The effectiveness of vaccination against long COVID

A rapid evidence briefing

Contents

Main messages

1. Fifteen studies were identified that reported on the effectiveness of vaccination against long COVID (search up to 12 January 2022): 7 studies examined whether vaccination before infection reduced the symptoms or incidence of long COVID, 7 studies examined whether vaccination in people with long COVID reduced or cleared the symptoms of long COVID, and one study examined both.

2. Six of the 8 studies assessing the effectiveness of vaccination before coronavirus (COVID-19) infection suggested that vaccinated cases (one or 2 doses) were less likely to develop symptoms of long COVID following infection, in the short term (4 weeks after infection), medium term (12 to 20 weeks after infection) and long term (6 months after infection). As all 8 studies included only participants who had COVID-19, the effect of vaccination on reduced incidence of COVID-19 is not accounted for. This means these studies do not give a total population estimate for the effectiveness of vaccines to prevent long COVID, but rather underestimate it. From 2 studies that measured individual long COVID symptoms, fully vaccinated cases were less likely to have the following symptoms in the medium or long term than unvaccinated cases: fatigue, headache, weakness in arms and legs, persistent muscle pain, hair loss, dizziness, shortness of breath, anosmia, interstitial lung disease, myalgia, and other pain.

3. In studies examining the effect of vaccination among people with long COVID, 3 of 4 studies comparing long COVID symptoms before and after vaccination suggested that more cases reported an improvement in symptoms after vaccination, either immediately or over several weeks. There were, however, some cases in all studies who reported a worsening in symptoms after vaccination.

4. Three studies of people with long COVID who were unvaccinated when they were initially infected, compared people who were subsequently vaccinated and people who remained unvaccinated. All these studies suggested that people with long-COVID were less likely to report long COVID symptoms shortly after vaccination, and over longer periods, than people with long COVID who were not subsequently vaccinated. One study looked at the timing of vaccination after COVID-19 diagnosis, and suggested that cases who were vaccinated sooner rather than later after diagnosis were much less likely to report symptoms of long COVID than cases who remained unvaccinated.

5. In 3 of the 5 studies reporting on symptom changes following vaccination of people with long COVID, there was a higher proportion of people with long COVID who reported unchanged symptoms following vaccination (up to 70%) than people whose symptoms improved or worsened.

6. All studies were observational, so the results may be from differences other than vaccination, and there was large heterogeneity between studies in the definition of long COVID.

Background

Long COVID, also known as post acute sequalae of a SARS-CoV-2 infection and post COVID-19 syndrome, has several definitions, but typically includes having persistent symptoms of COVID-19, usually for weeks but potentially for months or years (1,2). Symptoms commonly include fatigue, shortness of breath and a persistent cough, although many other symptoms have been reported (3). As of 6 December 2021, 1.3 million people in the UK (2% of the population) reported experiencing long COVID symptoms for more than 4 weeks after the initial infection (4). Vaccination against COVID-19 reduces the risk of symptomatic COVID-19 infection (5), though vaccination may additionally reduce the risk of long COVID if a vaccinated person is infected with COVID-19 (1,2). While there is no recommendation against vaccination in people with long COVID (6), it is unclear whether vaccination of previously unvaccinated people with long COVID is more likely to improve or worsen long COVID symptoms (7,8).

The purpose of this rapid evidence briefing is to provide evidence relating to the effectiveness of vaccination against long COVID, both for vaccinations given before infection with COVID-19 (effectiveness against incidence of long COVID), and for vaccinations given after infection with COVID-19 and development of long COVID symptoms (effectiveness for reducing or eliminating symptoms of long COVID).

Methods

A rapid search was undertaken on 12 January 2022 to identify primary studies related to the effectiveness of vaccination against long COVID. We searched a number of specialist COVID-19 review repositories and ran a broad search using Medline, Embase, NLM COVID portfolio (for preprints), WHO COVID Database and Google. As this work was conducted at pace, data was extracted directly into a narrative summary. The quality criteria checklist (QCC) tool was used to rate the quality of included studies as low, medium, or high quality. Full details of the methods are available in Appendix A.

Evidence

Fifteen studies reported on the effectiveness of vaccination against long COVID. Four studies were conducted in the UK (7 to 10), 4 studies in the US (11 to 14), one study in France (15), 2 studies in India (16, 17), one study in Indonesia (18), one study in Israel (19), and 2 studies were conducted online with participants from multiple countries (20 to 22). Seven studies examined whether vaccination before infection reduced the symptoms or incidence of long COVID (9, 11, 12, 16 to 19), 7 studies examined whether vaccination in people with long

COVID reduced or cleared the symptoms of long COVID ([7](#), [8](#), [10](#), [14](#), [15](#), [20 to 22](#)), and one study examined both ([13](#)). Table one shows the characteristics of each included study.

Most studies used different definitions of long COVID, as such these definitions are given in the summaries below. In all studies, fully vaccinated is defined as 2 doses of any 2 dose vaccine or one dose of a single dose vaccine, and partially vaccinated is defined as a single dose of a 2 dose vaccine. Where the vaccine brand (for example, Pfizer, AstraZeneca) is available, this is reported.

Vaccination before infection

Note that all 8 studies included in this section only include participants who had COVID-19, so the effect of vaccination to reduce incidence of COVID-19 is not accounted for. This means all studies will likely underestimate the effectiveness of vaccines to prevent long COVID. A nested case-control study by Antonelli and others (2022, rated as medium quality) examined whether vaccination for COVID-19 before infection was associated with long duration symptoms of COVID-19 (at least 28 days) in adults who reported testing positive on RT-PCR (reverse transcriptase polymerase chain reaction) or LFD (lateral flow device) for COVID-19 on the COVID symptom study phone app (ZOE) between 8 December 2020 and 4 July 2021 in the UK ([9](#)).

In total, 6,030 participants reported a positive test at least 14 days after their first vaccination but before their second (partially vaccinated, tested a median of 67 days after vaccination), and 2,370 at least 7 days after their second vaccine (fully vaccinated, tested a median of 44 days after vaccination). The same number of unvaccinated participants who tested positive were matched with those who were partially and fully vaccinated, accounting for date of positive test, healthcare worker status, sex, body mass index, and age.

The results suggested that:

- fully vaccinated participants were about half as likely to have symptoms lasting at least 28 days than unvaccinated participants (odds ratio [OR] = 0.51, 95% confidence interval [CI]: 0.32 to 0.82, p=0.005), whereas partially vaccinated participants were about as likely to have symptoms lasting at least 28 days than unvaccinated participants (OR = 1.04, 95% CI: 0.86 to 1.25, p=0.69)
- fully vaccinated younger adults (18 to 59 years) were much less likely to have symptoms lasting at least 28 days than younger unvaccinated adults (OR = 0.21, 95% CI: 0.08 to 0.59, p=0.003)

A retrospective cohort study by Al-Aly and others (2021, preprint, rated as medium quality) examined whether vaccination for COVID-19 before infection was associated with post-acute sequelae of COVID-19 (symptoms of COVID-19 at 6 months) in adults who had a positive test

for COVID-19 in the United States Veterans Health Administration electronic health databases between 1 February and 31 August 2021 in the US ([12](#)).

