# **EVIDENCE SYNTHESIS BRIEFING NOTE**

# TOPIC: UNDERSTANDING THE POST-COVID CONDITION

# Information finalized as of April 1, 2022.<sup>a</sup>

This Briefing Note was completed by the Research, Analysis, and Evaluation Branch (Ministry of Health) based on information provided by members of the COVID-19 Evidence Synthesis Network. Please refer to the <u>Methods</u> section for further information.

**<u>Purpose</u>**: This briefing note examines the definitions, prevalence, risk factors, symptoms, quality of life (QoL), and activities of daily living of the post COVID-19 condition for the general, working age adult, and low-income populations.

**<u>Research Findings</u>**: There was limited information identified about health system utilization, expected burdens, and working age and low-income populations. Evidence from systematic reviews, living reviews, and individual studies yielded the following details:

- <u>Definitions</u>: Post COVID-19 condition definitions share similar components such as persistent symptoms and/or delayed symptoms of SARS-CoV-2 infection beyond four weeks from symptom onset.
- <u>Prevalence</u>: Global prevalence of post COVID-19 condition is estimated at 43% of all cases. In North America, prevalence is estimated at 30%. Studies report the prevalence of post COVID-19 condition among people with confirmed COVID-19 symptoms varies across follow-up points: four weeks (83%), two to five months (55%), 12 weeks (59%), after 12 weeks (62%), and six months (54%).
- <u>Risk Factors</u>: Common risk factors include: severe/critical acute infection; female sex; older age; obesity; hospital admission at symptom initiation; dyspnea or abnormal chest auscultation; and number of symptoms during acute SARS-CoV-2 infection.
- <u>Symptomatology</u>: Commonly reported symptoms of post-COVID-19 condition are chronic fatigue, dysosmia (disordered smell perception), dyspnea (shortness of breath), taste dysfunction, headache, pain (e.g., chest, joint, muscle), poor sleep quality, and reduced exercise capacity.
- <u>QoL</u>: Post-COVID-19 condition symptoms may lead to decreased QoL and health-related quality of life in the general population and low-income populations.
- <u>Activities of Daily Living</u>: The need for care assistance among the general population significantly increases after COVID-19 infection, and individuals who were not dependent previously are reported to be partially dependent on others in the performance of daily activities.
- <u>Impact on the Working Age Population</u>: Work absences are variously reported: 9%-40% of those previously employed at two to three months after discharge; 12%-23% of mild-to-moderate and non-hospitalized cases for three to seven months after acute disease; and 70% of hospitalized and non-hospitalized cases for 13 weeks or more.

<u>Analysis for Ontario</u>: Based on the emerging available data, post COVID-19 condition has the potential to impact the physical and mental health of a substantial proportion of Ontario's population, as well as impact health care system resources in the coming years.

<sup>&</sup>lt;sup>a</sup> This briefing note includes current available evidence as of the noted date. It is not intended to be an exhaustive analysis, and other relevant findings may have been reported since completion.





# **Objectives and Search Methods**

This briefing note examines the research and jurisdictional reports on post COVID-19 condition for: 1) the general population; and 2) working age adults and low-income populations. In particular:

- **General Population**: Definitions; underlying causes; prevalence and associated symptoms and sequelae; risk factors and mitigation; health system utilization; functional limitations; use of long-term disability and employment; and expected burden for Ontario.
- Working Age/Low-Income Populations: Symptom prevalence by body system (e.g., neurological, respiratory); symptom duration and intensity over time; acuity level of illness; quality of life (QoL) and activities of daily living impacts; work-related impacts (e.g., leaves of absence); health care services received; and analysis/modelling considerations.

This briefing note is an update of <u>RAEB's Evidence Synthesis Briefing Note on Long COVID</u> (Oct 29, 2021) and a Science Advisory Table's (SAT) report on <u>Understanding the Post-COVID-19 Condition (Long</u> <u>COVD) and the Expected Burden for Ontario (Sept 14, 2021)</u>. The literature search was limited to sources published from October 1, 2021 to April 2022; however, where applicable, information was included outside of this date range if it was not present in the previously completed RAEB's Evidence Synthesis Briefing Note or SAT report listed above.

#### **Limitations**

- Most of the information identified on general aspects of post COVID-19 condition (i.e., definitions, method of diagnosis, prevalence, and risk factors) are largely unchanged from the RAEB and SAT reports listed above.
- There are no standardized definitions and diagnostic criteria (e.g., validated self-reported questionnaires versus clinical assessments) used across studies. In particular:
  - A report (Mar 16, 2022) by Public Health Ontario noted that study populations, follow-up periods, outcome measures, and analysis methods were highly heterogeneous across systematic reviews and primary studies, making direct comparisons challenging.<sup>1</sup>
  - A report (2021) by the World Health Organization (WHO) indicated that there are multiple names in use in the literature to refer to post COVID-19 condition, such as: long COVID; chronic COVID syndrome; late sequelae of COVID-19; post-acute sequelae of SARS-CoV-2 infection (PASC); and long haul COVID.<sup>2</sup> This Briefing Note will apply the term post COVID-19 condition.
- There was limited information identified on the following topics:
  - The impact of post COVID-19 condition on health system utilization, work- and disability-related impacts, and expected burdens across jurisdictions, including Ontario.
  - The impact of post COVID-19 condition on working age and low-income populations. For example, this was emphasized in the following studies:
    - A review (Oct 2021) on the acute and post-acute neurological manifestations of COVID-19 reported that population data from low- and middle-income countries are scarce, leading to uncertainties in measuring neurological impacts.<sup>3</sup>
    - A US study (Apr 2022) on Black, Indigenous, and Latinx communities noted few studies address inequities in outcomes associated with post COVID-19 condition.<sup>4</sup>
  - The impact of vaccination on post COVID-19 condition. In particular:
    - A Canadian Agency for Drugs and Technologies in Health (CADTH) draft scoping review (Mar 16, 2022) on the clinical classification and interventions for post COVID-19 condition did not identify many published studies assessing the impact of COVID-19 vaccination on post COVID-19 condition. The scoping review did not identify many studies of individuals who received the





COVID-19 vaccine, making it unclear whether receiving a COVID-19 vaccine before or after developing post COVID-19 condition will impact symptoms.<sup>5</sup>

 The clinical recommendations and/or methodological quality of most of the sources identified are unclear as the Research, Analysis, and Evaluation Branch does not have the expertise to make such assessments; methodological assessments published by other research groups are reported where available.

#### Supporting Evidence

<u>Table 1</u> below summarizes the scientific evidence and jurisdictional experiences on post COVID-19 condition among the general population, low-income populations, and working age population. In the <u>Appendix</u>, additional details are provided in <u>Table 2</u> (Summary of Systematic Reviews on Post COVID-19 Condition), and <u>Table 3</u> (Summary of Individual Studies on Post COVID-19 Condition). In terms of jurisdictional experience, information is mainly presented from Canada and the United Kingdom.

