

This management support tool is intended primarily for front-line physicians, pharmacists and nurses. However, it is also intended as a source of information for other front-line professionals. It is provided for information purposes only and should not replace the judgment of the clinician who performs activities reserved under a statute or regulation. The contents are based on a systematic review of the clinical practice guidelines available when it was being developed and is supported by the knowledge and experience of Québec experts who contributed to its development. This tool is intended to complement other INESSS publications. For further details, go to inesss.qc.ca/COVID-19.

POST-COVID-19 CONDITIONS

For the purposes of this tool, post-COVID-19 conditions refer to the health of an individual who meets the following 3 conditions:

- ▶ Initial infection confirmed (nucleic acid amplification test or serology) or plausible (epidemiological link);
- ▶ Presence of signs and symptoms beyond 4 weeks after the initial infection;
- ▶ Persistence of signs and symptoms that cannot be explained by another condition and that were not present before the infection.

GENERAL INFORMATION

- ▶ **Signs and symptoms** may be present regardless of the severity of the initial infection¹:
 - They can occur in children, adolescents and adults.
- ▶ **Clinical presentation is variable:**
 - Persistence of certain signs and symptoms present during the acute phase of the infection with or without the onset of new symptoms (e.g., postexertional malaise and mental fog);
 - Onset of signs and symptoms after a period of remission following the acute infection or following an asymptomatic infection.
- ▶ **The prevalence of signs and symptoms** of a post-COVID-19 condition varies between studies according to the severity of the initial infection, the participants' characteristics and the length of follow-up. According to studies, the proportion of individuals with at least 1 sign or symptom at least 4 weeks after infection was:
 - 13% to 41% in nonhospitalized persons;
 - 25% to 89% in hospitalized patients or patients admitted to intensive care.
- ▶ **Recovery** varies from person to person. There is limited experience and few available data, but it appears that:
 - Gradual improvement in health is observed in many persons up to 12 weeks after infection;
 - When symptoms persist beyond 12 weeks, subsequent improvement tends to be much slower. The long-term prognosis for these persons has not been clearly determined.

1. According to the World Health Organization classification: asymptomatic infection, mild disease (signs and symptoms with no signs of viral pneumonia or hypoxia), moderate disease (pneumonia), severe disease (severe pneumonia), critical disease (acute respiratory distress syndrome, sepsis, septic shock, acute thrombosis, or multisystemic inflammatory syndrome in children).

UNCERTAINTIES

INESSS remains on the lookout for new data and will update this tool accordingly.

Scientific evidence	Epidemiology	Etiology	Diagnosis	Risk factors
The currently available scientific data are limited and of low methodological quality.	A number of epidemiological aspects are still uncertain. There is little long-term data on the evolution of signs and symptoms.	The etiology of the signs and symptoms is still unknown, and could involve various mechanisms of action.	There are no recognized diagnostic criteria and no validated specific management.	No risk factors for developing a post-COVID-19 condition have been confirmed. Advanced age, female sex, comorbidities, severe initial infection and hospitalization have been suggested among others.

SIGNS AND SYMPTOMS

- ▶ **There are no signs or symptoms specific to post-COVID-19 conditions.**
- ▶ Signs and symptoms:
 - Are varied and can affect more than one system;
 - Can be constant or transient, vary in severity and change over time.

Signs and symptoms of post-COVID-19 conditions (list not exhaustive)

Cardiopulmonary

- Arrhythmia, palpitations, tachycardia
- Chest tightness or pain
- **Dyspnea***, cough
- Orthostatic intolerance

Dermatologic

- Hair loss
- Skin rash

Gastrointestinal

- Abdominal pain
- Decrease in or loss of appetite
- Nausea, diarrhea

General

- Fever
- **Postexertional malaise***
- **Sustained, disabling fatigue***

Musculoskeletal

- Muscle, tendon or joint pain

Neurological

- Delirium (elderly individuals)
- Memory or concentration problems
- Mental fog, headache
- Paresthesia, burning sensation
- Symptoms of sleep disorders

Otorhinolaryngologic

- Dizziness, odynophagia, tinnitus
- Taste or smell disturbances
- Sore throat or earache

Psychological

- Anxious or depressive symptoms
- Symptoms of posttraumatic stress disorder

*The most common signs and symptoms.

