EDCOVID-19 QUICK RESPONSE Report

Newfoundland & Labrador Centre for Applied Health Research

Medium-term and Long-term Health Impacts of COVID-19 on Infection Survivors

Disclaimer:

This *Quick Response Report* was published on September 23, 2020. Given the rapidly changing nature of the coronavirus pandemic, some of the references included in this report may quickly become out-of-date. We further caution readers that researchers at the Newfoundland & Labrador Centre for Applied Health Research are not experts on infectious diseases and are relaying work produced by others. This report has been produced quickly and it is not exhaustive, nor have the included studies been critically appraised.

Readers will note that some text below has been highlighted for emphasis.

Original Inquiry

What are the medium-term and long-term health impacts of COVID-19 on infection survivors?

Summary of Findings

- For the purposes of this *Quick Response Report*, we have included sources that discuss any health impacts that persist or emerge after the initial COVID-19 incubation and presentation phases.
- The available evidence indicates that COVID-19 is likely to have medium/long-term health impacts through prolonged disease progression as well as complications and sequelae (i.e., conditions which are the consequence of a previous disease or injury).
- Medium/long-term health impacts are multi-system and may involve the lungs, cardiovascular system, central and peripheral neurological systems, kidneys, eyes, and immune system.
- Survivors are also predicted to be at increased risk for anxiety, depression, and other mental health comorbidities.
- The pandemic is still relatively new and definitive research-based evidence is scant. Readers are encouraged to follow the progress of a large CIHR-funded research project in Canada tracking the physical, mental and psychosocial outcomes of COVID-19 Survivors (see Palepu et al. under Primary Research).

Guidance from Health Authorities

Centres for Disease Control. Symptom Duration and Risk Factors for Delayed Return to Usual Health among Outpatients with COVID-19 in a Multistate Health Care Systems Network — United States, March–June 2020. July 31, 2020. LINK

• "In a multistate telephone survey of symptomatic adults who had a positive outpatient test result for SARS-CoV-2 infection, 35% had not returned to their usual state of health when interviewed



COVID-19 *Quick Response Reports* Evidence for the Newfoundland & Labrador Health System Newfoundland and Labrador Centre for Applied Health Research September 23, 2020 | page 1 2–3 weeks after testing. Among persons aged 18–34 years with no chronic medical conditions, one in five had not returned to their usual state of health."

• "COVID-19 can result in prolonged illness, even among young adults without underlying chronic medical conditions. Effective public health messaging targeting these groups is warranted."

Public Health Ontario. Long-Term Sequelae and COVID-19 – What We Know So Far. September 10, 2020. LINK

- At this stage of the COVID-19 pandemic, there are few peer-reviewed studies examining the occurrence or prevalence of long-term sequelae associated with COVID-19.
 - There is some evidence that olfactory dysfunction (e.g., dysosmia) and gustatory dysfunction (e.g., dysgeusia) are relatively common long-term sequelae associated with COVID-19 infection.
 - Multisystem inflammatory syndrome in children (MIS-C) has been associated with SARS-CoV-2 infection in several studies. MIS-C may have long-term sequelae.
- Cardiovascular, pulmonary and other neurological sequelae may be expected based on the pathophysiology of COVID-19 or what is known regarding other infectious diseases.
- Additional longer-term sequelae that may be anticipated, based on knowledge of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), include anxiety, cardiovascular system abnormalities, depression, glucose metabolism disorders, hyperlipidemia, lipid metabolism dysregulation, post-traumatic stress disorder and reduced lung capacity.

Alberta Health Services. **COVID-19 Scientific Advisory Group Rehabilitation Needs Rapid Evidence Report**. May 19, 2020. <u>LINK</u>

- "The rehabilitation needs of COVID-19 patients are potentially extensive and encompass physical, respiratory, cognitive, and psychological needs."
- "The immediate focus is often on the respiratory rehabilitation needs of COVID-19 patients. However, guidance, recommendations and expert opinion expressed in the available sources indicate that COVID-19 patients experience a significant non-respiratory burden requiring rehabilitation needs to be recognized and screened for during the hospital admission in both the ICU and non-ICU settings."