#### Table 1: Scientific and Jurisdictional Information on Post COVID-19 Condition

Scientific	Definitions
Evidence	<ul> <li>Definitions of post COVID-19 condition have been defined by many studies and share similar components, such as persistent symptoms and/or delayed symptoms of SARS-CoV-2 infection beyond four weeks from symptom onset,<sup>6</sup> and signs and symptoms that develop during or after SARS-CoV-2 infection that are not explained by an alternative diagnosis, and continue for three weeks;<sup>7</sup> beyond four weeks;<sup>8</sup> or, at least two months.<sup>9</sup></li> </ul>
	Prevalence
	<ul> <li>Since the official name and definition for the condition are not yet established, determining an overall prevalence of post COVID-19 condition among COVID-19 survivors remains challenging. There is high heterogeneity in prevalence estimates.</li> <li><u>Prevalence at Follow-up Periods</u>: Eight identified systematic reviews (SRs) reported on post COVID-19 condition prevalence at multiple follow-up points, ranging from four to 12 weeks after COVID-19 diagnosis to 12 months after symptom onset.<sup>10,11,12,13,14,15,16,17</sup> For example:</li> <li>A SR (Dec 16, 2021) reporting on post COVID-19 condition prevalence estimated that 59% of people with confirmed COVID-19 had symptoms at 12 weeks and 62% had symptoms at &gt;12 weeks.<sup>18</sup></li> <li>A preprint SR (Nov 3, 2021) reporting on 36 studies estimated that 83% of people with confirmed COVID-19 had symptoms four weeks after diagnosis and 56% experienced symptoms after 12 weeks.<sup>19</sup></li> <li>A SR (Oct 13, 2021) reported on post COVID-19 condition prevalence at three follow-up periods: one month (54%); two to five months (55%); and six months (54%).<sup>20</sup></li> <li><u>Global Prevalence</u>: A preprint SR (Nov 16, 2021), reporting on 29 studies comprising 886,388 COVID-19 positive patients, estimated a global pooled prevalence of post COVID-19 condition at 43% of all cases (57% among patients hospitalized). Reports from North America had the lowest pooled prevalence at 30%. Overall, the SR estimated that about 100 million people had or are still living with post COVID-19 condition worldwide.<sup>21</sup></li> </ul>





S	<u>ymptomatology</u>
•	Emerging evidence about the type of symptoms and long-term health effects post COVID-19
	condition suggests that many adults can experience a range of symptoms after their initial
	COVID-19 infection.
	<ul> <li><u>Common Symptoms</u>: The most common symptoms reported are: chronic fatigue,</li> </ul>
	dysosmia (disordered smell perception), dyspnea (e.g., shortness of breath), taste
	dysfunction, headache, pain (e.g., chest, joint, muscle), poor sleep quality, and reduced
	exercise capacity. <sup>22,23,24,25,26,27,28,29,30,31</sup> In addition, persistent symptoms also affect the
	cognitive, musculoskeletal, respiratory, nervous, gastrointestinal, cardiac, and
	psychological systems (e.g., post-traumatic stress disorder, anxiety, depression). <sup>32,33,34,35</sup>
	For example:
	<ul> <li><u>Neuropsychiatric Symptoms</u>: A SR and meta-analysis (Dec 17, 2021) on the persistent</li> </ul>
	neuropsychiatric symptoms associated with post COVID-19 condition across 51 studies
	and 18,917 patients assessed at least 20 days after acute COVID-19 infection. The
	neuropsychiatric symptoms included cognitive dysfunction (20.2%, 10.3–35.7), and
	psychological outcomes, such as: sleep problems (27.4%), anxiety (19.1%), post
	traumatic stress disorder (PTSD) (15.7%), and depression (12.9%). <sup>36</sup>
<u> </u> <u>R</u> i	isk Factors
•	The identified literature reported that having five symptoms in the first week of illness (i.e.,
	fatigue, headache, shortness of breath, hoarse voice, and myalgia) may increase the risk for
	post COVID-19 condition. <sup>37</sup> The following factors also may increase the risk for the condition.
	<ul> <li>Number of symptoms during acute SARS-CoV-2 infection;<sup>38</sup> severe/critical acute</li> </ul>
	infection; <sup>39,40</sup> female sex; <sup>41,42</sup> older age; <sup>43</sup> obesity; <sup>44</sup> hospital admission at symptom
	Initiation;** and dysphea or abnormal chest auscultation.**
	<u>uality of Life (QoL)</u>
•	I wo identified studies investigated now post COVID-19 condition impacted QoL outcomes for
	patients, reporting that the symptoms led to a decreased QoL in the general population. $47,40,49$
	• A SR (Dec 10, 2021) of 39 studies examined post COVID-19 condition symptoms at 212
	at 12 works after initial infection. The provalence of Ool, work identified for: 1) pain or
	discomfort (36%): 2) mobility issues (32%): 3) depression or anyioty (27%): 4) decrease in
	usual activities (23%); and 5) issues with self-care (10%) 50
	$\sim$ A SR and meta-analysis (Aug 31, 2022) on symptoms of nost COVID-19 condition
	reported that an overall prevalence result was reported for poor Ool Additionally the
	study reported prevalence results of individual factors in the EQ-5D-5L questionnaire
	(higher scores represent more problems with the specified factor): 1) mobility (36%): 2)
	personal care (8%): 3) usual activities (28%): 4) pain/discomfort (42%): and 4)
	anxiety/depression (38%). Poor QoL was significantly higher among post COVID-19
	patients with admission to intensive care unit and fatigue.51,b
<u>A</u>	ctivities of Daily Living
•	A review (Jan 27, 2021) on the epidemiology of post COVID-19 condition among a general
	population reported that the need for care assistance significantly increased (52.4%) after
	COVID-19 infection compared to before (7.7%); 41.1% of cases who were not dependent

<sup>&</sup>lt;sup>b</sup> The EQ-5D-5L is a questionnaire that comprises five dimensions: mobility, self-care, usual activities, pain and/or discomfort and anxiety and/or depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems (<u>EQ-5D, n.d.</u>).





previously were at least partially dependent on others in the performance of daily activities subsequently. <sup>52</sup>
Impact on the Working Age Populations
<ul> <li>Prevalence: A SR (Oct 16, 2021) of 13 studies on post COVID-19 condition among working age patients (aged 15-67 years) reported that the prevalence of the condition ranged from 16% to 87% of workers.<sup>53</sup></li> </ul>
<ul> <li>Work Absences: A review (Mar 15, 2022) on post COVID-19 condition stated that almost 50% of 102 primary studies reported some degree of social and family-life impairment, long absence periods off work, adjusted workloads, and loss of employment. For example, the review reported on study findings on work-related implications:</li> <li>In studies on previously hospitalized participants, absence from work due to post COVID-</li> </ul>
19 condition was reported in 9%-40% of those previously employed at two to three months after discharge.
<ul> <li>Research on primarily mild-to-moderate and non-hospitalized SARS-CoV-2 cases reported that about 12%-23% remained absent from work (or had long absence periods) at three to seven months after acute disease.</li> </ul>
<ul> <li>A study with a mixed sample (hospitalized and non-hospitalized) reported that 70% of participants were absent from work for a period of 13 weeks or more, while another study (hospitalized and non-hospitalized) reported that 31% were still out of work at six weeks after acute illness.<sup>54</sup></li> </ul>
<ul> <li>Workload Adjustments: The review (Mar 15, 2022) also reported that many of those living with post COVID-19 condition are forced to adjust or reduce their workload.<sup>55</sup> For example:</li> <li>Two studies (July, 2020; Nov, 2021) included in the review followed up on previously hospitalized participants for two months and reported that their employed participants adjusted their employment to their current circumstances. In the UK study (July, 2020), 15% percent of hospitalized patients remained off-sick from work at the two-month follow-up 56 The LIC study (New 2021) reported that 40% of their employed participants had</li> </ul>
<ul> <li>control of the bost study (Nov, 2021) reported that 40% of their employed participants had reduced hours and/or modified duties upon their return to work.<sup>57</sup></li> <li>control of three studies (Feb, 2021; April, 2021; Jul, 2021) reported that, at follow-ups of three to the studies (Feb, 2021; April, 2021; Jul, 2021) reported that, at follow-ups of three to the studies (Feb, 2021; April, 2021; Jul, 2021) reported that the studies of three to the studies of the studies of the studies of the studies (Feb, 2021; April, 2021; Jul, 2021) reported that the studies of the stu</li></ul>
eight months, the proportions of hospitalized participants (mild to moderate cases) who adjusted or reduced their workloads ranged from 8%-45%. <sup>58,59,60</sup>
deteriorating health, with one reporting that 11% and the other 13.8% of their previously employed participants were unemployed at two months after acute disease. <sup>61,62</sup>
Impact on Low-Income Populations
Limited Data: A US study (Apr, 2022) on Black, Indigenous, and Latinx communities noted
few studies addressing inequities in post COVID-19 condition outcomes in the context of
material resource deprivation caused by low socio-economic status, chronic stress brought
on by racial/ethnic discrimination, or place-based risk. Moreover, the overall lack of complete
data for cases, deaths, and vaccine uptake by race and ethnicity complicates the ability to
understand the etiology and factors associated with mitigation of post COVID-19 condition in
the US.
Control and Prevention (CDC) Social Vulnerability Index (SVI) <sup>c</sup> to mitigate the impact of

