UK Health Security Agency

COVID-19 Omicron variant infectious period and transmission from people with asymptomatic compared with symptomatic infection: a rapid review

Contents

Main messages

This review (search up to 26 January 2023) identifies and summarises evidence on coronavirus (COVID-19) Omicron variant infectious period (82 studies), and the difference in transmission from people with asymptomatic compared with symptomatic COVID-19 infection (10 studies).

Infectious period of COVID-19 Omicron variant

1. Three studies directly examining transmission suggested that most transmission events happened around symptom onset, with the majority of transmission events occurring up to 5 days after symptom onset (100% in one study, 81% in another study, not reported in the third study).
2. Ten studies also reported that viral culture positivity was highest in the first 5 days after symptom onset or diagnosis, and 14 studies reporting on viral load suggested that peak viral loads occurred a median and mean of 2 to 5 days after symptom onset.
3. Nine studies measuring serial interval and generation time suggested the median and mean serial interval was between 2 and 4 days (with interquartile ranges between one and 9 days), and generation times of around 3 days.
4. Fifty-three studies measuring time to viral clearance suggested that there were substantial differences in viral clearance times between cases and populations. The majority of studies in the general population estimated viral clearance to take around 7 to 11 days, and most studies of hospitalised, immunodeficient, and other high-risk cases estimated viral clearance to take around 10 to 15 days. Whilst detectable viral load does not provide direct evidence on the risk of transmission, it does indicate potential infectivity.
5. Overall, the evidence suggests that COVID-19 Omicron variant cases were most infectious up to 5 days after symptom onset but could potentially be infectious for longer, especially if hospitalised, immunocompromised, or otherwise high-risk. Most studies included relatively few cases.

Asymptomatic compared with symptomatic transmission of COVID-19 Omicron variant

6. Three studies compared household secondary attack rates (SAR) of asymptomatic and symptomatic index cases, with 2 studies suggesting more transmission from symptomatic than asymptomatic index cases, and one study suggesting no clear difference.
7. Five studies compared viral loads (usually using Ct values) between asymptomatic and symptomatic cases, with 3 studies suggesting similar viral loads, and 2 studies suggesting higher viral loads in symptomatic compared with asymptomatic cases.
8. Overall, the evidence on differences in transmission from people with asymptomatic compared with symptomatic COVID-19 Omicron variant was mixed, with some studies suggesting that symptomatic cases were more likely to transmit infection than asymptomatic

cases and others showing no difference. The lack of precision due to small study samples combined with the variability between studies and the small number of studies limit the ability to draw firm conclusions.

Purpose

To identify and summarise evidence relating to COVID-19 Omicron variant coronavirus infectious period, and the difference in transmission from people with asymptomatic compared with symptomatic COVID-19.

Methods

There were 2 review questions:

1. What is the infectious period of COVID-19 Omicron variant?
2. What is the difference in transmission from people with asymptomatic compared with symptomatic COVID-19 Omicron variant?

We previously conducted reviews covering the infectious period of COVID-19 (searches to 23 February 2022 and 16 May 2022). However, these could not be used as a source of evidence for this current review (which looked at primary studies) as the previous searches were aimed at identifying existing rapid and systematic reviews. The primary study search for evidence on infectious period therefore started 1 December 2021, shortly after the start of the Omicron wave.

We also conducted a previous review looking at the difference in transmission of COVID-19 between symptomatic and asymptomatic index cases (search to 15 March 2022). This review was used as a source of evidence up to 15 March 2022.

A rapid review was conducted to search for primary studies up to 26 January 2023 for both review questions (from 1 December 2021 for infectious period, and from 15 March 2022 for asymptomatic transmission), following streamlined systematic methodologies to accelerate the review process (1). Only studies where the majority of the participants in the study were stated to have the Omicron variant of COVID-19 were included.