Mental fog: The subjective perception of not being able to think as clearly as usual.

Postexertional malaise: A worsening of signs and symptoms that occurs after effort, whether physical, mental or emotional. It usually occurs within 12 to 72 hours after the activity and can last for days or weeks.

MANAGEMENT

ASSESSMENT OF THE HEALTH CONDITION

OBJECTIVES

- To determine if the condition might be due to:
 - Complications or sequelae of the acute phase of COVID-19;
 - An exacerbation or worsening of an existing comorbidity.
- To rule out conditions unrelated to COVID-19.

⚠ **There are no recognized diagnostic criteria for post-COVID-19 conditions.**

GENERAL CONSIDERATIONS

- Exercise empathetic listening while the person expresses their concerns and worries.

SIGNS AND SYMPTOMS

- ▶ Document the signs and symptoms (onset, evolution and duration).
- ▶ Document their impact on the person's quality of life, psychological status and overall functioning.

⚠ **Individuals who have had an asymptomatic infection can develop post-COVID-19 conditions.**

The symptoms can affect more than one system, fluctuate over time, be different from those of the acute phase or be rare.

HEALTH HISTORY

- ▶ Document the COVID-19 episode in order to assess the presence of sequelae or complications associated with the acute phase.
 - Dates, signs and symptoms, severity, examinations performed, treatments provided, and rehabilitation performed in hospital.
- ▶ Inquire about the person's:
 - History and comorbidities (relating to physical and mental health) to determine if there is a worsening or exacerbation.
 - Medication history to determine if drugs might be having an effect on the signs and symptoms.
 - Personal situation (e.g., financial losses, worries about their health or that of a family member) to assess the psychosocial risks.

EXAMINATIONS

- ▶ Examinations should be chosen according to:
 - Signs and symptoms;
 - Health history.
 - ▶ Examinations to be considered:
 - Complete physical exam, including:
 - Weight and any recent changes in weight;
 - Temperature;
 - Heart rate and blood pressure in the supine and then upright positions;
 - Respiration;
 - Resting and exercise pulse oximetry if any dyspnea or tachypnea.
 - Mental status examination.
- ▶ A number of conditions and syndromes that are not mutually exclusive have been described in the context of post-COVID-19 conditions. There are currently no scientific data that permit determining if these conditions or syndromes are consequences of the SARS-CoV-2 virus, sequelae of prolonged hospitalization, or those of a health condition unrelated to COVID-19. The following list is subject to change as knowledge evolves and should be used as one tool among others to guide questions and examinations.

⚠ No scale has been validated for measuring the signs and symptoms of post-COVID-19 conditions.

The interpretation of the results of mental health problem screening tools may be distorted by the physical effects of post-COVID-19 conditions.

Categories	Conditions and syndromes to be considered
Cardiovascular	• Myocarditis, heart failure, pericarditis, orthostatic hypotension, POTS
Dermatology	• Alopecia, vasomotor disorders
Hematology	• Pulmonary embolism, arterial thrombosis, venous thromboembolism, other hypercoagulability
Mental and behavioural disorders	• Depression, anxiety disorders, posttraumatic stress disorder, psychosis
Neurology	• Transient ischemic attacks, cognitive impairments, memory problems, neuropathies, cerebellar problems, sleep disorders
Otorhinolaryngology	• Smell and taste disturbances, phantosmia, parosmia, tinnitus, hypoacusis, hearing loss
Respiratory	• Interstitial pneumopathy, hyperventilation syndrome, bronchial hyperresponsiveness
Renal	• Renal failure
Rheumatology	• Reactive arthritis, fibromyalgia, connective tissue disease
Others	• Progression of comorbidities, allergies, anorexia, undernutrition, malnutrition, vitamin D deficiency, diabetes, hypothyroidism, dysautonomia disorders, mastocyte activation syndrome, reactivation of other viruses, digestive disorders, urological disorders, sexual dysfunction, pain syndromes, functional problems, effort deconditioning

Orthostatic hypotension:

Excessive decrease in blood pressure in the standing position.

- A decrease > 20 mm Hg in systolic blood pressure or > 10 mm Hg in diastolic blood pressure.
- Occurs within 3 minutes of going from the supine position to the standing position.