<sup>c</sup> Indices, such as the SVI, are geographical-based statistical tools that capture the relative average advantage and disadvantage of those living in an area. These tools incorporate metrics such as income, levels of education completed, and housing quality.



	<ul> <li>systemic racism and socioeconomic adversity, which correlate with the disproportionately higher rates of COVID-19 morbidity, mortality, and transmission in black, Indigenous, and Latinx communities.<sup>63</sup></li> <li>Symptomatology: A review (Oct, 2021) on acute and post-acute neurological manifestations of COVID-19 indicated that data from low- and middle-income countries are scarce, leading to uncertainties in the measure of neurological findings of COVID-19.<sup>64</sup></li> <li>QoL: A review (Oct 28, 2021) on the impact of COVID-19 on health-related quality of life (HQoL) of patients reported that the impact on HRQoL was considerable among patients with post COVID-19 condition. In patients from low-income countries, there was a greater impact on HRQoL. The study noted that a higher HRQoL among COVID-19 patients in high-income countries (e.g., United Kingdom, Norway) may be due to better health services of the countries rather than other factors compared to low and middle income countries (e.g., United Kingdom, Norway) may be due to better health services of the countries rather than other factors compared to low and middle income countries.</li> </ul>
	Iran). <sup>65</sup>
International Scan	<ul> <li>Definition</li> <li>A WHO (Oct 6, 2021) study on standardizing the clinical case definition for long-term symptoms associated with COVID-19 uses the term post COVID-19 condition; however, the study notes that multiple names are in use, such as: long COVID; chronic COVID syndrome; late sequelae of COVID-19; post-acute sequelae of SARS-CoV-2 infection (PASC); and long haul COVID <sup>66</sup></li> </ul>
	<ul> <li>Prevalence</li> <li>The Office for National Statistics (Aug 5, 2021) in the United Kingdom reported that approximately 40% of all people with post COVID-19 condition will continue living with sequelae for over 12 months.<sup>67</sup></li> </ul>
Canadian Scan	<ul> <li>Definition</li> <li>A Government of Canada report (Sept 24, 2021) on post COVID-19 condition defined it as having COVID-19 symptoms for weeks or months after their initial recovery and may occur in some people after infection.<sup>68</sup></li> <li>Prevalence</li> </ul>
	<ul> <li>A living systematic review (Dec 4, 2021) on care models for long COVID reported that, at the time of writing, Canadian prevalence data were unavailable. Based on findings in a preprint SR (Nov 16, 2021) on the global prevalence of post-acute sequelae of COVID-19, the living review estimated that upward of 500,000 Canadians may need to seek care for long COVID.<sup>69</sup></li> </ul>
	<ul> <li>Symptomatology</li> <li>The Government of Canada report (Sept 24, 2021) on post COVID-19 condition reports that for adults the most common symptoms are different for adults and children:         <ul> <li><u>Adults</u>: Fatigue, memory problems, sleep disturbances, shortness of breath, anxiety and depression, general pain and discomfort, difficulty thinking or concentrating, and PTSD.</li> <li>There have been reports of more than 100 symptoms or difficulties with everyday activities. About 80% of adults reported one or more symptoms in the short-term (four to 12 weeks after their initial COVID-19 infection).</li> </ul> </li> </ul>

For example, using the data collected with the tools, entities can identify population groups who may benefit more from the COVID-19 vaccines (<u>Medeiros et al., 2022</u>).







# <u>Methods</u>

The COVID-19 Evidence Synthesis Network is comprised of groups specializing in evidence synthesis and knowledge translation. The group has committed to provide their expertise to provide high-quality, relevant, and timely synthesized research evidence about COVID-19 to inform decision makers as the pandemic continues. The following members of the Network provided evidence synthesis products that were used to develop this Evidence Synthesis Briefing Note:

- Canadian Agency for Drugs and Technologies in Health. (March 2022). Clinical Classification and Interventions for Post–COVID-19 Condition: A Scoping Review (Draft). CADTH.
- Decary, S., Dugas, M., Stefan, T., Langlois, L., Skidmore, B., Bhéreur, A., & LeBlanc, A. (December 4, 2021). <u>Care Models for Long COVID – A Living Systematic Review. First Update – December</u> <u>2021</u>. SPOR Evidence Alliance, COVID-END Network.
- Public Health Ontario. (March 16, 2022). Post-Acute COVID-19 Syndrome (PACS) in Adults What We Know So Far (Confidential). Public Health Ontario.

For more information, please contact the <u>Research</u>, <u>Analysis and Evaluation Branch</u> (<u>Ministry of Health</u>).





# Appendix

# Table 2: Summary of Systematic Reviews on Post COVID-19 Condition

Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
Working-Age Population				
<ul> <li>International</li> <li>N=13 studies</li> <li>Systematic review</li> </ul>	<ul> <li><u>Objective</u>: Evaluate the evidence on PCS among workers.</li> <li><u>Population</u>: Working-age patients (aged 15–67 years).</li> <li><u>Follow-up time</u>: From nine days to five months after symptom onset or after hospital discharge.</li> </ul>	<ul> <li><u>Symptom Prevalence</u>: A wide range of patients (16%–87%) have PCS.</li> <li><u>Symptoms</u>: The most common disorders reported were:         <ul> <li><u>Pneumological Symptoms</u>: Symptoms included continued shortness of breath, dyspnea, chest pain; and</li> <li><u>Neuropsychological Symptoms</u>: included muscle weakness, loss of smell, sleep difficulties, anxiety, depression, post-traumatic stress disorder [PTSD]).</li> <li><u>Organic sequelae</u>: The most frequent health condition associated with having had COVID-19 was:             <ul> <li>Pulmonary fibrosis.</li> </ul> </li> </ul></li></ul>	<ul> <li><u>Risk Factors</u>: High risk of post COVID-19 condition was related to:</li> <li>Number of symptoms during acute SARS-CoV-2 infection;</li> <li>Severity of the disease; and</li> <li>High serum levels of D-dimer.<sup>d</sup></li> </ul>	• None reported. <sup>72</sup>
General Population				
<ul> <li>International</li> <li>N=120 studies</li> <li>Systematic scoping review</li> </ul>	<ul> <li><u>Purpose</u>: To synthesize what is known from literature about persistent COVID-19, its signs and symptoms, its</li> </ul>	<ul> <li><u>Symptoms</u>: Predominant symptoms among individuals with post COVID-19 condition were:</li> <li>Fatigue;</li> </ul>	<ul> <li><u>Number of Symptoms</u>: Having five symptoms in the first week is a risk factor for post COVID-19 condition (i.e., fatigue; headache; shortness of breath; hoarse voice;</li> </ul>	None reported. <sup>73</sup>

<sup>d</sup> D-dimer is a protein fragment (small piece) that is made when a blood clot dissolves in the body. A D-dimer test identifies D-dimer in blood (MedlinePlus, November 8, 2021).





