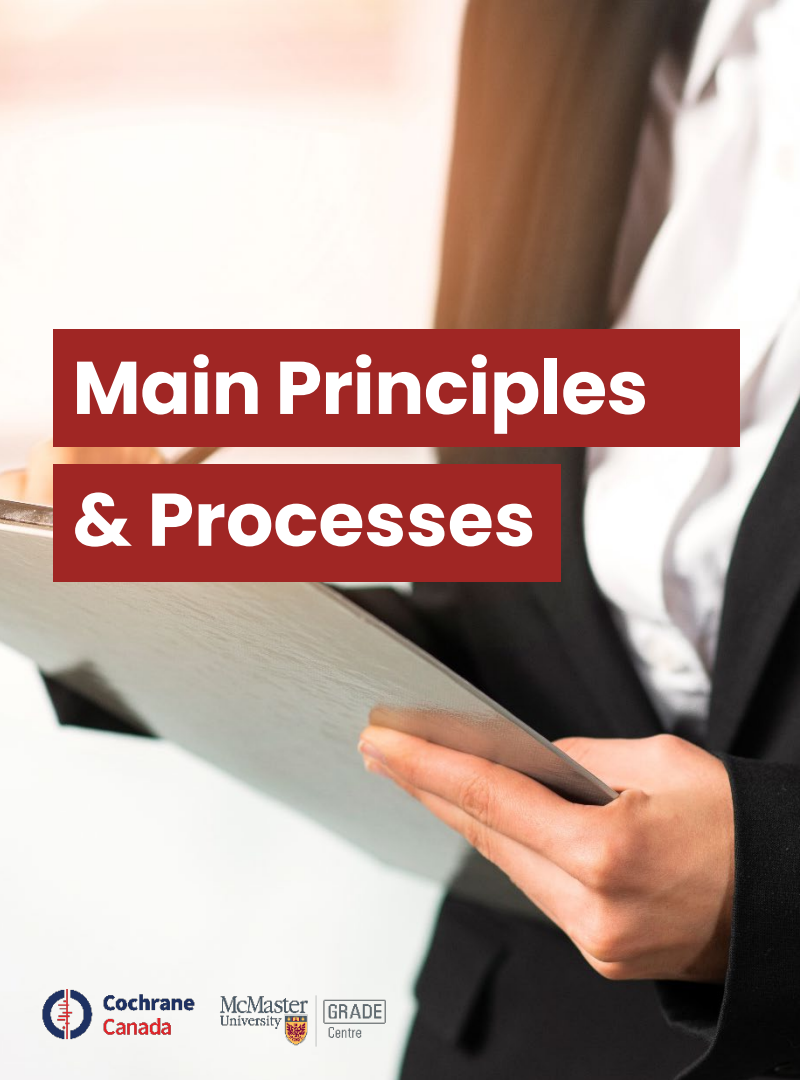


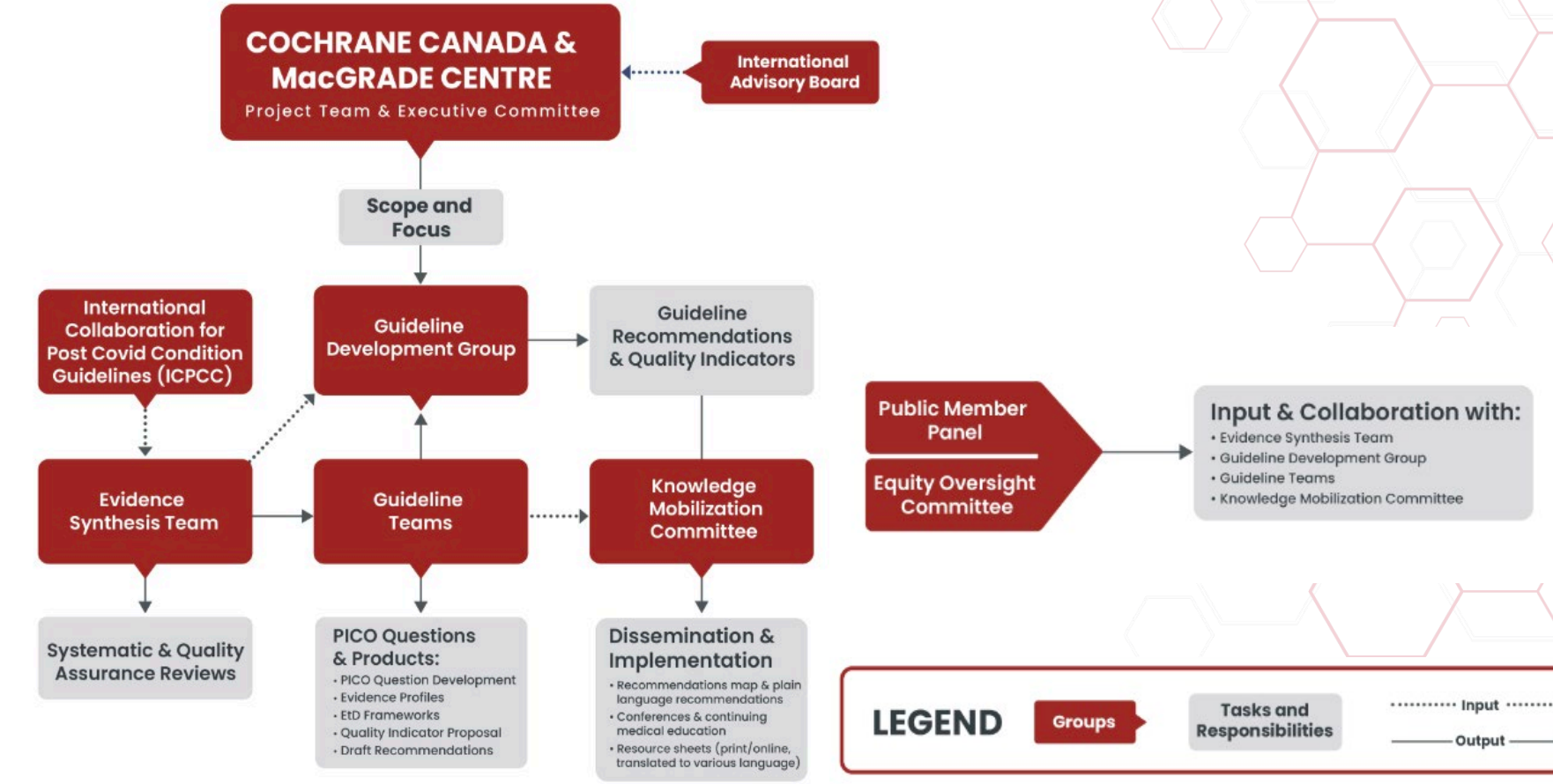
Main Principles & Processes

- **Balanced representation** of participants in decision-making roles, including people with lived experience and equity-seeking groups
- **Key groups and collaborators**, including representatives from prominent international guideline development organizations
- **A transparent and evidence-based systematic approach** based on best practices for guideline development
- **Independent management** of conflicts of interest
- **Standardized training** with certification from the International Guideline Training and Certification Program (INGUIDE)

INGUIDE

Source: FreePik, inguide.org

Project Groups: Roles, and Responsibilities



Equity in CAN-PCC

Equity Oversight Committee

An Equity Oversight Committee, first of its kind, will ensure health equity is incorporated during the guideline development process.

