Scientific Advisory Group

COVID-19 Scientific Advisory Group Rapid Evidence Report

Updated review of prolonged symptoms after acute COVID-19 infection

July 12, 2021

Alberta Health Services

Physical distancing works

Table of contents

Lay Summary

- Scientists are not yet sure exactly how common it is for people to have symptoms that last for a long time after COVID-19 (sometimes called “Long COVID”). Some early studies show that as many as 1/3 to 1/2 of people may have some symptoms that last more than 1 month, with some having symptoms for 6 months or more. Over 231,987 (as of July 2021) Albertans have been diagnosed with COVID-19 so this could affect the health of many people. This rapid evidence review brings together recent studies to help doctors and other health care workers plan care for people recovering from COVID.
- Because most people have been infected only in the last year, there are no long-term studies - our knowledge is increasing as groups of people are assessed for longer times after their infections.
- A variety of terms have been used, and after reviewing all of them, we suggest that for now (until there are standard terms across countries) “post-COVID conditions”, or PCC as short form, should be used. “Long COVID” as a description is popular but may leave out some conditions that occur after hospitalization, as it seems to describe a particular set of symptoms in as currently used.
- Some groups internationally have used standard sets of questions to check people for their risk of post-COVID conditions, compare groups of patients, or follow how patients do over time. Although this may be quite useful, studies on how well the question sets work to identify people at risk and to follow their progress are still needed.
- There are not many good quality reports on how common post-COVID conditions are. Most studies are in people who had been in in hospital or ICU so this may not be the same for people who stayed home with COVID-19. Based on the studies we have, after hospital care for COVID-19 over 80% of people have at least one symptom at 1 month and over half still have at least one symptom after 3 months.
- A number have studies looked at risk factors for post-COVID conditions. Four high quality studies found no specific risk factors for experiencing post COVID conditions. The rest of the studies are not that good, but the ones that showed risk differences showed possible higher risk of post COVID conditions with older age (at least >60 years) (5 studies); being female (4 studies); and having other medical conditions (including lung disease, diabetes, heart failure and chronic kidney disease) (3 studies). Other risk factors from two studies each included White ethnicity, ICU admission, needing oxygen in hospital, and being male. Better studies are needed.
- There is no good quality evidence around whether vaccination may change post COVID conditions, although studies are happening.
- A few studies describe COVID-19 survivors as requiring medical care after their initial infection through emergency departments, acute care, home care, outpatient specialty clinics, general practitioners, and telehealth lines.
- Surveys of people who have had COVID-19 show that 1/3-1/2 do not return to work (early retirement), half or more miss days of work, and around one to two thirds say they are less productive at work. A more objective and standardized assessment of this is needed.

The committee made 4 recommendations, suggesting the use of the term “post-COVID conditions”; using a list of identified risk factors; that Albertan healthcare use data be assessed for post COVID healthcare patterns; and that this review should be updated in 6-12 months with new studies as many are happening now.

Authorship and Committee Members

Name	Contribution
Kiran Pohar Manhas	Writing – Evidence screening and extraction; original draft preparation and editing
Ceara Cunningham, Cyndie Koning, Jamie Boisvenue	Writing – Evidence screening and extraction
Nicole Loroff	Research Librarian
Brandie Walker	Primary scientific reviewer
Chester Ho	Secondary scientific reviewer
Lynora Saxinger & Scott Klarenbach	Scientific Advisory Group chairs (oversight and leadership responsibility) L. Saxinger secondary review/lay summary writer
John Conly, Andre Corriveau, Alexander Doroshenko, Shelley Duggan, Elizabeth MacKay, Frank MacMaster, Andrew McRae, Jeremy Slobodan, Brandie Walker, Nathan Zelyas	Discussion, revision, and approval of document

Topic: Update to chronic COVID-19 symptoms review (a review of prolonged symptoms after acute COVID-19 infection)

1. **What are the most common terms and definitions used for symptoms that persist after resolution of suspected or confirmed acute COVID-19 infection across jurisdictions and what is the suggested terminology for Alberta?**
   a. **Are there validated screening or assessment tools for this phenomenon that may be used to identify patients requiring care linkage?**
2. **After a diagnosis of COVID-19, which symptoms (physical and/or neuropsychiatric) are most commonly noted to persist for at least 30 days after acute infection in children and adults?**
3. **Which patients with COVID-19 are at highest risk of developing these chronic symptoms? Is the severity of COVID-19 disease (e.g. hospitalized; ICU) associated with the probability of developing post-COVID conditions?**
4. **Does COVID-19 vaccination impact the course of post-COVID conditions?**
5. **What are the potential health system impacts and what could be the health care needs for patients with post-COVID conditions (e.g., emergency department visits, hospital use, home care, rehab, community programs)?**
   a. **Is it anticipated that health system resource use would continue indefinitely (chronic disease model) or would this decrease over time?**
   b. **What are the implications for return to work for employees, their employers, and for health care workers involved in assessments of return to work?**

Context

- On November 30, 2020, the Scientific Advisory Group released a rapid evidence review on chronic symptoms (defined as 30+ days) after COVID-19 diagnosis, as well as the risk factors for, and the potential mechanisms of, these chronic symptoms.
- This review was requested due to growing recognition that a subset of patients recovering from COVID-19 experience symptoms after the acute phase of illness. Colloquially, these people are often termed "long haulers", and experience "Long Covid", which are two terms/hashtags increasingly prominent in social media and in patient-driven campaigns.
- Since that review, Alberta has seen two further surges in cases of COVID-19. As of July 5, 2021, 231,987 individuals in Alberta were diagnosed with COVID-19 (Alberta Health, 2021), with 9618 hospital admissions and 2,301 deaths from COVID-19. A substantial population of survivors could be affected by these symptoms after COVID-19.
- Based on the prevalence rates of persistent symptoms noted in the first Scientific Advisory Group review on post-COVID conditions, as many as 1/3 to 1/2 of the 231,987 Albertans with confirmed COVID-19 and any unconfirmed cases may be affected by post COVID symptoms lasting at least a month. This review found the literature included hospitalized and non-hospitalized patients, and community based data was limited, including self reported disease and symptoms in social media based surveys but lacking population based survey data.
- In the November review, 46 unique chronic symptoms were noted from the literature, which involved diverse bodily systems. In that review, fatigue, headache and dyspnea were the most common chronic symptoms between 4-6 weeks after diagnosis, and dyspnea and sleep impairments were noted from 8-12 weeks.
- Between November 2020 and March 2021, the Post COVID-19 Rehabilitation Response Taskforce developed an implementation strategy for a provincial Post COVID Rehabilitation Response Framework. This framework informs screening, assessment and referral for care

across the continuum to support COVID-19 survivors with persistent symptoms and rehabilitation needs. Management of these post acute symptoms may require novel approaches and considerations.[1]

- This rapid evidence review aims to support clinicians caring for patients during post COVID recovery and inform AHS based care planning. We sought to determine the current best evidence regarding the following elements of symptoms that persist or arise 30 days or more after COVID-19 diagnosis: appropriate terminology and definitions; available and validated screening tools; symptomatology (frequency); risk factors; impact of vaccination; impact on health services utilization; and, impact on patients' return to work.
- This evidence review is intended for clinicians and healthcare and public health decision-makers.

Key Messages from the Evidence Summary

- Terminology & Definitions (based on 66 articles)
    - There is heterogeneity in the literature and no clear international consensus on definitions and terminology for prolonged symptoms after acute COVID-19 infection.
    - At least 22 unique terms are used. Some terms have several different definitions. Common points of contention include (a) when the "clock starts" on timing; (b) how long symptoms must persist; and (c) whether mechanisms inform inclusion. International consensus work is ongoing to clarify terminology and definitions.
    - "Long COVID" is a colloquial, non-specific terminology (14 articles with 9 heterogeneous definitions) and is frequently used by patients and the media. Diverse definitions were related to its use as a blanket term, its origins in a patient-driven movement, and an implication of a specific time-limited phenomena with a specific set of symptoms, which may exclude some complications of severe acute COVID.
    - "Post-COVID syndrome" is used relatively consistently, especially with health organizations, to describe signs and symptoms attributable to COVID-19 infection that appear or persist 4+ weeks after diagnosis of infection.
        - Qualifiers to "post-COVID syndrome" inform timing: "chronic" relates to symptoms at 12+ weeks after diagnosis; "post-acute" relates to symptoms that persist at 4-12 weeks after diagnosis.
        - However, "post-COVID syndrome" is an older term that is becoming replaced with "Post-COVID condition or conditions", as this may not be syndromic in nature, with the same definition and qualifiers attached. This term appears to have potential emerging consensus from the Public Health Agency of Canada and the Centers for Disease Control.
        - Currently therefore, the term "post-COVID conditions" (short form PCC) has the most clear, consistent usage.
- Validated Screening or Assessment Tools (based on n=10 articles)
    - Use and utility of screening or assessment tools is not well developed, and these tools are not well validated. Thirteen tools were identified (n=10 studies); only the Short-Form-36 (SF-36) and Post COVID Functional Status (PCFS) Scale were used in ≥1 study. Most are used for assessment versus screening.
    - Four studies proposed the use of (or used) a suite of tools originally developed and validated in non-COVID settings. Six studies described bespoke COVID-19 specific assessment tools, most of which are not fully validated.
        - All proposed tools and strategies attempt comprehensive assessment processes covering the diverse potential symptoms of post-COVID conditions.

[1] https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-management.html

    - Two papers attempted construct validation of two different tools. The PCFS Scale had modest findings relating to its construct validity (n=1,939) (Machado et al., 2021). Machado et al (2021) found weak-to-strong statistical associations between functional status and all domains of the EQ-5D-4L (r: 0.233-0.661); complementary but not statistically significant decreases in the PCFS Scale were associated with increases in work productivity and activity impairment (Machado et al., 2021). Tran et al (2021) (n=351) described moderate or high construct validity of two complementary tools (Long COVID Symptom Tool (ST) and Long COVID Impact Tool (IT)) in the areas of functional status, quality of life and perceived health state. This evaluation used the PCFS Scale as the gold standard to examine construct validity around functional status. Other forms of validity have not been tested.
- <u>Symptomatology (based on n=28 articles)</u>
    - This question was addressed by a parallel, [living systematic review](#) completed by the Public Health Agency of Canada (PHAC). The PHAC did not include preprints and included articles until January 15, 2021. This Scientific Advisory Group review was more inclusive and included recent literature search until May 28, 2021.
    - The PHAC systematic review completed a meta-analysis on 28 observational studies that included individuals with laboratory-confirmed COVID-19. Most studies had less than 200 participants. Most studies included hospitalized patients, but findings were mixed of hospitalized and non-hospitalized patients. Minimum follow-up was 4 weeks.
    - Over 100 post COVID-19 conditions were reported in laboratory-confirmed individuals. Eighty-three percent (95%CI: 65-93%; *low certainty*) and 56% (95%CI: 34-75%; *very low certainty*) reported persistence or presence of one or more symptoms in the short- and long-term, respectively.
        - The most prevalent symptoms in both periods included: fatigue, general pain or discomfort, sleep disturbances, shortness of breath and anxiety or depression (point estimates ranging from 22-51%; *low* to *very low certainty*).
    - 19 studies were at moderate risk of bias and 9 were of high risk of bias (GRADE tool), with common sources of bias as participant selection and poor objectivity/ validity of outcome measurement.
    - Results have limited generalizability to patients who experienced COVID-19 as an outpatient.
- <u>Risk Factors (based on n=45 articles)</u>
    - Fourteen studies assessed chronic symptoms or manifestations of post-COVID conditions in patients who had been hospitalized for COVID-19; these cases involved primarily laboratory-confirmed diagnoses and used either administrative data or observation surveys (Table 3A). None of these studies used social media surveys.
    - Four studies of high quality according to the adapted Mixed Methods Appraisal Tool (MMAT) found **no** risk factors were statistically associated with post-COVID conditions. Together, these studies examined 2,877 patients, with each study looking at a mean of 719 patients; two studies were specific to hospitalized patients. This adds uncertainty to the identified risk factors.
    - The outcomes assessed included composite outcomes of death, readmission +/- new medical diagnoses, pulmonary function/CT scan findings/symptoms, and various assessments of recovery to baseline Acknowledging this heterogeneity, the most commonly-recognized risk factors that have statistically significant associations with post-COVID conditions in <u>hospitalized patients</u> include older age (at least >60 years) (n=5 studies); being female (n=4 studies); and presence of co-morbidities (including COPD, diabetes, heart failure and chronic kidney disease) (n=3 studies). Other noted risk factors by two studies each included White ethnicity, ICU admission, oxygen delivery in hospital, and being male.

        - Of all the included studies, only one focused exclusively on pediatric populations (Osmanov et al., 2021). Osmanov et al (2021) found that in pediatric populations, risk factors for post-COVID conditions include older age (12- 18 years old) and allergic disease.
    - There must be caution taken in interpreting the “female” and “male” risk factor, as the studies varied widely on whether they were capturing a gender identity variable or a physiological sex variable; and on whether this information was captured through self-report or health team interpretation.
    - The most commonly-recognized risk factors that have statistically significant associations with post-COVID conditions in studies involving <u>all types of COVID-19 patients</u> include older age (n=4 studies); multiple symptoms at acute infection (n=4 studies); ICU admission (n=3 studies); hospitalization (n=3 studies); being female (n=2 studies); and, presence of co-morbidities (n=2 studies). These risk factors do corroborate those found in the hospitalized-only populations. However, the age threshold for “older age” is not as clearly defined for the diverse populations in these studies.
- <u>Impact of Vaccination (based on n=2 articles)</u>
    - The body of evidence on vaccination implications for post-COVID conditions is very preliminary. Two moderate-quality, preprint articles (from UK) examined the relationship between vaccination and patient symptoms using observational cohort designs. Only 1 study directly addressed the impact of vaccination on post-COVID conditions.
    - This low quality evidence suggests that patients with post-COVID conditions (a) may experience more peri-immunization adverse events within 24 hours of vaccination, but (b) may experience improvements in the longer-term (e.g. symptom resolution or less progression of symptoms).
        - The timing, likelihood and nature of such improvements is unclear and requires further rigorous, scientific study.
- <u>Impact on Health Service Utilization (based on n=22 articles)</u>
    - 22 articles informed this synthesis. They fall into 3 categories: (1) empirical studies that inform health service use by patients after COVID-19 infection (n=9); (2) empirical studies that provide limited insights (n=4); and (3) review articles that provide generic guidance and hypothetical considerations (n=9).
    - Adult COVID-19 survivors have accessed the following health services after acute infection: emergency department, acute care, home care, outpatient specialty clinics, general practitioners, and telehealth lines.
    - Adult COVID-19 survivors often undergo additional diagnostic testing and imaging after acute infection, including chest X-ray, blood tests, spirometry, trans-thoracic echocardiogram, autonomic reflex testing, as well as functional assessments (e.g. 6-minute walking test).
    - A proportion (18% per Menges et al (2021); odds ratio between 1.5-3.0 per Ayoubkhani et al (2021)) of adult COVID-19 survivors appear to receive new diagnoses of chronic medical conditions after the acute infection. Whether this proportion is consistently greater than age-matched controls is unclear.
    - The frequency and duration of health service use post-COVID-19 is not well described with only 2 studies identified:
        - Lund et al (2021) suggested that most COVID-19 survivors have 1 general practitioner visit with a minority requiring 5 or more visits over the 6 months from diagnosis.
        - Hernandez-Romieu et al (2021) found that the frequency of health service utilization post-COVID was 2-24 visits per 10,000 person-days in 28–59 days after COVID-19 diagnosis relative to 1-4 visits per 10,000 person-days 120–180 days after diagnosis.

- The prevalence of health service utilization post-acute COVID-19 ranged from 16-40% up to 9 weeks post-discharge (D'Cruz et al., 2021); 29.4% for re-hospitalization across 20-weeks post-discharge (Ayoubkhani et al., 2021); 8.5% re-admission rate if sent home with supplemental oxygen (Banerjee et al., 2021); or 10% re-hospitalizations, 36% visited their general practitioner, and 7% called a medical hotline at least once (Menges et al., 2021).
- A limited number of studies suggest that health service utilization decreases over time. These studies obviously do not extend beyond one year. Other papers suggest that post-COVID conditions have a relapsing-remitting nature and that follow-up for one year minimum is suggested. It is not possible to anticipate with any certainty whether health service needs will continue indefinitely or for a time-limited period. The data suggesting increased chronic medical diagnoses after active COVID-19 suggests prolonged or indefinite utilization might need to be the default for health service planning.

- Impact on Patients' Return to Work (based on n=8 articles)
  - On the basis of survey data, it appears patients with post-COVID conditions experience reduced workforce participation (e.g. early retirement) (31-54%), absenteeism (e.g. missed days) (48-61%) and presenteeism (e.g. at work but less productive) (25-69%). No study comparatively assessed COVID-19 patients with and without identified post COVID conditions.
  - The prevalence of these work related issues was statistically lower at 6 months compared to 3 months from the time of acute infection (n=3 studies, 1 using administrative data).
    - A Norwegian study suggested that reduced workforce participation brought about by post-COVID conditions resolves by 3 months after post-onset of acute symptoms.

Committee Discussion

The committee reached consensus on the recommendations. For question 1, the committee provided feedback on the emerging consensus from public health organizations in Canada and US using "post-COVID conditions" over "post-COVID syndrome." It was conditionally recommended to align with this emerging, interim definition until international consensus is reached. For question 1a, the committee discussed the different purposes of screening versus assessment tools, that the tools identified in this review were assessment tools; the clinical role of such tools were also discussed and suggested clearer delineation between these. For questions 2 and 3, the committee discussed the importance of framing the evidence according to patient populations and methodology. In particular, research with only hospitalized patients cannot be generalized to community-only patients; and, research using laboratory-confirmed cases of COVID-19 has a level of rigour beyond that of the studies using self report surveys via social media. For questions 4, 5 and 5a, the committee discussed the lack of research available on these topics, and that the guidance or recommendations should discuss research gaps and opportunities for the health system.

Recommendations

1. Common terminology should be used to describe the phenomenon of persistent or emerging symptoms 4+ weeks after diagnosis with COVID-19. As consensus terminology evolves we recommend AHS adopt interim use of the term "post-COVID conditions", (PCC) with the qualifiers of "post-acute" or "chronic" as needed if focused on time periods 4-12 weeks or 12+ weeks after diagnosis, respectively.

   Rationale: This recommendation is based on evaluation of the evolving terminology and reflects current use in many organizations. This term has also retained a clear, consistent definition when used in the literature and by organizations. Other terms, such *as "Long COVID, which is commonly used by patients and in the media, are associated with diverse definitions and may be more strongly associated with specific symptom complexes, which is less inclusive of some medical complications and affects clarity.*

2. Evidence is insufficient to recommend specific standard assessment tools for identification of patients with elevated risk of PCC, to screen for PCC, or to follow patients with clinically diagnosed PCC. If one of the reported tools is widely adopted by the AHS Post COVID rehabilitation response framework group, we recommend development of a validation framework to assess the performance and utility of the tool in our population.
   Rationale: *The activities to support the implementation of the Post-COVID Rehabilitation Response Framework involve provincially consistent recognition of patients with post-COVID conditions. Currently the PCFS Scale is highlighted by this group, and although it has been cited in publications, it has only been assessed for construct validity thus far.*

3. Infrastructure and resources to sustain analysis of organization-wide utilization of health services by Albertan COVID-19 patients should be provided to clarify health service utilization impacts of post-COVID conditions in Alberta. This research should be longitudinal, and extend beyond one year.
   Rationale: A limited number of studies suggest that post-COVID conditions are associated with increased medical diagnoses and increased health services utilization, but that it may decrease over time. Because of the recency of the pandemic there are no present studies beyond 1 year in duration, with most much shorter. Some authors suggested that post-COVID conditions have a relapsing-remitting nature, although this was discussed more than empirically presented. Assessing health system impact requires a longer time frame of follow-up to determine the frequency, intensity and duration of increased health service use of people with positive COVID tests versus those without. As a provincial organization, Alberta Health Services is well-positioned to conduct this work and inform a substantial gap in the literature.

4. An update on this evidence review will likely be required in 6-12 months' time as the literature matures, particularly relating to the questions on definition and terminology, screening and assessment tools, vaccination impact, health services utilization, and return to work implications.
   Rationale: The previous review examined symptoms and risk factors for post-COVID conditions; the body of evidence has grown and become more consistent between the previous evidence review and this one on those two aspects. The body of evidence is inconsistent, limited and emerging for the other questions in this review. Definitive conclusions are difficult to make based on the current body of evidence.

Practical Considerations

Despite the emerging, inconsistent nature of the evidence, this rapid evidence review may inform decision-making although more robust evidence is needed.

1. While the validation evidence is lacking to identify any gold standard screening or assessment tools, the PCFS Scale is the most widely used as an assessment tool and evidence is evolving on its psychometric validity. The current utilization of the PCFS Scale in the Post COVID Rehabilitation Response Framework is reasonable based on the current evidence base however it has only been formally assessed for construct validity and its usefulness in informing clinical care is not known.

2. The available evidence on symptomatology and risk factors is described largely in hospitalized cohorts with varied post COVID outcomes of interest. More information is required prior to use of risk factor based tools to identify or screen for PCC. Higher quality evidence on risk factors (including in non-hospitalized patients), the probability that consideration of risk factors identify patients with PCC that would not have been identified otherwise, consideration of the impact of 'labelling' (i.e. informing someone they are at 'high risk' of PCC), and if early identification has a meaningful impact on health outcomes is needed. Preliminary risk factors have been identified for some post-COVID conditions based on current data (although due to the quality of the studies this is preliminary, and subject to bias and uncertainty). The more commonly identified factors (for rehospitalization, pulmonary function problems) include older age (60+), hospitalization, female sex, having co-morbidities, having multiple symptoms during the acute phase, and need for critical care support, and in two studies each, other potential risks were white ethnicity, being male, ICU admission, and needing oxygen in hospital.

3. There is insufficient evidence to confirm or refute any association between vaccination and post-COVID conditions symptomatology, with only two relevant preprint studies evaluated. One small study suggested that vaccinated individuals with PCC symptoms may be more likely to have improvement or at least plateau of their symptoms than unvaccinated individuals
4. There is emerging evidence that post-COVID conditions may result in increased usage of health services and impairment of some patients' capacity to return to work. The frequency and duration of these impacts is unclear based on the emerging evidence and more research is required.

Research Gaps

As stated above, there is a lack of robust research on the frequency and duration of symptoms across patient groups including in pediatric age ranges, where hospitalization is uncommon and the outcome of mild-moderate community based infection is not well assessed. Risk factors for the development of specific well defined post-COVID conditions are not well described. Stronger research in the future would corroborate self-report with administrative data; seek out both physiological sex and gender identities; and would ensure adequate representation from ethnic minorities as well as patients who did and did not experience hospitalization due to COVID-19. Further, evidence on how (and if) risk factors can reliably identify patients at higher risk who would not otherwise have been identified, and whether early identification improves outcomes, or may "label" patients with negative impacts is required. Other areas of need include the impact of vaccination on post COVID conditions, which may be able to be assessed within post vaccination surveillance infrastructure; the implications of post COVID conditions on health services utilization; and, the impact of post COVID conditions on patients' capacity to return to work are also not well described. It is recommended that upcoming research include appropriate control groups to allow for control of confounding factors. In addition, the onset date or time of diagnosis (rather than discharge date) should be when the "clock starts" on assessing time since acute infection, and would ideally look at key implications at several time-points in the post-acute (4-12 weeks) and chronic (12+ weeks) stage, and go further into 6-12 months post-diagnosis.

Strength of Evidence

The body of evidence varied greatly with the question at issue. This review included 7 distinct topics: terminology, screening tools, symptoms, risk factors, vaccination impact, health service utilization, and return to work implications. The quality of evidence on question 2 (symptoms) is addressed by the PHAC in its systematic review and will not be discussed herein.

According to the adapted MMAT tool (Hong et al., 2018), 44 articles were of high quality, 9 were of moderate quality and 13 were of low quality. This tool does not capture the full nuances of the literature and the opportunities for bias. The literature on risk factors was the most robust and informative. The literature on screening tools, vaccination impact, health services utilization and return to work implications was less robust. While articles spoke to some degree on terminology and definitions, the over-arching lack of consensus is not directly tied to evidence quality but rather the emerging nature of this syndrome and the pandemic illness as a whole.

Limitations of this review

The process limitations of this review centred primarily on the fact that there were 7 distinct questions that had to be addressed separately. The nature and time of the questions relative to the development and implementation of the search strategy meant that the removal of inapplicable articles happened at the reviewer-screening stage versus the librarian-search-strategy stage within a constrained turnaround time.

While there were 15 review articles, only one was a rigourous systematic review and most did not detail their search strategies. This introduces concerns on the ability of those studies to unbiasedly inform the questions at issue.

For the observational studies, whether observational cohorts or cross sectional surveys, there were several common concerns. Some studies framed their design as an observational cohort but lacked any longitudinal features in implementation and were in fact cross sectional in design. Due to time constraints, we listed the design as proclaimed by the authors. A challenge in synthesizing the articles was the variation in defining the phenomena and the “starting point” of the follow-up time period. Implications vary greatly between follow-up that starts at symptoms onset or diagnosis, versus those that start at time of discharge.

In the empirical studies, recall and selection bias were common concerns. For the latter, recruitment techniques did not favour generalizability with no study using a randomization approach. Some studies were site-specific, while others looked across a few hospitals and few considered population-level databases. Studies generally used convenience sampling or a sequential approach to participant recruitment/inclusion. Many studies relied on self-report, which is susceptible to recall bias. The few studies that used social media for recruitment had large sample sizes but limited generalizability, as only technologically-savvy individuals were recruited. Conversely, studies that used large administrative databases faced concerns on data accuracy. Only one study specifically targeted persons from minority communities, which queries the accuracy of findings related to ethnicity and diversity as the other studies may not be representative enough in that regard. Few studies had contemporaneous control groups. Potential confounding factors that limit any insight into causation include presence of pre-existing symptoms or conditions prior to COVID-19, treatment effects, impact of hospitalization or ICU admission, and the effects of the novel, global pandemic itself (e.g. barriers to care, psychosocial impacts).

There was great variability in the sample sizes, and this corresponding to the heterogeneous data collection techniques: survey, administrative data, social media activity. The smallest sample size was 10 and the largest was 740,182. The median sample size was 417, which is relatively robust. This heterogeneity provided significant challenges in synthesizing the evidence, particularly for the questions related to risk factors, health service utilization, and return to work impacts.

Given the emerging nature of the pandemic and timeline since the introduction of the virus, the recommendations rely on preprints and peer-reviewed articles in equal stead. This review should be read as a rapid, emerging evidence summary, rather than a rapid evidence review.

Databases were searched for English-language evidence published in 2020, thus, evidence from outbreaks in jurisdictions where English is not common has not been included in this review.

Summary of Evidence

Literature for this review was collected from a database search covering Medline (OVID), Embase, APA PsycInfo, PubMed, TRIP Pro, MedRxiv, BioRxiv, WHO Global Research Database on COVID-19, National Institute of Health and Care Excellence (NICE), Google, and Google Scholar. The search strategy involved combinations of keywords and subject headings including: “COVID-19” and “long-term.” Because of the diversity of questions in this review, the literature search strategy was very broad, and the screening process determined inclusion as relating to the research questions.

389 articles (peer-reviewed and pre-prints) were identified by KRS with references and abstracts provided for further review. 29 additional articles were identified *ad hoc*. 418 articles were each independently screened by two reviewers using the title and abstract. After a title, abstract and paper review where each paper was assessed by two writers independently, 269 articles were excluded. Of the 149 articles that went to full-text screening, 82 were excluded by consensus of two independent reviewers. A total of four writers were involved in screening and extraction.

The search was limited by the parameters of the questions: determining terms and definitions, or screening tools, or risk factors, or associations with vaccinations, or associations with health service use, or associations with return to work for symptoms that remain with COVID-19 survivors after the acute infection stage of COVID-19. The search was limited to English articles published 2020-current. Since this study was framed as an update to the November 30, 2020 review, articles were sought between November 4, 2020 and May 28, 2021. Articles were not excluded based on population. While the research questions framed chronicity as at 30 days or beyond the date of diagnosis, as discussed above, we did not limit the search strategy by specific date and sought articles that examined or considered symptoms in the non-acute infection period of COVID-19.

The included studies were: 1 systematic review, 29 observational cohort studies (7 were pre-review), 11 cross sectional survey studies (3 were pre-review), 14 review articles (including narratives style reviews) (1 was pre-review), 1 quality improvement report, and 7 other style of reports and articles were included (1 was pre-review). The jurisdictional distribution of the studies was as follows: UK (n=19), USA (n=12), Spain (n=7), Norway (n=4), Canada (n=3), China (n=3), Belgium (n=2), Denmark (n=2), Germany (n=2), Switzerland (n=2), and 1 each from Chile, France, Greece, Italy, Korea, Malaysia, Romania, Russia, Sweden, and the Netherlands.

Research Question 1 (Terms & Definitions): What are the most common terms for and definitions used for symptoms that persist after resolution of suspected or confirmed acute COVID-19 infection across jurisdictions and what is the suggested terminology for Alberta?

Evidence from secondary and grey literature
In this synthesis on terminology and definitions for the phenomena of interest (i.e. symptoms that persist after resolution of suspected or confirmed acute COVID-19), we included all articles. This included 13 grey literature articles. They come from reputable organizations in Belgium, Canada, Norway, the UK, the USA and the World Health Organization.

Evidence from the primary literature
This synthesis on terminology and definitions includes 56 primary literature articles (43 peer-reviewed, 12 preprints). These articles arise from the UK (n=19), USA (n=12), Spain (n=7), Norway (n=4), Canada (n=3), China (n=3), Belgium (n=2), Denmark (n=2), Germany (n=2), Switzerland (n=2), and 1 each from Chile, France, Greece, Italy, Korea, Malaysia, Romania, Russia, Sweden, and the Netherlands.

We used the adapted MMAT to assess the quality of the article as whole, and not specifically its approach to defining this phenomena of persisting symptoms after acute COVID-19 infection (Hong et al., 2018). With that in mind, 44 articles were of high quality, 9 were of moderate quality and 15 were of low quality.

Synthesis of the Information Relating to Question 1
There is much heterogeneity in the literature and no clear consensus on definitions for prolonged symptoms after acute COVID-19 infection. At least 22 unique terms are used; many individual terms have several different definitions attached to them (Table 1). Definitions contain nuanced differences that are highly debated.

There are distinctions on (a) when the "clock starts" on timing, (e.g. date of first symptoms vs. diagnosis vs. hospitalization vs. discharge); (b) the timing within the definition itself (e.g. a syndrome or condition begins at what time after the "clock starts": 4 weeks, 2 months, 12 weeks, 100 days); and (c) whether or not to include previously-known causes of recognized signs or symptoms (e.g. post-ICU syndrome is included vs. must be ruled out). The terminology is consistent in three areas: mentioning COVID-19 as the origins, language to describe the "after" or "consequential" nature of this condition, and definitions that encompass myriad symptoms and bodily system involvement.

Several articles call for international consensus to determine disease definition and classification. The World Health Organization described such consensus building activities as planned, but the results of such consensus-building activities were not available at the time of writing this review.

Importantly, 32 included articles did not attempt to define this phenomena, but rather focused on examining the long-term impacts, effects or health care needs after COVID-19 without using any terms or definitions. This may reflect a confluence of the fact that there is no clear definition with the fact that it is still early in this disease's trajectory and researchers are approaching complications and sequelae more openly.

"Long COVID" appears as a more colloquial, non-specific terminology. Fourteen articles used this terminology, but we recorded 9 heterogeneous definitions. It is recognized as a patient-derived terminology; but it is used inconsistently in the scientific literature. Sometimes, it is used (a) as a blanket term that covers many phenomena; (b) to refer the patient-driven campaign that brought this phenomenon to decision-makers' attention; or (c) a defined phenomenon with a specific time frame. Unfortunately, even with explicit definitions, the time frame associated with "Long COVID" is inconsistent (e.g. 28 days, 12 weeks, or 100 days).

The NICE guidance is one of the earliest published, and seems to be the starting point for most subsequent articles. "Post-COVID syndrome" or "Post-COVID condition(s)" is used relatively consistently, especially with recognized health organizations, to describe signs and symptoms attributable to COVID-19 infection that appear or persist 4+ weeks after diagnosis. The "condition" terminology is valued for its appreciation of the diversity in the frequency, nature and duration of the signs and symptoms of this phenomena.

a. "Chronic" or "Persistent" qualifiers are frequently added to "Post-COVID conditions" when those symptoms persist 12 or more weeks after diagnosis.
b. Qualifiers for symptoms that persist between 4 and 12 weeks after diagnosis include "post-acute COVID", "acute post-COVID", "subacute/ongoing COVID-19" and "ongoing symptomatic COVID-19."
c. The exception here is the 'oldest' reputable definition from the National Institute for Health and Care Excellence (NICE), which defines the Post-COVID conditions as "signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis."

While "Post-COVID syndrome" has some consistency in use, there has been critique of term "syndrome" as inaccurate. "Post-COVID conditions" has consistent definitions similar to "Post-COVID syndrome" but less critique with the diversity of symptoms captured in the plural form of condition, and the terminology as having a more accurate connotation for this emerging illness. In the face of no international consensus, the use of "post-COVID conditions" over the early use of "post-COVID syndrome" or "Long COVID" is being touted as the interim solution by the Centres for Disease Control[2] and the Public Health Agency of Canada.[3]

There is insufficient consistency in the evidence base to definitively suggest permanent terminology and definitions should be used in Alberta. The upcoming international consensus work will be most informative. In the meantime, and in the remainder of this report, we use the term "post-COVID conditions" because of its relatively consistent definition, and its encompassing both "post-acute" and "chronic" time periods in the trajectory of these conditions. Because this condition is seen in those who are hospitalized and not hospitalized, it is recommended that the "clock start" in the definition at the time of diagnosis (or at start of symptoms if a diagnosis date is unavailable). In the future, if a health system were to make determinations on service availability based on time periods (e.g. 4-12 weeks or 12+ weeks) then qualifiers such as "post-acute" or "chronic" be used, as consistent with the literature.

Table 1. Summary of Terminology and Definitions Examined

[2] Centers for Disease Control, "Post-COVID Conditions" at https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects.html.
[3] Public Health Agency of Canada, "Update on Long-Term Effects of COVID-19: Post COVID-19 Condition" (June 29, 2021).