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
	<ul> <li>pathophysiology, and the current management recommendations.</li> <li><u>Population</u>: Adult and pediatric patients with post COVID-19 condition symptoms (population non-specified).</li> <li><u>Follow-Up Time</u>: Not reported.</li> </ul>	<ul> <li>Breathlessness;</li> <li>Arthralgia (joint stiffness);</li> <li>Sleep difficulties; and</li> <li>Chest pain.</li> <li>Long-Term Sequelae: Reports also point to the risk of long-term sequelae with cutaneous, respiratory, cardiovascular, musculoskeletal, mental health, neurologic, and renal involvement in those who survive the acute phase of the illness.</li> </ul>	<ul> <li>and myalgia [muscle aches and pains]).</li> <li>Prolonged Symptoms: Some prolonged COVID-19 symptoms are associated with: <ul> <li>Age 40 to 60 years;</li> <li>Hospital admission at symptom initiation;</li> <li>Severe COVID-19; and</li> <li>Dyspnea or abnormal chest auscultation.</li> </ul> </li> <li>Mental Health: Mental health risk factors include: <ul> <li>Loss of a loved one;</li> <li>Hospitalization;</li> <li>Containment measures such as isolation and quarantine;</li> <li>Being in low-income regions;</li> <li>Financial stressors;</li> <li>Having disabilities;</li> <li>Female gender; and</li> <li>Older age.</li> </ul> </li> </ul>	
<ul> <li>International (preprint)</li> <li>N=29 studies</li> <li>Systematic review and meta-analysis</li> </ul>	<ul> <li><u>Purpose</u>: Examine the prevalence of post-acute sequelae SARS- CoV-2 infection (PASC) across the world and to assess geographic heterogeneities.</li> <li><u>Population</u>: COVID-19 patients (population non-specified.</li> <li><u>Follow-Up Time</u>: 30 to 120 days.</li> </ul>	<ul> <li><u>PASC Prevalence</u>: Global estimated pooled PASC prevalence was 0.43 (95% CI: 0.35, 0.63).</li> <li><i>Hospitalized</i>: PASC prevalence estimate of 0.57 (95% CI: 0.45, 0.68), among those hospitalized during the acute phase of infection.</li> <li><i>Gender</i>: Estimates of PASC prevalence varied across gender:</li> <li><i>Females</i>: 0.49 [95% CI: 0.35, 0.63]; and</li> </ul>	<ul> <li><u>Risk Factors</u>: These groups have higher odds of having PASC:</li> <li><i>Female Sex</i>: 1.57 (95% CI: 1.09, 2.26); and</li> <li><i>Pre-Existing Asthma</i>: 2.15 (95% CI: 1.14, 4.05).</li> </ul>	<ul> <li>Health effects of COVID- 19 appear to be prolonged and can exert marked stress on the healthcare system.</li> <li>Worldwide, PASC comprises a significant fraction (0.43 [95% CI: 0.35, 0.63]) of COVID- 19 tested positive cases and more than half of hospitalized COVID-19 cases.<sup>74</sup></li> </ul>





