

COVID-19 Evidence Support Team RAPID REVIEW REPORT

What is the incidence and duration of long COVID cases?

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Full author statement available at the end of report.

Updated Key Findings

March 31, 2022

- Since the previous rapid review, a large amount of new research and reviews are available to draw upon. Many studies have addressed aspects previously identified as limitations such as the use of validated questionnaires, documenting pre-COVID health status, and control cohorts. Many studies now include only participants with RT-PCR verified infections and also focus on a range of disease severities from severe (hospitalized) to mild (managed in the community); PCR-validated infections ensure a higher quality of comparison between test-positive and control groups. Studies involving control groups contributed illuminating findings about prevalence and incidence of long COVID, which is lower than previous thought when compared to control groups. Comorbidities/factors that potentially indicate increased risk of developing long COVID-19 have been identified and widely agreed-upon, such as **diabetes, cardiovascular diseases, obesity, and gender (female)**.
- A case definition for long COVID has yet to be adopted but is commonly defined as **COVID-related symptoms that persist or emerge beyond 4 weeks of infection** with two subsequent phases: “ongoing symptomatic COVID-19 (OSC; signs and symptoms from 4 to 12 weeks from initial infection) and 2) post-COVID-19 syndrome (PCS; signs and symptoms beyond 12 weeks) with respect to symptomatology, abnormal functioning, psychological burden, and quality of life”. Long COVID includes *both* OSC and PCS.
- It is estimated that 32% of non-hospitalized and 51% of hospitalized people experience Long COVID symptoms within 12 weeks of infection; however, higher estimates up to 92% have been reported

in studies with a greater proportion in persons who were previously hospitalized. More than 200 symptoms affecting 10 organ systems have been identified in various reports or systematic reviews. Many patients (49%), experience at least one COVID-related symptom 12 months after infection (compared to 68% at 6 months).

- For many persons, symptoms improve over time while others experience persistent and/or new symptoms. At 3 months post-infection the most frequently reported symptoms are fatigue (up to 98%), dyspnoea (up to 88%), headache (up to 91%) and taste/smell disorders (up to 58%).
- Mechanism(s) leading to long COVID remain unclear, but these comorbidities/factors have been found to indicate potentially increased risk of developing long COVID:
 - Age (60+)
 - Greater number of symptoms during the acute phase of illness (typically 5+)
 - Manifestation of specific symptoms
 - Diabetes
 - Cardiovascular disease
 - Obesity or high BMI
 - Gender (female)
- There is limited evidence to support the contention that vaccination lowers incidence of long COVID.

Key Findings

July 9, 2021

- The frequency of Long COVID symptoms varies widely across studies based on populations studied, duration of follow up and methods of assessment of symptoms.
- It is estimated that 1 in 50 persons experience Long COVID symptoms after 12 weeks; however, higher estimates up to 80% have been reported in studies with a greater proportion of persons who were previously hospitalized. A recent study of a mixed cohort of 96 persons found that only 22.9% had no symptoms at 12 months post diagnosis.
- A wide range of symptoms affecting multiple organ systems has been reported. For many persons symptoms improve over time while others experience persistent and/or new symptoms. Among studies with the longest duration of follow up, the most frequently reported symptoms included fatigue (up to 65%), dyspnea (up to 50%), headache (up to 45%), anosmia/ageusia (up to 25%), cognitive memory/concentration (up to 39.6%) and sleep disorders (up to 26%).
- Few studies estimated the duration of symptoms with estimates ranging from 2.2% for 6 months and 27% for 7-9 months.
- The mechanism(s) leading to Long COVID remain unclear but those experiencing post acute sequelae tend to be older, have a greater number of symptoms during the acute phase of illness or manifest specific symptoms and live with multiple comorbid conditions such as obesity.
- The lack of consensus on a definition of Long COVID contributes to marked variations in robust prevalence estimates.

Limitations

- Data on the Delta and Omicron variants, which are believed to have different transmission/severity profiles compared to previously dominant variants are not specified in any studies/reviews
- Few studies focused on prevalence for pediatric populations.
- Most studies were based on self-reported symptoms and may be subject to recall bias.

- Few studies report on age and gender, which have been shown to have a positive association with persistent symptoms.
- Infection rates are considered to be underrepresented as many cases go unreported, which may result in long COVID prevalence rates being overestimated
- Few studies focus on psychological factors, but some research suggests persistent COVID-related symptoms could be attributed to pandemic-related stress, rather than infection.