Term	Definition	Citations
Not explicitly defined	-32 articles did not explicitly define this phenomenon -Almost all these articles framed their research as examining the long-term impacts, effects or health care needs after COVID-19. But, they did not use any of the terms listed in this table. - Castro-Avila et al (2021) and Hassenpflug et al (2021) focused on post-ICU syndrome, so did not speak to other phenomena.	(Augustin et al., 2021; Banerjee et al., 2021; Bellan et al., 2021; Bowles et al., 2021; Caronna et al., 2020; Castro-Avila, Jefferson, Dale, & Bloor, 2020; D'Cruz et al., 2021; Demelo-Rodríguez et al., 2021; Einvik, Dammen, Ghanima, Heir, & Stavem, 2021; Ekbom et al., 2021; Hassenpflug, Jun, Nelson, & Dolinay, 2020; Hernandez-Romieu et al., 2021; Iqbal et al., 2021; Islam et al., 2021; Lemhöfer et al., 2021; Lerum et al., 2020; Lund et al., 2021; Machado et al., 2021; Mei et al., 2021; O'Sullivan et al., 2021; Park et al., 2020; Pizarro-Pennarolli et al., 2021; Postigo-Martin et al., 2021; Public Health Ontario, 2021; Qu et al., 2021; Skyrud, Telle, Hernaes, Magnusson, & Skyrud, 2021; Taquet, Geddes, Husain, Luciano, & Harrison, 2021; Tudoran et al., 2021; Vaes et al., 2021; Whittaker et al., 2021; Wildwing & Holt, 2021; World Health Organization, 2021b)
Acute COVID-19 Potentially infection-related symptoms	-"signs and symptoms up to 4 weeks after disease onset, not explained by an alternative diagnosis: -defined by NICE, and used by 2 other articles OR -"symptoms up to 4-5 weeks"	(Fernández-de-Las-Peñas, Guijarro, Plaza-Canteli, Hernández-Barrera, & Torres-Macho, 2021; Maxwell, 2020; National Institute for Health and Care Excellence, Practitioners, & Scotland, 2020; Parkin et al., 2021)
Acute post-COVID symptoms	-"symptoms from week 5 to week 12" and "symptoms from week 12 to week 24"	(Fernández-de-Las-Peñas et al., 2021)
COVID-19 long haulers Long haulers Long-haul COVID Long-tail COVID	-" experience persistent symptoms for weeks or months after their COVID-19 diagnosis" -Yong et al (2021) reference other studies that define "Long-haul COVID" or "Long-tail COVID" as "symptoms lasting for >100 days"	(Hirschtick et al., 2021; Korompoki et al., 2021; Vehar, Boushra, Ntiamoah, & Biehl, 2021; Yong, 2020)
Chronic COVID-19	-"symptoms >12 weeks" OR -"chronic or post-COVID-19 syndrome, which includes symptoms and abnormalities persisting or present beyond 12 weeks of the onset of acute COVID-19 and not attributable to alternative diagnoses"	(Korompoki et al., 2021; Nalbandian et al., 2021; Yong, 2020)
Late sequelae of SARS-CoV-2 infection	-"Symptoms lasting for > 4 weeks after the initial infection or diagnosis"	(Yong, 2020)
Long COVID	-Term originated by patient groups	(Arnold et al., 2021; Ayoubkhani et al., 2021; Davis et al., 2021; Maxwell, 2020;

	-Has the most diverse usage, with many people using it with different definitions attributed. See below -Belgian Health Care Knowledge Centre (2021): “arbitrary” use of Long COVID OR -“patients with symptoms that persist or develop after the acute phase of a confirmed or suspected COVID-19” OR -Research & Analytics (Ontario) (2021) define Long COVID as the “persistence of any COVID signs and symptoms that continue or develop between four to 12 weeks after acute COVID-19, including both ongoing symptomatic COVID-19 and post-COVID-19 syndrome” OR -NICE (2021) says Long COVID “includes both ongoing symptomatic COVID-19 and post-COVID-19 syndrome. Long COVID may consist of a number of distinct syndromes, which could include post-ICU syndrome, post-viral fatigue syndrome, long-term COVID syndrome and permanent organ damage.” OR -Nurek et al. (2021) uses Long COVID but accepts terminology of “post COVID-19 condition” and “Post-Acute Sequelae of SARS-CoV-2.” OR -Osmanov et al. (2021) uses long COVID with post-COVID syndrome, and defines as “symptoms more than 6 months past acute phase.” OR -Raw et al. (2021) use research definition tied to vaccination: “Long-COVID was defined as symptoms persisting >2 months to vaccination.” OR -Sudre et al. (2021) use “symptoms persisting over 28 days: OR	Nurek et al., 2021; Public Health Ontario, 2021; Rando et al., 2021; Raw, Kelly, Rees, Wroe, & Chadwick, 2021; Research, 2021; Sudre et al., 2021; Tran et al., 2021; World Health Organization, 2021b; Yong, 2020; Zapatero & Hanquet, 2021)

	-Yong et al. (2021) found references defining Long COVID as “Symptoms lasting for > 2 months”	
Long post-COVID	-“symptoms from week 12 to week 24” -Authors indicate that must rule out potential sequelae related to hospitalization.	(Fernández-de-Las-Peñas et al., 2021)
Ongoing symptomatic COVID-19 Subacute symptomatic COVID-19	-“signs and symptoms, not explained by an alternative diagnosis, from 4 to 12 weeks after disease onset” OR -“subacute or ongoing symptomatic COVID-19, which includes symptoms and abnormalities present from 4–12 weeks beyond acute COVID-1” -defined by NICE, and used by 5 other articles	(Maxwell, 2020; National Institute for Health and Care Excellence et al., 2020; Office for National Statistics, 2021; Parkin et al., 2021; Sisó-Almirall et al., 2021)
Persistent post-COVID-19 symptoms	-“symptoms lasting longer than 24 weeks after the infection” -Authors indicate that must rule out potential sequelae related to hospitalization.	(Fernández-de-Las-Peñas et al., 2021)
Post-acute COVID-19 Post-Acute COVID19 Post-acute COVID-19 syndrome Post-acute effects of SARS-CoV-2	-“presence of symptoms >3 weeks from onset of COVID-19 symptoms) OR -“persistent symptoms that could be related to residual inflammation (convalescent phase), organ damage, non-specific effects from the hospitalization or prolonged ventilation (post-intensive care syndrome), social isolation or impact on pre-existing health conditions” OR -“ persistent symptoms and/or delayed or long-term complications of SARS-CoV-2 infection beyond 4 weeks from the onset of symptoms”	(Korompoki et al., 2021; Lund et al., 2021; Moreno-Pérez et al., 2021; Nalbandian et al., 2021; Public Health Ontario, 2021; Yong, 2020)
Post-acute sequelae of COVID-19 Post-acute sequelae of SARS-CoV-2 infection	-“at least three months past testing positive for SARS-CoV-2” OR -“sequelae at least 30 days beyond diagnosis”	(Al-Aly, Xie, & Bowe, 2020; Mermelstein et al., 2021)
Post-COVID-19 syndrome Post-COVID syndrome	-“signs and symptoms that develop during or after an infection consistent with COVID-19 which continue for more than 12 weeks	(Augustin et al., 2021; Ayoubkhani et al., 2021; Menges et al., 2021; Office for National Statistics, 2021; Parkin et al., 2021; Sisó-Almirall et al., 2021;

	and are not explained by an alternative diagnosis." -Some articles conflate long COVID and post-COVID syndrome (Ayoubkhani et al. (2021))	Vanichkachorn et al., 2021; World Health Organization, 2021b)

Research Question 1a (Validated Screening Tools): Are there validated screening or assessment tools for this phenomenon that may be used to identify patients requiring care linkage?

Evidence from secondary and grey literature

No secondary or grey literature was identified that addressed this question. The literature review for this question on validated screening or assessment tools is limited to primary literature or original research (including preprints).

Evidence from the primary literature

This synthesis is based on 10 primary literature articles (3 preprints, 7 peer-reviewed articles). The methodologies varied across the studies include observational cohorts (n=4), cross-sectional survey (n=2), review (n=2) and other (n=2). The research originated from the UK (n=4), as well as one study each from France, Germany, Russia, Spain, the Netherlands, and the USA. Table 1A overviews the key takeaways from these articles as relating to the availability, use and validation of screening or assessment tools for post-COVID conditions, while Table 6A in the Appendix contains the details information extracted from each article.

As demonstrated by this synthesis, the evidence on psychometric validation of screening tools is quite limited. We used the adapted MMAT to assess the quality of the article as whole, and not specifically its approach to screening tool validation (Hong et al., 2018). On the whole, the quality of these articles was high, with seven articles being high quality (Arnold et al., 2021; D'Cruz et al., 2021; Lemhöfer et al., 2021; Machado et al., 2021; O'Sullivan, 2021; Osmanov et al., 2021; Tran et al., 2021), 1 moderate quality (Postigo-Martin et al., 2021), and 2 of low quality (Parkin et al., 2021; Vehar et al., 2021).

Synthesis of the Information Relating to Question 1a

Approaches to use and validation of screening/assessment tools varies. The 10 included articles describe 13 distinct tools. Only two tools are mentioned more than once. All tools appeared more geared to assessment of patients who had COVID-19 rather than screening the general or COVID-19 populaces. First, the Short-Form-36 (SF-36) is a validated quality of life tool which is used independently (Arnold et al., 2021) or incorporated into a novel tool (C19-RehabNeS) (Lemhöfer et al., 2021). Second, the Post COVID Functional Status (PCFS) Scale is mentioned in 3 studies: (1) where it is tested for psychometric validity (Machado et al., 2021); (2) where it is used but not psychometrically tested (D'Cruz et al., 2021); and (3) where it is mentioned but considered not validated and not used (Vehar et al., 2021).

Four studies proposed the use of (or used) a suite of validated tools, which would cover the myriad potential symptoms and sequelae associated with post-COVID conditions (Arnold et al., 2021; O'Sullivan, 2021; Postigo-Martin et al., 2021; Vehar et al., 2021). The included tools often cover quality of life, functioning, cognition, fatigue and mental health.

Novel tools introduced in these articles as COVID-19-specific assessment tools include:

- C19-RehabNeS (Lemhöfer et al., 2021)
- Post-COVID Functional Status (PCFS) Scale (Machado et al., 2021)

- ISARIC COVID-19 Health and Wellbeing Follow Up Survey for Children (Osmanov et al., 2021)
- Covid 19 Yorkshire Rehab Screen (C19-YRS) (Parkin et al., 2021)
- Long COVID Symptom Tool (ST) and Long COVID Impact Tool (Tran et al., 2021)

Each tool aims to be comprehensive to cover the breadth and diversity of symptoms and functional impacts of post-COVID conditions. The C19-RehabNeS and ISARIC COVID-19 Health and Wellbeing Follow Up Survey for Children are presented and used, without any discussion or information on validity. The C19-YRS is described as recommended across the UK's National Health Service for outcome measurement for post-COVID clinics (Parkin et al., 2021). It is currently undergoing psychometric testing for construct validity, responsiveness and stability (Parkin et al., 2021).

Only two papers attempted (albeit initial) psychometric testing of two different tools. First, Machado et al (2021) (n=1939) investigated only construct validity of the PCFS comparing it to validated tools measuring quality of life (EQ-5D-5L), and work productivity (WPAI questionnaire). Regarding quality of life, weak-to-strong statistical associations were found between functional status and all domains of health-related quality of life using the EQ-5D-5L (r: 0.233–0.661) (Machado et al., 2021). Notably, the strongest association found was with the 'usual activities' domain of the 5-level EQ-5D questionnaire) (Machado et al., 2021). The WPAI findings revealed complementarity between gradual increases of activity impairment on the WPAI and decreases in functional status (Machado et al., 2021). However, the study was described as not having sufficient power to detect these "small but meaningful" differences (Machado et al., 2021).

Second, Tran et al (2021) (n=351) described the development of, and examination of the construct validity of, two complementary screening tools: Long COVID Symptom Tool (ST) and Long COVID Impact Tool (IT). Their study demonstrated moderate or high construct validity given moderate correlations to functional status (ST score rs = -0.39, p<0.0001; IT score rs = -0.55, p<0.0001) and perceived health state (MYMOP2 score and ST score moderate correlation at rs = -0.40, p<0.0001; MYMOP2 score and IT score high correlation at rs = -0.59, p<0.0001), and high correlations to quality of life (EQ-5D-5L rs = -0.59, p<0.0001; and EQ-5D VAS rs = -0.54, p<0.0001) (Tran et al., 2021). Concerningly, this study used the PCFS Scale to examine construct validity around functional status. The reliability of the two Long COVID tools (IT and ST) was strong given the test-retest reliability was high (ICC was 0.89 (95% CI, 0.88 to 0.90) (Tran et al., 2021).

In sum, there are myriad approaches to assessing patients to determine their experience of post-COVID conditions and potential care needs relating to post-COVID conditions. The PCFS Scale is the most prominently described and used tool, with modest findings relating to its construct validity. No truly validated tool has been identified for evaluation of post-COVID conditions at this point, however this is very likely to be rectified within the next 6 months.

Table 1A. Summary of Articles Informing Screening or Assessment Tools

Author	Study Details (Article Type, Country, Study Design)	Tools & Available Validation Data
(Arnold et al., 2021)	• Preprint • UK • Observational cohort	• Used previously validated survey tools • Quality of Life: Short-Form-36 (**SF-36**) • Mental Wellbeing: Warwick and Edinburgh Mental Wellbeing scores (**WEMWBS**)

(D'Cruz et al., 2021)	• Peer-reviewed article • UK • Observational cohort	• **Post-COVID Functional Status (PCFS) Scale** • Just used, did not try to validate it.

(Lemhöfer et al., 2021)	• Peer-reviewed article
	• Germany
	• Narrative review
		• **C19-RehabNeS**
		• Description: The C19-RehabNeS = 2 separate assessment tools: (i) the SF-36 on health-related quality of life; and (ii) the C19-RehabNeQ.
		• C19-RehabNeQ has 57 items assigned to 7 main categories:
		  • Time of infection (1 item)
		  • Health problems caused by SARS-CoV-2 (14 items)
		  • Treatment (9 items)
		  • Activity and participation (13 items)
		  • Quality of life and general health (6 items)
		  • Health service provisions (5 items)
		  • Personal information (9 items)

(Machado et al., 2021)	• Peer-reviewed article
	• The Netherlands
	• Cross-sectional Survey
		• **Post-COVID Functional Status (PCFS) Scale**
		• Description: The scale was designed to cover the entire range of functional limitations from: grade 0, "No functional limitations" to grade 4, "Severe functional limitations" and grade 5, "Death". The PCFS Scale stratification is composed of five scale grades:
		  • grade 0 (No functional limitations);
		  • grade 1 (Negligible functional limitations);
		  • grade 2 (Slight functional limitations);
		  • grade 3 (Moderate functional limitations)
		  • grade 4 (Severe functional limitations).
		• The final scale grade 5 'death', which is required to be able to use the scale as outcome measure in clinical trials, was left out for self-administered contexts.
		• Psychometric testing data: Investigated the construct validity of the PCFS Scale.

(Osmanov et al., 2021)	• Preprint • Russia • Observational cohort	• **ISARIC COVID-19 Health and Wellbeing Follow Up Survey for Children** • Description: captures demographics, parental perception of changes in their child's emotional and behavioural status, previous vaccination history, hospital stay and readmissions, mortality (after the initial index event), history of newly developed symptoms between discharge and the follow-up assessment, including symptom onset and duration, and overall health condition compared to prior to the child's Covid-19 onset.
(O'Sullivan et al., 2021)	• Peer-reviewed article • UK • Cross-sectional Survey	• **Remote COVID-19 Rehabilitation Assessment Tool** • No validation data. • Description: Incorporates a medical screening, identifying the acute course, severity and management of COVID-19. Identifies existence of post-COVID-19 symptoms, including pain, fatigue, sleep and mood, and functional limitations such as shortness of breath, exercise intolerance or cognitive problems on activities of daily living (ADLs) or occupation.

(Parkin et al., 2021)	• Peer-reviewed article • UK • Descriptive	• **Covid 19 Yorkshire Rehab Screen (C19-YRS)** • Description: 4-page tool. Asks patients to rate on scale of 0-10 how affected now versus pre-COVID on 19 domains including breathlessness, voice, swallowing, nutrition, mobility, fatigue, continence, cognition, pain, depression, and vocation. • C19-YRS recommended by NHS Clinical Guidance for use as an outcome measure in post-COVID-19 syndrome assessment clinics. • Work is ongoing to psychometrically validate the tool.

(Postigo-Martin et al., 2021)	• Peer-reviewed article
	• Spain
	• Review
		• **COVID-19 Prospective Surveillance Model (PSM)**
		• Meant for rehabilitation professionals
		• Description: Tool is more of a model. Divided into three sections: rapid screening, general assessment and specific assessments for each system likely to be affected.
		  ◦ (1) at the first evaluation, with rapid screening through exploratory questions;
		  ◦ (2) at general health assessment (vital signs, auscultation, dyspnea, body composition, physical activity level, sedentary lifestyle and quality of life); and
		  ◦ (3) at specific evaluation of cardiorespiratory, neuromuscular and mental levels.
		  ◦ The latter section includes reliable tools for making necessary assessments, cut-off points and orientation regarding treatment. Specific assessments are categorized as cardiopumonary, neuromuscular system and mental health

(Tran et al., 2021)	• Preprint
	• France
	• Cross sectional survey
		• Two tools: **Long COVID Symptom Tool (ST)** and **Long COVID Impact Tool**
		• Description:
		  ◦ Long COVID ST score reports the number of symptoms patients experienced over the last 30 days and has a theoretical range from 0 (no symptoms) to 53 (all symptoms identified during step 1).
		  ◦ Long COVID IT score has a theoretical range of 0 (no impact) to 60 (maximum impact) and represents the sum of item scores for the 6 questions related to the disease's impact on their personal activities, family lives, professional lives, social lives, their morale, and their relationships with care providers.
		• Paper is dedicated to development and validation of construct validity and reliability of the two tools (n=351). Qualitative patient work informed development.
		  ◦ The long COVID ST and IT scores were highly correlated (rs=0.54, p<0.0001) and did not seem to differ by time from symptom onset.
		  ◦ In sum, examinations of construct validity demonstrated moderate or high correlations with patients' quality of life, functional status, and perceived health state. Reliability was strong with an ICC ≥ 0.8 during the test-retest.

(Vehar et al., 2021)	• Peer-reviewed article	• Used previously validated screening measures for cognition and mental health (anxiety, depression and post-traumatic stress disorder).

	• USA • Review	• **The Montreal Cognitive Assessment (MoCA)** • **Hospital Anxiety and Depression Scale (HADS)** • **Impact of Event Scale-6** • Other testing includes medication reconciliation, screening for rehabilitation needs, and pulmonary function testing. • Authors discussed PCFS, but felt that "it has not been validated or widely implemented."

Research Question 2 (Symptomatology): After a diagnosis of COVID-19, which symptoms (physical and/or neuropsychiatric) are commonly noted to persist for at least 30 days after acute infection in children and adults?

The search strategy and literature review methods described in this review applied to all questions except for this one. The Public Health Agency of Canada (PHAC) was completing a living systematic review at the time of preparation of this Scientific Advisory Group Rapid Review. To avoid unnecessary duplication of efforts, it was determined that for this question on common symptomatology of post-COVID conditions, this review would summarize the PHAC review only.

The PHAC used a search strategy developed by the UK National Institute for Health and Care Excellence, and it was updated to search for new research published between October 2020 and January 15, 2021. The databases searched included Embase, Medline, PsycInfo, and Cochrane Central. Technically, this review is less up-to-date and covers different databases than the search strategy (PHAC did not include preprints) described herein. The living systematic review sought similar observational studies (n≥50) capable of meta-analysis, which was not a limitation in the review directed by the Scientific Advisory Group. The latter was more inclusive and heterogeneous compared to the former. Nevertheless, the strategies are comparable and both reputable. With recognition of these differences, the remainder of this section summarizes the key findings from the PHAC living systematic review. The PHAC review used the term "post COVID-19 conditions" for persistent or recurring symptoms at 4-12 and > 12 weeks.

The PHAC review can be found at https://www.medrxiv.org/content/10.1101/2021.06.03.21258317v1.

Evidence from secondary and grey literature
There was no secondary or grey literature included in this review.

Evidence from the primary literature
Of the 2807 unique citations, 36 observational studies met the inclusion criteria (after independent review by two screeners): 28 studies included prevalence data for individuals with laboratory-confirmed COVID-19 and 8 included prevalence data for individuals who were clinically-diagnosed with COVID-19. The PHAC review focused on the 28 laboratory-confirmed studies for their synthesis. The synthesis and findings provided by PHAC did not distinguish hospitalized versus non-hospitalized patients.

All studies were observational (cohort or cross-sectional), with samples sizes between 58 and 1733 individuals; most studies had n<200 (n=21 of 28). The majority were conducted in Europe (n=16), with the remaining in Asia (n=6), North America (n=3, 1 of which was from Canada) and others (3). Most articles recruited adults only (n=17), while a minority did not restrict recruitment by age (n=10). Only 1 study focused on a pediatric population. Forty-three percent of studies (n=12) only recruited participants who were hospitalized or admitted to the intensive care unit (ICU) due to COVID-19. Seventy-nine percent (n=22) of studies measured short-term outcomes (i.e., between 4-12 weeks from COVID-19 diagnosis) and 21% (n=6) measured outcomes beyond 12 weeks (5/6 measured outcomes up to 6 months).

Quality-wise, all studies of laboratory-confirmed COVID-19 had moderate to high risk of bias: 19 studies were at moderate risk of bias and the other 9 at high risk of bias using the GRADE tool. The most common sources of potential bias were participant selection (i.e. convenience samples or study population was not representative of the target population) and poor objectivity/validity of outcome measurement (i.e. many outcomes were self-reported or obtained using non-validated measures).

Synthesis of the Information Relating to Question 2

The PHAC review sought to clarify the prevalence of post COVID syndrome (terminology used in the review), including the frequency of symptoms, sequelae and impairments to daily living.

Over 100 post COVID-19 conditions were reported in laboratory-confirmed individuals. Eighty-three percent (95%CI: 65-93%; *low certainty*) and 56% (95%CI: 34-75%; *very low certainty*) reported persistence or presence of one or more symptoms in the short- and long-term, respectively. The most prevalent symptoms in both periods included: fatigue, general pain or discomfort, sleep disturbances, shortness of breath and anxiety or depression (point estimates ranging from 22-51%; *low* to *very low certainty*). Table 2 presents the most prevalent symptoms and frequencies as described in the PHAC review.

The PHAC interpreted their results as follows: “data indicate that a substantial proportion of individuals reported a variety of symptoms ≥4 weeks after COVID-19 diagnosis. Due to low certainty in the evidence, further research is needed to determine the true burden of post COVID-19 conditions.”

The PHAC recognized some evidence gaps and limits to their living systematic review. Most studies included adults or persons hospitalized or treated for moderate-to-severe COVID-19. The prevalence of post COVID syndrome in children, asymptomatic individuals, and those with mild COVID-19 (i.e. community only) may not be sufficiently represented in the results. Few studies reported beyond 12 weeks post-infection. Most studies had small sample sizes (< 200 participants) or were at risk of bias due to participant recruitment methods and outcome measures used. Most studies lack contemporaneous control groups, so causation is difficult and confounding likely. Possible contributing factors include presence of pre-existing symptoms or conditions prior to COVID-19, treatment effects, impact of hospitalization or ICU admission, and the effects of the novel, global pandemic itself (e.g. barriers to care, psychosocial impacts).

Table 2. Key Symptom Prevalence Findings for Post COVID Syndrome (per PHAC Living Systematic Review) in hospitalized adults with confirmed COVID-19

Data note: These results have very low or low certainty due to the low quality of available evidence, which was predominantly (not exclusively) from observational studies of hospitalized and critical care based populations with confirmed COVID-19, with all studies at graded at moderate to high risk of bias. Therefore, these results should not be extrapolated to outpatient populations; there findings have more generalizability to hospitalized patients.

<table>
<tr><th>Time Frame</th><th>Prevalent Symptoms</th></tr>
<tr><td>Short-Term (4-12 weeks after COVID-19 diagnosis)</td><td>Approximately 4 in 5 individuals (83%, 95% CI: 65-93%, low certainty) reported the persistence or presence of one or more symptoms in the short-term primarily after hospitalization for COVID-19.
The most prevalent symptoms in the short-term were:
Fatigue (51%, 95% CI: 39-64%, low certainty)
General pain or discomfort (40%, 95% CI: 24-58%, low certainty)
Shortness of breath (38%, 95% CI: 27-51%, very low certainty)
Sleep disturbances (36%, 95% CI: 10-74%, low certainty)
Anxiety (29%, 95% CI: 16-48%, very low certainty)
Cough (28%, 95% CI: 22-35%, low certainty).
52% percent of individuals (95% CI: 35-68%, low certainty) reported feeling ill or not back to full health in the short-term.</td></tr>
<tr><td>Long-Term (>12 weeks after COVID-19 diagnosis)</td><td>Approximately 3 in 5 individuals (56%, 95% CI: 34-75%, very low certainty) reported persistence or presence of one or more symptoms in the long-term primarily after hospitalization for COVID-19.
The most prevalent symptoms
Fatigue (47%, 95% CI: 27-68%, very low certainty)
General pain or discomfort (27%, 95% CI: 25-29%, low certainty)
Sleep disturbances (26%, 95% CI: 24-29%, low certainty).
Anxiety or depression (22-23%, low to very low certainty)
Depression or post-traumatic stress disorder (22-23%, low to very low certainty)
Shortness of breath (22-23%, low to very low certainty)
Hair fall/loss (22-23%, low to very low certainty)
The most prevalent complication from acute COVID-19 was unresolved impaired pulmonary function (42%, 95%CI: 25-29%, very low certainty).</td></tr>
</table>

Research Question 3 (Risk Factors): Which patients with COVID-19 are at highest risk of developing these chronic symptoms? Is the severity of COVID-19 disease (e.g. hospitalized; ICU) associated with the probability of developing post-acute COVID symptoms?

Evidence from secondary and grey literature

Six grey literature articles spoke on the topic of risk factors, and were included by two independent reviewers for this analysis. These articles came from reputable organizations in Belgium (Belgian Health Care Knowledge Centre), Canada (e.g. Public Health Ontario, Ministry of Ontario), Norway (Norwegian Institute of Public Health), and the World Health Organization.

Evidence from the primary literature

During the article screening process, 39 articles were included according to the established inclusion criteria (27 peer-reviewed, 5 preprint, in addition to the 6 grey literature articles described above). The study designs of these 38 articles include observational cohort (n=22), cross sectional survey (n=7), review (n=8) and systematic review (n=2).

These articles originated from across the globe: UK (n=8), USA (n=6), Spain (n=5), Canada (n=3, all reviews), China (n=3), Norway (n=3), and 1 each from Belgium, Denmark, Germany, Italy, Korea, Malaysia, Romania, Russia, Sweden, Switzerland, and The Netherlands. For the empirical studies, the median (minimum, maximum) sample size was 402 (10, 236,379). The mean (standard deviation) and median follow-up period for the empirical studies were 15.8 (9.7) and 12, respectively.

Using the below described adapted MMAT on the 38 included references (Hong et al., 2018), 28 articles were considered high quality (Al-Aly et al., 2020; Ayoubkhani et al., 2021; Banerjee et al., 2021; Bowles et al., 2021; Castro-Avila et al., 2020; D'Cruz et al., 2021; Hernandez-Romieu et al., 2021; Lund et al., 2021; Menges et al., 2021; Nurek et al., 2021; O'Sullivan, 2021; Vanichkachorn et al., 2021; Whittaker et al., 2021; Yong, 2020), 3 considered moderate quality, and 8 considered low quality. Common limitations of the empirical studies were that the recruitment techniques did not favour generalizability, concerns on recall and selection bias, and for some studies the sample sizes queried the accuracy of the statistical significance proclaimed.

For extraction, the writers and reviewers of this rapid review determined to include the review and systematic review articles as references, but they were not extracted or included as part of the synthesis. It should be noted, that we used the studies description to inform study design determination. Several observational cohorts on closer examination fell more in line with a cross sectional survey design, which some authors noted in their limitations section. Nevertheless, the extracted details are provided in full in the Appendix (Table 6B). In this section, Table 3A provides summaries of the studies that focused hospitalized patients (n=15 studies) and Table 3B summarizes the studies that focused on all types of COVID-19 patients (hospitalized and community-only experience) (n=24). It appears that no studies limited their examination to community-only experiences of COVID-19.

Synthesis of the Information Relating to Question 3

Studies Involving Only Patients Previously Hospitalized for COVID-19

Fourteen studies looked at the chronic symptoms or manifestation of post-COVID conditions in patients who had been hospitalized for COVID-19; these cases involved primarily laboratory-confirmed diagnoses and used either administrative data or observation surveys (Table 3A). None of these studies used social media.

Table 3C highlights the recognized risk factors from these studies. The most commonly recognized risk factors that have statistically significant associations with post-COVID conditions include older age (at least >60 years) (n=5 studies); being female (n=4 studies); and, presence of co-morbidities (including COPD, diabetes, heart failure and chronic kidney disease) (n=3 studies). Other noted risk factors by two studies each included White ethnicity, ICU admission, oxygen delivery in hospital, and being male. The male risk factor was associated with increased risk of post-traumatic stress disorder and risk of re-hospitalization. One study each noted risk factors associated with peri-acute manifestations: multiple symptoms in the acute infection, physical symptoms at discharge, and more than 2 emergency department visits up to 2 months before the acute infection.

Of all the included studies, only one focused exclusively on pediatric populations (Osmanov et al., 2021). Osmanov et al (2021) found that in pediatric populations, risk factors for post-COVID conditions include older age (12- 18 years old) and allergic disease.

There must be caution taken in interpreting the "female" and "male" risk factor, as the studies varied widely on whether they were capturing a gender identity variable or a physiological sex variable; and on whether this information was captured through self-report or health team interpretation.

Importantly, two studies of high quality according to the adapted MMAT found **no** risk factors were statistically associated with post-COVID conditions (Fernandez-de-Las-Penas et al., 2021; Liang et al., 2021).

Studies Involving Both Hospitalized and Non-Hospitalized Patients with COVID-19
The remaining 23 studies touched on all types of COVID-19 patients, including those who had been hospitalized and/or non-hospitalized patients. Ten articles were review articles that were not directly extracted.

Of the 13 articles, there was varying methodology with use of administrative data, cross-sectional surveys, or examination of social media application communities. Table 3D highlights the recognized risk factors from these studies. The most commonly recognized risk factors that have statistically significant associations with post-COVID conditions include older age (n=4 studies); multiple symptoms at acute infection (n=4 studies); ICU admission (n=3 studies); hospitalization (n=3 studies); being female (n=2 studies); and, presence of co-morbidities (n=2 studies). These risk factors do corroborate those found in the hospitalized-only populations. However, the age threshold for “older age” is not as clearly defined for the diverse populations in these studies. Three studies describe the risky age group as over 70, 54-64, and 40-59 each. Also, as described above, female as an age or gender is not clearly or consistently defined to inform interpretation. Twelve further, unique risk factors were noted by one study each (Table 3D). These generally related to some symptoms noted during the acute infection period: diarrhea, aguesia, anosomia, low baseline SARS-CoV-2 levels, no headache, and developing encephalopathy.

Importantly, two studies of high quality according to the adapted MMAT found **no** risk factors were statistically associated with post-COVID conditions (Einvik et al., 2021; Moreno-Perez et al., 2021).

The body of literature on risk factors for COVID-19 has evolved and strengthened since the first SAG review on the topic of chronic symptoms and risk factors post-acute COVID-19 (dated November 30, 2020). In the first review, four articles highlighted 3 risk factors: younger age, female, and previous diagnosis of a psychiatric disorder. With 28 empirical articles (not including the 9 reviews and 1 n=10 study), there is stronger, more corroborated evidence on at least some of the factors that may increase the likelihood of experiencing post-COVID conditions. The new batch of articles do not speak to mental health symptoms as much as the first review’s included articles. However, it appears that older age (not younger age) is the age-related risk factor; in this way, this new review refutes the previous set of evidence. This updated review points to several key risk factors: older age, being female, severity of acute infection (whether by requiring hospitalization, ICU admission, oxygen as well as by presenting with multiple symptoms), and the presence of co-morbidities (particularly chronic obstructive pulmonary disease (COPD)).

Table 3A. Summary of Studies assessing risks for morbidity after COVID-19 hospitalization.

Author	Study Details (Article Type, Country, Study Design)	Noted Risk Factors

<table>
<tr><td>(Ayoubkhani et al., 2021)</td><td>Peer-reviewed
UK
Observational cohort
Hospitalized COVID-19 patients, lab confirmed
Admin data</td><td>N=47,780
Aim: Estimate excess morbidity after severe COVID-19 (hospitalized) using administrative data (retrospective, matched cohort study)
Mean follow-up 20 weeks
RISK FACTORS:
Rates of all outcomes (e.g. death, readmission, respiratory disease, chronic kidney or liver disease) after discharge were greater in individuals with COVID-19 aged 70 or more than in those aged less than 70
Rates of all outcomes (e.g. death, readmission, respiratory disease, chronic kidney or liver disease) other than diabetes were greater in the white ethnic group than in the non-white group.
Rate ratios comparing patients with COVID-19 and matched controls were greater in individuals aged less than 70 than those aged 70 or more for all outcomes, however.
The largest differences in rate ratios were for death (14.1 (95% confidence interval 11.0 to 18.3) for age <70 years v 7.7 (7.1 to 8.3) for ≥70) and respiratory disease (10.5 (9.7 to 11.4) for age <70 v 4.6 (4.3 to 4.8) for ≥70).
Ethnic differences in rate ratios were greatest for respiratory disease (11.4 (9.8 to 13.3) for individuals in the non-white group v 5.2 (5.0 to 5.5) in the white ethnic group). Differences in rate ratios between men and women were generally small.
NOTE: focus on severe COVID-19, so likely many syndromes (e.g. post-ICU syndrome) implicated in post-discharge health service use.</td></tr>
<tr><td>(Bellan et al., 2021)</td><td>Peer-reviewed
Italy
Observational cohort
Hospitalized COVID-19 patients, lab confirmed</td><td>N=238
Aim: evaluate the prevalence of lung function anomalies, exercise function impairment, and psychological sequelae among patients hospitalized for COVID-19, 4 months after discharge.
RISK FACTORS:
In logistic regression analysis, risk factors associated with D_{LCO} less than 80% of expected (pulmonary function) at follow-up included female sex (odds ratio [OR], 4.33 [95% CI, 2.25-8.33]; P < .001), chronic kidney disease (OR, 10.12 [95% CI, 2.00-51.05]; P = .005), and the modality of oxygen delivery during hospital stay (OR, 1.68 [95% CI, 1.08-2.61]; P = .02).
Risk factors associated with D_{LCO} less than 60% at follow-up were female sex (OR, 2.70 [95% CI, 1.11-6.55]; P = .03), COPD (OR, 5.52 [95% CI, 1.32-23.08]; P = .02), and ICU admission during hospital stay (OR, 5.76 [95% CI, 1.37-24.25]; P = .02)
COPD was associated with an increased risk of physical impairment (OR, 12.70 [95% CI, 1.41-114.85]; P = .02), and higher D_{LCO} was associated with decreased risk of physical impairment (OR, 0.96 [95% CI, 0.94-0.98]; P < .001).</td></tr>
</table>

		• Authors describe **male sex** was the only factor independently associated with the presence of moderate to severe post-traumatic stress disorder symptoms (but in supplemental, the p=0.20).
(Bowles et al., 2021)	• Peer-reviewed • USA • Observational cohort • Hospitalized COVID-19 patients	• N=1,409 • Aim: To describe the home health recovery of patients with COVID-19 and risk factors associated with re-hospitalization or death • Mean follow-up 12 weeks • RISK FACTORS • Risk for re-hospitalization or death was higher among **male** patients (HR, 1.45 [CI, 1.04 to 2.03]); **White** patients (HR, 1.74 [CI, 1.22 to 2.47]); and **patients who had heart failure** (HR, 2.12 [CI, 1.41 to 3.19]), **diabetes with complications** (HR, 1.71 [CI, 1.17 to 2.52]), **2 or more emergency department visits** in the past 6 months (HR, 1.78 [CI, 1.21 to 2.62])

(D'Cruz et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
	• Hospitalized COVID-19 patients
		• N=119
		• Prospective, single-centre observational cohort
		• Follow-up 7-9 weeks post-discharge follow-up
		• Population: adults discharged after severe COVID-19 pneumonia (hospitalization ≥48hrs)
		• RISK FACTORS:
		  • **Comorbid obstructive lung disease** was associated with failure of mMRC recovery to baseline (OR 5.06, 95% CI 1.33–19.24; p=0.017) and PCFS grade ⩾2 (OR 2.84, 95% CI 1.01–7.98; p=0.047)
		  • **Pre-morbid obstructive lung disease** was associated with persistent (NRS ⩾1) breathlessness (OR 8.04, 95% CI 0.19–21.4; p=0.03) and cough (OR 3.43, 95% CI 0.98–12.0), but not burdensome (NRS ⩾4) breathlessness or cough (OR 1.97, 95% CI 0.60–6.47; p=0.26 and OR 2.27, 95% CI 0.38–13.69; p=0.37, respectively). There were no associations between the presence or absence of pre-existing comorbidities and persistent fatigue, sleep disturbance or pain.
		  • Ordinal logistic regression modelling was performed for the outcomes of return of mMRC grade to pre-COVID-19 baseline, PCFS grade ⩾2, positive mental health screening (PHQ-9 or GAD-7 >9 or Trauma Screening Questionnaire ⩾6) and physiological functional impairment (4MGS <0.8 m·s−1, STS repetitions <2.5th percentile or oxygen desaturation ⩾4% on STS) (table 3). Positive associations were found between **PCFS grade ⩾2, physiological impairment (4MGS <0.8 m·s−1 and STS repetitions <2.5th percentile) and positive mental health screening.** Critical care admission and need for IMV were associated with physiological functional impairment. Neither worst inpatient nor follow-up RALE score were associated with any modelled outcome measure.
		• LIMITS: not possible to do lung function on serial patients; conventional walking tests impractical; lack of standardized definition of post-COVID conditions; single centre

(Ekbom et al., 2021)	• Peer-reviewed
	• Sweden
	• Observational cohort
	• Hospitalized COVID-19 patients
		• N=60
		• Aim: prevalence of respiratory impairment as measured by pulmonary function tests (PFT) and associated factors in Intensive Care Unit (ICU)-treated COVID-19 patients 3–6 months after discharge.
		• RISK FACTORS
		  ◦ The most common impairment is reduced diffusing capacity, present in 45%. This risk increases with **age above 60**, **need for mechanical ventilation** and **time in ICU.**
		  ◦ Longer stay in the ICU as well as impaired FVC (<LLN) at follow-up were also associated with impaired DLCO. All these significant relations could be confirmed after further adjusting for age.
		• LIMITS: small sample size, no control, selection bias

(Fernández-de-Las-Peñas et al., 2021)	• Peer-reviewed • Spain • Observational cohort • Hospitalized COVID-19 patients	• N=1,950 • Population: Adults hospitalized with COVID-19 in first wave of 3 hospitals in Spain • Follow-up average 44.8 weeks • RISK FACTORS for post-COVID cough: **None found** • LIMITS: phone survey; no community-only perspectives; no data on diagnostics or severity; cross-sectional data

(Islam et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
	• Hospitalized COVID-19 patients
		• N=403
		• Population: Patients discharged during 4 month period from NHS
		• Follow-up average 8.6 weeks
		• RISK FACTORS
		  ◦ The standardized incidence rate (per 100 person-months) of readmission or death within 60 days of discharge was twice as high among **those aged 65 years** as those < 65 years [23.4 vs 10.6; standardized incidence rate ratio 2.21 (95% CI: 1.45–3.56)] and among **women** as men [34.9 vs 15.5; standardized incidence rate ratio 2.25 (1.05–4.18)].
		  ◦ There was no evidence of variation in incidence by ethnicity.
		• LIMITS: limited generalizability (1 region, limited diversity)

(Lerum et al., 2020)	• Peer-reviewed • Norway • Observational cohort • Hospitalized COVID-19 patients	• N=103 • Aim describe symptoms and pulmonary function 3-months following hospital admission for COVID-19 • Follow-up average 11.8 weeks for COVID-19 or viral pneumonia • RISK FACTORS: ◦ Age per year NOT associated with dyspnea (OR 0.81, p=0.231). **Age per year** associated with ground glass opacities (GGO) in chest CT (OR 1.81, p=0.004). Age per year NOT associated with parenchymal bands in chest CT (OR 1.19, p=0.376). • LIMITS: possible participation bias • STRENGTHS: multicenter, prospective design; age and prevalence similar between sample and population estimates; dyspnea is subjective so valuable to have diagnostic imaging.