International Society on Thrombosis and Haemostasis. **COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up.** June, 2020. <u>LINK</u>

- "COVID-19 may predispose patients to arterial and venous thrombosis. Initial series suggest the common occurrence of venous thromboembolic disease in patients with severe COVID-19. The optimal preventive strategy warrants further investigation."
- "The majority of [consensus group] panel members consider prophylactic anticoagulation, although a minority consider intermediate-dose or therapeutic dose to be reasonable."

Related:

- Oudkerk et al. Diagnosis, Prevention, and Treatment of Thromboembolic Complications in COVID-19: Report of the National Institute for Public Health of the Netherlands. April 23, 2020. LINK
 - "This report summarizes evidence for thromboembolic disease, potential diagnostic and preventive actions as well as recommendations for patients with COVID-19 infection."
- MedPage Today. COVID-19: Anticoagulation Recommended Even After Discharge. April 30, 2020. LINK



Systematic Reviews

Taherifard & Taherifard. **Neurological complications of COVID-19: a systematic review**. Neurological Research, July 23, 2020. LINK

 "The 22 records included for analysis provided 57 patients with neurological sequelae. The neurological complications reported ranged widely from ischemic cerebrovascular accidents to cerebral hemorrhage and were seen at both peripheral and central nervous system levels. The most frequently reported neurological complication was acute ischemic cerebrovascular accident, followed by Guillain–Barré syndrome."

Other Reviews

Ojo et al. **Pulmonary Fibrosis in COVID-19 Survivors: Predictive Factors and Risk Reduction Strategies**. Pulmonary Medicine, August 10, 2020. <u>LINK</u>

• "We conclude that, from the available literature, the predictors of pulmonary fibrosis in COVID-19 infection are advanced age, illness severity, length of ICU stay and mechanical ventilation, smoking and chronic alcoholism."

Sher. **The impact of the COVID-19 pandemic on suicide rates**. Quarterly Journal of Medicine, June 30, 2020. <u>LINK</u>

• "Multiple lines of evidence indicate that the COVID-19 pandemic has profound psychological and social effects... In this article, I suggest that the COVID-19 pandemic may increase the prevalence of psychiatric disorders and suicide rates during and after the pandemic."

Tng et al. **Psychological sequelae within different populations during the COVID-19 pandemic: a rapid review of extant evidence**. Singapore Medical Journal, June 30, 2020. <u>LINK</u>

• "The most common psychological responses across these subpopulations were anxiety (overall range 24.8%–49.5%), depression (overall range 18.6%–42.6%) and traumatic stress symptoms (overall range 12.7%–31.6%). Healthcare workers and those with pre-existing physical and mental illnesses were more severely affected."

Fiani et al. **A Contemporary Review of Neurological Sequelae of COVID-19**. Frontiers in Neurology, June 23, 2020. LINK

• "The authors then discuss the peripheral nervous system sequelae and COVID's impact on causing chemosensory dysfunction starting with viral attack on olfactory sensory neurons and cells types within the lining of the nose."

Iba et al. Coagulopathy in COVID-19. Journal of Thrombosis and Haemostasis, June 18, 2020. LINK

• "The information about coagulopathy in COVID-19 is still evolving; however, evidence shows that thrombotic coagulation disorder is quite common in severe cases... Compared with the high incidence of thrombotic events, bleeding complication is considerably rare in COVID-19, and therefore, standard anticoagulant therapy can strongly be recommended."

Langer et al. **Coagulopathy in COVID-19 and Its Implication for Safe and Efficacious Thromboprophylaxis**. Hamostaseologie, June 4, 2020. <u>LINK</u>

• "While the risk of venous thromboembolism (VTE) appears to be higher in patients requiring intensive care unit support compared to those admitted to general wards, recent autopsy



findings and data on the timing of VTE diagnosis relative to hospitalization clearly suggest that thromboembolic events also contribute to morbidity and mortality in the ambulatory setting."