Ten percent of the title and abstract screening was completed in duplicate for each review question, while full text screening and data extraction were performed by one reviewer and checked by another. Risk of bias assessment using the quality criteria checklist (QCC) (2) was performed by one reviewer and checked by another for all analytical studies (not descriptive studies). Full details on the methodology are provided in Annexe A.

The review questions were searched for and reported separately within the same report.

COVID-19 Omicron variant infectious period

Evidence

In total, 82 observational studies looking at different measures of COVID-19 Omicron variant infectious period were included in this report. As all studies were descriptive rather than analytical, quality was not assessed. Infectious period is difficult to measure directly, so studies reporting on related measures were also included.

In total, 3 studies reported directly on transmission period (3 to 5), 10 studies on culture positivity over time (6 to 15), 8 studies on incubation period (4, 5, 16 to 21), one study on latent period (5), 9 studies on serial interval (3, 4, 16 to 18, 21 to 24), 6 studies on time to peak viral load (14, 25 to 29), 53 studies on time to viral clearance (12, 14, 15, 27, 29 to 77), and 9 studies on viral load over time (7, 25, 78 to 84). Some studies provided evidence for multiple outcomes. Although some studies compared treatments for COVID-19, the effects of treatments on infectious period outcomes were not considered, only the infectious period within different groups in each study.

Studies directly assessing infectious period, large studies (especially those conducted in the UK), and studies of more recent Omicron variants (BA.3 and later) are individually summarised, whereas the remainder of studies are jointly summarised. Table 1 gives study characteristics of the 82 included studies.

Transmission period

There were 3 included studies (3 to 5) (no preprints) that included direct evidence for the transmission period of COVID-19 Omicron variant. These studies identified index cases and known secondary cases and estimated when transmission was likely to have taken place. These studies most directly estimate the period of infectiousness.

Of these studies, 2 studies were conducted in Europe (3, 4), and one in China (5). All studies were conducted between December 2021 and May 2022. One study was a prospective cohort study (3), one study was a retrospective cohort study (4), and one study was a cross-sectional study (5). These studies included cases with COVID-19 Omicron variant BA.1 and BA.2 (3), BA.1 (4), and BA.1.1 (5) variant.

All 3 studies are summarised in detail below, with study characteristics in Table 1a.

Summaries of individual studies

An der Heiden and others reported on transmission of COVID-19 Omicron variant BA.1 and BA.2 in n=11,512 households in Germany between January 2022 and May 2022 (3). The

results suggested that 81% of transmission occurred by day 5 of symptom onset in the index case, and 95% of transmission occurred by day 10 of symptom onset in the index case.

Del Aguila-Mejia and others reported on transmission of COVID-19 Omicron variant BA.1 between n=622 index cases and n=455 secondary cases in Spain in December 2021 (4). The median transmission period after symptom onset was 0 days (interquartile range [IQR]: -1 to 2 days).

Xin and others reported on transmission of COVID-19 Omicron variant BA.1.1 between n=113 pairs of cases in China between January and February 2022 (5). The estimated proportion of transmissions occurring 4 or more days before symptom onset was 4.4% (95% credible interval [CrI]: 0.9% to 8.0%), and the estimated proportion of transmissions occurring before symptom onset was 33.6% (95% CrI: 24.8% to 42.5%). Overall, transmission peaked at symptom onset, and all observed transmission events occurred within 5 days of symptom onset.

Viral culture positivity over time

There were 10 included studies (6 to 15) (one preprint (8)) that included evidence on viral culture positivity over time for COVID-19 Omicron variant. These studies typically took repeated viral samples from cases over the course of their illness and tested them for the presence of live virus using cultures. The presence of live virus in a sample does not necessarily indicate that the case would infect other people with whom they came into contact, but is a stronger indicator of infectiousness than just the presence of viral RNA as measured using RT-PCR.