Vaccinated cases (n=16,035, mean age of 67 years, 71% white race, 91% male) were matched (and weighted) with unvaccinated cases (n=48,536, mean age of 56 years, 71% white, 86% male), accounting for age, race, sex, socioeconomic deprivation, smoking status, health conditions and information, data of test and hospital information. Post-acute sequalae of COVID-19 included cardiovascular disorders, coagulation, fatigue, gastrointestinal disorders, kidney disorders, mental health disorders, metabolic disorders, musculoskeletal disorders, neurologic disorders, and pulmonary disorders.

The results suggested that:

- vaccinated cases were less likely to have at least one post-acute sequalae of COVID-19 at 6 months compared with unvaccinated cases (hazard ratio [HR] = 0.87, 95% confidence interval [CI]: 0.83 to 0.92).

A retrospective cohort study by Arjun and others (2022, preprint, rated as medium quality) examined whether vaccination for COVID-19 before infection (confirmed with RT-PCR) was associated with self-reported long COVID symptoms (including fatigue, cough, loss of taste and smell and cognitive dysfunction 4 weeks from the date of diagnosis) in adults (at least 18 years) who were diagnosed with COVID-19 between April and September 2021 in India ([16](#)). In total, 487 participants who tested positive for COVID-19 in a single hospital responded, with a mean age of 39 years, 41% female, and 59% of participants had 2 doses of a COVID-19 vaccine (the majority had Covaxin), 17% had one dose, and 25% were unvaccinated. The analysis was adjusted for age, sex, occupation, body mass index, substance use, past COVID-19 infection, comorbidities, number of COVID-19 symptoms and severity of COVID-19 disease.

The results suggested that:

- fully vaccinated participants were more likely to have long COVID symptoms 4 weeks from the date of diagnosis than unvaccinated participants (OR = 2.32, 95% CI: 1.17 to 4.58, p=0.01)
- note that these results are in the opposite direction to all other studies, that is, that cases who were fully vaccinated had a greater chance of subsequently developing long COVID symptoms, and more analysis is needed to understand why this may be the case

A retrospective cohort study (POST-COVID) by Herman and others (2022, preprint, rated as medium quality) examined whether vaccination for COVID-19 before infection with COVID-19 (confirmed by RT-PCR, Nucleic Acid Amplification Test [NAAT] or rapid antigen test) was associated with olfactory dysfunction (anosmia or hyposmia) 2 and 4 weeks after the end of

infection in cases recruited up to December 2021 in Indonesia ([18](#)). Fully vaccinated participants (2 doses, n=221, mean age of 32 years, 50% female) more than 14 days before infection were matched with participants who were not fully vaccinated more than 14 days before infection (including unvaccinated and partially vaccinated cases, n=221, mean age of 32 years, 50% female), accounting for occupation, education, island, type of living area, living companion, age and hypertension status.

The results suggested that:

- while fully vaccinated participants were less likely to develop olfactory dysfunction after infection than unvaccinated participants (OR = 0.31, 95% CI: 0.10 to 0.94), there was little evidence for an association between full vaccination and olfactory dysfunction 4 weeks after the end of infection (p=0.59)

A cross-sectional study nested in a prospective cohort study by Kuodi and others (2022, preprint, rated as medium quality) examined whether vaccination for COVID-19 before infection was associated with long-term physical, mental, and psychosocial consequences of COVID-19 in adults who tested positive for COVID-19 (RT-PCR) between 15 March 2020 and 15 June 2021 in Israel ([19](#)). Study participants (n=951, 294 fully vaccinated [2 doses], 340 partially vaccinated [one dose], 317 unvaccinated), who tested positive for COVID-19 in one of 3 government hospitals, completed a survey between 16 July and 18 November 2021 detailing their COVID-19 test results, vaccination status, number of doses, type of vaccine and date of administration, and symptoms experienced at the time of filling out the survey. In total, 337 of 951 participants (35%) reported not fully recovering from the initial COVID-19 symptoms at follow-up.

The results suggested that:

- compared with unvaccinated participants, participants with 2 or 3 doses of vaccine were 54% to 83% less likely to report 7 of the 10 most commonly reported symptoms (see below)
- for most symptoms, the vaccine effectiveness against symptoms reported at follow-up was highest for older participants (more than 60 years) and lowest for younger participants (19 to 35 years), with the exceptions of hair loss (highest in 36 to 60 year olds), persistent cough (similar in all age groups) and feeling fully recovered from COVID-19 (highest in 19 to 35 year olds).

Additionally, the relative risks (RR) of each symptom, comparing participants who received 2 or 3 doses of vaccine with unvaccinated participants (relative risks less than one indicate that fewer vaccinated compared with unvaccinated participants had the symptom at follow-up) were:

- fatigue: RR = 0.36 (95% CI: 0.19 to 0.71, p=0.003)

- headache: RR = 0.46 (95% CI: 0.26 to 0.83, p=0.01)
- weakness in arms and legs: RR = 0.43 (95% CI: 0.20 to 0.94, p=0.03)
- persistent muscle pain: RR = 0.32 (95% CI: 0.11 to 0.88, p=0.03)
- loss of concentration: RR = 0.59 (95% CI: 0.17 to 2.06, p=0.41)
- hair loss: RR = 0.17 (95% CI: 0.06 to 0.60, p=0.005)
- sleeping problems: RR = 0.53 (95% CI: 0.18 to 1.61, p=0.26)
- dizziness: RR = 0.26 (95% CI: 0.09 to 1.79, p=0.02)
- persistent cough: RR = 0.72 (95% CI: 0.28 to 1.83, p=0.48)
- shortness of breath: RR = 0.23 (95% CI: 0.07 to 0.84, p=0.03)
- feeling fully recovered from COVID-19: RR = 0.98 (95% CI: 0.80 to 1.21, p=0.86)

A cross-sectional study by Senjam and others (2021, preprint, rated as medium quality) examined whether vaccination for COVID-19 before infection was associated with symptoms of long COVID (symptoms present between 4 and 12 weeks [short-term] or beyond 12 weeks [long-term] after a positive RT-PCR or cartridge based NAAT) in adults (at least 18 years) who tested positive for COVID-19 between one January and 30 April 2021 in India ([17](#)). A total of 773 participants, who tested positive in a single hospital, completed a survey between June and July 2021 (median age of 34 years, 56% male, 33% with short-term long COVID symptoms, 13% with long-term long COVID symptoms, 53% unvaccinated, 25% fully vaccinated [2 doses]). The most commonly reported long COVID symptoms were fatigue, pain in the joints and muscle, hair loss, headache, cough, breathlessness, sleep disorders, sore throat and decrease of smell and taste.

