COVID-19 rapid guideline: managing the long-term effects of COVID-19

Main editor

National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) and Royal College of General Practitioners (RCGP)

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NICE, RCGP, and SIGN

Sections

1. How to use this guideline

Background

This guideline has been developed collaboratively by NICE, the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners (RCGP). It covers care for people who have signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 4 weeks and are not explained by an alternative diagnosis.

This new and emerging condition, which has been described using a variety of terms including 'long COVID', can have a significant effect on people's quality of life. It also presents many challenges when trying to determine the best-practice standards of care based on the current evidence. There is no internationally agreed clinical definition or clear treatment pathway, and there is an evolving, evidence base. This guideline provides clinical definitions of the effects of COVID-19 at different times (see below). It also provides advice on diagnosis and management based both on the best available evidence and the knowledge and experience of the expert panel.

NICE, SIGN and the RCGP have developed the guideline using a 'living' approach, which means that targeted areas of the guideline will be continuously reviewed and updated in response to emerging evidence.

We aim to update these recommendations frequently in line with new evidence or changes in practice and will produce new recommendations where gaps are identified. We search and screen the evidence weekly to produce living recommendations that reflect the latest best available evidence.

We have developed this guideline using our methods and processes for guidelines developed during health and social care emergencies. For more details of the methods and processes used for this guideline, including details of the expert advisory panel members and declarations of interests, see the methods and processes section.

Using the guideline in MAGICapp

In MAGICapp, each recommendation is accompanied by layered supporting information. The supporting information presented differs depending on whether the recommendation was developed by consensus or evidence review.

All recommendations are accompanied by a rationale and labelled as follows:

> **Consensus recommendation (Blue)**
>
> A consensus recommendation can be given for or against the intervention. This type of recommendation is used when there is not enough evidence to give an evidence-based recommendation, but the panel still regards it as important to give a recommendation.

If sufficient evidence becomes available, additional supporting information will be added as follows:

Recommendation labels

> **Recommendation for (Green)**
>
> A strong recommendation is given when there is high-certainty evidence showing that the overall benefits of the intervention are clearly greater than the disadvantages. This means that all, or nearly all, patients will want the recommended intervention.
>
> **Recommendation against (Red)**
>
> A strong recommendation against the intervention is given when there is high-certainty evidence showing that the overall disadvantages of the intervention are clearly greater than the benefits. A strong recommendation is also used when the examination of the evidence shows that an intervention is not safe.

Conditional recommendation for (Yellow)

A conditional recommendation is given when it is considered that the benefits of the intervention are greater than the disadvantages, or the available evidence cannot rule out a substantial benefit of the intervention while assessing that the adverse effects are few or absent. This recommendation is also used when patient preferences vary.

Conditional recommendation against (Orange)

A conditional recommendation is given against the intervention when it is judged that the disadvantages of the intervention are greater than the benefits, but when this is not substantiated by strong evidence. This recommendation is also used when there is strong evidence of both beneficial and harmful effects, but when the balance between them is difficult to determine. Likewise, it is also used when patient preferences vary.

Supporting information

Research evidence: The overall effect estimates and references to the studies.

Certainty of the evidence:

- **High**: We are very sure that the true effect is close to the estimated effect.
- **Moderate**: We are moderately sure of the estimated effect. The true effect is probably close to this one, but there is a possibility that it is statistically significantly different.
- **Low**: We have limited confidence in the estimated effect. The true effect may be statistically significantly different from the estimated effect.
- **Very low**: We have very little confidence in the estimated effect. The true effect is likely to be statistically significantly different from the estimated effect.

Evidence to decision: Brief description of beneficial and harmful effects, certainty of evidence and considerations of patient preferences.

Rationale: Description of how the panel reached its decision.

Practical information: Practical information about the treatment and information on any special patient considerations.

References: Reference list for the recommendation.

2. Identification

These recommendations are for healthcare professionals caring for people who have had suspected or confirmed acute COVID-19 and present to any healthcare setting, irrespective of whether they were hospitalised or had a positive or negative SARS-CoV-2 test (PCR, antigen or antibody). Be aware that both children and adults can be affected by ongoing symptomatic COVID-19.

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on case definition, signs, symptoms and prevalence, children and young people, risk factors, impact of vaccines and views and experiences of patients, their families and carers.

Recommended

Use the following clinical case definitions to identify and diagnose the long-term effects of COVID-19:

Acute COVID-19

Signs and symptoms of COVID-19 for up to 4 weeks.

Ongoing symptomatic COVID-19

Signs and symptoms of COVID-19 from 4 weeks up to 12 weeks.

Post-COVID-19 syndrome

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. It usually presents with clusters of symptoms, often overlapping, which can fluctuate and change over time and can affect any system in the body. Post-COVID-19 syndrome may be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed.

In addition to the clinical case definitions, the term 'long COVID' is commonly used to describe signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more).

Codes have been developed that align with this case definition. See the practical info section for further details.

Practical Info

To support recording of clinical information and enable data extraction and exchange, codes have been developed that align with the case definition and support diagnosis, management and referral. These can be found in NHS England and NHS Improvement's national guidance for post-COVID syndrome assessment clinics (Appendix B), as part of the primary care coding minimum dataset.

The Scottish Government's information support note for clinicians to support the management of the long-term effects of COVID-19 in primary and community care in Scotland provides information on the relevant codes for EMIS PCS and Vision. It also includes targeted information for clinicians and support for healthcare teams, including information and links to resources to support a consistent approach in Scotland to clinical assessment, shared decision making and individualised care planning conversations, including self-management and further referral where needed.

Evidence To Decision

Benefits and harms

Evidence on the case definition was reviewed and no changes were made. See the evidence review on case definition.

The panel recognised the importance of having a case definition for describing the long-term effects of COVID-19 and the need

to review it as more information on the condition becomes available. Having a case definition allows clinicians to effectively diagnose, treat and manage a condition and distinguish it from other conditions. The panel considered that the updated evidence review continued to support the current case definition and therefore no changes were made.

The panel acknowledged that this case definition may be interpreted as a diagnosis of exclusion. However, they discussed that ongoing symptomatic COVID-19 and post-COVID-19 syndrome have many features in common with other conditions, some of which could be considered life threatening. Therefore, ongoing symptomatic COVID-19 and post-COVID-19 syndrome should not be the first conditions to be excluded for reasons of patient safety.

Certainty of the Evidence

There is a lack of certainty in the evidence base. Most studies included in the review were cross-sectional surveys and were judged to be of high risk of bias due the retrospective nature of the studies. All the data in the studies were self-reported and therefore prone to recall bias. The surveys were disseminated to online social media groups which will have included participants who were self-selected and therefore may not be representative of the general population. Most participants were female and of white ethnicity. Some of the same social media groups were targeted for more than one survey so there is a possibility of duplication and double counting due to the similar nature of the questions. However, there were themes emerging from the evidence that were consistent across all studies, such as the variance and fluctuation of symptoms.

There is lower-certainty evidence paired with consistent panel expertise showing that the overall benefits of using the case definition are clearly greater than the disadvantages.

Values and preferences

The panel understood from the qualitative evidence that the fluctuating nature of symptoms and the trajectory of the disease led to increased fear and uncertainty and a sense of limited information and knowledge. The panel acknowledged the importance of having a case definition to reduce the uncertainty around the trajectory of illness.

Resources and other considerations

While there are concerns that a case definition may inadvertently exclude people who do not present in a typical way, including children and older adults, the panel discussed that the case definition was broad enough to capture people who need help and support for the long-term effects of COVID-19.

The panel expect that having a case definition for the long-term effects of COVID-19 would be acceptable to patients. This is because there is limited knowledge of the condition and patients reporting experiences of not being taken seriously. The key features of the case definition reflect patient experiences of illness trajectory seen in the evidence, including the fluctuating nature of symptoms.

The panel discussed the new World Health Organization definition A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021 (who.int) They agreed that it was very similar to the NICE definition of post-COVID-19 syndrome in that it usually occurs 3 months from the onset of COVD-19 and cannot be explained by alternative diagnosis. There is also agreement that symptoms may fluctuate over time. However, the expert panel agreed it was important to recognise the ongoing symptomatic COVID-19 population with symptoms between 4 and 12 weeks from onset of COVID-19 and therefore favoured to keep the NICE definition in place at this time.

Rationale

To effectively diagnose, treat and manage a condition it needs to be defined and distinguished from other conditions. A set of definitions was needed to distinguish 3 phases following infection consistent with COVID-19, and to define the term ‘long COVID’.

When developing the terms used in this guideline, many different factors were taken into account. The aim was to reduce the existing confusion about how to define the disease for clinical guidance. The panel recognised the significant progress made by patient groups using the term ‘long COVID’. However, the term ‘long COVID’ has been used in multiple ways across the literature. Other terms have also been used. Greenhaigh et al (2020) uses the terms ‘post-acute COVID-19’ (from 3 to 12 weeks) and ‘chronic COVID-19’ for symptoms extending beyond 12 weeks. The National Institute for Health Research themed review notes the

possibility of a number of different syndromes.

The evidence on and pros and cons of different terms were reviewed. Specific clinical diagnostic criteria were needed to facilitate access to support, provide the basis for planning services and to enable formal codes to be developed for clinical datasets. Three definitions were developed: acute COVID-19 (0 to 4 weeks), ongoing symptomatic COVID-19 (4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or longer).

In deciding these time periods, the panel were aware of evidence showing that most people's symptoms will resolve before 12 weeks from the start of acute COVID-19, while for a smaller proportion of people they will continue for longer. People may also develop signs or symptoms of a life-threatening complication at any time and these need to be investigated urgently.

The panel concluded that most people who have symptoms or had a positive COVID-19 test would no longer be self-isolating after 4 weeks and could be investigated for ongoing symptomatic COVID-19 (4 to 12 weeks) with the possibility of later being diagnosed with post-COVID-19 syndrome (12 or more weeks).

There is currently no long-term evidence base to help determine how long the ongoing effects currently seen after a SARS-CoV-2 infection will last. The term 'post' COVID-19 syndrome was agreed to reflect that the acute phase of the illness has ended, not that the person has recovered. Because it is not clear how long symptoms may last, the panel agreed that time-specific terms such as 'chronic' or 'persistent' were not appropriate. 'Syndrome' was agreed to reflect the 'running together' or concurrence of the multisystem, fluctuating and often overlapping 'clusters' of symptoms that people present with.

For the November 2021 update, the panel reviewed the evidence and agreed that it supported the current case definition, therefore no changes were made.

Clinical Question/ PICO

Population: Adults and children experiencing ongoing symptoms beyond the duration of acute COVID-19 illness (>4 weeks)

Intervention:

Comparator:

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Diagnoses of PCS or alternative conditions Up to 14 months from acute illness onset	Based on data from 23,704 participants in 2 studies. (Observational (non-randomized)) Follow up: up to 14 months.	One study found 23468/36507 (64.3%) of Long COVID codes used on electronic health records were for diagnosis of Post-COVID-19 syndrome and 2989/36507 (8.2%) were for the diagnosis of ongoing symptomatic disease. One study reported 27/77 (35%) people were diagnosed with a medically evaluated COVID-19 complication and 11 (14%) with a self-evaluated COVID-19 complication. 39 (51%) were diagnosed with a non-COVID-19 related diagnosis or was unclear		**Very low** Due to very serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [1]	Evidence from 2 studies found that coding for PCS was used more than coding for ongoing symptomatic disease but both remained low. People were diagnosed with COVID-19 related complications and non-COVID-19 related complications up to 14 months from acute illness.
Referral Up to 14 months from acute illness onset	Based on data from 23,273 participants in 1 studies. (Observational (non-randomized)) Follow up: up to 14 months.	One study found that coding was signposted to YOUR COVID Recovery (2.9%), referred to post-COVID assessment clinics (17.3%) and (4.9%) referred to YOUR COVID Recovery rehabilitation platform.		**Very low** Due to very serious risk of bias, Due to very serious imprecision [2]	Evidence from 1 study found coding for referral to COVID recovery services was low up to 14 months from acute illness.
Assessment Up to 14 months	Based on data from 23,273 participants in 14	One study found that assessment tools accounted for <1% of all the codes		**Very low** Due to very	Evidence from 1 study found coding for assessment tools was

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
from acute illness onset	studies. (Observational (non-randomized)) Follow up: up to 14 months.	used. The assessment tools coded included the Newcastle post-COVID syndrome follow-up screening questionnaire, COVID-19 Yorkshire Rehabilitation screening tool and the Post-COVID-19 Functional Status Scale patient self-report		serious risk of bias, Due to very serious imprecision [3]	very low up to 14 months from acute illness.
Healthcare utilisation A median of 7.2 months from acute illness onset	Based on data from 320 participants in 2 studies. (Observational (non-randomized)) Follow up: a median of 7.2 months.	One study reported that 8/81 (10%) of previously hospitalised patients had been re-hospitalised for reason related to COVID-19. A survey found that the number of people receiving physiotherapy or rehabilitation between 3 and 6 months of follow-up (31.8% and 11.7% respectively) was significantly higher compared to the period between initial infection and 3 months follow-up (4.2%; p<0.05)		**Very low** Due to very serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [4]	Evidence from 2 studies found that people were receiving care (re-hospitalisation, physiotherapy or rehabilitation) up to 6 months after acute illness.
Symptom duration Mean duration of symptoms was 7.2 months	Based on data from 11,475 participants in 3 studies. (Observational (non-randomized)) Follow up: no fixed time point.	One survey found that that 2454 (65.2%) respondents experienced symptoms for more than 180 days. Another survey found that symptom duration ranged from 2 weeks to over 100 days and another reported mean duration of illness to be 7.2 (SD 1.8) months		**Very low** Due to very serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [5]	Evidence from 3 studies found that people were still experiencing symptoms 6-7 months after acute illness
Number of symptoms Up to 6 months from acute illness	Based on data from 4,010 participants in 2 studies. (Observational (non-randomized)) Follow up: up to 6 months.	One study found that for those people that did not recover within 90 days, the average number of symptoms peaked at month 2 from initial illness. For those people experiencing symptoms for longer than 6 months, the mean number of symptoms was 13.79 (95% CI 12.68 to 14.88). Another study found that at 6 months, 98 (41%) people reported 1 to 5 symptoms, 69 (40%) people reported 6 to 10 symptoms and 32 (13%) reported >10 symptoms		**Very low** Due to very serious risk of bias, Due to very serious imprecision [6]	Evidence from 2 studies found that those people still experiencing symptoms reported having multiple symptoms. These ranged from <5 to up to a mean of 14 symptoms at 6 months after acute illness.
Course of illness Up to 7 months from acute illness	Based on data from 8,925 participants in 2 studies. (Observational (non-randomized)) Follow up: up to 7 months.	One study suggested that symptoms were clustered in three groups according to their time courses. Cluster 1 symptoms occur early in the illness peaking at 2-3 weeks; Cluster 2 symptoms remain stable over time; Cluster 3 symptoms rise sharply in the first 2 months, can remain stable, decrease over time or increase slightly in later months. Another study was similar in reporting 3 waves of symptoms. The first wave consists of neurological and cardiovascular symptoms, the second wave have microvascular symptoms and the third wave impacts endocrine function.		**Very low** Due to very serious risk of bias, Due to very serious imprecision [7]	Evidence from 2 studies found that symptoms occur in clusters or waves over the course of illness in the first 6 months.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Changes in symptoms Up to 7 months from acute illness	Based on data from 8,925 participants in 2 studies. (Observational (non-randomized)) Follow up: up to 7 months.	One study (n=3762) found that a minimum of 85.9% (95% CI 84.8% to 87%) people experienced relapses of symptoms which occur in an irregular pattern (52.8%, 95% CI 51.2% to 54.4%) and in response to a specific trigger (52.4%, 95% CI 50.8% to 54%). Another study (n=5163f) found that symptoms would temporarily resolve and then later return.		**Very low** Due to very serious risk of bias, Due to very serious imprecision [8]	Evidence from 2 studies found that people experience relapses of symptoms that occur in irregular patterns and often in response to triggers up at 7 months from acute illness.
Triggers of symptom relapses Up to 7 months from acute illness	Based on data from 8,925 participants in 2 studies. (Observational (non-randomized))	One study (n=3762) found that triggers of relapses were Physical activity: 70.7%, (95% CI 69.2% to 72.1%); Stress: 58.9%, (95% CI 57.3% to 60.5%); Exercise: 54.39%, (95% CI 52.8% to 56.0%); Mental activity: 46.2%, (95% CI 44.7% to 47.8%); during menstruation: 34.3%, (95% CI 32.0% to 36.5%) and before menstruation: 35.2%, (95% CI 33.0% to 37.3%). Another study (n= 5163) identified triggers of relapses to be physical activity (77.2%); stress (55.1%); disturbance in sleep patterns (46.9%); cognitive activity (42.2%) and domestic chores (35.0%).		**Very low** Due to very serious risk of bias, Due to very serious imprecision [9]	Evidence from 2 studies identified several triggers that led to relapses of symptoms at 7 months after acute illness. These triggers include physical activity, exercise, stress, mental/cognitive activity, menstruation, sleep disturbance and domestic chores.
Impact on activities - Daily activities Up to 6 months from acute illness	Based on data from 2,789 participants in 2 studies. (Observational (non-randomized)) Follow up: 6 weeks to 6 months.	One study (n=2550) symptoms impacted on the ability to carry out activities such as domestic chores (84.3%), leisure (84.8%) and social (77.1%) activities, work (74.9 %), self-care (50.0%), childcare (35.8%), and caring for other adults (26.1%). At 6 weeks 32.3% were unable to live alone without any assistance, and 34.5% reported moderate functional limitations. Another study (n=239) found that 62% still reported moderate to extreme problems with daily activities at 6 months. People were significantly less dependent of a partner or family for personal care at 6 months follow up but the proportion of people still needing help was still significantly higher compared to before COVID-19 illness		**Very low** Due to very serious risk of bias, Due to very serious imprecision [10]	Evidence from 2 studies found that symptoms affected people's ability to carry out daily activities including needing assistance at 6 weeks from acute illness. This dependence was significantly less at 6 months from acute illness but still had not reduced to pre-COVID levels.
Impact on activities - Work up to 7.7 months from acute illness	Based on data from 11,714 participants in 4 studies. (Observational (non-randomized)) Follow up: up to 7.7 months.	One study found that symptoms such as fatigue, personality change, sensation of 'brain pressure', inability to sleep, inability to exercise, difficulty concentrating, memory problems, confusion, shortness of breath, and the fluctuating nature of symptoms impacted on the ability to work. Another study (n=3762) found that 45.6% (95% CI 43.2% to 48%) of unrecovered respondents were working reduced hours at 7 months and 22.3% (95% CI 20.5% to 24.3%) were not		**Very low** Due to very serious risk of bias, Due to very serious imprecision [11]	Evidence from 4 studies found that symptoms and the fluctuating nature of symptoms experienced up to 7.7 months from acute illness impacted on ability to work. People work reduced hours or are unable to work due to their condition but there was some improvement at 6 months compared to 3 months.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		working due to their health condition. Another study found that at 7.7 months since COVID-19 illness, 9.7% of 2550 participants reported working reduced hours and 19.1% reported being unable to work. A fourth study (n=239) found that the mean work time missed due to ill health or impairment while working at 3 months compared to 6 months, reduced from 73% to 52% and 66% to 60% respectively.			

1. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported or clinician entered data. Coding could be retrospective. High risk of recall bias.. **Inconsistency: serious.** Studies enrolled patients in different ways. One study only included SARs-CoV-2 positive patients only.. **Indirectness: no serious. Imprecision: very serious.** Unable to pool data as descriptive only. Unable to measure imprecision.
2. **Risk of Bias: very serious.** Retrospective study design reliant on clinician entered data. Coding could be retrospective. High risk of recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data as descriptive only. Unable to measure imprecision. **Publication bias: no serious.**
3. **Risk of Bias: very serious.** Retrospective study design reliant on clinician entered data. Coding could be retrospective. High risk of recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data as descriptive only. Unable to measure imprecision. **Publication bias: no serious.**
4. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: serious.** Unable to pool due to different study designs. **Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
5. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: serious.** Unable to pool due to different study designs. **Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
6. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
7. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
8. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
9. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
10. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**
11. **Risk of Bias: very serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: very serious.** Unable to pool data or measure imprecision. **Publication bias: no serious.**

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37. COVID-19 rapid evidence review: Case definition. 2021;

Recommended

Give people who have had suspected or confirmed acute COVID-19 (and their families or carers, as appropriate) advice and written information on:

- the most common new or ongoing symptoms after acute COVID-19 (see the section on common symptoms)
- what they might expect during their recovery, including that:
  - recovery time is different for everyone but for most people symptoms will resolve by 12 weeks
  - the likelihood of developing ongoing symptomatic COVID-19 or post-COVID-19 syndrome is not considered to be linked to the severity of their acute COVID-19 (including whether they were in hospital)
  - if new or ongoing symptoms occur they can fluctuate, affecting them in different ways at different times
- how to self-manage ongoing symptomatic COVID-19 or post-COVID-19 syndrome (see the recommendations on self-management and supported self-management)
- who to contact if they are worried about new, ongoing or worsening symptoms, or if they are struggling to return to education, work or other usual activities, especially if it is more than 4 weeks after the start of acute COVID-19.

For signs or symptoms that could be caused by an acute or life-threatening complication, see the recommendation on referral.

Evidence To Decision

Benefits and harms

Adults

The panel discussed the importance of identifying the most common symptoms that present in people experiencing long term effects of COVID-19. Knowing the most common symptoms will help clinicians to recognise post-COVID-19 syndrome as a possible diagnosis. However, they were mindful that the most common symptoms will not always be present and should not be used as strict criteria for diagnosis as this could mean people who present atypically may be missed. Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19 syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

Children and young people

The panel noted the evidence indicating that children sometimes have a lack of concentration, short term memory loss, and/or difficulty doing everyday tasks ≥4 weeks after acute COVID-19 illness. Expert witnesses and the panel agreed there was a lack of recognition among healthcare professionals and the public that children can be affected by ongoing symptomatic COVID-19 or post-COVID-19 syndrome. For example, worse achievement or absenteeism at school is sometimes erroneously attributed to other causes, leading to an under-referral of cases to dedicated clinics, multidisciplinary teams (MDTs) and multidisciplinary rehabilitation services.

The expert witness and panel overwhelmingly agreed that worse performance or absenteeism at education, work, or training was a "red flag" for both children and adults. For example, in the studies above, common symptoms of long-COVID-19 include tiredness, fatigue, and lack of concentration. The panel agreed that it was important to highlight this because worse achievement or absenteeism could be wrongfully attributed to other causes. The panel agreed to use the term "worse achievement" because this encompasses a range of attainments, such as academic, athletic, attention to detail or other abilities that are important to that person.

The panel also agreed to retain the list of common symptoms of ongoing symptomatic COVID-19 and post-COVID-19 syndrome, which is consistent with the evidence and encompasses the common symptoms for all age groups, however they did note that cardiac and respiratory symptoms were less common in children than adults and agreed that this should be noted in the common symptoms list.

Certainty of the Evidence

Lower-certainty evidence paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

Adults

The panel recognised that the evidence base is still considered to be moderate to very low quality. All studies were considered to be of moderate to high risk of bias due to the ways the studies were conducted. The panel were also mindful that when considering prevalence data, it is important to know the denominator when interpreting the percentages. This varied across all studies. However, it is clear from the evidence that some symptoms such as fatigue and shortness of breath are reported consistently across studies and the panel commonly see them in clinical practice, which increases the certainty around these symptoms. The panel also acknowledged that some symptoms may be under-reported in the literature. In their experience, patients may not report a symptom, such as sleep disturbance, unless directly asked. They were mindful that the way participants were asked about their symptoms in the studies could impact on how symptoms were reported.

Children and young people

The evidence base for children and young people remains uncertain due to the small number of studies, the small size of them, and their risk of bias. Furthermore, there was heterogeneity across the studies in terms of how they selected participants who had symptoms of post-acute COVID-19. For example, some studies only included children with "long COVID-19" and others included all children who had COVID-19 and measured symptoms experienced after certain amount of time by that whole population overall. Most studies had a high risk of bias due to their retrospective design with the inherent risk of selection bias, and largely self-reported outcomes with an increased risk of recall bias.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

The panel identified worse performance or absenteeism at education, work, or training as being important to people. Therefore,

the panel decided that advice and information should be given on who to contact if people are worried about new, ongoing or worsening symptoms, or if they are struggling to return to education or work.

Resources and other considerations

Ongoing persistent symptoms can impact on an individual's ability to perform usual work activities. Healthcare workers have been considered at high risk of contracting SARS-CoV-2 infection. This could potentially mean a higher prevalence of long-term effects of COVID-19 in this population which may impact on resources within the NHS.

Rationale

People need good information after acute COVID-19 so they know what to expect and when to ask for more medical advice. This could help to relieve anxiety if people do not recover in the way they expect. Evidence from patient experience and the panel's own experiences supported this, particularly because symptoms can fluctuate and there are so many different symptoms reported. Information may be provided by GPs or community services, or by secondary care for people who were in hospital.

For the November 2021 update, the panel heard expert testimony that absence from or poor performance at work or education was associated with poor outcomes for people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome. The panel agreed that it is important for people to contact a health professional if they are struggling with returning to work or education after acute COVID-19 to ensure they receive support with any continuing symptoms.

The panel discussed whether there were any symptoms in particular that people should look out for that that may suggest they have ongoing symptomatic COVID-19 or post-COVID-19 syndrome. They agreed that there was no new evidence in this area and that the list of possible symptoms is too long to give people helpful advice on which symptoms to look out for. The panel agreed that people should contact a healthcare professional if they are concerned about any new, ongoing or worsening symptoms. The panel also noted that there is some helpful information on the Your COVID Recovery website that outlines when people should contact their healthcare professional.

Clinical Question/ PICO

Population: Adults experiencing symptoms beyond the duration of acute COVID-19 illness (>4 weeks)
Intervention: Not applicable
Comparator: Not applicable

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Fatigue (People with a history of laboratory-confirmed COVID-19) 4-12 weeks after COVID-19 diagnosis	Based on data from 1,292 participants in 9 studies. [1] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 51% 95% CI 39% to 64%		**Low** The systematic review did not report reasons for downgrading	9 studies found that 51% people reported fatigue 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 39% or as high as 64%.
Fatigue (People with a history of laboratory-confirmed	Based on data from 1,962 participants in 3 studies. [2] (Observational (non-randomized)) Follow up: 12 weeks or	Prevalence 47% 95% CI 27% to 68%		**Very low** The systematic review did not report reasons for downgrading	3 studies found that 47% people reported fatigue 12 weeks or more after COVID-19 diagnosis. The symptom prevalence

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
COVID-19) 12 weeks or more after COVID-19 diagnosis	more after COVID-19 diagnosis.				could be as low as 27% or as high as 68%.
Dyspnoea (People with a history of laboratory-confirmed COVID-19) 4-12 weeks after COVID-19 diagnosis	Based on data from 1,495 participants in 10 studies. [3] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 38% 95% CI 27% to 51%		**Very low** The systematic review did not report reasons for downgrading	10 studies found that 38% people reported shortness of breath 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 27% or as high as 51%.
Dyspnoea (People with a history of laboratory-confirmed COVID-19) 12 weeks or more after COVID-19 diagnosis	Based on data from 2,373 participants in 4 studies. [4] (Observational (non-randomized)) Follow up: 12 weeks or more after COVID-19 diagnosis.	Prevalence 22% 95% CI 12% to 35%		**Very low** The systematic review did not report reasons for downgrading	4 studies found that 22% people reported shortness of breath 12 weeks or more after COVID-19 diagnosis. The symptom prevalence could be as low as 12% or as high as 35%.
Cough (any type) (People with a history of laboratory-confirmed COVID-19 4-12 weeks after COVID-19 diagnosis	Based on data from participants in 6 studies. [5] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 28% 95% CI 22% to 35%		**Low** The systematic review did not report reasons for downgrading	6 studies found that 28% of people reported cough 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 22% or as high as 35%.
Sleep disturbances or difficulties (People with a history of laboratory-confirmed COVID-19) 4-12 weeks after COVID-19 diagnosis	Based on data from participants in 2 studies. [6] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 36% 95% CI 10% to 74%		**Low** The systematic review did not report reasons for downgrading	2 studies found that 36% of people reported sleep disturbances or difficulties 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 10% or as high as 74%.

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Sleep disturbances or difficulties (People with a history of laboratory-confirmed COVID-19) 12 weeks or more after COVID-19 diagnosis	Based on data from participants in 1 studies. [7] (Observational (non-randomized)) Follow up: 12 weeks or more after COVID-19 diagnosis.	Prevalence 36% 95% CI 10% to 74%		**Low** The systematic review did not report reasons for downgrading	2 studies found that 36% of people reported sleep disturbances or difficulties 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 10% or as high as 74%.
Anxiety or depression (People with a history of laboratory-confirmed COVID-19) 4-12 weeks after COVID-19 diagnosis	Based on data from participants in 2 studies. [8] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 22% 95% CI 19% to 25%		**Low** The systematic review did not report reasons for downgrading	2 studies found that 36% of people reported sleep disturbances or difficulties 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 10% or as high as 74%.
Anxiety or depression (People with a history of laboratory-confirmed COVID-19) 12 weeks or more after COVID-19 diagnosis	Based on data from participants in 1 studies. [9] (Observational (non-randomized)) Follow up: 12 weeks or more after COVID-19 diagnosis.	Prevalence 23% 95% CI 21% to 25%		**Low** The systematic review did not report reasons for downgrading	1 study found that 23% of people reported anxiety or depression 12 weeks or more after COVID-19 diagnosis. The symptom prevalence could be as low as 21% or as high as 25%.
Hair loss (People with a history of laboratory-confirmed COVID-19) 12 weeks or more after COVID-19 diagnosis	Based on data from participants in 1 studies. [10] (Observational (non-randomized)) Follow up: 12 weeks or more after COVID-19 diagnosis.	Prevalence 22% 95% CI 20% to 24%		**Low** The systematic review did not report reasons for downgrading	1 study found that 22% of people reported hair loss 12 weeks or more after COVID-19 diagnosis. The symptom prevalence could be as low as 20% or as high as 24%.