(Liang et al., 2020)	• Peer-reviewed • China • Observational cohort • Hospitalized COVID-19 patients	• N=67 • Aim: to evaluate symptoms and lung function of COVID-19 survivors post-discharge • Follow-up 12 weeks • RISK FACTORS: **None found** • LIMITS: small sample; single site; large decline rate so selection bias; some patients had no prior medical history so unclear if pre-existing or novel diagnoses
(Mei et al., 2021)	• Peer-reviewed • China • Cross sectional survey • Hospitalized COVID-19 patients	• N=3,677 • AIM: to record and investigate possible post-COVID-19 sequelae and herd immunity • Follow-up average 20.6 weeks • RISK FACTORS: ◦ The incidence of post-COVID-19 sequelae among elderly COVID-19 survivors (**age ≥60 years**) was slightly increased compared to that of young COVID-19 survivors (age <60 years; relative risk = 1.05, 95% CI = 1.02–1.10, p = 0.007). • LIMITS: no control; not designed to determine impact of treatment

(Osmanov et al., 2021)	• Peer-reviewed
	• Russia
	• Observational cohort
	• PEDIATRIC
	• Hospitalized COVID-19 patients
		• N=518
		• Population: children previously hospitalized with Covid-19,
		• Single survey, follow-up average 36 weeks, ¼ had symptoms, at >6months 9% had fatigue, 6 % sleep issues, 5% disturbed sense of smell
		• RISK FACTORS:
		  ◦ **Age & Allergic disease:** In multivariable regression analysis, older age group was associated with persistent symptoms. When compared with children under two years of ages, those ages 6-11 years had an odds ratio of 2.74 (95% confidence interval 1.37 to 5.75) of persistent symptoms and those 342 12-18 years of age (OR 2.68, 95% CI 1.41 to 5.4) both vs. <2 years.
		  ◦ Another predictor associated with persistent symptoms was allergic diseases (OR 1.67, 95% CI 1.04 to 2.67).
		  ◦ Similar patterns were seen for children with co-existence of persistent symptoms from 2 or more categories: 6-11 years of age (OR 2.49, 95% CI 1.02 to 6.72), 12-18 years of age (OR3.18, 95% CI 1.43 to 8.11) both vs. <2 years. Allergic disease in children were also associated with a higher risk of long COVID

(Park et al., 2021)	• Peer-reviewed • Korea • Cross sectional survey • Hospitalized COVID-19 patients	• N=10 • Aim: to assess mental health in patients with COVID-19 • Population: 10 patients recovering from COVID-19 pneumonia after discharge • Follow-up 4 weeks • LIMITS: Too small of a sample to appropriately perform any quantitative analyses. • Due to size of sample, not including in synthesis above.
(Qu et al., 2021)	• Peer-reviewed • China • Observational cohort	• N=540 • Population: COVID-19 patients who had been discharged from designated hospitals • Follow-up average 12 weeks

	• Hospitalized COVID-19 patients	• RISK FACTORS • Results of logistic regression showed that **female** (odds ratio (OR): 1.79, 95% confidence interval (CI): 1.04–3.06), **older age** (≥60 years) (OR: 2.44, 95% CI: 1.33–4.47) and the **physical symptom after discharge** (OR: 40.15, 95% CI: 9.68–166.49) were risk factors for poor physical component summary; the physical symptom after discharge (OR: 6.68, 95% CI: 4.21–10.59) was a risk factor for poor mental component summary. • LIMITS: confounding factors; reliability of SF-36 is low in study; design is cohort but implementation like cross-sectional survey so difficult to make causal inferences.
(Sigfrid et al., 2021)	• Preprint • UK • Observational cohort • Hospitalized COVID-19 patients	• N=327 • Population: adults, admitted to hospital during study period with suspected COVID-19 and discharged at least 90 days previous • Follow-up average 31.7 weeks. • RISK FACTORS • **Females under the age of 50 years** were five times less likely to report feeling recovered (adjusted OR 5.09, 95% CI 1.64 to 15.74), were more likely to have greater disability (adjusted OR 4.22, 95% CI 1.12 to 15.94), twice as likely to report worse fatigue (adjusted OR 2.06, 95% CI 0.81 to 3.31) and seven times more likely to become more breathless (adjusted OR 7.15, 95% CI 2.24 to 22.83) than men of the same age. • LIMITS: not generalizable; selection bias; design is cohort but implementation like cross-sectional survey so difficult to make causal inferences.
(Tudoran et al., 2021)	• Peer-reviewed • Romania • Cross sectional survey • Hospitalized COVID-19 patients	• N=125 • Population: aged under 55 years; patients hospitalized during the first COVID-19 outbreak for a mild/moderate form; confirmed COVID-19 diagnosis • Follow-up average 8 weeks • RISK FACTORS • **age and BMI ($r = 0.81$ and $r = 0.67$, $p < 0.001$) correlated with COVID TCT score** ($r = 0.79$, $p < 0.001$). • LIMITS: Hospitalized so not generalizable to general population. Results very specific to physiological functioning versus patient experience of symptoms, which is what primarily discussed in post COVID syndrome. Other studies have noted that physiological functioning does not predict symptomatology in post-COVID conditions.

Table 3B. Summary of Key Details from Included Articles on Risk Factors Associated from Studies Including All Types of COVID-19 Patients (Hospitalized & Non-Hospitalized)

Author	Study Details (Article Type, Country, Study Design)	Noted Risk Factors

(Augustin et al., 2021)	• Peer-reviewed
	• Germany
	• Observational cohort
	• All types of COVID-19 patients
		• N=958
		• Aim: explore the incidence, diagnostic criteria and management of long-term health consequences at 4 and 7 months after mild courses of COVID-19 at post-COVID outpatient clinic
		• Mean 22 weeks follow-up (2 follow-ups at 4 and 7 months)
		• RISK FACTORS:
		  ◦ Used univariate logistic regression revealed several factors and symptoms during acute COVID-19 that were associated with an increased risk of post COVID syndrome after 7 months.
		    ▪ **Multiple symptoms (2+)** (odds ratio (OR) 1.28; 95% confidence interval (95% CI): 1.13–1.46)
		    ▪ **Diarrhea** (OR 2.19; 95% CI 1.21–4.00)
		    ▪ **Ageusia** (OR 2.16; 95% CI 1.36–3.43)
		    ▪ **Anosmia** (OR 3.79; 95% CI 2.36–6.09)
		    ▪ **Baseline IgG titers** between 1.2 and 4 (OR 2.06; 95% CI 1.19–3.53)
		  ◦ Male **gender** was associated with a lower risk for post COVID syndrome (OR 0.49; 95% CI 0.31–0.77).
		  ◦ In the multivariable logistic regression model **a lower baseline level of SARS-CoV-2** was associated with a higher risk of developing post-COVID conditions after 7 months IgG (initial IgG 1.2–4; OR 2.06 (95% confidence interval (95%CI) 1.19–3.53), p = 0.009 and initial IgG ≤1.1; aOR 2.05 (95%CI 0.96–4.37), p = 0.054).
		  ◦ **Anosmia** and **diarrhea** during acute COVID-19 were independent predictors for a PCS after 7 months with an OR of 5.12 (95% CI 2.43–10.76, p=<0.001) and 2.35 (95%CI 1.13–4.90, p = 0.023), respectively.

(Caronna et al., 2020)	• Peer-reviewed • Spain • Observational cohort • Sub-population; unclear re: hospitalization	• N=130 • Aim: To define headache characteristics and evolution in relation to COVID-19 and its inflammatory response • Mean follow-up 6 weeks • RISK FACTORS ◦ For patients with and without headache, for whom data were available at follow-up, and adjusting for age and gender, we observed shorter COVID-19 disease duration in the **headache group** (23.9 and 11.6 vs. 31.2 and 12.0 days; p=0.028). We did not observe any difference in mortality (no mortality in this subgroup) or hospital length of stay (9.1 and 9.0 vs. 10.9 and 9.0 days; p=0.854). • LIMITS: not all patients had confirmed COVID-19 diagnosis; single centre; one symptom of focus
(Demelo-Rodríguez et al., 2021)	• Peer-reviewed • Spain • Observational cohort • All types of COVID-19 patients	• N=100 • Aim: describe the long-term outcomes of COVID-19 patients with VTE and to analyze the risk factors of poor prognosis. • Mean follow-up 13.9 weeks • RISK FACTORS: ◦ Development of main outcome (death) was significantly associated with ICU admission (OR 8.437, p<0.001),

		anemia (OR 2.918 p0.021), thrombocytopenia (3.211 OR, p0.025), and cancer (OR 7.187, p0.024). • Risk of death or major bleeding was independently associated with **ICU admission** (HR 12.2; 95% CI 3.0-48.3), **thrombocytopenia** (HR 4.5; 95% CI 1.2-16.5), and **cancer** (HR 21.6; 95% CI 1.8-259) • LIMITS: Describes risk factors for negative outcomes from COVID-19 and VTE, not other forms of post-COVID conditions. More about complication of COVID-19 vs. "long COVID."
(Einvik et al., 2021)	• Peer-reviewed • Norway • Cross sectional survey • All types of COVID-19 patients	• N=583 • Aim: Determine if prevalence of symptom-defined PTSD 1.5-6 months after COVID-19 was higher in hospitalized than non-hospitalized subjects; and, determine risk factors for persistent symptoms of PTSD in COVID-19 survivors • Population: 17% Norwegian population (subjects of 2 parallel cohort studies); adults with positive COVID test • Follow-up: 4-8 weeks post-discharge or 1-4 months post-diagnosis for non-hospitalized • RISK FACTORS: **none found**
(Himmels, 2021)	• Grey Literature • Norway • Review • All types of COVID-19 patients	• Review (n=43 articles) • Exact studies and findings not extracted.
(Hirschtick et al., 2021)	• Peer-reviewed • USA • Cross sectional survey • All types of COVID-19 patients	• N=593 • Aim: to estimate the prevalence and correlates of post-acute sequelae of SARS-CoV-2 infection (PASC). • Follow-up average 8.6 weeks • RISK FACTORS • Respondents reporting **very severe (vs. mild) symptoms** had 2.25 times higher prevalence of 30-day COVID-19 ([aPR] 2.25, 95% CI 1.46-3.46) and 1.71 times higher prevalence of 60-day COVID-19 (aPR 1.71, 95% 1.02-2.88). • **Hospitalized** (vs. non-hospitalized) respondents had about 40% higher prevalence of both 30-day (aPR 1.37, 95% CI 1.12-1.69) and 60-day COVID-19 (aPR 1.40, 95% CI 1.02-1.93). • In unadjusted analyses, **older age** was statistically significantly associated with 30-day and 60-day COVID-19 prevalence. Respondents aged 55-64 years had 1.71 times higher prevalence of 30-day COVID-19 (Prevalence Ratio [PR] 1.71, 95% CI 1.19-2.47) and 2.14 times higher prevalence of 60-day COVID-19 (PR 2.14, 95% CI 1.27-3.59) relative to 18-34 year-olds. • **Annual household income** was a strong and significant predictor of 30-day COVID-19. Even after adjusting for demographic and clinical factors, respondents with an income less than \$75,000 had about 40% higher prevalence of 30-day COVID-19 than respondents with an income at or above \$75,000 (<\$35,000 aPR 1.40, 95% CI 1.09-1.79; \$35,000-74,999 aPR 1.38, 95% CI 1.09-1.75). Income was not

		significantly associated with 60-day COVID-19 in fully adjusted models. • LIMITS: skip pattern means missed data; lack of diversity so underestimate socioeconomic disparities; recall and response bias; severe experiences more likely to participate
(Iqbal et al., 2021)	• Peer-reviewed • UK • Systematic Review • All types of COVID-19 patients	• Systematic Review • Exact studies and findings not extracted.

(Machado et al., 2021)	• Peer-reviewed
	• The Netherlands
	• Cross sectional survey
	• All types of COVID-19 patients
		• N=1,939
		• Population: adults with confirmed or suspected COVID-19 infection from online panel or social media groups for long-COVID
		• 12 week follow-up
		• Completed a battery of online surveys relating to symptoms, health-related quality of life (EQ-5D-5L), impairment in work and activities, and functional status
		• RISK FACTORS:
		  ◦ Subjects with no functional limitations were **older** (unclear) compared to subjects presenting slight, moderate and severe functional limitations. Subjects with severe functional limitations (Grade 4 on the PCFS Scale) **presented lower BMI** compared to all other groups.
		  ◦ Other factors associated with poorer functional status were **marital status** (prevalence of category 'alone' highest in Grade 4) and **presence of comorbidities** (prevalence of '≥ 2 comorbidities' highest in Grade 4).
		  ◦ All associations found significant is p<0.05 for grades 3/4 vs. 0/1/2. Specific odds ratio not provided.

(Menges et al., 2021)	• Preprint
	• Switzerland
	• Observational cohort
	• All types of COVID-19 patients
		• N=431
		• Population: Adults with positive COVID-19 test
		• Mean follow-up 21.7 weeks
		• Study provides frequency of contact/utilization with the healthcare system after COVID-19 positive test. Offers some insight on risk factors for healthcare usage.
		• RISK FACTORS:
		  ◦ In multivariable analyses among initially symptomatic participants, we found evidence that **severe to very severe symptoms during acute illness** (OR 2.05, 95% CI 1.27 to 3.34, p=0.003) and the **presence of comorbidities** (OR 2.08, 95% CI 1.24 to 3.50, p=0.005) were associated with higher odds of not having recovered. **Females** were less likely to have recovered at 6-8 months after diagnosis compared to males (OR 0.53, 95% CI 0.33 to 0.85, p=0.009)
		  ◦ DYSPNEA: In multivariable analyses, we found evidence for an association of grade ≥1 dyspnea with **female sex** (OR 2.24, 95% CI 1.31 to 3.87, p=0.003), initial hospitalization (OR 4.17, 95% CI 2.23 to 7.91,

		p<0.001) and body mass index (OR 1.14 per unit increase, 95% CI 1.08 to 1.20, p<0.001), but not with age, initial symptom severity, smoking or respiratory comorbidity • LIMITS: testing capacity early in pandemic might mean more severely-affected population; risk of self-selection bias; lack of baseline; not all health service utilization (i.e. no specialty use or diagnostic services);

(Mermelstein et al., 2021)	• Preprint
	• USA
	• Cross sectional survey
	• All types of COVID-19 patients
		• N=401
		• Population: Adults, self-identify as Hispanic/Latinx and Black
		• Follow-up average 16 weeks
		• RISK FACTORS
		  • In a multivariable logistic regression model, **older age** (40-59 vs. 18-39 years: adjusted odds ratio [aOR] = 0.46 [95% confidence interval, 0.24 to 0.90]) and having **been hospitalized with COVID-19** (vs. not hospitalized: aOR = 0.28 [0.12 to 0.64]) were independently associated with a lower likelihood of recovery within 3 months.
		  • A similar pattern was noted in participants who were age 60 years and older vs. age 18-39 years, though differences were not significant.
		  • Participants who were hospitalized with COVID-19 were significantly less likely to return to usual health within 3 months (vs. not hospitalized: aOR 0.28, 95% CI 0.12 to 0.64).
		• LIMITS: self-report re: COVID-19 positivity; no population-based sampling strategy and short window to participate so limited generalizability;

(Moreno-Pérez et al., 2021)	• Peer-reviewed • Spain • Observational cohort • All types of COVID-19 patients	• N=277 • Aim: to analyze the incidence of Post-acute COVID-19 syndrome (PCS) and its components, and to evaluate the acute infection phase associated risk factors. • Population: adults with COVID-19 who attended emergency department • Follow-up average 10 weeks • RISK FACTORS: **none found**
(O'Sullivan et al., 2021)	• Peer-reviewed • UK • Observational cohort • All types of COVID-19 patients	• N=155 • Report early use of a rehabilitation tool for clinical practice • Mean 13 weeks follow-up • RISK FACTORS: • Patients who self-managed at home (n=100, 64.5%) were 75% less likely to receive laboratory confirmation (OR 0.25 (0.12 to 0.50), **Patients admitted to hospital wards and intensive care unit** were more likely to receive laboratory confirmation (OR 4.43 (1.84 to 10.63), p<0.01and OR 4.72 (1.20 to 18.56), p=0.03, respectively). • LIMITS: Results are highly focused on sub-analysis of patient groups who received a COVID test and those who did not, and location of acute care or no hospitalization was used as a proxy for risk.

(Postigo-Martin et al., 2021)	• Peer-reviewed • Spain • Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.
(Public Health Ontario, 2021)	• Grey Literature • Canada • Systematic Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.
(Health Ontario, 2021)	• Grey Literature • Canada • Systematic Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.
(Research, 2021)	• Grey Literature • Canada • Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.

(Sudre et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
	• All types of COVID-19 patients
		• N=4,182
		• Aim: to compare users of an app based on persistence of symptoms post-COVID-19
		• Follow-up average 6 weeks
		• RISK FACTORS:
		    • Individuals who reported **more than five symptoms in the first week** (the median number reported) were significantly more likely to go on to experience LC28, (OR 3.95 (CI 3.10–5.04)). This strong risk factor was predictive in both sexes and in all age groups. The five symptoms experienced during the first week that were most predictive of LC28 in the individuals with COVID-19 were: **fatigue** (OR 2.83 (CI 2.09–3.83)), **headache** (OR 2.62 (2.04–3.37)), **dyspnea** (OR 2.36 (CI 1.91–2.91), **hoarse voice** (OR 2.33 (1.88–2.90)) and **myalgi**a (OR 2.22 (1.80–2.73)). Similar patterns were observed in both sexes.
		    • **In adults aged over 70 years, loss of smell** (which was generally less common in this age group) was the most predictive symptom of long COVID (OR 7.35 (CI 1.58–34.22)) before fever (OR 5.51 (CI 1.75–17.36) and hoarse voice (OR 4.03 (CI 1.21–13.42).
		• LIMITS: Selection bias as only those who contribute to an app. Self-report so recall bias.

(Taquet et al., 2021)	• Peer-reviewed • US • Observational Cohort	• N=236,379 • Population: adult COVID-19 survivors • Follow-up average 24 weeks • RISK FACTORS

	• All types of COVID-19 patients	• The severity of COVID-19 had a clear effect on subsequent neurological diagnoses. But the incidences and HRs of these were greater in patients who had required hospitalization, and markedly so in those who had **required ICU admission** or **had developed encephalopathy**, even after extensive propensity score matching for other factors (eg, age or previous cerebrovascular disease) (all p values <0.001). • LIMITS: Focus on specific sequelae as complications rather than on symptomatology of post-COVID conditions. Size of sample queries if number of analyses led to statistical significance or if there was a statistically significant analysis.
(Vanichkachorn et al., 2021)	• Peer-reviewed • USA • Observational Cohort • All types of COVID-19 patients	• N=100 • Description of patient population at a specialty, rehabilitation-focused outpatient clinic (COVID Activity Rehabilitation Program) • Most patient presented at 12 weeks post-diagnosis • RISK FACTORS • The CARP PCS population appears distinct from those who suffer more severe cases of acute SARS-CoV-2 infection. While advanced age and the presence of several comorbidities are positively associated with increased mortality and hospitalization during acute infections, CARP patients were younger (mean age 45.4 years old + 14.2) than groups associated with severe infection, high mortality, and hospitalization. In addition, most PCS patients had no significant medical conditions prior to their SARS-CoV-2 infection, making it difficult to predict which patients may be at risk for PCS. • LIMITS: Single clinic; post hoc analysis; no odds ratio or p-values provided; not clear on who comparing too • Not included in synthesis above.
(Vehar et al., 2021)	• Peer-reviewed • USA • Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.

(Whittaker et al., 2021)	• Preprint
	• UK
	• Observational Cohort
	• Sub-population, including all types of COVID-19 patients
		• N=46,687
		• Aim: To investigate new primary care-recorded symptoms, diseases, prescriptions and healthcare utilization in patients post-acute COVID-19 infection, comparing outcomes between community-only and hospitalized patients
		• RISK FACTORS:
		  • Women had higher rates of fatigue and older women in particular had higher rates of joint pain compared to men.
		  • This is a preprint that describes the statistical results as available in appendices, however those appendices are not available.
		• LIMITS: only wave 2 patients; no access to statistical tests to view p-values and odds ratios.

(World Health Organization, 2021b)	• Grey Literature • Denmark • Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.
(Yong, 2020)	• Peer-reviewed • Malaysia • Review • All types of COVID-19 patients	• Review • Exact studies and findings not extracted.
(Zapatero & Hanquet, 2021)	• Grey Literature • Belgium • Review • All types COVID-19 patients	• Pragmatic review • Exact studies and findings not extracted.

Table 3C. High Level Summary of Recognized Risk Factors Associated with Increased Risk of Post-COVID conditions for Hospitalized Patients

Risk Factor	Special Note	# of References	References
Older Age (> 60 years)	-defined as > 60 years old (Ekbom et al, 2021; Mei et al, 2021; Qu et al, 2021) -defined as >65 (Islam et al, 2021) -defined as >70 (Ayoubkhani et al., 2021) -defined as increasing age per year (Lerum et al, 2021)	5	(Ayoubkhani et al., 2021; Ekbom et al., 2021; Lerum et al., 2021; Mei et al., 2021; Qu et al., 2021)
Female	-Sigfrid et al found the risk specific to females < 50 years old -Concerns across studies on whether looking at gender identity (as self-reported) or sex (as perhaps attributed in health records), and lack of consistency thereof	4	(Bellan et al., 2021; Islam et al., 2021; Qu et al., 2021; Sigfrid et al., 2021)
Presence of co-morbidities	-Heart failure (Bowles et al., 2021) -Diabetes (Bowles et al., 2021) -COPD (Bellan et al., 2021) -Chronic Kidney Disease (Bellan et al., 2021) -Pre-morbid lung conditions (D'Cruz et al., 2021)	3	(Bellan et al., 2021; Bowles et al., 2021, D'Cruz et al., 2021)
White ethnicity	-compared to non-White ethnicity	2	(Ayoubkhani et al., 2021; Bowles et al., 2021)
ICU Admission	-for Ekbom et al (2021), framed as time in ICU	2	(Bellan et al., 2021; Ekbom et al., 2021)
Oxygen delivery in hospital	-Ekbom et al (2021), specific to needing mechanical ventilation	2	(Bellan et al., 2021; Ekbom et al., 2021)
Male	-Bellan et al (2021): for increased risk of post-traumatic stress disorder	2	(Bellan et al., 2021; Bowles et al., 2021)

	-Bowles et al (2021): for increased risk of re-hospitalization		
Multiple Symptoms during Acute Infection	-Qu et al (2021) framed as having physical symptoms after discharge	1	(Qu et al., 2021)
Physical symptoms after discharge	-Qu et al (2021) framed as having physical symptoms after discharge	1	(Qu et al., 2021)
>2 emergency department visits in previous 6 months	-Study follow-up was 12 weeks, so included months prior to acute infection	1	(Bowles et al., 2021)
Older Age Pediatric	12-18 years old	1	(Osmanov et al., 2021)
Allergic Disease	Pediatrics-only study	1	(Osmanov et al., 2021)

Table 3D. High Level Summary of Recognized Risk Factors Associated with Increased Risk of Post-COVID conditions

Risk Factor	Special Note	# of References	References
Older Age (variably defined)	-defined as > 70 years old (Sudre et al, 2021; Augustin et al, 2021) -defined as 54-64 (Hirschtick et al, 2021) -defined as 40-59 years old (Mermelstein et al, 2021)	4	(Augustin et al., 2021; Hirschtick et al., 2021; Mermelstein et al., 2021; Sudre et al., 2021)
Multiple Symptoms during Acute Infection	-Hirschtick et al (2021) and Menges et al (2021) both specified that was having very severe symptoms in acute phase -Sudre et al (2021) defined as 5+ symptoms in the first week. The most predict symptoms in the first week were fatigue (OR 2.83 (CI 2.09–3.83)), headache (OR 2.62 (2.04–3.37)), dyspnea (OR 2.36 (CI 1.91–2.91), hoarse voice (OR 2.33 (1.88–2.90)) and myalgia (OR 2.22 (1.80–2.73)). -Augustin et al (2021) included 2+ symptoms	4	(Augustin et al., 2021; Hirschtick et al., 2021; Menges et al., 2021; Sudre et al., 2021)
ICU Admission	-for those hospitalized	3	(Demelo-Rodríguez et al., 2021; O'Sullivan et al., 2021; Taquet et al., 2021)
Hospitalized	-during acute infection	3	(Hirschtick et al., 2021; Mermelstein et al., 2021; O'Sullivan et al., 2021)
Female	-Concerns across studies on whether looking at gender identity (as self-reported) or sex (as perhaps attributed in health records), and lack of consistency thereof	2	(Augustin et al., 2021; Menges et al., 2021)

Presence of co-morbidities	-specifically cancer in (Demelo-Rodriguez et al., 2021)	2	(Demelo-Rodriguez et al., 2021; Machado et al., 2021; Menges et al., 2021)
Diarrhea	During acute infection	1	(Augustin et al., 2021)
Ageusia	During acute infection	1	(Augustin et al., 2021)
Anosomia	During acute infection Single study, but OR 5.12 (95% CI 2.43-10.76)	1	(Augustin et al., 2021)
Baseline IgG titer between 1.2-4	During acute infection	1	(Augustin et al., 2021)
Lower baseline level of SARS-CoV-2	During acute infection	1	(Augustin et al., 2021)
No headache	During acute infection	1	(Caronna et al., 2021)
Thrombocytopenia		1	(Demelo-Rodríguez et al., 2021)
Annual household income		1	(Hirschtick et al., 2021)
Marital Status	Being alone	1	(Machado et al., 2021)
Lower BMI		1	(Machado et al., 2021)
Encephalopathy	During acute infection	1	(Taquet et al., 2021)

Research Question 4 (Vaccination): Does COVID-19 vaccination impact the course of post-acute COVID symptoms?

Evidence from secondary and grey literature

No secondary or grey literature was identified that addressed this question. The literature review for this question on vaccination impact is limited to primary literature or original research (including preprints).

Evidence from the primary literature

This synthesis on the impact of vaccination on post-COVID conditions is based on 2 primary articles (2 preprints), both using observational cohort designs (Arnold et al., 2021; Raw et al., 2021). Both articles are from the UK. Table 4 contains the key takeaways from these articles, while detailed information extracted from each articles is found in Table 6C.

The body of evidence on vaccination implications for post-COVID conditions is very small and emerging, given the preprint status of the 2 articles detected. Using the below described adapted MMAT (Hong et al., 2018), both were considered moderate quality (Arnold et al., 2021; Raw et al., 2021).

Synthesis of the Information Relating to Question 4

Published, peer-reviewed literature on the implications of vaccination on post-COVID conditions is lacking. Only 2 articles were found that touch upon associations between vaccination and the symptoms of post-COVID conditions (Arnold et al., 2021; Raw et al., 2021).

A single study (n=66) sought to distinguish the symptom burden in post-discharge for COVID-19 (Arnold et al., 2021). For patients describing post-COVID symptoms, there were small, but statistically significant, increases in symptom resolution (23.2% vaccinated vs. 15.4% unvaccinated) and decreases in worsening symptoms (5.6% vaccinated vs. 14.3% unvaccinated) (p=0.035, each) (Arnold et al., 2021). Upon vaccination, about 41% of all study participants described transient (< 72 hour duration) systemic effects, often associated with immunization (including fever, myalgia, and headache) (Arnold et al., 2021). There was no significant variation by type of vaccine. Study limitations include recall bias and selection bias in that a vaccinated population may vary in significant ways from unvaccinated persons. As a single study of a small, previously-hospitalized cohort, the generalizability of this study is also questioned.

The other study (n=974) took a broader, and different, approach to explore whether previous COVID-19 infection (including those with post-COVID conditions) is associated with different frequencies of vaccination-related adverse events: myalgia, fever, fatigue, arthralgia, and lymphadenopathy (Raw et al., 2021). This study focused on health care workers (Raw et al., 2021). Prior COVID-19 infection, but not post-COVID conditions, is associated with increased risk of vaccination-related adverse events (Raw et al., 2021). The proportion of participants reporting at least one moderate-to-severe symptom was higher in the prior COVID-19 infection group (56% v 47%, Odds Ratio (OR) =1.5 [95%CI, 1.1–2.0], p=0.009). Confidence that these symptoms were vaccination related lies in the finding that symptom onset was mostly within 24 hours (75%) with no onset >48 hours. After controlling for age and sex, higher symptom number (1.61 (2.26) vs 0.89 (2.02) symptoms, d=0.34 [0.20-0.49], p<0.001) and severity (2.7 (6.65) vs 1.5 (2.21) symptom-days, d=0.41 [0.27-0.55], p<0.001) were significantly associated with reporting previous COVID-19 infection. Symptom number and duration was not significantly higher in those with post-COVID conditions after accounting for gender and age effects and no individual symptom was significantly associated with this condition. Study limitations include recall bias around adverse event and positive COVID-19 status, and non-responder bias. Also, the subset of survey respondents with post-COVID conditions is relatively small, which impacts the insights possible on this specific population. Similar to the other study discussion vaccination in persons who experienced COVID-19, this is a single study of modest size, specific to health care workers and with limited numbers of patients with post-COVID conditions, so the generalizability of this study is also questioned.

Table 4. Summary of Articles Informing Impact of Vaccination

Author	Study Details (Article Type, Country, Study Design)	Implications of Vaccination
(Arnold et al., 2021)	• Preprint • UK • Observational cohort	• N=66 • Population: patients originally hospitalized with COVID-19 at 1 UK hospital • Aim: assess change in quality of life and symptoms after vaccination • Mean follow-up 32 weeks • No significant worsening in quality of life or mental wellbeing metrics pre- vs. post- vaccination. • About 41% reported transient (<72 hour duration) systemic effects (including fever, myalgia and headache) • When compared to matched unvaccinated participants from the same cohort, those who had received vaccine had a small improvement in Long COVID symptoms, with a decrease in worsening symptoms (5.6% vaccinated vs. 14.3% unvaccinated) and increase in symptom resolution (23.2% vaccinated vs. 15.4% unvaccinated) (p=0.035). • Does not vary with type of vaccine.
(Raw et al., 2021)	• Preprint • UK	• N=974 • Population: health care workers receiving first dose of Pfizer vaccine at 3 hospitals

	• Observational cohort	• Aim: Determine frequency of adverse events after vaccination for patients with and without previous COVID-19 infection • The proportion of participants reporting at least one moderate-to-severe symptom was higher in the previous COVID-19 group (56% v 47%, Odds Ratio (OR)=1.5 [95%CI, 1.1–2.0], p=0.009). • Symptom onset was mostly within 24 hours (75%) with no onset >48 hours. After controlling for age and sex, higher symptom number (1.61 (2.26) v 0.89 (2.02) symptoms, d=0.34 [0.20-0.49], p<0.001) and severity (2.7 (6.65) v 1.5 (2.21) symptom-days, d=0.41 [0.27-0.55], p<0.001) were significantly associated with reporting previous COVID-19. • Logistic regressions controlling for age and sex showed five systemic symptoms were significantly associated with previous COVID-19 status: fever (OR 2.87, p=0.044), fatigue (OR 1.78, p=0.011), myalgia (OR 2.34, p<0.001), arthralgia (OR 2.25, p=0.004) and lymphadenopathy (OR 5.18, p=0.033). • Symptom number and duration was not significantly higher in those with Long-COVID after accounting for gender and age effects and no individual symptom was significantly associated with this condition.

Given the dearth of studies in this area, and that only 1 study truly addresses the question of this review, it is not possible to conclusively determine whether COVID-19 vaccination impacts the course of post-COVID conditions. Conservatively, evidence suggests that patients with post-COVID conditions (a) may experience more peri-immunization adverse events within 24 hours of vaccination, but (b) may experience improvements in the longer-term such as symptom resolution or less worsening of symptoms. The timing, likelihood and nature of such improvements is unclear and requires further rigorous, scientific study.

Research Question 5 (Health System Impact): What are the potential health system impacts and what could be the health care needs for patients with PASC (e.g. emergency department visits, hospital use, home care, rehab, community programs)?

Research Question 5a (Health System Impact): Is it anticipated that any increased health system resource use would continue indefinitely (chronic disease model) or would this decrease over time?

Evidence from secondary and grey literature

Four grey literature documents were identified that addressed these two questions related to health system impact and implications of post-COVID conditions. The documents arise from reputable organizations: the World Health Organization (WHO) (World Health Organization, 2021b); and governmental organizations or ministries in Canada (Research, 2021) and the UK (Maxwell, 2020; National Institute for Health and Care Excellence et al., 2020). Nevertheless, from the MMAT quality assessment, these articles, which are all reviews, were ranked of low quality.

Evidence from the primary literature

Eighteen primary literature articles informed this synthesis (3 preprints, 15 peer-reviewed articles). Most of the primary literature came from the UK (n=8), USA (n=6), and one each from European or Asian countries (Belgium, Denmark, Malaysia, Switzerland). The primary literature included primarily observational cohorts (n=10), as well as cross-sectional surveys (n=2), and 1 each of a review, systematic review, and quality improvement project. Three articles fell into an "other" category and were primarily descriptions of clinical programs. Table 5A provides an overview of the key findings from these articles relating to health system impact for post-COVID conditions, while Table 6D in the Appendix section contains the detailed information extracted from each document.

Using the below described adapted MMAT (Hong et al., 2018), 14 primary-literature articles were considered high quality (Al-Aly et al., 2020; Ayoubkhani et al., 2021; Banerjee et al., 2021; Bowles et al., 2021; Castro-Avila et al., 2020; D'Cruz et al., 2021; Hernandez-Romieu et al., 2021; Lund et al., 2021; Menges et al., 2021; Nurek et al., 2021; O'Sullivan, 2021; Vanichkachorn et al., 2021; Whittaker et al., 2021; Yong, 2020); 3 considered moderate quality (Hassenpflug et al., 2020; Vaes et al., 2021; Wildwing & Holt, 2021), and 1 low quality (Parkin et al., 2021).

Synthesis of the Information Relating to Question 5 & 5a

While there are a total of 22 articles included in this synthesis, they fall into three categories: (1) empirical studies that inform actual health service utilization by patients after COVID-19 infection (n=9); (2) empirical studies that provide limited insights into health service utilization and impacts (n=4); and (3) review articles that provide generic guidance and hypothetical considerations around health service impact (n=9). For the empirical studies, median (minimum, maximum) sample size was 431 (33, 73,435). The mean (standard deviation) of 9144.0(21404.4) demonstrate highly variable sample sizes due to the mix of studies relying on administrative data (n=8) versus primary data collection (n=6). Even within the administrative data studies, there was substantial variation as some studies looked across populations or systems, while others used administrative data to describe a small, local clinic population.

The follow up period in these studies was limited given evolution of the pandemic, with the mean (standard deviation) was 13.44 (6.16) and mean 13 weeks – however, studies varied on the starting point of these follow-up periods: first symptoms of COVID-19, data of diagnosis, or date of hospital discharge which introduced potentially several weeks of additional variability.

All of these studies (primary and secondary literature) focused on adult populations. They varied in that 9 included all types of COVID-19 patients, while 7 focused on only those who had been hospitalized with COVID-19, 3 considered only those who had community-only experiences of COVID-19, and 1 focused on a specific sub-population (visitors to a specific clinic).

While all studies are elaborated in Tables 5A and 6D, the following synthesis will highlight select article in-text for the three categories.

Empirical Studies

Nine empirical studies attempted to quantify the health service utilization of patient populations directly affected by COVID-19, whether solely in the community or in hospital (Ayoubkhani et al., 2021; Banerjee et al., 2021; D'Cruz et al., 2021; Hernandez-Romieu et al., 2021; Lund et al., 2021; Menges et al., 2021; Vaes et al., 2021; Vanichkachorn et al., 2021; Whittaker et al., 2021). Most studies looked at a mix of hospitalized and non-hospitalized patients.

Menges et al (2021) found that, over a mean of 21.7 weeks of follow-up, 40% (170 of 431) of adults who tested positive for COVID-19 self-reported having had at least one contact with the healthcare system (i.e., re-hospitalization, general practitioner visits, or medical hotline calls) related to COVID-19. Specific COVID-19-related usage included 10% had re-hospitalizations (of the 81 who were initially hospitalized for COVID-19), 36% visited their general practitioner, and 7% called a medical hotline at least once (Menges et al., 2021). Among those, the median number of general practitioner visits and hotline calls were 2 and 1, respectively (Menges et al., 2021). Only 33% of those who had not fully recovered indicated they did not seek out healthcare. New physician-diagnosed medical conditions were reported by 18%. Not having fully recovered (OR 3.53, 95% CI 2.14 to 5.86, p<0.001), experiencing grade ≥1 dyspnea (OR 2.35, 95% CI 1.40 to 3.99, p<0.001), fatigue (OR 1.61, 95% CI 1.04 to 2.50, p=0.03) and symptoms of depression (OR 2.13, 95% CI 1.32 to 3.45, p=0.002) were independently associated with having contact with the healthcare system (Menges et al., 2021). Some study limitations include risk of self-selection and recall bias, and lack of baseline for comparison.

Whittaker et al (2021) (n=46,687) used administrative data to determine healthcare utilization post-acute COVID-19. This study found increase utilization in hospitalized vs. community-only groups of COVID-19 survivors (Whittaker et al., 2021). The hospitalized group utilized more healthcare (including GP visits, referrals, emergency department, hospitalization) than the community group post-COVID-19, with a 2.7-fold difference in rates per 100,000 person-weeks [95%CI] between groups (52,775 [50,570 to 55,105] v. 19,405 [19,142 to 19,673]) in hospitalized and community groups, respectively (Whittaker et al., 2021).