<ul> <li>Males: 0.37 [95% CI: 0.24, 0.51].</li> <li>Regional Estimates of PASC prevalence varied across regions:</li> <li>Asi: 0.49 (95% CI: 0.21, 0.42):</li> <li>Europe: 0.44 (95% CI: 0.30, 0.59); and</li> <li>North America: 0.30 (95% CI: 0.32, 0.66).</li> <li>Follow-Up Times: Estimates of global PASC prevalence varied by days after index test positive date:</li> <li>30 days: 0.36 (95% CI: 0.25, 0.46);</li> <li>60 days: 0.24 (95% CI: 0.30, 0.59); and</li> <li>North America: 0.30 (95% CI: 0.32, 0.66).</li> <li>Follow-Up Times: Estimates of global PASC prevalence varied by days after index test positive date:</li> <li>30 days: 0.36 (95% CI: 0.13, 0.39);</li> <li>90 days: 0.37 (95% CI: 0.12, 0.57); and</li> <li>120 days: 0.51 (95% CI: 0.42, 0.59).</li> <li>Symptoms: Prevalence estimates varied according to common symptoms:</li> <li>Falgue: 0.23 (95% CI: 0.13, 0.38); and</li> <li>Oygener: 0.13 (95% CI: 0.13, 0.38); and</li> <li>Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivos of COVID- 19.</li> <li>Pupulation: Adults (aged 18+ uncol but args of to bitmarg of to common symptoms include:</li> </ul>	Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
<ul> <li>International         <ul> <li>N=5/1 studies</li> <li>Purpose: Examine the prevalence             <ul> <li>Purpose: Examine the prevalence</li></ul></li></ul></li></ul>			<ul> <li>Males: 0.37 [95% CI:</li> <li>0.24, 0.511</li> </ul>		
<ul> <li>International         <ul> <li>None reported. 75</li> <li>Systematic review and meta-analysis</li> </ul> </li> <li>Purpose: Examine the prevalence         <ul> <li>Systematic review and meta-analysis</li> <li>Systematic review and meta-analysis</li> </ul> </li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.</li> <li>Systematic review and meta-analysis</li> <ul> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.</li> <li>Systematic review and meta-analysis</li> </ul> </ul>			<ul> <li>O.24, 0.31].</li> <li>○ Regional Estimates:</li> </ul>		
<ul> <li>International         <ul> <li>N=51 studies</li> <li>Purpose: Examine the prevalence             <ul> <li>Purpose: Examine the prevalence</li></ul></li></ul></li></ul>			Estimates of PASC		
<ul> <li>International</li> <li>Purpose: Examine the prevalence of neurological and mental health outcomes include:</li> <li>Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of neurological and mental health outcomes include:</li> </ul>			prevalence varied across		
<ul> <li>Asia: 0.49 (95% CI: 0.21, 0.42); Europe: 0.44 (95% CI: 0.30, 059); and North America: 0.30 (95% CI: 0.32, 0.66). Scillar 20, 20, 06).</li> <li>Follow-Up Times: Estimates of global PASC prevalence varied by days after index test positive date: </li></ul>			regions:		
• None reported. <sup>75</sup> • None reported. <sup>75</sup> • None reported. <sup>75</sup>			Asia: 0.49 (95% CI: 0.21,		
<ul> <li>International</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.</li> <li>Systematic review and meta-analysis</li> </ul>			0.42);		
<ul> <li>International</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric systematic review and meta-analysis</li> </ul>			Europe: 0.44 (95% CI:		
<ul> <li>North America .030         <ul> <li>(95% CI: 0.32, 0.66).</li> <li><i>Follow-Up Times:</i> Estimates of global PASC prevalence varied by days after index test positive date:                 <ul></ul></li></ul></li></ul>			0.30, 0.59); and		
<ul> <li>International N=51 studies Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence symptoms in survivors of COVID- 19, 2004</li> <li>Participant of the prevalence symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ symptoms of COVID- 19, 2004</li> <li>Population: Adults (aged 18+ symptoms of COVID</li></ul>			North America: 0.30		
<ul> <li>International N=51 studies Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ meta-analysis</li> <li>Population: Adults (aged 18+ meta-analysis</li> <li>Chlow-Up Time: Estimates of global PASC prevalence of global PASC prevalence 0.25, 0.48); 0.024 (95% CI: 0.12, 0.57); and 0.12, 0.57; and 0.12, 0.57; and 0.12</li></ul>			(95% CI: 0.32, 0.66).		
<ul> <li>of global PASC prevalence varied by days after index test positive date:         <ul> <li>30 days: 0.36 (95% CI: 0.25, 0.48);</li> <li>60 days: 0.24 (95% CI: 0.13, 0.39);</li> <li>90 days: 0.29 (95% CI: 0.12, 0.57); and</li> <li>120 days: 0.51 (95% CI: 0.42, 0.59).</li> <li>0.5 ymptoms: Prevalence estimates varied according to common symptoms:</li> <li>Fatigue: 0.23 (95% CI: 0.13, 0.38); and</li> <li>0.9yspnea: 0.13 (95% CI: 0.14, 0.59% CI: 0.13, 0.38); and</li> <li>0.9yspnea: 0.13 (95% CI: 0.14, 0.59% CI: 0.13, 0.38); and</li> <li>0.9yspnea: 0.13 (95% CI: 0.14, 0.59% CI: 0.59% CI: 0.14, 0.59% CI: 0.59\% CI:</li></ul></li></ul>			○ Follow-Up Times: Estimates		
<ul> <li>International N=51 studies Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence symptoms in survivors of COVID- 19.</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence symptoms in survivors of COVID- 19.</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence symptoms in survivors of COVID- 19.</li> <li>Purpose: Examine the prevalence symptoms in survivors of COVID- 19.</li> <li>Purpose: Examine the prevalence symptoms in survivors of COVID- 19.</li> <li>Purpose: Purpose: Examine the prevalence symptoms in survivors of COVID- 19.</li> <li>Purpose: Purpose: Purpose:</li></ul>			of global PASC prevalence		
<ul> <li>International N=51 studies Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence Suppose: Examine the prevalence Suppose: Examine the prevalence of persistent neuropsychiatric Suppose: Suppose: Suppose:</li></ul>			varied by days after index		
Systematic review and meta-analysis     Purpose: Examine the prevalence     Systematic review and meta-analysis     Purpose: Adults (aged 18+     Systematic review and meta-analysis     Population: Adults (aged 18+     Systematic review			test positive date:		
<ul> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ users) wilds</li> </ul>			■ 30 days: 0.36 (95% CI: 0.25, 0.48):		
<ul> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ years) with a bistory of formation and the bistory of formation and bistory of formation and the bistory of formation</li></ul>			0.23, 0.40), 60 days: 0.24 (95% CI:		
<ul> <li>International</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID- 19.</li> <li>Symptom Prevalence: The prevalence of neurological and mental health outcomes include:</li> </ul>					
<ul> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.</li> <li>Systematic review and meta-analysis</li> <li>Purpose: Istudits (aged 18+ woorn) with a history of</li> </ul>			■ 90 days: 0 29 (95% Cl		
<ul> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ verse) with a bistor of</li> </ul>			0 12 0 57); and		
• International       • Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.       • Symptoms: Prevalence estimates varied according to common symptoms:       • Fatigue: 0.23 (95% CI: 0.13, 0.38); and       • Dyspnea: 0.13 (95% CI: 0.09, 0.19).         • International       • Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID-19.       • Symptom Prevalence: The prevalence of neurological and mental health outcomes include:       • None reported.       • None reported.			<ul> <li>120 days: 0.51 (95% CI:</li> </ul>		
<ul> <li>Symptoms: Prevalence estimates varied according to common symptoms:</li> <li>Fatigue: 0.23 (95% CI: 0.13, 0.38); and</li> <li>Dyspnea: 0.13 (95% CI: 0.09, 0.19).</li> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ voors) with a bistory of</li> </ul>			0.42, 0.59).		
<ul> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ years) with a bictory of</li> </ul>			<ul> <li>Symptoms: Prevalence</li> </ul>		
International       • Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID- 19.       • Symptom Prevalence: The prevalence: The prevalence of persistent neuropsychiatric symptoms in survivors of COVID- 19.       • None reported. <sup>75</sup> • Population: Adults (aged 18+ years) with a bittory of       • Population: Adults (aged 18+ years) with a bittory of       • None reported.			estimates varied according		
<ul> <li>International</li> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ voors) with a biotory of</li> </ul>			to common symptoms:		
<ul> <li>International</li> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ voors) with a biotory of</li> </ul>			Fatigue: 0.23 (95% CI:		
<ul> <li>Dyspnea: 0.13 (95% CI: 0.09, 0.19).</li> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ veore) with a biotom of</li> </ul>			0.13, 0.38); and		
<ul> <li>International</li> <li>Purpose: Examine the prevalence of persistent neuropsychiatric symptoms in survivors of COVID- 19.</li> <li>Population: Adults (aged 18+ voors) with a biotory of</li> </ul>			<ul> <li>Dyspnea: 0.13 (95% CI:</li> </ul>		
<ul> <li>International</li> <li>N=51 studies</li> <li>Systematic review and meta-analysis</li> <li>Population: Adults (aged 18+ vacre) with a biotory of</li> </ul>			0.09, 0.19).		
N=51 studies     Systematic review and meta-analysis     Population: Adults (aged 18+     voors) with a biotory of	International	<u>Purpose</u> : Examine the prevalence	• <u>Symptom Prevalence</u> : The	None reported.	None reported. <sup>75</sup>
Systematic review and meta-analysis     19.     19.     Population: Adults (aged 18+ voors) with a bistory of	N=51 studies	or persistent neuropsychiatric	prevalence of neurological		
• <u>Population</u> : Adults (aged 18+	Systematic review and     meta analyzia		include:		
<u>ropulation</u> . Addits (aged for     )	meta-analysis	Population: Adults (aged 18+			
		vears) with a history of			





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
	<ul> <li>polymerase chain reaction (PCR)- confirmed or clinically suspected SARS-CoV-2 infection (population non-specified).</li> <li><u>Follow-up time</u>: The mean duration of follow-up after COVID- 19 was 77 days (range 14–182 days).</li> </ul>	<ul> <li>Neurological Symptoms: Common neurological symptoms were:</li> <li>Objective cognitive dysfunction (20.2%, 10.3–35.7);</li> <li>Dysosmia (disordered smell perception) (1.14%, 8.2–15.6);</li> <li>Taste dysfunction (7.4%, 4.7–11.4); and</li> <li>Headache (6.6%, 3.6– 12.0).</li> <li>Mental Health Symptoms: Common outcomes were:</li> <li>Sleep problems (27.4%, 21.4–34.4);</li> <li>Anxiety (19.1%, 13.3– 26.8);</li> <li>Post-traumatic stress disorder (PTSD) (15.7%, 9.9–24.1); and</li> <li>Depression (12.9%, 7.5– 21.5).</li> </ul>		
<ul> <li>International</li> <li>N=81 studies</li> <li>Systematic review and meta-analysis</li> </ul>	<ul> <li><u>Objective</u>: Examine the proportion of individuals experiencing fatigue and cognitive impairment 12 or more weeks following COVID-19 diagnosis.</li> <li><u>Population</u>: COVID-19 patients (n=25,268; population non-specified).</li> <li><u>Follow-Up Time</u>: Periods ranged from 2.8 to 11.2 months.</li> </ul>	<ul> <li><u>Symptom Prevalence</u>: Twelve or more weeks following COVID-19 diagnosis participants experienced:         <ul> <li><i>Fatigue</i>: Proportion of individuals experiencing fatigue 0.32 (95% CI, 0.27, 0.37);</li> <li><i>Cognitive Impairment</i>: Proportion of individuals exhibiting cognitive impairment was 0.22 (95% CI, 0.17, 0.28).</li> </ul> </li> </ul>	<ul> <li><u>Risk Factors</u>: Similar incidences of fatigue and cognitive impairment were observed amongst:         <ul> <li>Hospitalized; and</li> <li>Non-hospitalized populations.</li> </ul> </li> </ul>	• None reported. <sup>76</sup>