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Cognitive impairment (People with a history of laboratory-confirmed COVID-19) 4-12 weeks after COVID-19 diagnosis	Based on data from participants in 2 studies.[11] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 24% 95% CI 18% to 21%		**Low** The systematic review did not report reasons for downgrading	2 studies found that 24% of people had cognitive impairment 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 18% or as high as 21%.
Difficulty concentrating (People with a history of laboratory-confirmed COVID-19) 4-12 weeks after COVID-19 diagnosis	Based on data from participants in 2 studies.[12] (Observational (non-randomized)) Follow up: 4-12 weeks after COVID-19 diagnosis.	Prevalence 25% 95% CI 22% to 28%		**Moderate** The systematic review did not report reasons for downgrading	2 studies found that 25% of people reported difficulty concentrating 4-12 weeks after COVID-19 diagnosis. The symptom prevalence could be as low as 22% or as high as 28%.

1. Systematic review [4].
2. Systematic review [4].
3. Systematic review [4].
4. Systematic review [4].
5. Systematic review [4].
6. Systematic review [4]. N not reported for all prevalence outcomes in the systematic review.
7. Systematic review [4].
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Clinical Question/ PICO

Population: Adults experiencing symptoms beyond the duration of acute COVID-

Intervention: Not applicable

Comparator: Not applicable

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Risk factor: Female sex Symptoms lasting 4 weeks or more	Odds ratio 1.49 (CI 95% 1.24 — 1.79) Based on data from 6,525 participants in 9 studies. [1] (Observational (non-randomized)) Follow up: 4 weeks or more.			**Very low** Due to very serious risk of bias, Due to serious inconsistency [2]	10 studies found that female sex was significantly associated with increased risk of having symptoms lasting 4 weeks or more since acute COVID-19 illness.
Risk factor: Female sex Persistence of one or more symptoms at 12 weeks or more	Odds ratio 1.51 (CI 95% 1.46 — 1.55) Based on data from participants in 1 studies. [3] (Observational (non-randomized)) Follow up: 12 weeks of more.			**Low** Due to very serious risk of bias [4]	1 study found that female sex was significantly associated with increased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.
Risk factor: Non-white ethnicity Symptoms lasting 4 weeks or more	Odds ratio 0.8 (CI 95% 0.54 — 1.19) Based on data from 5,607 participants in 7 studies. [5] (Observational (non-randomized)) Follow up: 4 weeks or more.			**Very low** Due to very serious risk of bias, Due to serious imprecision [6]	Data from 7 studies could not differentiate whether non-white ethnicity was a risk factor for having symptoms lasting 4 weeks or more since acute COVID-19 illness.
Risk factor: Asian ethnicity Persistence of one or more symptoms at 12 weeks or more	Odds ratio 0.8 (CI 95% 0.74 — 0.88) Based on data from participants in 1 studies. [7] (Observational (non-randomized)) Follow up: 12 weeks or more.			**Low** Due to very serious risk of bias [8]	1 study found that Asian ethnicity was significantly associated with a decreased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Risk factor: Poor pre-pandemic mental health Symptoms lasting 4 weeks or more	Odds ratio 1.46 (CI 95% 1.17 — 1.83) Based on data from 5,467 participants in 9 studies. [9] (Observational (non-randomized)) Follow up: 4 weeks or more.			**Low** Due to very serious risk of bias [10]	9 studies found that poor-pre pandemic mental health was significantly associated with an increased risk of having symptoms lasting 4 weeks or more since acute COVID-19 illness.
Risk factor: Poor general health Symptoms lasting 4 weeks or more	Odds ratio 1.62 (CI 95% 1.25 — 2.09) Based on data from 4,429 participants in 7 studies. [11] (Observational (non-randomized)) Follow up: 4 weeks or more.			**Low** Due to very serious risk of bias [12]	7 studies found that poor general health was significantly associated with an increased risk of having symptoms lasting 4 weeks or more since acute COVID-19 illness.
Risk factor: Asthma Symptoms lasting 4 weeks or more	Odds ratio 1.32 (CI 95% 1.07 — 1.62) Based on data from 4,525 participants in 9 studies. [13] (Observational (non-randomized)) Follow up: 4 weeks or more.			**Low** Due to very serious risk of bias [14]	9 studies found that asthma was significantly associated with an increased risk of having symptoms lasting 4 weeks or more since acute COVID-19 illness.
Risk factor: Overweight or obese Symptoms lasting 4 weeks or more	Odds ratio 1.25 (CI 95% 1.01 — 1.55) Based on data from 4,327 participants in 8 studies. [15] (Observational (non-randomized)) Follow up: 4 weeks or more.			**Low** Due to very serious risk of bias [16]	8 studies found that being overweight or obese was significantly associated with an increased risk of having symptoms lasting 4 weeks or more since acute COVID-19 illness.
Risk factor: Overweight Persistence of one or more symptoms at 12 weeks or more	Odds ratio 1.16 (CI 95% 1.12 — 1.21) Based on data from participants in 1 studies. [17] (Observational (non-randomized)) Follow up: 12 weeks or more.			**Low** Due to very serious risk of bias [18]	1 study found that being overweight was significantly associated with an increased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.
Risk factor: Obesity Persistence of one or more symptoms at 12 weeks or more	Odds ratio 1.53 (CI 95% 1.47 — 1.59) Based on data from participants in 1 studies. [19] (Observational (non-randomized)) Follow up: 12 weeks or more.			**Low** Due to very serious risk of bias [20]	1 study found that obesity was significantly associated with an increased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.
Risk factor:	Odds ratio 1.35			**Low**	1 study found that

Outcome Timeframe	**Study results and measurements**	**Comparator** Not applicable	**Intervention** Not applicable	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Smoking Persistence of one or more symptoms at 12 weeks or more	(CI 95% 1.28 — 1.41) Based on data from participants in 1 studies. [21] (Observational (non-randomized))			Due to very serious risk of bias [22]	smoking was significantly associated with an increased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.
Risk factor: Vaping Persistence of one or more symptoms at 12 weeks or more	Odds ratio 1.26 (CI 95% 1.18 — 1.34) Based on data from participants in 1 studies. [23] (Observational (non-randomized)) Follow up: 12 weeks or more.			**Low** Due to very serious risk of bias [24]	1 study found that vaping was significantly associated with an increased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.
Risk factor: Hospitalisation Persistence of one or more symptoms at 12 weeks or more	Odds ratio 3.46 (CI 95% 2.93 — 4.09) Based on data from participants in 1 studies. [25] (Observational (non-randomized)) Follow up: 12 weeks or more.			**Low** Due to very serious risk of bias [26]	1 study found that being hospitalised for acute COVID-19 illness was significantly associated with an increased risk of persistence of at least 1 symptom at 12 weeks or more since acute COVID-19 illness.

1. Systematic review [11] . **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: very serious.** Risk of bias assessment not reported but most studies used self-reported outcomes that increases recall bias.. **Inconsistency: serious.** Significant heterogeneity (I2 >50%). **Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
3. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
5. Systematic review [11] . **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of Bias: very serious.** Risk of bias assessment not reported but most studies used self-reported outcomes that increases recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** 95% CI crosses the line of no effect. **Publication bias: no serious.**
7. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
9. Systematic review [11] . **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of Bias: very serious.** Risk of bias assessment not reported but most studies used self-reported outcomes that increases recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
11. Systematic review [11] . **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of Bias: very serious.** Risk of bias assessment not reported but most studies used self-reported outcomes that increases recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
13. Systematic review [11] . **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of Bias: very serious.** Risk of bias assessment not reported but most studies used self-reported outcomes that increases recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
15. Systematic review [11] . **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of Bias: very serious.** Risk of bias assessment not reported but most studies used self-reported outcomes that increases recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
17. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.

18. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
19. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
21. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.
22. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
23. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.
24. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
25. Primary study[8]. **Baseline/comparator:** Control arm of reference used for intervention.
26. **Risk of Bias: very serious.** Study rated as high risk of bias due to the retrospective study design and high probability of recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**

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Clinical Question/ PICO

Population: Children experiencing ongoing symptoms beyond the duration of acute COVID-19 illness (>4 weeks)
Intervention: Not applicable
Comparator: Not applicable

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Prevalence of individual symptoms	Based on data from 4,388 participants in 6 studies. (Observational (non-randomized))	Four studies (n=4222) found that 2.99%-87.10% of patients reported tiredness and weakness or hypersomnia. Five studies (n=1323) found that 10.69%-87% of patients reported fatigue. Six studies (n=4388) found that 3.50%-78.60% of patients reported headache and 2.00%-75.9% of patients reported abdominal pain. Six studies (n=4388) found that 0.82%-68.4% of patients reported muscle aches and pains. Five studies (n=3878) found that 1.39%-55.0% of patients reported shortness of breath. Four studies (n=3749) found that 1.0%-45.5% of patients reported loss of		Very low Due to serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [1]	Evidence from 6 studies found that the most common ongoing symptoms in children were tiredness, weakness and fatigue; headaches; abdominal pain; muscle aches and pain; shortness of breath; loss of smell; lack of concentration or delirium; dizziness or light headedness; skipped meals and skin rash or red welts.

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
		smell. Six studies (n=4388) found that 0.41%-60.6% of patients reported lack of concentration or delirium. Five studies (n=4259) found that 1.03%-48.0% of patients reported dizziness or light headedness. Two studies (n=3142) found that 9.7%-16.88% of patients reported skipped meals. Six studies (n=4388) found that 1.6%-52.4% of patients reported skin rash or red welts			
Prevalence of categories of symptoms	Based on data from 135 participants in 2 studies. (Observational (non-randomized))	Two studies (n=135) found that 16.36%-27.5% of patients reported general symptoms (including fatigue and fever). Two studies (n=135) found that 3.64%-22.5% of patients reported ear, nose, and throat symptoms (including reduced taste/smell). Two studies (n=135) found that 5.45%-21.2% of patients reported respiratory symptoms. Two studies (n=135) found that 5.45%-16.2% of patients reported neurological symptoms (including cognitive impairment/'brain fog' and headache). One study (n=80) found that 15% of patients reported dermatological symptoms. Two studies (n=135) found that 5.45%-13.80% of patients reported gastrointestinal symptoms. Two studies (n=135) found that 1.81%-11.20% of patients reported cardiovascular symptoms. Two studies (n=135) found that 5.45%-10% of patients reported psychiatric symptoms. One study (n=80) found that 8.80% of patients reported muscular symptoms.		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [2]	Evidence from 2 studies found that the most common ongoing categories of symptoms in children were general symptoms (including fatigue and fever); ear, nose, and throat (including reduced taste/smell); respiratory symptoms; neurological symptoms (including cognitive impairment/'brain fog' and headache); and dermatological symptoms.
Symptoms of paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 6 weeks to 6 months	Based on data from 46 participants in 1 studies. (Observational (non-randomized))	One study found that the most common symptoms of PIMS-TS reported at 6 weeks and 6 months were abnormal neurological examination (52.17% at 6 weeks, 39.13% at 6 months); could walk less than 3rd centile (43.48%, 39.13%); proximal myopathy or lower limb weakness (36.13%, 17.39%); bilateral or unilateral dysmetria (34.78%, 26.09%); and abnormal eye movements or saccades (32.61%, 15.21%).		**Very low** Due to serious risk of bias, Due to serious imprecision [3]	Evidence from 1 study found that the most common symptoms of PIMS-TS at 6 weeks and 6 months were abnormal neurological examination; could walk less than 3rd centile; proximal myopathy or lower limb weakness; bilateral or unilateral dysmetria; and abnormal eye movements or saccades.
Prevalence of new post-COVID diagnoses or conditions	Based on data from 2,673 participants in 1 studies. (Observational (non-randomized))	One study found that children with COVID were not more likely to experience new post-COVID diagnoses or conditions than children without COVID		**Very low** Due to serious risk of bias, Due to serious imprecision [4]	Evidence from one study found that children with COVID-19 were not more likely to experience new post-COVID diagnoses or conditions than children without COVID-19

1. **Risk of Bias: serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: serious.** Unable to pool due to different study designs. **Imprecision: very serious.** Unable to pool due to different study designs.
2. **Risk of Bias: serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: serious.** Unable to pool due to different study designs. **Imprecision: very serious.** Unable to pool due to different study designs.
3. **Risk of Bias: serious.** Retrospective observational study and therefore prone to selection bias.. **Imprecision: serious.** unable to assess statistical significance.
4. **Imprecision: serious.** Unable to measure precision.

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Recommended

Give people information on COVID-19 vaccines (see NHS information on COVID-19 vaccines). Encourage them to follow current government guidance for vaccination but explain that it is not known if vaccines have any effect on ongoing symptomatic COVID-19 or post-COVID-19 syndrome.

Evidence To Decision

Benefits and harms

The panel reviewed published evidence and considered expert testimony (Steves 2021) on the safety and therapeutic benefit of COVID-19 vaccines in the context of long term effects of COVID-19. The panel considered that the results from the existing studies were inconclusive and agreed that there remains uncertainty for the outcomes of change in ongoing symptoms, quality of life and mental wellbeing. Considering this, the panel decided that the findings could not justify a positive recommendation for COVID-19 vaccination to treat the long term effects of COVID-19, nor a negative recommendation against this intervention in the absence of evidence of harm.

However, the panel recognised the safety and effectiveness of vaccines in preventing acute infection and the importance of the national COVID-19 vaccination programme to protect all people, particularly those who are at highest risk from serious illness or death from COVID-19 or at risk of transmitting infection. Therefore, the panel emphasised the need to encourage patients with long- term effects of COVID-19 who have not been vaccinated to have the vaccination to reduce the risk of further SARS CoV-2 infection, but to explain that it is not known if vaccines have any effect on ongoing symptomatic COVID-19 or post-COVID-19 syndrome.

In August 2022, the panel were presented with an updated evidence review on COVID-19 vaccinations and the long-term effects of COVID-19. This evidence showed that there is a likely benefit for vaccination to reduce the occurrence of long-term effects of COVID-19 in people who were vaccinated prior to SAR-CoV-2 infection. However, the evidence remained uncertain for the effects of COVID-19 vaccination on symptoms in people experiencing long-term effects of COVID-19. Considering this, the panel agreed that the current recommendation still reflects the evidence base.

Certainty of the Evidence

All outcomes were considered to be of very low certainty. This was due to none of the studies being randomised and therefore findings of the studies being potentially impacted by confounding variables. Whilst there may have been attempts to minimise confounding bias by adjusting for different variables, there may still be some residual bias. Some studies were also prone to selection bias due to the sources of patient data they used. These biases make the data less applicable to the general population. Due to the vaccine schedule, there is likely to be an imbalance in the demographics of who was vaccinated at the time of the studies. For example, in the UK, older people and those at high risk were prioritised which may reflect the dominance of vaccinated older people in the studies.

Some studies used self-reported data in their analyses. This type of data is prone to recall bias. As the studies were mainly retrospective and therefore not blinded, there is the risk that people may have been influenced by knowledge that they had or had not received the vaccine in terms of how they reported symptoms. Other factors that contribute to the uncertainty relate to the directness of the evidence. All of the studies used data collected prior to the emergence of Omicron as the dominant variant. As the effectiveness of vaccines could be impacted by different variants, this could be an important variable in the effectiveness of the vaccine to reduce the risk of developing any long term effects from subsequent SARS-CoV-2 infections. The studies also noted that effectiveness could be related to the specific vaccine used but it was not possible to analyse by vaccine given because of inconsistent data collection.

There was also some level of inconsistency across studies in terms of diagnosing long-term effects of COVID-19. Whilst all studies were broadly using the same definition, only some studies used electronic health record data. Other studies, particularly online surveys, relied on participants in a self-selection process, which could lead to an inconsistent population across the body of evidence.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values, but they identified critical outcomes that would be important for decision making. These included all-cause adverse effects, change in symptoms, quality of life and wellbeing. It is likely that these outcomes would also be of similar importance to patients. In addition, other outcomes including return to usual activities including work, education or leisure, are likely to be of particular importance to patients. These outcomes were not reported in studies.

The panel inferred that, in view of the lack of meaningful benefit for people with long term effects of COVID-19 and the unknown potential for harm, most would not choose vaccination as an intervention for long term effects of COVID-19 but

would receive vaccination to prevent further acute infection, given the evidence for the safety and effectiveness of vaccines for their primary purpose of preventing acute COVID-19.

Resources

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Equity

The panel were not aware of any evidence for vaccines use in long term effects of COVID-19 in children or pregnancy. However, because the overall recommendation is to encourage vaccination in eligible groups for preventing acute disease, it is not expected to cause inequity among any subgroups.

Acceptability

The panel were not aware of any systematically collected evidence about acceptability. However, considering the importance of the national vaccination programme and implications for patients not receiving vaccination, use of vaccines in people with long term effects would be acceptable in preventing further acute infection unless there are contraindications.

Feasibility

The panel were not aware of any systematically collected evidence about feasibility.

COVID-19 vaccines are approved for use in the UK, so the recommendation supports current practice.

Rationale

Observational evidence and expert testimony on the safety and therapeutic benefit of COVID-19 vaccines in the context of long-term effects of COVID-19 were inconclusive for the outcomes of duration and change in symptoms, quality of life and mental wellbeing. The population included people with existing long-term effects of COVID-19 and people infected after vaccination who reported symptoms of 28 days or longer since vaccination.

The expert panel agreed that the findings could not justify a positive recommendation for COVID-19 vaccination to treat the long-term effects of COVID-19, nor a negative recommendation against this intervention in the absence of evidence of harm.

However, the panel recognised the safety and effectiveness of vaccines in preventing acute infection and the importance of the national COVID-19 vaccination programme to protect all people, particularly those who are at highest risk from serious illness or death from COVID-19 or at risk of transmitting infection. Therefore, the panel emphasised the need to encourage patients with long-term effects of COVID-19 who have not been vaccinated to have the vaccination to reduce the risk of a further SARS CoV-2 infection, but to explain the uncertainty about the effect of vaccination on ongoing symptomatic COVID-19 and post-COVID-19 syndrome.

In August 2022, the panel were presented with an updated evidence review on COVID-19 vaccinations and the long-term effects of COVID-19. However, they agreed that the cumulative evidence did not change the previous conclusions or have any impact on the current recommendation. This is because the evidence remained uncertain for the effects of COVID-19 vaccination on symptoms in people experiencing long-term effects of COVID-19.

Clinical Question/ PICO

Population: People with history of COVID-19 infection after vaccination
Intervention: COVID-19 vaccination (any)

Comparator: No vaccination

Summary

Vaccination prior to initial COVID-19 infection

Compared to people who are unvaccinated for COVID-19, two doses plus a booster or two doses alone of COVID-19 vaccine given to people prior to SARS-CoV-2 infection may reduce the occurrence of long term effects of COVID-19 at 12 weeks or more from acute onset infection. There is less certainty around the effectiveness of a single dose of COVID-19 vaccine in reducing long term effects of COVID-19 when administered prior to SARS-CoV-2 infection.

What is the evidence informing this conclusion?

Evidence comes from 9 studies (7 cohort studies [Al-Aly 2021; Ayoubkhani 2022, Azzolini 2022, Simon 2021, Tannous 2022, Taquet 2022 and Zisis 2022], 1 case control study [Antonelli 2021] and 1 cross-sectional study [Kuodi 2022]). These studies included participants with a history of SARS-CoV-2 infection after one or two doses of a COVID-19 vaccine compared to people who were unvaccinated at the time of COVID-19 onset.

Publication status

Four studies are only available as preprints (Ayoubkhani 2022, posted to medRxiv on 24 February 2022, Kuodi 2022 posted to medRxiv on 17 January 2022, Simon 2021 posted to medRxiv on 18 November 2021 and Tannous 2022 posted to MedRxiv on 2 July 2022) and have therefore not been peer reviewed.

Summary of included studies

A cohort study (Al-Aly 2022) using the national healthcare databases of the US Department of Veterans Affairs (n=33,940 cases; n=113,474 controls; mean age 62.82 years; 88.85% male) aimed to characterise 6-month risks of incident post-acute sequelae (lasting 30 days or more from diagnosis) in people with breakthrough COVID-19 (the disease that ensues following post-vaccination breakthrough SARS-CoV-2 infection) compared to people with COVID-19 without prior history of vaccination. Main limitations included a predominantly older aged group and male sample, which is not representative of the UK population and an unspecified number of vaccine doses at the time of breakthrough infection.

Using the COVID-19 Infection survey data (CIS), a UK cohort study (Ayoubkhani 2022 preprint) aimed to investigate whether SARS-CoV-2 infection following two doses of a COVID-19 vaccine is associated with a reduction in Long Covid symptoms after 12 weeks, relative to being unvaccinated when infected (n=3,090 cases; n=3,090 controls, mean age 47.85 years; 54% male). Main limitations included not being able to have contemporaneous matching for cases and controls due to questions on Long COVID not being added to CIS until after mass vaccination began in the UK. It was also not possible to investigate participants who received a single dose of vaccine because most people had their second dose within the 12 week follow-up period. The data was also collected before the Omicron variant became widespread in the UK.

A cohort study conducted in the USA (Simon 2021 preprint) used data from patient health records to identity factors influencing the development and progression of long-COVID. They included people who tested positive for COVID-19 who had been vaccinated prior to infection compared to those who had not (n=2392 cases; n=220,460 controls; 40.1% male; mean age not reported). Main limitations included the findings being based on opportunistic availability of large volumes of data where there could be geographic, temporal and socioeconomic gaps that could influence outcomes. The analysis was conducted on data collected prior to the emergence of the delta variant in the USA.

Two other cohort studies conducted in the USA (Taquet 2022 and Zisis 2022) also used data from patient electronic health records through the TriNetX Research Network platform. Both studies included people with confirmed SARS-COV-2 infection after a COVID-19 vaccination compared to those who were unvaccinated (n=9479 vaccinated, n=9479 unvaccinated matched controls; mean age 57 years, 40% male [Taquet 2022]; n= 25,225 cases; 25,225 unvaccinated matched controls; mean age 55 years; 40% male [Zisis 2022]). Main limitations included those who had COVID-19 but were asymptomatic or were untested not being included in the dataset. The studies pre-date Omicron variant dominance and SARS-CoV-2 variant(s) unknown in the populations studied. As both studies used the same source of data, there may be overlap with the findings.

Using longitudinal data obtained from the Houston Methodist COVID-19 Surveillance and Outcomes Registry (CURATOR), a cohort study (Tannous 2022 preprint) evaluated the efficacy of COVID-19 vaccines against Post-Acute Sequelae of SARS-CoV-2 infection (PASC) in people with breakthrough SARS-CoV-2 infection compared to those with PASC who remained unvaccinated (vaccinated PASC n= 332; unvaccinated PASC n=5597; 37.8% male; 28.1% aged ≥65 years; 47.9% aged 40 to 64 years; 23.9% aged 18 to 39 years). Main limitations included data being limited to a single healthcare system which may impact the generalisability of the findings. Details on SARS-CoV-2 variants were not reported in the study.

A cohort study conducted in Italy (Azzolini 2022; letter) followed healthcare workers with Long COVID who were required to have 3 doses of vaccine BNT162b2 and who had a documented positive result for SARS-CoV-2 between March 2020 and March 2022 (n=229; 21.4% male; mean age 44.3 years). They were compared to a reference group of females in wave 1 of the pandemic who were unvaccinated. Main limitations included that outcomes were self-reported and unclear reporting of the regression analysis. Characteristics and sample sizes of reference group of unvaccinated females in wave 1 were not

reported and the regression analysis includes data where vaccines were administered at least 14 days prior to infection therefore it is unclear whether the 176 people who were unvaccinated at the time of infection were included in the analysis.

A UK case-control study (Antonelli 2021) used self- or proxy-reported data from the Zoe app to assess illness duration and symptom profile in individuals with SARS-CoV-2 infection after first or second vaccination compared to unvaccinated individuals (n=4731 case; n=4731 controls; mean age 53 years; 37% male). Main limitations included the app data sample containing disproportionately more women than men and under-represented individuals in more deprived areas and reliance on self-reporting and daily logging.

A cross-sectional study (Kuodi 2022 preprint) used an online survey to collect data from adults (n=634) and determine whether vaccination was associated with the incidence of reporting long-term symptoms after SARS-CoV-2 infection.

Outcomes

Post-acute COVID-19 symptoms

The UK cohort study (Ayoubkhani 2022) found that Long COVID symptoms of any severity and activity limited symptoms were statistically significantly reduced at 12 weeks from acute onset of COVID-19 for people who were double vaccinated prior to SARS-CoV-2 infection compared to those who were not vaccinated (Long COVID symptoms: OR 0.59 95% CI 0.5 to 0.69; n=6180; Activity limited symptoms: OR 0.59 95% CI 0.48 to 0.73).

Similar findings were shown in 3 of the cohort studies conducted in the USA (Al-Aly 2022, Simon 2021, Tannous 2022 and Zisis 2022). Al-Aly 2022 found that the risk of having post-acute sequalae was statistically significantly reduced at 6 months from acute onset of COVID-19 for people with breakthrough COVID-19 (infection after vaccination) compared to those who had infection but were not vaccinated (HR 0.85 95% CI 0.82 to 0.89; n=147,414). Tannous 2022 reported that the likelihood of developing PASC was statistically significantly reduced in people with breakthrough COVID-19 who had received 2 doses of mRNA vaccines or a single dose of As26.COV2.S vaccine compared to those who were unvaccinated (aOR 0.58 95% CI 0.52 to 0.66; n=5929). Simon 2021 found that reporting any symptom or at least one symptom was statistically significantly reduced at 12 to 20 weeks from acute onset of COVID-19 for people who were vaccinated compared to those who were not vaccinated (Any symptom: OR 0.22 95% CI 0.2 to 0.25; n=243,040; >1 symptom: OR 0.46 95% CI 0.43 to 0.49; n=243,040). Zisis 2022 reported that vaccination prior to SARS-CoV-2 infection significantly reduced the risk of new symptoms since COVID-19 at 28 days and 90 days compared to those who were unvaccinated:

- (28 days Respiratory symptoms RR 0.70 95% CI 0.67 to 0.74; headache RR 0.56 95% CI 0.5 to 0.63; fatigue RR 0.65 95% CI 0.61 to 0.70; body ache RR 0.5 95% CI 0.42 to 0.57 and diarrhoea or constipation RR 0.60 95% CI 0.55 to 0.65)
- (90 days Respiratory symptoms RR 0.54 95% CI 0.50 to 0.57; headache RR 0.39 95% CI 0.34 to 0.45; fatigue RR 0.48 95% CI 0.43 to 0.52; body ache RR 0.34 95% CI 0.28 to 0.42 and diarrhoea or constipation RR 0.44 95% CI 0.40 to 0.49; n= 50,450).

In contrast, another cohort study from the USA, Taquet 2022 reported no difference in the outcome composite of death and any long-COVID feature for vaccinated people with COVID-19 compared to unvaccinated people (HR 1.01 95% CI 0.96 to 1.05; n= 18,958). Number of vaccination doses were not reported in Al-Aly 2022, Simon 2021, Taquet 2022 and Zisis 2022.

The UK case-control study (Antonelli 2021) found that symptoms lasting ≥ 28 days from acute onset of COVID-19 were no different for people with 1 dose of COVID-19 vaccination prior to infection compared to those who were unvaccinated (OR 1.03 95% CI 0.85 to 1.24; n=5241). However, symptoms lasting ≥ 28 days from acute onset of COVID-19 were statistically significantly reduced for people who had received 2 doses of vaccine compared to those who were unvaccinated (OR 0.51 95% CI 0.32 to 0.82; n=1074).

Similarly, the cohort study conducted in Italy on healthcare workers (Azzolini 2022) found that the probability of Long COVID with 2 or 3 vaccine doses given at least 14 days prior to infection was statistically significantly lower when compared to a reference group of unvaccinated females in wave 1 (2 vaccine doses OR 0.25 95% CI 0.07 to 0.87; 3 vaccine doses OR 0.16 95% CI 0.03 to 0.84, n= 229).

The cross-sectional study (Kuodi 2022) found no statistically significant difference for specified symptoms and recovery from COVID-19 at the time of follow-up for those people who had 1 dose of vaccine compared to those that were unvaccinated (n=657; fatigue: RR 1.06 95% CI 0.82 to 1.36; headache: RR 1.08 95% CI 0.81 to 1.44; weakness in limbs: RR 1.04 95% CI 0.74 to 1.47; persistent muscle pain: RR 1.17 95% CI 0.77 to 1.76; loss of concentration: RR 1.24 95% CI 0.81 to 1.9; hair loss: RR 1.11 95% CI 0.74 to 1.69; sleeping problems: RR 1.35 95% CI 0.86 to 2.11; dizziness: RR 0.87 95% CI 0.54 to 1.4; persistent cough: RR 1.01 95% CI 0.59 to 1.71; shortness of breath: RR 1.08 95% CI 0.65 to 1.81; recovery from COVID-19: RR 1.02 95% CI 0.89 to 1.16;).