Lopez et al. **COVID-19 Guide for the Rehabilitation Clinician: A Review of Non-Pulmonary Manifestations and Complications**. American Journal of Physical Medicine & Rehabilitation, May 26, 2020. <u>LINK</u>

- "The COVID-19 literature continues to expand; currently, observational single institution reports and case series with relatively small sample sizes are our primary sources of evidence. This report will summarize key non-pulmonary considerations to provide early guidance to rehabilitation clinicians who may be involved now in the care of COVID-19 survivors with the best available evidence to date."
- Focus areas include the following types of complications: neurologic, hematologic, musculoskeletal, ocular, cardiovascular, gastrointestinal, and dermatologic.

Zhang et al. Liver injury in COVID-19: management and challenges. Lancet Gastroenterology and Hepatology, May 5, 2020. LINK

- "2–11% of patients with COVID-19 had liver comorbidities and 14–53% cases reported abnormal levels of alanine aminotransferase and aspartate aminotransferase during disease progression. Patients with severe COVID-19 seem to have higher rates of liver dysfunction."
- "Liver damage in mild cases of COVID-19 is often transient and can return to normal without any special treatment. However, when severe liver damage occurs, liver protective drugs have usually been given to such patients in our unit."

Vittori et al. Coronavirus Disease 2019 Pandemic Acute Respiratory Distress Syndrome (ARDS) Survivors: Pain after the Storm? Anesthesia Analgesia, April 27, 2020. LINK

"Survivors of ARDS can develop a disorder that is characterized by persistent fatigue, weakness, and limited exercise tolerance (defined as the distance walked in 6 minutes). This limited exercise tolerance is related to the use of systemic corticosteroids to treat the disease and multi-organ dysfunction during the ICU stay. Chronic pain and weakness will develop in these survivors. To date, resources have been concentrated on efforts to prevent the spread of and to treat COVID-19. Concomitant efforts need to be ramped up to study the epidemiology and treatment of posttraumatic stress disorder (PTSD), chronic pain, sleep disorders, fibromyalgia, and fatigue in COVID-19 survivors."

Troyer et al. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain, Behavior, and Immunity, April 10, 2020. <u>LINK</u>

• "However, beyond acute infection, the delayed or chronic effects of this pandemic, particularly on public mental health, will not be fully appreciated for several years. Thus, timely and longitudinal investigations of potential COVID-19associated neuropsychiatric outcomes are critical in disease surveillance and evidence-based therapeutic strategies. Here we review the available studies of acute neuropsychiatric symptoms in the context of COVID-19 for timely evaluation of the evidence. Furthermore, we postulate possible delayed post-viral sequelae of COVID-19 based on findings from other coronavirus or past viral pandemics."



Expert Opinion

Raghu & Wilson. **COVID-19 interstitial pneumonia: monitoring the clinical course in survivors**. Lancet Respiratory Medicine, August 3, 2020. LINK

• "We hypothesise that most COVID-19 survivors will manifest early pulmonary abnormalities, which could range from being asymptomatic, to mild to severe, and debilitating. We further hypothesise that among patients without pre-existing lung disease, the duration of pulmonary abnormalities will be related to the severity of their acute COVID-19 course, with complete or near complete resolution within 6 months in patients who had a mild course (i.e., did not require admission to hospital) and within 12 months in patients who had a moderate course (i.e., admitted to hospital but did not require intensive care). However, persistent lung function abnormalities, including restrictive lung disease, decreased diffusing capacity, and fibrosis, are expected in patients who had a severe course, particularly those who required mechanical ventilation."

Cothran et al. A brewing storm: **The neuropsychological sequelae of hyperinflammation due to COVID-19**. Brain, Behaviour, and Immunity, June 23, 2020. LINK

• "The goal of this letter is to highlight the importance of understanding and assessing potential COVID-19 neuropsychological sequelae that may result from the effects of hyperinflammation."

Rayner et al. Covid-19: **Prolonged and relapsing course of illness has implications for returning workers**. BMJ, June 23, 2020. LINK

- "... we are seeing increasing evidence of a "long-tail" of covid-19 related illness, and we need to consider how to support patients with prolonged illness from covid-19"
- "Prolonged covid-19 illness follows a distinct pattern, reflecting a cluster of symptoms of longer duration and of unknown cause... It is now apparent that this is a multi-system disorder with a far wider range of symptoms than currently identified on the NHS website."