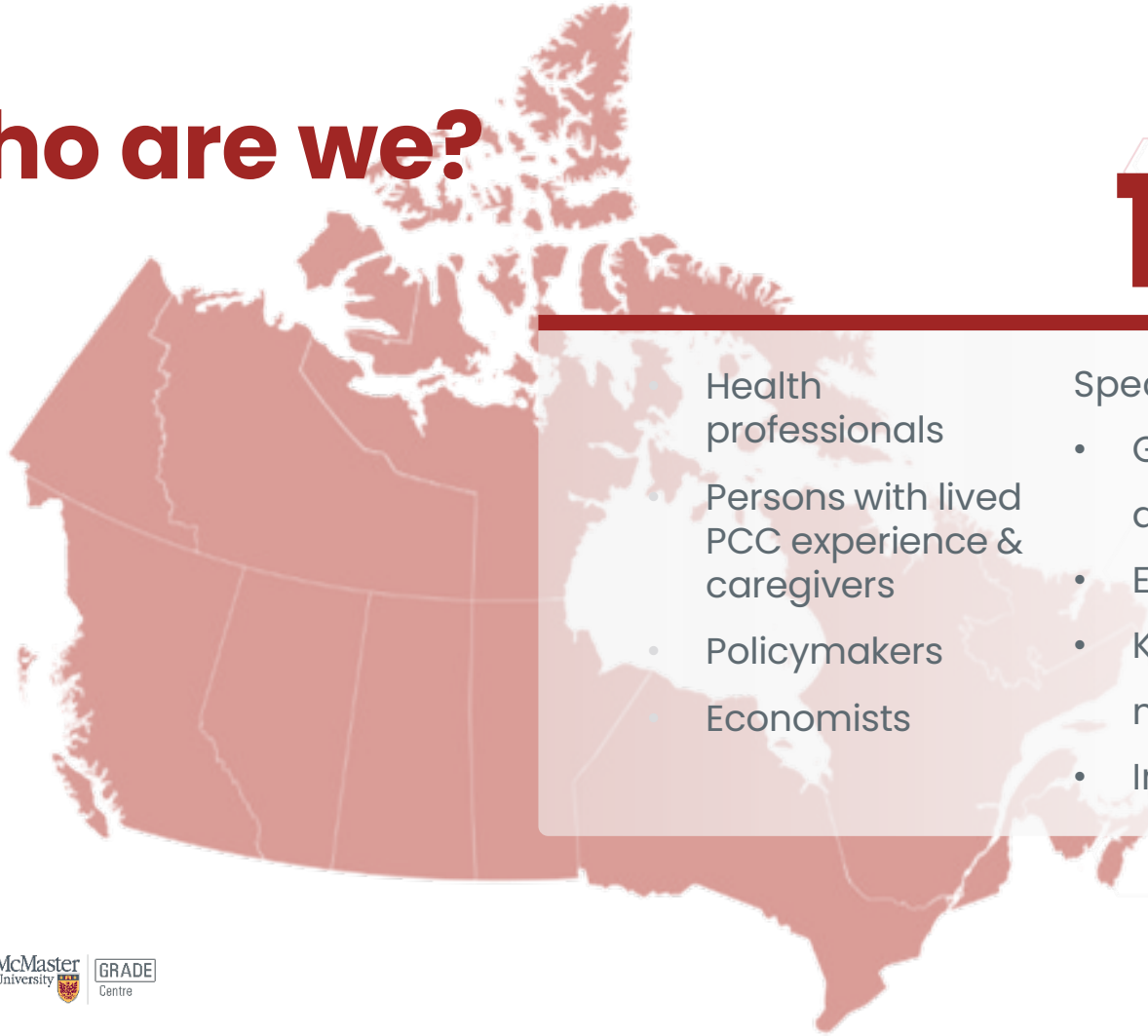
Partner equity-seeking groups

Prioritized groups include Indigenous Peoples, refugees and migrants, 2SLGBTQIA+, older adults, women, pregnant women, racialized groups, people experiencing homelessness, and justice-involved people.

Cochrane Canada | McMaster University | GRADE Centre

Source: FreePik

Who are we?



150+

- Health professionals
- Persons with lived PCC experience & caregivers
- Policymakers
- Economists

Specialists in:

- Guideline development
- Evidence synthesis
- Knowledge mobilization
- Impact evaluation

Involvement of persons with lived PCC experience

- Persons with lived PCC experience in equal guideline development roles
- Provide perspective of lived PCC experience during the guideline development process.

CAN-PCC

CANADIAN GUIDELINES FOR
POST COVID-19 CONDITION

*"As a person with Post COVID-19 Condition, I would like to see **clinicians** consider these guidelines in their practice.*

*I would like to encourage sensitivity when **patients** are expressing those concerns.*

*I would like to see the **public** use the guidelines to best inform and empower themselves in their health decisions."*

Kimberly, CAN-PCC Patient Representative

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How a CAN-PCC recommendation is made

Public input from:

- **Government**
- **Patients & Public**
- **Health Organizations**

1. **Select topics & questions**
2. **Identify outcomes**
3. **Identify, combine, & assess evidence**
4. **Develop draft recommendations**
5. **Public comment on draft Recommendations**
6. **Review comments and revise recommendations**
7. **Approve recommendations**
8. **Disseminate**

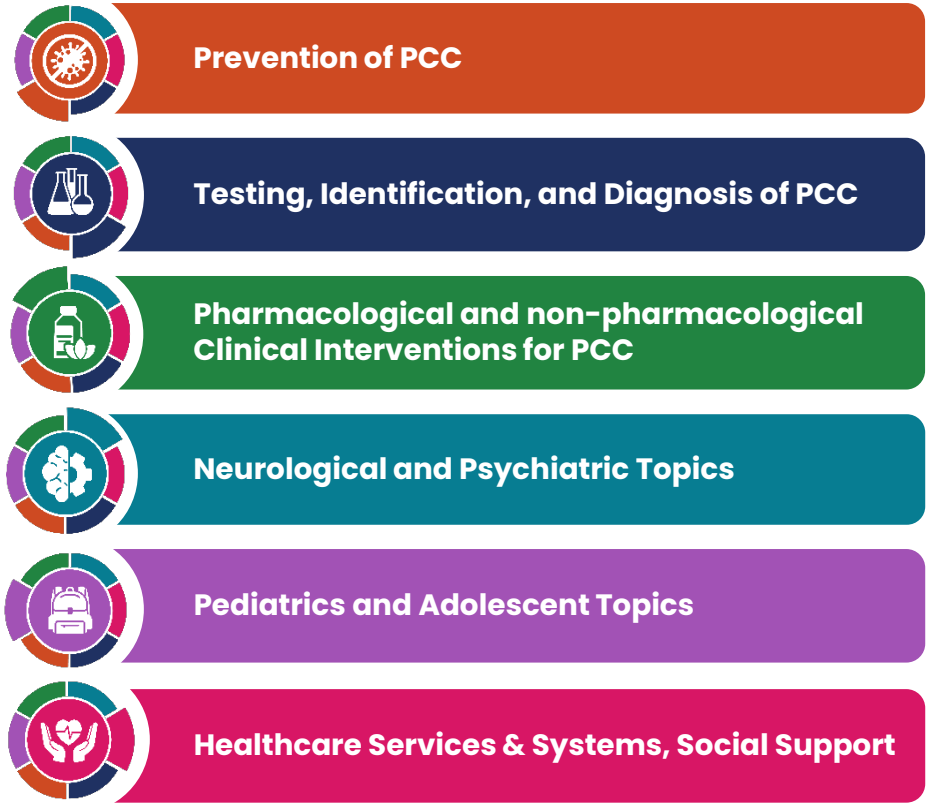
Diverse experts
including health professionals, patients, public, researchers & economists.

- Guideline Teams
- Guideline Development Group
- Equity Oversight Committee
- Public Member Panel
- KM Committee
- International Advisory Board
- Evidence Synthesis Teams

Canadian Guidelines for Post COVID-19 Condition

99 recommendations available, 13 more to be released by June 2025

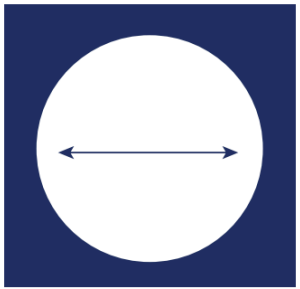
Recommendations cover:



What are recommendation strength and direction?