Of these studies, 5 were conducted in Asia (9 to 11, 13, 15), 2 in the US (7, 8), one in the UK (6), one in Turkey (12), and one in Brazil (14). Nine studies were prospective cohort studies (6 to 14), and the remaining study was a retrospective cohort study (15). All studies were conducted between November 2021 and May 2022. These studies included cases with COVID-19 Omicron B.1.1.529 (10), BA.1 (6, 14), and BA.1 and BA.2 (13) variant, and some studies did not report the sub-lineage (7, 9, 11, 12, 15), or report the variant at all, though were very likely Omicron variant (8). Study characteristics are given in Table 1b.

The study from the UK is summarised in detail below (6). The remaining studies did not include more than 100 cases and are jointly summarised below.

Summaries of individual studies

Boucau and others reported the time to negative culture in n=32 Omicron BA.1 variant cases in the UK up to January 2022 (6). The median time from the first positive RT-PCR to negative culture was 5 days (IQR: 3 to 9 days), and the median time from the first positive RT-PCR or symptom onset (whichever was earlier) to negative culture was 8 days (IQR: 5 to 10 days).

Joint summary of remaining studies

Three studies measured the median time from symptom onset to negative viral cultures (8, 10, 11). All 3 studies estimated a median time of 4 days, with interquartile ranges varying between 3 to 5 or 6 days (8, 10) and one to 7 days (11).

The remaining 6 studies reported on the proportion of cases (typically mild cases) with positive viral cultures on different days after either symptom onset or diagnosis (7, 9, 12 to 15). Culture positivity was highest in the first 5 days after symptom onset or diagnosis, with different studies reporting 46% at day 5 (14), a peak of around 30% at day 4 dropping to 10% at day 5 (7), 83% at day 5 (12), 51.5% and 86.5% at day one falling to 18.2% and 32.4% at day 5 depending on treatment (13), and 11.8% at days 0 to one rising to 41.7% at days 2 to 5 (15). Beyond 5 days after symptom onset or diagnosis, culture positivity fell, with different studies reporting 20% at day 7 after symptom onset (14), 52% at day 7,13.5% at day 10 and 8% at day 14 (12), and 18.8% at days 6 to 9 (15). The time from symptom onset or diagnosis to no further positive cultures was variable, taking 8 days (9), 10 days (14), 10 to 14 days (15), and 13 days (7) in different studies.

Incubation period

There were 8 included studies (4, 5, 16 to 21) (2 preprints (18, 21)) that included evidence for the incubation period of COVID-19 Omicron variant. The incubation period is the time from COVID-19 exposure and symptom onset in a case, and studies would typically ask participants about exposure and symptom onset times to measure this, often pairing up or otherwise matching index and secondary cases.

Of these studies, 4 were conducted in Asia (5, 17, 19, 21) and 4 in Europe (4, 16, 18, 20), including one in the UK (20). All studies were conducted between December 2021 and April 2022. Three studies were prospective cohort studies (16, 17, 19), 3 studies were retrospective cohort studies (4, 18, 20), and 2 studies were cross-sectional studies (5, 21). These studies included cases with COVID-19 Omicron variant BA.1 (4, 5, 19), BA.2 (21), and BA.1 and BA.2 (17, 20) , and some studies did not report the sub-lineage (16, 18). Study characteristics are given in Table 1c.

One study from the UK included had a large sample size and is summarised in detail below (20). The remaining studies typically included fewer than 1,000 cases in total and are jointly summarised below.

Summaries of individual studies

Ward and others reported on the incubation period of n=124,948 cases (n=116,163 BA.1, n=8,785 BA.2 Omicron variant) in the UK up to February 2022 (20). The estimated mean incubation period for Omicron BA.1 was 3.67 days (95% CrI: 3.61 to 3.72 days) with an

estimated standard deviation (SD) of 3.14 days (95% CrI: 3.06 to 3.22 days). Similarly, the estimated mean incubation period for Omicron BA.2 was 3.48 days (95% CrI: 3.43 to 3.53 days) with an estimated SD of 2.90 days (95% CrI: 2.82 to 2.98 days). The mean incubation period of both BA.1 and BA.2 Omicron did not appear to vary substantially by age group.