Strength of Evidence

- | | |
|--|--|
| <input type="checkbox"/> Mature evidence | <input checked="" type="checkbox"/> Emerging Supportive evidence |
| <input type="checkbox"/> Mixed evidence | <input type="checkbox"/> Weak evidence |

Quality of Evidence Assessment

- 1. Adequacy of primary studies:** A large number of studies, reviews, and reports are available on the topic. Here, we have synthesized a number of reports and systematic reviews to capture a broad understanding of the findings.
- 2. Methodological limitations:** Symptoms were often self-reported, and studies were limited to a 1-year follow-up period and did not indicate symptom reduction beyond that point. Studies focusing on children were limited in number and lacked consensus on the definition and presentation of long COVID in young people. Many studies do not report gender distribution or age, although these are commonly referred to as indicators of risk for long COVID. Although limited, some research supports the potential that some long COVID symptoms could be related to psychological and psychosocial effects of life experience during this pandemic; more research is needed in this area.
- 3. Methodological strengths:** Many studies have addressed aspects previously identified as limitations such as the use of validated questionnaires, documenting pre-COVID health status, and control cohorts. Many studies specifically included only participants with RT-PCR verified infections and also focused on a range of disease severity from severe (hospitalized) to mild (managed in the community) as well as comorbidities such as diabetes, cardiovascular diseases, and obesity. PCR-validated infections ensure a higher quality of comparison between test-positive and control groups. Studies involving control groups contributed illuminating findings about prevalence and incidence of long COVID.
- 4. Relevance to review question:** Many studies were relevant to the review question and objectives and have been synthesized in various reviews and reports, which will be the basis for this report.
- 5. Generalizability of findings:** Most studies were conducted in developed countries including United States, United Kingdom, Belgium, Italy, Spain, France, Germany, Switzerland, and China that may have different population profiles, pandemic experience and health system context than Canada. However, results (and study designs) are quite similar across geographies and in general, findings provide a strong case for confirming prevalence rates for northern-hemisphere populations.

Background/Context

1. Clinical Context

A case definition for Long COVID has yet to be adopted but is commonly defined as **COVID-related symptoms that persist or emerge beyond 4 weeks of infection**^{1,2} with two subsequent phases: “ongoing symptomatic COVID-19 (OSC; signs and symptoms from 4 to 12 weeks from initial infection) and 2) post-COVID-19 syndrome (PCS; signs and symptoms beyond 12 weeks) with respect to symptomatology, abnormal functioning, psychological burden, and quality of life”.³ Long COVID includes *both* OSC and PCS.

The WHO defines Long COVID, also referred to as “post acute sequelae of SARS CoV-2 (PASC)” or “post COVID condition”, as a condition where a patient “does not recover to baseline health after an initial infection or diagnosis of COVID-19”². Quite reliably, studies and reviews accept the idea that the acute phase of COVID lasts up to 4 weeks. Regardless of the temporal criteria threshold, the central tenet of the definition embraces prolonged recovery without return to pre COVID health and functioning. In a narrative analysis, one review found the absence of a more specific definition of long COVID to be a significant barrier in effectually diagnosing, supporting, and treating those experiencing persistent symptoms.⁴

There is growing recognition that many people experience persistent symptoms after acute SARS CoV-2 infection, even 12+ months later. It is important to note that most research focused on those infected in early 2020 to mid-2021, prior to the emergence of the Delta or Omicron variants. Continued research may find vastly different rates of prevalence and symptomatology for long COVID associated with the Delta variant, which emerged in early Fall 2021 and was quickly overshadowed by the two Omicron variants as the dominant strains worldwide. The potential impact on population health requires anticipation and preparation of health systems to cope with the demand for care and support among persons experiencing post acute sequelae of SARS CoV-2 (long COVID).

As new studies emerge that include control cohorts, new evidence shows that symptoms commonly exist (at varying rates) for both those who have been infected with SARS CoV-2 as well as participants within control cohorts. This review will be critical in determining treatment needs within and beyond the primary health care system in Saskatchewan.

2. Purpose

This review sought to describe the epidemiology of Long COVID and in particular to obtain estimates of the incidence/prevalence and duration of Long COVID symptoms to inform prediction models of the scale and impact of Long COVID on population health and health care systems.

3. Review Question(s)

- What is the incidence and duration of Long COVID?