In contrast, Kuodi 2022 found that specified symptoms were statistically significantly improved for people with 2 doses of COVID-19 vaccination compared to those who were unvaccinated except for loss of concentration, dizziness and persistent cough and recovery from COVID-19 which remained non-statistically significant (n=611; fatigue: RR 0.36 95% CI 0.19 to 0.71; headache: RR 0.46 95% CI 0.26 to 0.83; weakness in limbs: RR 0.48 95% CI 0.2 to 0.94; persistent muscle pain: RR

0.32 95% CI 0.11 to 0.88; loss of concentration: RR 0.59 95% CI 0.17 to 2.06; hair loss: RR 0.17 95% CI 0.06 to 0.6; sleeping problems: RR 0.53 95% CI 0.18 to 1.61; dizziness: RR 0.26 95% CI 0.09 to 1.79; persistent cough: RR 0.72 95% CI 0.28 to 1.83; shortness of breath: RR 0.23 95% CI 0.07 to 0.84; recovery from COVID-19: RR 0.98 95% CI 0.8 to 1.21).

Risk of death

One cohort study (Al-Aly 2022) found that the risk of death was statistically significantly reduced for people at 6 months from acute onset of COVID-19 with breakthrough COVID-19 (infection after vaccination) compared to those who had infection but were not vaccinated (HR 0.66 95% CI 0.58 to 0.74; n=147,414). Number of vaccination doses were not reported.

Our confidence in the results

All outcomes were considered to be of very low certainty. This was due to none of the studies being randomised and therefore findings of the studies being potentially impacted by confounding variables. Whilst there may have been attempts to minimise confounding bias by adjusting for different variables, there may still be some residual bias. Some studies were also prone to selection bias due to the sources of patient data they used. For example, Al-Aly 2022 used data from the US Department of Veterans Affairs national healthcare databases which meant that the majority of the population were male and relatively older. In contrast, the data sources used in Antonelli 2021 had a predominantly white female demographic. These biases make the data less applicable to the general population. Due to the vaccine schedule, there is likely to be an imbalance in the demographics of who was vaccinated at the time of the study. For example, in the UK, older people and those at high risk were prioritised which may reflect the dominance of vaccinated older people in the studies.

Antonelli 2021 and Kuodi 2021 used self-reported data in their analyses. This type of data is prone to recall bias. As the studies were mainly retrospective and therefore not blinded, there is the risk that people may have been influenced by knowledge that they had or had not received the vaccine in terms of how they reported symptoms. The data in Antonelli 2021 also relied on daily reporting by participants. This may lead to skewed data if those with symptoms were more likely to keep reporting symptoms.

Other factors that contribute to the uncertainty relate to the directness of the evidence. All of the studies used data collected prior to the emergence of Omicron as the dominant variant and 1 study, Simon 2021 used data collected prior to the emergence of the delta variant as the predominant variant. As the effectiveness of vaccines could be impacted by different variants, this could be an important variable in the effectiveness of the vaccine to reduce the risk of developing any long term effects from subsequent SARS-CoV-2 infections. The studies also noted that effectiveness could be related to the specific vaccine used but it was not possible to analyse by vaccine given because of inconsistent data collection.

Please see the full evidence review for further detail.

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 vaccination (any)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Probability of Long COVID (double vaccinated plus booster) Follow-up	Odds ratio 0.16 (CI 95% 0.03 — 0.84) Based on data from 229 participants in 1 studies. [1] (Observational (non-randomized))			**Very low** Due to very serious risk of bias [2]	Probability of Long COVID was statistically significantly reduced for healthcare workers who had received 2 doses of a COVID-19 vaccination plus a booster prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Probability of Long COVID (double vaccinated) Follow-up	Odds ratio 0.25 (CI 95% 0.07 — 0.87) Based on data from 229 participants in 1 studies. [3] (Observational (non-randomized))			**Very low** Due to very serious risk of bias [4]	Probability of Long COVID was statistically significantly reduced for healthcare workers who had received 2 doses of a COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 vaccination (any)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Likelihood of developing PASC (double vaccinated) Follow-up	Odds ratio 0.58 (CI 95% 0.52 — 0.66) Based on data from 5,929 participants in 1 studies. [5] (Observational (non-randomized))			**Very low** Due to serious risk of bias [6]	Likelihood of developing PASC was statistically significantly reduced for people who had received 2 doses of a COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Fatigue (double vaccinated) Follow-up	Odds ratio 0.36 (CI 95% 0.19 — 0.71) Based on data from 611 participants in 1 studies. [7] (Observational (non-randomized))			**Very low** Due to serious risk of bias [8]	Reporting of fatigue was statistically significantly reduced in people who had 2 doses of vaccine prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Symptoms lasting at least 28 days (double vaccinated) from onset of acute COVID-19	Odds ratio 0.51 (CI 95% 0.32 — 0.82) Based on data from 1,074 participants in 1 studies. [9] (Observational (non-randomized))			**Very low** Due to serious risk of bias, Due to serious indirectness [10]	Reporting of symptoms lasting at least 28 days was statistically significantly reduced for people who had received 2 doses of a COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Shortness of breath (double vaccinated) Follow-up	Odds ratio 0.23 (CI 95% 0.07 — 0.84) Based on data from 611 participants in 1 studies. [11] (Observational (non-randomized))			**Very low** Due to serious risk of bias [12]	Reporting of shortness of breath was statistically significantly reduced in people who had 2 doses of vaccine prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Shortness of breath (single vaccinated) Follow-up	Odds ratio 1.08 (CI 95% 0.65 — 1.81) Based on data from 657 participants in 1 studies. [13] (Observational (non-randomized))			**Very low** Due to serious risk of bias, Due to serious imprecision [14]	Reporting of shortness of breath at follow up was not statistically different between people who had a single dose of vaccine prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Fatigue (single vaccinated) Follow-up	Odds ratio 1.06 (CI 95% 0.82 — 1.36) Based on data from 657 participants in 1 studies. [15] (Observational (non-randomized))			**Very low** Due to serious risk of bias, Due to serious imprecision [16]	Reporting of fatigue at follow up was not statistically different between people who had a single dose of vaccine prior to SARS-CoV-2 infection compared to those who were unvaccinated.

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 vaccination (any)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Symptoms lasting at least 28 days (single vaccinated) from onset of acute COVID-19	Odds ratio 1.03 (CI 95% 0.85 — 1.24) Based on data from 5,241 participants in 1 studies. [17] (Observational (non-randomized))			**Very low** Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision [18]	There was no significant difference in reporting of symptoms lasting at least 28 days for people who had received 1 dose of COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Long COVID symptoms of any severity (double vaccinated) 12 weeks from acute onset of COVID-19	Odds ratio 0.59 (CI 95% 0.5 — 0.69) Based on data from 6,180 participants in 1 studies. [19] (Observational (non-randomized))			**Very low** Due to serious indirectness [20]	Long COVID symptoms of any severity were statistically significantly reduced at 12 weeks in people who had 2 doses of COVID-19 vaccine prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Any symptoms (unknown number of vaccination doses) 12 to 20 weeks from acute onset of COVID-19	Odds ratio 0.22 (CI 95% 0.2 — 0.25) Based on data from 222,852 participants in 1 studies. [21] (Observational (non-randomized))			**Very low** Due to serious risk of bias [22]	Reporting of any symptoms was statistically significantly reduced at 12 to 20 weeks for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Risk of death (unknown number of vaccination doses) 6 months from acute onset of COVID-19	Hazard ratio 0.66 (CI 95% 0.58 — 0.74) Based on data from 147,414 participants in 1 studies. [23] (Observational (non-randomized))			**Very low** Due to serious risk of bias, Due to serious imprecision, [24]	Risk of death was statistically significantly reduced at 6 months for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Activity limited symptoms (double vaccinated) 12 weeks from acute onset of COVID-19	Odds ratio 0.59 (CI 95% 0.48 — 0.73) Based on data from 6,180 participants in 1 studies. [25] (Observational (non-randomized))			**Very low** Due to serious indirectness [26]	Activity limited symptoms were statistically significantly reduced at 12 weeks in people who had 2 doses of COVID-19 vaccine prior to SARS-CoV-2 infection compared to those who were unvaccinated.
At least 1	Odds ratio 0.11			**Very low**	Reporting of at least 1

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 vaccination (any)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
symptom (unknown number of vaccination doses) 12 to 20 weeks from acute onset of COVID-19	(CI 95% 0.09 — 0.14) Based on data from 222,852 participants in 1 studies. [27] (Observational (non-randomized))			Due to serious risk of bias [28]	symptom was statistically significantly reduced at 12 to 20 weeks for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Risk of post-acute sequelae (unknown number of vaccination doses) 6 months from acute onset of COVID-19	Hazard ratio 0.85 (CI 95% 0.82 — 0.89) Based on data from 147,414 participants in 1 studies. [29] (Observational (non-randomized))			**Very low** Due to serious indirectness, Due to serious risk of bias [30]	Risk of post-acute sequelae was statistically significantly reduced at 6 months for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Respiratory symptoms (unknown number of vaccination doses) 28 days from acute onset of COVID-19	Relative risk 0.7 (CI 95% 0.67 — 0.74) Based on data from 50,450 participants in 1 studies. [31] (Observational (non-randomized))			**Very low** Due to serious risk of bias [32]	Reporting of respiratory symptoms at 28 day follow up was statistically significantly reduced at for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Respiratory symptoms (unknown number of vaccination doses) 90 days from acute onset of COVID-19	Relative risk 0.54 (CI 95% 0.5 — 0.57) Based on data from 50,450 participants in 1 studies. [33] (Observational (non-randomized))			**Very low** Due to serious risk of bias [34]	Reporting of respiratory symptoms at 90 day follow up was statistically significantly reduced at for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Fatigue (unknown number of vaccination doses) 28 days from acute onset of COVID-19	Relative risk 0.65 (CI 95% 0.61 — 0.7) Based on data from 50,450 participants in 1 studies. [35] (Observational (non-randomized))			**Very low** Due to serious risk of bias [36]	Reporting of fatigue at 28 day follow up was statistically significantly reduced at for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 vaccination (any)	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
					those who were unvaccinated.
Fatigue (unknown number of vaccination doses) 90 days from acute onset of COVID-19	Relative risk 0.48 (CI 95% 0.43 — 0.52) Based on data from 50,450 participants in 1 studies. [37] (Observational (non-randomized))			**Very low** Due to serious risk of bias [38]	Reporting of fatigue at 90 day follow up was statistically significantly reduced at for people who had received COVID-19 vaccination prior to SARS-CoV-2 infection compared to those who were unvaccinated.
Composite of death and any long-COVID feature 6 months from acute onset of COVID-19	Hazard ratio 1.01 (CI 95% 0.96 — 1.05) Based on data from 18,958 participants in 1 studies. [39]			**Very low** Due to serious risk of bias and serious imprecision [40]	A composite outcome of death and any long-COVID feature at 6 month follow up was not statistically different between people who were vaccinated prior to SARS-CoV-2 infection compared to those who were unvaccinated.

1. Systematic reviewwith included studies: [69]. **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of Bias: very serious.** Unclear how reference group was selected or who was included in the analysis. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
3. Systematic reviewwith included studies: [69]. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of Bias: very serious.** Unclear how reference group was selected or who was included in the analysis. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
5. Systematic reviewwith included studies: [68]. **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
7. Systematic reviewwith included studies: [53]. **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of Bias: serious.** Risk of reporting bias as well as confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
9. Systematic reviewwith included studies: [57]. **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of Bias: serious.** Self-reported outcomes that relied on individuals logging data daily. **Inconsistency: no serious. Indirectness: serious.** The app data sample contained disproportionately more women than men and under-represented individuals in more deprived areas.. **Imprecision: no serious. Publication bias: no serious.**
11. Systematic reviewwith included studies: [53]. **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of Bias: serious.** Risk of reporting bias as well as confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
13. Systematic reviewwith included studies: [53]. **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of Bias: serious.** Risk of reporting bias as well as confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** 95% CI crosses the line of no effect. **Publication bias: no serious.**
15. Systematic reviewwith included studies: [53]. **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of Bias: serious.** Risk of reporting bias as well as confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** 95% CI crosses the line of no effect. **Publication bias: no serious.**
17. Systematic reviewwith included studies: [57]. **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of Bias: serious.** Self-reported outcomes that relied on individuals logging data daily. **Inconsistency: no serious. Indirectness: serious.** The app data sample contained disproportionately more women than men and under-represented

individuals in more deprived areas.. **Imprecision: serious.** 95% CI crosses the line of no effect. **Publication bias: no serious.**
19. Systematic reviewwith included studies: [54]. **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of Bias: no serious.** No other risk of bias concerns other than some risk of confounding. **Inconsistency: no serious. Indirectness: serious.** No contemporaneous control group. **Imprecision: no serious. Publication bias: no serious.**
21. Systematic reviewwith included studies: [55]. **Baseline/comparator:** Control arm of reference used for intervention.
22. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious.**
23. Systematic reviewwith included studies: [66]. **Baseline/comparator:** Control arm of reference used for intervention.
24. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** Older, male-dominated population not representative of the UK. **Publication bias: no serious.**
25. Systematic reviewwith included studies: [54]. **Baseline/comparator:** Control arm of reference used for intervention.
26. **Risk of Bias: no serious.** No other risk of bias concerns other than some risk of confounding. **Inconsistency: no serious. Indirectness: serious.** No contemporaneous control group. **Imprecision: no serious. Publication bias: no serious.**
27. Systematic reviewwith included studies: [55]. **Baseline/comparator:** Control arm of reference used for intervention.
28. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
29. Systematic reviewwith included studies: [66]. **Baseline/comparator:** Control arm of reference used for intervention.
30. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: serious.** Older, male-dominated population not representative of the UK. **Imprecision: no serious. Publication bias: no serious.**
31. Systematic reviewwith included studies: [70]. **Baseline/comparator:** Control arm of reference used for intervention.
32. **Risk of Bias: serious.** Reporting of outcomes was reliant on data entered in electronic health records which may have been inconsistent across the network. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
33. Systematic reviewwith included studies: [70]. **Baseline/comparator:** Control arm of reference used for intervention.
34. **Risk of Bias: serious.** Reporting of outcomes was reliant on data entered in electronic health records which may have been inconsistent across the network. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
35. Systematic reviewwith included studies: [70]. **Baseline/comparator:** Control arm of reference used for intervention.
36. **Risk of Bias: serious.** Reporting of outcomes was reliant on data entered in electronic health records which may have been inconsistent across the network. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
37. Systematic reviewwith included studies: [70]. **Baseline/comparator:** Control arm of reference used for intervention.
38. **Risk of Bias: serious.** Reporting of outcomes was reliant on data entered in electronic health records which may have been inconsistent across the network. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
39. Systematic reviewwith included studies: [65]. **Baseline/comparator:** Control arm of reference used for intervention.
40. **Risk of Bias: serious.** Reporting of outcomes was reliant on data entered in electronic health records which may have been inconsistent across the network. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** 95% CI crosses line of no effect. **Publication bias: no serious.**

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Clinical Question/ PICO

Population: Adults and children who are experiencing new or ongoing symptoms: • 4-12 weeks from pre-vaccination onset of acute COVID-19 illness • 12 weeks from pre-vaccination onset of acute COVID-19 illness

Intervention: COVID-19 Vaccination

Comparator: No vaccination

Summary

Vaccination after initial COVID-19 infection

There remains uncertainty around the effect of COVID-19 vaccination on symptoms in people experiencing long term effects of COVID-19. The findings of the evidence are mixed which some studies reporting significant improvements in symptoms but others showing no effect on symptoms and sometimes worsening of symptoms. Due to the nature of the studies and confounding variables, it is not possible to confidently attribute the observed findings in the studies to COVID-19 vaccination.

What is the evidence informing this conclusion?

Evidence comes from 11 studies (6 cohort studies [Ayoubkhani 2021, Peghin 2022, Simon 2021, Tran 2021, Wisnivesky 2022 and Wynberg 2022], 3 cross-sectional studies [Scherlinger 2022, Strain 2022 and Wanga 2021] and 2 case series [Arnold 2021 and Tsuchida 2022]).

Publication status

Three studies are only available as preprints Ayoubkhani 2021, posted to medRxiv on 9 December 2021, Simon 2021 posted to medRxiv on 18 November 2021 and Tran 2021 posted to SSRN on 29 September 2021) and have therefore not been peer reviewed.

Summary of included studies

A UK cohort study (Ayoubkahni 2021 preprint) using responses from the COVID infection survey (CIS) and linked National Immunisation Management System (NIMS) records (n=6729; mean age 45.9 years; 44.4% male) aimed to estimate associations between one or two doses of COVID-19 vaccination and long-COVID symptoms in people who had SARS-CoV-2 infection prior to vaccination. Long COVID was defined as symptoms persisting for at least 12 weeks from confirmed or suspected coronavirus infection not explained by any other health condition. Main limitations included there being no comparison group and that the study was observational so causality cannot be inferred. Long-COVID status was self-reported with no formal clinical diagnosis.

A cohort study conducted in the USA (Simon 2021 preprint) used data from patient health records to identity factors influencing the development and progression of long-COVID. Long-COVID cases were classified as those where the patient presented one or more COVID-associated symptoms between 12 and 20 weeks after the initial COVID-19 diagnosis. The study included people who tested positive for COVID-19 who had been vaccinated up to 12 weeks after SARS-COV-2 infection compared to those who had not (n=17,796 cases; n=220,460 controls; 38.7% male; mean age not reported). Main limitations included the findings being based on opportunistic availability of large volumes of data where there could be geographic, temporal and socioeconomic gaps that could influence outcomes. The analysis was conducted on data collected prior to the emergence of the delta variant in the USA.

Another cohort study conducted in Italy (Peghin 2022) used data from a single centre hospital clinical database (n=479) to

evaluate vaccination on long-term symptoms of COVID-19 defined as signs and symptoms developed during or following an infection consistent with COVID-19 that continued for more than 12 weeks. The study included adults who were diagnosed with COVID-19 during the first wave. Main limitations included limited generalisability due to data coming from a single study centre and first wave COVID-19 infections only.

A cohort study conducted in France (ComPaRe long COVID; Tran 2021 preprint) included adults (n=455 vaccinated n=455 unvaccinated controls; mean age 47 years 19.5% male) with confirmed or suspected COVID-19 infection experiencing symptoms of Long COVID defined as symptoms persisting more than three weeks past the initial infection. The aim of the study was to evaluate the effect of first COVID-19 vaccine injection among patients with long COVID on the severity and impact of their symptoms. Main limitations included potential unmeasured confounders that could bias results and that the data was collected before the emergence of recent variants of concern.

Similarly, a small cohort study conducted in the Netherlands (RECoVERED; Wynberg 2022) included adults (n=36 vaccinated, n=32 unvaccinated controls; mean age 51 years; 35.5% male) with previous SARS-CoV-2 infection who developed post-acute sequalae of COVID-19 (PASC) symptoms defined as the WHO criteria as reporting at least one COVID-19 symptom that started within one month of overall illness onset and lasted beyond 3 months after illness onset. The study aimed to assess the effect of two doses of vaccine on recovery from PASC symptoms. Main limitations included the potential for residual confounding as participants were not randomised. There was no SARS-CoV-2 negative control group so it is not possible to determine whether symptoms are causally related to the infection as opposed to underlying comorbidities. All participants were infected with wild-type or Alpha SARS-CoV-2 so may not be generalisable to other variants.

A cohort study conducted in the USA (Wisnivesky 2022) included patients enrolled into an institutional Post-COVID-19 Registry at the Mount Sinai Health System (MSHS) in New York City who reported one PASC symptom and were unvaccinated at baseline (n=453; mean age 50 years; 35% male). The study aimed to assess whether vaccination was associated with resolution of or improvement in PASC symptoms at 6 month follow-up. Main limitations included being a non-randomised study so systematic differences between vaccinated and unvaccinated participants cannot be excluded. Different vaccines could be a limitation in determining effect of vaccination on changes in PASC symptoms.

An online survey among French speaking adults recruited through social media platforms (n=397; median age 44 years; 14.1% male) was used to evaluate the impact of two doses of SARS-CoV-2 vaccination on PASC burden (Scherlinger 2022). PASC symptoms were defined as symptoms persisting over 4 weeks following a confirmed or probable COVID-19, without any identified alternative diagnosis. Main limitations included recruitment from social media platforms not being representative of the general PASC population.

An international survey (Strain 2022) that was open to vaccinated adults with current or recent symptoms of long COVID (at the time of vaccination) sourced participants from Long COVID support groups (n=812; 0.4% age 20 years and under, 3.7% 21-30 years, 18.2% 31-40 years, 29.6% 41-50 years. 32.7% 51-60 years, 13% 61-70 years, 2.5% 71 years and over; 19.4% male). Main limitations included the study population being unlikely to be representative of the population as the recruitment was via social media. Participants were predominantly white and female.

Another online survey conducted in the USA (Wanga 2022) compared long-term symptom changes in people after receiving a COVID-19 vaccination in adults with and without a previous COVID-19 infection (with COVID-19 infection n=698, without COVID-19 infection n=2437; mean age: 39.3 years vs 45.3 years). Main limitations included the study being nonprobability-based which limits its generalisability. The responses to the survey were self-reported and subject to reporting bias.

A case series conducted in the UK (Arnold 2021) included consecutive patients who had previously been admitted to a single hospital with COVID-19 who remained symptomatic at 8 months and who subsequently received a COVID-19 vaccination (n=163, median age 64 years IQR 53-73; 58% male). It aimed to describe quality of life and symptoms after vaccination. Main limitations included a small sample size and the potential for recall bias.

Another case series was conducted in a Long COVID outpatient clinic in Japan (Tsuchida 2022). The aim was to evaluate changes in symptoms after a single COVID-19 vaccination in people who presented with several sequelae symptoms after at least 2 months since the onset of acute COVID-19 (n=52, median age 40 to 50 years; 56% male). Main limitations included being a single centre with a small sample size and the potential for confounding due to some participants already receiving treatment for symptoms.

Outcomes

Changes in symptoms

Studies reported a variation in changes of symptoms following COVID-19 vaccination. The Italian cohort study (Peghin 2022) found that of people with ongoing symptoms 1 year after acute infection who had been vaccinated with at least one dose of COVID-19 vaccine, 87 (65.9%) reported that their symptoms remained unaffected or unchanged compared to 247 (71.2%) of people who were unvaccinated. 30 (22.7%) of vaccinated people reported that their symptoms had worsened compared to 55 (15.8%) of unvaccinated people. Only 15 (11%) of vaccinated people reported that their symptoms had improved compared to 45 (13%) of unvaccinated people. Similarly, a cross-sectional study conducted in the USA (Wanga

2021) found that of participants who had received a positive COVID result and subsequently had at least one dose of vaccine, 28.7% reported that the vaccine made their symptoms better, 26.4% reported that the vaccine had no effect on their symptoms at all and 16.1% reported that the vaccine made symptoms worse. A UK case series reported similar findings (Arnold 2021) in that after at least one dose of COVID vaccine, 113/159 (71.1%) of participants reported that their symptoms were unchanged, 9/159 (5.6%) reported worsening of symptoms and 31/159 (23.2%) reported improvement in their symptoms.

Similarly, a cross-sectional study conducted in France (Scherlinger 2022) found that of participants who had one or two doses of COVID vaccination, 117/380 (31%) reported worsening of symptom severity compared to 83/380 (21.8%) who reported improvement in symptom severity. An international cross-sectional study (Strain 2022) conducted after one dose of COVID vaccine found that 470/812 (57.2%) participants reported an overall improvement in symptoms compared to 145/812 (17.9%) reporting an overall worsening of symptoms.

The cohort study conducted in the Netherlands (Wynberg 2022) reported no significant difference at 3 months for recovery from PASC for people who had received two doses of COVID vaccine 28 days apart, compared to those who remained unvaccinated (OR 1.57 95% CI 0.46 to 5.84; n = 68).

In contrast, the ComPaRe long COVID study (Tran 2021 preprint) reported that COVID vaccination significantly reduced long COVID symptoms and disease impact on patient lives after 120 days (long COVID symptom tool [ST] MD -1.8 95% CI-2.5 to -1.0; disease impact tool [IT] MD -3.3 95% CI -6.25 to -0.5; n=910). The study also reported that the rate of patients reporting complete remission of symptoms was almost doubled (remission rate HR 1.97 95% CI 1.23 to 3.15; n=910). The number of COVID vaccination doses was not reported.

Long COVID symptoms

A UK cohort study (Ayoubkhani 2021 preprint) reported that the odds of experiencing Long COVID symptoms initially decreased after first vaccination (12.8% decrease 95% CI -18.6% to -6.6%; n=6729) but this was followed by an increase per week until receiving the second dose (0.3 increase 95% CI -0.6% to 1.2%; n=6729). Second vaccination was associated with an initial decrease (8.8% decrease 95% CI -14.1% to -3.1%; n=6729) but this was followed by a decrease of 0.8% 95% CI -1.2% to -0.4% per week. Activity limitation initially decreased after first vaccination (12.3% decrease 95% CI-19.5% to -4.5%; n=4747) followed by an increase of 0.9% (-0.2% to +1.9%) per week until receiving the second dose. Second vaccination was associated with an initial 9.1% decrease (-15.6% to -2.1%; n=4747), followed by a decrease of 0.5% (-1.0% to +0.05%) per week.

The Italian cohort study (Peghin 2022) found that of people who had been vaccinated with at least one dose of COVID-19 vaccine, 73 (55.3%) reported no post-COVID symptoms compared to 180 (51.9%) who were unvaccinated. 44 (33.3%) of people who were vaccinated reported 1 or 2 post-COVID symptoms compared to 107 (30.8%) who were unvaccinated. 8 (6.1%) of people who were vaccinated reported 3 or 4 symptoms compared to 38 (11%) who were unvaccinated. 7 (5.3%) of people who were vaccinated reported 5 or more symptoms compared to 22 (6.3%) who were unvaccinated.

A cohort study conducted in the USA (Simon 2021) found that reporting any symptom was statistically significantly reduced at 12 to 20 weeks from acute onset of COVID-19 for people who were vaccinated 0-12 weeks after COVID diagnosis compared to those who were not vaccinated (Any symptom; Vaccine 0-4 weeks after diagnosis: OR 0.38 95% CI 0.35 to 0.41; Vaccine 4-8 weeks after diagnosis: OR 0.54 95% 0.51 to 0.57; Vaccine 8-12 weeks after diagnosis: OR 0.75 95% CI 0.71 to 0.78; n=243,040). The number of COVID vaccination doses was not reported.

Another cohort study from the USA (Wisnivesky 2022) reported on Post-COVID symptom scores in 324 people who were vaccinated and compared them to 129 unvaccinated people. The study found no significant difference in any reported symptom (anosmia MD -0.02 95% CI -0.35 to 0.31; dyspnoea MD 0.05 95% CI -0.15 to 0.25; cough MD -0.17 95% CI -0.55 to 0.22; depression symptoms MD 0.02 95% -1.18 to 1.22; COVID PTSD symptoms MD 2.53 95% CI -3.06 to 8.12; non-COVID PTSD Symptoms MD -2.53 95% CI -12.11 to 7.04). There was also no significant difference reported for quality of life outcomes (QoL physical function MD -1.16 95% CI -3.35 to 1.02; QoL anxiety MD -0.29 95% CI -2.84 to 2.27; QoL depression MD -1.12 95% CI -3.8 to 1.26; QoL: fatigue MD -1.42 95% CI -4.15 to 1.32; QoL social roles MD -0.17 95% CI -3.18 to 2.83; QoL: sleep MD 1.51 95% CI -0.86 to 3.87; QoL pain MD -0.02 95% CI -2.74 to 2.7).

Our confidence in the results

All outcomes were considered to be of very low certainty. This was due to none of the studies being randomised and therefore findings of the studies being potentially impacted by confounding variables. Whilst there may have been attempts to minimise confounding bias by adjusting for different variables, there may still be some residual bias. Some studies were also prone to selection bias due to the sources of patient data they used. For example, Strain 2022 used data from social media platforms with most respondents identifying as white and female. These biases make the data less applicable to the general population. Due to the vaccine schedule, there is likely to be an imbalance in the demographics of who was vaccinated at the time of the study. For example, in the UK, older people and those at high risk were prioritised which may reflect the dominance of vaccinated older people in the studies. Other factors that can limit generalisability of the findings include where the study was conducted. For example, Peghin 2022 was carried out in a single centre which limits its generalisability. It was not always possible to determine from the studies how long participants had been experiencing the long term effects of COVID-19. This is expected to be varied as people will have had the acute COVID-19 infection at

different points, prior to receiving a COVID-19 vaccine. Peghin 2022 and Wynberg 2022 only included people who had COVID-19 in the first wave of the pandemic so may not be generalisable to people who had COVID-19 in later waves, particularly when taking different variants into account.

There was also some level of inconsistency across studies in terms of diagnosing long-term effects of COVID-19. Whilst all studies were broadly using the same definition, only some studies such as Simon 2021 used electronic health record data. Other studies, particularly online surveys, relied on participants in a self-selection process, which could lead to an inconsistent population across the body of evidence.

Some studies used self-reported data in their analyses. This type of data is prone to recall bias. As the studies were mainly retrospective and therefore not blinded, there is the risk that people may have been influenced by knowledge that they had or had not received the vaccine in terms of how they reported symptoms. In addition to this, it remains uncertain whether changes in symptoms can be directly attributed to vaccination, considering the relapsing-remitting nature of symptoms reported by people experiencing long term effects of COVID-19.

Please see the full evidence review for further detail.