Joint summary of remaining studies

The remaining 7 studies estimated the median (4, 16, 17, 19, 21) or mean incubation period (5, 16, 18). The median incubation period was estimated to be between 2 and 5 days with interquartile ranges between one and 6 days (4, 16, 17, 19, 21), with one study suggesting little difference between the Omicron BA.1 and BA.2 variants (17). The mean incubation period was estimated to be between 3 and 5 days (5, 16, 18), with one study estimating that the 95th percentile to be less than 7 days (5).

Latent period

There was one included study that included evidence for the latent period of COVID-19 Omicron variant (5). The latent period is the time from exposure to COVID-19 and detectable viral levels in a case (potentially indicating the capability to infect other people), and studies would typically ask about COVID-19 exposure and first positive test times to measure this. Study characteristics are given in Table 1d.

Xin and others estimated the latent period of n=114 cases with COVID-19 Omicron BA.1.1 variant between January 2022 and February 2022 in China (5). The estimated mean latent period was 3.1 days (95% credible interval [CrI]: 2.8 to 3.5 days), with 95% of cases developing detectable virus levels 5.9 days after infection (95% CrI: 5.3 to 6.8 days).

Serial interval and generation time

There were 9 included studies (3, 4, 16 to 18, 21 to 24) (3 preprints (18, 21, 22)) that included evidence for the serial interval of COVID-19 Omicron variant. The serial interval is the time from symptom onset of an index case to symptom onset of a secondary case, and studies would typically ensure that transmission happened between individual cases, then ask about symptom onset times to measure this. The generation time is the time from infection of an index case and infection of a secondary case, and studies would typically estimate this in the same way as for serial interval.

Of these studies, 4 were conducted in Europe (3, 4, 16, 18), 4 in Asia (17, 21 to 23), and one in the US (24). All studies were conducted between November 2021 and April 2022. Six studies were prospective cohort studies (3, 16, 17, 22 to 24), 2 studies were retrospective cohort studies (4, 18), and one study was a cross-sectional study (21). These studies included cases with Omicron BA.1 (4, 23), BA.2 (21), and BA.1 and BA.2 (3, 17, 22, 24) variant COVID-19, and some studies did not report the sub-lineage of COVID-19 Omicron variant (16, 18). Study characteristics are given in Table 1e.

One study included over 11,000 households and is summarised in more detail below (3). The remaining studies typically included fewer than 1,000 cases and are jointly summarised below.

Summaries of individual studies

An der Heiden and others reported the serial interval estimated from household transmission of COVID-19 Omicron variant BA.1 and BA.2 in n=11,512 households in Germany between January 2022 and May 2022 (3). The mean serial interval was estimated to be 3.61 days (95% CI: 3.56 to 3.66 days) across all cases, 3.88 days (95% confidence interval [CI]: 3.79 to 3.97 days) for Omicron BA.1 cases, and 3.39 days (95% CI: 3.30 to 3.49 days) for Omicron BA.2 cases.

Joint summary of remaining studies

Of the remaining studies, 4 studies reported on estimated median serial interval (4, 17, 21, 24), 4 studies reported on estimated mean serial interval (16, 18, 22, 23), and 2 studies reported on the median generation time (17) or mean forward generation interval (18). The median serial interval was estimated to be between 2 and 4 days, the interquartile ranges between one and 9 days (4, 17, 21, 24), with one study suggesting little difference between Omicron BA.1 and BA.2 variants (17). The mean serial interval was estimated to be between 3 and 4 days (16, 18, 22, 23), with one study suggesting child index cases may have shorter serial intervals (3.0 days) than adult index cases (5.0 days) (23). Both the median generation time and mean forward generation interval were estimated to be around 3 days (17, 18).