Lund et al (2021) examined administrative data (n=8,983) after COVID-19 positive tests for a mean of 12 weeks. While 73.0% of non-hospitalized individuals with COVID-19 either visited their general practitioner, visited an outpatient clinic or were admitted to hospital, the number for COVID-19-negative controls was 77.1% (Lund et al., 2021). However, when PERR-adjusted risk ratios are presented, COVID-19-positive individuals have higher risks for general practitioner visits (1·18 [95% CI 1·15–1·22]) and outpatient clinic visits (1·10 [1·05–1·16]) compared to COVID-19-negative individuals (Lund et al., 2021). Among health-care users, most individuals had a single visit to the general practitioner or hospital outpatient clinic, and few individuals had five or more visits (Lund et al., 2021). There are no material differences between cohorts for emergency department visits (1·07 [0·88–1·30]) or inpatient hospitalizations (1·00 [0·87–1·14]; appendix pp 14–15) (Lund et al., 2021).

Hernandez-Romieu et al (2021) used administrative data (n=3,171) to clarify longer-term health care utilization of non-hospitalized adults after COVID-19 diagnosis (mean follow-up 21.7 weeks; range 1-6 months). In this population, 69% had 1+ outpatient visits (Hernandez-Romieu et al., 2021). Active COVID-19 diagnoses* (10%) and symptoms potentially related to COVID-19 (3%–7%) were among the top 20 new visit diagnoses; rates of visits for these diagnoses declined from 2–24 visits per 10,000 person-days 28–59 days after COVID-19 diagnosis to 1–4 visits per 10,000 person-days 120–180 days after diagnosis (Hernandez-Romieu et al., 2021). Among adults with one or more outpatient visits, 7,991 visits occurred 28–180 days after COVID-19 diagnosis, with a median of two (interquartile range = 1–4) visits per patient (Hernandez-Romieu et al., 2021). Among specialists visited, 1,627 (75%) patients visited a family, geriatric, or internal medicine provider, and 823 (38%) visited with a new specialist (Hernandez-Romieu et al., 2021). Common new specialty visits potentially related to COVID-19 included dermatology (16%), behavioral/mental health (11%), gastroenterology (11%), and cardiology (10%). Overall, 58 (3%) patients saw a pulmonologist; 41 (71%) of these patients had not been evaluated by this specialty in the 12 months preceding their COVID-19 diagnosis. Study limitations include a population of mostly privately-insured individuals who likely differ from general populations; a lack of control group; and lack of clarity when and how the COVID-19 diagnosis code was used across the system. Nevertheless, this study reveals a reduction in number of visits for COVID-19-related outpatient visits over time, especially compare weeks 4-8 to weeks 12-24.

Vaes et al (2021) elaborated self-reported health service utilization at 12 and 24 weeks post-onset of acute COVID-19 symptoms (n=1,556). More patients received physiotherapy or rehabilitation in the 3-6 months of follow-up period compared to the 0-3 months of follow-up (61.9% versus 31.8% and 11.7% versus 4.2%, respectively, p<0.001) (Vaes et al., 2021). However, between 3-6 months of follow-up, significant improvements were found in patients who did and did not receive physiotherapy or rehabilitation (Vaes et al., 2021). Patients receiving physiotherapy reported more symptoms (6 vs. 4, p<0.05) and a worse self-reported health (84.5% good vs. 91.7% good, p<0.05), functional status (grade 2.6 vs. 2.0, p<0.05) and quality of life (0.613 vs. 0.706 mean index EQ-5D-5L, p<0.05) compared to patients who did not receive physiotherapy or rehabilitation (Vaes et al., 2021). Similar differences found at 6 months (all p<0.05). This suggests that rehabilitation services may face increased demand further from the pandemic surges versus in the immediate aftermath. The quality of this paper was particularly questioned because the statistics reported in the article varied from that found in the article's supplemental material.

Banerjee et al (2021) completed a relatively short follow-up for 4 weeks to assess outcomes of those COVID-19 survivors sent home with home oxygen and nursing support post-discharge. This study demonstrated a 30-day readmission rate of 8.5% (95% CI, 6.2%-10.7%) with a median follow-up time of 26 days (interquartile range, 15-55 days), which was framed as lower than the overall post-acute care 30-day readmission rate for DHS patients (15.2%), as reported to California Department of Health Care Services in 2020 (Banerjee et al., 2021). This small study has many limitations include no control, very short follow-up period, and lack of contextualization of how many patients overall used this service. Nevertheless, the study would indicate some utility in use of home oxygen for COVID-19 survivors post-discharge, which would lead to health service impact in making such resources and services available.

Ayoubkhani et al (2021) looked at re-admission rates and new diagnoses post-discharge for patients who experienced severe COVID-19-related hospitalizations for an average of 20 weeks after discharge (n=47,780). After initial discharge, 29.4% of COVID-19 patients were readmitted to hospital (compared to 9.2% of controls with similar personal and clinical characteristics) (Ayoubkhani et al., 2021). Ayoubkhani et al (2021) determined that novel diagnoses after discharge with major adverse cardiovascular event, chronic liver disease, chronic kidney disease and diabetes were 3.0 (2.7 to 3.2), 2.8 (2.0 to 4.0), 1.9 (1.7 to 2.1), and 1.5 (1.4 to 1.6) times more frequent, respectively, in COVID-19 patients than in the matched control groups. It is likely that this population includes many syndromes (e.g. post-ICU syndrome) given its focus on severe COVID-19. Depending on one's definition of post-COVID conditions, this study may, or may not, inform the future health service impacts of post-COVID conditions.

Vanichkachorn et al (2021) (n=100) described the patient population at a specialty, rehabilitation-focused outpatient clinic. Most patients presented at 12-weeks post-diagnosis, and their health service utilization was noted. The clinic program included a function-focused interview, standard laboratory assessments and optional diagnostic tests or consultations (Vanichkachorn et al., 2021). Service-wise, common health services used included physical therapy (42%), occupational therapy (27%), brain rehabilitation consultation (22%), and infectious disease consultation (6%) (Vanichkachorn et al., 2021). Diagnostically, common imaging and testing ordered included chest X-ray (34%), spirometry with DLCO (27%), trans thoracic echocardiogram (29%), and autonomic reflex testing (20%) (Vanichkachorn et al., 2021). This study, while of limited generalizability, does provide insight on the health system cost and needs implications within specialty post-COVID clinics.

D'Cruz et al (2021) focused on post-discharge sequelae in the 7-9 week follow-up period (n=119). Using self-report, survey respondents indicated that 57 (48%) patients used hospital services following hospital discharge (D'Cruz et al., 2021). Herein, 23 (40%) attended outpatient appointments for monitoring of inpatient complications (hematology, renal, diabetes), 16 (28%) attended the emergency department, nine (16%) were re-hospitalized and nine (16%) attended planned outpatient appointments for pre-existing comorbidities. Thus, health service use post-discharge ranged between 16-40% up to 9 weeks post-discharge. This, like many other studies, lacks a control group and is susceptible to recall and selection bias (D'Cruz et al., 2021).

In sum, the following are some of the key insights from these articles (elaborated above in text and in Table 5A):

- Adult COVID-19 survivors have been recorded to access the following health services after the acute infection: emergency department, acute care, home care, outpatient specialty clinics, general practitioners, and telehealth lines.
- Adult COVID-19 survivors often undergo additional diagnostic testing and imaging after the acute infection. These tests include chest X-ray, blood tests, spirometry, trans thoracic echocardiogram, autonomic reflex testing, as well as functional assessments such as the six minute walking test.
- A regular proportion of adult COVID-19 survivors appear to receive new diagnoses of chronic medical conditions after the acute infection.
- The prevalence of health service utilization post-acute COVID-19 may range from 16-40% up to 9 weeks post-discharge (D'Cruz et al., 2021); 29.4% for re-hospitalization across 20-weeks post-discharge (Ayoubkhani et al., 2021); 8.5% re-admission rate if sent home with supplemental oxygen (Banerjee et al., 2021); or, 10% re-hospitalizations, 36% visited their general practitioner, and 7% called a medical hotline at least once (Menges et al., 2021).
- The frequency and duration of health service utilization post-COVID-19 is unclear. One study suggested that most COVID-19 survivors have 1 general practitioner visit with a minority requiring 5 or more visits (Lund et al., 2021). Another study suggested that 2-24 visits per 10,000 person-days in 28–59 days after COVID-19 diagnosis relative to 1–4 visits per 10,000 person-days 120–180 days after diagnosis (Hernandez-Romieu et al., 2021).
- A limited number of studies do suggest that health service utilization does decrease over time. However, these studies do not (and cannot) extend beyond one year. Other papers (cited below) highlight that post-COVID conditions have a relapsing-remitting nature and that follow-up for one year minimum is suggested. It is difficult to anticipate with any certainty whether health service needs will continue indefinitely or for a time-limited period. The data indicating many novel diagnoses of chronic health conditions suggests the former over the later.

Many of these studies had significant limitations, mostly due to a lack of control group or contextualization of the study participant utilization relative to a comparable or broader population. In addition, primary survey studies had concerns of recall bias and administrative data studies had concerns of inaccurate coding.

Empirical, but Limited Insight

Four articles are empirical in nature, but offered little insights into the exact utilization impacts of health services in the post-acute phase of COVID-19 (Al-Aly et al., 2020; Bowles et al., 2021; Castro-Avila et al., 2020; Hassenpflug et al., 2020). Castro-Avila et al (2020) provide qualitative interviews with clinicians, who describe current post-ICU practices with COVID-19 patients and how that is expected to continue into the future. Hassenpflug et al (2020) describe the care provided to those who transferred from acute care to a long-term care facility and the reasons for their short stays. The study's insights are quite limited as it is unclear what proportion of hospitalized COVID-19 patients require such care.

Al-Aly et al. (2020) performed a secondary data analysis (n=73,435) on never-hospitalized COVID-19 survivors (vs. controls) for around 18 weeks follow-up. The study reports increases in novel medication and medical diagnoses during follow-up, but does not clarify the size or frequency of such new health needs nor their impact on health service utilization (Al-Aly et al., 2020).

Bowles et al (2021) examined home care service utilization post-discharge for adult COVID-19 survivors (n=1,409). The majority (94%) of patients were discharged from home care after an average of 32 days of care (SD, 25.7); 1241 (87%) were discharged without any adverse events (re-hospitalization or death) (Bowles et al., 2021). More than half (57%) of those re-hospitalized returned to home care and were subsequently discharged (n= 78) (Bowles et al., 2021). Patients received an average of 11.1 home-care visits (95% CI, 10.8 to 11.4 visits), with 76% being in-person and 16% by phone or 8% by tele-video (Bowles et al., 2021). The home-care services were provided mostly by registered nurses (52%) or physical therapists (37%), but occasionally by social workers, occupational therapists, or speech language pathologists (Bowles et al., 2021). There are no controls or contextualization to determine how many hospitalized patients with COVID-19 required home care, this study does provide insights on the service utilization of those that do.

These studies perhaps best complement the next category of papers that provide general guidance to health systems on preparing for care of patients with post-COVID conditions.

General Guidance for Post COVID-19 Care

Nine articles, whether reviews or other study designs, offered general guidance on health service structuring and clinical approaches (Maxwell, 2020; National Institute for Health and Care Excellence et al., 2020; Nurek et al., 2021; O'Sullivan, 2021; Parkin et al., 2021; Research, 2021; Wildwing & Holt, 2021; World Health Organization, 2021b; Yong, 2020). These studies suggest the following:

- Prepare health systems with clear clinical pathways to support assessment and management of post-COVID conditions
- Ensure that care of patients with post-COVID conditions is multidisciplinary and integrated, with involvement of general practitioners, rehabilitation providers, and medical specialists
- Ensure that clinicians and patients are aware of the myriad bodily systems that can be implicated and affected by post-COVID conditions, as well as the relapsing-remitting nature of the syndrome
- Promote the use of patient-centred care principles and practices such as shared decision-making and patient-centred goal identification

- Make self-management information and advice readily available for those affected by post-COVID conditions
- Enable effective assessments by empowering clinicians with in-person opportunities as appropriate
- Recognize that traditional approaches to rehabilitation may need to be modified in the context of post-COVID conditions based on patient abilities
- Recognize that, while appropriate frequency and duration of follow-up of patients post-COVID is not clearly defined, one review recommended at least seven interactions (4 in-person) between health care providers and patients in the first 12 months, and likely four instances of follow-up assessment and imaging (i.e. CT scan, six-minute walk tests, blood tests, and antibody tests).

None of these recommendations were grounded in empirical evidence that involved patients post-COVID (whether cited studies or their own empirical work). Nevertheless, they represent expert opinions on how health systems may best approach the care of their population of individuals with post-COVID conditions.

Table 5A. Summary of Articles Informing Implications for Health Service Utilization

Author	Study Details (Article Type, Country, Study Design)	Implications around Health Services

(Al-Aly et al., 2020)	• Peer-reviewed
	• USA
	• Observational Cohort
	• COVID-19 negative controls, community and hospital
		• N=73,435
		• Secondary analysis of administrative data from Veterans' Affairs, included negative-outcome controls (
		• Median follow-up 18 weeks
		• Increased novel use of medication and medical diagnoses after COVID-19 infection even when never-hospitalized. Study does not clarify what health services are used to "get" to those diagnoses.
		  ◦ Observed an increased risk of the incident use of several classes of medication, including pain medications (opioid and non-opioid), antidepressant, anxiolytic, antihypertensive, anti-hyperlipidemic and oral hypoglycemic drugs and insulin.
		  ◦ An increased risk of a broad array of specific clinical manifestations that include acute coronary disease, arrhythmias, acute kidney injury, chronic kidney disease, memory problems and thromboembolic disease.

(Ayoubkhani et al., 2021)	• Peer-reviewed
	• UK
	• Observational Cohort
	• hospitalized, lab confirmed
		• N=47,780
		• Aim: Estimate excess morbidity after severe COVID-19 (hospitalized) using administrative data
		• Mean follow-up 20 weeks
		• Increased rates of re-admission and new diagnoses post-discharge for severe COVID-19 hospitalization. Study does not clarify what health services are used to "get" to those diagnoses.
		  ◦ After admission to hospital for COVID-19, 29.4% were readmitted (compared to 9.2% of controls with similar personal and clinical characteristics in control)
		  ◦ Those with COVID -19 were diagnosed with major adverse cardiovascular event, chronic liver disease, chronic kidney disease, and diabetes after discharge

		from hospital 3.0 (2.7 to 3.2), 2.8 (2.0 to 4.0), 1.9 (1.7 to 2.1), and 1.5 (1.4 to 1.6) times more frequently, respectively, than in the matched control group. • NOTE: focus on severe COVID-19, so likely many syndromes (e.g. post-ICU syndrome) implicated in post-discharge health service use.

(Banerjee et al., 2021)	• Peer-reviewed
	• USA
	• Observational Cohort
	• hospitalized, lab confirmed
		• N=621
		• Aim: Assess outcomes post-discharge with supplemental home oxygen (and nursing education)
		• Follow-up about 4 weeks
		• Study details mortality and readmission rate for patients post-COVID19 who received home oxygen. Does not indicate % of overall patients who used this, just outcomes of the ones that did use home oxygen.
		  • The all-cause mortality rate was 1.3% (95% CI, 0.6%-2.5%) and the 30-day return hospital admission rate was 8.5% (95% CI, 6.2%-10.7%) with a median follow-up time of 26 days (interquartile range, 15-55 days).
		  • The observed 30-day readmission rate for these home oxygen patients was also lower than the overall post-acute care 30-day readmission rate for DHS patients (15.2%), as reported to California Department of Health Care Services in 2020.
		  • LIMIT: no control in this study and short follow-up period

(Bowles et al., 2021)	• Peer-reviewed
	• USA
	• Observational Cohort
	• Hospitalized COVID-19 patients
		• N=1,409
		• Aim: Describe home health recovery of adults with COVID-19 and risk factors associated with re-hospitalization or death
		• Mean follow-up 12 weeks
		• Study elaborates usage of home health care services, including average visits and type of therapy used. No control comparison so difficult to predict how many will need home health care, but for those that go it does provide insights.
		  • Most visits (76%) were in person, 16% by telephone, and 8% by tele-video. Registered nurses provided 52% of the visits, physical therapists provided 37%, and the remainder were provided by social workers and occupational and speech therapists.
		  • The patients received average of 11.1 visits.
		  • 137 (10% [CI, 8.1% to 11.2%]) were re-hospitalized.
		  • After an average of 32 days of care (SD, 25.7), 94% of patients with COVID-19 in home health care were discharged (n= 1319); 1241 (87%) were discharged without any adverse events (re-hospitalization or death). More than half (57%) of those re-hospitalized returned to HHC and were subsequently discharged (n= 78)

(Castro-Avila et al., 2020)	• Peer-reviewed • UK • Sequential mixed-methods (qualitative)	• N=193 care staff and GPs • Sequential mixed methods (online survey and interviews) • Aim: Identify follow-up services available during and after UK's first wave of COVID-19 pandemic, and views of critical care staff and GPs on patients' future needs. • Population: critical care staff and GPs • Study describes clinician's perspectives on changes to health service provision in first wave of COVID-19. See post-

		ICU and rehabilitation support important. But, no metrics on actual utilization. Most care provided virtually, but not considered adequate by staff. ◦ Barriers to follow-up care service provision: funding complexities, remit and expertise, and communication between ICU and community services.
(D'Cruz et al., 2021)	• Peer-reviewed • UK • Observational Cohort • hospitalized, lab confirmed	• N=119 • Aim: investigate sequelae of severe COVID-19 pneumonia (hospitalization ≥48hrs), and identify risk factors • Follow-up 7-9 weeks post-discharge follow-up • Study noted hospital service use post-discharge and found 16-40% used some services. Time frame is lacking and no controls. ◦ 57 (48%) patients used hospital services following hospital discharge: 23 (40%) attended outpatient appointments for monitoring of inpatient complications (hematology, renal, diabetes), 16 (28%) attended the emergency department, nine (16%) were re-hospitalized and nine (16%) attended planned outpatient appointments for pre-existing comorbidities.
(Hassenpflug et al., 2020)	• Peer-reviewed • USA • Quality Improvement • hospitalized, lab confirmed	• N=41 • Aim: describe first series of patients with COVID-19 admitted to post-acute hospital • Based on administrative data • Median length of stay at post-acute hospital: 6 weeks • Study unclear on what proportion of hospitalized patients go to post-acute hospital. Few insights on health service utilization. ◦ Of 194 patients transferred to post-acute hospital during study period, 41 (21%) were admitted for continued recovery from confirmed COVID-19 pneumonia. ◦ Upon evaluation by the consulting pulmonologist on admission to facility, patients were determined not to be weaning candidates for the following reasons: physiologic instability (unmet readiness to wean parameters), and poor mentation or neurocognitive disorders. • LIMITS: Small cohort, unique population, relatively short follow-up, and unclear on service utilization fully in long-term care.
(Hernandez-Romieu et al., 2021)	• Peer-reviewed • USA • Observational Cohort • Non-hospitalized	• N=3171 • Aim: clarify longer-term health care utilization and clinical characteristics of non-hospitalized adults after COVID-19 diagnosis • Mean follow-up 21.7 weeks • Study provides frequency of contact/utilization with the healthcare system in the 28-180 days after COVID-19 diagnosis. Offers some insight on usage over time. ◦ 69% had one or more outpatient visits during the follow-up period of 28–180-days. ◦ Among adults with one or more outpatient visits, 7,991 visits occurred 28–180 days after COVID-19 diagnosis, with a median of two (interquartile range = 1–4) visits

		per patient. Fewer than 2% (32) of patients were hospitalized 28–180 days after COVID-19 diagnosis. More than two thirds of patients (1,617; 68%) had visits for a new primary diagnosis. Among specialists visited, 1,627 (75%) patients visited a family, geriatric, or internal medicine provider, and 823 (38%) visited with a new specialist. • COVID-19–related visits declined from 24 per 10,000 person-days during the 28–59-day interval to fewer than two per 10,000 person-days during the 120–180-day interval. Visits per 10,000 person-days for symptoms potentially related to COVID-19 declined during these same intervals, including those for throat or chest pain (from seven per 10,000 person-days to four), shortness of breath (from eight to three), cough (from four to two), and malaise and fatigue (from four to two). In contrast, rates of visits with chronic disease diagnoses (e.g., hypertension and diabetes) and urinary tract infections changed little over time. • LIMITS: mostly privately insured population; no non-COVID-19 control group; unclear whether use of COVID-19 diagnosis visit code used by providers.

(Lund et al., 2021)	• Peer-reviewed
	• Denmark
	• Observational Cohort
	• Community-only; lab-confirmed
		• N=8983
		• Aim: To examine prescription drug and health-care use after SARS-CoV-2 infection not requiring hospitalization
		• Administrative data
		• Mean follow-up 12 weeks
		• Study gives insights on health service utilization and compares with COVID-19 negative individuals over same period.
		  • 6557 (73·0%) of 8983 non-hospitalized individuals with SARS-CoV-2 infection and 62 391 (77·1%) of 80 894 SARS-CoV-2-negative individuals had visited their general practitioner, were seen at a hospital outpatient clinic, or were admitted to hospital (appendix p 5).
		  • Comparing overall health-care use between SARS-CoV-2-positive and SARS-CoV-2-negative individuals, we observed increased PERR-adjusted rate ratios for general practitioner visits (1·18 [95% CI 1·15–1·22]) and outpatient clinic visits (1·10 [1·05–1·16]) among SARS-CoV-2-positive individuals.
		  • We found no material difference between cohorts for emergency department visits (1·07 [0·88–1·30]) or inpatient hospitalizations (1·00 [0·87–1·14]; appendix pp 14–15).
		  • Among health-care users, most individuals had a single visit to the general practitioner or hospital outpatient clinic, and few individuals had five or more visits.
		• LIMITS: Follow-up was limited to 6 months after a test for SARS-CoV-2, which might not yet account for all long-term complications and persisting symptoms after COVID-19. Information on the indication for testing was not available.

(Maxwell, 2020)	• Grey Literature • UK	• Review

	• Review	• Makes recommendations about care in all settings for adults, children and young people with new or ongoing symptoms 4+ weeks after start acute COVID-19 • Recommendations more about generic good quality care. Nature of report means no insight on frequency of utilization. • Assessment recommendations for integrated multidisciplinary rehabilitation services (e.g. consider all bodily systems; personal goal identification; symptom management advice for all presenting symptoms; make follow-up strategy; and shared decision-making)

(Menges et al., 2021)	• Preprint
	• Switzerland
	• Observational Cohort
	• Lab-confirmed, community
		• N=431
		• Aim: assess prevalence of symptomatology and health care utilization at least 6 months after COVID-19 infection.
		• Mean follow-up 21.7 weeks
		• Study provides frequency of contact/utilization with the healthcare system after COVID-19 positive test. Offers some insight on risk factors for healthcare usage.
		  • A total of 170 (40%) participants reported having had at least one contact with the healthcare system (i.e., re-hospitalization, general practitioner visits, or medical hotline calls) for reasons related to COVID-19.
		  • Out of 81 individuals who were initially hospitalized due to COVID-19, eight (10%) were admitted to a hospital again at least once due to persistent symptoms or COVID-19 related complications, with a maximum of three re-hospitalizations.
		  • More than half of the participants (n=224, 52%) reported at least one general practitioner visit for any reason, and 150 (36%) had a general practitioner visit related to COVID-19. Among those, the median number of general practitioner visits related to COVID-19 was 2 (IQR 1 to 3).
		  • 31 (7%) participants reported to have called a medical hotline at least once for a reason related to COVID-19, with a median of 1 call (IQR 1 to 2).
		  • Among those that had not fully recovered, 37 (33%) did not report further healthcare contacts.
		  • Since SARS-CoV-2 infection, a new physician-diagnosed medical condition was reported by 77 (18%) participants. 27 (35%) of these diagnoses were considered to be related to COVID-19 by a physician.
		  • In multivariable regression analyses, we found evidence for an association between healthcare use and initial hospitalization, having experienced severe to very severe symptoms, sex, and age ≥40 years. Furthermore, not having fully recovered (OR 3.53, 95% CI 2.14 to 5.86, p<0.001), experiencing grade ≥1 dyspnea (OR 2.35, 95% CI 1.40 to 3.99, p<0.001), fatigue (OR 1.61, 95% CI 1.04 to 2.50, p=0.03) and symptoms of depression (OR 2.13, 95% CI 1.32 to 3.45, p=0.002) were independently associated with having contact with the healthcare system.
		• LIMITS: testing capacity early in pandemic might mean more severely-affected population; risk of self-selection bias; lack

		of baseline; not all health service utilization (i.e. no specialty use or diagnostic services);

(National Institute for Health and Care Excellence et al., 2020)	• Grey Literature
	• UK
	• Review
		• Review document
		• Aim: guidance to assist healthcare systems establish and maintain post-COVID assessment services
		• Paper provides recommendations on types of health services likely required, but nature of report means no insight on frequency of utilization.
		  ◦ Gives minimum standards for post-COVID assessment service (e.g. coverage, thresholds for referrals, communication strategy, access to diagnostics, multidisciplinary team).
		  ◦ Gives guidance on what support patients should receive (e.g. self-management advice; specialist referral; clear pathways; GP communication; multidisciplinary rehabilitation)

(Nurek et al., 2021)	• Preprint
	• UK
	• Delphi
		• N=33 physicians
		• Aim: Get consensus on physicians on recognition, diagnosis and management of post-COVID conditions
		• Expert Delphi panel provided strategies for health care providers and system, but nature of paper no exact % on implications of such recommendations on resource use.
		  ◦ Long COVID clinics must operate in context of rapidly evolving practice amongst both GPs and specialists.
		  ◦ Care pathways in holistic care, investigation of specific complications, management of potential symptom clusters in cardiac disease, dysautonomia and mast cell disorder, and individualized rehabilitation are needed.
		  ◦ Long COVID alone is insufficient diagnosis unless other causes have been excluded.
		  ◦ Require face-to-face assessment
		  ◦ Lots of diagnostic imaging and specialty referrals are recommended for appropriate assessment.

(O'Sullivan et al., 2021)	• Peer-reviewed article • UK • Cross-sectional Survey • Both hospitalized and non-hospitalized	• N=155 • Report early use of a rehabilitation tool for clinical practice • Population: GP assesses as having acute illness with ongoing rehabilitation needs (so COVID-19 diagnosis not required); military personnel • Mean 13 weeks follow-up • Narrative discussion on importance of referral to appropriate primary and/or specialty care based on principal symptoms. No empirical data on exact impacts and size of referrals, just that are likely to be some.
(Parkin et al., 2021)	• Peer-reviewed article • UK • Descriptive • Hospitalized	• N=225 • Article focuses on describing a functioning, comprehensive multidisciplinary rehabilitation pathway for patients with COVID-19 post-discharge. Eligibility included persistent symptoms 7 weeks after hospital discharge. • In describing this pathway, it provided a brief description of the demographics of the population who had been supported by this pathway.

		• Study overviews the services available and triggered by the pathway. The frequency of utilization is not elaborated in this study. • led by the patient's functional priorities and presenting symptoms, following the usual process of assessment, clinical reasoning and intervention planning. • No comparison and more descriptive study, so cannot speak definitively to impact or implications.

(Research, 2021)	• Grey Literature
	• Canada
	• Review
		• Review
		• Aim: to summarize evidence on Long COVID, including definitions, risk factors, symptomatology, prognosis, therapeutics, and other emerging research findings
		• Review gives general advice on health service implications.
		  • Research suggests that treating people with long COVID requires a multidisciplinary approach including evaluation, symptomatic treatment, treatment of underlying problems, physiotherapy, occupational therapy and psychological support.
		  • Some recommendations on management, with follow-up being most indicative of what health services may be required. But, no clarity on whether a chronic disease model or time-limited condition is at issue.

(Vaes et al., 2021)	• Peer-reviewed article
	• Belgium
	• Cross-sectional Survey
	• Both hospitalized and non-hospitalized
		• N=1556
		• Follow-up at 12 and 24 weeks post-onset of acute COVID-19 symptoms
		• Population: membership on online peer support for long COVID (social media)
		• Self-reported health service utilization
		  • The proportion of patients receiving physiotherapy or rehabilitation between 3 and 6 months of follow-up was significantly higher compared to the period from the infection to 3 months of follow-up (61.9% versus 31.8% and 11.7% versus 4.2%, respectively, $p<0.001$).
		  • After the onset of COVID-19 related symptoms, patients receiving physiotherapy reported more symptoms (6 vs. 4, $p<0.05$) and a worse self-reported health (84.5% good vs. 91.7% good, $p<0.05$), work productivity, functional status (grade 2.6 vs. 2.0, $p<0.05$) and quality of life (0.613 vs. 0.706 mean index EQ-5D-5L, $p<0.05$) compared to patients who did not receive physiotherapy or rehabilitation. Similar differences found at 6 months (all $p<0.05$).
		  • Between 3 and 6 months of follow-up, significant improvements were found in both patients who did and did not receive physiotherapy or rehabilitation.
		  • NOTE: concerns with this paper as % in text are different for same content in supplemental.

(Vanichkachorn et al., 2021)	• Peer-reviewed article • USA • Observational Cohort	• N=100 • Population: adults with positive COVID-19 test and symptoms four or more weeks after positive test. • Description of patient population at a specialty, rehabilitation-focused outpatient clinic (COVID Activity Rehabilitation Program) • Most patient presented at 12 weeks post-diagnosis

	• Hospitalized and non-hospitalized	• Describes elements of the program, and some utilization statistics ◦ Program elements include: function-focused interview; standard laboratory assessments; optional diagnostic tests; optional consultations ◦ Some statistics on the therapy, referral and diagnostic use by patients visiting outpatient clinic: Physical therapy (42%); Occupational therapy (27%); Brain rehabilitation consultation (22%); Infectious disease consultation (6%); Chest X-ray (34%); Spirometry with DLCO (27%); Trans Thoracic Echocardiogram (29%); Autonomic reflex testing (20%)
(Whittaker et al., 2021)	• Preprint • UK • Observational Cohort • Both hospitalized and non-hospitalized, lab confirmed	• N=46,687 • Aim: To investigate new primary care-recorded symptoms, diseases, prescriptions and healthcare utilization in patients post-acute COVID-19 infection, comparing outcomes between community-only and hospitalized patients • Increased health service utilization in hospitalized vs. community-only group. ◦ The hospitalized group utilized more healthcare (including GP visits, referrals, emergency department, hospitalization) than the community group post-COVID-19, with a 2.7-fold difference in rates per 100,000 person-weeks [95%CI] between groups (52,775 [50,570 to 55,105] v. 19,405 [19,142 to 19,673]) in hospitalized and community groups, respectively. ◦ Regarding utilization among the 6 and 12 months prior, healthcare utilization increased in both groups post-COVID-19 relative to pre-pandemic levels, this was much higher in the hospitalized group (61.2% increase v. 28.5%). Healthcare utilization was lower 6 months prior relative to other time-points for each group.
(World Health Organization, 2021b)	• Grey literature article • Denmark • Review	• Policy brief, provides a review of larger population-based studies of the various approaches taken across multiple countries to best define, understand, and provide care for post-COVID conditions. • A review that touches on health system implications in caring for patients with post-COVID conditions, specifically the persistent symptoms: ◦ Survey of UK general practitioners in 2020 found that 67% were looking after patients with COVID-19 symptoms lasting longer than 12 weeks. Only 23% had access to a Long COVID clinic that they could refer into (Royal College of General Practitioners, 2020). ◦ Recommendations on model of care for post-COVID conditions should include multidisciplinary assessment services; should bring together physicians with expertise in different body systems, as well as multidisciplinary rehabilitation services, with core teams that could include, but not be limited to, occupational therapy, physiotherapy, clinical psychology and psychiatry, and rehabilitation medicine.
(Wildwing & Holt, 2021)	• Peer-reviewed • UK	• Systematic Review (n=45 studies) • Aim: systematic review of reviews of neurological symptoms of COVID-19 and implications for health care services

	• Systematic Review
	• Neurologic symptom focus
		• Review speaks to likely but hypothetical needs of patients with post-COVID conditions. No empirical data.
		  • Symptoms seen in Long Covid such as facial pain, muscle issues, neuralgia, fatigue and insomnia, may become long term and disabling, requiring sustained support from healthcare services such as pain-, fatigue- and sleep-clinics, neurological services and primary care.
		  • The effects of COVID-19 on overstretched neurological services is hard to predict, as the neuropathy, myopathy and sensory deficits of SARS resolved within 3 months of recovery. However, as COVID-19 appears to be becoming Long Covid for up to 10% of patients, support is likely to be required, potentially for a significant number of people, if their symptoms do not resolve spontaneously.

(Yong, 2020)	• Peer-reviewed
	• Malaysia
	• Review
		• Narrative review
		• Focus on pathophysiology, risk factors and treatments in long COVID
		• Literature review describes broad need for rehabilitation for long COVID, but that has to be personalized to this condition and these patients. No empirical data, more recommendations. No data on size/frequency of this utilization.
		  • According to reviews, in rehabilitation, patients are advised to perform light aerobic exercise paced according to individual capacity. Exercise difficulty levels are increased gradually within tolerated levels until improvements in fatigue and dyspnea are seen, typically four to six weeks.
		  • Risks of physical rehabilitation must also be considered. Systematic and scoping reviews have identified that rehabilitation may not be suitable for survivors of critical COVID-19 with severe pulmonary or cardiac damage. Hence, exclusion criteria for post-COVID-19 rehabilitation have been proposed: high resting heart rate (>100 beats/min), low or high blood pressure (<90/60 or >140/90 mmHg), low blood oxygen saturation (<95%), or other conditions where exercise is a contraindication. Indeed, an international survey study found that 85.9% of participants with long COVID experienced symptom relapse following mental or physical activities.

Research Question 5b (Return to Work): What are the implications for return to work for employees, their employers and for health care workers involved in assessments for return to work?

Evidence from secondary and grey literature

This synthesis includes one grey literature document: a World Health Organization policy brief that touches upon the return-to-work implications of post-COVID conditions (World Health Organization, 2021b).

Evidence from the primary literature

This synthesis on return to work and post-COVID conditions is based on 7 primary articles (5 peer-reviewed articles and 2 preprints), including 4 cross-sectional surveys, 2 observational cohorts, and 1 article describing a clinical pathway. Three articles were from the UK, while 1 each were from the USA and four separate European countries (Belgium, Denmark, the Netherlands, and Norway). Table 5B summarizes the key takeaways from these articles relating to return to work implications for post-COVID conditions, while Table 6E in the Appendix section contains the information extracted from each document.

Synthesis of the Information Relating to Question 5b

Return to work reflects occupational productivity, which can manifest in 3 ways: (1) reduced workforce participation (either early retirement or other workforce withdrawal); (2) absenteeism (temporary in nature; where worker remains in the workforce but is required to take time off work due to being unwell); and (3) presenteeism (lower productivity at work, where a worker produces less due to lower capacity to work) (Smith & Hillner, 2019). In brief, illness can impact individuals' ability to return to work at all, or their regularity or capacity upon return. This narrative synthesis sought to elaborate scientific findings related to any of these three manifestations related to return to work and productivity.

The body of evidence on the return to work implications of post-COVID conditions is small, and suggest only emergent learning. Using the below described adapted Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018), 6 studies were of high quality; 1 of mixed quality (Davis et al., 2021; Vaes et al., 2021); and 2 of low quality (Parkin et al., 2021; World Health Organization, 2021b).

While 3 studies based findings on primary data collection using a survey, 4 studies used secondary analysis of administrative data, 1 study used a Delphi panel, and 1 study provided no empirical data but international guidance on impact of post-COVID conditions on return to work. The mean (standard deviation) and median sample size of the 7 empirical studies are 1,290 (1445.1) and 891, respectively. These 8 studies include a mean (standard deviation) of 16.1 (7.43) weeks of follow-up; the median length of follow-up is 13 weeks. Types of populations of focus included all COVID-19 patients (n=6), hospitalized-only COVID-19 patients (n=1), and a sub-population (employed persons) (n=1).

The 3 primary-data studies used online surveys with a mean of 2,419 participants, and recruited from social media platforms wherein respondents already self-identified as having post-COVID conditions (or 'Long COVID') (Davis et al., 2021; Machado et al., 2021; Vaes et al., 2021). In Davis et al (2021), 68.9% of unrecovered respondents had either reduced workforce participation or absenteeism, compared to 45.6% of recovered respondents. At least 45% of those who were working indicated that remote working accommodations were critical to their continued ability to work. In Machado et al (2021), a statistically significant association was found between level of functional impairment post-COVID and the experience of absenteeism ($p<0.05$), presenteeism ($p<0.05$) and work impairment ($p<0.05$). Finally, Vaes et al (2021) found that absenteeism and presenteeism was prevalent amongst survey respondents at 61% and 65%, respectively at 3 months. However, a statistically significant reduction in both were noted at 6 months, with absenteeism and presenteeism reducing to 48% and 57%, respectively (both $p<0.001$). Overall working impairment was 73% at 3 months and 62% at 6 months (different statistically significant, $p<0.001$).

Examinations of administrative data reveal utilization of formal sick leaves (Skyrud et al., 2021) or self-report to clinics about occupational productivity (O'Sullivan et al., 2021; Parkin et al., 2021; Vanichkachorn et al., 2021). Skyrud et al (2021) studied the working population of Norway (n=740,182) and found that use of sick leave increases for those testing positive for COVID-19 for the week of testing, but returns to pre-testing, population-level norm levels 3-4 months after testing. Skyrud et al (2021) was the only included study that used administrative data versus self-report. Amongst those who feel unwell and tested positive for COVID-19, 28.5% require sick leaves the test week and this population returns to 2.8% at month 3 post-testing. Amongst those who fell unwell and tested negative for COVID-19, 9.0% require sick leaves the test week and this population returns to 2.6% at month 3 post-testing.