Method

For each Rapid Review, the initial question is posed by a decision-maker in the health care system seeking the evidence base for a specific policy decision. According to the subject of the question, the COVID Evidence Support Team (CEST) Intake Committee allocates the question to the appropriate Working Group. Each Working Group may be comprised of a librarian, researcher, 1-2 clinicians, 1-2 subject matter experts, and a group leader. A reference interview is conducted to establish the

parameters of the question to ensure it is articulated in a clear, searchable manner. The librarians assigned to the team then conduct a thorough search of the indexed literature, grey literature, news sources, or other sources as agreed upon. Some reference lists for especially pertinent articles are also reviewed. An Evidence Search Report is thereby created. See Appendix for more details on the search strategy. A Rapid Review of the identified literature is then performed by the researcher using the approach of a systematic review, but without a double review, formal assessment of quality of reported study, or meta-analysis. Importantly, the review is completed in a time-sensitive manner. Relevant evidence is summarized in both tabular and narrative form, key findings and limitations articulated, and the quality of the body of evidence evaluated using a four-point grading system that assesses the methodologies, adequacy of the included studies, the direct relevance to the question and the generalizability of the findings related to the question. The draft Rapid Review Report is reviewed and edited by the Working Group clinicians, experts, and leader. Once revisions are complete, the Rapid Review is submitted to the requesting decision-maker and placed in the COVID-19 repository and database. For certain topics with rapidly changing evidence, after a period of time an updated evidence search is performed, the review process repeated, and an updated Rapid Review released.

Globally, many research teams and organizations have released various reviews and reports on this topic and as such, this report will provide a synthesis of these reports. This allows a broad view of current research by leveraging the high-quality analysis presented within these reports.

Summary of Evidence

A large number of studies and reviews have now been conducted about the incidence and prevalence of long COVID and its health impacts; amongst the most pertinent are documents released by the Canadian Institute for Health Information (CIHI), Quebec's Institut national d'excellence en santé et en services sociaux (INESS), Science Briefs of the Ontario COVID-19 Science Advisory Table, the Belgian Health Care Knowledge Centre, a living review by the NSW Government Agency for Clinical Innovation – COVID-19 Critical Intelligence Unit (Australia), and the World Health Organization (WHO). These comprehensive reports provide evidence about the incidence and severity of persistent SARS-CoV-2 symptoms as well as the unintended consequences of the pandemic, such as shutdowns and backlogs to various services, supports, and treatments—which have had broad range effects, even for health issues not directly related to the COVID-19 pandemic.

Studies are better aligned in collecting participant data at common intervals (compared to that of version 1 of this review)—typically 1, 3, 6, and 12 months with more standardized methodology, such as using data based on patient records, RT-PCR verified infections, and control cohorts. Specifically, the inclusion of control cohorts allows a better understanding of long COVID prevalence in comparison to control groups. Although persistent symptoms are more common for those who have been infected by SARS CoV-2, there is a smaller difference than previously reported when compared to control cohorts.⁵

Better parameters for diagnosis are needed but will continue to evolve as new research is conducted. A systematic review by Groff et al. supported the classification of symptomatology into “organ systems, i.e., neurologic; cardiovascular; respiratory; digestive; dermatologic; and ear, nose, and throat as well as mental health, constitutional symptoms, and functional mobility”.⁶ This may provide efficient pathways to diagnosis and treatment plans and allow patterns to emerge with regard to effective treatments and risk indicators.⁶

The advancement of long COVID research has identified risk factors for experiencing symptoms beyond 4 weeks from infection as **female gender, age, BMI, those with comorbidities** (especially cardiovascular diseases and diabetes), **severity of acute symptoms, and need for hospitalization**.⁷⁻⁹ However, it is difficult to determine the effect and prevalence of postintensive care syndrome (PICS), which refers to the onset of symptoms such as cognitive dysfunction, weakness, anxiety, depression, and PTSD¹⁰; PICS symptoms largely overlap with that of long COVID. Although gender and age are potential indicators for heightened risk of developing long COVID, few studies reported on these factors.