Health recommendations will have a **strength** and **direction.**

The **strength** can be either **strong** or **conditional (weak)**



The **direction** is about whether the recommendation is **for** or **against** an option

For example:

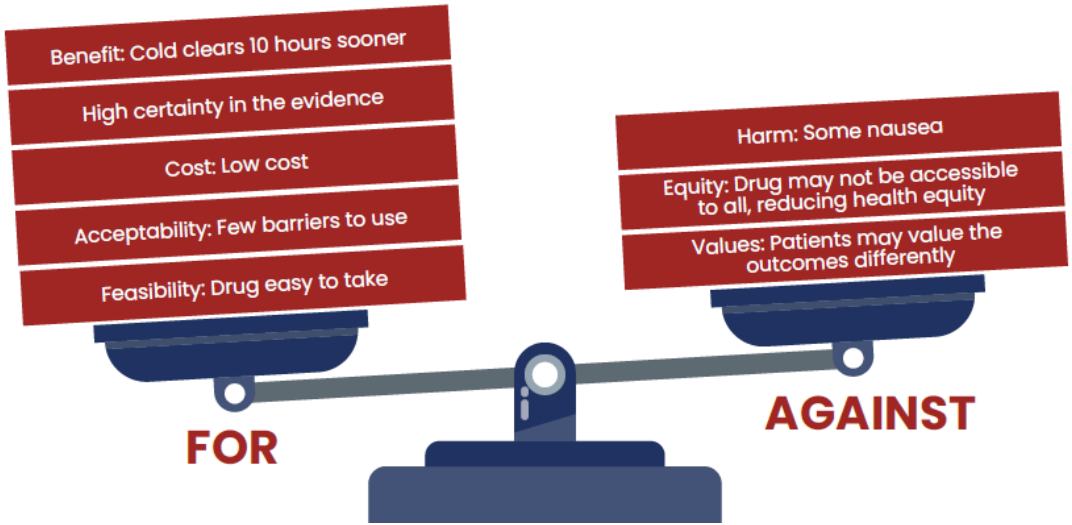
"The guideline group recommends **Drug A** to treat the common cold."

This is a **strong** recommendation **for** the intervention.

Conditional recommendation
Example

There are some factors that favour Drug B, but some factors do not.

In this case, the scale only slightly tips and this is a **conditional** recommendation **for** the option.
Clinicians and their patients will need to consider the conditions for using the option and if it is right for them.



When a recommendation is conditional

- The majority of people will want to follow it but they may want to talk with a healthcare professional first
- The majority of physicians will want to prescribe it but they may want to review all factors first
- Most policymakers will want to adopt it but they may want to review all factors first

Financial contribution:
Public Health Agency of Canada / Agence de la santé publique du Canada

What is certainty of evidence?

Certainty of evidence is also called **quality of evidence.**

Certainty of evidence refers to our confidence that our estimates of the effects are adequate to support the recommendation.

Conditional recommendations are issued when[9]:

The balance between benefits and harms is **small**

There is **low quality of evidence**

Values and preferences of patients **vary**

Most people would want to follow the recommendation, but many would not.

Your healthcare professional should understand that different options will be appropriate for different people and should support you in making decisions that align with your values and preferences.

TESTING RECOMMENDATIONS

Should electrocardiogram (EKG or ECG) be used for people with suspected post COVID-19 condition who have respiratory or cardiac complaints?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests the use of ECG versus not using ECG in adult patients with suspected post COVID-19 condition and cardiopulmonary symptoms (conditional recommendation, very low certainty in the evidence). **Remarks:** The benefits of this test are diagnosing important comorbidities, but not increasing suspicion of post COVID-19 condition or making a diagnosis of post COVID-19 condition.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

✓ conditional

Evidence-to-Decision Table

Intervention

ECG

Problem

High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits

Compared to no ECG

- Small

Harms

Compared to no ECG

- Small

Balance

Probably **favors ECG** vs. no ECG

Value

No important uncertainty or variability in how people value the main outcome

Resources

Negligible costs and savings
Cost: $12–50 CAD
Population size:
it is estimated that 19.6% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 conditions have respiratory and/or cardiac complaints

Cost-effectiveness

No included studies

Acceptability

Yes
Acceptable to payer, patients and practitioners

Feasibility

Yes
ECGs are widely available in small and large medical centers

Equity

Probably increased

Should a Holter monitor be used for people with suspected post COVID-19 condition who have respiratory or cardiac complaints?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests using Holter monitoring versus not using Holter monitoring in adults with suspected post COVID-19 condition and certain cardiopulmonary symptoms (Conditional recommendation, very low certainty in the evidence). **Remarks:** The benefits of this test are diagnosing or ruling out important comorbidities, but not increasing suspicion of post COVID-19 condition or making a diagnosis of post COVID-19 condition. Examples of cardiopulmonary symptoms include chest pain, dyspnea, palpitations, tachycardia or bradycardia that can be sustained or intermittent and of short duration.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

✓ conditional

Evidence-to-Decision Table

Intervention
24-hr Holter

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no Holter
- Small

Harms
Compared to no Holter
- Small

Balance
Probably **favors Holter** vs. no Holter

Value
No important uncertainty or variability in how people value the main outcome

Resources
Large costs
Cost: $100-300 CAD
Population size:
it is estimated that 19.6% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 conditions have respiratory and/or cardiac complaints

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Acceptable to patients, probably acceptable to practitioners and payers

Feasibility
Probably Yes
Holter is generally available and monitors can be shipped to remote areas

Equity
Probably reduced
Increased wait times and difficulty accessing the test depending on resources available and access to care

Should the 10-minute stand test be used for adults with suspected post COVID-19 condition who have dizziness?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests using the 10-minute standing test versus not using the 10-minute standing test in adults with suspected post COVID-19 condition and dizziness (conditional recommendation, very low certainty in the evidence). **Remarks:** The benefits of this test are increasing suspicion of post COVID-19 condition, by potentially diagnosing POTS or other forms of cardiac dysautonomia as a condition often associated with post COVID-19 condition, and diagnosing or ruling out important comorbidities, but not making a diagnosis of post COVID-19 condition.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

✓ conditional

Evidence-to-Decision Table

Intervention
10-minute stand test

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no 10-min stand test
- Moderate

Harms
Compared to 10-min stand test
- Trivial

Balance
Probably **favors 10-min stand test** vs. no 10-min standing test

Value
Possibly no important uncertainty or variability in how people value the main outcome

Resources
Negligible costs and savings
Cost: $0-25.75 CAD
Population size:
it is estimated that 11% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 conditions have dizziness

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Acceptable to patients and payers, probably acceptable to practitioners (requires time of trained personnel)

Feasibility
Varies
Depends on having the appropriate staff and equipment available (e.g., automated blood pressure machine)

Equity
Varies
Members of certain equity-seeking groups may have difficulty accessing clinical visits for evaluation for suspected post COVID-19 condition

Should Troponin (High sensitive Troponin I) be used for adults with suspected post COVID-19 condition who have respiratory or cardiac complaints?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests the use of Troponin I / High-Sensitivity Troponin I tests in adults with suspected post COVID-19 condition and cardiac or pulmonary symptoms (conditional recommendation, very low certainty in the evidence). **Remarks:** The roles of this test include ruling out myocardial infarction, assessing prognosis, since elevated levels are associated with a wide range of patients, and identifying potential causes of cardiopulmonary symptoms. Cardiac or respiratory symptoms may include chest pain, which may also include referred pain to another part of the body such as the neck or shoulders, palpitations and/or shortness of breath (at rest or on exertion).