Time to peak viral load

There were 6 included studies (14, 25 to 29) (one preprint (29)) that included evidence for time to peak viral load of COVID-19 Omicron variant cases. The time to peak viral load is the time from exposure, first positive RT-PCR test, or symptom onset to the peak viral load. Studies would typically repeatedly test cases for COVID-19 using RT-PCR, recording the peak viral load as the time of the lowest Ct value to measure this. Higher viral loads, as measured by Ct values (lower Ct values indicate higher viral loads), may be indicative of a higher chance of being infectious, but high viral loads (or low Ct values) do not necessarily indicate infectiousness.

Of these studies, 2 were conducted in the US (27, 29), and one each in Spain (26), Canada (28), Brazil (14), and South Korea (25). All studies were conducted between December 2021 and March 2022. Three studies were prospective cohort studies (14, 28, 29), and 3 studies were retrospective cohort studies (25 to 27). These studies included cases with COVID-19 Omicron variant BA.1 (14, 27 to 29), and BA.1 and BA.2 (26) , and one study did not report the sub-lineage (25). Study characteristics are given in Table 1f.

One study included over 5,000 cases and is summarised in more detail below (25). The remaining studies included fewer than 1,000 cases in total and are jointly summarised below.

Summaries of individual studies

Choi and others reported time to peak viral load for n=5,187 Omicron variant cases in South Korea in January 2022 (25). The results suggested the peak viral load occurred 2.4 days (95% CI: 2.2 to 2.5 days) after symptom onset.

Joint summary of remaining studies

The remaining 5 studies estimated the mean time to peak viral load (14, 26 to 29). The studies suggested the mean time to peak viral load was between 2 and 5 days for the Omicron variant BA.1 (14, 26 to 29), with one study suggesting the Omicron variant BA.2 may have a shorter mean time to peak viral load (one day) (26).

Time to viral clearance

There were 53 included studies (12, 14, 15, 27, 29 to 77) (15 preprints (29 to 31, 34, 36, 37, 39, 54, 55, 57, 58, 60, 66, 69, 77)) that included evidence for time to viral clearance of COVID-19 Omicron variant cases. The time to viral clearance is the time either from exposure, first positive RT-PCR test, or symptom onset to the last positive RT-PCR test or first negative RT-PCR test. These studies typically repeatedly tested cases for COVID-19 using RT-PCR, recording the date at which the last positive or first negative RT-PCR test was conducted, sometimes requiring a repeat negative RT-PCR test to ensure viral clearance. A detectable viral load (as measured using RT-PCR) does not necessarily indicate that a case is infectious.

Of these studies, 33 were conducted in China (33, 34, 39, 40, 43 to 48, 51 to 55, 58, 59, 61 to 72, 74 to 77), 8 in Europe (12, 30, 32, 35, 38, 49, 56, 57), 6 in the US (27, 29, 36, 37, 41, 42), 4 in the rest of Asia (60, 73) (15, 50), and 2 in Brazil (14, 31). Most studies were conducted between March 2022 and July 2022, though some studies were conducted earlier, and some studies were conducted up to August and October 2022 (34, 44). In total, 28 studies were prospective cohort studies (12, 14, 29 to 33, 36 to 38, 41 to 44, 46, 47, 49, 53, 54, 56 to 58, 63, 65, 67, 72, 74, 76) (6 of which were randomised controlled trials [RCTs] or quasi-experimental studies but reported as prospective cohort studies (31, 32, 46, 54, 58, 63)), and 25 studies were retrospective cohort studies (15, 27, 34, 35, 39, 40, 45, 48, 50 to 52, 55, 59 to 62, 64, 66, 68 to 71, 73, 75, 77). These studies included cases with COVID-19 Omicron variant BA.1 (14, 27, 29, 49), BA.2 (39, 40, 45, 46, 51, 54, 55, 57, 60 to 62, 64, 67 to 73, 76, 77), BA.1 and BA.2 (38), and BA.5 (44) , and some studies did not report the sub-lineage (12, 15, 30, 32 to 37, 41 to 43, 47, 48, 50, 52, 53, 56, 58, 59, 63, 65, 66, 74, 75), or report the variant at all, though were very likely Omicron variant (31). Study characteristics are given in Table 1g.