Overall, rates of persistent symptoms are significant, even at one-year post-infection. A large systematic review (N=8591 participants) that has been highlighted in a number of guidance documents reviewed studies with one-year follow-up studies in China, Italy, Spain, and Germany. Findings showed significant rates of fatigue/weakness (28%), dyspnoea (18%), arthromyalgia (26%), depression (23%), anxiety (22%), memory loss (19%), concentration difficulties (18%), and insomnia (12%).¹¹ These are in alignment with the most commonly identified long COVID symptoms reported.¹² In extreme cases, some reviews have found studies that report rates of over 80% for persistent symptoms 3-24 weeks post-infection.¹³ Another systematic review found that even those with mild symptoms during acute infection experience symptoms beyond 3 weeks and up to 3 months at a rate between 10% and 35%.¹²

Figure 1 shows the broad range of organ systems effected by long COVID and SARS CoV-2 infections.

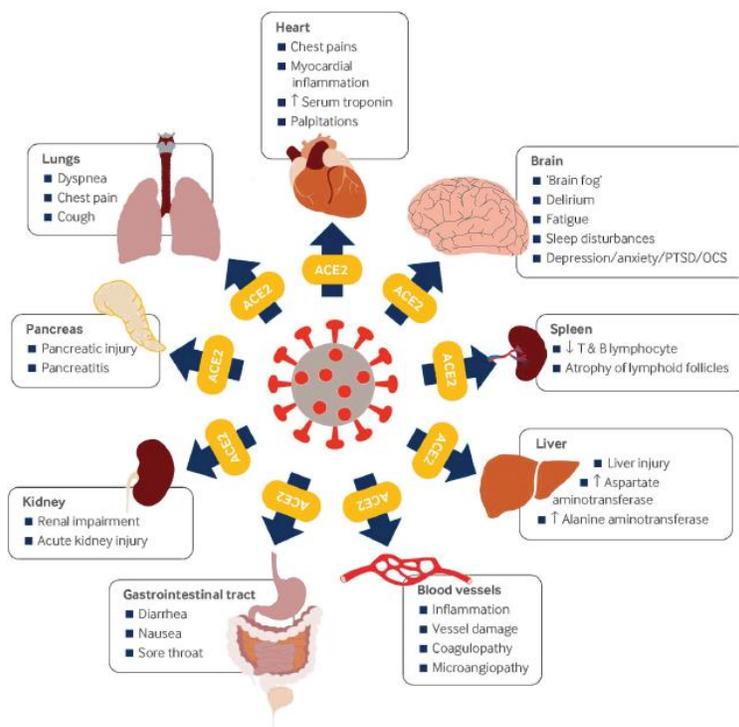


Figure 1: Impact of SARS CoV-2 and Post-COVID Condition on Various Organ Systems

PTSD, post-traumatic stress disorder. OCS, obsessive-compulsive symptoms.

Reproduced from Crook et al (2021) as shown in Razak F, et al. (2021).²

A living systematic review by Michelen et al. reviewed studies with mostly severe infections requiring hospitalization and reported higher rates of several symptoms at 12 weeks post-infection or later: “weakness (41%), general malaise (33%), fatigue (31%), concentration impairment (26%) and

breathlessness (25%). 37% of patients reported reduced quality of life; 26% of studies presented evidence of reduced pulmonary function”.¹⁴

Jennings, through a systematic review, studied the two phases of long COVID, which are: “**ongoing symptomatic COVID-19** (OSC; signs and symptoms from 4 to 12 weeks from initial infection) and 2) **post-COVID-19 syndrome** (PCS; signs and symptoms beyond 12 weeks) with respect to symptomatology, abnormal functioning, psychological burden, and quality of life”.³ They found that abnormalities in lung function, confirmed through imaging, seemed to be more common in patients experiencing OSC, whilst anxiety, depression, and poor quality of life seemed more frequent in patients with PCS; “decreased quality of life was reported by 40% of those with OSC and 57% with PCS”.³

Mental Health

The stresses of living during this global pandemic appears to have had mental health impacts for the general population, whether they have been infected by SARS CoV-2 or not. Some research findings show that new diagnoses of depression and anxiety have similar rates when comparing SARS CoV-2 cases and control cohorts with only slightly higher risk differences for confirmed cases.¹⁵

More focused research is needed to explore the incidence of psychosomatic symptoms caused by stresses associated with living during this pandemic. This would explain control cohorts reporting persistent symptoms, such as fatigue, chronic pain, depression, and anxiety and calls into question the need to create new pathways following multidisciplinary approaches for treatment within primary care systems. Although more research is needed, treatment for long COVID may lay outside the scope of primary healthcare and could be better hosted by auxiliary treatments, such as dietetic, psychological, and physical therapies. However, it is possible that certain more severe cases of long COVID could follow pathways within primary care that currently exist for similar conditions.