Postural orthostatic tachycardia syndrome (POTS):

- Increase in pulse ≥ 30 /minute in adults or ≥ 40 /minute in individuals under 19 years of age.
- Occurs within 10 minutes of going from the supine position to the standing position.
- Presence of signs and symptoms in the standing position that improve when the person returns to the supine position (dizziness, palpitations, tremor or atypical chest discomfort).
- No orthostatic hypotension.

TESTS AND INVESTIGATIONS

- ▶ The tests and investigations should be chosen on the basis of:
 - Signs and symptoms;
 - Health history;
 - Findings of the physical examination;
 - Other suspected conditions.
- ▶ Depending on the clinical picture, one might consider not ordering tests and investigations during post-infection weeks 4 to 12 since signs and symptoms may improve.

There are no specific tests or investigations for post-COVID-19 conditions, and no standard workup has yet been defined.

The results of the tests and investigations are mainly used to rule out associated complications. It appears that these results are often normal in the context of post-COVID-19 conditions.

The detection of antibodies against SARS-CoV-2 is not very informative, especially because a negative result does not rule out exposure to the virus.

 **AVOID OVERINVESTIGATING**

Tests and investigations to be considered

CHOOSE ON THE BASIS OF THE CLINICAL PICTURE

CATEGORIES	TESTS
Basic tests	
Hemogram, electrolytes and renal function	<ul style="list-style-type: none"> • CBC • Electrolytes (Na, K, Mg, Ca) • Creatinine • Urinalysis
Liver function	<ul style="list-style-type: none"> • ALT • Alkaline phosphatase • Total bilirubin
Inflammatory marker	<ul style="list-style-type: none"> • CRP • Ferritin
Thyroid function	<ul style="list-style-type: none"> • TSH
Diabetes	<ul style="list-style-type: none"> • Fasting blood glucose • HbA1c (at least 3 months after the initial infection)
Existing comorbidities	<ul style="list-style-type: none"> • Any test that can be used to check the stability of the comorbidities
Specialized tests	
Coagulation disorder	<ul style="list-style-type: none"> • D-dimer • Fibrinogen
Myocardial injury	<ul style="list-style-type: none"> • Troponin
Differentiate symptoms of cardiac versus pulmonary origin	<ul style="list-style-type: none"> • NT-pro-BNP
Viral infection if included in the initial differential diagnosis	<ul style="list-style-type: none"> • EBV • CMV • HIV
Rheumatological conditions	<ul style="list-style-type: none"> • Antinuclear antibodies • Rheumatoid factor • Anti-CCP • Anticardiolipin • CK
Investigations	
Respiratory system	<ul style="list-style-type: none"> • Chest x-ray if: <ul style="list-style-type: none"> • Pneumonia is suspected • Overload during the acute phase (in this case, to be done 12 weeks after infection)
Cardiovascular system	<ul style="list-style-type: none"> • ECG (12-lead) if symptoms of cardiac involvement • Echocardiography if elevated NT-pro-BNP, a picture of overload and pericarditis during the acute phase

ALT: alanine aminotransferase; anti-CCP: anti-cyclic citrullinated peptides; CBC: complete blood count; CK: creatine kinase; CMV: cytomegalovirus; CRP: C-reactive protein; EBV: Epstein-Barr virus; ECG: electrocardiogram; HbA1c: glycated hemoglobin; HIV: human immunodeficiency virus; NT-pro-BNP: N-terminal fraction of B-type natriuretic peptide; TSH: thyroid-stimulating hormone.

THERAPEUTIC MANAGEMENT

OBJECTIVES

- To eliminate the signs and symptoms or reduce their frequency and severity.
- To support optimal self-management and a safe return to activities.
- To refer the person to specialized resources, if necessary.

GENERAL CONSIDERATIONS

- Establish a care plan in partnership with the person via a shared decision-making process.
- Keep abreast of the progress in knowledge regarding post-COVID-19 conditions.
- Assess the resumption of daily activities on a case-by-case basis (e.g., return to school or work).
- Draw on interdisciplinary collaboration.
- Self-management is a complementary intervention to others and requires a certain amount of supervision in order to be optimal.