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

✓ conditional

Evidence-to-Decision Table

Intervention
Troponin

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no Troponin *(per 1000)*:
- Small

Harms
Compared to no Troponin *(per 1000)*:
- Small

Balance
Probably **favors Troponin** vs. no Troponin

Value
Possibly no important uncertainty or variability in how people value the main outcome

Resources
Negligible costs and savings
Cost: $6.75 CAD
Population size: it is estimated that 5-30% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 condition have respiratory and/or cardiac complaints)

Cost-effectiveness
No included studies

Acceptability
Yes
Acceptable to payer, patient and practitioner

Feasibility
Yes
Tests are widely available in small and large medical centers

Equity
Probably no impact
Troponin tests are widely available and easy to access

Should C-reactive protein (CRP) be used for adults with suspected post COVID-19 condition?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests not ordering C-reactive protein in adults with suspected post COVID-19 condition (conditional recommendation, very low certainty of the evidence). **Remarks:** This recommendation does not mean withholding care or diagnostic testing that may be clinically appropriate. For example, this test may be added after other tests are performed (i.e. used as an add-on test) or the test may be performed at the same time as other tests (i.e., parallel test) in a specific subgroup of people with suspected post COVID-19 condition, such as those with symptoms consistent with an autoimmune condition as it might have a prognostic role (Enocsson et al., 2021). Consideration may also be given to testing individuals presenting with symptoms associated with acute pericarditis (Ashram et al., 2022). In both of these clinical scenarios, the test would need to be accompanied by appropriate additional diagnostic tests.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

⊗ conditional

Evidence-to-Decision Table

Intervention
CRP

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no CRP
(per 1000):
- Trivial

Harms
Compared to no CRP
(per 1000):
- Small

Balance
Probably **favors not using CRP** vs. using CRP

Value
Possibly important uncertainty or variability in how people value the main outcome

Resources
Moderate costs
Cost: $9.57 CAD
Population size:
it is estimated that 2.1 million Canadians reported symptoms associated with post COVID-19 conditions

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Acceptable to patients, probably acceptable to health care professionals and payers

Feasibility
Yes
Generally available in small and large medical centers

Equity
Probably reduced
The test itself may be less accessible in remote communities as would potential clinical follow-up and/or investigations

Should questionnaires be used for Post-exertional malaise (PEM)/Post-exertional symptom exacerbation (PESE) screening in adults with suspected post COVID-19 condition?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests the use of questionnaires to screen for post-exertional malaise over not using them in adult patients with suspected post COVID-19 condition (conditional recommendation, very low certainty in the evidence). **Remarks:** The benefits of using a questionnaire, such as the DePaul Symptom Questionnaire-Post-Exertional Malaise (DSQ-PEM) short form, are increasing suspicion of post COVID-19 condition and important manifestations often associated with post COVID-19 condition (i.e., post-exertional malaise/post-exertional symptom exacerbation [PEM/PESE]) but not making a diagnosis of post COVID-19 condition.

Certainty of evidence
⊕◯◯◯ Very low

Recommendation strength
✓ conditional

Evidence-to-Decision Table

Intervention
PEM questionnaire

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no PEM questionnaires
(per 1000):
- Moderate

Harms
Compared to no PEM questionnaires
(per 1000):
- Trivial

Balance
Probably **favors PEM questionnaires** vs. PEM questionnaires

Value
No important uncertainty or variability in how people value the main outcome

Resources
Moderate costs and savings
Cost: time needed to the administer the test
Population size:
it is estimated that 2.1 million Canadians reported symptoms associated with post COVID-19 conditions

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Acceptable for patients but probably acceptable for payers and practitioners (depending on time and expertise)

Feasibility
Yes
Widely available, can be easily done in clinic, and has a negligible cost

Equity
Probably increased
People who are usually not tested as fatigue is attributed to other conditions would now be tested (e.g., people with chronic conditions, pregnant women, frail elderly, people experiencing homelessness or incarceration)

Should tools to assess functional status and quality of life (i.e., Post COVID-19 functional status scale, and EuroQol-5D [EQ-5D]) be used for adults with suspected post COVID-19 condition who have fatigue or dizziness?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests the use of tools (i.e., Post COVID-19 functional status scale, and EuroQol-5D [EQ-5D]) to evaluate adults with suspected post COVID-19 condition and dizziness and/or fatigue (conditional recommendation, very low certainty in the evidence).

Remarks: The role of these tools is to increase suspicion of post COVID-19 condition and important complications often associated with post COVID-19 condition (e.g., myalgic encephalitis/chronic fatigue syndrome) while providing assessments of impact on quality of life and functional status, but not making a diagnosis of post COVID-19 condition.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

✓ conditional

Evidence-to-Decision Table

Intervention
Tools to assess functional status and quality of life

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no tools to assess functional status and quality of life
(per 1000):
- Moderate

Harms
Compared to no tools to assess functional status and quality of life
(per 1000):
- Trivial

Value
No important uncertainty or variability in how people value the main outcome

Resources
Moderate costs
Cost: time needed to the administer the test
Population size:
it is estimated that 75% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 conditions have fatigue

Balance
Probably **favors tools to assess functional status and quality of life** vs. no tools to assess functional status and quality of life

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Acceptable to patients, probably acceptable to payers and healthcare professionals

Feasibility
Varies
Depends on having available time and trained healthcare professionals which may be limited in certain settings

Equity
Probably increased
It could lead to a more standardized approach to estimating impact on quality of life and functional status, and this could improve acknowledgement of patient symptoms

Should chest x-ray be used for adults with suspected post COVID-19 condition who have respiratory or cardiac complaints?

Certainty of evidence
⊕◯◯◯ Very low

Recommendation strength
✓ conditional

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests using chest x-rays in adults with suspected post COVID-19 condition and cardiac or respiratory symptoms (conditional recommendation, very low certainty in the evidence). **Remarks:** This recommendation was supported by data from people who were hospitalized during their acute COVID-19 infection. Based on available evidence, the pre-test probability is likely to be higher in people who were hospitalized during their acute COVID-19 infection. Pre-test probability could not be determined in people who were not hospitalized due to lack of evidence but is assumed to be lower than in people who were hospitalized during their acute COVID-19 infection. The benefits of this test are diagnosing or ruling out important conditions, such as a pneumonia, fibrosis/lung scarring or heart failure but not making a diagnosis of post COVID-19 condition.

Evidence-to-Decision Table

Intervention
Chest X-ray

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no Chest X-ray:
- Small

Harms
Compared to no Chest X-ray:
- Small

Balance
Varies using **Chest Xray** vs. no Chest Xray

Value
Possibly important uncertainty or variability in how people value the main outcome

Resources
Large costs
Cost: $ 230-600 CAD
Population size:
it is estimated that 20% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 conditions have cardiac or respiratory symptoms

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Acceptable to healthcare professionals, probably acceptable to patients and payers

Feasibility
Probably Yes
Usually accessible but can be challenging to obtain for people who have limited mobility

Equity
Probably reduced
Staff to administer and interpret the test may be limited in remote communities. Certain people may not be able to access the test due to mobility issues

Should computed tomography of the chest (CT Chest) be used for adults with suspected post COVID-19 condition who have respiratory complaints (low risk of pulmonary complications)?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests not using non-contrast chest CT scans in adults with suspected post COVID-19 conditions and respiratory symptoms who are at **low risk** of pulmonary complications (conditional recommendation, very low certainty of evidence). **Remarks:** Patients considered to be at low risk for pulmonary complications are those **without any of the following**: current respiratory symptoms, previously identified important abnormalities on chest X-ray or CT chest or pulmonary function tests, patients who were previously hospitalized during the acute phase of their COVID-19 infection, patients with a high clinical suspicion for pulmonary disease. The benefits of this test are diagnosing or ruling out important conditions, such as pulmonary fibrosis/lung scarring, but not making a diagnosis of post COVID-19 condition.