Youth

Children and young people who have been infected with SARS CoV-2 showed slightly elevated pooled risk differences compared with control cohorts with the following most common symptoms: cognitive difficulties (3%), headache (5%), loss of smell (8%), sore throat (2%) sore eyes (2%) but NOT abdominal pain, cough, fatigue, myalgia, insomnia, diarrhoea, fever, dizziness or dyspnoea.⁵

Vaccination

Many of the systematic reviews and 12-month follow up data are for people infected before the availability of vaccines, thus subsequent reviews will better reflect new evidence regarding the effect of vaccination on the prevalence and severity of long COVID. Although a growing number of studies include data on the efficacy of vaccination in lowering rates of long COVID, at the time of our search only emerging primary research was available which has not yet been synthesized into systematic reviews/guidance documents.

Fortunately, primary findings show strong evidence for the efficacy of vaccination to reduce incidence and severity and a number of long COVID symptoms.^{2,16,17} One study found significantly lowered rates of long COVID rates for participants who had received just one dose of the COVID vaccine, whether before or after SARS-CoV-2 infection:

“Patients who received at least one dose of any of the three COVID vaccines prior to their diagnosis with COVID-19 were 7-10 times less likely to report two or more long-COVID symptoms compared to unvaccinated patients. Furthermore, unvaccinated patients who received their first COVID-19 vaccination within four weeks of SARS-CoV-2 infection were 4-6

times less likely to report multiple long-COVID symptoms, and those who received their first dose 4-8 weeks after diagnosis were 3 times less likely to report multiple long-COVID symptoms compared to those who remained unvaccinated”.¹⁸

Conclusions

Our understanding of the longer-term consequences of SARS CoV-2 infections is still evolving as more prospective studies have stronger foundational knowledge to work from. The lack of consensus on the definition continues to pose a challenge as well as characterization of sub-syndromes and phenotypes that comprise long COVID. More longitudinal studies with comparison cohorts are surfacing which helps to disentangle background frequency of common symptoms that also occur in the general population. Use of standardized tools to assess symptoms perhaps embedded within electronic medical records would be helpful for comparisons across studies. Further research is needed about at-risk populations, such as females, aging people, those with obesity or higher BMIs, diabetes, cardiovascular diseases, or other co-morbidities. Further, more attention toward those experiencing challenges with regard to socio-economic status is needed as this population has been disproportionately affected by the COVID-19 pandemic as well as its unintended consequences of the pandemic. For instance, supports for at-risk populations have been backlogged or discontinued to redistribute resources and staff toward treating SARS CoV-2 patients, and by the resignation of various support personnel. More information is needed about pediatric populations since little is known about the presentation of long COVID in this population and particularly as younger children (0-4 years) remain vulnerable due to their inability to be vaccinated.

Table 1: Summary of Evidence

Consult the Summary of Evidence table using the following link:

- <https://covid19evidencereviews.saskhealthauthority.ca/en/permalink/coviddoc343>

This link provides access to the database where it is possible to view the spreadsheet for review.

Reference List

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Appendix 1: Evidence Search Details

Note: To view full search strategy details, please consult the associated Evidence Search Report.

Filters, Limits & Exclusions:	English only June 25, 2021 – March 3, 2021	
Sources Searched:	<ul style="list-style-type: none"> • Alberta Health Services • BCCDC • CDC-US • CEBM • COVID-19 Best Evidence Front Door • COVID-END • Embase • Europe PMC • Evidence Check Australia • Evidence Synthesis Network • Google • Google Scholar • HSE Ireland • LitCovid 	<ul style="list-style-type: none"> • L-OVE • McMaster Plus Evidence Alerts • Medline • medRxiv • NCCMT • Newfoundland Quick Response Reports • PHAC • Public Health Ontario • SPOR Evidence Alliance • TRIP PRO • Veterans Affairs Database • WHO Global Research Database • WHO
Librarian(s):	Brianna Howell-Spooner, Clinical Librarian, Saskatchewan Health Authority Mark Mueller, Clinical Librarian, Saskatchewan Health Authority	

Appendix 2: Evidence Search Strategies

Medline

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/ or covid-19/) and (disease outbreaks/ or epidemics/ or pandemics/)	76057
2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,nm,ox,rx,px.	221876
3	((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf.	64235
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf.	11515
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf.	386