The results suggested that:

- fully vaccinated (2 doses) participants were less likely to have long COVID symptoms (not stated if these were short-term, long-term or both) than unvaccinated participants (OR = 0.55, 95% CI: 0.37 to 0.85)

A retrospective cohort study by Simon and others (2021, preprint, rated as high quality) examined whether vaccination for COVID-19 before or after infection was associated with long COVID (COVID-19 symptoms present between 12 and 20 weeks after COVID-19 diagnosis) in cases who were diagnosed with, or tested positive for (NAAT or antigen test), COVID-19 between one January 2020 and 31 May 2021 in the US ([13](#)). In total, 240,648 cases were included, 220,460 (92%) cases were unvaccinated by 12 weeks after their COVID-19 diagnosis, 2,392 (1.0%) cases received one dose of vaccine before their diagnosis, and 17,796 (7.4%) cases received one dose of vaccine within 12 weeks of their diagnosis. COVID-19 symptoms included: chest pain, palpitations, altered mental state, anorexia, chills, fatigue, fever, malaise, loss of sense of smell, loss of sense of taste, nasal congestion, sore throat, abdominal pain, diarrhoea, digestive changes, nausea, vomiting, arthralgia, muscle weakness, general weakness, myalgia, headache, cough and dyspnoea.

The results suggested that:

- cases who were vaccinated before diagnosis were much less likely to have any symptoms of long COVID between 12 and 20 weeks after diagnosis than cases who were unvaccinated up to 12 weeks after their diagnosis (OR = 0.22, 95% CI: 0.20 to 0.25, p<0.005), and even less likely to have more than one symptom of long COVID (OR = 0.11, 95% CI: 0.09 to 0.14, p<0.005)

A matched case-control study by Taquet and others (2021, preprint, rated as high quality) examined whether vaccination for COVID-19 before infection (confirmed diagnosis or positive RT-PCR test) was associated with documented consequences of COVID-19 in people in the 6 months after an infection, with infection occurring between one January and 31 August 2021, primarily in the US (11). Data was obtained from TriNetX Analytics, which contains data from 59 healthcare organisations and 81 million patients. In total, 9,479 vaccinated cases (n=2,996 with one dose and n=6,957 with 2 doses of any vaccine received at least 14 days before infection during the study) were matched with the same number of unvaccinated cases (who had received an influenza vaccine), accounting for age, sex, ethnicity, obesity, socioeconomic deprivation and specific health conditions, as well as date of infection. The mean age of participants was 57 years, 59% were female, and of those who were vaccinated, 65% had the Pfizer vaccine, 9% the Moderna vaccine, 1.6% the Januaryssen vaccine, and 24% had an unspecified vaccine. A composite long COVID outcome was defined as having a diagnosis of any of the following symptoms in the 6 months after infection: abdominal symptoms, abnormal bleeding, anxiety or depression, chest or throat pain, cognitive symptoms, fatigue, headache, myalgia and other pain, as well as death (to account for differences in survival between vaccinated and unvaccinated participants).

The results suggested that:

- there was no association between vaccination (comparing participants with 2 doses of vaccine with unvaccinated participants) and the composite long COVID outcome in the 6 months after infection: hazard ratio (HR) = 1.00 (95% CI: 0.95 to 1.06); 64.9% and 65.6% of vaccinated and unvaccinated participants had a long COVID symptom respectively.

However, participants with 2 doses of vaccine, when compared with unvaccinated participants, were less likely to be diagnosed with:

- anosmia: HR = 0.68 (95% CI: 0.55 to 0.84, p=0.0004)
- fatigue: HR = 0.86 (95% CI: 0.77 to 0.96, p=0.005)
- hair loss: HR = 0.66 (95% CI: 0.54 to 0.81, p<0.0001)
- interstitial lung disease: HR = 0.74 (95% CI: 0.62 to 0.88, p=0.0006)
- myalgia: HR = 0.70 (95% CI: 0.59 to 0.84, p<0.0001)
- other pain: HR = 0.85 (95% CI: 0.76 to 0.96, p=0.007)

Vaccination after infection

A prospective cohort by Arnold and others (2021, preprint, rated as medium quality) examined the effect of vaccination (with Pfizer or AstraZeneca) on long COVID symptoms in previously unvaccinated participants who were hospitalised with COVID-19 in April and May 2020 and either remained unvaccinated or were vaccinated (Pfizer or AstraZeneca) in January or February 2021 in the UK (7). Vaccinated participants (n=44, median age 64 years, 64% male, 82% symptomatic 8 months after infection) were matched with unvaccinated participants (n=22, median age 55 years, 59% male, 82% symptomatic 8 months after infection), accounting for symptomatology and quality of life at 8 months after infection, and all participants were asked about whether they had symptoms, and whether they had improved, stayed the same, or worsened following vaccination.

The results suggested that:

- at one month after vaccination (or a matched time for unvaccinated cases), more vaccinated participants reported their symptoms improved than unvaccinated participants (23.2% versus 15.4%), and fewer vaccinated participants reported their symptoms worsened than unvaccinated participants (25.6% versus 14.3%, p=0.035 for all differences). A similar percentage of vaccinated and unvaccinated participants had unchanged symptoms (71.1% versus 70.3%)

A prospective cohort (the Office of National Statistics COVID-19 infection survey [CIS]) study by Ayoubkhani and others (2021, preprint, rated as high quality) examined the effect of vaccination on long COVID symptoms in previously unvaccinated adults (18 to 69 years) between 3 February and 5 September 2021 in the UK (8). Participants in the CIS were randomly sampled from UK households, and were visited monthly to both provide a swab for RT-PCR testing and to be asked if they would describe themselves are currently experiencing long COVID (in this analysis, symptoms persisting at least 12 weeks from a confirmed or suspected COVID-19 infection that could not be explained by another health condition).

All participants had their first vaccine dose by 5 September 2021 (n=28,356), 45.7% after 3 February 2021, and 83.8% had their second vaccine dose by 5 September 2021 (n=23,753). There were 6,729 participants (23.7%) that reported they had long COVID symptoms, including fever, headache, muscle ache, weakness or tiredness, nausea or vomiting, abdominal pain, diarrhoea, loss of appetite, loss of taste, loss of smell, sore throat, cough, shortness of breath, chest pain, palpitations, vertigo or dizziness, worry or anxiety, low mood or not enjoying anything, trouble sleeping, memory loss or confusion, or difficulty concentrating.

The results suggested that both the first and second vaccine doses were associated with reduced odds of reporting long COVID symptoms shortly after vaccination:

- first vaccine dose: OR = 0.87 (95% CI: 0.81 to 0.93, p<0.001)
- second vaccine dose: OR = 0.91 (95% CI: 0.86 to 0.97, p=0.003)
- the second vaccine dose was also associated with a long-term decrease in the odds of reporting long COVID symptoms (p=0.03)

Additionally, the results were similar for activity limiting long COVID (n=4,747 reported activity limiting long COVID):

- first vaccine dose: OR = 0.88 (95% CI: 0.81 to 0.96, p=0.003)
- second vaccine dose: OR = 0.91 (95% CI: 0.84 to 0.98, p=0.01)
- the second vaccine dose was also associated with a long-term decrease in the odds of reporting long COVID symptoms (p=0.03)

Finally, there was little evidence for differences in results between mRNA and adenovirus vaccine types, and the results suggested that the odds of experiencing most symptoms of long COVID decreased with the first and second doses of vaccine, though these results were relatively imprecise.