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
<ul> <li>International</li> <li>N=18 studies</li> <li>Systematic review and meta-analysis</li> </ul>	<ul> <li><u>Objective</u>: Systematically synthesize evidence on post COVID-19 condition symptoms persisting for at least 12 months.</li> <li><u>Population</u>: COVID-19 survivors (n=8,591); hospitalized and non- hospitalized.</li> <li><u>Follow-Up Time</u>: 12 months after symptom onset or hospital admission.</li> </ul>	<ul> <li><u>Symptom Prevalence</u>: One year after infection, a sizeable proportion of COVID-19 survivors still experience residual symptoms involving various body systems. The most prevalent symptoms were:         <ul> <li>Fatigue/weakness (28%, 95% CI: 18–39);</li> <li>Dyspnoea (18%, 95% CI: 13–24);</li> <li>Arthromyalgia (bone pain) (26%, 95% CI: 8–44);</li> <li>Depression (23%, 95% CI: 12–34);</li> <li>Anxiety (22%, 95% CI: 15–29);</li> <li>Memory loss (19%, 95% CI: 7–31);</li> <li>Concentration difficulties (18%, 95% CI: 2–35); and</li> <li>Insomnia (12%, 95% CI: 7–17).</li> </ul> </li> </ul>	<ul> <li><u>Risk Factors</u>: Existing evidence suggests that the following are risk factors for experiencing long- term post COVID-19 condition symptoms:         <ul> <li>Female sex; and</li> <li>Severe/critical acute infection.</li> </ul> </li> </ul>	• None reported. <sup>77</sup>
<ul> <li>International</li> <li>N=44 observational studies</li> <li>Systematic review</li> </ul>	<ul> <li><u>Objective</u>: Evaluate the extent and timing of olfactory recovery following loss due to COVID-19 infection.<sup>e</sup></li> <li><u>Population</u>: Adult patients (≥18 years) and children diagnosed with COVID-19 infection by positive PCR test, and who reported olfactory dysfunction (anosmia or hyposmia).</li> </ul>	<ul> <li><u>Symptoms</u>: Olfactory recovery was found to occur as early as seven days, with most patients recovering olfaction within 30 days.</li> <li>Olfactory recovery most often occurred within the first two weeks from symptom onset with a rate of recovery at one month as</li> </ul>	<ul> <li><u>Risk Factors</u>: Patients with initial poor olfactory scores had slow rates of olfactory recovery.</li> <li>However, the majority of studies did not observe medical co-morbidities, demographics, or general symptoms to be a pertinent factor in olfactory recovery.</li> </ul>	None reported. <sup>78</sup>

e Olfactory loss (anosmia) has been identified as one of the common symptoms related to COVID-19 infection and may sometimes be the primary presenting symptom or the sole manifestation of disease in patients with COVID-19. Recovery of olfactory function has an important impact on patients' quality of life (<u>Jafar et al., November 9, 2021</u>).





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
	<ul> <li><u>Follow-Up Time</u>: Timing of</li> </ul>	high as 94.6%; at six		
	evaluations ranged from 10 days	months the rate of recovery		
	to six months.	was as nigh as 85.7%.		
International	Objective: Compare ongoing	<u>Symptoms Prevalence of</u>	None reported.	<ul> <li>None reported.<sup>79</sup></li> </ul>
N=39 studies	(four to 12 weeks) and post	USC: Between four and 12		
Systematic review		symptoms were:		
	(after 12 weeks) with respect to	$\sim$ Eatique (43%: range 5-		
	symptomatology, abnormal	83%)		
	functioning, psychological burden.	<ul> <li>○ Sleep disorders (36%: 10–</li> </ul>		
	and quality of life.	69%)		
	Population: Adults (18+ years)	<ul> <li>Respiratory symptoms:</li> </ul>		
	with post COVID-19 condition	<ul> <li>Dyspnoea (31%; 2–64%);</li> </ul>		
	(population non-specified).	<ul> <li>Cough (26%; 5–45%).</li> </ul>		
	<ul> <li>Follow-Up Time: Four to 12</li> </ul>	<ul> <li>Other symptoms: These</li> </ul>		
	weeks after infection; and, beyond	Included:		
	12 weeks.	Arthraigia (23%; 10– 48%):		
		40 /0), ■ Myalaia (18%: 1_32%):		
		<ul> <li>■ Chest nain (17%: 3–</li> </ul>		
		35%):		
		<ul> <li>Headache (17%; 4–36%);</li> </ul>		
		Fever (15%; 1–51%);		
		Expectoration (14%; 1–		
		25%);		
		<ul> <li>Weight loss (13%; 6–</li> </ul>		
		17%);		
		<ul> <li>Skin problems (12%; 8– 15%);</li> </ul>		
		15%;		
		<ul> <li>Anosinia (11%, 2-21%),</li> <li>Aneusia (11%: 1_25%)</li> </ul>		
		and		
		<ul> <li>Confusion (11%; 9–14%).</li> </ul>		
		Symptoms Prevalence of		
		PCS: Over 12 weeks post-		
		disease onset the most		
		common symptoms were:		





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
Studies, and Review Type		<ul> <li>Fatigue: 44% (10–71%);</li> <li>Dyspnoea (shortness of breath): 40% (6–73%);</li> <li>Myalgia (muscle aches and pains): 34% (2–86%); and</li> <li>Sleep disorder: 33% (18–57%).</li> <li>Other symptoms included:         <ul> <li>Cough (22%; 3–59%);</li> <li>Hair loss (20%; 6–29%);</li> <li>Palpitations (20%; 4–62%);</li> <li>Arthralgia (joint stiffness; 13%; 6–29%);</li> <li>Arthralgia (loss of smell): 10% (5–13%); and</li> <li>Chest pain (12%; 3–29%);</li> <li>Anosmia (loss of smell): 10% (5–13%); and</li> <li>Chest pain (10%; 1–22%).</li> </ul> </li> <li>Quality of Life (QoL): A decreased QoL was recorded by 40% (23-53%) in those with OSC and 57% (51–67%) in those with PCS including:         <ul> <li>Pain or discomfort (36%; 27–48%);</li> <li>Mobility issues (32%; 7–56%);</li> <li>Depression or anxiety (27%; 14–46%);</li> <li>A decrease in usual activities (23%; 2–37%); and</li> </ul> </li> </ul>		
		$\circ$ Issues with self-care (10%; 1–17%).		