6	or/1-5	230188
7	public health informatics/ or models, statistical/ or models, theoretical/ or logistic models/ or models, biological/ or computer simulation/ or nonlinear dynamics/	878128
8	(novel agent-based simulation framework* or novel agent based simulation framework* or agent based model* or public health informatics or public-health informatics or ((statistical or probabilistic or theoretic* or biologic* or experimental or mathematical or logistic or logit or computer* or non-linear or nonlinear) adj2 model*) or computer simulation* or nonlinear dynamic* or non-linear dynamic*).tw,kf.	350846
9	7 or 8	1117730
10	("post-COVID-19 syndrome" or "post COVID-19 syndrome" or "post COVID syndrome" or "long haulers" or "long-haulers" or "long-term COVID" or "long term COVID" or "chronic COVID syndrome" or "chronic COVID symptoms" or persistent post-COVID syndrome or PPCS or PASC or post-acute COVID syndrome or PACS or post-COVID condition? or long COVID or long-haul* COVID or long haul* COVID or long-COVID).ti,ab.	7206
11	incidence/ or probability/ or exp risk/	1542830
12	(incidence? or secondary attack rate? or attack rate? or person-time rate? or person time rate? or probabilit* or risk? or health correlates or protective factor? or likelihood function? or likelihood estimate? or likelihood ratio? or bayes theorem or (bayesian adj (forecast? or analys#s or prediction? or approach* or method?)) or odds ratio? or cross-product ratio? or relative odds or risk ratio? or chance).ti,ab.	3511902
13	11 or 12	4001331
14	6 and 10 and 13	284
15	COVID-19/co [Complications]	8554
16	10 or 15	15282
17	6 and 9 and 13 and 16	218
18	17 not 14	211
19	13 and 16	4453
20	limit 19 to (english language and yr="2020 -Current")	3597
21	("post COVID syndrome" or "long haulers" or "long-haulers" or "long-term COVID" or "long term COVID" or persistent COVID or long COVID or long-haul* COVID or long haul* COVID).ti,ab.	1012
22	20 and 21	219

23	((duration or length or time) adj1 (illness or sickness or post-treatment or post-hospital* or "after hospitalization" or "after treatment")) or duration or time or length or day? or month? or week?).tw ,kf.	7539401
24	10 and 23	2694
25	21 and 24	414
26	limit 25 to (english language and yr="2020 -Current")	397
27	26 not 22	259
28	14 or 18 or 20 or 26 or 27	3871
29	limit 28 to dt=20210625-20220303	1223
30	limit 29 to english language	1214
31	("post COVID syndrome" or "long haulers" or "long-haulers" or "long-term COVID" or "long term COVID" or persistent COVID or long COVID or long-haul* COVID or long haul* COVID).ti,ab.	1012
32	30 and 31	352

Medline

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/ or covid-19/) and (disease outbreaks/ or epidemics/ or pandemics/)	75487
2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,nm,ox,rx,px.	138755
3	((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf.	40806
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf.	7167
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf.	276
6	or/1-5	145604
7	limit 6 to (english language and yr="2021 -Current")	88998
8	Long Term Adverse Effects/ or Recurrence/ or Symptom Flare Up/	195099
9	((long-term or long term or long-tail or long tail or longitudinal* or chronic* or persist* or permanent or prolong* or ongoing or recurr* or lasting or long-lasting* or linger*) adj2 (symptom* or complicat* or	302321

	consequence* or outcome* or effect* or aftereffect? or after-effect? or after effect? or manifest*).ti,ab,kw ,kf.	
10	(sequela* or long-COVID* or long COVID* or chronic-COVID or chronic COVID or long-hauler? or long hauler?).ti,ab,kw ,kf.	67945
11	8 or 9 or 10	546201
12	(post-acute or postacute or post-hospital* or posthospital* or post-discharg* or postdischarg*).ti,ab,kw ,kf.	16680
13	(postcovid* or post-covid* or postcoronavirus* or post-coronavirus*).ti,ab,kw ,kf.	1728
14	("post COVID syndrome" or "long haulers" or "long-haulers" or "long-term COVID" or "long term COVID" or persistent COVID or long COVID or long-haul* COVID or long haul* COVID).ti,ab.	585
15	12 or 13 or 14	18705
16	7 and 11 and 15	736
17	(sequela* or long-COVID or long COVID or chronic-COVID or chronic COVID).ti.	11697
18	7 and 17	398
19	16 or 18	813
20	limit 19 to (english language and yr="2021 -Current")	813
21	Longitudinal Studies/ or Follow -Up Studies/	820557
22	((study or studies) adj1 (follow -up or follow up or follow up or longitudinal)).ti,ab,kw ,kf.	130344
23	((((duration or length or time) adj1 (illness or sickness or post-treatment or post-hospital* or "after hospitalization" or "after treatment"))) or duration or time or length or day? or month? or week?).tw ,kf.	6465815
24	21 or 22 or 23	6871380
25	incidence/ or probability/ or exp risk/	1541471
26	(incidence? or secondary attack rate? or attack rate? or person-time rate? or person time rate? or probabilit* or risk? or health correlates or protective factor? or likelihood function? or likelihood estimate? or likelihood ratio? or bayes theorem or (bayesian adj (forecast? or analys#s or prediction? or approach* or method?)) or odds ratio? or cross-product ratio? or relative odds or risk ratio? or chance).ti,ab.	3037328
27	25 or 26	3526557
28	20 and 24	429
29	20 and 27	239