A prospective cohort study by Gaber and others (2021, rated as medium quality) asked health care workers in the UK with long COVID whether vaccination between December 2020 and January 2021 changed their long COVID symptoms ([10]). Of 67 healthcare workers with long COVID receiving the vaccine, 75% had fatigue, 53% had shortness of breath, and 18% had anxiety.

The results suggested that:

- several weeks after vaccination, 14 (21%) participants reported an improvement in one or more of their symptoms, 8 (12%) participants reported a worsening in symptoms, and 45 (67%) participants reported no change in their symptoms

An online survey (LongCovidSOS) by Strain and others (2021, preprint, rated as medium quality) asked people in the UK and elsewhere with long COVID (positive RT-PCR or antigen test not required) whether their symptoms improved or worsened following vaccination ([21],[22]). The survey was completed by 812 respondents (96% above 30 years old, 80% women) in March and April 2021, 41% of participants had a confirmed COVID-19 infection, 50% had the AstraZeneca vaccine, 40% the Pfizer vaccine, 8.6% the Moderna vaccine, 14% had 2 doses of any vaccine, and 40% of participants had at least 30 days between their last vaccine and completing the survey. Long COVID symptoms included fatigue, brain fog, myalgia, shortness of breath, insomnia, chest pain or palpitations, gastrointestinal symptoms, anosmia, autonomic dysfunction, postural orthostatic tachycardia syndrome, persistent cough, fever, rash (including COVID toes) and vascular complications.

The results suggested that:

- of all participants, 57% reported an improvement in symptoms after vaccination, 25% of participants reported no change in symptoms, while 19% of participants reported a worsening of symptoms, with Moderna having the most participants report an improvement and least report a deterioration.

Additionally, when responses to individual symptoms were grouped together, more participants had all or some of their symptoms improve than worsen:

- all improved: 11%
- some improved: 16%
- mixture: 24%
- no change: 42%
- some got worse: 3.8%
- all got worse: 2.9%

An online survey by Scherlinger and others (2022, rated as medium quality) asked French-speaking adults with post-acute sequelae of COVID-19 (PASC, persistent symptoms lasting more than 4 weeks after probable or confirmed COVID-19 infection and no alternative diagnosis to explain the symptoms) whether their symptoms improved or worsened following vaccination (Pfizer [78%], Moderna [16%], AstraZeneca [4%]) ([20](#)). The survey was completed by 567 respondents (median age 44 years, 83% women) in August 2021, 64% of participants had a confirmed COVID-19 infection, 25% had one vaccine dose and 45% had 2 vaccine doses. Symptoms of PASC included fever or chills, fatigue, brain fog, headaches, changing mood or impact on morale, sleeping issues, costal pain, dyspnoea, cough, palpitations, muscle aches, joint pain, paraesthesia or tingling, anosmia or ageusia, diarrhoea or vomiting, spontaneous bruises, and pruritus.

The results suggested that:

- of the 380 participants who reported long COVID at the time of vaccination, 117 (31%) reported a global worsening of symptoms (including fever/chills [74%], gastro-intestinal symptoms [70%], paraesthesia [64%] and arthralgia [63%]), whereas 83 (21.8%) reported a global improvement in symptoms (including anosmia [62%] and brain fog [51%]), and 179 (47%) reported no change in symptoms following vaccination.
- the symptoms thought to be affected by vaccination persisted for more than 2 weeks after vaccination in 64% of participants reporting a worsening in symptoms, and in 73% of participants reporting an improvement.
- there was little evidence of differences in results between vaccine types (p=0.60)

A retrospective cohort study by Simon and others (2021, preprint, rated as high quality), detailed above, examined whether vaccination for COVID-19 before or after infection was associated with long COVID (COVID-19 symptoms present between 12 and 20 weeks after COVID-19 diagnosis) in cases who were diagnosed with, or tested positive for (NAAT or antigen test), COVID-19 between one January 2020 and 31 May 2021 in the US (13).

The results suggested that:

- cases who were vaccinated 0 to 4 weeks after diagnosis were much less likely to have any symptoms of long COVID between 12 and 20 weeks after diagnosis than cases who were unvaccinated up to 12 weeks after their diagnosis (OR = 0.38, 95% CI: 0.35 to 0.41, p<0.005), and even less likely to have more than one symptom of long COVID (OR = 0.19, 95% CI: 0.16 to 0.22, p<0.005)
- cases who were vaccinated 4 to 8 weeks after diagnosis were less likely to have any symptoms of long COVID between 12 and 20 weeks after diagnosis than cases who were unvaccinated up to 12 weeks after their diagnosis (OR = 0.54, 95% CI: 0.51 to 0.57, p<0.005), and much less likely to have more than one symptom of long COVID (OR = 0.32, 95% CI: 0.29 to 0.35, p<0.005)
- cases who were vaccinated 8 to 12 weeks after diagnosis were less likely to have any symptoms of long COVID between 12 and 20 weeks after diagnosis than cases who were unvaccinated up to 12 weeks after their diagnosis (OR = 0.75, 95% CI: 0.71 to 0.78, p<0.005), and much less likely to have more than one symptom of long COVID (OR = 0.46, 95% CI: 0.43 to 0.49, p<0.005)

A prospective cohort (ComPaRe long COVID cohort) study by Tran and others (2021, preprint, rated as high quality) examined the effect of vaccination on long COVID symptoms in adults (at least 18 years old) who had a COVID-19 infection (confirmed or suspected) and subsequent long COVID symptoms (symptoms persisting more than 3 weeks past initial infection) between November 2020 and May 2021 in France (15). Participants (n=910, median age of 47 years, 80.5% female, median of 10.7 months of symptoms) were contacted every 60 days and asked about 53 COVID-19 symptoms (to form a COVID ST score, from 0 to 53, representing the number of different symptoms), and every 45 days and asked about vaccination status. Vaccinated (n=455) and unvaccinated (n=455) participants were matched on sex, age, education, comorbidities, confirmed COVID-19 infection, hospitalisation for COVID-19, time from COVID-19 infection and COVID-19 symptoms.