Canadian Association of Physical Medicine & Rehabilitation. **Post-acute Covid-19 Sequelae: Preparing for Recovery to Rehabilitation (Webinar).** Released April 27, 2020. <u>LINK</u>

- Review of sequelae for a broad range of body systems, including pulmonary, cardiac, vascular, peripheral nervous system (i.e., smell and taste), neurological, kidney, in addition to psychiatric consequences and overall fatigue/myalgia.
- Includes discussion about how health systems, particularly rehabilitation, can plan and adapt to address increased numbers of COVID-19 survivors.

Primary Research

Mid- and Long-Term Impacts

Palepu et al. Canadian COVID-19 Prospective Cohort Study (CanCOV). Ongoing. LINK

- "Canadian study to provide a comprehensive evaluation of early to 1-year outcomes in 2000 patients with COVID-19 infection and their family caregivers."
- "Through the CANCOV program of research, we will: 1) characterize the myriad health consequences of COVID-19 including their short and long-term outcomes (recruited from the community and hospitals) and those of their family caregivers, 2) determine the clinical risk factors, timing and pace of recovery across the spectrum of COVID-19 disease, 3) provide detailed clinical descriptions for genetic, basic science, translational and multi-omics research inquiry, and



4) facilitate the creation of prediction models and tools using machine learning and artificial intelligence, as well as secondary clinical studies."

Carfi et al. Persistent Symptoms in Patients after Acute COVID-19. JAMA, August 11, 2020. LINK

"Patients were assessed a mean of 60.3 (SD, 13.6) days after onset of the first COVID-19 symptom; at the time of the evaluation, only 18 (12.6%) were completely free of anyCOVID-19—related symptom, while 32% had 1 or 2 symptoms and 55% had 3 or more. None of the patients had fever or any signs or symptoms of acute illness. Worsened quality of life was observed among 44.1% of patients... a high proportion of individuals still reported fatigue (53.1%), dyspnea (43.4%), joint pain, (27.3%) and chest pain (21.7%)."

Puntmann et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). JAMA Cardiology, July 27, 2020. LINK

"In this cohort study including 100 patients recently recovered from COVID-19 [median (IQR) time interval between COVID-19 diagnosis and cardiac magnetic resonance (CMR) was 71 (64-92) days] ... CMR imaging revealed cardiac involvement in 78 patients (78%) and ongoing myocardial inflammation in 60 patients (60%), which was independent of pre-existing conditions, severity and overall course of the acute illness, and the time from the original diagnosis."

Related:

- Lindner et al. Association of Cardiac Infection with SARS-CoV-2 in Confirmed COVID-19 Autopsy Cases. JAMA Cardiology, July 27, 2020. LINK
 - "Among individuals with cardiac infection [by SARS-CoV-2], overt myocarditis was not observed in the acute phase, but the long-term consequences of this cardiac infection needs to be studied."
- Yancy & Fonarow. Coronavirus Disease 2019 (COVID-19) and the Heart—Is Heart Failure the Next Chapter? JAMA Cardiology, July 27, 2020. LINK
 - "... if this high rate of risk is confirmed, the pathologic basis for progressive left ventricular dysfunction is validated, and especially if longitudinal assessment reveals new-onset heart failure in the recovery phase of COVID-19, then the crisis of COVID-19 will not abate but will instead shift to a new de novo incidence of heart failure and other chronic cardiovascular complications."

Garner. For 7 weeks I have been through a roller coaster of ill health, extreme emotions, and utter exhaustion. BMJ Opinion, May 5, 2020. LINK

• First person account by Paul Garner, professor of infectious diseases at Liverpool School of Tropical Medicine, discusses his experience of having covid-19 (not hospitalized).