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 Vaccination	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Recovery from PASC (double vaccinated) 3 months	Odds ratio 1.57 (CI 95% 0.46 — 5.84) Based on data from 68 participants in 1 studies. (Observational (non-randomized))			**Very low** Due to serious risk of bias and serious imprecision [1]	There was no statistically significant difference in recovery from PASC at 3 months for people with new or ongoing symptoms who had received 2 doses of vaccine compared to those who were unvaccinated
Complete remission of symptoms (unknown doses of vaccine) 120 days	Hazard ratio 1.97 (CI 95% 1.23 — 3.15) Based on data from 910 participants in 1 studies. (Observational (non-randomized))			**Very low** Due to serious risk of bias [2]	Complete remission of symptoms was statistically significantly more likely at 120 days in people with new or ongoing symptoms who had been vaccinated compared to those who were unvaccinated.
Any long COVID symptom (Vaccine 0-4 weeks after diagnosis)	Odds ratio 0.38 (CI 95% 0.35 — 0.41) Based on data from 243,040 participants in 1 studies. (Observational (non-randomized))			**Very low** Due to serious risk of bias [3]	Reporting of any symptoms was statistically significantly reduced for people with new or ongoing symptoms who had received COVID-19 vaccination 0-4 weeks after to SARS-CoV-2 infection compared to those who were unvaccinated.
Any long COVID symptom (Vaccine 4-8 weeks after diagnosis)	Odds ratio 0.54 (CI 95% 0.51 — 0.57) Based on data from 243,040 participants in 1 studies. (Observational			**Very low** Due to serious risk of bias [4]	Reporting of any symptoms was statistically significantly reduced for people with new or ongoing

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 Vaccination	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
	(non-randomized))				symptoms who had received COVID-19 vaccination 4-8 weeks after to SARS-CoV-2 infection compared to those who were unvaccinated.
Any long COVID symptom (Vaccine 8-12 weeks after diagnosis)	Odds ratio 0.75 (CI 95% 0.71 — 0.78) Based on data from 243,040 participants in 1 studies. (Observational (non-randomized))			**Very low** Due to serious risk of bias [5]	Reporting of any symptoms was statistically significantly reduced for people with new or ongoing symptoms who had received COVID-19 vaccination 8-12 weeks after to SARS-CoV-2 infection compared to those who were unvaccinated.
Long COVID symptoms (unknown doses of vaccine) 120 days	Measured by: Long COVID symptom tool (ST) Lower better Based on data from 910 participants in 1 studies. (Observational (non-randomized))	Difference:	**MD 1.8 lower** (CI 95% 2.5 lower — 1 lower)	**Very low** Due to serious risk of bias [6]	Reporting of Long COVID symptoms was statistically significantly lower in people with new or ongoing symptoms who had received a COVID vaccine compared to those who were unvaccinated.
Disease impact on patient lives (unknown doses of vaccine) 120 days	Measured by: Disease impact tool (IT) Lower better Based on data from 910 participants in 1 studies. (Observational (non-randomized))	Difference:	**MD 3.3 lower** (CI 95% 6.25 lower — 0.5 lower)	**Very low** Due to serious risk of bias [7]	Disease impact on patient lives was statistically significantly lower in people with new or ongoing symptoms who had received a COVID vaccine compared to those who were unvaccinated.
Dyspnoea symptom score (at least one dose of COVID-19 vaccine) 6 months	Lower better Based on data from 453 participants in 1 studies. (Observational (non-randomized))	Difference:	**MD 0.02 lower** (CI 95% 0.35 lower — 0.31 higher)	**Very low** Due to serious risk of bias [8]	Dyspnoea symptom scores were statistically significantly lower at 6 months in people with new or ongoing symptoms who had received at least one COVID-19 vaccine compared to those who were unvaccinated.
QoL: Fatigue symptom score (at least one dose of COVID-19 vaccine) 6 months	Lower better Based on data from 453 participants in 1 studies. (Observational (non-randomized))	Difference:	**MD 1.42 lower** (CI 95% 4.15 lower — 1.32 higher)	**Very low** Due to serious risk of bias [9]	Fatigue symptom scores were not statistically significantly different at 6 months in people with new or ongoing symptoms who had received at least one

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 Vaccination	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
					COVID-19 vaccine compared to those who were unvaccinated.
QoL: Physical function score (at least one dose of COVID-19 vaccine) 6 months	Lower better Based on data from 453 participants in 1 studies. (Observational (non-randomized))	Difference:	**MD 1.16 lower** (CI 95% 3.35 lower — 1.02 higher)	**Very low** Due to serious risk of bias [10]	Physical function scores were not statistically significantly different at 6 months in people with new or ongoing symptoms who had received at least one COVID-19 vaccine compared to those who were unvaccinated.
At least one post-COVID symptom (at least one dose of COVID-19 vaccine)	Based on data from 479 participants in 1 studies. (Observational (non-randomized))	The Italian cohort study (Peghin 2022) found that of people who had been vaccinated 44 (33.3%) reported 1 or 2 post-COVID symptoms. 8 (6.1%) of people who were vaccinated reported 3 or 4 symptoms. 7 (5.3%) of people who were vaccinated reported 5 or more symptoms.		**Very low** Due to serious risk of bias and serious imprecision [11]	At least one post-COVID symptom was reported 44.7% of people with new or ongoing symptoms who received at least one dose of COVID-19 vaccine
No post-COVID symptoms (at least one dose of COVID-19 vaccine)	Based on data from 479 participants in 1 studies. (Observational (non-randomized))	The Italian cohort study (Peghin 2022) found that 73 (55.3%) people who were vaccinated reported no post-COVID symptoms compared to 180 (51.9%) who were unvaccinated.		**Very low** Due to serious risk of bias, Due to serious imprecision [12]	No post-COVID symptoms were reported 55.3% of people with new or ongoing symptoms who received at least one dose of COVID-19 vaccine compared to 180 (51.9%) who were unvaccinated.
Worsening of post-COVID 19 symptoms (at least one dose of COVID 19 vaccine) Up to 1 year from acute COVID-19 infection	Based on data from 1,930 participants in 5 studies. (Observational (non-randomized))	One cohort study (Peghin 2022) found that 30 (22.7%) reported that their symptoms had worsened. In a cross-sectional study (Wanga 2021) 16.1% reported that the vaccine made symptoms worse. Another cross-sectional study found that 117/380 (31%) reported worsening of symptom severity. An international cross-sectional study found that 145/812 (17.9%) reported an overall worsening of symptoms. A case series found that 9/159 (5.6%) reported worsening of symptoms.		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [13]	Worsening of post-COVID-19 symptoms was reported in 5.6% to 31% of participants with new or ongoing symptoms in who received at least one dose of COVID-19 vaccine.
Improvement in post-COVID 19 symptoms (at least one dose of COVID-19 vaccine) Up to 1 year from acute COVID-19	Based on data from 1,930 participants in 5 studies. (Observational (non-randomized))	One cohort study (Peghin 2022) found that 15 (11%) of vaccinated people reported that their symptoms had improved. In a cross-sectional study (Wanga 2021) reported that 28.7% reported that the vaccine made their symptoms better. Another cross-sectional study found that 83/380 (21.8%) reported improvement in		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [14]	Improvement in post-COVID-19 symptoms was reported in 11% to 57.2% of participants with new or ongoing symptoms who received at least one dose of COVID-19 vaccine.

Outcome Timeframe	**Study results and measurements**	**Comparator** No vaccination	**Intervention** COVID-19 Vaccination	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
infection		symptom severity. An international cross-sectional study found that 470/812 (57.2%) reported an overall improvement in symptoms. A case series found that 31/159 (23.2%) reported improvement in their symptoms.			
No change in post-COVID 19 symptoms (at least one dose of COVID 19 vaccine) Up to 1 year from acute COVID-19 infection	Based on data from 738 participants in 3 studies. (Observational (non-randomized))	One cohort study (Peghin 2022) found that 87 (65.9%) reported that their symptoms remained unaffected or unchanged. In a cross-sectional study (Wanga 2021) 26.4% reported that the vaccine had no effect on their symptoms at all. A case series found that 113/159 (71.1%) of participants reported that their symptoms were unchanged		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision [15]	No change in post-COVID-19 symptoms was reported in 26.4% to 71.1% of participants with new or ongoing symptoms in who received at least one dose of COVID-19 vaccine.
Activity limitation (single vaccinated)	Based on data from 4,747 participants in 1 studies. (Observational (non-randomized))	A UK cohort study (Ayoubkhani 2021 preprint) reported that activity limitation initially decreased after first vaccination (12.3% decrease 95% CI-19.5% to -4.5%) followed by an increase of 0.9% (-0.2% to +1.9%) per week until receiving the second dose.		**Very low** Due to serious risk of bias [16]	Activity limitation statistically significantly decreased after first vaccination but increase non-statistically significantly until second vaccination
Odds of experiencing long COVID symptoms (single vaccinated)	Based on data from 6,729 participants in 1 studies. (Observational (non-randomized))	A UK cohort study (Ayoubkhani 2021 preprint) reported that the odds of experiencing Long COVID symptoms initially decreased (12.8% decrease 95% CI -18.6% to -6.6%) but this was followed by an increase per week until receiving the second dose (0.3% increase 95% CI -0.6% to 1.2%).		**Very low** Due to serious risk of bias [17]	Odds of experiencing long COVID symptoms was statistically significantly decreased after first vaccination but increased non-statistically significantly until second vaccination
Odds of experiencing long COVID symptoms (double vaccinated)	Based on data from 6,729 participants in 1 studies. (Observational (non-randomized))	A UK cohort study (Ayoubkhani 2021 preprint) reported that the odds of experiencing Long COVID symptoms initially decreased (8.8% decrease 95% CI -14.1% to -3.1%) but this was followed by a decrease of 0.8% 95% CI -1.2% to -0.4% per week.		**Very low** Due to serious risk of bias [18]	Odds of experiencing long COVID symptoms was statistically significantly decreased after second vaccination and continued to statistically significantly decrease thereafter
Activity limitation (double vaccinated)	Based on data from 4,747 participants in 1 studies. (Observational (non-randomized))	A UK cohort study (Ayoubkhani 2021 preprint) reported that activity limitation initially decreased 9.1% decrease (-15.6% to -2.1%), followed by a decrease of 0.5% (-1.0% to +0.05%) per week.		**Very low** Due to serious risk of bias [19]	Activity limitation statistically significantly decreased after second vaccination but continued to decrease non-statistically significantly thereafter

1. **Risk of Bias: serious.** Potential for residual confounding and lack of control group. **Inconsistency: no serious. Indirectness:**

no serious. Imprecision: serious. 95% CI crosses the line of no effect . **Publication bias: no serious.**
2. **Risk of Bias: serious.** Potential unmeasured confounders. Data did not take motivation to receive COVID 19 vaccination into account.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
3. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
4. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
5. **Risk of Bias: serious.** Risk of selection bias in addition to confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
6. **Risk of Bias: serious.** Potential unmeasured confounders. Data did not take motivation to receive COVID 19 vaccination into account.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
7. **Risk of Bias: serious.** Potential unmeasured confounders. Data did not take motivation to receive COVID 19 vaccination into account.. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
8. **Risk of Bias: serious.** Risk of reporting bias and selection bias in addition to residual confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
9. **Risk of Bias: serious.** Risk of reporting bias and selection bias in addition to residual confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
10. **Risk of Bias: serious.** Risk of reporting bias and selection bias in addition to residual confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
11. **Risk of Bias: serious.** Self-reporting of symptoms may introduce recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** No 95% CI reported . **Publication bias: no serious.**
12. **Risk of Bias: serious.** Self-reporting of symptoms may introduce recall bias. **Inconsistency: no serious. Indirectness: no serious. Imprecision: serious.** No 95% CI reported . **Publication bias: no serious.**
13. **Risk of Bias: serious.** Some studies did not have a control group. Self-reporting of symptoms may introduce recall bias. **Inconsistency: serious.** Participants had varying amounts of time experiencing symptoms prior to vaccination. **Indirectness: no serious. Imprecision: serious.** No 95% CI reported in these studies. **Publication bias: no serious.**
14. **Risk of Bias: serious.** Some studies did not have a control group. Self-reporting of symptoms may introduce recall bias. **Inconsistency: serious.** Participants had varying amounts of time experiencing symptoms prior to vaccination. **Indirectness: no serious. Imprecision: serious.** No 95% CI reported in these studies. **Publication bias: no serious.**
15. **Risk of Bias: serious.** Some studies did not have a control group. Self-reporting of symptoms may introduce recall bias. **Inconsistency: serious.** Participants had varying amounts of time experiencing symptoms prior to vaccination. **Imprecision: serious.** No 95% CI reported in these studies.
16. **Risk of Bias: serious.** Risk of recall bias in addition for confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
17. **Risk of Bias: serious.** Risk of recall bias in addition for confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
18. **Risk of Bias: serious.** Risk of recall bias in addition for confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**
19. **Risk of Bias: serious.** Risk of recall bias in addition for confounding. **Inconsistency: no serious. Indirectness: no serious. Imprecision: no serious. Publication bias: no serious.**

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Consensus recommendation

Provide all information in accessible and age-appropriate formats so that people can understand and take part in decisions about their care. Follow relevant national guidance on communication, providing information (including different formats and languages) and shared decision making, for example:

- NICE's guidelines on patient experience in adult NHS services and shared decision making
- Healthcare Improvement Scotland's website 'What Matters To You'
- NHS England's Accessible information standard.

NICE, RCGP and SIGN's patient booklet on Long COVID provides accessible information for people who have had acute COVID-19 and have ongoing signs and symptoms.

Evidence To Decision

Benefits and harms

The panel acknowledged that patient information must be accessible in order to help people understand and be involved in decisions about their care. They discussed that the content must be age-appropriate and also provided in different languages where possible. The panel also discussed that the format of the information is also important and acknowledged that digital content has become more common, especially in the context for the pandemic. However, they highlighted that digital formats are not always suitable so alternatives need to be available to suit a wide range of preferences. Similarly, the panel acknowledged that some people experiencing symptoms such as 'brain fog' or fatigue may have some difficulties to take in long and complex information so this needs to be considered when choosing the format of the information.

Certainty of the Evidence

Evidence was not reviewed for accessibility of information but the panel thought it was important to make a consensus recommendation. This was because there is a legal requirement for accessibility of information and there is a need to consider requirements of people experiencing the long-term effects of COVID-19. In addition, there remains uncertainty in managing the condition.

Values and preferences

The qualitative evidence highlighted that patients experiencing the long-term effects of COVID-19 reported difficulty accessing care. The panel expected that people would value having information in an accessible format and that this would help to minimise barriers to accessing healthcare and other support available.

Resources and other considerations

The panel acknowledged that creating accessible information in different formats and languages may not always be feasible. They discussed resources which may be of use to people when producing accessible information.

Rationale

Accessibility of information is a legal requirement and is particularly important after acute COVID-19 because people may have cognitive symptoms ('brain fog') or fatigue, making it difficult for them to take in long or complex information.

Recommended

For people with new or ongoing symptoms after acute COVID-19, suspect:

- ongoing symptomatic COVID-19 if people present with symptoms 4 to 12 weeks after the start of acute COVID-19 **or**
- post-COVID-19 syndrome if the person's symptoms have not resolved 12 weeks after the start of acute COVID-19.

Evidence To Decision

Benefits and harms

The panel discussed the importance of identifying the most common symptoms that present in people experiencing long term effects of COVID-19. Knowing the most common symptoms will help clinicians to recognise post-COVID-19 syndrome as a possible diagnosis. However, they were mindful that the most common symptoms will not always be present and should not be used as strict criteria for diagnosis as this could mean people who present atypically may be missed.

Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19 syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

The panel acknowledged that this case definition may be interpreted as a diagnosis of exclusion. However, they discussed that ongoing symptomatic COVID-19 and post-COVID-19 syndrome have many features in common with other conditions, some of which could be considered life threatening. Therefore, ongoing symptomatic COVID-19 and post-COVID-19 syndrome should not be the first conditions to be excluded for reasons of patient safety.

Certainty of the Evidence

There is a lack of certainty in the evidence base. Most studies included in the review were cross-sectional surveys and were judged to be of high risk of bias due the retrospective nature of the studies. All the data in the studies were self-reported and therefore prone to recall bias. The surveys were disseminated to online social media groups which will have included participants who were self-selected and therefore may not be representative of the general population. Most participants were female and of white ethnicity. Some of the same social media groups were targeted for more than one survey so there is a possibility of duplication and double counting due to the similar nature of the questions. However, there were themes emerging from the evidence that were consistent across all studies, such as the variance and fluctuation of symptoms.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

Resources and other considerations

Whilst there are concerns that a case definition may inadvertently exclude people who do not present in a typical way, including children and older adults, the panel discussed that the case definition was broad enough to capture people who need help and support for the long-term effects of COVID-19.

The panel expect that having a case definition for the long-term effects of COVID-19 would be acceptable to patients. This is due to there being limited knowledge of the condition and patients reporting experiences of not being taken seriously. The key features of the case definition reflect patient experiences of illness trajectory seen in the evidence, including the fluctuating nature of symptoms.

Rationale

Healthcare professionals in all services need to be alert to whether people may need support. Although most people with ongoing symptoms will start to improve between 4 and 12 weeks, some will need further investigation and others will need rehabilitation to help them recover. The panel therefore agreed that ongoing symptomatic COVID-19 and post-COVID-19 syndrome should be considered as part of the differential diagnosis at 4 to 12 weeks and beyond 12 weeks, respectively.

The panel reviewed the evidence on the case definitions for the November 2012 update and agreed that no changes should be made to this recommendation. See the rationale for the case definition for more information. The panel also emphasised that this recommendation applies to children and young people as well as adults.

Recommended

For people who are experiencing new or ongoing symptoms 4 weeks or more after acute COVID-19, offer an initial consultation and use shared decision making to discuss and agree with the person whether it should be remote or in person.

Evidence To Decision

Benefits and harms

Adults

For people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome, the panel heard evidence from expert testimony that an in-depth consultation between the individual and an appropriately skilled healthcare professional can be an informative part of the assessment process. Expert testimony (Nicol 2021 and Nuffield Health 2021) suggested that some practice is moving away from conducting lots of clinical tests towards a model where discussion is held with the individual to determine what matters to them and what their goals are, which was viewed as helpful for determining which are the most appropriate tests for that individual.

Members of the panel agreed that while clinical tests may still be indicated, particularly to identify the presence of other conditions, a conversation can be more reassuring and reduce anxiety by explaining what is known about ongoing COVID-19 and post-COVID-19 syndrome.

The panel also heard evidence from expert testimony (Locke 2021) that people value a range of formats for interactions with health services, with requests to use video formats which might allow the individual to watch the session back at a later date.

Children and young people

Expert witness testimony advised that many children with new or ongoing symptoms after acute COVID-19 were experiencing

anxiety caused by unnecessary investigations and referrals to different specialists. Therefore, the panel advised that the NICE guideline on shared decision making should be signposted to. The panel agreed there should not be a recommendation cautioning against unnecessary investigations or referrals because there was already under-referral to dedicated clinics or MDTs.

Certainty of the Evidence

The panel acknowledged that the three testimonies all had limitations in terms of generalisability. People employed by the military may differ in characteristics from the rest of the population; the Nuffield model had fewer resource considerations than in the rest of the healthcare system; and the testimony from Scotland is in the context of the service model in NHS Scotland only. However, they noted that these findings were consistent with their own experiences, and were internally coherent.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to initial consultations. However, they agreed that this recommendation aligns with other NICE guidance about shared decision making, and therefore is taking account of people's preferences.

Resources

The recommendation is unchanged since the last publication of this guideline, so no change in resources is expected.

Equity

This recommendation takes into account considerations raised in the Equality Impact Assessment by making an initial consultation as accessible as possible.

Acceptability

The panel considered that the acceptability of this recommendation would be high, as it considers the needs of individuals.

Feasibility

Although there is no systematically collected evidence about feasibility, the panel noted that services have increasingly been offered in a variety of formats since the start of the pandemic, to facilitate social distancing.

Rationale

The expert panel agreed that an initial consultation would help identify people who need further assessment. A detailed discussion between the person and a healthcare professional is an important part of understanding their symptoms, and the way in which the symptoms affect their daily life. This discussion will form the first part of an assessment, and inform decisions about whether further assessment and investigations are needed (see the section on assessment). The panel also agreed that the format of the consultation should be discussed and agreed with the person according to their needs and preferences and local availability of services.

The panel reviewed expert testimonies from Nicol 2021, Nuffield Heath 2021 and Locke 2021, provided for the November 2021 update, that supported this recommendation and so the panel agreed that it should be retained.

Conditional recommendation

Consider using a screening questionnaire as part of the initial consultation to help capture all of the person's symptoms. These should only be used in conjunction with clinical assessment.

Evidence To Decision

Benefits and harms

Some screening questionnaires are being used in practice, but none are fully validated for this use. Questionnaires can be useful in preparation for or during the initial consultation but the panel did not want them to be used on their own to decide if further assessment is needed. Examples of questionnaires include the COVID-19 Yorkshire rehabilitation questionnaire, recommended by NHS England, and the modified International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) global paediatric COVID-19 follow-up questionnaire. Questionnaires should ideally be developed in partnership with patients and be fully validated.

Certainty of the Evidence

No new evidence was identified in the evidence review and the panel concluded that it was important to retain the recommendation made by consensus.

Values and preferences

The panel agreed to retain the advice to consider using screening questionnaire as part of the initial consultation to help capture the person's symptoms, which applies to all age groups. It was considered important to emphasise that the purpose of the screening questionnaire is to facilitate discussion with the patient about their symptoms and the impact that the long-term effects of COVID-19 has on them, to help make a decision about whether referral to a dedicated clinic or MDT would be appropriate.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Some screening questionnaires are being used in practice, but none are fully validated for this use. Questionnaires can be useful in preparation for or during the initial consultation but the panel did not want them to be used on their own to decide if further assessment is needed. Examples of questionnaires include the COVID-19 Yorkshire rehabilitation questionnaire, recommended by NHS England, and the modified International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) global paediatric COVID-19 follow-up questionnaire. Questionnaires should ideally be developed in partnership with patients and be fully validated.

Info Box

Some people (including children and older people) may not have the most commonly reported new or ongoing symptoms after acute COVID-19.

The following symptoms and signs are less commonly reported in children and young people than in adults:

- *shortness of breath*
- *persistent cough*
- *pain on breathing*
- *palpitations*
- *variations in heart rate*
- *chest pain.*

Evidence To Decision

Benefits and harms

The panel agreed to retain the list of common symptoms of ongoing symptomatic COVID-19 and post-COVID-19 syndrome, to reflect the evidence and encompass the common symptoms for all age groups, however they did note that cardiac and respiratory symptoms were less common in children than adults and agreed that this should be noted in the guideline.

The panel discussed that older people may present with atypical symptoms that could be overlooked. For example, older people can present with gradual decline, deconditioning, worsening frailty or dementia and may not be eating and drinking which can have a variety of causes. It would be reasonable to consider post-COVID-19 syndrome as a cause of these symptoms.

The updated evidence review supported the initial list of common symptoms. In addition, the updated evidence review identified additional common symptoms. The panel agreed that these additional common symptoms were consistently identified in the evidence and agreed that they should be added to the common symptoms list.

Certainty of the Evidence

The evidence base for children and young people remains uncertain due to the small number, size and risk of bias of studies. Most studies had a high risk of bias due to their retrospective design with the inherent risk of selection bias, and largely self-reported outcomes with an increased risk of recall bias.

All outcomes were rated as very low certainty. This is due to the high risk of bias of most of the studies but also the inability to measure imprecision.

No evidence was identified for older people.

Values and preferences

The qualitative evidence highlighted that patients reported negative experiences when seeking help for their symptoms with some people feeling dismissed or misdiagnosed by their healthcare professional. The panel considered this may be further complicated where people present atypically. It is expected that by highlighting that atypical presentation can occur will encourage consideration of Post-COVID-19 syndrome as well as other possible diagnoses.

Resources and other considerations

Not applicable

Rationale

In the panel's experience, some people, including children and older people, may report different symptoms from those most commonly seen in the adult population. The panel highlighted this to make sure their needs are still identified.

For the November 2021 update, the evidence for children and young people was reviewed. The evidence on the most common symptoms and signs in children and young people remains uncertain because of the small number and size of studies and the risk of bias. However, the panel did note that some cardiac and respiratory symptoms were less commonly reported in children than adults and agreed that these symptoms should be noted to inform investigation of alternative diagnoses.

Clinical Question/ PICO

Population: Children experiencing ongoing symptoms beyond the duration of acute COVID-19 illness (>4 weeks)
Intervention: Not applicable
Comparator: Not applicable

Outcome Timeframe	**Study results and measurements**	**Comparator**	**Intervention**	**Certainty of the Evidence** (Quality of evidence)	**Plain language summary**
Prevalence of individual symptoms	Based on data from 4,388 participants in 6 studies. (Observational (non-randomized))	Four studies (n=4222) found that 2.99%-87.10% of patients reported tiredness and weakness or hypersomnia. Five studies (n=1323) found that 10.69%-87% of patients reported fatigue. Six studies (n=4388) found that 3.50%-78.60% of patients reported headache and 2.00%-75.9% of patients reported abdominal pain. Six studies (n=4388) found that 0.82%-68.4% of patients reported muscle aches and pains. Five studies (n=3878) found that 1.39%-55.0% of patients reported shortness of breath. Four studies (n=3749) found that 1.0%-45.5% of patients reported loss of smell. Six studies (n=4388) found that 0.41%-60.6% of patients reported lack of concentration or delirium. Five studies (n=4259) found that 1.03%-48.0% of patients reported dizziness or light headedness. Two studies (n=3142) found that 9.7%-16.88% of patients reported skipped meals. Six studies (n=4388) found that 1.6%-52.4% of patients reported skin rash or red welts		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [1]	Evidence from 6 studies found that the most common ongoing symptoms in children were tiredness, weakness and fatigue; headaches; abdominal pain; muscle aches and pain; shortness of breath; loss of smell; lack of concentration or delirium; dizziness or light headedness; skipped meals and skin rash or red welts.
Prevalence of categories of symptoms	Based on data from 135 participants in 2 studies. (Observational (non-randomized))	Two studies (n=135) found that 16.36%-27.5% of patients reported general symptoms (including fatigue and fever). Two studies (n=135) found that 3.64%-22.5% of patients reported ear, nose, and throat symptoms (including reduced taste/smell). Two studies (n=135) found that 5.45%-21.2% of patients reported respiratory symptoms. Two studies (n=135) found that 5.45%-16.2% of patients reported neurological symptoms (including cognitive impairment/'brain fog' and headache). One study (n=80) found that 15% of patients reported dermatological symptoms. Two studies (n=135) found that 5.45%-13.80% of patients reported gastrointestinal symptoms. Two studies (n=135) found that 1.81%-11.20% of patients reported cardiovascular symptoms. Two studies (n=135) found		**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to very serious imprecision [2]	Evidence from 2 studies found that the most common ongoing categories of symptoms in children were general symptoms (including fatigue and fever); ear, nose, and throat (including reduced taste/smell); respiratory symptoms; neurological symptoms (including cognitive impairment/'brain fog' and headache); and dermatological symptoms.

Outcome Timeframe	Study results and measurements	Comparator	Intervention	Certainty of the Evidence (Quality of evidence)	Plain language summary
		that 5.45%-10% of patients reported psychiatric symptoms. One study (n=80) found that 8.80% of patients reported muscular symptoms.			
Symptoms of paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 6 weeks to 6 months	Based on data from 46 participants in 1 studies. (Observational (non-randomized))	One study found that the most common symptoms of PIMS-TS reported at 6 weeks and 6 months were abnormal neurological examination (52.17% at 6 weeks, 39.13% at 6 months); could walk less than 3rd centile (43.48%, 39.13%); proximal myopathy or lower limb weakness (36.13%, 17.39%); bilateral or unilateral dysmetria (34.78%, 26.09%); and abnormal eye movements or saccades (32.61%, 15.21%).		**Very low** Due to serious risk of bias, Due to serious imprecision [3]	Evidence from 1 study found that the most common symptoms of PIMS-TS at 6 weeks and 6 months were abnormal neurological examination; could walk less than 3rd centile; proximal myopathy or lower limb weakness; bilateral or unilateral dysmetria; and abnormal eye movements or saccades.
Prevalence of new post-COVID diagnoses or conditions	Based on data from 2,673 participants in 1 studies. (Observational (non-randomized))	One study found that children with COVID were not more likely to experience new post-COVID diagnoses or conditions than children without COVID		**Very low** Due to serious risk of bias, Due to serious imprecision [4]	Evidence from one study found that children with COVID-19 were not more likely to experience new post-COVID diagnoses or conditions than children without COVID-19

1. **Risk of Bias: serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: serious.** Unable to pool due to different study designs. **Imprecision: very serious.** Unable to pool due to different study designs.
2. **Risk of Bias: serious.** Retrospective study design reliant on self-reported data. High risk of recall bias.. **Inconsistency: serious.** Unable to pool due to different study designs. **Imprecision: very serious.** Unable to pool due to different study designs.
3. **Risk of Bias: serious.** Retrospective observational study and therefore prone to selection bias.. **Imprecision: serious.** unable to assess statistical significance.
4. **Imprecision: serious.** Unable to measure precision.

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Info Box

In addition to clinical symptoms, people who report increased absence or reduced performance in their education, work or training after acute COVID-19 may have ongoing symptomatic COVID-19 or post-COVID-19 syndrome.

People with ongoing symptomatic COVID-19 or post-COVID-19 syndrome who report increased absence or reduced performance in education or work may need extra support and recovery time.

Evidence To Decision

Benefits and harms

The panel noted the evidence indicating that children sometimes have a lack of concentration, short term memory loss, and/or difficulty doing everyday tasks ≥4 weeks after acute COVID-19 illness. Expert witnesses and the panel agreed there was a lack of recognition among healthcare professionals and the public that children can be affected by ongoing symptomatic COVID-19 or post-COVID-19 syndrome. For example, worse achievement or absenteeism at school is sometimes erroneously attributed to other causes, leading to an under-referral of cases to dedicated clinics, multidisciplinary teams (MDTs) and multidisciplinary rehabilitation services.