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
<ul> <li>International</li> <li>N=12 observational studies</li> <li>Systematic review and meta-analysis.</li> </ul>	<ul> <li><u>Objective</u>: Evaluate the pooled prevalence of poor QoL in post-acute COVID-19 syndrome (PACS) and evaluate the effects of persistent symptoms and intensive care unit (ICU) admission on the poor QoL.</li> <li><u>Population</u>: Adult PACS patients (n=4,828); population non-specified.</li> <li><u>Follow-Up Time</u>: Ranged from 30 to 180 days.</li> </ul>	<ul> <li><u>Prevalence</u>: Amongst PCS patients, the pooled prevalence of poor QoL was (59%; 95% CI: 42%–75%).</li> <li><u>Individual Factor Prevalence</u>: Prevalence of individual factors (measured by the EQ-5D-5L questionnaire) included:<sup>f</sup></li> <li>Mobility (36%, 10–67%);</li> <li>Personal care (8%, 1–21%);</li> <li>Usual activities (28%, 2–65%);</li> <li>Pain/discomfort (42%, 28–55%); and</li> <li>Anxiety/depression (38%, 19–58%).</li> <li><u>Persistent Symptom</u> <u>Prevalence</u>: Prevalence of persistent symptoms included:</li> <li>Fatigue (64%, 54–73%);</li> <li>Dyspnea (39.5%, 20–60%);</li> <li>Antralgia (24.3%, 14–36%);</li> <li>Headache (21%, 3–47%);</li> <li>Sleep disturbances (47%, 7–89%); and</li> <li>Mental health (14.5%, 4–29%).</li> </ul>	<ul> <li>Poor QoL was significantly higher among PSC patients with:         <ul> <li>ICU admission (p = 0.004); and</li> <li>Fatigue (p = 0.0015).</li> </ul> </li> </ul>	None reported. <sup>80</sup>
<ul> <li>Mernational</li> <li>N=18 studies</li> <li>Systematic review and meta-analysis</li> </ul>	<u>Objective</u> : Determine the prevalence of neurological and neuropsychiatric symptoms	<ul> <li><u>Symptom Prevalence</u>: Overall prevalence for neurological post COVID-19 symptoms were:</li> </ul>	<ul> <li>Neuropsychiatric symptoms substantially increased in prevalence between mid- and long-term follow-up.</li> </ul>	• None reported.

<sup>&</sup>lt;sup>f</sup> The EQ-5D-5L is a validated questionnaire to evaluate a patient's quality of life by assessing the following five factors: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Categorization within each factor is divided into five levels that range from no problems to extreme problems (Malik, et al., 2021).





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
	<ul> <li>reported after acute COVID-19 onset.</li> <li><u>Population</u>: Adult (18+ years) 10,530 COVID-19 patients (hospitalized and non- hospitalized).</li> <li><u>Follow-up time</u>: Three (12 weeks) to six months after acute COVID- 19 onset.</li> </ul>	<ul> <li>Fatigue (37%, 95% CI: 25%–48%);</li> <li>Brain fog (32%, 10%–54%);</li> <li>Memory issues (28%, 22%– 35%);</li> <li>Attention disorder (22%, 7%–36%);</li> <li>Myalgia (17%, 9%–25%);</li> <li>Anosmia (12%, 8%–16%);</li> <li>Dysgeusia (10%, 6%–14%); and</li> <li>Headache (15%, 4%–26%).</li> <li>Neuropsychiatric conditions included:</li> <li>Sleep disturbances (31%, 19%–42%);</li> <li>Anxiety (23%, 14%–32%); and</li> <li>Depression (17%, 10%– 24%).</li> </ul>	<ul> <li>Hospitalized patients: At three (or more) months post- infection, patients hospitalized for acute COVID-19 had reduced frequency of:         <ul> <li>Anosmia;</li> <li>Anxiety;</li> <li>Depression;</li> <li>Dysgeusia;</li> <li>Fatigue;</li> <li>Headache;</li> <li>Myalgia; and</li> <li>Sleep disturbance.</li> <li>Hospital admission: Hospital admission was associated with higher frequency of:             <ul> <li>Memory issues (OR: 1.9, 95% CI: 1.4–2.3).</li> <li>ICU admission: Compared to cohorts with &lt;20% of ICU admission during acute COVID- 19, cohorts with &gt;20% of patients admitted experienced higher prevalence of:             <ul> <li>Fatigue;</li> <li>Anxiety;</li> <li>Depression; and</li> <li>Sleep disturbances.</li> </ul> </li> </ul></li></ul></li></ul>	
<ul> <li>International</li> <li>N=9 observational studies</li> <li>Systematic review</li> </ul>	<ul> <li><u>Objective</u>: Examine the nature and frequency of persistent symptoms experienced by patients after mild COVID-19 infection.</li> <li><u>Population</u>: Adult patients who had been through a mild COVID- 19 infection (population non- specified).</li> </ul>	<ul> <li><u>Symptom Prevalence</u>: The frequency of persistent symptoms in patients after mild COVID-19 infection ranged between 10% and 35%.</li> <li><u>Symptoms</u>: Symptoms persisting after a mild COVID-19 infection:</li> </ul>	• None reported.	None reported. <sup>82</sup>





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
	<ul> <li><u>Follow-Up Time</u>: Three to 16 weeks.</li> </ul>	<ul> <li>Fatigue (most frequent):</li> <li>Dyspnoea;</li> <li>Cough;</li> <li>Chest pain;</li> <li>Headache; and</li> <li>Decreased mental and cognitive status and olfactory dysfunction.</li> </ul>		
<ul> <li>International</li> <li>N=57 studies</li> <li>Systematic review</li> </ul>	<ul> <li><u>Objective</u>: Estimate organ system–specific frequency and evolution of PASC.</li> <li><u>Population</u>: Survivors of COVID- 19 (n=250,351; median age: 54.4 yrs.; 56% male) of which 79% were hospitalized during acute COVID-19.</li> <li><u>Follow-Up Time</u>: Three follow-up periods: one month; two to five months; and six months.</li> </ul>	<ul> <li><u>Prevalence</u>: PACS prevalence (at least one symptom) was reported at three follow-up periods:         <ul> <li>Short Term: 54.0% (45.0%- 69.0%; 13 studies) at one month;</li> <li>Intermediate Term: 55.0% (34.8%-65.5%; 38 studies) at two to five months; and</li> <li>Long Term: 54.0% (31.0%- 67.0%; nine studies) at six or more months.</li> </ul> </li> <li>Symptom Prevalence: Symptom prevalence was reported for these systems:         <ul> <li>Pulmonary Sequelae: Most prevalent symptom was:</li> <li>Chest imaging abnormality (median [interquartile range], 62.2% [45.8%-76.5%]);</li> <li>Neurologic Disorders: Most prevalent symptom was:</li> <li>Difficulty concentrating (median, 23.8% [20.4%- 25.9%]);</li> </ul> </li> </ul>	None reported.	• None reported. <sup>83</sup>





Jurisdiction, Number of Relevant Studies, and Review Type	Objective, Population, Follow-up time Inclusion	Long-term Symptom(s) and Prevalence	Risk Factors for Post COVID-19 Condition	Health Care Utilization
		<ul> <li>Mental Health Disorders:</li> </ul>		
		Most prevalent symptom		
		was:		
		<ul> <li>Generalized anxiety</li> </ul>		
		disorder (median, 29.6%		
		[14.0%-44.0%]);		
		<ul> <li>Functional Mobility</li> </ul>		
		Impairments: Most		
		prevalent symptom was:		
		<ul> <li>General functional</li> </ul>		
		impairments (median,		
		44.0% [23.4%-62.6%]);		
		and		
		<ul> <li>General and Constitutional</li> </ul>		
		Symptoms: Most prevalent		
		symptom was:		
		<ul> <li>Fatigue or muscle</li> </ul>		
		37.5% [25.4%-54.5%]).		
		Other Symptoms: Other		
		inequentily reported symptoms		
		dermetelogia digestive and		
		dermatologic, digestive, and		
		ear, nose, and throat		
		disorders.		