The results suggested that:

- long COVID symptoms were less severe in vaccinated compared with unvaccinated participants 120 days after recruitment (mean difference in COVID ST score = -1.8, 95% CI: -2.5 to -1.0), and more vaccinated than unvaccinated participants had remission of all long COVID symptoms (16.6% versus 7.5%, HR = 1.97, 95% CI: 1.23 to 3.15)

- the impact of long COVID on the lives of vaccinated participants was also less than unvaccinated participants (mean difference in COVID impact score = -3.3, 95% CI: -6.2 to -0.5), and fewer vaccinated participants found their symptoms unacceptable (38.9% versus 46.4%, risk difference = -7.5%, 95% CI: -14.4% to -0.5%)

An online survey conducted by Wanga and others (2021, rated as medium quality) compared long-term symptom changes after receiving a COVID-19 vaccination in adults with and without a previous COVID-19 infection in the US ([14]). The survey was completed in April 2021 (n=100 COVID-19 cases, n=285 adults who had always received a negative COVID-19 test result), and long-term symptoms were defined as symptoms lasting longer than 4 weeks after a positive test for COVID-19 cases, and symptoms lasting longer than 4 weeks after they first started for adults who never had COVID-19. The analysis accounted for sex, age, region, race and ethnicity and education. Long-term symptoms included change in mood, change in smell or taste, chest pain or pressure, cough, diarrhoea, difficulty thinking clearly, concentrating, forgetfulness, memory loss or "brain fog", fatigue, tired, or weakness, fever or chills, hair loss, headache, joint or muscle pain, nausea or vomiting, palpitations (heart racing or pounding), post-exertional malaise (worsening of symptoms after even minor physical, mental, or emotional exertion), problems sleeping, shortness of breath or breathlessness, sore throat, stomach pain, or other symptoms.

The results suggested that:

- COVID-19 cases were more likely to report that the vaccine improved their long-term symptoms than adults who never tested positive for COVID-19 (28.7% versus 15.7%, p=0.023)
- however COVID-19 cases were also more likely to report that their symptoms worsened following the vaccination (although this was not statistically significant, 16.1% versus 11.2%, p=0.27), and that their symptoms were gone before receiving the vaccine (28.4% versus 13.1%, p=0.007)
- fewer COVID-19 cases reported that the vaccine did not affect their symptoms at all (26.4% versus 59.2%)

Research in progress

Four additional studies were identified that are still in progress:

- an NIHR funded study by Prieto-Alhambra and others will examine the effect of different COVID-19 vaccines on long COVID in the UK (23)
- a study by Massey and others ('Project COVID recovery: vaccination study') will measure the changes in participants' moderate to severe PASC symptoms at 6, 12 and 15 weeks after vaccination in the US (24)
- a study by Premkumar others (EvaLongCovid, NCT05107271) will measure long haul COVID-19 related symptoms in adults with chronic liver disease in India (25)
- a randomised controlled trial by the Área de Ensayos Clínicos (EUCTR2021-003331-28-ES) will randomise adults with COVID symptoms persisting 3 weeks after the acute phase of COVID-19 in Spain to either the Pfizer vaccine or placebo, and measure the change in frequency and intensity of symptoms (26)

Research limitations

Most studies included in this report compared people with COVID-19 or long COVID who were vaccinated with people who were not vaccinated. As there are many differences between people who are and are not vaccinated, there is a risk in all these studies that factors other than vaccination status may have influenced the results (in any direction), although some studies accounted for this well (8,11 to 13,15). The selection of participants may also have affected the results, especially for the online surveys, as people may have chosen to take part because they had either good or poor experiences with long COVID and vaccination, and for studies that recruited from hospitals, where participants may have had more severe disease or comorbidities. In studies where participants report on symptom change shortly after vaccination, the results may reflect short-term reactions to vaccination in addition to changes in long-term symptoms.

Long COVID was defined inconsistently across studies, both in terms of the symptoms that would comprise long COVID, but also the time frame in which the symptoms needed to be present (long COVID, or post-COVID syndrome, in the UK is typically defined as COVID-19 symptoms beyond 12 weeks). This is particularly true of the studies were long COVID was defined as a composite of several different symptoms. This increased the heterogeneity between studies, though as the results were still relatively consistent, this may also be considered a strength. The studies were also conducted at different points in the pandemic and in different countries, and notably no studies accounted for, or reported on, the COVID-19 variant in their analyses.

The studies where vaccination occurred before infection only included people who were infected with COVID-19, meaning no effect of vaccination on preventing COVID-19 infection in the first place was included in the results. As such, the total effect of vaccination on prevention of long COVID will have been underestimated.

Review limitations

This summary was produced at pace over several days so formal data extraction was not conducted. Most of the work was completed by one reviewer, although all narrative summaries were checked by a second reviewer.

Conclusion

There is evidence that vaccinated people who are subsequently infected with COVID-19 are less likely to report symptoms of long COVID than unvaccinated people, in the short term (4 weeks after infection), medium term (12 to 20 weeks after infection) and long term (6 months after infection). This is in addition to any benefit of vaccination in preventing COVID-19 infection (5). There is also evidence that unvaccinated people with long COVID who were subsequently vaccinated had, on average, reduced long COVID symptoms (though some people reported worsened symptoms after vaccination). Additionally, there was evidence that unvaccinated people with long COVID who were subsequently vaccinated reported fewer long COVID symptoms than those who remained unvaccinated. However, there is a risk of bias across all studies due to differences in people who were vaccinated and unvaccinated, the measurement of outcomes, and in the selection of participants.

Acknowledgement

We would like to thank colleagues within the Public Health Advice, Guidance and Expertise function who either reviewed or input into aspects of the review, particularly Graham Burns, Andrew Lee, Jamie Lopez Bernal, and Allison Streetly.

Disclaimer

UKHSA's rapid reviews aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, unpublished reports and papers on preprint servers. Please note that the reviews:

1. Use accelerated methods and may not be representative of the whole body of evidence publicly available.
2. Have undergone an internal, but not independent, peer review.
3. Are only valid as of the date stated on the review.

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Table 1a. Study characteristics: vaccination before infection

Acronyms: LFD = lateral flow device, NAAT = nucleic acid amplification test, NR = not reported, RT-PCR = reverse transcriptase polymerase chain reaction.
Fully vaccinated = 2 doses of a 2 dose vaccine or one dose of a single dose vaccine; partially vaccinated = one dose of a 2 dose vaccine; unvaccinated = no vaccine received.
[A] Simon and others looked at vaccination before and after infection