⚠ There is no specific treatment for post-COVID-19 conditions.

Management should be pragmatic, symptomatic and individualized.

Certain delays in accessing specialized care and services can complicate the person's therapeutic management.

MEDICAL MANAGEMENT

- ▶ Treat signs and symptoms according to standard practice.
- ▶ Optimize management of any comorbidities and treat complications according to standard practice.
- ▶ Consider self-monitoring based on signs and symptoms (e.g., blood pressure, pulse oximetry).
- ▶ Reassess appropriateness of any pharmacological treatments that might be having an effect on the signs and symptoms, and adjust dosage as needed.
- ▶ Consider referring the person to a medical specialist or a nearby post-COVID-19 service*, if available:
 - If the acute infection occurred ≥ 12 weeks ago and the person's health is not improving or is deteriorating;
 - If the person has a condition that suggests an abnormality or a persistent neurological, cardiovascular or pulmonary problem.

⚠ The usual emergency criteria prevail.

**Services are expanding and the criteria in place for access may vary according to the location and any ongoing research projects at the site.*

FUNCTIONAL RECOVERY

- ▶ Offer counselling tailored to the person's needs and abilities in order to support resuming their activities (e.g., mobility and technical aids).
 - ⚠ Resuming activities too quickly could pose a risk of relapse.
- ▶ Adjust management if postexertional malaise:
 - Avoid evaluations that could trigger or exacerbate signs and symptoms (e.g., walking test);
 - Do not encourage resuming activities for the purpose of increasing exercise endurance.
- ▶ Do not prescribe fixed or standardized physical exercise programs.
- ▶ Consider referring the person to rehabilitation services if they have:
 - Difficulty managing their energy or their pain that is causing a significant functional disability;
 - Significant, persistent respiratory impairment;
 - Severe cognitive, cardiac, neurological or musculoskeletal involvement;
 - Post-intensive care syndrome.

SOCIAL AND PSYCHOLOGICAL SUPPORT

- ▶ Treat signs and symptoms related to mental status according to standard practice.
- ▶ Provide support for social and psychological impact of post-COVID-19 conditions (e.g., inability to look after children, loss of employment, inability to return to school or work, and feelings of distress or isolation).
- ▶ Consider referring the person to support and evaluation services according to standard practice and the organization of services (e.g., a CLSC's general social services, community organizations, and mental health entry points).

SELF-MANAGEMENT OF SIGNS AND SYMPTOMS

- ▶ Ask the person to record their signs and symptoms (onset, deterioration and resolution) in order to identify triggers and exacerbators.
- ▶ Stress a healthy lifestyle (e.g., rest, nutrition).
- ▶ Ask the person to resume their activities according to their abilities and the effort thresholds that trigger their signs and symptoms.
- ▶ Instruct persons with postexertional malaise on how to manage their energy by balancing their activity periods and rest periods. These individuals should:
 - Identify the thresholds of physical, cognitive and emotional effort that trigger their signs and symptoms;
 - Adjust the intensity of their activities and plan their activity and rest periods so as to not exceed the identified effort thresholds;
 - Increase their activities cautiously and gradually, even if they are feeling well, to avoid relapses.
- ⚠ Inform them that optimal energy management may take some time to learn.
- ▶ Explain to the person how to alleviate their signs and symptoms (e.g., pharmacological treatment).
- ▶ Set incremental and realistic goals.
- ▶ Provide instructions for self-monitoring, if necessary (e.g., blood pressure, pulse oximetry).

FOLLOW-UP

- ▶ Decide with the person on the follow-up to be done: method (by telephone or in-person), frequency (every 3 months at the longest), professionals involved.
- ▶ Maintain standard follow-up for comorbidities.
- ▶ During follow-up:
 - Assess evolution of the person's signs and symptoms;
 - Repeat tests and investigations as needed;
 - Reassess the possible causes;
 - Monitor the care plan, including self-management.

MAIN REFERENCES

Centers for Disease Control and Prevention (CDC). Evaluating and Caring for Patients with Post-COVID Conditions: Interim Guidance. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-index.html>.

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For details on the process used to develop this management support tool for post-COVID-19 conditions and the stakeholders consulted, as well as for the complete references, see the supporting project report, which will be published in the summer of 2021.