Related:

• Re'em. My Covid-19 symptoms have lasted more than 100 days, and I'm not alone. Will they ever end? STAT, July 8, 2020. LINK

The following articles are preprints and have not been peer-reviewed. They report new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

Arnold et al. **Patient outcomes after hospitalisation with COVID-19 and implications for follow-up;** results from a prospective UK cohort. August 14, 2020. LINK



- "Patients with COVID-19 remain highly symptomatic at 8-12 weeks, however, clinical abnormalities requiring action are infrequent, especially in those without a supplementary oxygen requirement during their acute illness."
- COVID-19 patients (n=163) were recruited from hospital, with median LOS 5 days (IQR 2-8) and 19 deaths. Follow up at 8-12 weeks post admission (110/134) indicated 74% had "persistent symptoms (notably breathlessness and excessive fatigue) with reduced [health-related quality of life]. Only patients who required oxygen therapy in hospital had abnormal radiology, clinical examination or spirometry at follow up. Thirteen (12%) patients had an abnormal chest X-ray with improvement in all but 2 from admission. Eleven (10%) had restrictive spirometry. Blood test abnormalities had returned to baseline in the majority (104/110)."

COVID Symptom Study. How long does COVID-19 last? June 6, 2020. LINK

• Summary of results from COVID Symptom Study app users in Wales and Scotland, UK (n = 4,238,773). Includes information on length of disease, symptom profiles, and quality of life / return to normal living.

Patient-Led Research Team. What Does COVID-19 Recovery Actually Look Like? An Analysis of the Prolonged COVID-19 Symptoms Survey. May 11, 2020. LINK

- Survey conducted (n=640) and reported by a self-organized group of "long-haul" COVID-19 patients that arose from the <u>Body Politic COVID-19 Support Group</u>.
- Report covers the following areas:
 - o Impacts of the timing of testing on the status of results
 - o Cyclical symptoms experienced unexpectedly for over six weeks at time of response
 - The nature, severity, and recovery-time course of symptoms week by week
 - An analysis on differences in time course of symptoms reported by patients with positive and negative test results
 - o Internal and external stigmas experienced by patients in recovery
 - Impacts on lifestyle including physical activity and self-isolation

Additional Resources

Klok et al. **Incidence of thrombotic complications in critically ill ICU patients with COVID-19**. Thrombosis Research, July 1, 2020. <u>LINK</u>

• "The 31% incidence of thrombotic complications in ICU patients with COVID-19 infections is remarkably high. Our findings reinforce the recommendation to strictly apply pharmacological thrombosis prophylaxis in all COVID-19 patients admitted to the ICU, and are strongly suggestive of increasing the prophylaxis towards high-prophylactic doses, even in the absence of randomized evidence."

Mazza et al. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain, Behaviour, and Immunity, June 30, 2020. LINK

• "We screened for psychiatric symptoms 402 adults surviving COVID-19 (265 male, mean age 58), at one month follow-up after hospital treatment... A significant proportion of patients self-rated in the psychopathological range: 28% for PTSD, 31% for depression, 42% for anxiety, 20% for OC symptoms, and 40% for insomnia. Overall, 56% scored in the pathological range in at least one clinical dimension. Despite significantly lower levels of baseline inflammatory markers, females suffered more for both anxiety and depression. Patients with a positive previous psychiatric diagnosis showed increased scores on most psychopathological measures, with similar baseline



inflammation. Baseline systemic immune-inflammation index (SII), which reflects the immune response and systemic inflammation based on peripheral lymphocyte, neutrophil, and platelet counts, positively associated with scores of depression and anxiety at follow-up."

• "There is the need to diagnose and treat psychiatric sequelae in COVID-19 survivors."

Meng et al. **CT imaging and clinical course of asymptomatic cases with COVID-19 pneumonia at admission in Wuhan, China**. Journal of Infection, April 12, 2020. <u>LINK</u>

• "The predominant feature of CT findings in asymptomatic patients with COVID-19 pneumonia was ground glass opacity with peripheral distribution, unilateral location and, mostly involving one or two lobes, often combined with subpleural curvilinear line, fine reticulation, air bronchogram, halo sign or vascular enlargement signs. After a short-term follow-up, a few asymptomatic patients presented clinical symptom, mainly fever, cough and fatigue. And the evolution of CT findings was shown in patients with the progression of disease."