Study	Country, date	Population	Sample size	Vaccine(s)	Long COVID definition
Antonelli (9)	UK, December 2020 to July 2021	Adults with positive COVID-19 test (RT-PCR or LFD) reported to the ZOE app	n=4,740 (2,370 unvaccinated, 2,370 fully vaccinated)	NR	Long duration symptoms of COVID-19 (at least 28 days)
Al-Aly (12)	US, February to August 2021	Adults with positive COVID-19 test recorded in the US VHA database	n=64,571 (48,536 unvaccinated, 16,035 vaccinated)	NR	Post-acute sequelae of COVID-19 (symptoms of COVID-19 at 6 months, including cardiovascular disorders, coagulation, fatigue, gastrointestinal disorders, kidney disorders, mental health disorders, metabolic disorders, musculoskeletal disorders, neurologic disorders, and pulmonary disorders)
Arjun (16)	India, April to September 2021	Adults with positive COVID-19 test (RT-PCR) from a hospital	n=487 (122 unvaccinated, 287 vaccinated [doses NR])	Covaxin (majority)	Self-reported long COVID symptoms (including fatigue, cough, loss of taste and smell and cognitive dysfunction 4 weeks from the date of diagnosis)
Herman (18)	Indonesia, up to December 2021	People (age NR) with positive COVID-19 test (RT-PCR, NAAT or LFD) from across the country	n=442 (221 unvaccinated, 221 fully vaccinated)	NR	Olfactory dysfunction (anosmia or hyposmia) 2 and 4 weeks after the end of infection
Kuodi (19)	Israel, March to June 2021 (COVID-19 infection), Jul to Nov 2021 (survey completion)	Adults with positive COVID-19 test from a hospital	n=951 (317 unvaccinated, 294 fully vaccinated)	NR	Long-term physical, mental, and psychosocial consequences of COVID-19, including fatigue, headache, weakness in arms and legs, persistent muscle pain, loss of concentration, hair loss, sleeping problems, dizziness, persistent cough, shortness of breath, and feeling fully recovered from COVID-19
Senjam (17)	India, January to April 2021	Adults with positive COVID-19 test (RT-PCR or NAAT) from a hospital	n=773 (407 unvaccinated, 193 fully vaccinated)	NR	Long COVID symptoms present between 4 and 12 weeks (short-term) or beyond 12 weeks (long-term), including fatigue, pain in the joints and muscle, hair loss, headache, cough, breathlessness, sleep disorders, sore throat and decrease of smell and taste
Simon (13) [A]	US, January 2020 to May 2021	People (any age) with positive COVID-19 test (NAAT or antigen test) from across the country	n=240,648 (220,460 unvaccinated, 17,796 fully vaccinated by 12 weeks after infection)	Pfizer, AstraZeneca, Moderna (all approved for use)	COVID-19 symptoms present between 12 and 20 weeks after COVID-19 diagnosis, including chest pain, palpitations, altered mental state, anorexia, chills, fatigue, fever, malaise, loss of sense of smell, loss of sense of taste, nasal congestion, sore throat, abdominal pain, diarrhoea, digestive changes, nausea, vomiting, arthralgia, muscle weakness, general weakness, myalgia, headache, cough and dyspnoea
Taquet (11)	US, January to August 2021	People (age NR) with confirmed COVID-19 or positive COVID-19 test (RT-PCR) from across the country	n=18,958 (9479 unvaccinated, 2,996 partially vaccinated, 6,957 fully vaccinated)	Pfizer (65%), Moderna (9%), Januaryssen (1.6%), unspecified (24%)	Any of the following diagnosed symptoms in the 6 months after infection: abdominal symptoms, abnormal bleeding, anxiety/depression, chest/throat pain, cognitive symptoms, fatigue, headache, myalgia and other pain, and death

Table 1b. Study characteristics: Vaccination after infection

Study	Country, date	Population	Sample size	Vaccine(s)	Long COVID definition
Arnold ([7])	UK, April to May 2020 (COVID-19 hospitalisation), January to February 2021 (vaccination)	Adults previously hospitalised with COVID-19	n=66 (22 unvaccinated, 44 partially vaccinated)	Pfizer, AstraZeneca	Persistent symptoms of long COVID, including fatigue, breathlessness, insomnia, ear, nose and throat symptoms, brain fog, muscle aches, anosmia, joint pain, cough, headache, palpitations, chest pain, diarrhoea, abdominal pain and nausea
Ayoubkhani ([8])	UK, February to September 2021	Adults with confirmed COVID-19 (RT-PCR) and long COVID symptoms (self-classified)	n=28,356 (all partially vaccinated by study end, 23,753 fully vaccinated by study end)	mRNA vaccine (45%), adenovirus vector vaccine (55%)	Long duration symptoms of COVID-19 (at least 28 days) that could not be explained by another condition, including fever, headache, muscle ache, weakness or tiredness, nausea or vomiting, abdominal pain, diarrhoea, loss of appetite, loss of taste, loss of smell, sore throat, cough, shortness of breath, chest pain, palpitations, vertigo or dizziness, worry or anxiety, low mood or not enjoying anything, trouble sleeping, memory loss or confusion, or difficulty concentrating
Gaber ([10])	UK, December 2020 to January 2021	Healthcare workers with long COVID	n=77 (10 unvaccinated, 67 partially vaccinated)	Pfizer (100%)	Long COVID symptoms, including fatigue, shortness of breath and anxiety
Strain ([21])	UK, March to April 2021	Adults with confirmed (RT-PCR/serology) or suspected COVID-19, and long COVID symptoms	n=812 (698 partially vaccinated, 114 fully vaccinated)	AstraZeneca (50%), Pfizer (40%), Moderna (8.6%)	Current or recent symptoms of long COVID-19, including fatigue, brain fog, myalgia, shortness of breath, insomnia, chest pain or palpitations, gastrointestinal symptoms, anosmia, autonomic dysfunction, postural orthostatic tachycardia syndrome, persistent cough, fever, rash (including COVID toes) and vascular complications.
Scherlinger ([20])	France, August 2021	Adults with confirmed (RT-PCR/serology) or suspected COVID-19, and long COVID symptoms	n=567 (170 unvaccinated, 255 partially vaccinated, 142 fully vaccinated)	Pfizer (78.1%), Moderna (16.4%), AstraZeneca (4.3%), mRNA/vector vaccine combination (0.5%)	Post-acute sequelae of COVID-19 symptoms (at least 28 days) and no alternative diagnosis, with symptoms including fever or chills, fatigue, brain fog, headaches, changing mood or impact on morale, sleeping issues, costal pain, dyspnoea, cough, palpitations, muscle aches, joint pain, paraesthesia or tingling, anosmia or ageusia, diarrhoea or vomiting, spontaneous bruises, and pruritus
Tran ([15])	France, November 2020 to May 2021	Adults with confirmed or suspected COVID-19, and at least one long COVID symptom	n=910 (455 unvaccinated, 455 vaccinated)	Pfizer (78.9%), AstraZeneca (10.5%), Moderna (10.3%), Januaryssen (0.2%)	Long duration symptoms of COVID-19 (at least 3 weeks), including 53 symptoms
Wanga ([14])	US, January 2020 to April 2021 (symptoms), April 2021 (survey)	Adults tested for COVID-19 (whether positive or negative)	n=385 at least 1 vaccine dose (100 COVID-19 cases, 285 all prior COVID-19 tests negative)	NR	Long duration symptoms of COVID-19 (at least 28 days), including change in mood, change in smell or taste, chest pain or pressure, cough, diarrhoea, difficulty thinking clearly, concentrating, forgetfulness, memory loss or "brain fog", fatigue, tired, or weakness, fever or chills, hair loss, headache, joint or muscle pain, nausea or vomiting, palpitations (heart racing or pounding), post-exertional malaise (worsening of symptoms after even minor physical, mental, or emotional exertion), problems sleeping, shortness of breath or breathlessness, sore throat, stomach pain, or other symptoms

Appendix A. Methods

This report employed a rapid review approach to address the review question:

"Are vaccinations against COVID-19, before or after infection, effective against long COVID?"