Some studies included both treated and untreated arms, for instance in trials of different drugs compared with standard care or no treatment. In these studies, only the no treatment groups are summarised below, although results for both groups are available in Table 1g. Studies in this section are split into those including cases from the general population, and those that only

included cases who were at high-risk from COVID-19, including cases who were hospitalised (either for COVID-19 or another condition), and cases with immunodeficiency.

One study reported on the Omicron variant BA.5, and 3 studies included over 25,000 cases (with likely substantial overlap in cases between these studies), and all are individually summarised below. The remaining studies typically included fewer than 1,000 cases in total and are jointly summarised below. The jointly summarised studies are split into studies including cases from the general population (including studies of cases quarantining in hospitals, particularly in China) and studies including hospitalised, immunodeficient, or otherwise high-risk cases.

Summaries of individual studies

Li and others reported the duration of viral shedding (Ct value of less than 35 on a nucleic acid test) for n=27 cases with COVID-19 Omicron variant BA.5 and n=51 cases with Omicron variant BA.2 in August 2022 in China (44). Of the Omicron BA.5 cases, 96.30% shed virus for at least 7 days, 88.89% shed virus for at least 10 days, and 48.15% shed virus for at least 14 days. Of the Omicron BA.2 cases, 54.38% shed virus for at least 7 days, 21.92% shed virus for at least 10 days, and 4.51% shed virus for at least 14 days.

The following 3 studies reported on cases admitted to shelter hospitals in Shanghai, China between March and May 2022, and therefore likely included a substantial overlap in cases.

Pei and others reported time between first positive and first negative RT-PCR test for n=198,262 asymptomatic and mild cases with likely COVID-19 Omicron variant BA.2 between March and May 2022 in China (51). The median time from first positive to first negative RT-PCR test was 8.29 days (IQR: 5.33 to 11.27 days) in all cases, and 9.29 days (IQR: 6.33 to 12.28 days) in n=33,896 cases with comorbidities.

Yin and others reported the time between first positive and first negative RT-PCR test for n=199,590 asymptomatic or mild cases with Omicron variant BA.2 between March and May 2022 in China (70). The mean time from illness onset to negative RT-PCR test was 7.17 days (SD: 3.42 days).

Ying-Hao and others reported the time between first positive and first negative RT-PCR test for n=25,168 asymptomatic or mild cases with Omicron variant BA.2 between April and May 2022 in China (71). The median time from first positive to first negative RT-PCR test was 6 days (IQR: 4 to 9 days).

Joint summary of remaining studies: cases from the general population

In total, 19 studies reported the duration of positivity on a COVID-19 test (typically RT-PCR test, but also rapid antigen tests, and other nucleic acid tests), usually reporting either the mean or median time from either symptom onset or diagnosis to the first of 2 negative tests (27, 29 to 31,

36, 37, 40, 41, 46, 50, 57, 58, 60, 61, 63 to 65, 72, 73). Many studies did not specify the outcome, making comparison between studies more difficult. Nonetheless, the time to viral clearance was markedly different across studies, ranging from 4 to 29 days, though most studies estimated viral clearance to take around 7 to 11 days (27, 29 to 31, 36, 37, 40, 50, 57, 60, 63, 72, 73).

The remaining 7 studies including cases from the general population reported the proportion of cases who were still positive on a COVID-19 test (typically RT-PCR test, but also rapid antigen tests, and other nucleic acid tests) at certain days after symptom onset or diagnosis (12, 14, 15, 32, 42, 45, 62). As with the studies above, many studies did not specify the outcome and different time periods were reported on, making comparison between studies more difficult. However, all studies reported the proportion of positive tests at day 7, which varied between 20.4% and 100%, which most studies reporting positive test proportions between 87% and 100% (12, 14, 15, 32).