The expert witness highlighted that a worse performance or absenteeism at education, work, or training was a “red flag” for both children and adults. For example, in the studies above, common symptoms of long-COVID-19 include tiredness, fatigue, and lack of concentration. The panel agreed that it was important to highlight this because worse achievement or absenteeism could be wrongfully attributed to other causes. The panel agreed to use the term “worse achievement” because this encompasses a range of attainments, such as academic, athletic, attention to detail or other abilities that are important to that person.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus.

Values and preferences

The qualitative evidence highlighted that patients reported negative experiences when seeking help for their symptoms with some people feeling dismissed or misdiagnosed by their healthcare professional. The panel considered this may be further complicated where people present atypically. It is expected that by highlighting that atypical presentation can occur will encourage consideration of post-COVID-19 syndrome as well as other possible diagnoses.

Resources and other considerations

Resource impact was not assessed.

Rationale

Based on expert testimony and the panel's experience, the panel agreed that poor performance or increased absence in education, work or training may suggest ongoing symptomatic COVID-19 or post-COVID syndrome. Awareness of this may be helpful to healthcare professionals in identifying people who may need further assessment.

Recommended

Based on the initial consultation, use shared decision making to discuss and agree with the person whether they need a further assessment and whether this should be remote or in person. Take into account whether they may have symptoms that need investigating in person or require urgent referral to an appropriate service.

For advice on working with people to make decisions about their treatment and care, see NICE's guidelines on shared decision making and decision-making and mental capacity and Healthcare Improvement Scotland's What Matters To You website.

Evidence To Decision

Benefits and harms

Expert witness testimony advised that many adults with new or ongoing symptoms after acute COVID-19 were experiencing anxiety caused by unnecessary investigations and referrals to different specialists. Therefore, the panel advised that the NICE guideline on shared decision making should be signposted to. The panel agreed there should not be a recommendation cautioning against unnecessary investigations or referrals because there was already under-referral to dedicated clinics or MDTs.

Certainty of the Evidence

Lower-certainty evidence from expert testimony paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

People with experience of the condition highlighted that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

The panel also noted the expert testimony advising that many people with new or ongoing symptoms after acute COVID-19 were experiencing anxiety caused by unnecessary investigations and referrals to different specialists. Therefore, the panel agreed that for people who are concerned about new or ongoing symptoms 4 weeks or more after acute COVID-19, shared

decision making should be used to discuss and agree with the person whether they need a further assessment.

Resources and other considerations

Resource use was not assessed but the panel acknowledged that there may be impact on resources depending on the type of investigations required.

Rationale

There was evidence supporting further assessment in person after the initial consultation and the panel agreed this was important to fully assess people who need it. A consultation in person might not be suitable for everyone, so this should be agreed as a shared decision. However, the panel agreed that decisions about whether consultations should be remote or in person should always take into account any safeguarding concerns.

Consensus recommendation

Support access to assessment and care for people with new or ongoing symptoms after acute COVID-19, particularly for those in underserved or vulnerable groups who may have difficulty accessing services, for example by:

- providing extra time or additional support (such as an interpreter or advocate) during consultations
- raising awareness about possible new or ongoing symptomatic COVID-19 or post-COVID-19 syndrome – this may include working with local community leaders or organisations – particularly in vulnerable groups and black, Asian and minority ethnic groups.

See the equality impact assessment for more information about the equality issues considered.

Evidence To Decision

Benefits and harms

The panel agreed on the need to address health inequalities in care for people after acute COVID-19. Some people are less likely to seek help for symptoms or may be at risk of not being followed up after hospital care, for example because of language barriers, mental health conditions, mobility or sensory impairments, a learning disability or cultural differences in seeking help. Providing extra support and raising awareness could improve access to care.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The panel were aware from the evidence that some common symptoms experienced are fatigue and ‘brain fog’ which may make it harder to access services or understanding information. The panel considered this and other health inequalities and would expect that people would value the offer of more information, additional support or extra time in consultations.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel agreed on the need to address health inequalities in care for people after acute COVID-19. Some people are less likely to seek help for symptoms or may be at risk of not being followed up after hospital care, for example, because of language barriers, mental health conditions, mobility or sensory impairments, learning disabilities or cultural differences in seeking help. Providing extra support and raising awareness could improve access to care.

Conditional recommendation

Consider follow up by primary care or community services for people in vulnerable or high-risk groups who have self-managed in the community after suspected or confirmed acute COVID-19.

Evidence To Decision

Benefits and harms

Expert testimony supported panel experience that people who have had acute COVID-19 in the community who are in underserved or vulnerable groups, such as older people and people who are isolated may need proactive patient follow-up, together with accessible advice. This would help to identify people who could be at increased risk of complications following acute COVID-19.

Certainty of the Evidence

It is considered that the benefits of the intervention are greater than the disadvantages. Available lower certainty evidence from expert testimony cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. The panel expect that providing proactive follow up for vulnerable people will help minimise this uncertainty in these groups.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel agreed, based on expert testimony and their experience, that proactive follow up of people from underserved or vulnerable groups who are known to have had acute COVID-19 in the community could improve access to care and identify people who could be at increased risk of complications.

Recommended

A healthcare professional in secondary care should offer a follow-up consultation at 6 weeks after discharge to people who have been in hospital with acute COVID-19 to check for new or ongoing symptoms or complications.

Evidence To Decision

Benefits and harms

The panel recommended active follow-up at 6 weeks to help identify if people are still struggling with symptoms. It may not be needed for all patients but it would be backed up by the information about self-referring for reassessment if people felt their health wasn't improving.

Certainty of the Evidence

Lower-certainty evidence from patient experience paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. The panel expect by providing proactive follow up for people who have been in hospital with acute COVID-19 will help minimise this uncertainty in this group.

Resources and other considerations

Resource use was not assessed.

Rationale

The panel recommended active follow up at 6 weeks to help identify if people are still struggling with symptoms. It may not be needed for all patients, but it would be backed up by the information about self-referring for reassessment if people felt their health wasn't improving. For the November 2021 update, the panel agreed that this consultation can be in person or remote, and therefore updated the previous version of the recommendation, which advised video or phone consultation.

3. Assessment

These recommendations are for healthcare professionals assessing people in any healthcare setting, 4 weeks or more after the start of suspected or confirmed acute COVID-19.

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on signs, symptoms and prevalence, children and young people, risk factors, investigations and views and experiences of patients, their families and carers.

Recommended

For people with ongoing symptomatic COVID-19 or suspected post-COVID-19 syndrome who have been identified as needing an assessment, use a holistic, person-centred approach. Include a comprehensive clinical history and appropriate examination that involves assessing physical, cognitive, psychological and psychiatric symptoms, as well as functional abilities.

Include in the comprehensive clinical history:

- *history of acute COVID-19 (suspected or confirmed)*
- *the nature and severity of previous and current symptoms*
- *timing and duration of symptoms since the start of acute COVID-19*
- *history of other health conditions*
- *exacerbation of pre-existing conditions.*

Evidence To Decision

Benefits and harms

Adults

Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19 syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

Children and young people

The panel noted the evidence indicating that children sometimes have a lack of concentration, short term memory loss, and/or difficulty doing everyday tasks ≥4 weeks after acute COVID-19 illness. Expert witnesses and the panel agreed there was a lack of recognition among healthcare professionals and the public that children can be affected by ongoing symptomatic COVID-19 or post-COVID-19 syndrome. For example, worse achievement or absenteeism at school is sometimes erroneously attributed to other causes, leading to an under-referral of cases to dedicated clinics, multidisciplinary teams (MDTs) and multidisciplinary rehabilitation services.
The expert witness and panel overwhelmingly agreed that worse performance or absenteeism at education, work, or training was a “red flag” for both children and adults. For example, in the studies above, common symptoms of long-COVID-19 include tiredness, fatigue, and lack of concentration. The panel agreed that it was important to highlight this because worse achievement or absenteeism could be wrongfully attributed to other causes. The panel agreed to use the term “worse achievement” because this encompasses a range of attainments, such as academic, athletic, attention to detail or other abilities that are important to that person.

Certainty of the Evidence

Lower-certainty evidence from patient experience paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

People with lived experience highlighted that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

Resources and other considerations

The panel agreed that it would be difficult to do a full examination and fully comprehensive history for a patient, especially considering the time constraints. However, they concluded that a full examination, including clinical history was very important. The panel emphasised the need to focus the examination on both what was appropriate to the patient and their symptoms and what matters most to the patient. The panel also highlighted that in their experience there are people who have had mild symptoms of COVID-19 and not realised, then later develop new symptoms. This also supports the need for taking a full history.

The panel agreed to retain the advice to consider using screening questionnaire as part of the initial consultation to help capture the person's symptoms, which applies to all age groups. It was considered important to emphasise that the purpose of the screening questionnaire is to facilitate discussion with the patient about their symptoms and the impact that the long-term effects of COVID-19 has on them, to help make a decision about whether referral to a dedicated clinic or MDT would be appropriate.

Rationale

The evidence suggested that healthcare professionals should use a holistic approach to assessment and the panel agreed that assessment should cover both symptoms and how they affect the person overall. Evidence from patient experience showed that many people feel their symptoms are not taken seriously. There are also people who don't realise that their symptoms are connected with COVID-19, so taking time to listen, showing empathy, taking a careful history and making an assessment are important.

Recommended

Be aware that people can have wide-ranging and fluctuating symptoms after acute COVID-19, which can change in nature over time (see the section on common symptoms).

Evidence To Decision

Benefits and harms

The panel discussed the importance of identifying the most common symptoms that present in people experiencing long term effects of COVID-19. Knowing the most common symptoms will help clinicians to recognise post-COVID-19 syndrome as a possible diagnosis. However, they were mindful that the most common symptoms will not always be present and should not be used as strict criteria for diagnosis as this could mean people who present atypically may be missed. Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19 syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

Certainty of the Evidence

Lower-certainty evidence from patient experience paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

The panel recognised that the evidence base is still considered to be moderate to very low quality. All studies were considered to be of moderate to high risk of bias due to the ways the studies were conducted. The panel were also mindful that when

considering prevalence data, it is important to know the denominator when interpreting the percentages. This varied across all studies. However, it is clear from the evidence that some symptoms such as fatigue and shortness of breath are reported consistently across studies and the panel commonly see them in clinical practice, which increases the certainty around these symptoms. The panel also acknowledged that some symptoms may be under-reported in the literature. In their experience, patients may not report a symptom, such as sleep disturbance, unless directly asked. They were mindful that the way participants were asked about their symptoms in the studies could impact on how symptoms were reported.

Values and preferences

The panel understood from the qualitative evidence that the fluctuating nature of symptoms and the trajectory of the disease led to increased fear and uncertainty and a sense of limited information and knowledge. The panel acknowledged the importance of having a case definition to reduce the uncertainty around the trajectory of illness.

Resources and other considerations

Not applicable

Rationale

The panel noted that evidence from patient experience showed that symptoms can fluctuate and healthcare professionals should be aware of this when carrying out a holistic assessment. The panel reviewed evidence on the case definition for the November 2021 update, which emphasised the fluctuating nature of symptoms, so they agreed to retain this recommendation.

Recommended

Discuss the person's experience of their symptoms and how their life and activities have been affected, including work, education, mobility and independence. Ask about any feelings of worry or distress. Listen to their concerns with empathy and acknowledge the impact on their day-to-day life.

Evidence To Decision

Benefits and harms

The panel discussed the importance of identifying the most common symptoms that present in people experiencing long term effects of COVID-19. Knowing the most common symptoms will help clinicians to recognise post-COVID-19 syndrome as a possible diagnosis. However, they were mindful that the most common symptoms will not always be present and should not be used as strict criteria for diagnosis as this could mean people who present atypically may be missed. Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19 syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

Certainty of the Evidence

Lower-certainty evidence from patient experience paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

The panel recognised that the evidence base is still considered to be moderate to very low quality. All studies were considered to be of moderate to high risk of bias due to the ways the studies were conducted. The panel were also mindful that it when considering prevalence data, it is important to know the denominator when interpreting the percentages. This varied across all studies. However, it is clear from the evidence that some symptoms such as fatigue and shortness of breath are reported consistently across studies and the panel commonly see them in clinical practice, which increases the certainty around these symptoms. The panel also acknowledged that some symptoms may be under-reported in the literature. In their experience,

patients may not report a symptom, such as sleep disturbance, unless directly asked. They were mindful that the way participants were asked about their symptoms in the studies could impact on how symptoms were reported.

Values and preferences

People with lived experience highlighted that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

Resources and other considerations

Ongoing persistent symptoms can impact on an individual's ability to perform usual work activities. Healthcare workers have been considered at high risk of contracting SARS-CoV-2 infection. This could potentially mean a higher prevalence of long-term effects of COVID-19 in this population which may impact on resources within the NHS.

Rationale

Evidence from patient experience showed that many people feel their symptoms are not taken seriously. There are also people who don't realise that their symptoms are connected with COVID-19, so taking time to listen, showing empathy, taking a careful history and making an assessment are important.

Consensus recommendation

For people who may benefit from support during their assessment, for example, to help describe their symptoms, include a family member or carer in discussions if the person agrees.

For more advice on supporting adults to make their own decisions if they lack mental capacity, see NICE's guideline on decision-making and mental capacity and the Adults with Incapacity Act (Scotland) (2000), with further guidance available from the Mental Welfare Commission for Scotland.

Evidence To Decision

Benefits and harms

The panel highlighted the value of talking to family members or carers, with the person's agreement, to help get a full clinical picture for people who need extra support with communication.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus.

Values and preferences

The panel were aware from the evidence that some common symptoms experienced are fatigue and 'brain fog' which may make it harder to access services or understanding information. The panel considered this and other health inequalities and would

expect that people would value the offer of additional support in consultations.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Some people may need help to describe their symptoms, including those who experience cognitive symptoms, such as 'brain fog', confusion and loss of memory, after acute COVID-19. The panel highlighted the value of talking to family members or carers, with the person's agreement, to help get a full clinical picture for people who need extra support with communication.

Not recommended

Do not predict whether a person is likely to develop post-COVID-19 syndrome based on whether they had certain symptoms (or clusters of symptoms) or were in hospital during acute COVID-19.

Evidence To Decision

Benefits and harms

The panel discussed that identifying risk or protective factors associated with developing post-COVID-19 syndrome may help to determine which individuals could be more likely to develop the condition. They can be used to inform the shared decision making process. However, the panel were concerned that using risk factors as part of diagnosis can potentially lead to people who do not have specific risk factors being overlooked. The panel stressed the importance of ongoing monitoring of people who do not have the main risk factors under consideration. These people may be recovering as expected up to 12 weeks but might develop symptoms thereafter.

Certainty of the Evidence

The expert panel concluded that lower-certainty evidence paired with important contextual factors showed that the overall disadvantages of the intervention are clearly greater than the benefits.

The evidence base remains uncertain. All risk and protective factors were assessed in GRADE as being low to very low certainty. Most of the evidence came from a non-systematic meta-analysis of longitudinal studies in the UK although the findings were consistent with data in electronic health records. The panel's main concerns were around the bias that may be introduced due to the self-reporting of symptom persistence, which could mean that the data may not be generalisable to the whole population.

Values and preferences

People with lived experience highlighted that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to fear and anxiety for patients. It would be helpful to discuss risk factors for developing post-COVID-19 syndrome as part of a shared decision-making conversation on expectations around recovery, but the evidence base is currently low quality. The panel did not want to emphasis certain groups and inadvertently miss groups who are not considered 'at risk'.

Resources and other considerations

The panel noted resource implications of time and expertise needed to assess all the risk factors in a consultation. However, the panel doubted whether the cost could be justified based on such limited evidence, especially since there could be resource savings longer-term by preventing inappropriate service use. The panel wished to avoid directing people along specific

pathways inappropriately, for example where asthma is suspected but unconfirmed.

There was no evidence available for risk and protective factors for long-term effects of COVID-19 in children.

Rationale

There were too many uncertainties in the evidence to provide any symptoms that could predict whether people might develop post-COVID-19 syndrome. The panel also did not want healthcare professionals to assume that people who had been hospitalised were more likely to develop post-COVID-19 syndrome because the current evidence and the panel's own experience do not support this.

Info Box

When investigating possible causes of a gradual decline, deconditioning, worsening frailty or dementia, or loss of interest in eating and drinking in older people, bear in mind that these can be signs of ongoing symptomatic COVID-19 or suspected post-COVID-19 syndrome.

Evidence To Decision

Benefits and harms

Adults

The panel discussed and agreed that healthcare professionals should be aware that older people may not present with the common symptoms associated with ongoing symptomatic COVID-19 or post-COVID-19 syndrome. The panel agreed on signs that might prompt a healthcare professional to consider ongoing symptomatic COVID-19 or post-COVID-19 syndrome in an older person.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The qualitative evidence highlighted that patients reported negative experiences when seeking help for their symptoms with some people feeling dismissed or misdiagnosed by their healthcare professional. The panel considered this may be further complicated where people present atypically. It is expected that by highlighting that atypical presentation can occur will encourage consideration of Post-COVID-19 syndrome as well as other possible diagnoses.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel discussed and agreed that healthcare professionals should be aware that older people may not present with the common symptoms associated with ongoing symptomatic COVID-19 or post-COVID-19 syndrome. The panel agreed on signs that might prompt a healthcare professional to consider ongoing symptomatic COVID-19 or post-COVID-19 syndrome alongside other possible causes in an older person.

Consensus recommendation

If the person reports new cognitive symptoms, use a validated screening tool to measure any impairment and impact.

Evidence To Decision

Benefits and harms

Many people experience cognitive symptoms, such as 'brain fog', confusion and loss of memory. The panel agreed that validated screening tools are useful for measuring and monitoring any impairment and the impact of this. The panel were aware of several tools but were unable to recommend any specifically because these had not been reviewed in the evidence. They also agreed that the type of tool will differ depending on the setting and level of assessment needed.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

People with lived experience highlighted that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Many people experience cognitive symptoms, such as 'brain fog', confusion and loss of memory. The panel agreed that validated screening tools are useful for measuring and monitoring any impairment and the impact of this. The panel were aware of several tools but were unable to recommend any specifically because the evidence was not reviewed. They also agreed that the type of tool will differ depending on the setting and level of assessment needed.

4. Investigations and referral

These recommendations are for healthcare professionals carrying out initial investigations in primary care or community services for people with new or ongoing symptoms 4 weeks or more after the start of suspected or confirmed acute COVID-19. See the NICE guideline on shared decision making for advice on how to make appropriate investigations and referrals.

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on investigations, monitoring and referral and views and experiences of patients, their families and carers.

Recommended

Offer tests and investigations tailored to people's signs and symptoms to rule out acute or life-threatening complications and find out if symptoms are likely to be caused by ongoing symptomatic COVID-19, post-COVID-19 syndrome or could be a new, unrelated diagnosis.

Evidence To Decision

Benefits and harms

The panel were minded that when carrying out investigations for ongoing symptoms following acute COVID-19, it was important that other potential diagnoses are not ignored whilst trying to determine if the symptoms are due to post-COVID-19 syndrome. The panel suggested that it would be useful to carry out blood tests that are commonly carried out to rule out or confirm other conditions. They also considered that people might not associate their symptoms with COVID-19, particularly if another event, for example, a stroke, has happened since. The panel were also aware that people might not always present in a typical way, which may particularly be the case with older adults and children. For these reasons, the panel agreed with the conclusions from D'Cruz 2020 that a holistic and preferably face to face assessment is very important from both a clinical and patient perspective. If a clinician can see the patient, then they may identify concerns that the patient may not be aware of themself and may not have reported in a telephone consultation for example.
Blood tests, chest X-rays and exercise tolerance tests, e.g. sit-to-stand test were the most commonly reported tests in the evidence. The panel considered that these tests would be useful for most people as investigations and to obtain baseline measures. The panel however agreed that clinical judgment would be needed for exercise tolerance tests because it could be harmful to some people (for example, people with chest pain or severe fatigue). The evidence showed that chest X-ray may be a poor marker of improvement so the panel suggested it should only be used to inform a holistic assessment on further care needs.

Certainty of the Evidence

The expert panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

The overall certainty in the evidence was very low. The study designs were limited to mainly cohort studies. Whilst this was expected in terms of SARS-CoV-2 being a novel virus, it means that the data is limited and unlikely to lead to any firm conclusions at this point in time. The aims of the studies did not directly answer the question on which investigations to carry out in people with ongoing symptoms. The panel were also particularly concerned with the generalisability of the evidence. They acknowledged that most of the participants recruited were previously hospitalised with acute COVID-19 and some of the results of the investigations carried out would be reflective of this. The panel also considered that the type of investigations carried out in the literature were more likely to be carried out in secondary care settings.
In addition to this, the panel considered that comorbidities and history of related illness were important in understanding the outcomes of investigations but these were not consistently reported across the studies. The panel highlighted that the quantitative evidence often excluded children and older people and were unable to extrapolate the evidence for these groups of people.

Values and preferences

The expert panel would have expected to see outcomes of investigations carried out to rule out other diagnoses or confirm post-COVID-19 syndrome or dual diagnoses. As the evidence was indirect for this question, the panel were unable to draw conclusions from this evidence. However, they were able to identify the most commonly used tests in the literature during follow-up from acute COVID-19 and determine where abnormalities were often seen in these cohorts of people.

Resources and other considerations

Investigations

The panel were concerned that some of the investigations reported in the literature were unlikely to be readily available everywhere. For example, spirometry currently has a long waiting list in the UK, due to it being an aerosol-generating procedure and therefore fewer tests are being carried out. Many of the tests in the literature are generally not carried out in primary care so the panel agreed it is important to consider the setting, availability and resources needed to carry out investigations. The panel had concerns about further over-loading both primary and secondary care clinicians. The evidence suggests that a face-to-face consultation is preferable, but this is currently difficult in the pandemic setting.

The panel noted the need to also ensure that any symptom scores do not miss out other people who present with less common symptoms, with a concern over potential inequalities. They noted that vulnerable groups, such as older people and people who are isolated may need proactive patient follow-up, together with accessible advice.
The panel discussed the need for co-ordinated care and communication when referring to specialist services.

Rationale

The panel agreed that no one set of investigations and tests would be suitable for everyone because of the wide range of symptoms and severity. Investigations need to be tailored to the person's signs and symptoms and whether they are being assessed in primary care (blood tests, the 1-minute sit-to-stand test) or secondary care (exercise tolerance tests). They agreed that blood tests and exercise tolerance tests (if safe and appropriate for the person) would be useful for most people as investigations and baseline measures. These were also the tests most commonly reported in the evidence, along with chest X-rays.

Recommended

Refer people with ongoing symptomatic COVID-19 or suspected post-COVID-19 syndrome urgently to the relevant acute services if they have signs or symptoms that could be caused by an acute or life-threatening complication, including (but not limited to):

- hypoxaemia or oxygen desaturation on exercise
- signs of severe lung disease
- cardiac chest pain
- paediatric inflammatory multisystem syndrome – temporally associated with SARS-CoV-2 (PIMS-TS).

Evidence To Decision

Benefits and harms

Whilst the evidence presented was insufficient to directly inform knowledge of benefits and harms of different monitoring and referral options, the panel used their experience to consider benefits and harms when drafting recommendations.
The panel noted that people may need to be referred urgently to acute services for physical health symptoms, or to psychiatric services, to prevent potentially serious consequences.

Certainty of the Evidence

The expert panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise showed that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Investigations are important to identify symptoms that could be caused by an acute or life-threatening complication, and to assess for other underlying conditions and complications.

For signs and symptoms to help identify PIMS-TS, see the guidance on PIMS from the Royal College of Paediatrics and Child Health.

Recommended

If another diagnosis unrelated to COVID-19 is suspected, offer investigations and referral in line with relevant national or local guidance.

Evidence To Decision

Benefits and harms

The expert panel would have expected to see outcomes of investigations carried out to rule out other diagnoses or confirm post-COVID-19 syndrome or dual diagnoses. As the evidence was indirect for this question, the panel were unable to draw conclusions from this evidence. However, they were able to identify the most commonly used tests in the literature during follow-up from acute COVID-19 and determine where abnormalities were often seen in these cohorts of people.

The panel were minded that when carrying out investigations for ongoing symptoms following acute COVID-19, it was important that other potential diagnoses are not ignored whilst trying to determine if the symptoms are due to post-COVID-19 syndrome. The panel suggested that it would be useful to carry out blood tests that are commonly carried out to rule out or confirm other conditions. They also considered that people might not associate their symptoms with COVID-19, particularly if another event, for example, a stroke, has happened since. The panel were also aware that people might not always present in a typical way, which may particularly be the case with older adults and children. For these reasons, the panel agreed with the conclusions from D'Cruz 2020 that a holistic and preferably face to face assessment is very important from both a clinical and

patient perspective. If a clinician can see the patient, then they may identify concerns that the patient may not be aware of themself and may not have reported in a telephone consultation for example.
Blood tests, chest X-rays and exercise tolerance tests, e.g. sit-to-stand test were the most commonly reported tests in the evidence. The panel considered that these tests would be useful for most people as investigations and to obtain baseline measures. The panel however agreed that clinical judgment would be needed for exercise tolerance tests because it could be harmful to some people (for example, people with chest pain or severe fatigue). The evidence showed that chest X-ray may be a poor marker of improvement so the panel suggested it should only be used to inform a holistic assessment on further care needs.

Certainty of the Evidence

The expert panel concluded that lower-certainty evidence paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

The overall certainty in the evidence was very low. The study designs were limited to mainly cohort studies. Whilst this was expected in terms of SARS-CoV-2 being a novel virus, it means that the data is limited and unlikely to lead to any firm conclusions at this point in time. The aims of the studies did not directly answer the question on which investigations to carry out in people with ongoing symptoms. The panel were also particularly concerned with the generalisability of the evidence. They acknowledged that most of the participants recruited were previously hospitalised with acute COVID-19 and some of the results of the investigations carried out would be reflective of this. The panel also considered that the type of investigations carried out in the literature were more likely to be carried out in secondary care settings.
In addition to this, the panel considered that comorbidities and history of related illness were important in understanding the outcomes of investigations but these were not consistently reported across the studies. The panel highlighted that the quantitative evidence often excluded children and older people and were unable to extrapolate the evidence for these groups of people.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

The panel were concerned that some of the investigations reported in the literature were unlikely to be readily available everywhere. For example, spirometry currently has a long waiting list in the UK, due to it being an aerosol-generating procedure and therefore fewer tests are being carried out. Many of the tests in the literature are generally not carried out in primary care so the panel agreed it is important to consider the setting, availability and resources needed to carry out investigations. The panel had concerns about further over-loading both primary and secondary care clinicians. The evidence suggests that a face-to-face consultation is preferable, but this is currently difficult in the pandemic setting.

Rationale

The panel agreed that when carrying out investigations for ongoing symptoms following acute COVID-19, it is important that other potential diagnoses are not ignored. Healthcare professionals should follow relevant clinical guidance if a diagnosis unrelated to COVID-19 is suspected.

Conditional recommendation

Decisions about blood tests should be guided by the person's symptoms. If clinically indicated, offer blood tests, which may include a full blood count, kidney and liver function tests, C-reactive protein, ferritin, B-type natriuretic peptide (BNP), HbA1c and thyroid function tests.

Evidence To Decision

Benefits and harms

The panel did not think a specific battery of tests should be carried out in patients presenting with ongoing symptoms as this might include tests that will not affect how the patient is managed as well as being time and resource intensive. In addition, the evidence reviewed did not provide conclusive information on a battery of tests that should be conducted for this population. Instead, the panel considered that investigations should be focused on what a patient presents with, covering any 'red flags' that require urgent referral, as well as picking up on any 'pink flags' which would be less critical, but cumulatively would be causing significant problems for the patient. These tests should include assessment of cognitive, psychological, and psychiatric symptoms, as well as any physical assessments. As the panel were unable to recommend specific screening tools to be used in these assessments, they suggested research recommendations to determine which tools are the most useful. These research recommendations are outlined in the guideline.

For people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome, the panel heard evidence from expert testimony that an in-depth consultation between the individual and an appropriately skilled healthcare professional can be an informative part of the assessment process. Expert testimony (Nicol 2021 and Nuffield 2021) suggested that some practice is moving away from conducting lots of clinical tests towards a model where discussion is held with the individual to determine what matters to them and what their goals are. One programme (Nicol 2021) progressively removed tests from its rehabilitation assessment, as it found that they did not inform whether a person was referred to rehabilitation, and what that rehabilitation looked like for them.

Certainty of the Evidence

It is considered that the benefits of the intervention are greater than the disadvantages. available evidence from expert testimony and observational studies cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

The overall certainty in the evidence was very low. The study designs were limited to mainly cohort studies. Whilst this was expected in terms of SARS-CoV-2 being a novel virus, it means that the data is limited and unlikely to lead to any firm conclusions at this point in time. The aims of the studies did not directly answer the question on which investigations to carry out in people with ongoing symptoms. The panel were also particularly concerned with the generalisability of the evidence. They acknowledged that most of the participants recruited were previously hospitalised with acute COVID-19 and some of the results of the investigations carried out would be reflective of this. The panel also considered that the type of investigations carried out in the literature were more likely to be carried out in secondary care settings. In addition to this, the panel considered that comorbidities and history of related illness were important in understanding the outcomes of investigations but these were not consistently reported across the studies. The panel highlighted that the quantitative evidence often excluded children and older people and were unable to extrapolate the evidence for these groups of people

The panel acknowledged that the three testimonies all had potential limitations in terms of generalisability. People employed by the military may differ in characteristics from the rest of the population; the Nuffield model had fewer resource considerations than in the rest of the healthcare system; and the testimony from Scotland is in the context of the service model in NHS Scotland. However, they noted that these findings were consistent with their own experiences, and were internally coherent.

They discussed the fact that it is not possible to conduct randomised studies which actively withhold testing to investigate the effect on the referral pathway for ethical reasons, and therefore different types of evidence must be used.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to the use of

clinical tests as part of rehabilitation assessment. However, they agreed that only offering tests where clinically indicated is likely to be the preferred option for most patients.