Certainty of evidence
⊕◯◯◯ Very low

Recommendation strength
⊗ conditional

Should computed tomography of the chest (CT Chest) be used for adults with suspected post COVID-19 condition who have respiratory complaints (high risk of pulmonary complications)?

Topic: **Testing, identification and diagnosis related to PCC**

The CAN-PCC Collaborative suggests using non-contrast chest CT scans in adults with suspected post COVID-19 condition and respiratory symptoms who are at **high risk** of pulmonary complications (conditional recommendation, very low certainty of evidence). **Remarks:** Patients considered to be at high risk for pulmonary complications are: 1) patients with current respiratory symptoms and previously identified important abnormalities on chest X-ray or CT chest or pulmonary function tests, OR 2) patients who were previously hospitalized during the acute phase of their COVID-19 infection with a high clinical suspicion for pulmonary disease. The benefits of this test are diagnosing or ruling out important conditions, such as pulmonary fibrosis/lung scarring, but not making a diagnosis of post COVID-19 condition.

Certainty of evidence
⊕◯◯◯ Very low

Recommendation strength
✓ conditional

Evidence-to-Decision Table

Intervention
CT chest

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations

Benefits
Compared to no CT chest *(per 1000)*:
- Varies according to if patients were hospitalized or not

Harms
Compared to no CT chest *(per 1000)*:
- Moderate

Balance
Varies

Value
Possibly important uncertainty or variability in how people value the main outcome

Resources
Large costs
Cost: $ 249-949 CAD
Population size:
it is estimated that 20% of the 2.1 million Canadians reporting symptoms associated with post COVID-19 conditions have respiratory symptoms

Cost-effectiveness
No included studies

Acceptability
Probably Yes
Probably acceptable to patients and healthcare professionals, probably not acceptable to payers

Feasibility
Varies
Depends on comorbidities and mobility of patients, whether they live in a remote community or resource-limited setting

Equity
Probably reduced
Expensive test that is not easily accessible, especially for those with low socioeconomic status, living in remote communities, and/or with mobility issues

CLINICAL INTERVENTION RECOMMENDATIONS

Should activity, movement, or exercise-based interventions be used for adults with confirmed post COVID-19 condition who do not experience post-exertional malaise (PEM) or post-exertional symptom exacerbation (PESE)?

Topic: **Clinical interventions for PCC**

The CAN-PCC Collaborative suggests activity, movement, or exercise-based interventions for adults with confirmed post COVID-19 condition who do not experience post-exertional malaise (PEM)/post-exertional symptom exacerbation (PESE) (conditional recommendation, very low certainty of evidence). **Remarks:** Exercise may be considered rehabilitation but not all rehabilitation involves exercise. Rehabilitation interventions were individually tailored according to patient's dynamic symptoms and energy budget. Screening and monitoring for PEM/PESE is critical as it may be precipitated by participation in some rehabilitation interventions.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

✓ conditional

Should activity, movement, or exercise-based interventions be used for adults with confirmed post COVID-19 condition who experience post-exertional malaise (PEM) or post-exertional symptom exacerbation (PESE)?

Topic: **Clinical interventions for PCC**

The CAN-PCC Collaborative suggests activity, movement, or exercise-based interventions for adults with confirmed post COVID-19 condition who do experience post-exertional malaise (PEM)/post-exertional symptom exacerbation (PESE) in the context of research settings only **(research recommendation)**. **Remarks:** Exercise may be considered rehabilitation but not all rehabilitation involves exercise. Rehabilitation interventions were individually tailored according to patient's dynamic symptoms and energy budget. Screening and monitoring for PEM/PESE is critical as it may be precipitated by participation in some rehabilitation interventions.

Certainty of evidence

⊕◯◯◯ Very low

Evidence-to-Decision Table

Intervention
Exercise (in people without PEM/PESE)

Problem

High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits

Compared to no exercise
(per 1000): ⊕OOO
- Fatigue: 215 fewer
- Physical function: 49.4 m more in 6 min walk test
- Daily functioning: varied results
- Overall: Moderate

Harms

Compared to no exercise
(per 1000):
- Adverse events: 44 fewer ⊕⊕OO
- Overall: Small

Balance

Probably **favors exercise** vs. no exercise

Value

Probably no important uncertainty or variability in how people value the main outcome

Resources

Large costs
Supervised exercises with trained physiotherapist, occupational therapist or kinesiologist

Cost-effectiveness

No included studies

Acceptability

Varies
Patients: risk of PEM/PESE and energy envelope
Providers: time to explain risks
Payers: variable due to costs

Feasibility

Varies
Availability of trained providers for individually tailored therapy varies across Canada

Equity

Varies
May increase for those with resources and ability to access
May be reduced for those with less access, mobility issues, limited resources

Evidence-to-Decision Table

Intervention
Exercise (in people with PEM/PESE)

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits
Compared to no exercise
- Fatigue: 215 fewer
- Physical function: 49.4 m more in 6 min walk test
- Most trials did not include PEM/PESE; self-selection effect
- Overall: Moderate ⊕OOO

Harms
Compared to no exercise
- concerns that trials that did not measure PEM/PESE may not have detected adverse events related to PEM, especially because these events occur 24-48 hours after activity
- Overall: Moderate ⊕OOO

Value
Probably no important uncertainty or variability in how people value the main outcome

Resources
Large costs
Supervised exercises with trained physiotherapist, occupational therapist or kinesiologist

Balance
Does **not favour either** exercise or no exercise

Cost-effectiveness
No included studies

Acceptability
Varies
Patients: risk of PEM/PESE and energy envelope
Providers: time to explain risks
Payers: variable due to costs

Feasibility
Varies
Availability of trained providers for individually tailored therapy varies across Canada

Equity
Varies
May increase for those with resources and ability to access
May be reduced for those with less access, mobility issues, limited resources

Should metformin vs. Paxlovid be used for adults with confirmed post COVID-19 condition who have a new acute COVID-19 infection?

Topic: **Clinical interventions for PCC**

The two interventions were ranked in order of decreasing preference as follows (conditional recommendation; very low certainty in the evidence): (i) metformin; (ii) nirmatrelvir/ritonavir (Paxlovid). **Remarks:** Each drug has an individual conditional recommendation favouring their use, over no treatment. The panel did not have sufficient evidence to evaluate a recommendation on the concurrent use of both drugs. Access the full multiple comparison evidence to decision framework **here**.

Recommendation strength

conditional

Evidence-to-Decision Table

Intervention
Metformin

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits
Compared to no metformin *(per 1000)*: ⊕OOO
- ER visit: 20 fewer
- Hypoxemia (QoL): 11 fewer
- Mortality: 2 fewer
- Overall: Small

Harms
Compared to no metformin *(per 1000)*: ⊕OOO
- All adverse events: 5 more
- Serious adverse events: 4 more
- Considered safe in hospitalized patients
- Overall: Trivial

Balance
Probably **favors metformin** vs. no metformin

Value
Possibly important uncertainty or variability in how people value the main outcome

Resources
Negligible costs and savings
Metformin per person = $1.50 to $1.95

Cost-effectiveness
No included studies

Acceptability
Yes
Approximately 2.8 million people use metformin in Canada

Feasibility
Yes
Metformin is commonly used off-label

Equity
Probably no impact
Widely available and accessible

Evidence-to-Decision Table

Intervention
Paxlovid

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits
Compared to no Paxlovid
(per 1000): ⊕OOO
- Severe adverse events: 23 fewer
- Fatigue: 3 fewer
- Mortality: 5 fewer
- Overall: Small

Harms
Compared to no Paxlovid
(per 1000): ⊕OOO
- Sustained alleviation of all acute "targeted symptoms and signs" at 28 days: 15 fewer
- Overall: Trivial

Balance
Probably **favors paxlovid** vs. no paxlovid

Value
Probably no important uncertainty or variability in how people value the main outcome

Resources
Large costs
The cost of a single five-day treatment course for acute COVID-19 infection with nirmatrelvir/ritonavir in Canada is $1,288.88

Cost-effectiveness
No included studies

Acceptability
Varies

Feasibility
Probably yes

Equity
Varies

Multiple Intervention Comparison

	Metformin		Nirmatrelvir/Ritonavir (Paxlovid)	
BALANCE OF EFFECTS	★★★☆☆		★★★☆☆	
RESOURCES REQUIRED	★★★★☆		★☆☆☆☆	
COST EFFECTIVENESS	☆☆☆☆☆		☆☆☆☆☆	
EQUITY	★★★☆☆		★★☆☆☆	
ACCEPTABILITY	★★★☆☆		★★☆☆☆	
FEASIBILITY	★★★★☆		★★★☆☆	

Should ivabradine, beta-blockers, pyridostigmine, or midodrine in isolation or in combination be used for people with post COVID-19 condition and co-existing cardiac dysautonomia (postural orthostatic tachycardia syndrome [POTS], inappropriate sinus tachycardia [IST])?