Our rapid review approach follows streamlined systematic methodologies (27). In particular, title and abstract screening was completed by one reviewer, and full text screening and summarisation of the studies were performed by one reviewer and checked by another. Risk of bias was assessed by one reviewer, using the quality criteria checklist (QCC) tool (28).

We searched a number of specialist COVID-19 review repositories and ran a broad search using Medline, Embase, NLM COVID portfolio (for preprints), World Health Organization (WHO) COVID Database and Google. Searches were conducted for papers published between 1 January 2020 and 12 January 2022. Search terms covered key aspects of the review question. The search strategy for Ovid Medline is presented in below.

Search strategy Ovid Medline

1   vaccinat*.tw,kw. (175921)
2   vaccine*.tw,kw. (271324)
3   previously-vaccin*.tw,kw. (1021)
4   post-vaccin*.tw,kw. (5742)
5   early-vaccin*.tw,kw. (423)
6   late-vaccin*.tw,kw. (84)
7   moderna.tw,kw. (618)
8   mRNA-1273.tw,kw. (451)
9   pfizer.tw,kw. (4091)
10   BNT162b2.tw,kw. (1349)
11   JNJ-78436735.tw,kw. (5)
12   "Johnson & Johnson*".tw,kw. (943)
13   Astrazeneca.tw,kw. (1690)
14   Oxford-Astrazeneca.tw,kw. (172)
15   AZD 1222.tw,kw. (3)
16   AZD1222.tw,kw. (165)
17   BNT 162b2.tw,kw. (14)
18   ChAdOx1.tw,kw. (564)
19   Novavax.tw,kw. (38)
20   NVX-CoV2373.tw,kw. (24)
21   Sputnik V.tw,kw. (57)
22   Ad26.tw,kw. (83)
23   "Ad26.COV2".tw,kw. (15)
24   Ad5.tw,kw. (2669)

25   Januaryssen.tw,kw. (1173)

26   Sinovac.tw,kw. (77)

27   sinopharm.tw,kw. (52)

28   covaxin.tw,kw. (43)

29   exp Vaccination/ (95675)

30   COVID-19 Vaccines/ (7849)

31   one or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (372560)

32   transmiss*.tw,kw. (426659)

33   transmit*.tw,kw. (180675)

34   viral load*.tw,kw. (36428)

35   viral burden.tw,kw. (1064)

36   ((severity or severe) adj2 (disease or illness)).tw,kw. (117155)

37   Viral Load/ (37202)

38   exp Disease Transmission, Infectious/ (77194)

39   32 or 33 or 34 or 35 or 36 or 37 or 38 (769168)

40   exp coronavirus/ (116957)

41   exp Coronavirus Infections/ (142168)

42   COVID-19/ (131372)

43   ((corona* or corono*) adj1 (virus* or viral* or virinae*)).ti,ab,kw. (4131)

44   (coronavirus* or coronovirus* or coronavirinae* or CoV or HCoV*).ti,ab,kw. (121211)

45   covid*.nm. (7853)

46   (2019-nCoV or 2019nCoV or nCoV2019 or nCoV-2019 or COVID-19 or COVID19 or CORVID-19 or CORVID19 or WN-CoV or WNCoV or HCoV-19 or HCoV19 or 2019 novel* or Ncov or n-cov or SARS-CoV-2 or SARSCoV-2 or SARSCoV2 or SARS-CoV2 or SARSCov19 or SARS-Cov19 or SARSCov-19 or SARS-Cov-19 or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese* or SARS2 or SARS-2 or SARScoronavirus2 or SARS-coronavirus-2 or SARScoronavirus 2 or SARS coronavirus2 or SARScoronovirus2 or SARS-coronovirus-2 or SARScoronovirus 2 or SARS coronovirus2).ti,ab,kw. (204081)

47   (respiratory* adj2 (symptom* or disease* or illness* or condition*) adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw. (700)

48   ((seafood market* or food market* or pneumonia*) adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw. (2159)

49   ((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (Wuhan* or Hubei or China* or Chinese* or Huanan*)).ti,ab,kw. (465)

50   or/40-49 (238986)

51   31 and 39 and 50 (4420)

52   COVID-19/tm [Transmission] (4367)

53   31 and 52 (520)

54   COVID-19 Vaccines/ (7849)

55   39 and 54 (815)

56   COVID-19/vi [Virology] (8817)

57   31 and 56 (1561)

58   51 or 53 or 55 or 57 (5712)

59   limit 58 to yr="2020 - 2022" (5195)

60   exp SARS-CoV-2/ (104107)

61   exp COVID-19/ (131372)

62   (corona* adj1 (virus* or viral*)).tw,kw,kf. (4621)

63   (CoV not (Coefficien* or "co-efficien*" or covalent* or Covington* or covariant* or covarianc* or "cut-off value*" or "cutoff value*" or "cut-off volume*" or "cutoff volume*" or "combined optimi?ation value*" or "central vessel trunk*" or CoVR or CoVS)).tw,kw,kf. (73907)

64   (coronavirus* or 2019nCoV* or 19nCoV* or "2019 novel*" or Ncov* or "n-cov" or "SARS-CoV-2*" or "SARSCoV-2*" or SARSCoV2* or "SARS-CoV2*" or "severe acute respiratory syndrome*" or COVID*2).tw,kw,kf. (225343)

65   exp COVID-19 Vaccines/ (7849)

66   exp COVID-19 Testing/ (7905)

67   or/60-66 (231660)

68   ((medium or long-term or long-haul or expanded or extended or recurr* or sustain* or persist* or prolong* or continu* or debilitating) adj2 (effect* or symptom* or impact* or outcome* or recover* or suffer* or sequela* or impair*)).ti,ab. (305145)

69   "post acute".tw. (3871)

70   68 or 69 (308748)

71   67 and 70 (3551)

72   ((long* or post) adj4 covid*).tw. (5319)

73   71 or 72 (7953)

74   59 and 73 (166)

75   limit 74 to (english language and yr="2021 - 2022") (141)

Article eligibility criteria are summarised in Table A.1.