# Table 3: Summary of Individual Studies on Post COVID-19 Condition

Jurisdiction, Number of Participants, and Study Type	Objective, Population, Follow-up Time	Reported Outcomes	Risk Factors	Health Care Utilization
General Population				
<ul> <li>United States</li> <li>N=153,760; also, two sets of control cohorts with 5,637,647 (contemporary controls) and 5,859,411 (historical controls) individuals</li> <li>Retrospective cohort study</li> </ul>	<ul> <li><u>Purpose</u>: Examine the post- acute cardiovascular manifestations of COVID-19 after one year.</li> <li><u>Population</u>: Individuals with COVID-19 included in healthcare databases from the US Department of Veterans Affairs (population non- specified).</li> <li><u>Follow-Up Time</u>: Median follow-up times for participant groups included:</li> <li>COVID-19 group: 347 days;</li> <li>Contemporary control group: 348 days; and</li> <li>Historical control group: 347 days.</li> </ul>	<ul> <li><u>Outcomes</u>: Beyond the first 30 days of infection, people with COVID-19 exhibited increased risks and 12-month burdens of incident cardiovascular disease. Disease includes:         <ul> <li>Cerebrovascular disorders;</li> <li>Dysrhythmias;</li> <li>Ischemic and non-ischemic heart disease;</li> <li>Pericarditis;</li> <li>Heart failure and thromboembolic disease.</li> </ul> </li> </ul>	<ul> <li><u>Risk Factors</u>: Risks of cardiovascular disease were evident regardless of:         <ul> <li>Age;</li> <li>Race;</li> <li>Sex; and</li> <li>Other cardiovascular risk factors, including:                 <ul> <li>Obesity;</li> <li>Hypertension;</li></ul></li></ul></li></ul>	• Not reported. <sup>84</sup>
<ul> <li>United States (preprint)</li> <li>N=2,965,506 electronic health records (EHR)</li> <li>Retrospective cohort study</li> </ul>	<ul> <li><u>Purpose</u>: Examine the incidence of new-onset long-term psychiatric manifestations for patients who have recovered from COVID-19 infection.</li> <li><u>Population</u>: Adult COVID-19 positive patients (population non-specified).</li> <li><u>Follow-Up Time</u>: Two periods following COVID-19 infection:</li> </ul>	<ul> <li><u>Outcomes</u>: Patients who have recovered from COVID-19 are at an increased risk for developing new-onset mental illness, especially anxiety disorders; risk is most prominent in the first 120 days following infection.</li> <li><u>New Onset Mental</u> <u>Disorders</u>: There was a significant increase in incidence of new-onset</li> </ul>	None reported.	<ul> <li>Study recommends that to cope with the excess in psychiatric morbidity experienced by survivors of COVID-19, health services should focus efforts early in the post COVID-19 clinical course.<sup>85</sup></li> </ul>





Jurisdiction, Number of Participants, and Study Type	Objective, Population, Follow-up Time	Reported Outcomes	Risk Factors	Health Care Utilization
	<ul> <li>○ 21-120 days; and</li> <li>○ 121-365 days.</li> </ul>	mental disorders in the period of 21-120 days following COVID-19 (3.8%, 3.6-4.0) compared to patients with respiratory tract infections (3%, 2.8- 3.2).		
<ul> <li>United States</li> <li>N=1,726,683 veterans</li> <li>Observational study</li> </ul>	<ul> <li><u>Purpose</u>: Examined kidney outcomes in long COVID (i.e., risks of acute kidney injury [AKI], estimated glomerular filtration rate [eGFR] decline, end stage kidney disease [ESKD], and major adverse kidney events [MAKE]).<sup>g,h</sup></li> <li><u>Population</u>: 30-day survivors of COVID-19 (population non-specified).</li> <li><u>Follow-Up Time</u>: 30 days.</li> </ul>	<ul> <li><u>Outcomes</u>: Compared with non-infected controls, 30-day survivors of COVID-19 exhibited excess eGFR declines during the acute phase of COVID-19 infection:</li> <li><i>Non-hospitalized</i>: -3.26 ml/min per 1.73 m<sup>2</sup> per year (-3.58 to -2.94);</li> <li><i>Hospitalized</i>: -5.20 ml/min per 1.73 m<sup>2</sup> per year (-6.24 to -4.16); and</li> <li><i>Admitted to intensive care</i>: -7.69 ml/min per 1.73 m<sup>2</sup> per year (-8.27 to -7.12).</li> </ul>	<ul> <li><u>Risk Factors</u>: Beyond the acute illness, 30-day survivors of COVID-19 exhibited higher risks of:         <ul> <li>AKI (adjusted hazard ratio [aHR], 1.94);</li> <li>eGFR decline ≥30% (aHR, 1.25);</li> <li>eGFR decline ≥40% (aHR, 1.44);</li> <li>eGFR decline ≥50% (aHR, 1.62);</li> <li>ESKD (aHR, 2.96); and</li> <li>MAKE (aHR, 1.66).</li> </ul> </li> </ul>	None reported. <sup>86</sup>
<ul> <li>Italy</li> <li>N=402,216, and 192 COVID- 19 survivors respectively at one, six, and 12 months; 95 (subgroup) evaluated longitudinally at one-, six- and 12-months follow ups</li> <li>Single cohort study</li> </ul>	<ul> <li><u>Purpose</u>: Investigate the psychopathological impact of COVID-19 in Italy one year after infection, outlining the trajectory of symptomatology.</li> <li><u>Population</u>: COVID-19 survivors (population non-specified).</li> <li><u>Follow-Up Times</u>: One, six, and twelve months after the COVID-19 outbreak.</li> </ul>	<ul> <li><u>Outcomes</u>: Study examined results for depression, anxiety, PTSD, and fatigue.</li> <li>At six months:</li> <li>94 (44%) patients self-rated in the clinical range in at least one psychopathological dimension.</li> <li>At 12 months:</li> </ul>	<ul> <li><u>Risk Factors</u>: The following factors were reported:         <ul> <li>The following groups exhibit increased scores in all the psychopathological domains:</li> <li>Females; and</li> <li>Patients with a positive psychiatric history.</li> <li>Sex and Time: There was an interaction effect of sex</li> </ul> </li> </ul>	None reported. <sup>87</sup>

<sup>&</sup>lt;sup>9</sup> The estimated glomerular filtration rate (eGFR) is a calculation used to estimate how well kidneys are filtering certain agents produced by the body, such as creatinine (a waste product that comes from the normal wear and tear on muscles), and cystatin C (a protein that slows down the breakdown of other protein cells (<u>National Kidney Foundation, n.d.</u>). <sup>h</sup> Major adverse kidney event [MAKE] was defined as estimated glomerular filtration rate decline ≥50%, end stage kidney disease, or all-cause mortality (<u>Bowe et al., 2021</u>).





Jurisdiction, Number of Participants, and Study Type	Objective, Population, Follow-up Time	Reported Outcomes	Risk Factors	Health Care Utilization
		<ul> <li>86 (45%) patients self- rated in the clinical range in at least one psychopathological dimension;</li> <li>63 (33%) patients experienced pathological fatigue.</li> </ul>	<ul> <li>and time was observed for depression (F = 8.63, p &lt; 0.001) and anxiety (F = 5.42, p = 0.005).</li> <li>Males showed a significant increasing trend of depression and anxiety symptoms; and</li> <li>Females showed a decreasing trend of depression anxiety symptoms.</li> </ul>	





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