Grillet et al. Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected with Pulmonary CT Angiography. Radiology, April 23, 2020. LINK

• "Our study points to a high prevalence of acute pulmonary embolism in patients with coronavirus disease 2019 (23% [95% confidence interval: 15%, 33%]). Pulmonary embolus was diagnosed a mean of 12 days from symptom onset."

Related:

- Leonard-Lorant et al. Acute Pulmonary Embolism in Patients with COVID-19 at CT Angiography and Relationship to d-Dimer Levels. Radiology, April 23, 2020. LINK
 - "Our study demonstrated that of 106 pulmonary CT angiograms performed for patients with COVID-19 over a 1-month period in a tertiary care center, 32 of 106 patients (30%) had acute pulmonary embolus. This rate of pulmonary embolus is higher than usually encountered in critically ill patients without COVID-19 infection (1.3%) or in patients treated in the emergency department (3%–10%)."
- Barco et al. Incomplete echocardiographic recovery at 6 months predicts long-term sequelae after intermediate-risk pulmonary embolism. A post-hoc analysis of the Pulmonary Embolism Thrombolysis (PEITHO) trial. Clinical Research in Cardiology, December 18, 2018. LINK
 - "CTEPH or PPEI occurs in almost one out of seven patients after acute intermediate-risk PE. Six-month echocardiographic follow-up may be useful for timely detection of late sequelae"

Diao et al. Human Kidney is a Target for Novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection. April 10, 2020. LINK

• "SARS-CoV-2 induces [acute renal failure] in COVID-19 patients. Viruses directly infect human kidney tubules to induce acute tubular damage. The viruses not only have direct cytotoxicity, but also initiate CD68+ macrophage together with complement C5b-9 deposition to mediate tubular pathogenesis.

Wu et al. Characteristics of Ocular Findings of Patients with Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. JAMA Ophthalmology, March 31, 2020. LINK

• "In this study (n=38), one-third of patients with COVID-19 had ocular abnormalities, which frequently occurred in patients with more severe COVID-19."



Li et al. Caution on Kidney Dysfunctions of COVID-19 Patients. March 27, 2020. LINK

• "... we suggest exercising a high degree of caution in monitoring kidney functions of COVID-19 patients regardless of comorbid chronic illnesses."

Shi et al. Association of Cardiac Injury with Mortality in Hospitalized Patients with COVID-19 in Wuhan, China. JAMA Cardiology, March 25, 2020. LINK

• Cardiac injury is common among hospitalized COVID-19 patients, ~20%, is highly correlated to comorbidities.

Wang et al. **Temporal Changes of CT Findings in 90 Patients with COVID-19 Pneumonia: A Longitudinal Study**. Radiology, March 19, 2020. LINK

• "The extent of lung abnormalities at CT peaked during illness days 6–11. The temporal changes of the diverse CT manifestations followed a specific pattern, which might indicate the progression and recovery of the illness."

News Articles

The Atlantic. What Young, Healthy People Have to Fear From COVID-19. September 7, 2020. LINK

- "COVID-19 presents an array of health challenges that are serious, if not imminently fatal."
- "We know that hepatitis C leads to liver cancer, we know that human papillomavirus leads to cervical cancer, we know that HIV leads to certain cancers," Howard Forman, a health-policy professor at Yale, told James Hamblin and Katherine Wells of The Atlantic. "We have no idea whether having had this infection means that, 10 years from now, you have an elevated risk of lymphoma."

Science Magazine. The Long Haul. August 7, 2020. LINK

• "Collectively, these "long-haulers" describe dozens of symptoms, including many that could have multiple causes, such as fatigue, joint pain, and fever."

STAT. Covid-19 infections leave an impact on the heart, raising concerns about lasting damage. July 27, 2020. LINK

• Summarizes two studies that "suggest that in many patients, Covid-19 could presage heart failure".

The Conversation. Here's what we know so far about the long-term symptoms of COVID-19. July 26, 2020. LINK

• Summarizes a broad range of research on non-pulmonary disease manifestations, mechanisms of pathology, experiences of long-term COVID-19 patients, and similarities to other coronaviruses.