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	All populations	
Settings	All community settings, including households	Healthcare settings
Context	COVID-19 pandemic	Other diseases
Intervention or exposure	Partial or full vaccination against COVID-19; any COVID-19 specific vaccination; vaccination before or after COVID-19 infection.	
Outcomes	Incidence or prevalence of long COVID using any definition given by individual studies, including symptoms of COVID-19 more than 28 days after the initial infection.	
Language	English	
Date of publication	1 January 2020 to 12 January 2022	
Study design	- randomised controlled trials - cohort studies - case-control studies	- systematic or narrative reviews - other observational studies - guidelines - opinion pieces - outbreak investigations, unless they include an analytical component
Publication type	Published and preprint	

Title and abstract screening was completed by one reviewer. Full text screening and study summaries were completed by one reviewer and checked by a second. Only results directly relevant to the review questions were summarised.
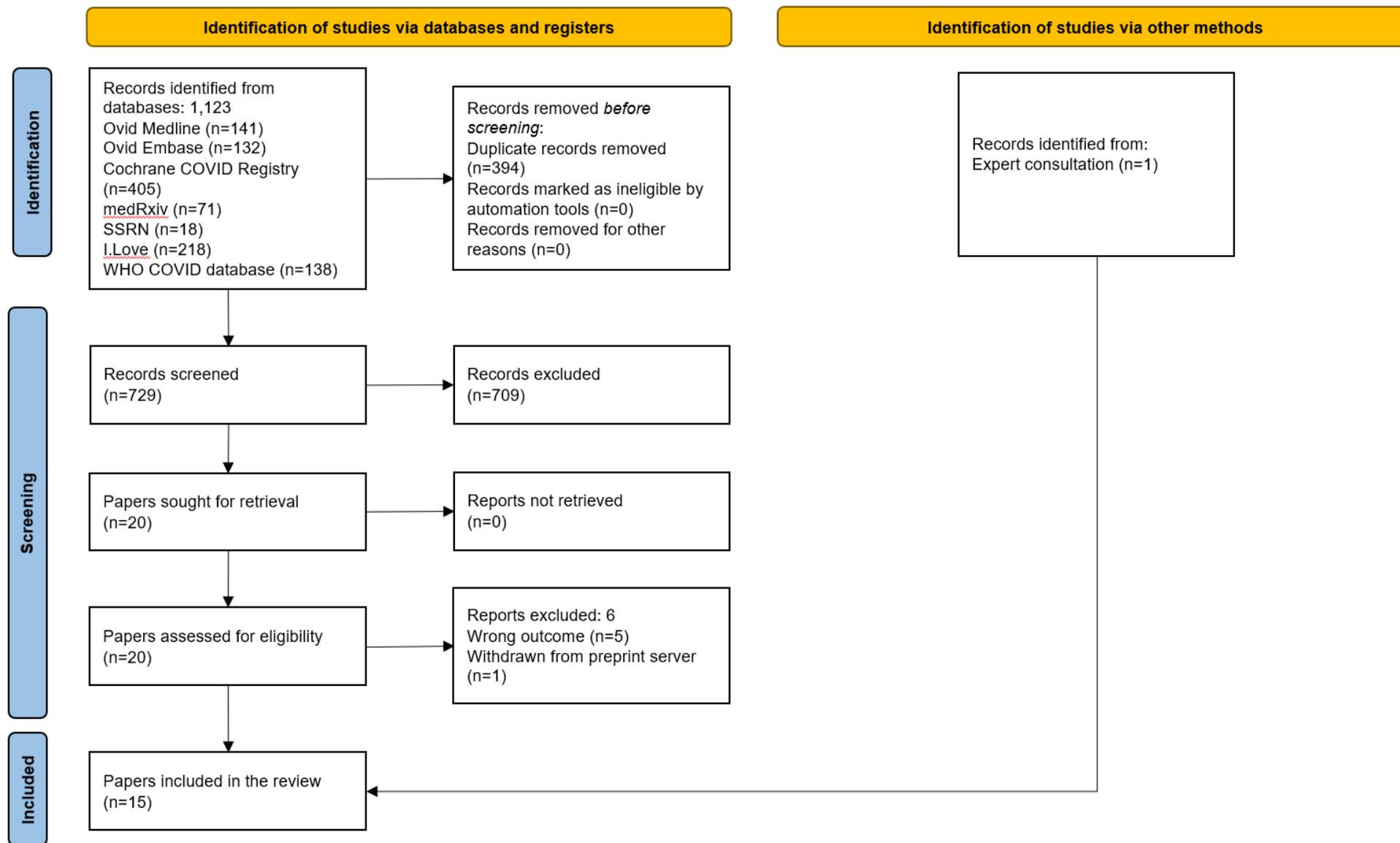
Studies were assessed by one reviewer, using the QCC for primary research (28). This risk of bias tool can be applied to most study designs (observational and interventional) and is therefore suitable for rapid reviews of mixed type of evidence. It is composed of 10 validity questions based on the criteria and domains identified by the Agency for Healthcare

Research and Quality to assess the methodological quality of a study (that is, the extent to which a study has minimised selection, measurement and confounding biases) (29).

In the QCC tool, 4 questions are considered critical (on selection bias, group comparability and confounding, interventions or exposure, and outcome). A study will be rated as high quality if the answers to the 4 critical questions are 'yes' (and at least one additional 'yes'). The study will be rated as low quality if 2 or more of the critical questions are answered 'no' and/or if greater than or equal to 50% of the remaining questions are answered 'no'. Otherwise, the study will be rated as medium quality. Judgments were made on case by case for questions answered as 'unclear'. To note that we report these ratings as 'quality' ratings for consistency with the name of the tool, although here quality needs to be understood as 'methodological quality' as part of a risk of bias assessment.

The PRISMA diagram showing the flow of citations is provided in Figure A.1.

Figure A.1. PRISMA flowchart

Identification of studies via databases and registers

Identification of studies via other methods

Identification

Records identified from databases: 1,123
Ovid Medline (n=141)
Ovid Embase (n=132)
Cochrane COVID Registry (n=405)
medRxiv (n=71)
SSRN (n=18)
I.Love (n=218)
WHO COVID database (n=138)

Records removed *before screening*:
Duplicate records removed (n=394)
Records marked as ineligible by automation tools (n=0)
Records removed for other reasons (n=0)

Records identified from:
Expert consultation (n=1)

Screening

Records screened (n=729)

Records excluded (n=709)

Papers sought for retrieval (n=20)

Reports not retrieved (n=0)

Papers assessed for eligibility (n=20)

Reports excluded: 6
Wrong outcome (n=5)
Withdrawn from preprint server (n=1)

Included

Papers included in the review (n=15)

Accessible text version of Figure A.1. PRISMA diagram

This is a PRISMA diagram showing the flow of studies through this review.

From identification of studies via databases and registers, n=1,123 records identified from databases:

- Ovid Medline (n=141)
- Ovid Embase (n=132)
- Cochrane COVID registry (n=405)
- medRxiv (n=71)
- SSRN (n=18)
- i.Love (n=218)
- WHO COVID database (n=138)

From these, records removed before screening:

- duplicate records removed (n=394)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=729 records screened, of which n=709 were excluded, leaving n=20 papers sought for retrieval, all of which were retrieved and assessed for eligibility.

Of these, n=6 reports were excluded:

- wrong outcome (n = 5)
- withdrawn from preprint server (n=1)

n=1 record identified from identification of studies via other methods:

- expert consultation (n=1)

n=15 papers included in this review

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