The patient lived experience evidence indicated that having someone in a supportive role who could co-ordinate and guide investigations would be beneficial. The panel concluded that whilst such investigations are important, clinicians should ensure that people have clear instructions and know who to contact for support if needed.

Resources

The panel agreed that testing is costly and therefore only undertaking it where necessary would ensure resources are being used efficiently.

Equity

The panel noted the possible under-representation of ethnic minorities and other groups with protected characteristics in the military (Nicol 2021) and accessing rehabilitation run by fee-paying organisations (even where the programme is free – Nuffield Health 2021). They felt that a reliance on an in-depth conversation about how symptoms impact on the individuals' health and well-being may be especially important in these groups, and so did not expect the change to this current recommendation to result in equality issues.

Acceptability

The panel were not aware of any systematically collected data on acceptability in relation to the use of clinical tests as part of rehabilitation assessment. However, they agreed that only offering tests where clinically indicated is likely to be an acceptable option for most patients.

Feasibility

Although there is no systematically collected evidence about feasibility, the panel noted that the change to this recommendation should not make it less feasible.

Rationale

The panel suggested some blood tests, such as a full blood count and kidney, liver and thyroid function tests, that are commonly carried out to help rule out or confirm other conditions.

For the November 2021 update, the panel decided to update this recommendation to be clear that blood tests should only be offered if clinically indicated. They discussed that tests should be carried out as needed when an alternative diagnosis is suspected. However, they recognised that multiple tests can be a negative experience for some people and may not always be needed to inform management of the person's symptoms. They agreed that testing should be guided by the person's symptoms and used to supplement a detailed holistic assessment.

The panel agreed to add HbA1c to the list of tests because they agreed that it was important to check for metabolic disease such as undiagnosed diabetes.

Conditional recommendation

Consider supported self-monitoring at home, if this is agreed through shared decision making as part of the person's assessment. This may include heart rate, blood pressure, pulse oximetry or symptom diaries. Ensure that people have clear instructions on how to use any equipment and parameters for when to seek further help.

Be aware that some pulse oximeters can underestimate or overestimate oxygen saturation levels, especially if the saturation level is borderline. Overestimation has been reported in people with dark skin. For more information about this, see NHS England's guide on how to look after yourself at home if you have COVID-19 or symptoms of COVID-19.

Evidence To Decision

Benefits and harms

The panel considered that monitoring should be tailored to each person. Based on their own experience and the patient lived experience evidence, the panel agreed on the value of people recording or tracking their symptoms, goals and progress. The panel were aware of digital tracking apps that could be used for self-monitoring and, although they acknowledged that these would not be suitable or accessible for everyone, they concluded that it would be useful to highlight these as potentially helpful approaches to recording symptoms.

Certainty of the Evidence

The panel considered that the benefits of the intervention are greater than the disadvantages. Available lower-certainty evidence from expert testimony cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

Values and preferences

The panel, considered, from their experience, that self-monitoring at home can be useful and is used in practice. However, the panel noted that it might not be suitable for everyone, and without the right information and support can cause unnecessary anxiety. People need good guidance to use equipment, interpret the results and understand when to contact a healthcare professional. However, the panel were also mindful that some investigations could be anxiety-inducing. For example, some panel members reported that some patients are being asked to record pulse-oximetry readings at home. These readings can fluctuate and therefore cause a patient to worry unnecessarily.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

In the panel's experience, self-monitoring at home can be useful and is used in practice. But it might not be suitable for everyone, and without the right information and support can cause unnecessary anxiety. People need good guidance to use equipment, interpret the results and understand when to contact a healthcare professional. The panel agreed that this advice also applies to parents or carers monitoring children at home.

Conditional recommendation

If appropriate, offer an exercise tolerance test suited to the person's ability (for example, the 1-minute sit-to-stand test). During the exercise test, record level of breathlessness, heart rate and oxygen saturation. Follow an appropriate protocol to carry out the test safely (see the rationale for suggested protocols).

Sharing skills between services can help community services to manage these assessments, for advice see the recommendation on sharing skills and training in the section on service organisation.

Evidence To Decision

Benefits and harms

Blood tests, chest X-rays and exercise tolerance tests, e.g. sit-to-stand test were the most commonly reported tests in the evidence. The panel considered that these tests would be useful for most people as investigations and to obtain baseline measures. The panel however agreed that clinical judgment would be needed for exercise tolerance tests because it could be harmful to some people (for example, people with chest pain or severe fatigue). The evidence showed that chest X-ray may be a poor marker of improvement so the panel suggested it should only be used to inform a holistic assessment on further care needs.

Certainty of the Evidence

The panel considered that the benefits of the intervention are greater than the disadvantages. Available evidence from expert testimony cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

The overall certainty in the evidence was very low. The study designs were limited to mainly cohort studies. Whilst this was expected in terms of SARS-CoV-2 being a novel virus, it means that the data is limited and unlikely to lead to any firm conclusions at this point in time. The aims of the studies did not directly answer the question on which investigations to carry out in people with ongoing symptoms. The panel were also particularly concerned with the generalisability of the evidence. They acknowledged that most of the participants recruited were previously hospitalised with acute COVID-19 and some of the results of the investigations carried out would be reflective of this. The panel also considered that the type of investigations carried out in the literature were more likely to be carried out in secondary care settings. In addition to this, the panel considered that comorbidities and history of related illness were important in understanding the outcomes of investigations but these were not consistently reported across the studies. The panel highlighted that the quantitative evidence often excluded children and older people and were unable to extrapolate the evidence for these groups of people.

Values and preferences

The panel experience was consistent with the patient lived experience evidence. Patient data and consensus asserted that people feel more reassured when investigations are carried out. However, the panel were also mindful that some investigations could be anxiety-inducing. For example, some panel members reported that some patients are being asked to record pulse-oximetry readings at home. These readings can fluctuate and therefore cause a patient to worry unnecessarily.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel discussed the usefulness of carrying out a sit-to-stand test but also agreed clinical judgement would be needed because it is not suitable for everyone (for example, people with chest pain or severe fatigue). They agreed skill sharing between services could help with gaps in knowledge and that a protocol should be followed in order to carry a sit-to-stand test out safely. The panel discussed that appropriate protocols could be found in these studies: Ozalevli S, Ozden A, and Akkoclu A (2007) Comparison of the sit-to-stand test with 6 min walk test in patients with chronic obstructive pulmonary disease and Briand J, Behal H, Chenivesse C et

al. (2018) The 1-minute sit-to-stand test to detect exercise-induced oxygen desaturation in patients with interstitial lung disease. The panel could not recommend any one in particular as their effectiveness is undetermined.

Consensus recommendation

For people with postural symptoms, for example palpitations or dizziness on standing, carry out lying and standing blood pressure and heart rate recordings (3-minute active stand test for orthostatic hypotension, or 10 minutes if you suspect postural tachycardia syndrome, or other forms of orthostatic intolerance).

Evidence To Decision

Benefits and harms

The panel were aware from their experience that postural symptoms are common in people with ongoing symptoms of COVID-19 and therefore should be investigated.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to the use of clinical tests as part of rehabilitation assessment. However, they agreed that only offering tests where clinically indicated is likely to be the preferred option for most patients.

The patient lived experience evidence indicated that having someone in a supportive role who could co-ordinate and guide investigations would be beneficial. The panel concluded that whilst such investigations are important, clinicians should ensure that people have clear instructions and know who to contact for support if needed.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Postural symptoms are common, so the panel agreed that these should be investigated by taking lying and standing blood pressure and heart rate. Advice on carrying this out is available from the Royal College of Physicians' brief guide on measuring lying and standing blood pressure.

Conditional recommendation

Offer a chest X-ray by 12 weeks after acute COVID-19 only if the person has continuing respiratory symptoms and it is clinically indicated. Chest X-ray appearances alone should not determine the need for referral for further care.

Be aware that a normal plain chest X-ray does not rule out lung disease.

Evidence To Decision

Benefits and harms

Based on limited evidence from one study in the review, the panel considered that a chest X-ray should be done if the person had continuing respiratory symptoms. The panel agreed that a chest X-ray should not be carried out if the person has already had one and there have been no subsequent clinical changes. The panel agreed that a chest X-ray should only be used as part of a holistic assessment to decide if referral or further care are needed. The panel also agreed that the lack of abnormal findings on a person's chest X-ray should not be used as a reason to not refer the person for further assessment and rehabilitation. The panel discussed that the chest X-ray should be done (if needed) before 12 weeks to help rule out any other pathology before the person moves onto a treatment pathway for post-COVID-19 syndrome.

Certainty of the Evidence

The panel considered that the benefits of the intervention are greater than the disadvantages. Available lower-certainty evidence from expert testimony cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

Values and preferences

The expert panel would have expected to see outcomes of investigations carried out to rule out other diagnoses or confirm post-COVID-19 syndrome or dual diagnoses. As the evidence was indirect for this question, the panel were unable to draw conclusions from this evidence. However, they were able to identify the most commonly used tests in the literature during follow-up from acute COVID-19 and determine where abnormalities were often seen in these cohorts of people.

Resources and other considerations

Many of the tests in the literature are generally not carried out in primary care so the panel agreed it is important to consider the setting, availability and resources needed to carry out investigations.

Rationale

The evidence suggested that not all pathology shows up on a chest X-ray so the panel agreed it should only be used as part of a holistic assessment to decide if referral or further care are needed in people with respiratory symptoms. The panel agreed that a chest X-ray should not be carried out if the person has already had one and there have been no subsequent clinical changes.

Recommended

Refer people with ongoing symptomatic COVID-19 or suspected post-COVID-19 syndrome urgently for psychiatric assessment if they have severe psychiatric symptoms or are displaying high risk of self-harm or suicide.

Evidence To Decision

Benefits and harms

While the evidence presented was insufficient to directly inform knowledge of benefits and harms of different monitoring and referral options, the panel used their experience to consider benefits and harms when drafting recommendations.

The panel noted that people may need to be referred urgently to acute services for physical health symptoms, or to psychiatric services, to prevent potentially serious consequences. The panel discussed appropriate tests which may need to be carried out as part of monitoring and follow-up; and agreed that these should be based on the person and their symptoms.

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Certainty of the Evidence

The expert panel concluded that lower-certainty evidence from expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages. See the evidence reviews on monitoring and referral.

The study populations in 2 of the 3 publications (D'Cruz et al, 2020; Salawu et al, 2020) focused on hospitalised patients, whereas the guideline is intended to cover both hospitalised and non-hospitalised people. Therefore, not all of the evidence included was generalisable to the wider population the panel wished to provide guidance for. It was acknowledged that the evidence was lacking for this review, with only a narrative review with practice recommendations, a single descriptive cohort study, and a practice model proposal included. Risk of bias was deemed to be high for the applicable study (D'Cruz et al, 2020) and, as the next section describes, the panel used its own expertise and the patient experience data to supplement the lack of an evidence base for this review question.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Evidence and expert testimonies from the Royal College of Psychiatry 2020 and Nicol 2021 highlighted that mental health symptoms are common after acute COVID-19. The committee agreed that it is important that people with severe psychiatric symptoms or at risk of harm are identified during assessment and urgently referred for psychiatric assessment and support in line with relevant guidance (see the Royal College of Psychiatrists' position statement [2019] The role of liaison psychiatry in integrated physical and mental healthcare).

Conditional recommendation

Follow relevant national or local guidelines on referral for people who have anxiety and mood disorders or other psychiatric symptoms. Consider referral:

- for psychological therapies if they have common mental health symptoms, such as symptoms of mild anxiety and mild depression **or**
- to a liaison psychiatry service if they have more complex needs (especially if they have a complex physical and mental health presentation).

Evidence To Decision

Benefits and harms

Whilst the evidence presented was insufficient to directly inform knowledge of benefits and harms of different monitoring and referral options, the panel used their experience to consider benefits and harms when drafting recommendations.
The panel noted that people may need to be referred urgently to acute services for physical health symptoms, or to psychiatric services, to prevent potentially serious consequences.
The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Certainty of the Evidence

The expert panel concluded that the benefits of the intervention are greater than the disadvantages. Available lower-certainty evidence from patient lived experience cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Evidence suggested that many people struggle to adjust to changes in their life, abilities and self-identity and reported feelings of helplessness and isolation. This was also supported by expert testimony, which suggested that symptoms of low mood and anxiety are common. The panel agreed that when mental health symptoms are identified during assessment, people need to be referred for support in line with relevant guidance (see the Royal College of Psychiatrists' position statement [2019] The role of liaison psychiatry in integrated physical and mental healthcare).

Conditional recommendation

After ruling out acute or life-threatening complications and alternative diagnoses, consider referring people to an appropriate service, such as an integrated multidisciplinary assessment service, any time from 4 weeks after the start of acute COVID-19.

Many people experience a spontaneous improvement in symptoms between 4 and 12 weeks after the start of acute COVID-19 and should be offered self-management support and monitoring during this time, with consideration of onward referral to further services if they do not improve. People with concerning symptoms during this time may need referral for assessment by acute medical services.

Evidence To Decision

Benefits and harms

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

For the November 2021 update, the panel discussed, based on expert testimony (Locke 2021), that in some areas of the UK provision of an integrated multidisciplinary assessment service is not feasible and so added wording to take into account the other services that people may be referred to.

Certainty of the Evidence

Patient preference may vary, but based on their own experience and the patient lived experience evidence, the panel agreed that the earlier people received help, the more effective the interventions. Lower-certainty qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

Resource use not assessed.

Rationale

For many people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome, this will mean referral to an integrated multidisciplinary assessment clinic for investigation, support to manage their symptoms and rehabilitation. Prompt referral is needed to avoid delays in getting people the support they need. In the panel's experience, the earlier people received help the more effective the interventions. The panel were also concerned that a lack of support could negatively affect people's mental health. They agreed that referral should be offered to those who would benefit from these services from 4 weeks after the start of acute COVID-19.

For the November 2021 update, the panel discussed expert testimony from Locke 2021, which reported that in some areas of the UK provision of an integrated multidisciplinary assessment service is not feasible. The recommendation was updated to take into account that people may be referred to other appropriate services. Different service pathways are in place across the UK, and this guideline is not intended to cover the diagnostic or management approaches delivered by the more specialist services involved in caring for patients with persistent symptoms or complications after acute COVID-19, such as post COVID assessment services in England or specialist clinics.

Not recommended

Do not exclude people from referral to an integrated multidisciplinary assessment service or for further investigations or specialist input based on the absence of a positive SARS-CoV-2 test (PCR, antigen or antibody) as long as the case definition criteria are met.

Evidence To Decision

Benefits and harms

The panel discussed the patient lived experience evidence, describing how some people were not offered tests, and how others were denied referral due to not having a positive SARS-CoV-2 test result. Since many people with ongoing symptoms of COVID-19 or post-COVID-19 syndrome will not have been tested, particularly those who had COVID-19 illness earlier in the pandemic, the panel recommended that access to services should not be restricted by the need for a positive test.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient lived experience paired with important contextual factors, show that the overall disadvantages of the intervention are clearly greater than the benefits.

The patient experience evidence described how some people were not offered tests and other people were refused a referral by healthcare professionals because they did not have a positive SARS-CoV-2 test result. Many people who had acute COVID-19 were not tested, particularly earlier in the pandemic.

Values and preferences

The panel expect that by not restricting referral based on history of a positive SARS-CoV-2 test would be acceptable to most patients as many would not have had access to tests, especially at the beginning of the pandemic. However, this preference may change over time as testing becomes more accessible.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The patient experience evidence described how some people were not offered tests and other people were refused a referral by healthcare professionals because they did not have a positive SARS-CoV-2 test result. Many people who had acute COVID-19 were not tested, particularly earlier in the pandemic. The panel were clear that access to services should not be restricted by the need for a positive SARS-CoV-2 test (PCR, antigen or antibody) if the case definition criteria in the section on identification are met.

5. Planning care

These recommendations are for healthcare professionals caring for people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome who have been assessed in primary care or a multidisciplinary assessment service.

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on interventions and monitoring and referral.

Recommended

After the holistic assessment, discuss with the person (and their family or carers, if appropriate) the options available and what each involves. These should include:

- advice on self-management, with the option of supported self-management (see the section on self-management and supported self-management) **and**
- one or more of the following, depending on clinical need and local pathways:
  - support from integrated and coordinated primary care, community, rehabilitation and mental health services
  - referral to an integrated multidisciplinary assessment service
  - referral to specialist care for specific complications.

Evidence To Decision

Benefits and harms

The panel discussed the need for patient information, including advice for patients on trends in symptoms, management of symptoms, and when to call professionals. There needs to be good communication with patients, including how to manage subsequent symptoms if they occur.

The panel noted there are likely to be waiting lists for referral into services and that people should be provided with clear information about what to expect, red flags and who to contact during this time. Patients could feel more empowered, with heightened sense of agency and control, if there are things they can do at home while waiting for referral, including potentially to aid their recovery.

The panel, considered, from their experience, that self-monitoring at home can be useful and is used in practice. However, the panel noted that it might not be suitable for everyone, and without the right information and support can cause unnecessary anxiety. People need good guidance to use equipment, interpret the results and understand when to contact a healthcare professional. The panel therefore recommended supported self-monitoring at home, if agreed as part of a person's assessment, and combined with clear instructions including on when to seek further help.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

Evidence from patients' lived experience suggested that some people struggled to access appropriate care, and some had experienced fragmented care. The panel agreed on the need to improve integration and coordination of care across different services. The panel agreed that having regular multidisciplinary meetings would help share information more efficiently and allow professionals to make decisions quickly about tests and referral. The patient experience evidence also described how

people could benefit from continuity of care, and the panel agreed this should be an aim for well-integrated services.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

To ensure people get the right care and support, the expert panel agreed that a tiered approach could be used in which everyone gets advice for self-management, with the additional option of supported self-management if needed. People can then also be offered care from different services to match the level of their needs. The recommendation applies to all age groups and therefore the panel updated the recommendation in November 2021 to allow for discussion with the family or carers of the person if appropriate.

Recommended

Use shared decision making to agree what support and rehabilitation the person needs, including how and when it should be provided.

When discussing with the person the appropriate level of support and management:

- *take account of the overall impact their symptoms are having on their life and usual activities, even if each individual symptom alone may not warrant referral*
- *look at the overall trajectory of their symptoms, taking into account that symptoms often fluctuate and recur so they might need different levels of support at different times.*

For advice on working with people to make decisions about their treatment and care, see NICE's guidelines on shared decision making and decision-making and mental capacity and Healthcare Improvement Scotland's What Matters To You website.

Evidence To Decision

Benefits and harms

With insufficient evidence to recommend specific criteria for referral, the panel agreed the right level of care would be agreed in shared decision making with the person after their holistic assessment.

The panel updated the recommendation in November 2021 to include more information about the decisions that people should be involved in about their care, including whether or not they are referred and when and how support will be provided. The panel agreed that the person should be central in planning their care. This was based on qualitative evidence of patient experience and expert testimony.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to initial consultations. However, they agreed that this recommendation aligns with other NICE guidance about shared decision making, and therefore is taking account of people's preferences.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

There was not enough evidence to recommend specific criteria for referral and the panel agreed the right level of care would be agreed in shared decision making with the person after their holistic assessment.

The panel updated the recommendation for the November 2021 update to include more information about the decisions that people should be involved in about their care, including whether or not they are referred and when and how support will be provided. The panel agreed that the person should be central in planning their care. This was based on qualitative evidence of patient experience and expert testimony.

6. Management

These recommendations are for healthcare professionals providing care for people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome in primary care and community settings or in multidisciplinary assessment and rehabilitation services

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on interventions, monitoring and referral and service models.

Info Box

There are established treatments for managing the common symptoms often seen with ongoing symptomatic COVID-19 and post-COVID-19 syndrome, as set out in current national and local guidance, which can be followed for symptomatic relief. However, there is a lack of evidence for pharmacological interventions to treat the condition itself.

Advice for patients on managing common symptoms is available from the Your COVID Recovery and NHSinform websites.

Evidence To Decision

Benefits and harms

The panel noted the absence of evidence for pharmacological treatments for ongoing symptomatic COVID-19 or post-COVID-19 syndrome, but that there are established treatments for some of the common symptoms of ongoing symptomatic COVID-19 or post-COVID-19 syndrome.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

The panel noted that there is currently a lack of clinical trials open for people to participate in but that this might be a possibility to consider for people in the future. The panel considered that the research recommendations for interventions remain appropriate to stimulate research for pharmacological treatments.

Values and preferences

The panel noted there are likely to be waiting lists for referral into services and that people should be provided with clear information about what to expect, red flags and who to contact during this time. Patients could feel more empowered, with heightened sense of agency and control, if there are things they can do at home while waiting for referral, including potentially to aid their recovery

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel discussed that although there was no evidence to support the use of specific pharmacological treatments for ongoing symptomatic COVID-19 or post-COVID-19 syndrome, there are established treatments for some of the common symptoms. For

example, antihistamines can be used to treat skin rashes. The panel noted that, given the fluctuating nature of the symptoms, regular review and monitoring is needed for people receiving any form of treatment.

There is currently a lack of clinical trials open for people to participate in, but this might be a possibility to consider for people in the future. The panel considered that the research recommendations for interventions for post-COVID-19 syndrome remain appropriate to stimulate research for pharmacological treatments.

NICE will continue to monitor and review new evidence in this area as part of its living approach to maintaining the guideline.

6.1 Self-management and supported self-management

Recommended

Give advice and information on self-management to people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome, starting from their holistic assessment. This should include:

- ways to self-manage their symptoms, such as setting realistic goals
- who to contact if they are worried about their symptoms or they need support with self-management
- sources of advice and support, including support groups, social prescribing, online forums and apps
- how to get support from other services, including social care, housing and employment, and advice about financial support
- information about new or continuing symptoms of COVID-19 that the person can share with their family, carers and friends (see the section on common symptoms).

Evidence To Decision

Benefits and harms

The panel expressed concern over the use of interventions to manage short term symptoms that might cause harm in the longer term, indicating the need for the guideline to advise caution over such interventions, including over the counter medicines. The panel emphasised the need for differentiation in support to address differing symptoms and circumstances, such as difficulty using digital platforms for people with cognitive problems or accessibility issues.

The panel agreed that there is a need for the guideline to acknowledge social and financial factors in supporting patient recovery. The panel highlighted that sources of advice and support should include support groups, social prescribing, online forums and apps. This was supported by patient lived experience evidence, which indicated that patients valued these types of interventions. The panel were aware of the online support service YourCOVIDRecovery. Support from other services was also considered to be important, including social care, housing, employment, and advice about financial support. Based on their own experience, the panel agreed on the value of symptom diaries and symptom tracking apps in self-monitoring.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience and expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The panel noted there are likely to be waiting lists for referral into services and that people should be provided with clear information about what to expect, red flags and who to contact during this time. Patients could feel more empowered, with heightened sense of agency and control, if there are things they can do at home while waiting for referral, including potentially to aid their recovery.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

There was very little evidence on interventions, but the panel agreed that everyone should have self-management support and information. There was a lack of COVID-19-specific evidence on managing many of the common symptoms related to COVID-19, such as fatigue, dizziness and cognitive problems (such as 'brain fog'). However, there are established treatments for managing individual common symptoms.

Patient organisations and online support groups can help to support self-management. The Your COVID recovery website was also highlighted as a potential source of reliable, up-to-date information and support.

Info Box

It is not known if over-the-counter vitamins and supplements are helpful, harmful or have no effect in the treatment of new or ongoing symptomatic COVID-19 or post-COVID-19 syndrome.

Evidence To Decision

Benefits and harms

The panel expressed concern over the use of interventions to manage short term symptoms that might cause harm in the longer term, indicating the need for the guideline to advise caution over such interventions, including over the counter medicines.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The panel noted there are likely to be waiting lists for referral into services and that people should be provided with clear information about what to expect, red flags and who to contact during this time. Patients could feel more empowered, with heightened sense of agency and control, if there are things they can do at home while waiting for referral, including potentially to aid their recovery

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel were concerned that people are buying over-the-counter vitamins and supplements that may not help with their symptoms. They agreed that it would be helpful to highlight the lack of knowledge in this area.

Recommended

Support people in discussions with their school, college or employer about returning to education or work, for example by having a phased return. For advice on returning to work, follow national guidance, for example NICE's guideline on workplace health: long-term sickness absence and capability to work.

Evidence To Decision

Benefits and harms

The panel agreed that there is a need for the guideline to acknowledge social and financial factors in supporting patient recovery. The panel highlighted that sources of advice and support should include support groups, social prescribing, online forums and apps. This was supported by patient lived experience evidence, which indicated that patients valued these types of interventions. The panel were aware of the online support service YourCOVIDRecovery. Support from other services was also considered to be important, including social care, housing, employment, and advice about financial support. Based on their own experience, the panel agreed on the value of symptom diaries and symptom tracking apps in self-monitoring.

For the November 2021 update, the panel heard expert testimony (Stark 2021 and Whittaker 2021) that absence from or poor performance in education was associated with poor outcomes for children and young people with ongoing symptoms or post-COVID syndrome. The panel agreed that this would also apply to adults returning to work or education. Health professionals should be aware that people who are struggling to return to work or education may have symptoms that persist for longer than other people and may need additional support.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience and expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

The panel identified worse performance or absenteeism at education, work, or training as being important to people. Therefore, the panel decided that advice and information should be given on who to contact if people are worried about new, ongoing or worsening symptoms, or if they are struggling to return to work or education.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The panel agreed that support to return to education or work, such as setting achievable goals, should be tailored to the person's needs. This might involve support to work or study at home, flexible working or a phased return.

For the November 2021 update, the panel heard expert testimonies from Stark 2021 and Whittaker 2021 describing that absence from or poor performance in education was associated with poor outcomes for children and young people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome. The panel agreed that this would also apply to adults returning to work or education. Healthcare professionals should be aware that people who are struggling to return to work or education may have symptoms that persist for longer than other people and may need additional support.

Further advice on returning to work can be found in the Society for Occupational Health Medicine guidance on COVID-19 return to work guide for recovering workers and COVID-19 return to work guide for managers.

6.2 Multidisciplinary rehabilitation

Reviewed, no new evidence

Info Box

Definition

Rehabilitation: a set of interventions designed to optimise functioning, health and wellbeing, and reduce disability in people with health conditions in interaction with their environment. In the context of ongoing COVID-19 symptoms, this may include providing information, education, supported self-management, peer support, symptom management strategies and physical rehabilitation. (Informed by the World Health Organization's fact sheet on rehabilitation.)

Recommended

Use a multidisciplinary approach to guide rehabilitation, including physical, psychological and psychiatric aspects of management. Ensure that any symptoms that could affect the person being able to start rehabilitation safely have been investigated first. See also the recommendation on multidisciplinary rehabilitation teams.

Evidence To Decision

Benefits and harms

The panel agreed that multidisciplinary rehabilitation teams should work with people to make a personalised plan for their rehabilitation needs, but they emphasised that rehabilitation planning should only happen after checking for symptoms that would need investigating before the person can safely start rehabilitation. The panel agreed on the potential value of a multidisciplinary approach to rehabilitation, including fatigue management, breathing retraining, and psychological or psychiatric support. This was supported by expert testimony.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience and expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The patient lived experience evidence indicated that having someone in a supportive role who could co-ordinate and guide investigations and management would be beneficial.

Resources and other considerations

The panel highlighted the current resource constraints of pulmonary rehabilitation services and that post COVID-19 syndrome would require additional resources to fund rehabilitation. The panel also expressed concern over the impact on existing services for other conditions and agreed that resources should not be diverted from these services to new COVID-19 rehabilitation services.

Rationale

The panel agreed that multidisciplinary rehabilitation teams should work with people to make a plan for their rehabilitation once any symptoms had been investigated that could affect the safety of rehabilitation. Physical, psychological and psychiatric aspects of rehabilitation should be addressed, with fatigue management being a key component of this. The evidence showed that breathlessness, fatigue and ‘brain fog’ are among the most commonly reported long-term symptoms, so support for these should be part of the person’s rehabilitation plan.

Recommended

Work with the person (and their family or carers, if appropriate) to develop a personalised rehabilitation and management plan that is recorded in a rehabilitation prescription and should include:

- areas of rehabilitation and interventions based on their assessment
- helping the person to decide and work towards goals
- how to manage and monitor their symptoms, taking into account that these may fluctuate, and what to do if symptoms return or change.

For people who may benefit from support during consultations, follow the recommendation on supporting access to assessment and care, including providing extra time or additional support (such as an interpreter or advocate).

Evidence To Decision

Benefits and harms

The panel expressed concern over the use of interventions to manage short term symptoms that might cause harm in the longer term, indicating the need for the guideline to advise caution over such interventions, including over the counter medicines. The panel discussed the ongoing debate over self-pacing and graded forms of exercise. The panel considered careful self-pacing of exercise to be an important element of self-management. However, the panel concluded that in the absence of evidence relating to people with ongoing symptoms from COVID-19 it could not make specific recommendations and it agreed to include a research recommendation to determine the effectiveness of exercise interventions for this population.

The panel agreed that multidisciplinary rehabilitation teams should work with people to make a personalised plan for their rehabilitation needs, but they emphasised that rehabilitation planning should only happen after checking for symptoms that would need investigating before the person can safely start rehabilitation, which was also emphasised by expert testimony. The panel agreed on the potential the value of a multidisciplinary approach to rehabilitation, including fatigue management, breathing retraining, and psychological or psychiatric support.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to initial consultations. However, they agreed that this recommendation aligns with other NICE guidance about shared decision making, and therefore is taking account of people's preferences.

Resources and other considerations

The panel highlighted the current resource constraints of pulmonary rehabilitation services and that post COVID-19 syndrome would require additional resources to fund rehabilitation. The panel also expressed concern over the impact on existing services for other conditions and agreed that resources should not be diverted from these services to new COVID-19 rehabilitation services.