Vanichkachorn et al (2021) found that 31% of patients presenting to post-COVID outpatient clinics at 12 weeks post-diagnosis had not returned to work; of the 69% who returned to work, only 46% (32% total) had returned to unrestricted work duty. Parkin et al (2021) found that 54% of patients supported by a multidisciplinary rehabilitation pathway experienced reduced workforce participation or absenteeism when symptoms persisted beyond 7 weeks from hospital discharge. It is likely that those who attend post-COVID clinics have higher rates of work impairment than the general population experiencing post COVID syndrome. Finally, O'Sullivan et al (2021) found that military personnel with ongoing rehabilitation needs post-COVID require assessment and management support to return to work. There was no prevalence data provided in this study.

This small set of studies, which have varied design and potential bias, suggest the following implications:

- Implications for employees
    - It appears patients with post-COVID conditions experience reduced workforce participation (31-54%), absenteeism (48-61%) and presenteeism (25-69%).
    - The prevalence of these experiences is statistically lower at 6 months than 3 months from the time of acute infection. A Norwegian study suggests that reduced workforce participant brought about by post-COVID conditions dissipates by 3 months post-onset of acute symptoms.
- Implications for employers
    - Employees who experience post-COVID conditions may require compensated leaves and/or remote working accommodations to overcome the illness' impact on productivity.
    - Employers should discuss suitable arrangements with employees to aid return to work.
- Implications for health care providers
    - The symptoms of post-COVID conditions impact patients' workforce participation and productivity. Occupational implications should be both at assessment of functional impairment, and in developing rehabilitation care plans to manage functional impairment.
    - Employers and employees should be provided with written advice from the health system, including information on the relapsing-remitting nature of the illness.
    - Health care providers should take care in providing medical notes of fitness or lack thereof, and the connection to a medically-recognized diagnosis.
    - The ability to return to (productive) work after illness is a marker of recovery and should be recorded in clinical notes.
    - There may be a potential need to develop standardized assessment tools to assist in return to work assessment and the need for further research, to reflect the notes gaps.

Table 5B. Summary of Articles Informing Return to Work Implications

Author	**Study Details** (Article Type, Country, Study Design)	Return to Work Implications

(Davis et al., 2021)	• Preprint
	• UK
	• Cross-sectional Survey
		• N=3,762
		• Population: adults with confirmed or suspected COVID-19 infection recruited by social media
		• Online survey at mean 28 weeks post-diagnosis
		• Study demonstrated impact on return to work, absenteeism and presenteeism.
		    • 68.9% of unrecovered respondents reported reduced work hours or not working at all as a direct result of their COVID-19 illness (vs. 45.6% [95%CI 43.2-48.0%] of unrecovered respondents)
		    • 27.3% [95%CI 25.3-39.4%] of unrecovered respondents who worked before illness were working as many hours as prior to becoming ill at the time of survey (compared to 49.3% [95%CI 40.8-57.9%]
		    • 23.3% [95%CI 21.3-25.4%] not working as direct result of illness.
		    • At least 45% of working respondents were working remotely, which they indicated was critical to their continued ability to work.

(Machado et al., 2021)	• Peer-reviewed article • The Netherlands • Cross-sectional Survey	• N=1,939 • Population: adults with confirmed or suspected COVID-19 infection from online panel or social media groups for long-COVID • 12 week follow-up • Study demonstrates statistically significant association between level of functional impairment post-COVID and facets of return to work as self-reported by respondents: • Compared to respondents with grade 0, 1 or 2 on the PCFS Scale, respondents with grade 3 or 4 on the PCFS Scale more often experienced absenteeism ($p<0.05$), presenteeism ($p<0.05$), and work impairment ($p<0.05$).

(Nurek et al., 2021)	• Preprint
	• UK
	• Modified Delphi
		• N=33
		• Population: UK physicians using a social media platform
		• Delphi process (2 online surveys) to get consensus on post-COVID conditions diagnosis and management.
		• Expert Delphi panel provided strategies for employers and health care providers, including:
		    • Employers should discuss with their employee suitable adjustments to aid a return to work, and both parties should be provided with written advice
		    • Must emphasize relapsing-remitting nature of illness
		    • Doctor with current clinical responsibility required to complete the fit note. The content of the fit note should be agreed between the patient and doctor, including a “medically-recognized diagnosis”. In UK, NHS staff’s fit note must mention COVID for “COVID pay” during absence.
		    • The ability to return to work after illness is a marker of recovery and clinicians must, therefore, record work

		status in the clinical notes in situations of chronic ill-health.

(Parkin et al., 2021)	• Peer-reviewed article
	• UK
	• Descriptive
		• N=225
		• Description of a functioning, comprehensive multidisciplinary rehabilitation pathway for patients with COVID-19 post-discharge. Eligibility included persistent symptoms 7 weeks after hospital discharge.
		• Describe demographics of population supported by pathway
		• Study reveals impact on return to work
		  • 54% of patient population on this pathway were unable to work or had to reduce hours (absenteeism)
		  • Undisclosed % "many" only remain at work due to current work from home arrangements.
		• No comparison and more descriptive study, so cannot speak definitively to impact or implications.

(O'Sullivan et al., 2021)	• Peer-reviewed article • UK • Cross-sectional Survey	• N=155 • Report early use of a rehabilitation tool for clinical practice • Population: GP assesses as having acute illness with ongoing rehabilitation needs (so COVID-19 diagnosis not required); military personnel • Mean 13 weeks follow-up • Study findings are unclear, but suggest occupational rehabilitation is required for patients with post-COVID as they require assessment and management support to return to work.

(Skyrud et al., 2021)	• Preprint
	• Norway
	• Observational Cohort
		• N=740,182
		• Population: every adult Norwegian who tested positive for COVID-19 and had an employment contract
		• Mean 17 week follow-up
		• Sick leave increases for those testing positive for the week of testing and returns to pre-testing levels 3-4 months after testing. Higher sick leave levels in those testing positive vs. negative.
		  • Employees testing positive had a sick leave of 2.5% in 3 months before testing positive; increasing to 28.5% in the test week; dropped to pre-testing levels at month 3 (2.8%) and 4 (2.2%) after testing.
		  • Employees testing negative had 2.0% sick leave in the 3 months before testing, increasing to 9.0% in test week, and returning toward pre-testing level in month 3 (2.6%) and 4 (2.5 %) after testing.

(Vaes et al., 2021)	• Peer-reviewed article • Belgium • Cross-sectional Survey	• N=1556 • Survey follow-up at 12 and 24 weeks post-onset of acute COVID-19 symptoms • Population: membership on online peer support for long COVID (social media) • The majority of persons self-identifying as having long COVID experience absenteeism and presenteeism, but there are modest (but statistically significant) improvements from 3 to 6 months post-onset of acute symptoms. • 87.9% patients had job before the infection.

		• The mean proportion of work time missed in the previous week due to ill health (absenteeism) and impairment while working (presenteeism) reduced from 61% to 48% and from 65% to 57%, respectively (both p<0.001). • The average work productivity loss reduced from 82% to 74%, resulting in an overall working impairment of 73% and 62% after 3 and 6 months, respectively (both p<0.001). • NOTE: concerns with this paper as % in text are different for same content in supplemental.

(Vanichkachorn et al., 2021)	• Peer-reviewed article
	• USA
	• Observational Cohort
		• N=100
		• Population: adults with positive COVID-19 test and symptoms four or more weeks after positive test.
		• Aim to describe patients reporting prolonged symptoms after COVID-19 infection visiting outpatient clinic
		• Most patient presented at 12 weeks post-diagnosis
		• Return to work is often associated with limited activities, but approximately a third of patients do not return to work.
		  ◦ At intake: 69% patients returned to some form of work at presentation to clinic, of which only 46% returned to unrestricted work duty.
		  ◦ At intake: 31% of previously-employed patients had not returned to work.

(World Health Organization, 2021b)	• Grey literature article • Denmark • Review	• Policy brief reviews larger population-based studies on how to best define, understand, and provide care for post-COVID conditions. • Speaks to challenges in diagnosing post-COVID conditions and its return to work assessment. ◦ "Although there is no simple symptom or test for diagnosing it, many people experience severe fatigue and a range of troubling physical symptoms that make it difficult for those who are employed to return to work."

Evolving Evidence

Research on SARS-CoV-2 is continually evolving and as such the evidence will continue to be assessed as new information is provided. As stated above, international consensus processes are currently underway to confirm the appropriate terminology and case definitions of post-COVID conditions. Similarly, work is ongoing on the validation of screening tools, including the PCFS Scale. Inclusion of research on areas under-represented in this review (i.e. health service implications, impact of vaccination, and return to work implications) will need to be included in future iterations of this work.

Appendix

List of Abbreviations

BMI	Body Mass Index
C19-YRS	Covid 19 Yorkshire Rehab Screen
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
EQ-5D-5L	EuroQoL version 5D-5L
HADS	Hospital Anxiety and Depression Scale
HR	Hazard Risk
ICC	Inter-class Correlation
ICU	Intensive Care Unit
IT	Impact Tool
MMAT	Mixed Methods Appraisal Tool
MoCA	Montreal Cognitive Assessment
OR	Odds Ratio
PASC	Post-Acute Sequelae of COVID-19
PCFS	Post-COVID Functional Status
PFT	Pulmonary Function Test
PHAC	Public Health Agency of Canada
PSM	Prospective Surveillance Model
SF-36	Short-Form-36
ST	Symptom Tool
WEMWBS	Warwick and Edinburg Mental Wellbeing
UK	United Kingdom
USA	United States of America
VTE	Venous Thromboembolism

Table 6A. Details on Articles Informing Screening Tools

Author	Study Details (Article Type, Country, Study Design)	Screening Tool & Available Validation Data
(Arnold et al., 2021)	• Preprint • UK • Observational cohort	• Used previously validated survey tools • Quality of Life: Short-Form-36 (**SF-36**) • Mental Wellbeing: Warwick and Edinburgh Mental Wellbeing scores (**WEMWBS**)
(D'Cruz et al., 2021)	• Peer-reviewed article • UK • Observational cohort	• **Post-COVID Functional Status (PCFS) Scale** • Just used, did not try to validate it.

(Lemhöfer et al., 2021)	• Peer-reviewed article
	• Germany
	• Narrative review
		• **C19-RehabNeS**
		• Description: The C19-RehabNeS = 2 separate assessment tools: (i) the SF-36 on health-related quality of life; and (ii) the C19-RehabNeQ.
		• C19-RehabNeQ has 57 items assigned to 7 main categories:
		  • Time of infection (1 item)
		  • Health problems caused by SARS-CoV-2 (14 items)
		  • Treatment (9 items)
		  • Activity and participation (13 items)
		  • Quality of life and general health (6 items)
		  • Health service provisions (5 items)
		  • Personal information (9 items)
		• History: The C19-RehabNeS was first developed in German and the single dimensions were then translated into English. The items of the C19-RehabNeQ comprise individual questions from existing questionnaires and include newly developed questions to illustrate the particularities of a SARS-CoV-2 infection.
		• The paper describes tool development by 5 specialists. There is not psychometric testing of its validity. Some of the tool has been validated on its own (i.e. previously-validated tools incorporated herein), but others have not and the tool as a whole has not been validated.

(Machado et al., 2021)	• Peer-reviewed article
	• The Netherlands
	• Cross-sectional Survey
		• **Post-COVID Functional Status (PCFS) Scale**
		• Description: The scale was designed to cover the entire range of functional limitations from: grade 0, "No functional limitations" to grade 4, "Severe functional limitations" and grade 5, "Death". The PCFS Scale stratification is composed of five scale grades:
		  • grade 0 (No functional limitations);
		  • grade 1 (Negligible functional limitations);
		  • grade 2 (Slight functional limitations);
		  • grade 3 (Moderate functional limitations)
		  • grade 4 (Severe functional limitations).
		• The final scale grade 5 'death', which is required to be able to use the scale as outcome measure in clinical trials, was left out for self-administered contexts.

		• The PCFS Scale can be used both at the time of hospital discharge, and to monitor functional status post discharge.
		• Psychometric testing data: Investigated the construct validity of the PCFS Scale.
		  ◦ N=1,939 subjects about 3 months after the onset of infection-related symptoms.
		  ◦ Found weak-to-strong statistical associations between functional status and all domains of health-related quality of life using the EQ-5D-5L (r: 0.233–0.661). Notably, the strongest association found was with the ‘usual activities’ domain of the 5-level EQ-5D questionnaire.
		  ◦ Using the WPAI questionnaire, absenteeism, presenteeism and work impairment were different considering all pairwise comparisons with exception of the comparison between subjects with no and negligible functional limitations and between subjects with moderate and severe functional limitations. Activity impairment increased gradually according to the decrease in functional status.
		  ◦ Limit: a lack of power to detect small but meaningful differences among the latter groups might have affected these results.

(Osmanov et al., 2021)	• Preprint • Russia • Observational cohort	• **ISARIC COVID-19 Health and Wellbeing Follow Up Survey for Children** • Description: captures demographics, parental perception of changes in their child’s emotional and behavioural status, previous vaccination history, hospital stay and readmissions, mortality (after the initial index event), history of newly developed symptoms between discharge and the follow-up assessment, including symptom onset and duration, and overall health condition compared to prior to the child’s Covid-19 onset. • Just used, no validation attempts. • Used in interviews with parents as standardized tool.
(O’Sullivan et al., 2021)	• Peer-reviewed article • UK • Cross-sectional Survey	• **Remote COVID-19 Rehabilitation Assessment Tool** • No validation data. • Description: Incorporates a medical screening, identifying the acute course, severity and management of COVID-19. Identifies existence of post-COVID-19 symptoms, including pain, fatigue, sleep and mood, and functional limitations such as shortness of breath, exercise intolerance or cognitive problems on activities of daily living (ADLs) or occupation. ◦ From this problem list, and in conjunction with the patient’s ideas, concerns and expectations, rehabilitation management is arranged. • The tool was introduced into clinical practice in late April 2020, using the NHSX-approved web-based VTC platform, Attend Anywhere (Attend Anywhere, Australia), the first such tool in clinical use in the UK. • Used on military personnel.
(Parkin et al., 2021)	• Peer-reviewed article • UK	• **Covid 19 Yorkshire Rehab Screen (C19-YRS)** • Description: 4-page tool. Asks patients to rate on scale of 0-10 how affected now versus pre-COVID on 19 domains

	• Descriptive	including breathlessness, voice, swallowing, nutrition, mobility, fatigue, continence, cognition, pain, depression, and vocation. • C19-YRS recommended by NHS Clinical Guidance for use as an outcome measure in post-COVID-19 syndrome assessment clinics. • Available as a self-report version gathers symptom severity and functional disability in post-COVID-19 syndrome and acts a triage tool to the most appropriate clinician or treatment modality. • Described as being patient-centered, and able to significantly reduce clinician assessment time, enabling face to face therapy to be focused on gathering further information as required and providing therapeutic intervention. • Work is ongoing to psychometrically validate the tool: “In partnership with the University of Leeds Psychometric Lab for Health Sciences, the C19-YRS is currently being developed and psychometrically tested for construct validity, responsiveness and stability using Rasch analysis.”

(Postigo-Martin et al., 2021)	• Peer-reviewed article
	• Spain
	• Review
		• **COVID-19 Prospective Surveillance Model (PSM)**
		• Meant for rehabilitation professionals
		• Description: Tool is more of a model. Divided into three sections: rapid screening, general assessment and specific assessments for each system likely to be affected.
		  ◦ (1) at the first evaluation, with rapid screening through exploratory questions;
		  ◦ (2) at general health assessment (vital signs, auscultation, dyspnea, body composition, physical activity level, sedentary lifestyle and quality of life); and
		  ◦ (3) at specific evaluation of cardiorespiratory, neuromuscular and mental levels.
		  ◦ The latter section includes reliable tools for making necessary assessments, cut-off points and orientation regarding treatment. Specific assessments are categorized as cardiopumonary, neuromuscular system and mental health
		• Model that incorporates validated tools, each likely used as validated.
		• Does not present validation data, but likely not necessary.

(Tran et al., 2021)	• Preprint
	• France
	• Cross sectional survey
		• Two tools: **Long COVID Symptom Tool (ST)** and **Long COVID Impact Tool**
		• Description:
		  ◦ Long COVID ST score reports the number of symptoms patients experienced over the last 30 days and has a theoretical range from 0 (no symptoms) to 53 (all symptoms identified during step 1).
		  ◦ Long COVID IT score has a theoretical range of 0 (no impact) to 60 (maximum impact) and represents the sum of item scores for the 6 questions related to the disease's impact on their personal activities, family lives, professional lives, social lives, their morale, and their relationships with care providers.

		• Paper is dedicated to development and validation of construct validity and reliability of the two tools (n=351). Qualitative patient work informed development.
		    • The long COVID ST and IT scores were highly correlated (rs=0.54, p<0.0001) and did not seem to differ by time from symptom onset.
		    • CONSTRUCT VALIDITY: The long COVID ST score was moderately and negatively correlated with the EQ-5D-5L questionnaire (rs = -0.45, p<0.0001) and the EQ-VAS (rs = -0.39, p<0.0001), while the long COVID IT score had a strongly negative correlation with the EQ-5D-5L questionnaire (rs = -0.59, p<0.0001) and the EQ-VAS (rs = -0.54, p<0.0001). For functional assessments using the PCFS, they found a moderate correlation between the long COVID ST score and the PCFS score (rs = -0.39, p<0.0001) and a high correlation between the long COVID IT score and the PCFS score (rs = -0.55, p<0.0001). For patients' perceived health state, the long COVID ST score was moderately correlated with the MYMOP2 score (rs = -0.40, p<0.0001) while the long COVID IT score was highly correlated with it (rs = -0.59, p<0.0001)
		    • RELIABILITY: Of the 351 patients invited to complete the long COVID ST and IT twice for the test-retest, 235 (67%) did so. The symptom score had an ICC of 0.83 (95% CI 0.80 to 0.86), with Bland and Altman plots showed a mean difference of 0.8 (95% limits of agreement, -14 and 16). The impact score's ICC was 0.84 (95% CI 0.80 to 0.87), with Bland and Altman plots showing a mean difference of 0.5 (95% limits of agreement, -11 to 12 (Figure 2). Finally, Cronbach's alpha was 0.89 (95% CI, 0.88 to 0.90) for the long COVID ST score and 0.86 (95% CI, 0.85 to 0.88) for the IT score.
		    • In sum, examinations of construct validity demonstrated moderate or high correlations with patients' quality of life, functional status, and perceived health state. Reliability was strong with an ICC ≥ 0.8 during the test-retest.

(Vehar et al., 2021)	• Peer-reviewed article • USA • Review	• Used previously validated screening measures for cognition and mental health (anxiety, depression and post-traumatic stress disorder). • **The Montreal Cognitive Assessment (MoCA)** • **Hospital Anxiety and Depression Scale (HADS)** • **Impact of Event Scale-6** • Other testing includes medication reconciliation, screening for rehabilitation needs, and pulmonary function testing. • Authors discussed PCFS, but felt that "it has not been validated or widely implemented."

Table 6B. Details from Articles on Risk Factors

Author	Study Details (Article Type, Country, Study Design)	Noted Risk Factors

(Augustin et al., 2021)	• Peer-reviewed
	• Germany
	• Observational cohort
		• N=958
		• Aim: explore the incidence, diagnostic criteria and management of long-term health consequences at 4 and 7 months after mild courses of COVID-19 at post-COVID outpatient clinic
		• Population: adults with previous positive COVID-19 test
		• Mean 22 weeks follow-up (2 follow-ups at 4 and 7 months)
		• RISK FACTORS:
		  • Used univariate logistic regression revealed several factors and symptoms during acute COVID-19 that were associated with an increased risk of post COVID syndrome after 7 months.
		    • **Multiple symptoms** (odds ratio (OR) 1.28; 95% confidence interval (95% CI): 1.13–1.46)
		    • **Diarrhea** (OR 2.19; 95% CI 1.21–4.00)
		    • **Ageusia** (OR 2.16; 95% CI 1.36–3.43)
		    • **Anosmia** (OR 3.79; 95% CI 2.36–6.09)
		    • **Baseline IgG titers** between 1.2 and 4 (OR 2.06; 95% CI 1.19–3.53)
		  • Male **gender** was associated with a lower risk for post COVID syndrome (OR 0.49; 95% CI 0.31–0.77).
		  • In the multivariable logistic regression model **a lower baseline level of SARS-CoV-2** was associated with a higher risk of developing post-COVID conditions after 7 months IgG (initial IgG 1.2–4; OR 2.06 (95% confidence interval (95%CI) 1.19–3.53), p = 0.009 and initial IgG ≤1.1; aOR 2.05 (95%CI 0.96–4.37), p = 0.054).
		  • **Anosmia** and **diarrhea** during acute COVID-19 were independent predictors for a PCS after 7 months with an OR of 5.12 (95% CI 2.43–10.76, p=<0.001) and 2.35 (95%CI 1.13–4.90, p = 0.023), respectively.

(Ayoubkhani et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
		• N=47,780
		• Aim: Estimate excess morbidity after severe COVID-19 (hospitalized) using administrative data (retrospective, matched cohort study)
		• Mean follow-up 20 weeks
		• RISK FACTORS:
		  • Rates of all outcomes after discharge were greater in individuals with COVID -19 **aged 70 or more** than in those aged less than 70
		  • Rates of all outcomes (e.g. death, readmission, respiratory disease, chronic kidney or liver disease) other than diabetes were greater in the **white ethnic group** than in the non-white group.
		  • Rate ratios comparing patients with COVID-19 and matched controls were greater in individuals aged less than 70 than those aged 70 or more for all outcomes, however.

		◦ The largest differences in rate ratios were for death (14.1 (95% confidence interval 11.0 to 18.3) for age <70 years v 7.7 (7.1 to 8.3) for ≥70) and respiratory disease (10.5 (9.7 to 11.4) for age <70 v 4.6 (4.3 to 4.8) for ≥70). ◦ Ethnic differences in rate ratios were greatest for respiratory disease (11.4 (9.8 to 13.3) for individuals in the non-white group v 5.2 (5.0 to 5.5) in the white ethnic group). Differences in rate ratios between men and women were generally small (supplementary table 4). • NOTE: focus on severe COVID-19, so likely many syndromes (e.g. post-ICU syndrome) implicated in post-discharge health service use.
(Bellan et al., 2021)	• Peer-reviewed • Italy • Observational cohort	• N=238 • Aim: evaluate the prevalence of lung function anomalies, exercise function impairment, and psychological sequelae among patients hospitalized for COVID-19, 4 months after discharge. • Population: consecutive patients discharged from hospital during 4 month period • RISK FACTORS: ◦ In logistic regression analysis, risk factors associated with D_{LCO} less than 80% of expected (pulmonary function) at follow-up included **female sex** (odds ratio [OR], 4.33 [95% CI, 2.25-8.33]; *P* < .001), **chronic kidney disease** (OR, 10.12 [95% CI, 2.00-51.05]; *P* = .005), and the **modality of oxygen delivery during hospital stay** (OR, 1.68 [95% CI, 1.08-2.61]; *P* = .02). ◦ Risk factors associated with D_{LCO} less than 60% at follow-up were **female sex** (OR, 2.70 [95% CI, 1.11-6.55]; *P* = .03), **COPD** (OR, 5.52 [95% CI, 1.32-23.08]; *P* = .02), and **ICU admission during hospital stay** (OR, 5.76 [95% CI, 1.37-24.25]; *P* = .02) ◦ **COPD** was associated with an increased risk of physical impairment (OR, 12.70 [95% CI, 1.41-114.85]; *P* = .02), and higher D_{LCO} was associated with decreased risk of physical impairment (OR, 0.96 [95% CI, 0.94-0.98]; *P* < .001). ◦ Authors describe **male sex** was the only factor independently associated with the presence of moderate to severe post-traumatic stress disorder symptoms (but in supplemental, the p=0.20).
(Bowles et al., 2021)	• Peer-reviewed • USA • Observational cohort	• N=1,409 • Aim: To describe the home health recovery of patients with COVID-19 and risk factors associated with re-hospitalization or death • Population: COVID-19 survivors discharged to home care • Mean follow-up 12 weeks • RISK FACTORS ◦ Risk for re-hospitalization or death was higher among **male** patients (HR, 1.45 [CI, 1.04 to 2.03]); **White** patients (HR, 1.74 [CI, 1.22 to 2.47]); and **patients who had heart failure** (HR, 2.12 [CI, 1.41 to 3.19]), **diabetes with complications** (HR, 1.71 [CI, 1.17 to 2.52]), **2 or**

		more emergency department visits in the past 6 months (HR, 1.78 [CI, 1.21 to 2.62])
(Caronna et al., 2020)	• Peer-reviewed • Spain • Observational cohort	• N=130 • Aim: To define headache characteristics and evolution in relation to COVID-19 and its inflammatory response • Population: Consecutive patients with COVID-19 symptoms visiting emergency department • Mean follow-up 6 weeks • RISK FACTORS • For patients with and without headache, for whom data were available at follow-up, and adjusting for age and gender, we observed shorter COVID-19 disease duration in the **headache group** (23.9 and 11.6 vs. 31.2 and 12.0 days; p=0.028). We did not observe any difference in mortality (no mortality in this subgroup) or hospital length of stay (9.1 and 9.0 vs. 10.9 and 9.0 days; p=0.854). • LIMITS: not all patients had confirmed COVID-19 diagnosis; single centre; one symptom of focus

(D'Cruz et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
		• N=119
		• Aim: investigate sequelae of severe COVID-19 pneumonia (hospitalization ≥48hrs), and identify risk factors
		• Prospective, single-centre observational cohort
		• Follow-up 7-9 weeks post-discharge follow-up
		• Population: adults discharged after severe COVID-19 pneumonia (hospitalization ≥48hrs)
		• Study noted hospital service use post-discharge and found 16-40% used some services. Time frame is lacking and no controls.
		• RISK FACTORS:
		  • **Comorbid obstructive lung disease** was associated with failure of mMRC recovery to baseline (OR 5.06, 95% CI 1.33–19.24; p=0.017) and PCFS grade ⩾2 (OR 2.84, 95% CI 1.01–7.98; p=0.047)
		  • **Pre-morbid obstructive lung disease** was associated with persistent (NRS ⩾1) breathlessness (OR 8.04, 95% CI 0.19–21.4; p=0.03) and cough (OR 3.43, 95% CI 0.98–12.0), but not burdensome (NRS ⩾4) breathlessness or cough (OR 1.97, 95% CI 0.60–6.47; p=0.26 and OR 2.27, 95% CI 0.38–13.69; p=0.37, respectively). There were no associations between the presence or absence of pre-existing comorbidities and persistent fatigue, sleep disturbance or pain.
		  • Presence of COVID-19-related CT abnormalities was associated with mental health screening questionnaires (PHQ-9 >9, GAD-7 >9 and/or Trauma Screening Questionnaire ⩾6) (Chi-squared=3.98, 95% CI 0.02–0.54; p=0.046), but not with any measure of patient-reported or physiological functional impairment (mMRC, PCFS, 4MGS <0.8 m·s−1 or oxygen desaturation ⩾4% during STS testing). Only 21% of patients with abnormal CT findings had an abnormal follow-up chest radiograph; however, 78% of those with oxygen desaturation ⩾4% during STS also had abnormal CT findings.

		• Ordinal logistic regression modelling was performed for the outcomes of return of mMRC grade to pre-COVID-19 baseline, PCFS grade ⩾2, positive mental health screening (PHQ-9 or GAD-7 >9 or Trauma Screening Questionnaire ⩾6) and physiological functional impairment (4MGS <0.8 m·s−1, STS repetitions <2.5th percentile or oxygen desaturation ⩾4% on STS) (table 3). Positive associations were found between **PCFS grade ⩾2, physiological impairment (4MGS <0.8 m·s−1 and STS repetitions <2.5th percentile) and positive mental health screening.** Critical care admission and need for IMV were associated with physiological functional impairment. Neither worst inpatient nor follow-up RALE score were associated with any modelled outcome measure. • LIMITS: not possible to do lung function on serial patients; conventional walking tests impractical; lack of standardized definition of post-COVID conditions; single centre

(Demelo-Rodríguez et al., 2021)	• Peer-reviewed
	• Spain
	• Observational cohort
		• N=100
		• Aim: describe the long-term outcomes of COVID-19 patients with VTE and to analyze the risk factors of poor prognosis.
		• Population: consecutive patients diagnosed with VTE during hospital admission and outpatients
		• Mean follow-up 13.9 weeks
		• RISK FACTORS:
		  • Development of main outcome was significantly associated with ICU admission (OR 8.437, p<0.001), anemia (OR 2.918 p0.021), thrombocytopenia (3.211 OR, p0.025), and cancer (OR 7.187, p0.024).
		  • Risk of death or major bleeding was independently associated with **ICU admission** (HR 12.2; 95% CI 3.0-48.3), **thrombocytopenia** (HR 4.5; 95% CI 1.2-16.5), and **cancer** (HR 21.6; 95% CI 1.8-259)
		• LIMITS: Describes risk factors for negative outcomes from COVID-19 and VTE, not other forms of post-COVID conditions. More about complication of COVID-19 vs. “long COVID.”

(Ekbom et al., 2021)	• Peer-reviewed
	• Sweden
	• Observational cohort
		• N=60
		• Aim: prevalence of respiratory impairment as measured by pulmonary function tests (PFT) and associated factors in Intensive Care Unit (ICU)-treated COVID-19 patients 3–6 months after discharge.
		• RISK FACTORS
		  • The most common impairment is reduced diffusing capacity, present in 45%. This risk increases with **age above 60**, **need for mechanical ventilation** and **time in ICU.**
		  • Longer stay in the ICU as well as impaired FVC (<LLN) at follow-up were also associated with impaired DLCO. All these significant relations could be confirmed after further adjusting for age.
		  • Longer stay in the ICU as well as impaired FVC (<LLN) at follow-up were also associated with impaired DLCO. Level of C-reactive protein (CRP) at admission to the ICU was lower in the group with impaired DLCO and the

		same was found regarding the lowest values for blood leukocytes and lymphocytes during the ICU-period. No relationship with impaired DLCO was found for D-dimer at admission or for the maximum value during the ICU-period. All these significant relations could be confirmed after further adjusting for age. Regarding FVC at follow-up, only severe ARDS was associated with having FVC < LLN at follow-up in a similar analysis. ◦ When analyzed as a continuous variable, DLCO (%predicted) at follow up was confirmed to significantly related (p < 0.05) to all variables that were significantly associated with impaired DLCO, with exception for CRP at admission (p = 0.11). • LIMITS: small sample size, no control, selection bias
(Einvik et al., 2021)	• Peer-reviewed • Norway • Cross sectional survey	• N=583 • Aim: Determine if prevalence of symptom-defined PTSD 1.5-6 months after COVID-19 was higher in hospitalized than non-hospitalized subjects; and, determine risk factors for persistent symptoms of PTSD in COVID-19 survivors • Population: 17% Norwegian population (subjects of 2 parallel cohort studies); adults with positive COVID test • Follow-up: 4-8 weeks post-discharge or 1-4 months post-diagnosis for non-hospitalized • RISK FACTORS: **none found** ◦ In multivariable logistic regression analysis, there was no association between being hospitalized and the presence of symptom-defined PTSD (OR 0.83, p=0.667). ◦ Being born in Norway compared to outside Norway was associated with PTSD (OR 0.40, p=0.012) ◦ None of the other covariates were significantly associated with PTSD
(Fernández-de-Las-Peñas et al., 2021)	• Peer-reviewed • Spain • Observational cohort	• N=1,950 • Aim: resents prevalence data and associated risk factors of post-COVID-19 cough one year after hospital discharge in a sample of subjects who had survived hospitalization for COVID-19. • Population: Adults hospitalized with COVID-19 in first wave of 3 hospitals in Spain • Follow-up average 44.8 weeks • RISK FACTORS: **None found** ◦ The regression model did not reveal any clinical variable associated with the presence of post-COVID-19 cough: age (OR1.01, 95%CI 0.99–1.03, P = 0.237), female gender (OR 0.96, 95%CI 0.72–1.29, P = 0.468), height (OR0.97, 95%CI 0.82–1.14, P = 0.681), weight (OR1.037, 95%CI 0.87–1.23, P = 0.717), or number of pre-existing medical comorbidities (OR1.39, 95%CI 0.69–2.81, P = 0.477). ◦ No significant association of long-term post-COVID-19 cough with hospitalization variables was either observed: the number of symptoms at hospital admission (OR1.26, 95%CI 0.59–2.69, P = 0.142), number of days at hospital (OR1.02, 95%CI 0.99–1.04,

		P = 0.141), or ICU admission (OR1.24, 95%CI 0.44–3.50, P = 90.687) • LIMITS: phone survey; no community-only perspectives; no data on diagnostics or severity; cross-sectional data
(Himmels, 2021)	• Grey Literature • Norway • Review	• Review (n=43 articles) • Aim to gather information on patient groups most at risk of long-term effects of COVID-19, and what characterizes them. • Exact studies and findings not extracted.

(Hirschtick et al., 2021)	• Peer-reviewed
	• USA
	• Cross sectional survey
		• N=593
		• Aim: to estimate the prevalence and correlates of post-acute sequelae of SARS-CoV-2 infection (PASC).
		• Population: non-institutionalized adults with COVID-19 onset during study period
		• Follow-up average 8.6 weeks
		• RISK FACTORS
		  ◦ Respondents reporting **very severe (vs. mild) symptoms** had 2.25 times higher prevalence of 30-day COVID-19 ([aPR] 2.25, 95% CI 1.46-3.46) and 1.71 times higher prevalence of 60-day COVID-19 (aPR 1.71, 95% 1.02-2.88).
		  ◦ **Hospitalized** (vs. non-hospitalized) respondents had about 40% higher prevalence of both 30-day (aPR 1.37, 95% CI 1.12-1.69) and 60-day COVID-19 (aPR 1.40, 95% CI 1.02-1.93).
		  ◦ In unadjusted analyses, **older age** was statistically significantly associated with 30-day and 60-day COVID-19 prevalence. Respondents aged 55-64 years had 1.71 times higher prevalence of 30-day COVID-19 (Prevalence Ratio [PR] 1.71, 95% CI 1.19-2.47) and 2.14 times higher prevalence of 60-day COVID-19 (PR 2.14, 95% CI 1.27-3.59) relative to 18-34 year-olds. Point estimates for respondents aged 65+ were similar to respondents aged 55-64, though slightly lower. After adjusting for other demographic factors, pre-existing comorbidities, and illness severity, older age (45+ years) was not statistically significantly associated with increased 30-day or 60-day COVID-19. Additionally, although females had a higher prevalence of 30-day and 60-day COVID-19 than males, this difference was not statistically significant.
		  ◦ Hispanic adults had 48% higher prevalence of 30-day COVID-19 (PR 1.48, 95% CI 1.17-1.86) and 67% higher prevalence of 60-day COVID-19 (PR 1.67, 95% CI 1.18-2.36) than NH White adults in unadjusted models. However, there were no statistically significant differences in 30-day or 60-day COVID-19 by race/ethnicity in the adjusted models.
		  ◦ **Annual household income** was a strong and significant predictor of 30-day COVID-19. Even after adjusting for demographic and clinical factors, respondents with an income less than $75,000 had about 40% higher prevalence of 30-day COVID-19 than respondents with an income at or above $75,000 (<$35,000 aPR 1.40, 95% CI 1.09-1.79; $35,000-74,999

		aPR 1.38, 95% CI 1.09-1.75). Income was not significantly associated with 60-day COVID-19 in fully adjusted models. • Results from the sensitivity analysis restricting the sample to non-hospitalized respondents were largely consistent with results from the primary analysis for 30-day COVID-19, with one exception. Although cardiovascular disease was not associated with 30-day COVID-19 among the entire sample, non-hospitalized respondents with (vs. without) cardiovascular disease had 54% higher prevalence of 30-day COVID-19 (aPR 1.54, 95% CI 1.01-2.34). • LIMITS: skip patter means missed data; lack of diversity so underestimate socioeconomic disparities; recall and response bias; severe experiences more likely to participate
(Iqbal et al., 2021)	• Peer-reviewed • UK • Systematic Review	• Systematic Review • Aim: clarify characteristics and predictors of acute and chronic post-COVID conditions • Exact studies and findings not extracted.

(Islam et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
		• N=403
		• Aim: describe the variation in the risk of readmission or death within 60 days of discharge following hospitalization for COVID-19, by age, sex and ethnicity.
		• Population: Patients discharged during 4 month period from NHS
		• Follow-up average 8.6 weeks
		• RISK FACTORS
		  • The standardized incidence rate (per 100 person-months) of readmission or death within 60 days of discharge was twice as high among **those aged 65 years** as those < 65 years [23.4 vs 10.6; standardized incidence rate ratio 2.21 (95% CI: 1.45–3.56)] and among **women** as men [34.9 vs 15.5; standardized incidence rate ratio 2.25 (1.05–4.18)].
		  • There was no evidence of variation in incidence by ethnicity.
		• LIMITS: limited generalizability (1 region, limited diversity)

(Lerum et al., 2020)	• Peer-reviewed
	• Norway
	• Observational cohort
		• N=103
		• Aim describe symptoms and pulmonary function 3-months following hospital admission for COVID-19
		• Patients: Patients aged >18 years who had been admitted for >8 h with a discharge diagnosis
		• Follow-up average 11.8 weeks for COVID-19 or viral pneumonia
		• RISK FACTORS:
		  • Age per year NOT associated with dyspnea (OR 0.81, p=0.231). **Age per year** associated with ground glass opacities (GGO) in chest CT (OR 1.81, p=0.004). Age per year NOT associated with parenchymal bands in chest CT (OR 1.19, p=0.376).
		  • Male sex not associated with dyspnea (OR 0.39, p=0.69); not associated with GGO in chest CT (OR

		1.25, p=0.662); not associated parenchymal bands in chest CT (OR 1.35, p=0.584). • ICU survivors had similar dyspnea scores to hospitalized but non-ICU patients (OR 0.67, p=0.553), similarly for pulmonary function (OR 1.54, p=0.517), but higher prevalence of GGO (adjusted OR 4.2, 95% CI 1.1–15.6) and lower performance in usual activities. • LIMITS: possible participation bias • STRENGTHS: multicenter, prospective design; age and prevalence similar between sample and population estimates; dyspnea is subjective so valuable to have diagnostic imaging.