30	28 or 29	510
31	limit 30 to dt=20210625-20220303	326

Embase

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/ or covid-19/) and (disease outbreaks/ or epidemics/ or pandemics/)	30989
2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kw ,ox,px.	234729
3	((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kw .	62488
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kw .	13398
5	((Wuhan or Hubei) adj5 pneumonia).ti,ab, kw .	442
6	or/1-5	242357
7	limit 6 to (english language and yr="2021 -Current")	158511
8	Long Term Adverse Effects/ or Recurrence/ or Symptom Flare Up/	404331
9	((long-term or long term or long-tail or long tail or longitudinal* or chronic* or persist* or permanent or prolong* or ongoing or recurr* or lasting or long-lasting* or linger*) adj2 (symptom* or complicat* or consequence* or outcome* or effect* or aftereffect? or after-effect? or after effect? or manifest*)).ti,ab,kw .	493806
10	(sequela* or long-COVID* or long COVID* or chronic-COVID or chronic COVID or long-hauler? or long hauler?).ti,ab,kw .	95907
11	8 or 9 or 10	964033
12	(post-acute or postacute or post-hospital* or posthospital* or post-discharg* or postdischarg*).ti,ab,kw .	31182
13	(postcovid* or post-covid* or postcoronavirus* or post-coronavirus*).ti,ab,kw .	3835
14	("post COVID syndrome" or "long haulers" or "long-haulers" or "long-term COVID" or "long term COVID" or persistent COVID or long COVID or long-haul* COVID or long haul* COVID).ti,ab.	1159
15	12 or 13 or 14	35561
16	7 and 11 and 15	1673

17	(sequela* or long-COVID or long COVID or chronic-COVID or chronic COVID).ti.	10972
18	7 and 17	778
19	16 or 18	1832
20	limit 19 to (english language and yr="2021 -Current")	1832
21	Longitudinal Studies/ or Follow -Up Studies/	1467258
22	((study or studies) adj1 (follow -up or follow up or follow up or longitudinal)).ti,ab,kw .	183765
23	((((duration or length or time) adj1 (illness or sickness or post-treatment or post-hospital* or "after hospitalization" or "after treatment"))) or duration or time or length or day? or month? or week?).tw ,kw .	10329176
24	21 or 22 or 23	10928010
25	incidence/ or probability/ or exp risk/	3204609
26	(incidence? or secondary attack rate? or attack rate? or person-time rate? or person time rate? or probabilit* or risk? or health correlates or protective factor? or likelihood function? or likelihood estimate? or likelihood ratio? or bayes theorem or (bayesian adj (forecast? or analys#s or prediction? or approach* or method?)) or odds ratio? or cross-product ratio? or relative odds or risk ratio? or chance).ti,ab.	4959875
27	25 or 26	5726907
28	20 and 24	1199
29	20 and 27	569
30	28 or 29	1362
31	limit 30 to dd=20210625-20220303	492
32	limit 31 to (human and english language)	488
33	limit 32 to medline	74
34	32 not 33	414

Keywords Used in Other Resources

- Long COVID; Post-Acute COVID; Post-COVID; COVID sequelae; Long Haulers; Chronic COVID; PASC; PPCS
- syndrome; symptoms; conditions; complications; effects; sequelae duration; incidence; rates; frequency

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Appendix 3: Review History

List in reverse chronological order (newest first)

Previous Review Date	Review Code
July 9, 2021	EPM210601 RR

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