Topic: **Clinical interventions for PCC**

In adults with post COVID-19 condition and co-existing cardiac dysautonomia (postural orthostatic tachycardia syndrome [POTS], inappropriate sinus tachycardia [IST]), the CAN-PCC Collaborative suggests using ivabradine, beta-blockers, pyridostigmine or midodrine as appropriate (conditional recommendation; low certainty in the evidence). **Remarks:** The evidence we evaluated was for the different medications in isolation. We did not have evidence for combination therapy. The doses and frequency of administration for the following therapies were assessed in this guideline: Ivabradine: range of 2.5 mg to 10 mg twice daily; Beta blockers: Carvedilol: range of 3.125 mg to 12.5 mg twice daily, Metoprolol 25 mg to 350 mg per day; Pyridostigmine 30 mg or 60 mg per day; Midodrine 10 mg per day. It is important for healthcare providers to identify the predominant sign/symptom of cardiac dysautonomia to help guide their choice of therapy. These include: 1) tachycardia (ivabradine, beta-blockers); and 2) supine hypotension (midodrine, pyridostigmine).

Certainty of evidence

⊕⊕◯◯ Low

Recommendation strength

✓ conditional

Evidence-to-Decision Table

Intervention

Cardiac Dysautonomia Rx

Problem

High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits

Compared to no Cardiac Dysautonomia Rx ⊕⊕OO

- Quality of life: physical (SMD 0.57) & social functioning (SMD 0.48) – moderate improvement
- Overall: Moderate

Harms

Compared to no Cardiac Dysautonomia Rx ⊕⊕OO

- No brachycardia, hypotension, worsening of POTS symptoms
- Slightly more withdrawals due to, fatigue, phosphenes
- Overall: Small

Balance

Probably **favors Cardiac Dysautonomia Rx** vs. no Cardiac Dysautonomia Rx

Value

Possibly important uncertainty or variability in how people value the main outcome

Resources

Varies
Based on costs and prevalence of specific class of drug prescribing; moderate for ivabradine to negligible for beta-blockers

Cost-effectiveness

No included studies

Acceptability

Varies

- People with PCC and POTS may wish to try treatment
- Providers -extra time for discussion
- Payers may find some costs unacceptable

Feasibility

Yes
Cardiac Dysautonomia Rx is available at most pharmacies and can be self-administered

Equity

Varies
May increase equity in those that can access and benefit from them. May reduce equity for those that cannot obtain prescriptions or afford cost

Should antiplatelet drugs be used for adults with post COVID-19 condition?

Topic: **Clinical interventions for PCC**

In adults with post COVID-19 condition who do not have a pre-existing indication for antiplatelet treatment (e.g., myocardial infarction, stroke/transient ischemic attack), the CAN-PCC Collaborative suggests against using antiplatelet therapies (conditional recommendation; very low certainty in the evidence). **Remarks**: The population for this recommendation is adults with post COVID-19 condition overall. In people with post COVID-19 condition who develop recurrent acute COVID-19, especially if they require hospitalization (but have no other indication for antiplatelet therapy), both the desirable (reduction in mortality and thrombotic events) and undesirable (major bleeding) impacts are likely to be more significant due to inherently higher baseline risks. For the type and duration of antiplatelet drugs used in the included studies please see the implementation considerations.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

⊗ conditional

Evidence-to-Decision Table

Intervention
Antiplatelets

Problem
High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits
Compared to no antiplatelets
(per 1000): ⊕OOO
- Mortality: 0 fewer deaths
- Venous thrombotic event: 1-2 fewer
- Arterial thrombotic event: 0 fewer
- Overall: Trivial

Harms
Compared to no antiplatelets
(per 1000): ⊕OOO
- Major bleeding: 2 to 13 more
- Serious adverse events: 3 more
- Any adverse event: little to no difference
- Overall: Small

Balance
Probably **favors no antiplatelets** vs. antiplatelets

Value
Possibly important uncertainty or variability in how people value the main outcome

Resources
Moderate costs
$176 million CAD* for Canada per year (note costs would be expected to be somewhat higher if we include clopidogrel and other newer antiplatelet agents)

Cost-effectiveness
Probably favours the comparison
Harms probably outweigh the benefits of the intervention with a moderate cost

Acceptability
Yes
Widely used for many conditions

Feasibility
Yes
Commonly used oral medications that are self-administered at home

Equity
Varies
Some equity-seeking groups may not be able to obtain prescriptions or afford out of pocket costs

Should low-dose naltrexone (1.5-6 mg) be used for people with post COVID-19 condition?

Topic: **Clinical interventions for PCC**

The CAN-PCC Collaborative suggests not using low-dose naltrexone for people with post COVID-19 condition (conditional recommendation; very low certainty in the evidence). **Remarks:** This recommendation will be re-evaluated in 2026 or earlier if higher certainty evidence for critical outcomes becomes available. Current evidence evaluated the use of low-dose naltrexone at a dose ranging between 1.5-6.0 mg. In light of very limited direct evidence for the potential benefits or harms of low-dose naltrexone among people with post COVID-19 condition, some people with post COVID-19 condition may still decide to trial low-dose naltrexone if they place a relatively higher value on some desirable outcomes and a relatively lower value on the undesirable outcomes (such as adverse effects), especially if they live in a jurisdiction where low-dose naltrexone treatment is feasible.

Certainty of evidence

⊕◯◯◯ Very low

Recommendation strength

⊗ conditional

Evidence-to-Decision Table

Intervention

Low-dose naltrexone

Problem

High priority
based on literature, surveys from key interest groups, web searching, and deliberations.

Benefits

Compared to no low-dose naltrexone ⊕⊕OO

- Little to no difference in health-related quality of life, physical functioning, pain intensity, fatigue
- Overall: Trivial

Harms

Compared to no low-dose naltrexone *(per 1000)*:

- Mortality: 0 fewer ⊕⊕OO
- Adverse events: 21 fewer ⊕OOO
- Overall: Trivial

Balance

Does **not favor either** low-dose naltrexone or no low-dose naltrexone

Value

Possibly important uncertainty or variability in how people value the main outcome

Resources

Moderate costs
Compounding pharmacy required to produce low-dose; coverage mainly out of pocket

Cost-effectiveness

Probably favours no low-dose naltrexone

- No net benefit but costs are moderate

Acceptability

Varies

- Has not been shown to have addictive effects
- Providers may not find acceptable due to lack of benefits and cost