Rationale

A personalised rehabilitation and management plan records the person's needs and how they will be met. In some settings a

'rehabilitation prescription' may be used to capture this information. The rehabilitation prescription is held by the person and includes an individualised description of rehabilitation needs or recommendations to inform the future planning and delivery of a person's ongoing rehabilitation. The panel recognised that some people may need additional support, such as an interpreter or advocate, in developing the rehabilitation and management plan.

For the November 2021 update, the panel reviewed evidence that emphasised the fluctuating nature of ongoing symptomatic COVID-19 and post-COVID-19 syndrome. Based on this evidence, the panel agreed that it was key that a management plan should take into account that symptoms may fluctuate.

Conditional recommendation

Encourage people to keep a record of, or use a tracking app to monitor, their goals, recovery and any changes in their symptoms (see also the section on follow up, monitoring and discharge).

Evidence To Decision

Benefits and harms

The panel considered that monitoring should be tailored to each person. Based on their own experience and the patient lived experience evidence, the panel agreed on the value of people recording or tracking their symptoms, goals and progress.

Certainty of the Evidence

The panel considered that the benefits of the intervention are greater than the disadvantages, and the available lower-certainty evidence from patient experience cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

Values and preferences

The panel were aware of digital tracking apps that could be used for self-monitoring and, although they acknowledged that these would not be suitable or accessible for everyone, they concluded that it would be useful to highlight these as potentially helpful approaches to recording symptoms.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Based on their experience, the panel agreed on the value of symptom diaries and symptom tracking apps in self-monitoring. The evidence for different symptom tracking apps was not reviewed so the panel could not recommend a specific product.

6.3 Additional support

Consensus recommendation

Consider additional support for people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome who may be vulnerable, for example, older people and people with complex needs. Additional support may include short-term care packages, advance care planning and support with social isolation, loneliness and bereavement, if relevant.

Evidence To Decision

Benefits and harms

There was a lack of evidence for specific age groups on managing ongoing symptomatic COVID-19 or post-COVID-19 syndrome. Based on their clinical experience, the panel made a recommendation for older people who may be vulnerable to ensure that they receive additional care and support, if needed, that is tailored to the particular needs of this population.

For the November 2021 update, the panel agreed that the recommendation should be broadened to include other vulnerable groups who may also benefit from additional support, such as people with complex needs.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The panel discussed the difficulties many people are facing as a result of the pandemic which may mean that some people may have complex needs that require additional support.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

There was a lack of evidence for specific age groups on managing ongoing symptomatic COVID-19 or post-COVID-19 syndrome. Based on their clinical experience, the panel made a recommendation for older people who may be vulnerable to ensure that they receive additional care and support, if needed, that is tailored to the particular needs of this population.

For the November 2021 update, the panel agreed that the recommendation should be broadened to include other vulnerable groups who may also benefit from additional support, such as people with complex needs.

Conditional recommendation

Consider referral from 4 weeks for specialist advice for children and young people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome.

Evidence To Decision

Benefits and harms

There was a lack of evidence on managing ongoing symptomatic COVID-19 or post-COVID-19 syndrome in children and young people. Based on their experience, the panel agreed that referral should be considered so that children and young people can be supported to manage their symptoms early and recover quickly.

Certainty of the Evidence

The panel considered that the benefits of the intervention are greater than the disadvantages, and the available lower certainty evidence from patient experience cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

There was a lack of evidence on managing ongoing symptomatic COVID-19 or post-COVID-19 syndrome in children and young people. Based on their experience, the panel agreed that referral should be considered so that children and young people can be supported to manage their symptoms early and recover quickly. The recommendation covers all children and young people, including those aged 16 to 18 who should be supported to access specialist advice through either adult or paediatric services depending on local referral pathways.

7. Follow up, monitoring and discharge

These recommendations are for healthcare professionals providing care for people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome in any setting, including primary care and community settings, secondary care and rehabilitation services.

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on interventions, monitoring and referral, service models and views and experiences of patients, their families and carers.

Recommended

Use shared decision making to decide how often follow up and monitoring are needed, which healthcare professionals should be involved and whether appointments should be carried out in person or remotely. Take into account:

- the person's needs and the services involved
- the person's symptoms, including new or worsening symptoms, and the effects of these on the person's life and wellbeing
- availability, clinical suitability and the person's preferences for in-person or remote appointments.

Evidence To Decision

Benefits and harms

The panel considered it was important to be able to effectively assess whether a patient had recovered or not, as part of monitoring/follow-up. Recovery would be considered as both symptom improvement - which might include links with quality of life and/or wellbeing - and an ability to return to usual activities, including work, education or leisure, or caring duties.

There was a lack of evidence on monitoring, but the panel agreed it is important so that people's support can be adapted if their symptoms or ability to carry out their usual activities change. The patient experience evidence highlighted the importance of follow-up and 'check ins' to access further care. The panel did not want to limit monitoring to specific tests or symptoms, or to a particular timeframe, because people with ongoing symptomatic COVID-19 and post-COVID19 syndrome have such a wide range of care needs. They decided it should be tailored to each person.

In the panel's experience, self-monitoring at home can be useful and is used in practice. But it might not be suitable for everyone, and without the right information and support can cause unnecessary anxiety. People need good guidance to use equipment, interpret the results and understand when to contact a healthcare professional.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

It was acknowledged that the evidence was lacking for this review, with only a narrative review with practice recommendations, a single descriptive cohort study, and a practice model proposal included. Risk of bias was considered to be high, and the panel used its own expertise and the patient experience data to supplement the lack of an evidence base for this review question.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to initial consultations. However, they agreed that this recommendation aligns with other NICE guidance about shared decision making, and therefore is taking account of people's preferences.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

There was a lack of evidence on monitoring, but the panel agreed it is important so that people's support can be adapted if their symptoms or ability to carry out their usual activities change. The patient experience evidence highlighted the importance of follow-up and 'check-ins' to access further care. The panel did not want to limit monitoring to specific tests or symptoms, or to a particular timeframe, because people with ongoing symptomatic COVID-19 and post-COVID19 syndrome have such a wide range of care needs. They decided it should be tailored to each person's needs and preferences.

Consensus recommendation

Be alert to symptoms developing that could mean referral or investigation is needed, following recommendations in the section on assessment.

Evidence To Decision

Benefits and harms

Whilst the evidence presented was insufficient to directly inform knowledge of benefits and harms of different monitoring and referral options, the panel used their experience to consider benefits and harms when drafting recommendations.

The panel noted that people may need to be referred urgently to acute services for physical health symptoms, or to psychiatric services, to prevent potentially serious consequences. The panel discussed appropriate tests which may need to be carried out as part of monitoring and follow-up; and agreed that these should be based on the person and their symptoms.

The panel discussed potential active monitoring of symptoms which would be considered below a threshold for referral. They concluded that whilst it is important not to miss these symptoms, neither should all decisions be based on them. The panel noted that thresholds in screening tools, whilst capturing symptoms where they are high in one area, may miss so-called 'pink flags', whereby a patient may be experiencing multiple relatively low-level symptoms (e.g. a little shortness of breath, fatigue) which may still indicate very significant illness, needing multidisciplinary team input. The panel therefore concluded that it was crucial for the referral to be based on a holistic assessment, not just a checklist of symptoms.

Certainty of the Evidence

The expert panel concluded that there is not enough evidence to give an evidence-based recommendation, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions. Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The evidence on when to refer was limited and based mostly on people who had been hospitalised, so it was not relevant to everyone. The panel agreed that healthcare professionals should be alert to any changes and that the recommendations in the

assessment section would also apply to monitoring.

Recommended

Use shared decision making to discuss and agree plans for discharge from rehabilitation and care, taking into account the person's preferences, goals and social support.

Follow local referral pathways to enable re-referral if needed.

Evidence To Decision

Benefits and harms

The panel heard evidence from expert testimony about various rehabilitation programmes (Nicol 2021 and Nuffield Health 2021). The length of these programmes varied: Nicol 2021 described a 2-week residential programme followed by monitoring and a gradual return to work. Nuffield Health 2021 described a 12-week programme (the first 6 weeks is completely virtual, the second 6 weeks has an in-person element) followed by continued access to support resources to use in the individual's own time.

The panel considered how long rehabilitation should last and agreed that it was dependent on the severity of symptoms at baseline; the change in these symptoms over time; and the goals set by the person (which might depend on the level of support they had access to from other services, groups, or family members and friends). They agreed that, although it might be easiest not to set a timeline for discharge, this might result in a large increase to the resources needed by rehabilitation services and could divert resources from other parts of the health system, resulting in an opportunity cost. They therefore recommended that plans should be made, but that both the individual and the healthcare professional should take part in these decisions.

The panel also heard evidence (Locke 2021) about the fluctuating nature of ongoing symptomatic COVID-19 and post-COVID-19 syndrome. Expert testimony put forward the importance of people being able to re-enter rehabilitation services after being discharged if their symptoms worsened. The panel recognised that symptoms may fluctuate and recur with patients needing to re-access support and services in the most efficient way possible. However, following shared decision making, local referral pathways would need to be followed due to variation in practice and funding.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

The panel acknowledged that the three testimonies all had potential limitations in terms of generalisability. People employed by the military may differ in characteristics from the rest of the population; the Nuffield model had fewer resource considerations than in the rest of the healthcare system; and the testimony from Scotland is in the context of the service model in NHS Scotland. Despite the indirect elements of these models, the principles of shared decision making in discharge planning highlighted by the testimonies informed the panel decision making.

Values and preferences

The panel were not aware of any systematically collected data on peoples' preferences and values in relation to timing of discharge from rehabilitation services in people with ongoing symptomatic COVID-19 or post-COVID-19 syndrome. However, they agreed a decision which took into account their preferences and goals was likely to be the preferred option for most patients.

Resources

The panel agreed that, although it might be easiest not to set a timeline for discharge, this might result in a large increase to the resources needed by rehabilitation services and could divert resources from other parts of the health system, resulting in an

opportunity cost. They therefore recommended that plans should be made, but that both the individual and the healthcare professional should take part in these decisions.

Equity

The panel noted the possible under-representation of ethnic minorities and other groups with protected characteristics in the military (Nicol 2021) and accessing rehabilitation run by fee-paying organisations (even where the programme is free – Nuffield Health 2021). They felt that a reliance on an in-depth conversation about how symptoms impact on the individuals' health and well-being may be especially important in these groups, and so did not expect the change to this current recommendation to result in equality issues.

Acceptability

The panel considered that the acceptability of this recommendation would be high, as it considers the needs of individuals.

Feasibility

Although there is no systematically collected evidence about feasibility, the panel noted that this recommendation is not significantly different from established practice in rehabilitation for other conditions, which is an indicator of feasibility.

Rationale

The panel discussed when a person should be discharged from rehabilitation and care. They agreed that a timepoint could not be specified, because this is dependent on the person's symptoms, the goals that were set, the progress made and the amount of social support the person has. However, they agreed that making a discharge plan with the person would support motivation, ensure the person gets the support they need and help to manage rehabilitation resources. The panel also agreed that transition to adult services should be considered in discharge planning for young people.

Expert testimony highlighted the importance of people being able to re-enter rehabilitation services after being discharged if their symptoms worsen. The panel recognised that symptoms may fluctuate and recur with patients needing to re-access support and services in the most efficient way possible. However, following shared decision making, local referral pathways would need to be followed because of variation in practice and funding.

8. Sharing information and continuity of care

Info Box

Full details of the evidence and the panel's discussion are in the evidence reviews on monitoring and referral and views and experiences of patients, their families and carers.

Recommended

Ensure effective information sharing and integrated working by sharing clinical records and care and rehabilitation plans promptly between services and through multidisciplinary meetings, either virtual or in person.

Evidence To Decision

Benefits and harms

Evidence from patients' lived experience suggested that some people struggled to access appropriate care, and some had experienced fragmented care. The panel agreed on the need to improve integration and coordination of care across different services. The panel agreed that having regular multidisciplinary meetings would help share information more efficiently and allow professionals to make decisions quickly about tests and referral. The patient experience evidence also described how people could benefit from continuity of care, and the panel agreed this should be an aim for well-integrated services.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The panel expected that people would value an integrated and coordinated approach to their care and that this would minimise the difficulties highlighted by patient experience.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

There was evidence that people struggled to access appropriate care and some had experienced fragmented care. The panel agreed on the need to improve integration and coordination of care across different services. Having regular multidisciplinary meetings would help share information more efficiently and allow professionals to make decisions quickly about tests and referral.

Consensus recommendation

Give people a copy of their care plans or records to keep, including their discharge letters, clinical records and rehabilitation plans and prescriptions.

Evidence To Decision

Benefits and harms

The panel wanted to make sure that information is also shared with people using services so that they know what is happening with their care.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients' experience of having their symptoms dismissed when seeking help. Enabling people to be involved and informed about their care may help to minimise uncertainty around the condition.

Resources and other considerations

Resource use not assessed.

Rationale

The panel wanted to make sure that information is also shared with people using services so that they know what is happening with their care.

Consensus recommendation

Include baseline measures as well as ongoing assessments in information shared between services, including when the person is discharged from hospital. For example, resting oxygen saturation and heart rate, and the results of functional assessment.

Evidence To Decision

Benefits and harms

Sharing clinical records and care plans between services, with the agreement of the person, will help healthcare professionals provide integrated care, and avoid gaps in care or duplication of effort. In particular, sharing baseline measures is essential for monitoring as people move between services.

Certainty of the Evidence

The expert panel concluded that there is not enough evidence to give an evidence-based recommendation, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition.

Values and preferences

The panel expected that people would value an integrated and coordinated approach to their care and that this would minimise the difficulties highlighted by patient experience.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Sharing clinical records and care plans between services, with the agreement of the person, will help healthcare professionals provide integrated care, and avoid gaps in care or duplication of effort. In particular, sharing baseline measures is essential for monitoring as people move between services.

Recommended

Provide continuity of care with the same healthcare professional or team as much as possible, for example, by providing a care coordinator or a single point of contact.

Evidence To Decision

Benefits and harms

Evidence from patients' lived experience suggested that some people struggled to access appropriate care, and some had experienced fragmented care. The panel agreed on the need to improve integration and coordination of care across different services. The panel agreed that having regular multidisciplinary meetings would help share information more efficiently and allow professionals to make decisions quickly about tests and referral. The patient experience evidence also described how people could benefit from continuity of care, and the panel agreed this should be an aim for well-integrated services.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

The patient lived experience evidence supported other components proposed by the published service models, in particular the need for personalised care and a case manager or single point of contact to overcome barriers to accessing services, and the need for meaningful referral pathways.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The patient experience evidence described how people could benefit from continuity of care, and the panel agreed this should always be an aim for well-integrated services.

9. Service organisation

Info Box

Full details of the evidence and the panel's discussion are in the evidence review on service models.

Recommended

Provide access to multidisciplinary services, if available, (these could be 'one-stop' clinics) for assessing physical and mental health symptoms and carrying out further tests and investigations. Services should be led by a doctor with relevant skills and experience and appropriate specialist support, taking into account the variety of presenting symptoms.

Evidence To Decision

Benefits and harms

The quantitative outcomes the expert panel expected to see in the evidence were the proportion of post-COVID-19 patients being correctly identified; assessed and referred; and effectively managed and supported thereafter, using a particular service model. Further outcomes of interest were accessibility and timely referral, and individual components of service models. However, in the absence of any patient data, only components of proposed service models were reported in the studies. These components informed the panel discussions and reinforced some recommendations in the guideline sections on investigation and assessment, and management and rehabilitation.

The main components of a service model advocated by the panel were the use of MDTs with specialist expertise, individualised interventions beginning with self-management, and the use of both remote and in-person modes of delivery. However, differing patient views and experiences of face-to-face and remote assessment emerged from the patient lived experience evidence, which further underlines the need to allow for patient preferences in the mode of service delivery. Some patients reported a desire for face-to-face consultations to support the holistic assessment and care they thought they needed, whilst a positive view expressed about telemedicine was that it did increase accessibility of primary care during periods of societal restrictions aimed at controlling the spread of COVID-19.

The panel agreed that as well as ensuring the right breadth of expertise, having an MDT with input from other services and clear referral pathways can help to prevent people receiving disjointed care from multiple specialists and delayed appointments. This was supported by the patient lived experience evidence, which described both the difficulty in accessing the GP service and variability in GP's knowledge and understanding of the wide range of symptoms covered by the condition. Some patients favoured a 'one-stop' clinic with multidisciplinary teams there to assess symptoms affecting a wide range of body systems. In addition to the core composition of the MDT, the panel stressed that expertise from other disciplines should be added depending on the person's age and symptoms. For example, this might include rheumatology, neurology rehabilitation, cardiology, paediatrics, dietetics, speech and language therapy, nursing and pharmacy.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience and expert testimony paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

The panel noted the lack of evidence on service models and agreed that expert testimony would be of value to this question to capture evidence outside the published literature. Expert testimony was provided from a service that specialised in post COVID-19 complications, The Royal College of Psychiatrists and from the online support service YourCOVIDRecovery.

Values and preferences

Differing patient views and experiences of face-to-face and remote assessment emerged from the patient lived experience evidence, which further underlines the need to allow for patient preferences in the mode of service delivery. Some patients

reported a desire for face-to-face consultations to support the holistic assessment and care they thought they needed, whilst a positive view expressed about telemedicine was that it did increase accessibility of primary care during periods of societal restrictions aimed at controlling the spread of COVID-19.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Different regional and geographical challenges mean that areas have different service needs and resources, so the panel agreed that one model would not fit all areas. The panel agreed a multidisciplinary service for assessment could avoid multiple referrals and would provide a single point for care. This could be a 'one-stop' clinic to help keep appointments to a minimum, although this might not be feasible for all services or wanted by all patients. In areas where multidisciplinary services are not available, services may be provided through integrated and coordinated primary care, community, rehabilitation and mental health services.

Recommended

Provide integrated, multidisciplinary rehabilitation services, based on local need and resources. Healthcare professionals should have a range of specialist skills, with expertise in managing fatigue and respiratory symptoms (including breathlessness). Additional expertise may be needed depending on the age and symptoms of the person. The core team could include, but not be limited to, the following specialist areas:

- occupational therapy
- physiotherapy
- clinical psychology and psychiatry
- rehabilitation medicine.

Other areas of expertise could also include, but are not limited to, rheumatology, neurology rehabilitation, cardiology, paediatrics, dietetics, speech and language therapy, nursing, pharmacy, social care and support to return to education or work or usual activities.

Evidence To Decision

Benefits and harms

The main components of a service model advocated by the panel were the use of MDTs with specialist expertise, individualised interventions beginning with self-management, and the use of both remote and in-person modes of delivery. However, differing patient views and experiences of face-to-face and remote assessment emerged from the patient lived experience evidence, which further underlines the need to allow for patient preferences in the mode of service delivery. Some patients reported a desire for face-to-face consultations to support the holistic assessment and care they thought they needed, whilst a positive view expressed about telemedicine was that it did increase accessibility of primary care during periods of societal restrictions aimed at controlling the spread of COVID-19.

The panel agreed that as well as ensuring the right breadth of expertise, having an MDT with input from other services and clear referral pathways can help to prevent people receiving disjointed care from multiple specialists and delayed appointments. This was supported by the patient lived experience evidence, which described both the difficulty in accessing the GP service and variability in GP's knowledge and understanding of the wide range of symptoms covered by the condition. Some patients favoured a 'one-stop' clinic with multidisciplinary teams there to assess symptoms affecting a wide range of body systems. In addition to the core composition of the MDT, the panel stressed that expertise from other disciplines should be added depending on the person's age and symptoms. For example, this might include rheumatology, neurology rehabilitation, cardiology, paediatrics, dietetics, speech and language therapy, nursing and pharmacy.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

In the absence of conclusive evidence on specific service delivery components, the panel considered that recommendations should take the form of general principles.

Values and preferences

Providing integrated, multidisciplinary rehabilitation services would help to keep appointments to a minimum which would be preferable for some people although the panel acknowledged that this might not be feasible for all services or desirable for all people.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

The limited evidence described different models of rehabilitation services. The panel agreed that some of the common elements, such as integration and multidisciplinary team working, would help provide effective, well-organised care for people with ongoing symptomatic COVID-19 and post-COVID-19 syndrome.

Because symptoms are so wide-ranging, many other areas of expertise could also be added as needed and examples of these have been added for the November 2021 update as an additional remark to the recommendation.

Consensus recommendation

Share knowledge, skills and training between services to help practitioners in the community provide assessments and interventions, such as 1-minute sit-to-stand tests and breathlessness training.

Evidence To Decision

Benefits and harms

Based on their experience, the panel concluded that different services sharing knowledge and expertise with each other could provide benefits in helping to expand the choice of tests and interventions available in the community. This could be done through local clinical networks or clinical hubs.

Certainty of the Evidence

No evidence was identified in the evidence review, but the panel still regards it as important to give a recommendation by consensus because of the uncertainty in managing the condition and potential variation in service organisation.

Values and preferences

Some people would prefer not to have to go to many different appointments for different assessments or other aspects of care. The panel agreed that sharing knowledge, skills and training between services may help to keep referrals and appointments to a minimum for some individuals.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

Based on their experience, the panel wanted to encourage different services to share knowledge and expertise with each other, to help expand the choice of tests and interventions available in the community. This could be done through local clinical networks or clinical hubs.

Recommended

Agree local, integrated referral pathways between primary and community care, rehabilitation services and specialist services, multidisciplinary assessment clinics (where available) and specialist mental health services.

Evidence To Decision

Benefits and harms

The panel concluded that ensuring the right breadth of expertise and having a multidisciplinary team with input from other services and clear referral pathways could benefit people by preventing disjointed care and helping to avoid long waiting times for appointments with multiple specialists. This was supported by the patient experience evidence, which described the challenges of attending multiple appointments and repeated investigations and difficulties in accessing the GP service and variability in GP's knowledge and understanding of the wide range of symptoms covered by the condition.

Certainty of the Evidence

The panel concluded that lower-certainty evidence from patient experience paired with consistent panel expertise show that the overall benefits of the intervention are clearly greater than the disadvantages.

Values and preferences

Providing integrated referral pathways would help to keep appointments to a minimum which would be preferable for some people although the panel acknowledged that this might not be feasible for all services or desirable for all people.

Resources and other considerations

Resource use was not assessed as part of the evidence review but a resource impact statement is available.

Rationale

As well as ensuring the right breadth of expertise, having a multidisciplinary team with input from other services and clear referral pathways can prevent disjointed care and people waiting a long time for appointments with multiple specialists. This was supported by the patient experience evidence, which described the challenges of attending multiple appointments and repeated investigations.

10. Common symptoms

Info Box

Symptoms after acute COVID-19 are highly variable and wide ranging. The most commonly reported symptoms include (but are not limited to) the following:

Respiratory symptoms

- Breathlessness
- Cough

Cardiovascular symptoms

- Chest tightness
- Chest pain
- Palpitations

Generalised symptoms

- Fatigue
- Fever
- Pain

Neurological symptoms

- Cognitive impairment ('brain fog', loss of concentration or memory issues)
- Headache
- Sleep disturbance
- Peripheral neuropathy symptoms (pins and needles and numbness)
- Dizziness
- Delirium (in older populations)
- Mobility impairment
- Visual disturbance

Gastrointestinal symptoms

- Abdominal pain
- Nausea and vomiting
- Diarrhoea
- Weight loss and reduced appetite

Musculoskeletal symptoms

- Joint pain
- Muscle pain

Ear, nose and throat symptoms

- Tinnitus
- Earache
- Sore throat
- Dizziness
- Loss of taste and/or smell
- Nasal congestion

Dermatological symptoms

- Skin rashes
- Hair loss

Psychological/psychiatric symptoms

- Symptoms of depression
- Symptoms of anxiety
- Symptoms of post-traumatic stress disorder

The following symptoms and signs are less commonly reported in children and young people than in adults:

- *shortness of breath*
- *persistent cough*
- *pain on breathing*
- *palpitations*
- *variations in heart rate*
- *chest pain.*

Evidence To Decision

Benefits and harms

Adults

The panel discussed the importance of identifying the most common symptoms that present in people experiencing long term effects of COVID-19. Knowing the most common symptoms will help clinicians to recognise post-COVID-19 syndrome as a possible diagnosis. However, they were mindful that the most common symptoms will not always be present and should not be used as strict criteria for diagnosis as this could mean people who present atypically may be missed. Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19 syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

Children and young people

The panel noted the evidence indicating that children sometimes have a lack of concentration, short term memory loss, and/or difficulty doing everyday tasks ≥4 weeks after acute COVID-19 illness. Expert witnesses and the panel agreed there was a lack of recognition among healthcare professionals and the public that children can be affected by ongoing symptomatic COVID-19 or post-COVID-19 syndrome. For example, worse achievement or absenteeism at school is sometimes erroneously attributed to other causes, leading to an under-referral of cases to dedicated clinics, multidisciplinary teams (MDTs) and multidisciplinary rehabilitation services.

The expert witness and panel overwhelmingly agreed that worse performance or absenteeism at education, work, or training was a “red flag” for both children and adults. For example, in the studies above, common symptoms of long-COVID-19 include tiredness, fatigue, and lack of concentration. The panel agreed that it was important to highlight this because worse achievement or absenteeism could be wrongfully attributed to other causes. The panel agreed to use the term “worse achievement” because this encompasses a range of attainments, such as academic, athletic, attention to detail or other abilities that are important to that person.

The panel also agreed to retain the list of common symptoms of ongoing symptomatic COVID-19 and post-COVID-19 syndrome, which is consistent with the evidence and encompasses the common symptoms for all age groups, however they did note that cardiac and respiratory symptoms were less common in children than adults and agreed that this should be noted in the common symptoms list.

Certainty of the Evidence

Adults

The panel recognised that the evidence base is still considered to be moderate to very low quality. All studies were considered to be of moderate to high risk of bias due to the ways the studies were conducted. The panel were also mindful that it when considering prevalence data, it is important to know the denominator when interpreting the percentages. This varied across all studies. However, it is clear from the evidence that some symptoms such as fatigue and shortness of breath are reported consistently across studies and the panel commonly see them in clinical practice, which increases the certainty around these symptoms. The panel also acknowledged that some symptoms may be under-reported in the literature. In their experience, patients may not report a symptom, such as sleep disturbance, unless directly asked. They were mindful that the way participants were asked about their symptoms in the studies could impact on how symptoms were reported.

Children and young people

The evidence base for children and young people remains uncertain due to the small number of studies, the small size of them, and their risk of bias. Furthermore, there was heterogeneity across the studies in terms of how they selected participants who had symptoms of post-acute COVID-19. For example, some studies only included children with “long COVID-19” and others included all children who had COVID-19 and measured symptoms experienced after certain amount of time by that whole population overall. Most studies had a high risk of bias due to their retrospective design with the inherent risk of selection bias, and largely self-reported outcomes with an increased risk of recall bias.

Values and preferences

People with experience of the condition highlighted to the panel that one of the most important issues around the long-term effects of COVID-19 is the uncertainty around what to expect when recovering from acute COVID-19. This can lead to people experiencing fear and anxiety because they do not know what to expect or who to contact for support. This fear and anxiety can be intensified by patients’ experience of having their symptoms dismissed when seeking help. Determining the main signs and symptoms of post-COVID-19 syndrome will help address these concerns.

Resources and other considerations

Ongoing persistent symptoms can impact on an individual’s ability to perform usual work activities. Healthcare workers have been considered at high risk of contracting SARS-CoV-2 infection. This could potentially mean a higher prevalence of long-term effects of COVID-19 in this population which may impact on resources within the NHS.

Rationale

The evidence review on symptoms and signs was updated for the November 2021 update and supported the original list of common symptoms. The updated evidence review identified additional common symptoms of hair loss, nasal congestion, symptoms of post-traumatic stress disorder, weight loss, vomiting, visual disturbances and mobility impairment. These additional common symptoms were consistently identified in the evidence and the panel agreed that they should be added to the common symptoms list. The panel also discussed that menstrual symptoms and ‘COVID toes’ are common symptoms in their experience, but noted that they were not identified in the evidence and so were not added to the common symptoms list. It was further noted that adjustment disorder was highlighted as a symptom in the patient experience review, however this too was not commonly reported in other studies so was not added to the common symptoms list.

Expert testimonies from Stephenson 2021 and Whittaker 2021 and evidence on signs and symptoms in children and young people indicated that cardiac and respiratory symptoms are less common in young people. The panel agreed that it is important to highlight the specific symptoms identified as less common in this population.

The panel noted that people typically experience a constellation of symptoms and the presence of an isolated symptom should prompt thorough consideration of other possible causes.

11. Recommendations for research

Key recommendations for research

1 Interventions for post-COVID-19 syndrome

What are the most clinically effective interventions (including social prescribing and structured community support) for managing post-COVID-19 syndrome?

Does effectiveness vary for different population groups (for example, sex, age, socioeconomic group, black, Asian and minority ethnic group communities or people with a learning disability)?

Do any symptoms of post-COVID-19 syndrome predict the need for specialist intervention?

Are there clusters of symptoms that identify response to interventions in post-COVID-19 syndrome?

What is the clinical effectiveness of different service models of multimodality/multidisciplinary post-COVID-19 syndrome rehabilitation in improving patient-reported outcomes (such as quality of life)?

What is the clinical effectiveness of exercise interventions for people with post-COVID-19 syndrome? Does effectiveness vary for different population groups (for example, sex, age, socioeconomic group, black, Asian and minority ethnic group communities or people with a learning disability)?

Does early exercise rehabilitation assist in improving symptoms of post-COVID-19 syndrome?