(Liang et al., 2020)Liang	• Peer-reviewed
	• China
	• Observational cohort
		• N=67
		• Aim: to evaluate symptoms and lung function of COVID-19 survivors post-discharge
		• Population: Discharged from hospital
		• Follow-up 12 weeks
		• RISK FACTORS: **None found**
		  • The characteristics of patients with or without impaired PFT at 3-months after discharge were not statistically significant between the two groups.
		  • Multivariate analysis found that none of the prognostic factors (including age (OR 1.022, p=0.196), sex (OR 0.795, p=0.662), comorbidities (OR 0.911, p=0.921), and length of hospital days(1.025, p=0.331)) were significantly associated with the impaired lung function tests at 3-months after discharge.
		  • In accordance with the ATS recommendations, 12 five patients received a bronchodilator and post-bronchodilator spirometry values were used in the analysis.
		• LIMITS: small sample; single site; large decline rate so selection bias; some patients had no prior medical history so unclear if pre-existing or novel diagnoses

(Machado et al., 2021)	• Peer-reviewed • The Netherlands • Cross sectional survey	• N=1,939 • Population: adults with confirmed or suspected COVID-19 infection from online panel or social media groups for long-COVID • 12 week follow-up • Completed a battery of online surveys relating to symptoms, health-related quality of life (EQ-5D-5L), impairment in work and activities, and functional status • Subjects with no functional limitations were **older** compared to subjects presenting slight, moderate and severe functional limitations. Subjects with severe functional limitations (Grade 4 on the PCFS Scale) **presented lower BMI** compared to all other groups. • Other factors associated with poorer functional status were **marital status** (prevalence of category 'alone' highest in Grade 4) and **presence of comorbidities** (prevalence of '≥ 2 comorbidities' highest in Grade 4). • Subjects with severe functional limitations also had the highest prevalence of a 'symptom-based' COVID-19 diagnosis.

		• All associations found significant is p<0.05 for grades 3/4 vs. 0/1/2. Specific odds ratio not provided.
(Mei et al., 2021)	• Peer-reviewed • China • Cross sectional survey	• N=3,677 • AIM: to record and investigate possible post-COVID-19 sequelae and herd immunity • Population: post-hospital discharge with confirmed COVID-19 • Follow-up average 20.6 weeks • RISK FACTORS: ◦ The incidence of post-COVID-19 sequelae among elderly COVID-19 survivors (**age ≥60 years**) was slightly increased compared to that of young COVID-19 survivors (age <60 years; relative risk = 1.05, 95% CI = 1.02–1.10, p = 0.007). • LIMITS: no control; not designed to determine impact of treatment

(Menges et al., 2021)	• Preprint
	• Switzerland
	• Observational cohort
		• N=431
		• Aim: assess prevalence of symptomatology and health care utilization at least 6 months after COVID-19 infection.
		• Population-based prospective cohort study using online survey
		• Population: Adults with positive COVID-19 test
		• Mean follow-up 21.7 weeks
		• Study provides frequency of contact/utilization with the healthcare system after COVID-19 positive test. Offers some insight on risk factors for healthcare usage.
		• RISK FACTORS:
		  ◦ A higher percentage of female participants reported not having recovered compared to males (31% versus 21%). We observed a higher percentage of non-recovered participants among 40-64 year-olds compared to older and younger age groups (32% versus 24% in ≥65 year-olds and 19% in 18-39 year-olds). A higher percentage of initially hospitalised individuals reported not to have recovered compared to those that did not require hospitalization (36% versus 23%).
		In multivariable analyses among initially symptomatic participants, we found evidence that **severe to very severe symptoms during acute illness** (OR 2.05, 95% CI 1.27 to 3.34, p=0.003) and the **presence of comorbidities** (OR 2.08, 95% CI 1.24 to 3.50, p=0.005) were associated with higher odds of not having recovered. **Females** were less likely to have recovered at 6-8 months after diagnosis compared to males (OR 0.53, 95% CI 0.33 to 0.85, p=0.009)
		  ◦ DYSPNEA: In multivariable analyses, we found evidence for an association of grade ≥1 dyspnea with **female sex** (OR 2.24, 95% CI 1.31 to 3.87, p=0.003), initial hospitalization (OR 4.17, 95% CI 2.23 to 7.91, p<0.001) and body mass index (OR 1.14 per unit increase, 95% CI 1.08 to 1.20, p<0.001), but not with age, initial symptom severity, smoking or respiratory comorbidity

		MENTAL HEALTH: The proportion of participants reporting depressive symptoms was higher in older age groups and in females. In multivariable analyses, we found **no evidence** for an association of depression with age, sex, initial hospitalization, severity of symptoms at diagnosis, or the presence of comorbidities. • LIMITS: testing capacity early in pandemic might mean more severely-affected population; risk of self-selection bias; lack of baseline; not all health service utilization (i.e. no specialty use or diagnostic services);
(Mermelstein et al., 2021)	• Preprint • USA • Cross sectional survey	• N=401 • Aim: to describe the methods and results of a multipronged strategy to rapidly (over a 1-week period) identify and enroll a diverse sample, and to characterize post-acute sequelae of COVID-19 (PASC) in a predominantly Hispanic/Latinx and Black population in Illinois • Population: Adults, self-identify as Hispanic/Latinx and Black • Follow-up average 16 weeks • RISK FACTORS - In a multivariable logistic regression model, **older age** (40-59 vs. 18-39 years: adjusted odds ratio [aOR] = 0.46 [95% confidence interval, 0.24 to 0.90]) and having **been hospitalized with COVID-19** (vs. not hospitalized: aOR = 0.28 [0.12 to 0.64]) were independently associated with a lower likelihood of recovery within 3 months. - A similar pattern was noted in participants who were age 60 years and older vs. age 18-39 years, though differences were not significant. - Participants who were hospitalized with COVID-19 were significantly less likely to return to usual health within 3 months (vs. not hospitalized: aOR 0.28, 95% CI 0.12 to 0.64). • LIMITS: self-report re: COVID-19 positivity; no population-based sampling strategy and short window to participate so limited generalizability;
(Moreno-Pérez et al., 2021)	• Peer-reviewed • Spain • Observational cohort	• N=277 • Aim: to analyze the incidence of Post-acute COVID-19 syndrome (PCS) and its components, and to evaluate the acute infection phase associated risk factors. • Population: adults with COVID-19 who attended emergency department • Follow-up average 10 weeks • RISK FACTORS: **none found** After multivariate adjustment, no baseline clinical features, neither age, sex, comorbidity, severity of acute COVID-19 infection, COVID-GRAM score, inflammatory markers, ICU-admission, hospital/ICU length of stay, or treatment behave as independent predictors of post-COVID conditions.
(Osmanov et al., 2021)	• Peer-reviewed • Russia	• N=518 • Aim: to assess long-term outcomes in children previously hospitalized with Covid-19 and associated risk factors.

	• Observational cohort	• Population: children previously hospitalized with Covid-19
		• Follow-up average 36 weeks
		• RISK FACTORS:
		  ◦ **Age & Allergic disease:** In multivariable regression analysis, older age group was associated with persistent symptoms. When compared with children under two years of ages, those ages 6-11 years had an odds ratio of 2.74 (95% confidence interval 1.37 to 5.75) of persistent symptoms and those 342 12-18 years of age (OR 2.68, 95% CI 1.41 to 5.4) both vs. <2 years.
		  ◦ Another predictor associated with persistent symptoms was allergic diseases (OR 1.67, 95% CI 1.04 to 2.67).
		• Similar patterns were seen for children with co-existence of persistent symptoms from 2 or more categories: 6-11 years of age (OR 2.49, 95% CI 1.02 to 6.72), 12-18 years of age (OR3.18, 95% CI 1.43 to 8.11) both vs. <2 years. Allergic disease in children were also associated with a higher risk of long COVID

(O'Sullivan et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
		• N=155
		• Report early use of a rehabilitation tool for clinical practice
		• Population: GP assesses as having acute illness with ongoing rehabilitation needs (so COVID-19 diagnosis not required); military personnel
		• Mean 13 weeks follow-up
		• RISK FACTORS:
		  ◦ Patients who self-managed at home (n=100, 64.5%) were 75% less likely to receive laboratory confirmation (OR 0.25 (0.12 to 0.50), **Patients admitted to hospital wards and intensive care unit** were more likely to receive laboratory confirmation (OR 4.43 (1.84 to 10.63), p<0.01and OR 4.72 (1.20 to 18.56), p=0.03, respectively).
		  ◦ LIMITS: Results are highly focused on sub-analysis of patient groups who received a COVID test and those who did not, and location of acute care or no hospitalization was used as a proxy for risk.

(Park et al., 2021)	• Peer-reviewed
	• Korea
	• Cross sectional survey
		• N=10
		• Aim: to assess mental health in patients with COVID-19
		• Population: 10 patients recovering from COVID-19 pneumonia after discharge
		• Follow-up 4 weeks
		• RISK FACTORS:
		  ◦ Patients with high perceived stigma (n = 4) tended to have higher scores for PTSD symptoms (their IES-R-K mean score = 16.3 vs. 3.5 in patients with low perceived stigma; P = 0.067), especially in the hyper-arousal (mean score = 4.8 vs. 0.2, P = 0.010) and numbness (mean score = 3.3 vs. 0.5, P = 0.019) domains.
		  ◦ Survivors with a previous history of psychiatric treatment (n = 3) also had higher scores for PTSD symptoms (mean score = 20.3 vs. 3.6 in patients without a previous history of psychiatric treatment, P = 0.017); still, they did not show scores for depression and anxiety that differed significantly from survivors without such a history.

		• There were no significant differences in the scores for depression, anxiety, or PTSD by pneumonia severity and whether their tracing routes were disclosed to the public. • LIMITS: Too small of a sample to appropriately perform any quantitative analyses. • Due to size of sample, not including in synthesis above.
(Postigo-Martin et al., 2021)	• Peer-reviewed • Spain • Review	• Review • Aim: describes a prospective surveillance model and includes some literature. • Exact studies and findings not extracted.
(Public Health Ontario, 2021)	• Grey Literature • Canada • Systematic Review	• Review • Aim: updates the evidence on the persistent symptoms of post-acute COVID-19 by organ system, explores the risk factors associated with persistent symptoms, and outlines the implications of post-acute COVID-19. • Exact studies and findings not extracted.
(Health Ontario, 2021)	• Grey Literature • Canada • Systematic Review	• Review • Aim: Explore what is known about pediatric post-acute COVID-19 and multisystem inflammatory syndrome in children • Exact studies and findings not extracted.
(Qu et al., 2021)	• Peer-reviewed • China • Observational cohort	• N=540 • Aim: To determine the health-related quality of life (HRQoL) of COVID-19 patients after discharge and its predicting factors • Population: OVID-19 patients who had been discharged from designated hospitals • Follow-up average 12 weeks • RISK FACTORS • Results of logistic regression showed that **female** (odds ratio (OR): 1.79, 95% confidence interval (CI): 1.04–3.06), **older age** (≥60 years) (OR: 2.44, 95% CI: 1.33–4.47) and the **physical symptom after discharge** (OR: 40.15, 95% CI: 9.68–166.49) were risk factors for poor physical component summary; the physical symptom after discharge (OR: 6.68, 95% CI: 4.21–10.59) was a risk factor for poor mental component summary. • LIMITS: confounding factors; reliability of SF-36 is low in study; design is cohort but implementation like cross-sectional survey so difficult to make causal inferences.
(Research, 2021)	• Grey Literature • Canada • Review	• Review • Summarizes the research evidence associated with "long COVID", including definitions, risk factors (i.e., sex/gender, age), symptomatology, prognosis, therapeutics, and other emerging research findings. • Exact studies and findings not extracted.
(Sigfrid et al., 2021)	• Preprint • UK • Observational cohort	• N=327 • Aim: to establish the long-term effects of Covid-19 following hospitalization. • Population: adults, admitted to hospital during study period with suspected COVID-19 and discharged at least 90 days previous • Follow-up average 31.7 weeks.

		• RISK FACTORS ◦ **Females under the age of 50 years** were five times less likely to report feeling recovered (adjusted OR 5.09, 95% CI 1.64 to 15.74), were more likely to have greater disability (adjusted OR 4.22, 95% CI 1.12 to 15.94), twice as likely to report worse fatigue (adjusted OR 2.06, 95% CI 0.81 to 3.31) and seven times more likely to become more breathless (adjusted OR 7.15, 95% CI 2.24 to 22.83) than men of the same age. • LIMITS: not generalizable; selection bias; design is cohort but implementation like cross-sectional survey so difficult to make causal inferences.

(Sudre et al., 2021)	• Peer-reviewed
	• UK
	• Observational cohort
		• N=4,182
		• Aim: to compare users of an app based on persistence of symptoms post-COVID-19
		• Population: Used app when age ≥ 18 years; BMI greater than 15 and less than 55, a positive SARS-CoV-2 swab test (PCR) confirming the diagnosis of COVID-19; disease onset between 14 d before and 7 d after the test date, and before the 30 June 2020
		• Follow-up average 6 weeks
		• RISK FACTORS:
		  ◦ Individuals who reported **more than five symptoms in the first week** (the median number reported) were significantly more likely to go on to experience LC28, (OR 3.95 (CI 3.10–5.04)). This strong risk factor was predictive in both sexes and in all age groups. The five symptoms experienced during the first week that were most predictive of LC28 in the individuals with COVID-19 were: **fatigue** (OR 2.83 (CI 2.09–3.83)), **headache** (OR 2.62 (2.04–3.37)), **dyspnea** (OR 2.36 (CI 1.91–2.91), **hoarse voice** (OR 2.33 (1.88–2.90)) and **myalgi**a (OR 2.22 (1.80–2.73)). Similar patterns were observed in both sexes.
		  ◦ **In adults aged over 70 years, loss of smell** (which was generally less common in this age group) was the most predictive symptom of long COVID (OR 7.35 (CI 1.58–34.22)) before fever (OR 5.51 (CI 1.75–17.36) and hoarse voice (OR 4.03 (CI 1.21–13.42).
		• LIMITS: Selection bias as only those who contribute to an app. Self-report so recall bias.

(Taquet et al., 2021)	• Peer-reviewed • US • Observational Cohort	• N=236,379 • Aim: investigate the incidence of neurological and psychiatric diagnoses in survivors in the 6 months after documented clinical COVID-19 infection, and we compared the associated risks with those following other health conditions • Population: adult COVID-19 survivors • Follow-up average 24 weeks • RISK FACTORS ◦ The severity of COVID-19 had a clear effect on subsequent neurological diagnoses. But the incidences and HRs of these were greater in patients who had required hospitalization, and markedly so in those who had **required ICU admission** or **had developed**

		encephalopathy, even after extensive propensity score matching for other factors (eg, age or previous cerebrovascular disease) (all p values <0.001). • LIMITS: Focus on specific sequelae as complications rather than on symptomatology of post-COVID conditions. Size of sample queries if number of analyses led to statistical significance or if there was a statistically significant analysis.

(Tudoran et al., 2021)	• Peer-reviewed
	• Romania
	• Cross sectional survey
		• N=125
		• Aim: to explore cardiac function in patients not yet recovered from COVID-19
		• Population: aged under 55 years; patients hospitalized during the first COVID-19 outbreak for a mild/moderate form; confirmed COVID-19 diagnosis
		• Follow-up average 8 weeks
		• RISK FACTORS
		  • Referring to LV-GLS as the most sensitive parameter characterizing the LV function, if we take into account only the 11 patients with impaired LV-SF, the statistical analysis by using Spearman's correlation, reveal statistically significant correlations with several inflammatory markers like Interleukin-6, CRP, and with CK-MB ($r = 0.88$, $r = 0.829$, and $r = 0.72$, with $p < 0.001$, $p = 0.002$, and $p = 0.012$, respectively) and moderate ones with age, BMI, and TCT score ($r = 0.69$, $r = 0.53$, and $r = 0.59$ with $p = 0.017$, $p = 0.09$, and $p = 0.05$, respectively).
		  • A strong correlation with MAPSE (0.85, $p = 0.001$) was also documented, as well as moderate ones with LVEF, RV-GLS, and TRV ($r = -0.55$, $r = 0.61$ and $r = 0.64$).
		  • Considering that elevated values of E/ e' ratio were the most common finding in patients with DD, by using the Spearman's correlation, the statistical analysis **evidenced statistically significant correlation of the E e' ratio with age and BMI ($r = 0.81$ and $r = 0.67$, $p < 0.001$), with COVID TCT score** ($r = 0.79$, $p < 0.001$), and with markers of inflammation determined at the admission in the hospital: CRP, interleukin-6, and fibrinogen ($r = 0.9$ with $p < 0.001$, respectively $r = 0.63$ with $p = 0.002$). We evidenced moderate correlations with other parameters characterizing DD: LAVI ($r = 0.77$, $p < 0.001$), TRV ($r = 0.47$, $p = 0.029$), and the number of days until negativation of PCR ($r = 0.7$ $p < 0.001$). Although LVMI should be a factor that strongly influences DD, due to different limits for men and women, the correlation was not statistically significant.
		• LIMITS: Hospitalized so not generalizable to general population. Results very specific to physiological functioning versus patient experience of symptoms, which is what primarily discussed in post COVID syndrome. Other studies have noted that physiological functioning does not predict symptomatology in post-COVID conditions.

(Vanichkachorn et al., 2021)	• Peer-reviewed • USA • Observational Cohort	• N=100 • Population: adults with positive COVID-19 test and symptoms four or more weeks after positive test.

		• Aim to describe patients reporting prolonged symptoms after COVID-19 infection • Description of patient population at a specialty, rehabilitation-focused outpatient clinic (COVID Activity Rehabilitation Program) • Most patient presented at 12 weeks post-diagnosis • Describes elements of the program, and some utilization statistics • RISK FACTORS ◦ The CARP PCS population appears distinct from those who suffer more severe cases of acute SARS-CoV-2 infection. While advanced age and the presence of several comorbidities are positively associated with increased mortality and hospitalization during acute infections, CARP patients were younger (mean age 45.4 years old + 14.2) than groups associated with severe infection, high mortality, and hospitalization. In addition, most PCS patients had no significant medical conditions prior to their SARS-CoV-2 infection, making it difficult to predict which patients may be at risk for PCS. • LIMITS: Single clinic; post hoc analysis; no odds ratio or p-values provided; not clear on who comparing too • Not included in synthesis above.
(Vehar et al., 2021)	• Peer-reviewed • USA • Review	• Review • Aim: review post-acute sequelae of COVID-19 • Exact studies and findings not extracted.

(Whittaker et al., 2021)	• Preprint
	• UK
	• Observational Cohort
		• N=46,687
		• Aim: To investigate new primary care-recorded symptoms, diseases, prescriptions and healthcare utilization in patients post-acute COVID-19 infection, comparing outcomes between community-only and hospitalized patients
		• Population-based cohort study (non-COVID-19 controls)
		• Population: adults registered with general practice
		• RISK FACTORS:
		  ◦ Women had higher rates of fatigue and older women in particular had higher rates of joint pain compared to men.
		  ◦ Younger women had higher rates of headache and anxiety compared to men and higher rates of skin rash, depression, and sore throat compared to men and older adults
		  ◦ This is a preprint that describes the statistical results as available in appendices, however those appendices are not available.
		• LIMITS: only wave 2 patients; no access to statistical tests to view p-values and odds ratios.

(World Health Organization, 2021b)	• Grey Literature • Denmark • Review	• Review • Policy brief, provides a review of larger population-based studies of the various approaches taken across multiple countries to best define, understand, and provide care for post-COVID conditions. • Exact studies and findings not extracted.
(Yong, 2020)	• Peer-reviewed • Malaysia	• Review

	• Review	• Aim: review of literature on Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments • Exact studies and findings not extracted.
(Zapatero & Hanquet, 2021)	• Grey Literature • Belgium • Review	• Pragmatic review • Review of risk factors (older age, co-morbidities, obesity, pre-existing psychiatric disorder, Blood type A) • Exact studies and findings not extracted.

Table 6C. Details from Articles Informing Vaccination Implications

Author	Study Details (Article Type, Country, Study Design)	Vaccination Implications

(Arnold et al., 2021)	• Preprint
	• UK
	• Observational cohort
		• N=66
		• Population: patients originally hospitalized with COVID-19 at 1 UK hospital (established cohort, including subset with persistent post-acute symptoms)
		• Aim: assess change in quality of life and symptoms after vaccination
		• Data collection included surveys for quality of life, symptoms, well-being
		• Mean follow-up 32 weeks
		• Small, statistically-significant improvements in post COVID syndrome symptoms and less worsening symptoms in those patients who are vaccinated versus those unvaccinated. Does not vary with type of vaccine.
		  ◦ No significant worsening in quality of life or mental wellbeing metrics pre- vs. post- vaccination.
		  ◦ About 41% reported transient (<72 hour duration) systemic effects (including fever, myalgia and headache)
		  ◦ When compared to matched unvaccinated participants from the same cohort, those who had received vaccine had a small improvement in Long COVID symptoms, with a decrease in worsening symptoms (5.6% vaccinated vs. 14.3% unvaccinated) and increase in symptom resolution (23.2% vaccinated vs. 15.4% unvaccinated) (p=0.035).
		  ◦ No difference in response was identified between Pfizer-BioNTech or Oxford-AstraZeneca vaccines.

(Raw et al., 2021)	• Preprint • UK • Observational cohort	• N=974 • Population: patients receiving first dose of Pfizer vaccine at 3 hospitals • Aim: Determine frequency of adverse events after vaccination for patients with and without previous COVID-19 infection • Survey regarding demographics, and self-reported adverse events (nature, severity, duration and onset) • Timing is self-reported, but analysis compared <24 hours vs. > 48 hours of adverse event onset • Findings suggest

		• The proportion of participants reporting at least one moderate-to-severe symptom was higher in the previous COVID-19 group (56% v 47%, Odds Ratio (OR)=1.5 [95%CI, 1.1–2.0], p=0.009). • Symptom onset was mostly within 24 hours (75%) with no onset >48 hours. After controlling for age and sex, higher symptom number (1.61 (2.26) v 0.89 (2.02) symptoms, d=0.34 [0.20-0.49], p<0.001) and severity (2.7 (6.65) v 1.5 (2.21) symptom-days, d=0.41 [0.27-0.55], p<0.001) were significantly associated with reporting previous COVID-19. • Logistic regressions controlling for age and sex showed five systemic symptoms were significantly associated with previous COVID-19 status: fever (OR 2.87, p=0.044), fatigue (OR 1.78, p=0.011), myalgia (OR 2.34, p<0.001), arthralgia (OR 2.25, p=0.004) and lymphadenopathy (OR 5.18, p=0.033). • Symptom number and duration was not significantly higher in those with Long-COVID after accounting for gender and age effects and no individual symptom was significantly associated with this condition.

Table 6D. Details from Articles Informing Health Service Implications

Author	Study Details (Article Type, Country, Study Design)	Implications around Health Services

(Al-Aly et al., 2020)	• Peer-reviewed
	• USA
	• Observational Cohort
		• N=73,435
		• Secondary analysis of administrative data from Veterans' Affairs, included negative-outcome controls
		• Population: never-hospitalized (community-only) patients who survived at least 30 days post COVID-19 diagnosis
		• Median follow-up 18 weeks
		• Increased novel use of medication and medical diagnoses after COVID-19 infection even when never-hospitalized. Study does not clarify what health services are used to "get" to those diagnoses.
		  • Observed an increased risk of the incident use of several classes of medication, including pain medications (opioid and non-opioid), antidepressant, anxiolytic, antihypertensive, antihyperlipidaemic and oral hypoglycaemic drugs and insulin.
		  • An increased risk of a broad array of specific clinical manifestations that include acute coronary disease, arrhythmias, acute kidney injury, chronic kidney disease, memory problems and thromboembolic disease.
		  • The risk gradient that increased across the care setting of the acute COVID-19 infection from non-hospitalized individuals to those who were hospitalized, and risk

		was highest in patients who were admitted to intensive care

(Ayoubkhani et al., 2021)	• Peer-reviewed
	• UK
	• Observational Cohort
		• N=47,780
		• Aim: Estimate excess morbidity after severe COVID-19 (hospitalized) using administrative data (retrospective, matched cohort study)
		• Mean follow-up 20 weeks
		• Increased rates of re-admission and new diagnoses post-discharge for severe COVID-19 hospitalization. Study does not clarify what health services are used to "get" to those diagnoses.
		  • After admission to hospital for COVID-19, 29.4% were readmitted (compared to 9.2% of controls with similar personal and clinical characteristics in control)
		  • Diabetes, major adverse cardiovascular event, chronic kidney disease, and chronic liver disease were diagnosed after discharge in 4.9%, 4.8%, 1.5%, and 0.3% of individuals with COVID-19, respectively, occurring at rates of 127 (122 to 132) for diabetes, 126 (121 to 131) for major adverse cardiovascular event, 39 (36 to 42) for chronic kidney disease, and 7 (6 to 9) for chronic liver disease diagnoses per 1000 person years.
		  • Those with COVID-19 were diagnosed with major adverse cardiovascular event, chronic liver disease, chronic kidney disease, and diabetes after discharge from hospital 3.0 (2.7 to 3.2), 2.8 (2.0 to 4.0), 1.9 (1.7 to 2.1), and 1.5 (1.4 to 1.6) times more frequently, respectively, than in the matched control group.
		  • NOTE: focus on severe COVID-19, so likely many syndromes (e.g. post-ICU syndrome) implicated in post-discharge health service use.

(Banerjee et al., 2021)	• Peer-reviewed
	• USA
	• Observational Cohort
		• N=621
		• Retrospective cohort
		• Population: Adults discharged from hospital after COVID-19 pneumonia
		• Follow-up about 4 weeks
		• Aim: Assess outcomes post-discharge with supplemental home oxygen (and nursing education)
		• Study details mortality and readmission rate for patients post-COVID19 who received home oxygen. Does not indicate % of overall patients who used this, just outcomes of the ones that did use home oxygen.
		  • The all-cause mortality rate was 1.3% (95% CI, 0.6%-2.5%) and the 30-day return hospital admission rate was 8.5% (95% CI, 6.2%-10.7%) with a median follow-up time of 26 days (interquartile range, 15-55 days).
		  • 30 days readmission: 30-day return hospital admission rate was 8.5% (95% CI, 6.2%-10.7%) stratified by those with discharged home with oxygen.
		  • The observed 30-day readmission rate for these home oxygen patients was also lower than the overall post-acute care 30-day readmission rate for DHS patients (15.2%), as reported to California Department of Health Care Services in 2020.

		• LIMIT: no control in this study; very short follow-up period

(Bowles et al., 2021)	• Peer-reviewed
	• USA
	• Observational Cohort
		• N=1,409
		• Aim: Describe home health recovery of patients with COVID-19 and risk factors associated with re-hospitalization or death
		• Retrospective observational cohort
		• Population: Adults with COVID-19 discharged from a short-stay acute care hospital and admitted to home health care
		• Mean follow-up 12 weeks
		• Study elaborates usage of home health care services, including average visits and type of therapy used. No control comparison so difficult to predict how many will need home health care, but for those that go it does provide insights.
		    • The 1409 patients with COVID-19 on HHC service between 1 April and 15 September 2020 received 13 926 home health visits.
		    • Most visits (76%) were in person, 16% by telephone, and 8% by tele-video. Registered nurses provided 52% of the visits, physical therapists provided 37%, and the remainder were provided by social workers and occupational and speech therapists.
		    • The patients received 11.1 visits on average (marginal means 95% CI, 10.8 to 11.4 visits).
		    • Compared with the under-65 age group, the 80-and-older group received more visits overall (11.9 [CI, 11.1 to 12.6] vs. 10.9 [CI, 10.4 to 11.4]), more in-person visits (9.1 [CI, 8.5 to 9.7] vs. 8.1 [CI, 7.7 to 8.5]), and more physical therapy visits (4.6 [CI, 4.0 to 5.1] vs. 3.8 [CI, 3.5 to 4.1]).
		    • 137 (10% [CI, 8.1% to 11.2%]) were re-hospitalized. Only 23 patients remain on service.
		    • After an average of 32 days of care (SD, 25.7), 94% of patients with COVID-19 in home health care were discharged (n= 1319); 1241 (87%) were discharged without any adverse events (re-hospitalization or death). More than half (57%) of those re-hospitalized returned to HHC and were subsequently discharged (n= 78)

(Castro-Avila et al., 2020)	• Peer-reviewed • UK • Sequential mixed-methods	• N=193 care staff and GPs • Sequential mixed methods (online survey and interviews) • Aim: Identify follow-up services available during and after UK's first wave of COVID-19 pandemic, and views of critical care staff and GPs on patients' future needs. • Population: critical care staff and GPs • Study describes clinician's perspectives on changes to health service provision in first wave of COVID-19. See post-ICU and rehabilitation support important. But, no metrics on actual utilization. Most care provided virtually, but not considered adequate by staff. • During first wave, follow-up services were offered in 80 units (71% sampled); of these, 20 reported ceasing provision and 53 modifying provision of services during the pandemic. 8 units implemented a new follow-up

		service after the peak of the pandemic. Occupational therapy and physiotherapy were the services with the greatest increase.
		• Over 60% of GPs were unaware of the follow-up services generally provided by their local hospitals and whether or not these were functioning during the pandemic. On average, four patients from their patients' list had been through ICU due to severe COVID-19. Physical and mental healthcare needs were ranked similarly high in terms of areas of concern with future patients recovering after a critical care stay.
		• Interview key themes:
		  ◦ They expected patients with COVID-19 to suffer a longer-lasting deterioration of lung function, potential issues with renal function, a high incidence of shoulder injuries due to proning and cognitive problems related to the incidence of delirium.
		  ◦ Before COVID-19, most ICU interviewees reported having a post-ICU follow-up service; the few who did not were planning to implement one after the pandemic. Most follow-up services were suspended during the peak of the first wave, as staff returned to in-hospital clinical duties. The few places that continued to provide such services used telephone follow-up, delivered by staff that were shielding.
		  ◦ All unit staff we interviewed follow patients up 2–3 months after ICU discharge, but a minority also routinely call patients weekly (ICUnurse04, North East) or monthly (ICUnurse08, East Midlands).
		  ◦ Two ICU interviewees said that they were implementing separate clinics for patients with COVID-19 to carry out extra recommended assessments, such as a chest X-ray at 6 weeks post-discharge as recommended by the British Thoracic Society.
		  ◦ Some ICU interviewees questioned the capacity of community rehabilitation services to improve patients' functioning. Both GPs and ICU staff felt that previous notions of thresholds for functional status post-ICU (several commented on assessments of patients climbing a flight of stairs) were arbitrary and not suitable for the wider age group of patients affected by COVID-19.
		  ◦ Barriers to follow-up care service provision: funding complexities, remit and expertise, and communication between ICU and community services.

(D'Cruz et al., 2021)	• Peer-reviewed • UK • Observational Cohort	• N=119 • Aim: investigate sequelae of severe COVID-19 pneumonia (hospitalization ≥48hrs), and identify risk factors • Prospective, single-centre observational cohort • Follow-up 7-9 weeks post-discharge follow-up

		• Population: adults discharged after severe COVID-19 pneumonia (hospitalization ≥48hrs) • Study noted hospital service use post-discharge and found 16-40% used some services. Time frame is lacking and no controls. • 57 (48%) patients used hospital services following hospital discharge: 23 (40%) attended outpatient appointments for monitoring of inpatient complications (haematology, renal, diabetes), 16 (28%) attended the emergency department, nine (16%) were re-hospitalized and nine (16%) attended planned outpatient appointments for pre-existing comorbidities.

(Hassenpflug et al., 2020)	• Peer-reviewed
	• USA
	• Quality Improvement
		• N=41
		• Aim: describe first series of patients with COVID-19 admitted to post-acute hospital
		• Single-centre observational descriptive report, based on administrative data
		• Median length of stay at post-acute hospital: 6 weeks
		• Study unclear on what proportion of hospitalized patients go to post-acute hospital. Few insights on health service utilization.
		    • Of 194 patients transferred to post-acute hospital during study period, 41 (21%) were admitted for continued recovery from confirmed COVID-19 pneumonia.
		    • All mechanical ventilation and hemodialysis interventions were initiated at the transferring hospital.
		    • None of the seven patients excluded from weaning were chronically ventilated prior to admission to the transferring hospital.
		    • Upon evaluation by the consulting pulmonologist on admission to facility, patients were determined not to be weaning candidates for the following reasons: physiologic instability (unmet readiness to wean parameters), and poor mentation or neurocognitive disorders.
		    • Patient characteristics: 51.2% on invasive mechanical ventilation; 67% admitted for weaning; 80.5% tracheostomy tube; hemodialysis 22%; 78% pressure injury ≥ stage 2.
		• LIMITS: Small cohort, unique population, relatively short follow-up, and unclear on service utilization fully in long-term care.

(Hernandez-Romieu et al., 2021)	• Peer-reviewed • USA • Observational Cohort	• N=3171 • Aim: clarify longer-term health care utilization and clinical characteristics of non-hospitalized adults after COVID-19 diagnosis • Population: non-hospitalized adults with positive COVID-19 test and 180 or more days since testing date • Mean follow-up 21.7 weeks • Study provides frequency of contact/utilization with the healthcare system in the 28-180 days after COVID-19 diagnosis. Offers some insight on usage over time.

		• Among 3,171 non-hospitalized adults who had COVID-19, 69% had one or more outpatient visits during the follow-up period of 28–180-days. • Compared with patients without an outpatient visit, a higher percentage of those who did have an outpatient visit were aged ≥50 years, were women, were non-Hispanic Black, and had underlying health conditions. Among adults with outpatient visits, 68% had a visit for a new primary diagnosis, and 38% had a new specialist visit. • Active COVID-19 diagnoses* (10%) and symptoms potentially related to COVID-19 (3%–7%) were among the top 20 new visit diagnoses; rates of visits for these diagnoses declined from 2–24 visits per 10,000 person-days 28–59 days after COVID-19 diagnosis to 1–4 visits per 10,000 person-days 120–180 days after diagnosis. The presence of diagnoses of COVID-19 and related symptoms in the 28–180 days following acute illness suggests that some non-hospitalized adults, including those with asymptomatic or mild acute illness, likely have continued health care needs months after diagnosis. • Among adults with one or more outpatient visits, 7,991 visits occurred 28–180 days after COVID-19 diagnosis, with a median of two (interquartile range = 1–4) visits per patient. Fewer than 2% (32) of patients were hospitalized 28–180 days after COVID-19 diagnosis. More than two thirds of patients (1,617; 68%) had visits for a new primary diagnosis. Among specialists visited, 1,627 (75%) patients visited a family, geriatric, or internal medicine provider, and 823 (38%) visited with a new specialist. Common new specialty visits potentially related to COVID-19 included dermatology (16%), behavioral/mental health (11%), gastroenterology (11%), and cardiology (10%). Overall, 58 (3%) patients saw a pulmonologist; 41 (71%) of these patients had not been evaluated by this specialty in the 12 months preceding their COVID-19 diagnosis. • COVID-19–related visits declined from 24 per 10,000 person-days during the 28–59-day interval to fewer than two per 10,000 person-days during the 120–180-day interval. Visits per 10,000 person-days for symptoms potentially related to COVID-19 declined during these same intervals, including those for throat or chest pain (from seven per 10,000 person-days to four), shortness of breath (from eight to three), cough (from four to two), and malaise and fatigue (from four to two). In contrast, rates of visits with chronic disease diagnoses (e.g., hypertension and diabetes) and urinary tract infections changed little over time. • LIMITS: mostly privately insured population; no non-COVID-19 control group; unclear whether use of COVID-19 diagnosis visit code used by providers.
(Lund et al., 2021)	• Peer-reviewed • Denmark	• N=8983

	• Observational Cohort	• Aim: To examine prescription drug and health-care use after SARS-CoV-2 infection not requiring hospitalization
		• Population-based cohort study using administrative data
		• Mean follow-up 12 weeks
		• Study gives insights on health service utilization and compares with COVID-19 negative individuals over same period.
		  ◦ By the end of follow-up, 6557 (73·0%) of 8983 non-hospitalised individuals with SARS-CoV-2 infection and 62 391 (77·1%) of 80 894 SARS-CoV-2-negative individuals had visited their general practitioner, were seen at a hospital outpatient clinic, or were admitted to hospital (appendix p 5).
		  ◦ Comparing overall health-care use between SARS-CoV-2-positive and SARS-CoV-2-negative individuals, we observed increased PERR-adjusted rate ratios for general practitioner visits (1·18 [95% CI 1·15–1·22]) and outpatient clinic visits (1·10 [1·05–1·16]) among SARS-CoV-2-positive individuals.
		  ◦ We found no material difference between cohorts for emergency department visits (1·07 [0·88–1·30]) or inpatient hospitalizations (1·00 [0·87–1·14]; appendix pp 14–15).
		  ◦ Among health-care users, most individuals had a single visit to the general practitioner or hospital outpatient clinic, and few individuals had five or more visits.
		• LIMITS: Follow-up was limited to 6 months after a test for SARS-CoV-2, which might not yet account for all long-term complications and persisting symptoms after COVID-19. Information on the indication for testing was not available.