Feasibility

Probably no

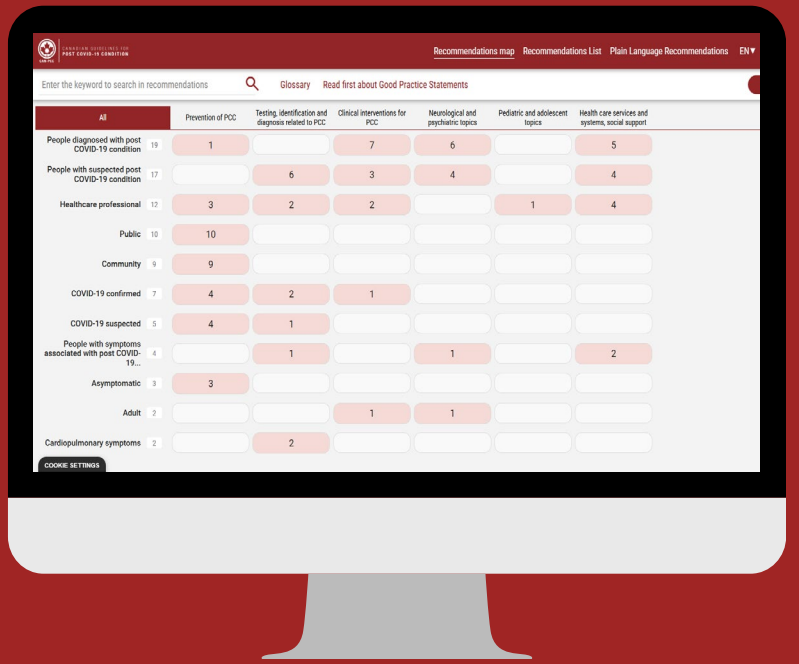
- Considered "off-label" use
- Some provinces do not provide compounding as standard practice

Equity

Probably reduced
Requires access to a prescription and to pharmacies able to provide compounding service

Recommendations Map (RecMap)

Free online tool that allows you to search for CAN-PCC recommendations



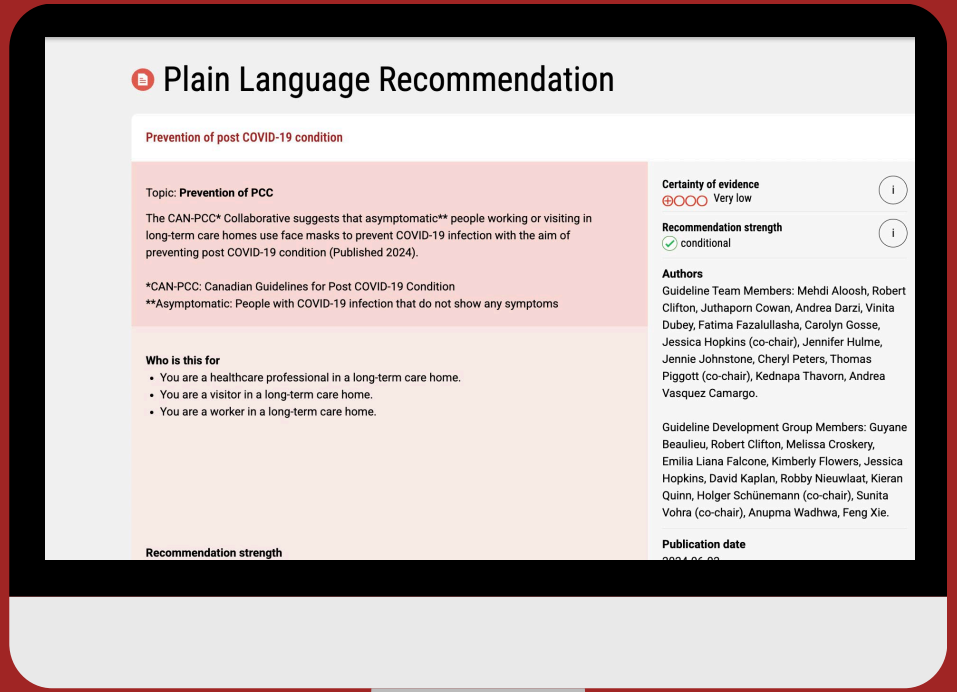
can-pcc.recmap.org

Cochrane Canada | McMaster University | GRADE Centre

Source: canpcc.recmap.org

Plain Language Recommendations

This format summarizes a recommendation and key supporting information in a user-friendly one-page view.



can-pcc.recmap.org

Source: canpcc.recmap.org

Resources for Patients

canpcc.ca/resources

MyGuide | longcovidguide.ca:
Customizable online self-management tool

Interactive infographics and online resource sheets:
Digital, user-friendly graphics summarizing the recommendations

Webinars:
Webinar recordings, slides, transcripts, are available.

Resources for Patients

Testing, Identification, Diagnosis

Online Resource Sheets

Cochrane Canada | McMaster University | GRADE Centre

CANADIAN GUIDELINES FOR POST COVID-19 CONDITION

Last Updated: 17-MAR-2025

GUIDELINE TOPIC:

Testing, Identification, and Diagnosis related to Post COVID-19 Condition

(also known as long COVID)

Do you suspect that you or a loved one has post COVID-19 condition?

Post COVID-19 condition (PCC) usually appears within three months from an acute COVID-19 infection and lasts at least two months. Symptoms (e.g., brain fog, fatigue, shortness of breath, pain) vary, can change or worsen over time, and significantly impact daily life, according to the **World Health Organization**.

If you suspect that you or a loved one has PCC, talk to a healthcare provider for more guidance.

On the right are some recommendations that you can discuss with a healthcare provider to support symptom identification and diagnosis.

Who made these recommendations?

These recommendations were made by **CAN-PCC committee members** from coast to coast to coast in Canada. Members included researchers, persons with lived PCC experiences, healthcare providers, and health economists.

How were these recommendations made?

These recommendations were made by carefully reviewing the scientific evidence and following a systematic **guideline development process**.

How strong are these recommendations?

A recommendation can be **strong or conditional**.

When a recommendation is strong, people will want to follow it. When a recommendation is conditional, the majority of people will want to follow it, but they may want to talk with a healthcare provider first. To learn more about the strength of recommendations and what it means for you, click **here**.

What is certainty of evidence?

Certainty of evidence is about how confident we are that the result from the review of the evidence comes close to the truth. To learn more about certainty of evidence, click **here**.

Adults with suspected PCC may want to talk to their healthcare provider about:

Some suggested ways that can help increase suspicion for PCC and guide management:

- 10-minute standing test[1]
  - adults who feel dizzy may want to talk to a healthcare provider about taking this test in a clinic.
- Screening questionnaires[2]
  - adults whose symptoms worsen after doing physical, mental, emotional, or social activities may want to talk to a healthcare provider about completing a questionnaire to screen for PEM/PESE*.

Some suggested tests that can help identify other conditions and guide management:

Adults with heart and/or lung symptoms may want to talk to a healthcare provider about taking these tests to check for irregularities:

- EKG/ECG*[3]
- Holter monitor[4]
- BNP/NT-proBNP* blood tests[5]
- Troponin blood tests[6]

Heart or lung symptoms may include shortness of breath, chest pain, and a feeling as if your heart is racing, pounding, or fluttering.

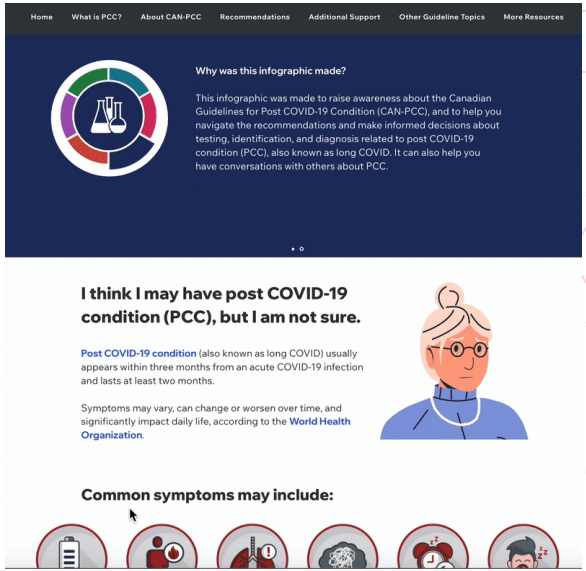
*PEM: Post-exertional malaise; PESE: Post-exertional symptom exacerbation; EKG/ECG: Electrocardiograms; BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro b-type natriuretic peptide

All numbered recommendations (1-6) are **conditional** and based on **low to very low certainty of evidence**. This does not mean that we should not do what is recommended but that the certainty of evidence may change as more research is done.