2 Prevalence of post-COVID-19 syndrome

What is the prevalence and incidence of post-COVID-19 syndrome in people who have received single, double or boosted doses of the approved vaccinations in the UK? Does this vary across different population groups (for example in black, Asian and minority ethnic group communities)? [updated 2021]

Other recommendations for research

Prognostic markers of developing post-COVID-19 syndrome

What is the clinical effectiveness of D-dimer and other blood tests and clinical features as prognostic markers of developing post-COVID-19 syndrome?

Presentation of post-COVID-19 syndrome in children, young people, pregnant women and older people

What symptoms do children, young people, pregnant women and older people with suspected post-COVID-19 syndrome present with?

Clinical course of post-COVID-19 syndrome

What is the natural history of post-COVID-19 syndrome?

What pathophysiological mechanism(s) underlie the most common presentations of post-COVID-19 syndrome? For example, generalised fatigue, breathlessness and 'brain fog'? [new, 2021]

Validated tools for screening for post-COVID-19 syndrome

Develop and validate new and existing screening tools (including physical, psychological and psychiatric aspects) for post-COVID-19 syndrome in a UK population.

What tools are validated for screening for post-COVID-19 syndrome, which are the most accurate at identifying post-COVID-19 syndrome in a UK population and what is their effectiveness in guiding management?

12. Equality considerations

12.1 Equalities impact assessment during scope development

Is the proposed primary focus of the guideline a population with a specific communication or engagement need, related to disability, age, or other equality consideration?

No. The scope of the guideline is adults, children and young people.

Have any potential equality issues been identified during the check for an update or during development of the draft scope, and, if so, what are they?

Exacerbating inequalities

The existing guideline (NG188 COVID-19 rapid guideline: managing the long-term effects of COVID-19) is being updated. Potential equality issues identified during the development of the previous guideline were documented in an EIA and are summarised here. Characteristics and individual circumstances were considered to ensure that recommendations did not exacerbate inequalities.

Age
It was suggested that ongoing symptomatic COVID-19 and post-COVID-19 syndrome may be more likely to be reported in older people generally, but that older adults with acquired communication impairments may be less likely to report symptoms, or symptoms may be attributed to other conditions. There could be difficulty accessing care for older people who cannot easily ask for help because of mobility or sensory impairments. These factors may lead to older people becoming less likely to seek help. In addition, it was highlighted that prevalence of post-COVID-19 syndrome (PCS) is unknown in care homes.
The pandemic may have led to limitations in carer arrangements. This may mean that some of the difficulties faced by older people who require additional support may be exacerbated.
Existing services may use exclusion criteria relating to age, which could lead to inequality of access.
There seem to be different clusters of symptoms in different age groups, which means that there could be different presentations for children and younger people and adults compared with people aged over 65.

Disability
Healthcare services may be less accessible to people with disabilities due to additional safety measures for patients. They may require reasonable adjustments to be made. In addition, people with disabilities who are immunocompromised may fear accessing care due to the risk of COVID-19 re-infection.
People with learning disabilities and autistic people may present late to services because of atypical presentations or diagnostic overshadowing. People with communication, speech and language difficulties may also not be able to describe, explain or communicate subtle or complex symptoms. Limitations in carer arrangements as a result of the pandemic may exacerbate these issues.

Gender reassignment
Some evidence suggests that there may be a number of factors that can dissuade trans people from seeking healthcare e.g., lack of providers that are knowledgeable on the topic, discrimination etc. This could lead to delayed diagnosis.

Pregnancy and maternity
People with symptoms who are pregnant or caring for young children may have difficulty accessing health and social care services where they could gain advice and assistance. This may increase the likelihood of a delay in seeking help.
There is a lack of evidence about the effect of maternal COVID-19 or PCS on the unborn child.

Race
There is some evidence of poorer outcomes from COVID-19 in black, Asian and minority ethnic populations, related either to higher rates of comorbidities (which may be due to biological factors, or to social determinants of health and systemic racism) or

occupation.
People from black, Asian and minority ethnic groups may also have had negative experiences of the healthcare service, which could be a barrier to engagement or help-seeking.

Religion or belief
People may feel or have experienced stigma based on their religion or belief when accessing healthcare services that may create challenges for seeking help.

Sex
While there are known differences in terms of poorer outcomes from COVID-19 for men compared to women, there is emerging evidence that women are more likely to report ongoing symptomatic COVID-19 and post-COVID-19 syndrome compared to men. Lower help-seeking behaviours in men may contribute to this.
Stakeholders highlighted that women may have had negative experiences of the healthcare service, and may have informal caring responsibilities to a greater extent than men, both of which could be barriers to engagement or help-seeking.

Sexual orientation
People may feel or have experienced stigma based on their sexual orientation when accessing healthcare services. There are also higher incidences of mental ill health in LGBTQ+ people. Both these factors may create challenges for seeking help.

Socioeconomic factors
People may feel or have experienced stigma based on their socio-economic background when accessing healthcare services that may create challenges for seeking help.
Poverty may also reduce accessibility of healthcare resources through mechanisms such as distance from healthcare, access to online support and access to childcare.

Other definable characteristics
Refugees, asylum seekers and migrant workers
For people whose first language is not English, there may be communication difficulties and a need for an interpreter especially for seeking help and effective shared decision making.
People who are homeless
People who are homeless may face challenges accessing care or may present late to services, so they may be more likely to have adverse outcomes compared to if they accessed services sooner.
Mental health and pre-existing comorbidities
There may be some situations when pre-existing comorbidities or mental health illness may create challenges for people seeking help and accessing services.
People at higher risk of COVID-19
Stakeholders highlighted that low levels of literacy and pervasive language disorders are known to exist in communities at higher risk of COVID-19 which can create challenges seeking help.
New barriers caused by ongoing COVID-19 symptoms or Post-COVID-19 symptoms
People with PCS may be experiencing symptoms that may prevent access to digital services, such as fatigue. They may also be experiencing new difficulties and may also have new transportation barriers due to new mobility, cognitive, or sensory impairments which may create barriers in attending face to face appointments.

Others identified
Stakeholders highlighted that inequalities are faced by groups such as people in prison, Gypsies and Travellers.
Stakeholders highlighted that groups such as people in prison, Gypsy, Roma and Traveller communities, armed forces personnel and people who have been trafficked should be considered when drafting recommendations.

Digital accessibility
Increased use of digital and virtual methods for delivering healthcare could create challenges for people with disabilities, low digital literacy, or people who do not have the devices or connectivity to use these services. These factors may lead to some groups of people becoming less likely to seek help.

What is the preliminary view on the extent to which these potential equality issues need addressing by the Committee?

The guideline will need to address the potential equality issues by looking at data from studies either focused on the groups identified or by looking at subgroup data. They will be captured by subgroup analyses in the review questions as well as qualitative data on patient experience. No groups will be excluded from the population.

12.2 Equalities impact assessment during scoping - final scope

Have any potential equality issues been identified during consultation, and, if so, what are they?

The following points were discussed at the Scoping Workshop for the guideline update.

Age
It was suggested that using a post 12-week referral point might be a barrier for children. 'Post-COVID-19' suggests a time point, whereas it was suggested that children should be assessed over time as they may deteriorate progressively. It was also noted that when considering problems people may have carrying out usual activities, education should be considered a usual activity.
Stakeholders noted that post-COVID-19 syndrome (PCS) may be more common in people of working age than in older people, but this may be influenced by under-reporting among older people. Symptoms experienced by people with PCS may make them unable to work, and therefore may have financial impacts at an individual level and socioeconomic impacts on a population level.
Stakeholders also highlighted that older, frailer people may struggle to attend services which they may be especially in need of. Older people may also have symptoms of PCS attributed to cognitive impairment, leading to missed diagnosis. Older people may also be less likely to report symptoms and the consequent gaps in reporting of PCS should be taken into account in reviewing evidence to avoid exacerbating inequalities for older people.

Disability
It was noted that people with disabilities may be reluctant to make or attend appointments about PCS symptoms due to a fear of reinfection with COVID-19, particularly if their disabilities put them at risk of worse symptoms or outcomes. This may also be the case for people who have been shielding, for example those with health conditions like kidney disease, and may increase the likelihood of a delay in seeking help.
Stakeholders also noted that people with a learning disability may have symptoms of PCS attributed to that disability, leading to missed diagnosis.

Gender reassignment
None identified at this time.

Pregnancy and maternity
None identified at this time.

Race
It was suggested that data from studies shows that the prevalence of PCS is not higher in ethnic minority groups. This is contrary to expectations based on the higher rates of COVID-19 in ethnic minorities, so stakeholders discussed the need to interpret these studies in light of contextual factors. For example, people from black, Asian and minority ethnic groups may have had negative experiences of the healthcare service, which could be a barrier to engagement or help-seeking.

Religion or belief
None identified at this time.

Sex
It was suggested that rates of PCS are higher in women than in men. The mechanism by which this would occur is not known, but stakeholders noted anecdotal evidence related to fluctuating symptoms being linked with ovulation.
It was highlighted that some women may have had negative experiences of the healthcare service and may have had PCS symptoms dismissed and not investigated fully.
Women may also have informal care responsibilities to a greater extent than men, which may be a barrier to seeking help for

symptoms.
One stakeholder also suggested that antibody tests may work less well in women, who may sero-revert faster than men. It was noted that any investigations should be considered carefully to make sure that they aren't introducing inequalities.

Sexual orientation
None identified at this time.

Socioeconomic factors
Stakeholders highlighted that symptoms experienced by people with PCS may make them unable to work. Those in vulnerable employment types or with casual contracts may be particularly at risk of losing their jobs.
One stakeholder had observed lower levels of referrals to COVID-19 clinics from deprived areas, indicating an inequality of access.

Other definable characteristics
Refugees, asylum seekers and migrant workers
No further issues were identified specifically for these groups in addition to those identified under the 'Race' section.
People who are homeless
None identified at this time.
Mental health and pre-existing comorbidities
Stakeholders noted that people with pre-existing comorbidities may have symptoms of PCS attributed to those conditions, leading to missed diagnosis.
Geographical location
Stakeholders highlighted that geographical inequalities in service provision exist across the UK, affecting people's access to service and the opportunity for healthcare staff in those areas to develop expertise and greater understanding of PCS to aid management of the syndrome. This inequality may interact with others (for example, socioeconomic inequality), exacerbating the results.

Hospitalisation
It was discussed that people who were not hospitalised for COVID-19 may be less clear on timepoints for disease onset and duration of symptoms. They may therefore experience difficulty in being assessed as having PCS, although the guideline scope specifies that a positive COVID-19 antibody test is not necessary to a diagnosis of PCS. There was a suggestion that people who were hospitalised may also experience more severe symptoms of PCS.
Help-seeking behaviour plays a part in hospitalisation, and so it may be that groups less willing or able to seek help from healthcare services for COVID-19 are disproportionately affected by these factors.

Healthcare professionals
Stakeholders highlighted that 77,000 healthcare professionals contracted COVID-19 last year and should be considered as a group of interest. They noted that many of these are nurses or occupational therapists who fit into the young female risk group and are experiencing significant professional and personal challenges as a result of PCS.

Have any changes to the scope been made as a result of consultation to highlight potential equality issues?
The scope did not exclude any groups. However, children and young people have been added as a named subgroup to clarify that they will be included in the update.
Inequalities will be considered throughout the update, and recommendations will aim to reduce inequalities identified.

Have any of the changes made led to a change in the primary focus of the guideline which would require consideration of a specific communication or engagement need, related to disability, age, or other equality consideration?
Not applicable.

12.3 Equalities impact assessment during guideline development

Have the potential equality issues identified during the scoping process been addressed by the Committee, and, if so, how?

Age

A recommendation has been added that alerts clinicians to be aware that long-term effects of COVID-19 may present in children and adults as reduced performance or increased absence in education or work.

There is an existing recommendation which was unchanged at the update which alerts clinicians to be aware that children and older people may not present with the more common symptoms associated with post-COVID-19 syndrome and that their symptoms may not be picked up by initial screening. Advice has been added about which symptoms are less commonly reported in children.

An existing recommendation which has been retained alerts clinicians to be aware that when investigating possible causes of a gradual decline, deconditioning, worsening frailty or dementia, or loss of interest in eating and drinking in older people, bear in mind that these can be signs of ongoing symptomatic COVID-19 or suspected post-COVID-19 syndrome.

Disability

There are existing recommendations which have been retained that encourages healthcare services to support access for people in underserved or vulnerable groups and sets out a number of suggested proactive actions to reduce barriers and improve awareness and contact. An exisiting recomendation has been amended to prompt healthcare professionals to consider additional support for vulnerable people, for example older people and disabled people.

An existing recommendation in the section on assessments details that the user of the guideline should talk to family members about the person's symptoms for people who might need help with describing symptoms, for example people who have learning disabilities.

Race

Existing recommendations which were retained at update encourage healthcare services to support access for people in underserved or vulnerable groups and sets out a number of suggested proactive actions to reduce barriers and improve awareness and contact.

Sex

The evidence identified did not provide any subgroup data to that compared prevalence of symptoms by sex.

It was highlighted at scoping that women may have informal care responsibilities to a greater extent than men, which may be a barrier to seeking help for symptoms. Recommendations have been retained which encourages healthcare services to support access for people in underserved or vulnerable groups and sets out a number of suggested proactive actions to reduce barriers and improve awareness and contact.

Socioeconomic factors

The guideline contained recommendations which state that users of the guideline should provide information to people with symptoms after acute COVID-19 illness about sources of support and how to get support from other services including social care, housing, benefits and employment.

Other definable characteristics

There are recommendations that encourage clinicians to use a holistic, person-centred approach and to include a comprehensive medical history, including co-morbidities and history of acute COVID-19 when assessing patients.

Have any other potential equality issues (in addition to those identified during the scoping process) been identified, and, if so, how has the Committee addressed them?

Sex and race

The evidence suggested that being female is a possible risk factor for developing ongoing symptomatic COVID-19 and post-COVID-19 syndrome and that Asian ethnicity maybe a protective factor. However, the panel agreed that the evidence was not sufficient to draw strong conclusions. The panel considered that introduction of these risk factors in the recommendations could have unintended consequences such as males or people of Asian ethnicity being overlooked when presenting with ongoing symptoms after acute COVID-19 illness.

Have the Committee's considerations of equality issues been described in the guideline for consultation, and, if so, where?

Equalities issues have been discussed in the recommendations outlined in the first section above, and the relevant rationales (assessment, information and follow-up after acute COVID-19, assessment, planning and agreeing management, sharing information and continuity of care and accessing care).

Do the preliminary recommendations make it more difficult in practice for a specific group to access services compared with other groups? If so, what are the barriers to, or difficulties with, access for the specific group?

No. No recommendations were deemed to make it more difficult in practice for a specific group to access services compared with other groups.

Is there potential for the preliminary recommendations to have an adverse impact on people with disabilities because of something that is a consequence of the disability?
No. No other adverse impacts on people with disabilities as a result of the recommendations were identified.

Are there any recommendations or explanations that the Committee could make to remove or alleviate barriers to, or difficulties with, access to services, or otherwise fulfil NICE's obligation to advance equality?
The recommendations acknowledge and seek to address NICE's obligation to advance equality. The panel acknowledged that particular issues may make it more difficult for certain groups to access services, for example due to mobility issues or location, and the recommendations emphasise the importance of options for contact with services, including remote or face to face.

12.4 Equalities impact assessment final guideline

Have any additional potential equality issues been raised during the consultation, and, if so, how has the Committee addressed them?

One stakeholder identified a new potential equalities consideration for people who have had negative experiences of healthcare in the past which might mean they are more reluctant to seek treatment for the long-term effects of COVID-19. The stakeholder suggests healthcare providers should reach out to these patients and ensure a supportive relationship is in place.

One stakeholder noted that those who have no fixed abode may be lost to follow up through the healthcare system.

The recommendations encourage a holistic, person-centred approach which encourages discussion around personal experiences. The recommendations also encourage the use of shared decision-making where appropriate which should accommodate patient preferences and ensure a supportive relationship. There is also a recommendation to follow-up people in vulnerable and high-risk groups which will go some way to minimising loss to follow-up in the healthcare system.

If the recommendations have changed after consultation, are there any recommendations that make it more difficult in practice for a specific group to access services compared with other groups? If so, what are the barriers to, or difficulties with, access for the specific group?

None.

If the recommendations have changed after consultation, is there potential for the recommendations to have an adverse impact on people with disabilities because of something that is a consequence of the disability?

None.

If the recommendations have changed after consultation, are there any recommendations or explanations that the Committee could make to remove or alleviate barriers to, or difficulties with, access to services identified above, or otherwise fulfil NICE's obligations to advance equality?

None.

Have the Committee's considerations of equality issues been described in the final guideline, and, if so, where?

Recommendations and the corresponding rationales outline the panel's consideration of equality issues. This includes encouraging a holistic and person-centred approach to assessment, providing extra time or additional support during consultations and raising awareness about possible symptoms and how they might impact on daily activities. One recommendation and corresponding rationale encourages following up people in underserved or vulnerable/high risk groups who have self-managed in the community.

13. Methods and evidence reviews

13.1 Methods and processes

Development
This guideline was developed and updated by NICE, SIGN and the RCGP using the methods and process in NICE's interim process and methods for guidelines, which was developed in response to health and social care emergencies.

Advisory panel
NICE has set up an expert advisory panel including representatives from relevant medical specialties with direct experience in the long-term effects of COVID-19 and people with lived experience of the long-term effects of COVID-19. The panel develop new content, provide ongoing advice for surveillance and assist with updates to recommendations.

Declarations of interest
The expert advisory panel's declarations of interest (DOI) are recorded according to NICE's policy on declaring and managing interests for advisory committees. DOIs are reviewed on an ongoing basis and the DOI registry updated as needed. For a list of panel members and corresponding DOI registry for this guideline, see NICE's guideline page on managing the long-term effects of COVID-19.

All NICE staff are asked to declare all interests in line with NICE's policy on declaring and managing interests for board members and employees. If a member of the NICE internal development team is conflicted, they are not permitted to help in developing that particular topic.

Scope development
The original scope was agreed in October 2020. As part of NICE's, SIGN's and the RCGP's commitment to keep the review living and the scope up to date, the scope was reviewed in April 2021. For this review, all of the relevant evidence identified through COVID-19 surveillance since publishing NICE's guideline on managing the long-term effects of COVID-19 was assessed for its effect on the current guidance. A targeted stakeholder workshop was held in June 2021 in which stakeholder views on the current scope, guideline and evidence base were sought. The scope was updated in light of stakeholder feedback, and was refined and agreed on by the expert advisory panel. Additional review questions were developed to address any new themes outlined in the scope. The scope is reviewed as part of ongoing surveillance and updating of the guideline, which is known as a 'living' approach.

See the current scope of this guideline.

Equality impact assessment
The impact on equality was assessed during guidance development according to NICE's manual on developing guidelines. Potential equality issues identified were discussed with the expert advisory panel to ensure they were addressed, if appropriate. Equality issues are reassessed with the expert advisory panel during updates, and new issues are added to the equality impact assessment when identified.

See equalities considerations for details about the equality impact assessment.

Developing review questions
The review questions developed for this guideline were based on the key areas identified in the updated guideline scope. They were drafted by the NICE team, and refined and validated by the guideline panel.

Literature searches, critical appraisals and evidence reviews were completed for all review questions.

Identifying the evidence
Searching for evidence
There was an evidence search for each review question using NICE's interim process and methods for guidelines developed in response to health and social care emergencies.

For the new key questions listed in the scope, full literature searches were done if it was deemed that these areas would not be picked up from the master surveillance search, for example, for qualitative questions. Results from the searches were screened against the relevant review protocol.

All search strategies are available on request.

Expert testimony
If limited or no relevant studies are found on a key question, the panel can request expert testimony or expert evidence to be

presented. This is to help them make recommendations on an identified evidence gap. A call for evidence was not appropriate because of the short development time, and very specific knowledge and expertise that was needed. Expert witnesses were needed for the areas of rehabilitation, vaccines and managing the long-term effects of COVID-19 in people under 18. The experts were chosen based on their knowledge, skills and experience in these areas, as well as their involvement with active research in this area. Expert witnesses were asked specific questions to answer in their testimony. A summary of each expert testimony was recorded in a standard form and can be found in the evidence reviews section. When considering expert testimony, the panel consider the applicability, validity and consistency (when there is more than 1 testimony on a subject) of the testimonies. When recommendations are wholly or partly based on expert testimony, the evidence to decision or rationale sections of relevant recommendations in MAGICapp set out the panel considerations of the expert testimony.

Selecting studies for inclusion

All references identified by the literature searches and from other sources (for example, previous versions of the guideline or studies identified by stakeholders or expert panel members) were uploaded into EPPI reviewer software (version 5) and deduplicated. Titles and abstracts were assessed for possible inclusion using the criteria specified in the review protocol. Ten per cent of the abstracts were reviewed by 2 reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.

The full text of potentially eligible studies was retrieved and assessed according to the criteria specified in the review protocol. A standardised form was used to extract data from included studies.

For the review questions on risk factors and the prevalence of symptoms, because of the high volume of primary evidence in these areas, these additional selection criteria were applied:

- highest quality systematic reviews published in 2021 covering all signs, symptoms and risk factors
- large primary studies (n more than 10,000) not covered by included systematic reviews.

Note that this approach does not apply to children and young people, for which a separate evidence review was done without the additional selection criteria. This was because of the lack of evidence in this area.

This approach was approved by the expert advisory panel and follows NICE's interim process and methods for guidelines developed in response to health and social care emergencies. The rationale for refining the approach from the original review protocol was that important primary studies should be captured by the systematic reviews, which could be supplemented by large primary studies published subsequently. Some of the included reviews have a living approach. It is anticipated that they will be updated to include important primary research in future iterations. This could inform living surveillance and updating of the guideline. Studies of larger sample sizes were prioritised as being more representative of the general population. From the studies identified, the larger studies sampled over 10,000 people while smaller studies were clustered below this number.

Reviewing the evidence

Living review approach

Recommendations were considered up to date and no further review was done for areas:

- in which evidence supported current recommendations
- that were not identified as priorities for update at the targeted stakeholder workshop.

Studies that were not considered robust enough to support a revision to a recommendation have been retained for future consideration. This is if any further confirmatory evidence is identified.

Evidence was reviewed for areas in which there was:

- new evidence that affected current recommendations
- stakeholder feedback indicating that recommendations needed updating.

When evidence was assessed as having no effect on current recommendations, expert testimony or expert evidence was sought.

Methods of combining evidence

Data synthesis for intervention studies

When possible, meta-analyses are done to combine the results of quantitative studies for each outcome. When there are 2 treatment alternatives, pairwise meta-analysis is used to compare interventions. Network meta-analysis has not been used in this guideline.

Data synthesis for association data

In this guideline, association data is defined as measures of association between 1 or more factors (a single variable or a group of variables) and an outcome variable (when the data is not reported in terms of outcome classification, that is, diagnostic or predictive

accuracy). Examples could include (but were not limited to) data assessing the association between variables and:

- diagnosis (diagnostic association studies)
- a future outcome (prognostic association studies).

Ideally, data is reported as hazard ratios (if measured over time), or odds ratios or risk ratios (if measured at a specific time point).

If hazard ratios, and odds ratios or risk ratios are reported, the same methods for meta-analysis of odds ratios and relative risks are used. This is described in the section on data synthesis for intervention studies. When these measures are not reported, the approach to reporting is agreed with NICE staff with responsibility for quality assurance.

Data synthesis for qualitative reviews
SIGN reviewed the qualitative evidence for the initial guideline and first update. Relevance for the included studies was established via the exclusion and inclusion criteria agreed within the scoping process. The included studies were critically appraised using the Critical Appraisal Skills Programme (CASP) qualitative checklist.

A full thematic synthesis was not done because of the limited amount of relevant information available, but key themes were identified and grouped into concepts. These concepts were presented against the review questions, for example, what people's experiences of symptoms or investigations were. They were also supported by quotes from the data.

Appraising the quality of evidence

Intervention studies (relative effect estimates)
Randomised controlled trials and quasi-randomised controlled trials are quality assessed using the Cochrane Risk of Bias Tool. Non-randomised controlled trials and cohort studies are quality assessed using the ROBINS-I tool. Other study types (for example, controlled before and after studies) are assessed using the preferred option specified in NICE's guidelines manual 2018 (appendix H).

GRADE for intervention studies analysed using pairwise analysis
GRADE is used to assess the quality of evidence for the outcomes specified in the review protocol. Outcomes from randomised controlled trials, non-randomised controlled trials and cohort studies (which are quality assessed using the Cochrane Risk of Bias Tool or ROBINS-I) are initially rated as high quality. Data from other study types is initially rated as low quality. The quality of the evidence for each outcome is downgraded or not from this initial point.

Association studies
Individual prognostic studies presenting data on association are quality assessed using the Quality in Prognostic Studies (QUIPS) checklist. Other cohort and case-control studies are quality assessed using the CASP cohort study checklist and CASP case-control checklist respectively. Individual cross-sectional studies are quality assessed using the Joanna Briggs Institute critical appraisal checklist for analytical cross-sectional studies (2016). This contains 8 questions covering: inclusion criteria, description of the sample, measures of exposure, measures of outcomes, confounding factors and statistical analysis.

Modified GRADE for association data
GRADE has not been developed for use with association studies, so a modified approach is applied using the GRADE framework. Data from cohort, cross-sectional and case-control studies is initially rated as high quality, with the quality of the evidence for each outcome then downgraded or not from this initial point.

Qualitative studies
Individual qualitative studies are quality assessed using the CASP qualitative checklist to consider appropriateness of the methodology applied, validity and relevance to the key question. GRADE CERQual (Confidence in the Evidence from Reviews of Qualitative Research) is only used if there is sufficient evidence.

Cost effectiveness
Because of the urgency for publishing guidance on long-term effects of COVID-19, no health economic analyses have been done.

Developing recommendations
Recommendations are developed or updated based on the expert advisory panel's discussions of:

- the overall quality of the evidence or confidence in the expert opinion
- the trade-off between benefits and harms
- the impact on equity and equality
- the feasibility of implementation (for example, resources, capacity, settings and acceptability).

Research recommendations
Research recommendations are developed by the expert advisory panel when:

- there is a lack of evidence
- the evidence is uncertain.

Quality assurance
Pragmatic checks and review are done iteratively throughout guideline development and during updates by NICE and SIGN staff with responsibility for quality assurance.

Consultation
Final recommendations are ratified by the expert advisory panel and external stakeholders through a targeted peer-review process. A range of stakeholders are invited to take part, including relevant national professional, and patient or carer groups.

NICE staff collate all comments from stakeholders, so the independent advisory expert panel can consider them. The panel then advises on changes to the recommendation(s) and responses to stakeholder comments. Comments from stakeholders are grouped into themes. Thematic responses are provided to address these themes, instead of responding to individual comments.

All stakeholder comments and thematic responses are available on the NICE guideline page on managing the long-term effects of COVID-19.

Sign off
NICE's guidance executive sign off the guideline, either when new recommendations are published or when recommendations are updated.

Surveillance and future updates
Guideline recommendations are maintained using a continuous 'living' surveillance approach. This ensures that recommendations are updated continuously to reflect changes in:

- the evidence base
- clinical or healthcare practice
- the health and social care system, and government policy.

Living surveillance uses a multifactorial approach to identify 'triggers' for update. This approach includes:

- identifying studies relevant to the scope through weekly evidence searches
- looking at relevant professional guidance in the area
- intelligence gathering, including feedback from the broader health and social care system
- monitoring ongoing research and checking for publication of these ongoing studies regularly.

Surveillance decisions and outcomes are based on continual assessment of the impact of all the new evidence and intelligence that has been identified. There are 4 possible surveillance outcomes:

No update: recommendations will not be updated if new evidence or intelligence does not suggest that any changes are needed.

Refresh of the recommendations: this involves simple editorial changes that improve the usability of the recommendations without changing the intent, or correction of factual errors.

Rapid update of the recommendations: the recommendations could be updated if changes are needed (for example, new evidence emerges). Examples of updates include:

- covering additional populations or settings
- addressing new review questions
- changes to the original review questions, which mean a new search of the evidence is needed
- when new evidence contradicts existing recommendations.

Withdrawal of recommendations: recommendations may be withdrawn if:

- they are no longer needed, for example, because service delivery has changed (such as normal services resuming) or the recommendations are likely to have limited relevance because of changes in context
- there are safety issues (for example, there is evidence of harm to people using the service)
- the recommendations are duplicated somewhere else (for example, if the recommendations are merged with another guideline).

Funding
NICE is an executive non-departmental public body sponsored by the Department of Health and Social Care.

A range of organisations, including the Department of Health and Social Care, arms-length bodies, professional associations, and voluntary and community sector groups are invited to become stakeholders. Stakeholders review and comment on draft recommendations as part of a targeted peer review. Stakeholders do not contribute to the systematic review and evidence appraisal process, or determine the final wording of recommendations.

13.2 Evidence reviews

In August 2022, a new evidence review was undertaken for the key question on:

- Impact of COVID-19 vaccines

For the November 2021 update, new evidence reviews were undertaken for key questions on:

- case definition (quantitative and qualitative reviews)
- referral to services (qualitative)
- children and young people
- impact of vaccines on the long-term effects of COVID-19.

Additionally, updates were undertaken to evidence reviews on:

- signs, symptoms and prevalence
- risk factors.

Expert testimony was heard for the key questions of

- vaccines (Steves 2021)
- rehabilitation (Nicol 2021, Nuffield Health 2021, Locke 2021)
- children and young people (Whittaker 2021, Stark 2021, Stephenson 2021).

There were no updates to evidence reviews on investigations, monitoring and referral, interventions, service organisation and views and experiences of patients, their families and carers. The evidence reviews for the first version of the guideline are available as follows:

- Prevalence 2020 review
- Risk factors 2020 review
- Investigations 2020 review
- Interventions 2020 review
- Monitoring and referral 2020 review
- Service organisation 2020 review

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