(Maxwell, 2020)	• Grey Literature • UK • Review	• Review • Makes recommendations about care in all settings for adults, children and young people with new or ongoing symptoms 4+ weeks after start acute COVID-19 • Recommendations more about generic good quality care. Nature of report means no insight on frequency of utilization. ◦ Assessment recommendations for integrated multidisciplinary rehabilitation services (e.g. consider all bodily systems; personal goal identification; symptom management advice for all presenting symptoms; make follow-up strategy; and shared decision-making)
(Menges et al., 2021)	• Preprint • Switzerland • Observational Cohort	• N=431 • Aim: assess prevalence of symptomatology and health care utilization at least 6 months after COVID-19 infection. • Population-based prospective cohort study using online survey • Population: Adults with positive COVID-19 test • Mean follow-up 21.7 weeks • Study provides frequency of contact/utilization with the healthcare system after COVID-19 positive test. Offers some insight on risk factors for healthcare usage. ◦ A total of 170 (40%) participants reported having had at least one contact with the healthcare system (i.e., re-

		hospitalization, general practitioner visits, or medical hotline calls) for reasons related to COVID-19. • Out of 81 individuals who were initially hospitalized due to COVID-19, eight (10%) were admitted to a hospital again at least once due to persistent symptoms or COVID-19 related complications, with a maximum of three re-hospitalizations. • More than half of the participants (n=224, 52%) reported at least one general practitioner visit for any reason, and 150 (36%) had a general practitioner visit related to COVID-19. Among those, the median number of general practitioner visits related to COVID-19 was 2 (IQR 1 to 3). • Older individuals (53% in those aged ≥65 years compared to 43% in 40-64 year-olds and 20% in 18-39 year-olds) and those initially hospitalized (63% versus 29% in non-hospitalized) more frequently reported to have seen their general practitioner. • 31 (7%) participants reported to have called a medical hotline at least once for a reason related to COVID-19, with a median of 1 call (IQR 1 to 2). • Among those that had not fully recovered, 37 (33%) did not report further healthcare contacts. • Since SARS-CoV-2 infection, a new physician-diagnosed medical condition was reported by 77 • (18%) participants. 27 (35%) of these diagnoses were considered to be related to COVID-19 by a physician. • In multivariable regression analyses, we found evidence for an association between healthcare use and initial hospitalization, having experienced severe to very severe symptoms, sex, and age ≥40 years. Furthermore, not having fully recovered (OR 3.53, 95% CI 2.14 to 5.86, p<0.001), experiencing grade ≥1 dyspnea (OR 2.35, 95% CI 1.40 to 3.99, p<0.001), fatigue (OR 1.61, 95% CI 1.04 to 2.50, p=0.03) and symptoms of depression (OR 2.13, 95% CI 1.32 to 3.45, p=0.002) were independently associated with having contact with the healthcare system. • LIMITS: testing capacity early in pandemic might mean more severely-affected population; risk of self-selection bias; lack of baseline; not all health service utilization (i.e. no specialty use or diagnostic services);
(National Institute for Health and Care Excellence et al., 2020)	• Grey Literature • UK • Review	• Review document • Aim: guidance to assist healthcare systems establish and maintain post-COVID assessment services • Paper provides recommendations on types of health services likely required, but nature of report means no insight on frequency of utilization. • Some patients will need further therapeutic input, rehabilitation, psychological support, specialist investigation or treatment once they have been assessed, and it is the responsibility of the assessment service to refer patients on to existing services as needed, so that care is coordinated and joined-up.

		Advice or signposting as a one-off intervention in the assessment service may also be offered. • Gives minimum standards for post-COVID assessment service (e.g. coverage, thresholds for referrals, communication strategy, access to diagnostics, multidisciplinary team). • Gives guidance on what support patients should receive (e.g. self-management advice; specialist referral; clear pathways; GP communication; multidisciplinary rehabilitation)

(Nurek et al., 2021)	• Preprint
	• UK
	• Modified Delphi
		• N=33 physicians
		• Population: UK physicians using a social media platform specific to physicians interested in long COVID
		• Aim: Get consensus on physicians on recognition, diagnosis and management of post-COVID conditions
		• Delphi process included 2 online surveys.
		• Expert Delphi panel provided strategies for health care providers and system, but nature of paper no exact % on implications of such recommendations on resource use.
		  ◦ Long COVID clinics must operate in context of rapidly evolving practice amongst both GPs and specialists.
		  ◦ Care pathways in holistic care, investigation of specific complications, management of potential symptom clusters in cardiac disease, dysautonomia and mast cell disorder, and individualized rehabilitation are needed.
		  ◦ Long COVID alone is insufficient diagnosis unless other causes have been excluded.
		  ◦ Require face-to-face assessment
		  ◦ Lots of diagnostic imaging and specialty referrals are recommended for appropriate assessment.

(O'Sullivan et al., 2021)	• Peer-reviewed article
	• UK
	• Cross-sectional Survey
		• N=155
		• Report early use of a rehabilitation tool for clinical practice
		• Population: GP assesses as having acute illness with ongoing rehabilitation needs (so COVID-19 diagnosis not required); military personnel
		• Mean 13 weeks follow-up
		• Narrative discussion on importance of referral to appropriate primary and/or specialty care based on principal symptoms. No empirical data on exact impacts and size of referrals, just that are likely to be some.
		  ◦ Given the uncertainty of the clinical course of post-COVID-19 syndrome, patients were reassured that re-referral from primary care was welcomed where necessary.
		  ◦ Further involvement of specialist services, including dietitians, psychology or DMRC COVID-19 Recovery Service was also performed when needed.
		  ◦ These principal symptoms should be a key consideration for the rehabilitation of individuals with post-COVID-19 syndrome.

(Parkin et al., 2021)	• Peer-reviewed article • UK	• N=225 • Article focuses on describing a functioning, comprehensive multidisciplinary rehabilitation pathway for

	• Descriptive	patients with COVID-19 post-discharge. Eligibility included persistent symptoms 7 weeks after hospital discharge. • In describing this pathway, it provided a brief description of the demographics of the population who had been supported by this pathway. • Study overviews the services available and triggered by the pathway. The frequency of utilization is not elaborated in this study. ◦ The Community COVID-19 MDT pathway was established in September 2020, as part of the NHS England "Five-point plan" to embed post-COVID-19 syndrome assessment clinics across England.7 the establishment of a 3 tier model of post COVID management. ◦ Patients with typical symptoms lasting between 1 and 2 months self-manage using the online resources outlined in Figure 1. Those who have Level 2 low/moderate complexity (such as single discipline needs) are supported by non-COVID specific care and therapy services, such as community occupational and physiotherapy. For patients who meet the Level 1 criteria of having prolonged symptoms over 3 months with a clear need for more than 1 specialist role are eligible for referral into the Community COVID-19 MDT. ◦ The Level 1 Community COVID-19 MDT consists of 2 Allied Health Professional (AHP) Pathway Co-ordinators, 2 Physiotherapists, 2 Occupational Therapists, and 3 Consultants with specialisms in Rehabilitation Medicine, Respiratory Medicine and Cardiology; with specialist support from a Respiratory nurse, Respiratory Physiotherapists, 2 Dieticians, and 2 Neurological Occupational Therapists ◦ Where patients present with complex symptoms of cognitive communication or voice and upper airways disorders such as Inducible Laryngeal Obstruction, referrals are made to the Community Speech and Swallow service or the Acute Trust Specialist ENT Speech and Language therapy team. ◦ There are also referral pathways from the Community COVID-19 MDT to established local mental health and psychology services for patients who are experiencing distressing thoughts and feelings that impact on their participation of valued activities and/or roles. ◦ Article describes referral process and assessment. ◦ A traditional pulmonary rehabilitation approach is not taken by the team due to the predominance of fatigue in many cases, taking caution from the experience of those with chronic fatigue syndrome, in which incremental exercise programs are advised against. Those patients who require consideration of ambulatory oxygen are assessed as per British Thoracic Society (BTS) guidelines. Interventions are led by the patient's functional priorities and presenting

		symptoms, following the usual process of assessment, clinical reasoning and intervention planning. • No comparison and more descriptive study, so cannot speak definitively to impact or implications.

(Research, 2021)	• Grey Literature
	• Canada
	• Review
		• Review
		• Aim: to summarize evidence on Long COVID, including definitions, risk factors, symptomatology, prognosis, therapeutics, and other emerging research findings
		• Review gives general advice on health service implications.
		  • Research suggests that treating people with long COVID requires a multidisciplinary approach including evaluation, symptomatic treatment, treatment of underlying problems, physiotherapy, occupational therapy and psychological support.
		  • Some recommendations on management, with follow-up being most indicative of what health services may be required. But, no clarity on whether a chronic disease model or time-limited condition is at issue herein:
		    • Treatment of Minor Symptoms: Cough, pain, myalgia can be treated symptomatically with paracetamol (i.e., acetaminophen), cough suppressants, and oral antibiotics (if secondary bacterial infection is suspected)
		    • Etiology: Etiology behind the symptoms, if any, like pulmonary embolism, cerebrovascular accident, coronary artery disease, has to be treated as per the standard protocol; chest physiotherapy and neuro rehabilitation is important in patients with pulmonary and neuromuscular sequelae.
		    • Follow-up: The ideal frequency and duration of follow up is not clearly defined. In people with COVID-19 interstitial pneumonia, in the first 12 months, seven interactions with health care professionals (four face-to-face) are recommended, alongside four high-resolution CT scans, four six-minute walk tests (6MWT); four blood tests (including blood count and metabolic panel); and two SARS-CoV-2-IgG tests (i.e., antibody tests).
		    • Social and Economic Impact: As the disease continues to spread, more people may need health care support in the future, which could put more demand on the health care system. Clear guidelines regarding management of long COVID may help clear confusion among health care providers.

(Vaes et al., 2021)	• Peer-reviewed article • Belgium • Cross-sectional Survey	• N=1556 • Surveys looking at symptoms, quality of life, functional status and work productivity at 6 months follow-up after onset COVID-19 symptoms. • Follow-up at 12 and 24 weeks post-onset of acute COVID-19 symptoms • Population: membership on online peer support for long COVID (social media) • Self-reported health service utilization

		• The proportion of patients receiving physiotherapy or rehabilitation between 3 and 6 months of follow-up was significantly higher compared to the period from the infection to 3 months of follow-up (61.9% versus 31.8% and 11.7% versus 4.2%, respectively, p<0.001). • After the onset of COVID-19 related symptoms, patients receiving physiotherapy reported more symptoms (6 vs. 4, p<0.05) and a worse self-reported health (84.5% good vs. 91.7% good, p<0.05), work productivity, functional status (grade 2.6 vs. 2.0, p<0.05) and quality of life (0.613 vs. 0.706 mean index EQ-5D-5L, p<0.05) compared to patients who did not receive physiotherapy or rehabilitation. Similar differences found at 6 months (all p<0.05). • Between 3 and 6 months of follow-up, significant improvements were found in both patients who did and did not receive physiotherapy or rehabilitation. • NOTE: concerns with this paper as % in text are different for same content in supplemental.

(Vanichkachorn et al., 2021)	• Peer-reviewed article
	• USA
	• Observational Cohort
		• N=100
		• Population: adults with positive COVID-19 test and symptoms four or more weeks after positive test.
		• Aim to describe patients reporting prolonged symptoms after COVID-19 infection
		• Description of patient population at a specialty, rehabilitation-focused outpatient clinic (COVID Activity Rehabilitation Program)
		• Most patient presented at 12 weeks post-diagnosis
		• Describes elements of the program, and some utilization statistics
		  • Program elements include: function-focused interview (assess for fatigue, dyspnea, depression/anxiety, brain fog, BP/HR fluctuations, sleep quality, appetite, signs of pulmonary embolism/DVT; review pre-existing conditions; ability with ADLS and IADL; pre-COVID functional status; complete occupational history; goal identification); standard laboratory assessments (CBC, CMP, vitamin d, vitamin b-12, thyroid stimulating hormone); optional diagnostic tests; optional consultations
		  • Some statistics on the therapy, referral and diagnostic use by patients visiting outpatient clinic:
		    • Physical therapy (42%)
		    • Occupational therapy (27%)
		    • Brain rehabilitation consultation (22%)
		    • Infectious disease consultation (6%)
		    • Chest X-ray (34%)
		    • Spirometry with DLCO (27%)
		    • Trans Thoracic Echocardiogram (29%)
		    • Autonomic reflex testing (20%)

(Whittaker et al., 2021)	• Preprint • UK • Observational Cohort	• N=46,687 • Aim: To investigate new primary care-recorded symptoms, diseases, prescriptions and healthcare utilization in patients post-acute COVID-19 infection, comparing

		outcomes between community-only and hospitalized patients
		• Population-based cohort study (non-COVID-19 controls)
		• Population: adults registered with general practice
		• Increased health service utilization in hospitalized vs. community-only group.
		  ◦ The hospitalized group utilized more healthcare (including GP visits, referrals, emergency department, hospitalization) than the community group post-COVID-19, with a 2.7-fold difference in rates per 100,000 person-weeks [95%CI] between groups (52,775 [50,570 to 55,105] v. 19,405 [19,142 to 19,673]) in hospitalized and community groups, respectively.
		  ◦ Regarding utilization among the 6 and 12 months prior, healthcare utilization increased in both groups post-COVID-19 relative to pre-pandemic levels, this was much higher in the hospitalized group (61.2% increase v. 28.5%). Healthcare utilization was lower 6 months prior relative to other time-points for each group.

(World Health Organization, 2021b)	• Grey literature article
	• Denmark
	• Review
		• Policy brief, provides a review of larger population-based studies of the various approaches taken across multiple countries to best define, understand, and provide care for post-COVID conditions.
		• A review that touches on health system implications in caring for patients with post-COVID conditions, specifically the persistent symptoms:
		  ◦ Survey of UK general practitioners in 2020 found that 67% were looking after patients with COVID-19 symptoms lasting longer than 12 weeks. Only 23% had access to a Long COVID clinic that they could refer into (Royal College of General Practitioners, 2020).
		  ◦ Recommendations on model of care for post-COVID conditions should include multidisciplinary assessment services; should bring together physicians with expertise in different body systems, as well as multidisciplinary rehabilitation services, with core teams that could include, but not be limited to, occupational therapy, physiotherapy, clinical psychology and psychiatry, and rehabilitation medicine.
		  ◦ These services should be part of a model of care that includes integrated referral patterns between primary, secondary and community care.
		  ◦ Recommended process includes: an initial assessment should be undertaken in primary or secondary care to exclude serious underlying pathology, using a screening tool included in the documentation. Onward referral would then be negotiated by a single point of access to triage and refer on to one or more of three possible pathways for those whose symptoms persist beyond 12 weeks: post-COVID assessment clinics, local rehabilitation clinics or online self-management resources.

(Wildwing & Holt, 2021)	• Peer-reviewed
	• UK
	• Systematic Review
		• Systematic Review (n=45 studies)
		• Aim: systematic review of reviews of neurological symptoms of COVID-19 and implications for health care services
		• Review speaks to likely but hypothetical needs of patients with post-COVID conditions. No empirical data.
		  ◦ This review highlight the impact that short- and long-term neurological symptoms of COVID-19 may have on current health services.
		  ◦ Symptoms seen in Long Covid such as facial pain, muscle issues, neuralgia, fatigue and insomnia, may become long term and disabling, requiring sustained support from healthcare services such as pain-, fatigue- and sleep-clinics, neurological services and primary care.
		  ◦ Neurological symptoms of Long Covid may increase demand for already overstretched consultant-led neurological services clinics and may indicate a need for more qualified health professionals and specialists in neurology. The effects of COVID-19 on these services is hard to predict, as the neuropathy, myopathy and sensory deficits of SARS resolved within 3 months of recovery. However, as COVID-19 appears to be becoming Long Covid for up to 10% of patients, support is likely to be required, potentially for a significant number of people, if their symptoms do not resolve spontaneously.

(Yong, 2020)	• Peer-reviewed • Malaysia • Review	• Narrative review • Focus on pathophysiology, risk factors and treatments in long COVID • Literature review describes broad need for rehabilitation for long COVID, but that has to be personalized to this condition and these patients. No empirical data, more recommendations. No data on size/frequency of this utilization. ◦ According to reviews, in rehabilitation, patients are advised to perform light aerobic exercise paced according to individual capacity. Exercise difficulty levels are increased gradually within tolerated levels until improvements in fatigue and dyspnoea are seen, typically four to six weeks. Rehabilitation also includes breathing exercises that aim to control slow, deep breaths to strengthen respiratory muscles' efficiency, especially the diaphragm. The breath should be inhaled through the nose, expanding the abdominal region, and exhaled via the mouth. Such light aerobic and breathing exercises should be performed daily in 5–10 min sessions throughout the day. Complementary behavioural modification and psychological support may also help improve survivors’ well-being and mental health. Reviews have also recommended that rehabilitation programs be personalized since long COVID manifestation and pathophysiology may vary in each case.

		• Risks of physical rehabilitation must also be considered. Systematic and scoping reviews have identified that rehabilitation may not be suitable for survivors of critical COVID-19 with severe pulmonary or cardiac damage. Hence, exclusion criteria for post-COVID-19 rehabilitation have been proposed: high resting heart rate (>100 beats/min), low or high blood pressure (<90/60 or >140/90 mmHg), low blood oxygen saturation (<95%), or other conditions where exercise is a contraindication. Indeed, an international survey study found that 85.9% of participants with long COVID experienced symptom relapse following mental or physical activities.

Table 6E. Details from Articles Informing Return to Work Implications

Author	Study Details (Article Type, Country, Study Design)	Return to Work Implications

(Davis et al., 2021)	• Preprint
	• UK
	• Cross-sectional Survey
		• N=3,762
		• Population: adults with confirmed or suspected COVID-19 infection
		• Online survey at mean 28 weeks post-diagnosis
		• International study using social media, with more than 56 countries represented.
		• Study demonstrated impact on return to work, absenteeism and presenteeism.
		  ◦ 68.9% of unrecovered respondents reported reduced work hours or not working at all as a direct result of their COVID-19 illness, and on average the unrecovered group felt they were less than 60% returned to their pre-illness baseline.
		  ◦ 27.3% [95%CI 25.3-39.4%] of unrecovered respondents who worked before illness were working as many hours as prior to becoming ill at the time of survey (compared to 49.3% [95%CI 40.8-57.9%]
		  ◦ 45.6% [95%CI 43.2-48.0%] of unrecovered respondents worked reduced hours (absenteeism)
		  ◦ 23.3% [95%CI 21.3-25.4%] not working as direct result of illness. This included being on sick leave, disability leave, being fired, quitting, and being unable to find a job that would accommodate them.
		  ◦ 45.2% (42.9% to 47.2%) of respondents reported requiring a reduced work schedule compared to pre-illness. 22.3% [95%CI 20.5-24.3%] were not working at the time of survey due to their health conditions.
		  ◦ At least 45% of working respondents were working remotely, which they indicated was critical to their continued ability to work.

(Machado et al., 2021)	• Peer-reviewed article	• N=1,939

	• The Netherlands • Cross-sectional Survey	• Population: adults with confirmed or suspected COVID-19 infection from online panel or social media groups for long-COVID • 12 week follow-up • Completed a battery of online surveys relating to symptoms, health-related quality of life (EQ-5D-5L), impairment in work and activities, and functional status • Most of the subjects reported moderate-to-slight functional limitations according to the PCFS Scale (85%) while only 3% of the subjects reported to currently have no limitations in daily life • Study demonstrates statistically significant association between level of functional impairment post-COVID and facets of return to work as self-reported by respondents: ◦ Compared to respondents with grade 0, 1 or 2 on the PCFS Scale, respondents with grade 3 or 4 on the PCFS Scale more often experienced absenteeism ($p<0.05$), presenteeism ($p<0.05$), and work impairment ($p<0.05$).

(Nurek et al., 2021)	• Preprint
	• UK
	• Modified Delphi
		• N=33
		• Population: UK physicians using a social media platform specific to physicians interested in long COVID
		• Aim: Get consensus on physicians on recognition, diagnosis and management of post-COVID conditions
		• Delphi process included 2 online surveys.
		• Expert Delphi panel provided strategies for employers and health care providers, including
		  ◦ Employers should discuss with their employee suitable adjustments to aid a return to work, and both parties should be provided with written advice such as the leaflet "COVID-19 return to work guide for recovering workers" by the Society of Occupational Medicine.
		  ◦ The relapsing-remitting nature of the illness needs to be emphasized as employer pressure may result in patients returning to work too soon.
		  ◦ The onus is on the doctor with current clinical responsibility for the patient to complete the fit note; this includes secondary care doctors.
		  ◦ The content of the fit note should be agreed between the patient and doctor, including a "medically-recognized diagnosis". For NHS staff to receive "COVID pay" during absence, the fit note must mention COVID.
		  ◦ The ability to return to work after illness is a marker of recovery and clinicians must, therefore, record work status in the clinical notes in situations of chronic ill-health.
		  ◦ From a public health perspective, counting days lost to sickness and lost income on account of long COVID is essential.

(Parkin et al., 2021)	• Peer-reviewed article • UK • Descriptive	• N=225 • Article focuses on describing a functioning, comprehensive multidisciplinary rehabilitation pathway for patients with COVID-19 post-discharge. Eligibility included persistent symptoms 7 weeks after hospital discharge.

		• In describing this pathway, it provided a brief description of the demographics of the population who had been supported by this pathway.
		• Study reveals impact on return to work
		  ◦ 54% of patient population on this pathway were unable to work or had to reduce hours (absenteeism)
		  ◦ Undisclosed % "many" only remain at work due to current work from home arrangements.
		• No comparison and more descriptive study, so cannot speak definitively to impact or implications.

(O'Sullivan et al., 2021)	• Peer-reviewed article • UK • Cross-sectional Survey	• N=155 • Report early use of a rehabilitation tool for clinical practice • Population: GP assesses as having acute illness with ongoing rehabilitation needs (so COVID-19 diagnosis not required); military personnel • Mean 13 weeks follow-up • Study findings are unclear, but suggest occupational rehabilitation is required for patients with post-COVID as they require assessment and management support to return to work. ◦ "A significant proportion of patients require assessment and management, with symptoms such as SOB, fatigue and mood disorders impacting on ADLs and return to work, amenable to bespoke rehabilitation programmes."

(Skyrud et al., 2021)	• Preprint
	• Norway
	• Observational Cohort
		• N=740,182
		• Population level study
		• Population: every adult Norwegian who tested positive for COVID-19 and had an employment contract
		• Administrative data analysis
		• Mean 17 week follow-up
		• Sick leave increases for those testing positive for the week of testing and returns to pre-testing levels 3-4 months after testing. Higher sick leave levels in those testing positive vs. negative.
		  ◦ More sick leave of employees testing positive, compared to those testing negative, for ~2 months after infection for young and older men.
		    ▪ Employees testing positive had a sick leave of 2.5% in 3 months before testing positive; increasing to 28.5% in the test week; dropped to pre-testing levels at month 3 (2.8%) and 4 (2.2%) after testing.
		    ▪ Employees testing negative had 2.0% sick leave in the 3 months before testing, increasing to 9.0% in test week, and returning toward pre-testing level in month 3 (2.6%) and 4 (2.5 %) after testing.
		    ▪ Aside from the couple of months around testing, sick leave remains similar from before testing (2.5%) to 5-6 months after testing (2.4%) for those who tested positive, but in line with the overall increase in sick leave in Norway during the pandemic.

		• For women, the excessive sick leave of those testing positive (compared to those testing negative) depended on age. Short-term elevation in sick leave (up to 2 months) for women aged 20-44 years, and a short- and long-term elevation in sick leave (up to 4 months) for women aged 45-70 years.

(Vaes et al., 2021)	• Peer-reviewed article
	• Belgium
	• Cross-sectional Survey
		• N=1556
		• Surveys looking at symptoms, quality of life, functional status and work productivity at 6 months follow-up after onset COVID-19 symptoms.
		• Follow-up at 12 and 24 weeks post-onset of acute COVID-19 symptoms
		• Population: membership on online peer support for long COVID (social media)
		• The majority of persons self-identifying as having long COVID experience absenteeism and presenteeism, but there are modest improvements from 3 to 6 months post-onset of acute symtpoms.
		  • The majority of patients (87.9%) reported having a job before the infection.
		  • The mean proportion of work time missed in the previous week due to ill health (absenteeism) and impairment while working (presenteeism) reduced from 61% to 48% and from 65% to 57%, respectively (both $p<0.001$).
		  • The average work productivity loss reduced from 82% to 74%, resulting in an overall working impairment of 73% and 62% after 3 and 6 months, respectively (both $p<0.001$).
		  • 3 and 6 months after the onset of COVID-19 related symptoms, patients receiving physiotherapy reported more symptoms and a worse self-reported health, work productivity, functional status and quality of life compared to patients who did not receive physiotherapy or rehabilitation.
		  • Between 3 and 6 months of follow-up, significant improvements were found in both patients who did and did not receive physiotherapy or rehabilitation.

(Vanichkachorn et al., 2021)	• Peer-reviewed article
	• USA
	• Observational Cohort
		• N=100
		• Population: adults with positive COVID-19 test and symptoms four or more weeks after positive test.
		• Aim to describe patients reporting prolonged symptoms after COVID-19 infection
		• Description of patient population at a specialty, outpatient clinic
		• Most patient presented at 12 weeks post-diagnosis
		• Return to work is often associated with limited activities, but approximately a third of patients do not return to work.
		  • Prior to their infection, 91% of the cohort was employed and 63 patients had returned to some form of gainful employment at the time of presentation to clinic.
		  • Of the 63 patients who had returned to work, only 46% had returned to unrestricted work duty at the time of presentation to clinic.

		• At initial intake, 31% of employed patients (28 of 91 patients) had not returned to work in any capacity after their SARS-CoV-2 infection.
(World Health Organization, 2021b)	• Grey literature article • Denmark • Review	• Policy brief, provides a review of larger population-based studies of the various approaches taken across multiple countries to best define, understand, and provide care for post-COVID conditions. • Speaks to challenges in diagnosing post-COVID conditions and its return to work assessment. • “Although there is no simple symptom or test for diagnosing it, many people experience severe fatigue and a range of troubling physical symptoms that make it difficult for those who are employed to return to work.”

Methods

Literature Search

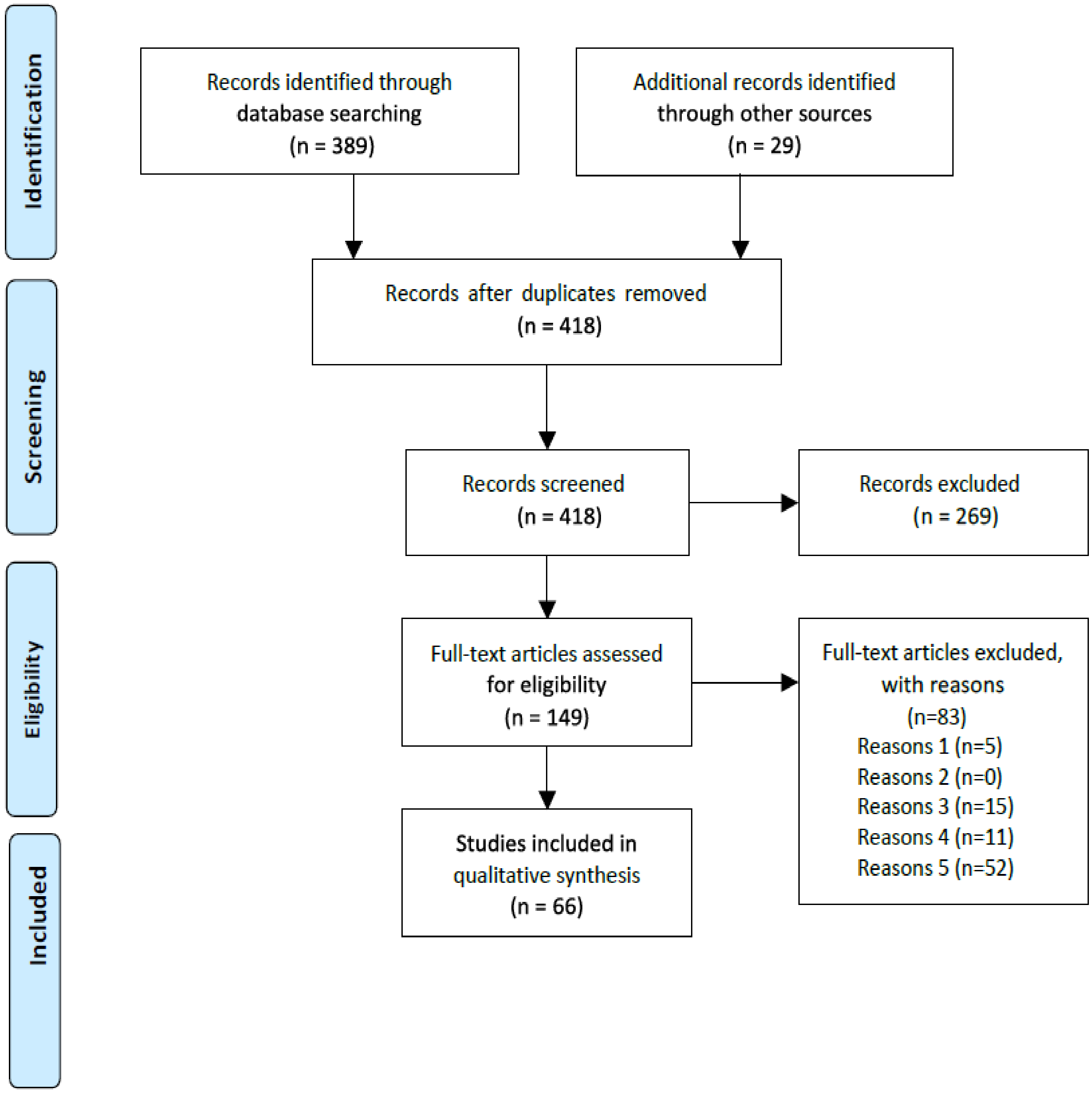
A literature search was conducted by Nicole Loroff from Knowledge Resources Services (KRS) within the Knowledge Management Department of Alberta Health Services. Since this review was framed as an update, KRS searched databases for articles published from November 4, 2020 to December 31, 2021. The librarian conducted the searches on May 24 and 28th, 2021. The searched databases included: Medline (OVID), Embase, APA PsycInfo, PubMed, TRIP Pro, MedRxiv, BioRxiv, WHO Global Research Database on COVID-19, National Institute of Health and Care Excellence (NICE), Google, and Google Scholar. The previous was completed on November 3, 2020. The search strategy is included below. Briefly, the search strategy involved combinations of keywords and subject headings including: "COVID-19" and "long-term." Because of the diversity of questions in this review, the literature search strategy was very broad, and the screening process determined inclusion as relating to the research questions.

Articles identified by KRS in their search were initially screened by title against the inclusion/exclusion criteria listed in Table 7 below. 389 articles were identified by KRS with references and abstracts provided for further review. 29 additional articles were identified *ad hoc*. 418 articles were each independently screened by two reviewers using the title and abstract. 269 articles were excluded based on information in the title and abstract. Of the 149 articles that went to full-text screening, 82 were excluded by consensus of two independent reviewers. The reasons for exclusion were not in English language (n=5), wrong type of article (e.g. editorial, protocol) (n=15), wrong population (n=11), and wrong content (i.e. inapplicable to the research questions) (n=51) (Figure ? for PRISMA table) (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009). In total, 67 articles were included to address one or more of the review questions.

Table 7. Inclusion and exclusion criteria for results of the literature search

Inclusion Criteria	Exclusion Criteria
• COVID-19 • Post-diagnosis (and/or post-discharge) • Long-term (or chronic) symptoms or outcomes (i.e. post-diagnosis) • Relates to any of: terminology or definitions of chronic symptoms post-COVID-19; screening tools; risk factors for long-term (or chronic) symptoms; impact of vaccination; impact on (or association with) health service utilization; or, impact on (or association with) return to work. • All COVID-19 positive populations (i.e. no limit on age, hospitalization) • November 4, 2020 to present • Limited to empirical studies • English language only • All publication status: pre-print, ahead of print, accepted, published, grey literature • Any jurisdiction • Full-text available	• Article is not from a credible source (author or publisher) • Non-COVID-19 conditions (e.g. SARS, MERS) • Focused on solely on acute symptoms or on mechanisms leading to acute symptoms. Acute was framed as during the infectious period or acuity of experience, not by number of days post-diagnosis • Presented data/evidence is not sufficient to address the research questions • Non-empirical research methods including editorial, commentary, case report (n=1) • Full-text not available (i.e. just abstract or conference proceedings)

Figure 1. PRISMA Flow Chart



Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses:* The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Critical Evaluation of the Evidence

Exclusion criteria for study quality were adapted from the Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018). Potential articles were evaluated on three criteria: 1) Peer reviewed or from a reputable source; 2) Clear research question or issue; 3) Whether the presented data/evidence is appropriate to address the research question. Preprints and non-peer-reviewed literature (such as commentaries and letters from credible journals) are not excluded out of hand due to the novelty of COVID-19 and the speed with which new evidence is available.

Table 8 below is a narrative summary of the body of evidence included in this review. The categories, format, and suggested information for inclusion were adapted from the Oxford Centre for Evidence-Based Medicine, the Cochrane Library, and the AGREE Trust (Brouwers et al., 2010; Urwin, Gavinder, & Graziadio, 2020; Viswanathan et al., 2012; Wynants et al., 2020).

Table 8. Narrative overview of the literature included in this review.

	Description
Volume	1 systematic review was included, 29 observational cohort studies were included (7 were pre-review), 11 cross sectional survey studies were included (3 were pre-review), 14 review articles (including narratives style reviews) were included (1 was pre-review), 1 quality improvement report was included, and 7 other style of reports and articles were included (1 was pre-review).
Quality	The body of evidence varied greatly with the question at issue. This review included 7 distinct topics: terminology, screening tools, symptoms, risk factors, vaccination impact, health service utilization, and return to work implications. The quality of evidence on question of symptoms is addressed in the PHAC review, as summarized above. We used the adapted MMAT to assess the quality of the article as whole (Hong et al., 2018). According to this adapted tool, 44 articles were of high quality, 9 were of moderate quality and 13 were of low quality. This tool does not capture the full nuances of the literature and the opportunities for bias. The literature on risk factors was the most robust and informative. The literature on vaccination impact, health services utilization and return to work implications was less robust. While there were 15 review articles, only one was a rigourous systematic review and most did not detail their search strategies. This introduces concerns on the ability of those studies to unbiasedly inform the questions at issue. For the observation studies, whether observational cohorts or cross sectional surveys, there were several common concerns. First, some studies framed their design as an observational cohort but lacked any longitudinal features in implementation and were in fact cross sectional in design. Due to time constraints, we listed the design as proclaimed by the authors. A challenge in synthesizing the articles was the variation in defining the phenomena and the “starting point” of the follow-up time period. Implications vary greatly between follow-up that starts at symptoms onset or diagnosis, versus those that start at time of discharge. In the empirical studies, recall and selection bias were common concerns. For the latter, recruitment techniques did not favour generalizability with no study using a randomization approach. Some studies were site-specific, while others looked across a few hospitals and few considered population-level databases. Studies generally used convenience sampling or a sequential approach to participant recruitment/inclusion. Many studies relied on self-report, which is susceptible to recall bias. This is especially concerning for the few studies that used social media for recruitment, as only technologically-savvy individuals are recruited. Conversely, studies that used large administrative

	databases faced concerns on data accuracy. Only one study specifically targeted persons from minority communities, which queries the accuracy findings related to ethnicity and diversity as the other studies may not be representative enough in that regard. Few studies had contemporaneous control groups, as found in the separate PHAC review. Potential confounding factors that limit any insight into causation include presence of pre-existing symptoms or conditions prior to COVID-19, treatment effects, impact of hospitalization or ICU admission, and the effects of the novel, global pandemic itself (e.g. barriers to care, psychosocial impacts). There was great variability in the sample sizes, and this corresponding to the heterogeneous data collection techniques: survey, administrative data, social media activity. The smallest sample size was 10 and the largest was 740,182. The median sample size was 417, which is relatively robust. The grey literature was from reputable sources, and can be used to inform other jurisdictions' perceptions and approaches to the topics of these questions.
Applicability	No evidence was identified from Alberta. Only 3 studies were from Canada, and they were all narrative reviews, which did not inform an empirical insights into any relevant questions. The included articles were mostly from the UK, which has a comparable population and health system. Most articles, except for a minority, were from Western industrialized countries in North America and Europe. The study evidence is applicable to the review questions, with some questions have literature of more alignment than others.
Consistency	The consistency of the evidence varies by question, with only the risk factor data being relatively consistent. For terminology, screening tools, vaccination impact, health service utilization and return to work implications, the evidence is not consistent across included studies.