To learn more about the 18 recommendations and 3 good practice statements on testing, identification, and diagnosis related to PCC, please visit canpcc.ca

Financial contributor: Public Health Agency of Canada | Agence de la santé publique du Canada

Interactive infographics



Home | What is PCC? | About CAN-PCC | Recommendations | Additional Support | Other Guideline Topics | More Resources

Why was this infographic made?

This infographic was made to raise awareness about the Canadian Guidelines for Post COVID-19 Condition (CAN-PCC), and to help you navigate the recommendations and make informed decisions about testing, identification, and diagnosis related to post COVID-19 condition (PCC), also known as long COVID. It can also help you have conversations with others about PCC.

I think I may have post COVID-19 condition (PCC), but I am not sure.

Post COVID-19 condition (also known as long COVID) usually appears within three months from an acute COVID-19 infection and lasts at least two months.

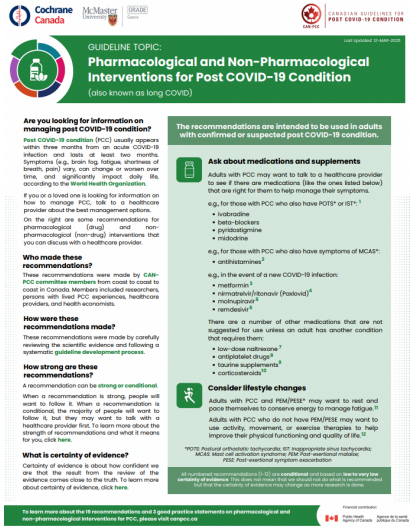
Symptoms may vary, can change or worsen over time, and significantly impact daily life, according to the **World Health Organization**.

Common symptoms may include:

Resources for Patients

Clinical Interventions

Online Resource Sheets



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GUIDELINE TOPIC:

Pharmacological and Non-Pharmacological Interventions for Post COVID-19 Condition

(also known as long COVID)

Last updated: 12-MAR-2025

Are you looking for information on managing post COVID-19 condition?

Post COVID-19 condition (PCC) usually appears within three months from an acute COVID-19 infection and lasts at least two months. Symptoms (e.g., brain fog, fatigue, shortness of breath, pain) vary, can change or worsen over time, and significantly impact daily life, according to the **World Health Organization**.

If you or a loved one is looking for information on how to manage PCC, talk to a healthcare provider about the best management options.

On the right are some recommendations for pharmacological (drug) and non-pharmacological (non-drug) interventions that you can discuss with a healthcare provider.

Who made these recommendations?

These recommendations were made by **CAN-PCC committee members** from coast to coast to coast in Canada. Members included researchers, persons with lived PCC experiences, healthcare providers, and health economists.

How were these recommendations made?

These recommendations were made by carefully reviewing the scientific evidence and following a systematic **guideline development process**.

How strong are these recommendations?

A recommendation can be **strong or conditional**.

When a recommendation is strong, people will want to follow it. When a recommendation is conditional, the majority of people will want to follow it, but they may want to talk with a healthcare provider first. To learn more about the strength of recommendations and what it means for you, click **here**.

What is certainty of evidence?

Certainty of evidence is about how confident we are that the result from the review of the evidence comes close to the truth. To learn more about certainty of evidence, click **here**.

The recommendations are intended to be used in adults with confirmed or suspected post COVID-19 condition.

Ask about medications and supplements

Adults with PCC may want to talk to a healthcare provider to see if there are medications (like the ones listed below) that are right for them to help manage their symptoms.

e.g., for those with PCC who also have POTS* or IST*:[1]
- Ivabradine
- beta-blockers
- pyridostigmine
- midodrine

e.g., for those with PCC who also have symptoms of MCAS*:
- antihistamines[2]

e.g., in the event of a new COVID-19 infection:
- metformin[3]
- nirmatrelvir/ritonavir (Paxlovid)[4]
- molnupiravir[5]
- remdesivir[6]

There are a number of other medications that are not suggested for use unless an adult has another condition that requires them:
- low-dose naltrexone[7]
- antiplatelet drugs[8]
- taurine supplements[9]
- corticosteroids[10]

Consider lifestyle changes

Adults with PCC and PEM/PESE* may want to rest and pace themselves to conserve energy to manage fatigue.[11]

Adults with PCC who do not have PEM/PESE may want to use activity, movement, or exercise therapies to help improve their physical functioning and quality of life.[12]

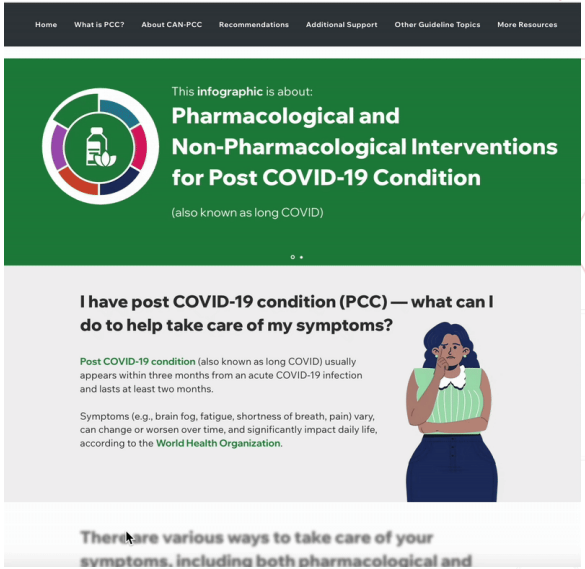
*POTS: Postural orthostatic tachycardia; IST: Inappropriate sinus tachycardia; MCAS: Mast cell activation syndrome; PEM: Post-exertional malaise; PESE: Post-exertional symptom exacerbation

All numbered recommendations (1–12) are **conditional** and based on **low to very low certainty of evidence**. This does not mean that we should not do what is recommended but that the certainty of evidence may change as more research is done.

To learn more about the 19 recommendations and 3 good practice statements on pharmacological and non-pharmacological interventions for PCC, please visit canpcc.ca

Financial contribution: Public Health Agency of Canada / Agence de la santé publique du Canada

Interactive infographics



Home | What is PCC? | About CAN-PCC | Recommendations | Additional Support | Other Guideline Topics | More Resources

This **infographic** is about:

Pharmacological and Non-Pharmacological Interventions for Post COVID-19 Condition

(also known as long COVID)

I have post COVID-19 condition (PCC) — what can I do to help take care of my symptoms?

Post COVID-19 condition (also known as long COVID) usually appears within three months from an acute COVID-19 infection and lasts at least two months.

Symptoms (e.g., brain fog, fatigue, shortness of breath, pain) vary, can change or worsen over time, and significantly impact daily life, according to the **World Health Organization**.

There are various ways to take care of your symptoms, including both pharmacological and

Resources for Health Professionals

canpcc.ca/resources

CME Accredited Webinars

Webinar recordings, slides, transcripts, are available.

Online CPD Course:

A free bilingual 2-hour course covering PCC diagnosis, referral, and management strategies.

EBM Connect Canada | ccirhken.ca/ebm-connect-canada:

A training program for internationally trained health professionals covering evidence-based medicine and PCC.

Acknowledgements

- CAN-PCC Collaborative and groups
- Members of the public
- Health organizations
- CCMOH/FPT
- PHAC PCC Secretariat

Thank you to those who have provided valuable input throughout the project!

Visit us online!

canpcc.ca

Source: canpcc.ca

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