Vox. The emerging long-term complications of Covid-19, explained. June 12, 2020. LINK

• Very well referenced article summarizing the existing evidence for long-term complications in several areas: lung scarring, strokes, embolism and clotting, heart damage, neurocognitive and mental health impacts, childhood inflammation, male infertility, and other possible lasting effects.

The Atlantic. COVID-19 Can Last for Several Months. June 4, 2020. LINK

• "About 80 percent of infections, according to the World Health Organization, "are mild or asymptomatic," and patients recover after two weeks, on average. Yet support groups on Slack



and Facebook host thousands of people like LeClerc, who say they have been wrestling with serious COVID-19 symptoms for at least a month, if not two or three. Some call themselves "long-termers" or "long-haulers."

- "Most have never been admitted to an ICU or gone on a ventilator, so their cases technically count as "mild." But their lives have nonetheless been flattened by relentless and rolling waves of symptoms that make it hard to concentrate, exercise, or perform simple physical tasks. Most are young. Most were previously fit and healthy."
- "Even though the world is consumed by concern over COVID-19, the long-haulers have been largely left out of the narrative and excluded from the figures that define the pandemic. I can pull up an online dashboard that reveals the numbers of confirmed cases, hospitalizations, deaths, and recoveries—but LeClerc falls into none of those categories. She and others are trapped in a statistical limbo, uncounted and thus overlooked."

The Guardian. Lingering and painful: the long and unclear road to coronavirus recovery. May 1, 2020. LINK

• "In a survey of group members [for people who have experienced Covid-19], 89% of the 465 respondents said they had symptoms that fluctuated in intensity and frequency; 23% had tested positive for coronavirus, taking on average just over nine days to be tested from the onset to symptoms; 28% tested negative and were, on average, tested after about 15 days; and just 3.5% were admitted to hospital, although 38% visited an emergency department."

Science Magazine. How does coronavirus kill? Clinicians trace a ferocious rampage through the body, from brain to toes. April 17, 2020. LINK

• Comprehensive and linked review to research-based evidence of sequelae to COVID-19.

Los Angeles Times. **Coronavirus infection may cause lasting damage throughout the body, doctors fear**. April 10, 2020. <u>LINK</u>

• Early reporting on concerns of morbidity to lungs, liver, heart and cardiovascular system.

The Guardian. Learning to breathe again: the long road to recovery from Covid-19. April 7, 2020. LINK

• Reporting on ICU COVID-19 patients' recovery and potential long-term psychological morbidity.



Methodology

Newfoundland and Labrador Centre for Applied Health Research (NLCAHR) COVID-19 Quick Response reports are initiated by, and shared with, our partners in the provincial health system, including the four Regional Health Authorities, the Departments of Health and Community Services and Children, Seniors and Social Development, and public health officials.

NLCAHR staff work with topic submitters to clarify the research question. We then search for related systematic reviews, meta-analyses, other reviews, interim and other guidance statements, primary research, expert opinion and health and science reporting.

Two researchers carried out individual internet searches (Google and Google Scholar), and divided, and searched, the following databases:

- <u>Alberta Health Services</u>
- <u>CADTH</u>
- <u>Canadian Pharmacists Association</u>
- <u>Campbell Collaboration</u>
- <u>Cochrane Collaboration</u>
- <u>Centre for Disease Control</u>
- <u>Centre for Evidence Based Medicine</u>
- <u>Evidence for Policy and Practice</u> Information and Co-ordinating Centre
- <u>European Centre for Disease Prevention</u> and Control
- Health Canada

- <u>HIQA (Ireland)</u>
- Joanna Briggs Institute
- <u>MedRxiv</u>
- <u>National Collaborating Centres on</u> Methods and Tools (NCCMT)
- National Institutes of Health
- <u>National Institute of Allergy and</u> Infectious Diseases
- National Library of Medicine
- Public Health Agency of Canada
- <u>Trip Database</u>
- World Health Organization

Each researcher screened their search results and extracted data, and checked the others work.

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