Table 4c. Critical Quality Appraisal of Included Studies

Author	Study Design	Type of Article	Is there clear research question?	Data appropriate to research question?	Type of COVID patients
(Al-Aly et al., 2020)	Observational cohort	Peer-reviewed	Yes	Yes	Community Only
(Arnold et al., 2021)	Observational cohort	Preprint	Yes	Yes	Hospitalized
(Augustin et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Community Only
(Ayoubkhani et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Banerjee et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Bellan et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Bowles et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized

(Caronna et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Sub-population
(Castro-Avila et al., 2021)	Other	Peer-reviewed	Yes	Yes	Hospitalized
(Davis et al., 2021)	Cross sectional Survey	Preprint	Yes		Sub-population
(D'Cruz et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Demelo-Rodríguez et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	All
(Ekbom et al., 2021)	Observational cohort	Peer-reviewed	No	No	Hospitalized
(Einvik et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	Yes	All
(Fernández-de-Las-Peñas et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Fernández-De-las-peñas, Palacios-Ceña, Gómez-Mayordomo, Cuadrado, & Florencio, 2021)	Other	Peer-reviewed	No	No	All
(Hassenpflug et al., 2021)	Quality Improvement	Peer-reviewed	Yes	No	Hospitalized
(Hernandez-Romieu et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Community Only
(Hirschtick et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	Yes	All
(Iqbal et al., 2021)	Systematic Review	Peer-reviewed	Yes	Yes	All
(Islam et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Korompoki et al., 2021)	Review	Peer-reviewed	Yes	Yes	All
(Lemhöfer et al., 2021)	Other	Peer-reviewed	Yes	Yes	NOT CLEAR
(Lerum et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Liang et al., 2020)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Lund et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Community Only
(Machado et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	Yes	All

(Maxwell et al., 2021)	Review	Grey literature	No		NOT CLEAR
(Mei et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	No	Hospitalized
(Menges et al., 2021)	Observational cohort	Preprint	Yes	Yes	All
(Mermelstein et al., 2021)	Cross sectional Survey	Preprint	Yes	Yes	All
(Moreno-Pérez et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	All
(Nalbandian et al., 2021)	Review	Peer-reviewed	Yes	Yes	All
(National Institute for Health and Care Excellence et al., 2020)	Review	Grey literature	No	No	All
(Himmels, 2021)	Review	Grey literature	No	No	Hospitalized
(Nurek et al., 2021)	Other	preprint	Yes	Yes	All
(Office for National Statistics, 2021)Office for National Statistics (UK)	Cross sectional Survey	Grey literature	Yes	Yes	Sub-population
(Osmanov et al., 2021)	Observational cohort	Preprint	Yes	Yes	Hospitalized
(O'Sullivan et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	All
(Park et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	No	Hospitalized
(Parkin et al., 2021)	Other	Peer-reviewed	No	No	Hospitalized
(Postigo-Martin et al., 2021)	Other	Peer-reviewed	Yes	No	All
(Public Health Ontario, 2021)	Review	Grey literature	No	No	All
(Health Ontario, 2021)	Systematic Review	Grey literature	No	No	Sub-population
(Qu et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	Hospitalized
(Rando et al., 2021)	Review	Preprint	Yes	Yes	All
(Raw et al., 2021)	Observational cohort	Preprint	Yes	No	All

(Sigfrid et al., 2021)	Observational cohort	Preprint	Yes	Yes	Hospitalized
(Sisó-Almirall et al., 2021)	Review	Peer-reviewed	Yes	Yes	Community Only
(Skyrud et al., 2021)	Observational cohort	Preprint	Yes	Yes	Sub-population
(Sudre et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	All
(Taquet et al., 2021)	Observational cohort	Peer-reviewed	Yes	Yes	All
(Tran et al., 2021)	Cross sectional Survey	Preprint	Yes	Yes	All
(Tudoran et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	Yes	Hospitalized
(Vaes et al., 2021)	Cross sectional Survey	Peer-reviewed	Yes	Yes	All
(Vanichkachorn et al., 2021)Vanichkachorn, Greg;	Observational cohort	Peer-reviewed	Yes	Yes	All
(Vehar et al., 2021)	Review	Peer-reviewed	No	No	All
(Whittaker et al., 2021)	Observational cohort	Preprint	Yes	Yes	Sub-population
(World Health Organization, 2021a)	Review	Grey literature	No	No	All
(World Health Organization, 2021b)	Review	Grey literature	No	No	All
(Wildwing et al., 2021)	Systematic Review	Peer-reviewed	Yes	No	All
(Yong et al., 2021)	Review	Peer-reviewed	Yes	Yes	All
(Zapatero & Hanquet, 2021)	Review	Grey literature	No	No	All

Search Strategy

Database(s): **Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily** 1946 to May 24, 2021

Search Strategy:

#	Searches	Results
1	COVID-19/ or SARS-CoV-2/ or Coronavirus/ or Betacoronavirus/ or Coronavirus Infections/	87247

2	(covid or coronavirus* or corona viru* or coronavirinae* or covid2019 or covid19 or covid-19 or nCoV* or n-CoV* or novel CoV* or 2019-nCoV* or 2019nCoV or 19nCov or hCoV* or h-Cov* or 2019-hCoV* or 2019hCoV* or 19 hCoV* or SARS-CoV-2 or SARSCoV2 or SARSCov-2 or SARS-CoV-19 or SARSCoV19 or SARSCoV-19 or SARS-Cov-2019 or SARSCoV2019 or SARSCoV-2019 or "severe acute respiratory syndrome CoV 2" or "severe acute respiratory syndrome coronavirus 2").tw.	124463
3	1 or 2	130142
4	Long term Adverse Effects/ or exp Recurrence/	189704
5	Patient Discharge/ or Aftercare/ or Long-Term Care/ or Convalescence/ or Subacute Care/ or Survivors/	96061
6	((longterm or long-term or longstanding or chronic* or persist* or prolong* or ongoing or recurr* or lasting or long-lasting or linger* or endur* or permanent* or continuous or continuing or continued or continual or residual* or delay* or post-viral or postviral* or postacute or post-acute or post-hospitalisation or post-hospitalization or post-discharge* or post-infect* or discharge* or subacute or sub-acute) adj3 (symptom* or complicat* or consequence* or outcome* or effect* or illness* or sequela* or syndrome or sign or signs or convalescence or prognosis or recover* or rehab* or aftercare or after care or follow-up or survivor*)).tw.	620848
7	4 or 5 or 6	865925
8	exp "Signs and Symptoms"/	2148038
9	Follow-Up Studies/ or Longitudinal Studies/	791939
10	(follow-up stud* or longitudinal stud*).tw.	128243
11	9 or 10	844494
12	8 and 11	114458
13	7 or 12	961319
14	3 and 13	4202
15	(longcovid* or long-covid* or longhaul* or long-haul* or long SARS-Cov-2 or postcovid* or post-covid* or postcoronavirus or post-coronavirus).tw.	1997
16	((longterm or long-term or longstanding or chronic* or persist* or prolong* or ongoing or recurr* or lasting or long-lasting or linger* or endur* or permanent* or continuous or continuing or continued or continual or residual* or delay* or post-viral or postviral* or postacute or post-acute or post-hospitalisation or post-hospitalization or post-discharge* or post-infect* or discharge* or subacute or sub-acute) adj5 (symptom* or complicat* or consequence* or outcome* or effect* or illness* or sequela* or syndrome or sign or signs or convalescence or prognosis or recover* or rehab* or aftercare or after care or follow-up or survivor*) adj10 (covid or coronavirus* or corona viru* or coronavirinae* or covid2019 or covid19 or covid-19 or nCoV* or n-CoV* or novel CoV* or 2019-nCoV* or 2019nCoV or 19nCov or hCoV* or h-Cov* or 2019-hCoV* or 2019hCoV* or 19 hCoV* or SARS-CoV-2 or SARSCoV2 or SARSCov-2 or SARS-CoV-19 or SARSCoV19 or SARSCoV-19 or SARS-Cov-2019 or SARSCoV2019 or SARSCoV-2019 or "severe acute respiratory syndrome CoV 2" or "severe acute respiratory syndrome coronavirus 2")).tw.	1668
17	14 or 15 or 16	6388
18	limit 17 to english language	6203
19	limit 18 to dt=20201104-20211231	2642
20	limit 19 to (letter or comment or editorial or news)	261
21	19 not 20	2381
22	remove duplicates from 21	2293

Database(s): **Embase** 1974 to 2021 May 24
Search Strategy:

#	Searches	Results
1	COVID-19/ or SARS-CoV-2/ or Coronavirinae/ or Betacoronavirus/ or Coronavirus infection/	31519
2	(covid or coronavirus* or corona viru* or coronavirinae* or covid2019 or covid19 or covid-19 or nCoV* or n-CoV* or novel CoV* or 2019-nCoV* or 2019nCoV or 19nCov or hCoV* or h-Cov* or 2019-hCoV* or 2019hCoV* or 19 hCoV* or SARS-CoV-2 or SARSCoV2 or SARSCov-2 or SARS-CoV-19 or SARSCoV19 or SARSCoV-19 or SARS-Cov-2019 or SARSCoV2019 or SARSCoV-2019 or "severe acute respiratory syndrome CoV 2" or "severe acute respiratory syndrome coronavirus 2").tw.	148733
3	1 or 2	151088
4	*Adverse Outcome/ or *Recurrent Disease/ or *Relapse/	48300
5	*Hospital Discharge/ or *Aftercare/ or *Long Term Care/ or *Convalescence/ or *Subacute Care/ or *Survivor/	58737
6	((longterm or long-term or longstanding or chronic* or persist* or prolong* or ongoing or recurr* or lasting or long-lasting or linger* or endur* or permanent* or continuous or continuing or continued or continual or residual* or delay* or post-viral or postviral* or postacute or post-acute or post-hospitalisation or post-hospitalization or post-discharge* or post-infect* or discharge* or subacute or sub-acute) adj3 (symptom* or complicat* or consequence* or outcome* or effect* or illness* or sequela* or syndrome or sign or signs or convalescence or prognosis or recover* or rehab* or aftercare or after care or follow-up or survivor*)).tw.	919007
7	4 or 5 or 6	1007745
8	Follow Up/ or Longitudinal Study/	1814035
9	(follow-up stud* or longitudinal stud*).tw.	170344
10	8 or 9	1864727
11	7 or 10	2603189
12	3 and 11	11460
13	(longcovid* or long-covid* or longhaul* or long-haul* or long SARS-Cov-2 or postcovid* or post-covid* or postcoronavirus or post-coronavirus).tw.	2523
14	((longterm or long-term or longstanding or chronic* or persist* or prolong* or ongoing or recurr* or lasting or long-lasting or linger* or endur* or permanent* or continuous or continuing or continued or continual or residual* or delay* or post-viral or postviral* or postacute or post-acute or post-hospitalisation or post-hospitalization or post-discharge* or post-infect* or discharge* or subacute or sub-acute) adj5 (symptom* or complicat* or consequence* or outcome* or effect* or illness* or sequela* or syndrome or sign or signs or convalescence or prognosis or recover* or rehab* or aftercare or after care or follow-up or survivor*) adj10 (covid or coronavirus* or corona viru* or coronavirinae* or covid2019 or covid19 or covid-19 or nCoV* or n-CoV* or novel CoV* or 2019-nCoV* or 2019nCoV or 19nCov or hCoV* or h-Cov* or 2019-hCoV* or 2019hCoV* or 19 hCoV* or SARS-CoV-2 or SARSCoV2 or SARSCov-2 or SARS-CoV-19 or SARSCoV19 or SARSCoV-19 or SARS-Cov-2019 or SARSCoV2019 or SARSCoV-2019 or "severe acute respiratory syndrome CoV 2" or "severe acute respiratory syndrome coronavirus 2")).ti,ab.	2217
15	12 or 13 or 14	14027
16	limit 15 to english language	13713
17	limit 16 to dc=20201104-20211231	9110
18	limit 17 to exclude medline journals	1716

Database(s): **APA PsycInfo** 1806 to May Week 3 2021
Search Strategy:

#	Searches	Results
1	Coronavirus/	2569
2	(covid or coronavirus* or corona viru* or coronavirinae* or covid2019 or covid19 or covid-19 or nCoV* or n-CoV* or novel CoV* or 2019-nCoV* or 2019nCoV or 19nCov or hCoV* or h-Cov* or 2019-hCoV* or 2019hCoV* or 19 hCoV* or SARS-CoV-2 or SARSCoV2 or SARSCov-2 or SARS-CoV-19 or SARSCoV19 or SARSCoV-19 or SARS-Cov-2019 or SARSCoV2019 or SARSCoV-2019	6133

	or "severe acute respiratory syndrome CoV 2" or "severe acute respiratory syndrome coronavirus 2").tw.	
3	1 or 2	6144
4	Hospital Discharge/ or Aftercare/ or Long Term Care/ or Survivors/	23313
5	((longterm or long-term or longstanding or chronic* or persist* or prolong* or ongoing or recurr* or lasting or long-lasting or linger* or endur* or permanent* or continuous or continuing or continued or continual or residual* or delay* or post-viral or postviral* or postacute or post-acute or post-hospitalisation or post-hospitalization or post-discharge* or post-infect* or discharge* or subacute or sub-acute) adj3 (symptom* or complicat* or consequence* or outcome* or effect* or illness* or sequela* or syndrome or sign or signs or convalescence or prognosis or recover* or rehab* or aftercare or after care or follow-up or survivor*)).tw.	111793
6	4 or 5	131568
7	exp Symptoms/	250468
8	Followup Studies/ or Longitudinal Studies/	28178
9	(follow-up stud* or longitudinal stud*).tw.	68382
10	8 or 9	86087
11	7 and 10	6907
12	6 or 11	137348
13	3 and 12	296
14	(longcovid* or long-covid* or longhaul* or long-haul* or long SARS-Cov-2 or postcovid* or post-covid* or postcoronavirus or post-coronavirus).tw.	388
15	((longterm or long-term or longstanding or chronic* or persist* or prolong* or ongoing or recurr* or lasting or long-lasting or linger* or endur* or permanent* or continuous or continuing or continued or continual or residual* or delay* or post-viral or postviral* or postacute or post-acute or post-hospitalisation or post-hospitalization or post-discharge* or post-infect* or discharge* or subacute or sub-acute) adj5 (symptom* or complicat* or consequence* or outcome* or effect* or illness* or sequela* or syndrome or sign or signs or convalescence or prognosis or recover* or rehab* or aftercare or after care or follow-up or survivor*) adj10 (covid or coronavirus* or corona viru* or coronavirinae* or covid2019 or covid19 or covid-19 or nCoV* or n-CoV* or novel CoV* or 2019-nCoV* or 2019nCoV or 19nCov or hCoV* or h-Cov* or 2019-hCoV* or 2019hCoV* or 19 hCoV* or SARS-CoV-2 or SARSCoV2 or SARSCov-2 or SARS-CoV-19 or SARSCoV19 or SARSCoV-19 or SARS-Cov-2019 or SARSCoV2019 or SARSCoV-2019 or "severe acute respiratory syndrome CoV 2" or "severe acute respiratory syndrome coronavirus 2")).tw.	99
16	13 or 14 or 15	692
17	limit 16 to english language	558
18	limit 17 to up=20201101-20211231	168

PubMed (May 28, 2021)

("longcovid*"[tiab] OR "long covid*"[tiab] OR "longhaul*"[tiab] OR "long haul*"[tiab] OR "long sars-cov-2"[tiab] OR "postcovid*"[tiab] OR "post covid*"[tiab] OR "postcoronavirus"[tiab] OR "post-coronavirus"[tiab] OR "postacute covid*"[tiab] OR "post-acute covid*"[tiab])

Filters applied: English, from 2021/5/1 - 2021/12/31 (166)

TRIP Pro (May 28, 2021)

(longcovid* OR "long-covid" OR “long-covid-19” OR “long covid” OR “long covid-19” or longhaul* OR "long-haul" OR “long-hauler” OR “long-haulers” OR "long sars-cov-2" OR postcovid* OR "post-covid" OR “post-covid-19" or “post covid-19” or postcoronavirus OR "post-coronavirus" OR “post coronavirus” OR "postacute covid" OR “postacute covid-19” OR "post-acute covid" OR “post-acute covid-19”)from:2020 (168)

medrXiv & biorXiv/WHO COVID-19 Global Research Database/National Institute of Health and Care Excellence (NICE)/Google/Google Scholar [first 50 results screened]

(longcovid* OR "long-covid" OR “long-covid-19” OR “long covid” OR “long covid-19” or longhaul* OR "long-haul" OR “long-hauler” OR “long-haulers” OR "long sars-cov-2" OR postcovid* OR "post-covid" OR “post-covid-19" or “post covid-19” or postcoronavirus OR "post-coronavirus" OR “post coronavirus” OR "postacute covid" OR “postacute covid-19” OR "post-acute covid" OR “post-acute covid-19”)

References

Al-Aly, Z., Xie, Y., & Bowe, B. (2020). High Dimensional Characterization of Post-acute Sequalae of COVID-19. *Research Square*, *pre-print*, 1–22. Retrieved from https://www.nature.com/articles/s41586-021-03553-9

Alberta Health. (2021). Cases in Alberta. Retrieved June 21, 2021, from https://www.alberta.ca/coronavirus-info-for-albertans.aspx

Arnold, D. T., Milne, A., Samms, E., Stadon, L., Maskell, N. A., & Hamilton, F. W. (2021). Are vaccines safe in patients with Long COVID? A prospective observational study. *MedRxiv*, 2021.03.11.21253225-2021.03.11.21253225. Retrieved from https://www.medrxiv.org/content/10.1101/2021.05.24.21257738v2.full.pdf

Augustin, M., Schommers, P., Stecher, M., Dewald, F., Gieselmann, L., Gruell, H., … Lehmann, C. (2021). Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. *The Lancet Regional Health. Europe*. https://doi.org/10.1016/j.lanepe.2021.100122

Ayoubkhani, D., Khunti, K., Nafilyan, V., Maddox, T., Humberstone, B., Diamond, I., & Banerjee, A. (2021). Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. *BMJ*, *372*, n693. https://doi.org/10.1136/bmj.n693

Banerjee, J., Canamar, C. P., Voyageur, C., Tangpraphaphorn, S., Lemus, A., Coffey, C., … Spellberg, B. (2021). Mortality and Readmission Rates among Patients with COVID-19 after Discharge from Acute Care Setting with Supplemental Oxygen. *JAMA Network Open*. https://doi.org/10.1001/jamanetworkopen.2021.3990

Bellan, M., Soddu, D., Balbo, P. E., Baricich, A., Zeppegno, P., Avanzi, G. C., … Pirisi, M. (2021). Respiratory and psychophysical sequelae among patients with covid-19 four months after hospital discharge. *JAMA Network Open*. https://doi.org/10.1001/jamanetworkopen.2020.36142

Bowles, K. H., McDonald, M., Barrón, Y., Kennedy, E., O'Connor, M., & Mikkelsen, M. (2021). Surviving COVID-19 After Hospital Discharge: Symptom, Functional, and Adverse Outcomes of Home Health Recipients. *Annals of Internal Medicine*. https://doi.org/10.7326/M20-5206

Brouwers, M., Kho, M., Browman, G., Cluzeau, F., Feder, G., B., F., … Consortium, A. N. S. (2010). AGREE II: Advancing guideline development, reporting and evaluation in health. *Canadian Medical Association Journal*, *182*, E839-842. https://doi.org/10.1503/cmaj.090449

Caronna, E., Ballvé, A., Llauradó, A., Gallardo, V. J., María Ariton, D., Lallana, S., … Pozo-Rosich, P. (2020). Headache: A striking prodromal and persistent symptom, predictive of COVID-19 clinical evolution. *Cephalalgia : An International Journal of Headache*, *40*(13), 1410–1421. https://doi.org/10.1177/0333102420965157

Castro-Avila, A., Jefferson, L., Dale, V., & Bloor, K. (2020). Support and follow-up needs of patients discharged from intensive care after severe COVID-19: A mixed-methods study of the views of UK general practitioners and intensive care staff during the pandemic's first wave. *MedRxiv*. https://doi.org/10.1101/2020.12.23.20248798

D'Cruz, R. F., Waller, M. D., Perrin, F., Periselneris, J., Norton, S., Smith, L.-J., … Jolley, C. J. (2021). Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. *ERJ Open Research*, *7*(1), 655–2020. https://doi.org/10.1183/23120541.00655-2020

Davis, H. E., Assaf, G. S., McCorkell, L., Wei, H., Low, R. J., Re'em, Y., … Akrami, A. (2021). Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact. *SSRN Electronic Journal*. https://doi.org/10.2139/ssrn.3820561

Demelo-Rodríguez, P., Ordieres-Ortega, L., Ji, Z., del Toro-Cervera, J., de Miguel-Díez, J., Álvarez-Sala-Walther, L. A., & Galeano-Valle, F. (2021). Long-term follow-up of patients with venous thromboembolism and COVID-19: Analysis of risk factors for death and major bleeding. *European Journal of Haematology*. https://doi.org/10.1111/ejh.13603

Einvik, G., Dammen, T., Ghanima, W., Heir, T., & Stavem, K. (2021). Prevalence and risk factors for post-traumatic stress in hospitalized and non-hospitalized COVID-19 patients. *International Journal of Environmental Research and Public Health*. https://doi.org/10.3390/ijerph18042079

Ekbom, E., Frithiof, R., Emilsson, O., Larson, I., Lipcsey, M., Rubertsson, S., … Malinovschi, A. (2021). Impaired diffusing capacity for carbon monoxide is common in critically ill Covid-19 patients at four months post-discharge. *Respiratory Medicine*. https://doi.org/10.1016/j.rmed.2021.106394

Fernández-de-Las-Peñas, C., Guijarro, C., Plaza-Canteli, S., Hernández-Barrera, V., & Torres-Macho, J. (2021). Prevalence of Post-COVID-19 Cough One Year After SARS-CoV-2 Infection: A Multicenter Study. *Lung*, 1–5. https://doi.org/10.1007/s00408-021-00450-w

Fernández-De-las-peñas, C., Palacios-Ceña, D., Gómez-Mayordomo, V., Cuadrado, M. L., & Florencio, L. L. (2021). Defining post-covid symptoms (Post-acute covid, long covid, persistent post-covid): An integrative classification. *International Journal of Environmental Research and Public Health*, *18*(5), 1–9. https://doi.org/10.3390/ijerph18052621

Hassenpflug, M. S., Jun, D., Nelson, D. R., & Dolinay, T. (2020). Post-COVID recovery: characteristics of chronically critically ill patients admitted to a long-term acute care hospital. *F1000Research*. https://doi.org/10.12688/f1000research.26989.1

Health Ontario, P. (2021). *Pediatric Post-acute COVID-19 and Multisystem Inflammatory Syndrome in Children (MIS-C)-What We Know So Far Updates to Latest Version Key Findings*.

Hernandez-Romieu, A. C., Leung, S., Mbanya, A., Jackson, B. R., Cope, J. R., Bushman, D., … Lobelo, F. (2021). Health Care Utilization and Clinical Characteristics of Nonhospitalized Adults in an Integrated Health Care System 28-180 Days After COVID-19 Diagnosis - Georgia, May 2020-March 2021. *MMWR. Morbidity and Mortality Weekly Report*, *70*(17), 644–650. https://doi.org/10.15585/mmwr.mm7017e3

Himmels, J. P. (2021). *COVID-19: Long-Term Effects of COVID-19*.

Hirschtick, J. L., Titus, A. R., Slocum, E., Power, L. E., Hirschtick, R. E., Elliott, M. R., … Fleischer, N. L. (2021). Population-based estimates of post-acute sequelae of SARS-CoV-2 infection (PASC) prevalence and characteristics: A cross-sectional study. *Clinical Infectious Diseases*. https://doi.org/10.1093/cid/ciab408

Iqbal, F. M., Lam, K., Sounderajah, V., Clarke, J. M., Ashrafian, H., & Darzi, A. (2021). Characteristics and predictors of acute and chronic post-COVID syndrome: A systematic review and meta-analysis. *EClinicalMedicine*, *36*, 100899. https://doi.org/10.1016/j.eclinm.2021.100899

Islam, M. S., Ferdous, M. Z., Islam, U. S., Mosaddek, A. S. M., Potenza, M. N., & Pardhan, S. (2021). Treatment, persistent symptoms, and depression in people infected with covid-19 in bangladesh. *International Journal of Environmental Research and Public Health*. https://doi.org/10.3390/ijerph18041453

Korompoki, E., Gavriatopoulou, M., Hicklen, R. S., Ntanasis-Stathopoulos, I., Kastritis, E., Fotiou, D., … Kontoyiannis, D. P. (2021). Epidemiology and organ specific sequelae of post-acute COVID19: A Narrative Review. *The Journal of Infection*. https://doi.org/10.1016/j.jinf.2021.05.004

Lemhöfer, C., Gutenbrunner, C., Schiller, J., Loudovici-Krug, D., Best, N., Bökel, A., & Sturm, C. (2021, April). Assessment of rehabilitation needs in patients after COVID-19: Development of the COVID-19-rehabilitation needs survey. *Journal of Rehabilitation Medicine*. https://doi.org/10.2340/16501977-2818

Lerum, T. V., Aaløkken, T. M., Brønstad, E., Aarli, B., Ikdahl, E., Lund, K. M. A., … Einvik, G.

(2020). Dyspnoea, lung function and CT findings three months after hospital admission for COVID-19. *European Respiratory Journal*. https://doi.org/10.1183/13993003.03448-2020
Liang, L., Yang, B., Jiang, N., Fu, W., He, X., Zhou, Y., … Wang, X. (2020, December). Three-month Follow-up Study of Survivors of Coronavirus Disease 2019 after Discharge. *Journal of Korean Medical Science*. https://doi.org/10.3346/JKMS.2020.35.E418
Lund, L. C., Hallas, J., Nielsen, H., Koch, A., Mogensen, S. H., Brun, N. C., … Pottegård, A. (2021). Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study. *The Lancet. Infectious Diseases*. https://doi.org/10.1016/S1473-3099(21)00211-5
Machado, F. V. C., Meys, R., Delbressine, J. M., Vaes, A. W., Goërtz, Y. M. J., van Herck, M., … Spruit, M. A. (2021). Construct validity of the Post-COVID-19 Functional Status Scale in adult subjects with COVID-19. *Health and Quality of Life Outcomes*, *19*(1), 1–10. https://doi.org/10.1186/s12955-021-01691-2
Maxwell, E. (2020). *Living with Covid19. A dynamic review of the evidence around ongoing Covid19 symptoms (often called Long Covid)*. *NIHR CED. National Institute for Health Research Centre for Engagement and Dissemination*. Retrieved from https://evidence.nihr.ac.uk/themedreview/living-with-covid19/
Mei, Q., Wang, F., Yang, Y., Hu, G., Guo, S., Zhang, Q., … Li, J. (2021). Health Issues and Immunological Assessment Related to Wuhan’s COVID-19 Survivors: A Multicenter Follow-Up Study. *Frontiers in Medicine*. https://doi.org/10.3389/fmed.2021.617689
Menges, D., Ballouz, T., Anagnostopoulos, A., Aschmann, H. E., Domenghino, A., Fehr, J. S., & Puhan, M. A. (2021). Estimating the burden of post-COVID-19 syndrome in a population-based cohort study of SARS-CoV-2 infected individuals: Implications for healthcare service planning. *MedRxiv*, 2021.02.27.21252572-2021.02.27.21252572. Retrieved from https://www.medrxiv.org/content/medrxiv/early/2021/03/01/2021.02.27.21252572.full.pdf
Mermelstein, R. J., Aiyer, M., Canfield, C., Chestek, D., Cook, J. A., Del Rios, M., … Illendula, S. D. (2021). Rapid implementation of cross-sectional study: Post-acute sequelae of SARS-CoV-2 (PASC) in a racially and ethnically diverse sample in Illinois. *MedRxiv*. Retrieved from https://www.medrxiv.org/content/10.1101/2021.04.29.21256304v1.full.pdf
Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ (Clinical Research Ed.)*, *339*, b2535. https://doi.org/10.1136/BMJ.B2535
Moreno-Pérez, O., Merino, E., Leon-Ramirez, J. M., Andres, M., Ramos, J. M., Arenas-Jiménez, J., … Gil, J. (2021). Post-acute COVID-19 syndrome. Incidence and risk factors: A Mediterranean cohort study. *Journal of Infection*, *82*(3), 378–383. https://doi.org/10.1016/j.jinf.2021.01.004
Nalbandian, A., Sehgal, K., Gupta, A., Madhavan, M. V, McGroder, C., Stevens, J. S., … Sehrawat, T. S. (2021). Post-acute COVID-19 syndrome. *Nature Medicine*, 1–15. Retrieved from https://www.nature.com/articles/s41591-021-01283-z?fbclid=IwAR0mbv6H9EpAQt1d2S-FVFNfSf-ZoM5n7MzwiSOg5sOmlX14TCRWJeCpmro
National Institute for Health and Care Excellence, Practitioners, R. C. of G., & Scotland, H. I. (2020). COVID-19 rapid guideline : managing the long-term effects of COVID-19. *NICE Guidelines*, (18 December 2020), 1–35.
Nurek, M., Rayner, C., Freyer, A., Taylor, S., Järte, L., MacDermott, N., & Delaney, B. C. (2021). Recommendations for the Recognition, Diagnosis, and Management of Patients with Post COVID-19 Condition ('Long COVID’): A Delphi Study. *SSRN Electronic Journal*. https://doi.org/10.2139/ssrn.3822279
O’Sullivan, O. (2021). Long-term sequelae following previous coronavirus epidemics. *Clinical Medicine, Journal of the Royal College of Physicians of London*, *21*(1), E68–E70. https://doi.org/10.7861/CLINMED.2020-0204
O’Sullivan, O., Barker-Davies, R. M., Thompson, K., Bahadur, S., Gough, M., Lewis, S., …

Cranley, M. (2021). Rehabilitation post-COVID-19: cross-sectional observations using the Stanford Hall remote assessment tool. *BMJ Military Health*. https://doi.org/10.1136/bmjmilitary-2021-001856
Office for National Statistics. (2021). Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK -. Retrieved June 23, 2021, from https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021
Osmanov, I. M., Spiridonova, E., Bobkova, P., Gamirova, A., Shikhaleva, A., Andreeva, M., … Munblit, D. (2021). Risk factors for long covid in previously hospitalised children using the ISARIC Global follow-up protocol: A prospective cohort study. *MedRxiv*, 2021.04.26.21256110-2021.04.26.21256110. Retrieved from http://medrxiv.org/content/early/2021/04/26/2021.04.26.21256110.abstract
Park, H. Y., Jung, J., Park, H. Y., Lee, S. H., Kim, E. S., Kim, H. Bin, & Song, K. H. (2020, December). Psychological Consequences of Survivors of COVID-19 Pneumonia 1 Month after Discharge. *Journal of Korean Medical Science*. https://doi.org/10.3346/jkms.2020.35.e409
Parkin, A., Davison, J., Tarrant, R., Ross, D., Halpin, S., Simms, A., … Sivan, M. (2021). A Multidisciplinary NHS COVID-19 Service to Manage Post-COVID-19 Syndrome in the Community. *Journal of Primary Care and Community Health*, *12*, 21501327211010990–21501327211010990. https://doi.org/10.1177/21501327211010994
Pizarro-Pennarolli, C., Sánchez-Rojas, C., Torres-Castro, R., Vera-Uribe, R., Sanchez-Ramirez, D. C., Vasconcello-Castillo, L., … Rivera-Lillo, G. (2021). Assessment of activities of daily living in patients post COVID-19: A systematic review. *PeerJ*. https://doi.org/10.7717/peerj.11026
Postigo-Martin, P., Cantarero-Villanueva, I., Lista-Paz, A., Castro-Martín, E., Arroyo-Morales, M., & Seco-Calvo, J. (2021). A COVID-19 Rehabilitation Prospective Surveillance Model for Use by Physiotherapists. *Journal of Clinical Medicine*, *10*(8), 1691. https://doi.org/10.3390/jcm10081691
Public Health Ontario. (2021). Persistent Symptoms and Post-Acute COVID-19 in Adults – What We Know So Far, 1–21.
Qu, G., Zhen, Q., Wang, W., Fan, S., Wu, Q., Zhang, C., … Sun, Y. (2021). Health-related quality of life of COVID-19 patients after discharge: A multicenter follow-up study. *Journal of Clinical Nursing*. https://doi.org/10.1111/jocn.15733
Rando, H. M., Bennett, T. D., Byrd, J. B., Bramante, C., Callahan, T. J., Chute, C. G., … Haendel, M. A. (2021). Challenges in defining Long COVID: Striking differences across literature, Electronic Health Records, and patient-reported information. *MedRxiv : The Preprint Server for Health Sciences*. https://doi.org/10.1101/2021.03.20.21253896
Raw, R. K., Kelly, C., Rees, J., Wroe, C., & Chadwick, D. R. (2021). Previous COVID-19 infection but not Long-COVID is associated with increased adverse events following BNT162b2/Pfizer vaccination. *MedRxiv*, 2021.04.15.21252192-2021.04.15.21252192. Retrieved from https://www.medrxiv.org/content/medrxiv/early/2021/04/22/2021.04.15.21252192.full.pdf
Research, A. & I. B. (Ministry of H. (2021). *Evidence Synthesis Briefing Note: Understanding Long COVID-19*. Toronto, ON. Retrieved from https://esnetwork.ca/wp-content/uploads/2021/04/Evidence-Synthesis-BN_Understanding-Long-COVID_May-15-2021_v2.pdf
Sigfrid, L., Drake, T. M., Pauley, E., Jesudason, E. C., Olliaro, P., Shen Lim, W., … Scott, J. T. (2021). Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. *MedRxiv*, 2021.03.18.21253888-2021.03.18.21253888. Retrieved from

https://www.medrxiv.org/content/10.1101/2021.03.18.21253888v3.full
Sisó-Almirall, A., Brito-Zerón, P., Ferrín, L. C., Kostov, B., Moreno, A. M., Mestres, J., … Ramos-Casals, M. (2021). Long covid-19: Proposed primary care clinical guidelines for diagnosis and disease management. *International Journal of Environmental Research and Public Health*, *18*(8). https://doi.org/10.3390/ijerph18084350
Skyrud, K., Telle, K., Hernaes, K., Magnusson, K., & Skyrud, K. D. (2021). Impacts of COVID-19 on sick leave. *MedRxiv*, 2021.04.09.21255215. https://doi.org/10.1101/2021.04.09.21255215
Smith, T. J., & Hillner, B. E. (2019). The Cost of Pain. *JAMA Network Open*, *2*(4), e191532. https://doi.org/10.1001/jamanetworkopen.2019.1532
Sudre, C. H., Murray, B., Varsavsky, T., Graham, M. S., Penfold, R. S., Bowyer, R. C., … Steves, C. J. (2021). Attributes and predictors of long COVID. *Nature Medicine*. https://doi.org/10.1038/s41591-021-01292-y
Taquet, M., Geddes, J. R., Husain, M., Luciano, S., & Harrison, P. J. (2021). 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *The Lancet Psychiatry*, *8*(5), 416–427. https://doi.org/10.1016/s2215-0366(21)00084-5
Tran, V.-T., Riveros, C., Clepier, B., Desvarieux, M., Collet, C., Yordanov, Y., & Ravaud, P. (2021). Development and validation of the long covid symptom and impact tools, a set of patient-reported instruments constructed from patients' lived experience. *Clinical Infectious Diseases*. https://doi.org/10.1093/cid/ciab352
Tudoran, M., Tudoran, C., Lazureanu, V. E., Marinescu, A. R., Pop, G. N., Pescariu, A. S., … Cut, T. G. (2021, March). Alterations of left ventricular function persisting during post-acute COVID-19 in subjects without previously diagnosed cardiovascular pathology. *Journal of Personalized Medicine*. https://doi.org/10.3390/jpm11030225
Urwin, S., Gavinder, K., & Graziadio, S. (2020). *What prognostic clinical risk prediction scores for COVID-19 are currently available for use in the community setting?* Retrieved from https://www.cebm.net/covid-19/what-prognostic-clinical-risk-prediction-scores-for-covid-19-are-currently-available-for-use-in-the-community-setting/
Vaes, A. W., Goërtz, Y. M. J., Van Herck, M., Machado, F. V. C., Meys, R., Delbressine, J. M., … Spruit, M. A. (2021). Recovery from COVID-19: a sprint or marathon? 6-month follow-up data from online long COVID-19 support group members. *ERJ Open Research*, *7*(2), 141–2021. https://doi.org/10.1183/23120541.00141-2021
Vanichkachorn, G., Newcomb, R., Cowl, C. T., Murad, M. H., Breeher, L., Miller, S., … Higgins, S. (2021). Post COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at the Mayo Clinic and Characteristics of the Initial Patient Cohort. In *Mayo Clinic Proceedings*. Elsevier. https://doi.org/10.1016/j.mayocp.2021.04.024
Vehar, S., Boushra, M., Ntiamoah, P., & Biehl, M. (2021). Post-acute sequelae of SARS-CoV-2 infection: Caring for the "long-haulers". *Cleveland Clinic Journal of Medicine*. https://doi.org/https://dx.doi.org/10.3949/ccjm.88a.21010
Viswanathan, M., Ansari, M. T., Berkman, N. D., Chang, S., Hartling, L., McPheeters, M., & Treadwell, J. R. (2012). Assessing the risk of bias of individual studies in systematic reviews of health care interventions. In *Methods guide for effectiveness and comparative effectiveness reviews [Internet].* Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK91433/
Whittaker, H. R., Gulea, C., Koteci, A., Kallis, C., Morgan, A. D., Iwundu, C., … Quint, J. (2021). Post-Acute COVID-19 Sequelae in Cases Managed in the Community or Hospital in the UK: A Population Based Study. *SSRN Electronic Journal*. https://doi.org/10.2139/ssrn.3820510
Wildwing, T., & Holt, N. (2021). The neurological symptoms of COVID-19: a systematic overview of systematic reviews, comparison with other neurological conditions and

implications for healthcare services. *Therapeutic Advances in Chronic Disease*, *12*. https://doi.org/10.1177/2040622320976979
World Health Organization. (2021a). *Expanding our understanding of Post COVID-19 condition*. Retrieved from https://www.who.int/publications/i/item/9789240025035
World Health Organization. (2021b). *In the wake of the pandemic: Preparing for Long COVID*. Copenhagen. Retrieved from https://apps.who.int/iris/bitstream/handle/10665/339629/Policy-brief-39-1997-8073-eng.pdf
Wynants, L., Van Calster, B., Collins, G. S., Riley, R. D., Heinze, G., Schuit, E., … Van Smeden, M. (2020). Prediction models for diagnosis and prognosis of covid-19: Systematic review and critical appraisal. *The BMJ*, *369*. https://doi.org/10.1136/bmj.m1328
Yong, S. J. (2020). Long-Haul COVID-19: Putative Pathophysiology, Risk Factors, and Treatments. Retrieved from https://www.tandfonline.com/doi/full/10.1080/23744235.2021.1924397
Zapatero, D. C., & Hanquet, G. (2021). *EPIDEMIOLOGY OF LONG COVID: A PRAGMATIC REVIEW OF THE LITERATURE*.