Joint summary of remaining studies: hospitalised, immunodeficient, and other high-risk cases

In total, 21 studies reported the duration of positivity on a COVID-19 test (typically RT-PCR test, but also rapid antigen tests, and other nucleic acid tests), usually reporting either the mean or median time from either symptom onset, diagnosis, or hospitalisation to the first of 2 negative tests for cases who were hospitalised (for COVID-19 or another condition), immunodeficient, or otherwise at high-risk from COVID-19 (33 to 35, 39, 43, 47 to 49, 52, 53, 55, 56, 59, 66 to 69, 74 to 77). Many studies did not specify the outcome, and cases had variable severity of COVID-19 and other conditions, making comparison between studies more difficult. In general, however, the time to viral clearance was longer than for cases from the general population, ranging from 4 to 21 days across studies, though most studies estimated viral clearance to take around 10 to 15 days (33, 35, 39, 48, 49, 52, 53, 55, 56, 66, 67, 69, 75 to 77). Studies comparing hospitalised cases with and without chronic kidney disease or cases on haemodialysis suggested viral clearance was quicker in cases without chronic kidney disease or on haemodialysis (39, 66, 75).

Two further studies including cases who were hospitalised (for COVID-19 or another condition), immunodeficient, or otherwise at high-risk from COVID-19 reported the proportion of cases who were still positive on a COVID-19 test (typically RT-PCR test, but also rapid antigen tests, and other nucleic acid tests) at certain days after symptom onset or diagnosis (38,54). In one study, 27.9% of immunodeficient cases still showed viral shedding (threshold set at 1,000,000 SARS-CoV-2 RNA copies per ml) 21 days after starting sotrovimab compared with 7.1% for immunocompetent cases (38). In another study, 31.1% of cases had a negative RT-PCR test within 7 days of entry into the study (54).

Viral load over time

There were 9 included studies (7, 25, 78 to 84) (4 preprints (78, 80, 83, 84)) that included evidence for the viral load over time for COVID-19 Omicron variant cases. These studies typically repeatedly tested cases for COVID-19 using RT-PCR, and typically expressed the results in a graph indicating mean or median viral loads of participants over a course of infection, either from diagnosis or from symptom onset (or both). For these studies, if no data were presented in the text (and the study reported in a previous section), the graphs were briefly summarised to give an overall impression of how viral load changed over the course of an infection. As with time to viral clearance, a detectable viral load (as measured using RT-PCR) does not necessarily indicate that a case is infectious.

Of these studies, 4 were conducted in Europe (78, 80, 82, 83), including 2 that were conducted in the UK (78, 83), 3 were in Asia (25, 79, 84), and 2 were in the US (7, 81). All studies were conducted between November 2021 and May 2022. Five studies were prospective cohort studies (7, 80 to 83), 3 studies were retrospective cohort studies (25, 79, 84), and one study was a cross-sectional study (78). These studies included cases with COVID-19 Omicron variant B.1.1529 (84), BA.1 (81), BA.2 (79), and BA.1 and BA.2 (78, 80, 82, 83), and some studies did not report the sub-lineage (7, 25). Study characteristics are given in Table 1h.

One study from England including over a million cases (78), and a study from South Korea include over 5,000 cases (25), and both are summarised in detail below. The remaining studies included fewer than 250 cases and are jointly summarised below.

Summaries of individual studies

Funk and others (preprint) reported on the Ct values over time for n=1,212,234 cases (n=1,083,976 BA.1, n=128,258 BA.2 Omicron variant) in England between December 2021 and January 2022 (78). Data extracted from a figure suggested Ct values decreased (viral load increased) in the first 2 days after symptom onset, then increased (viral load decreased) from days 2 to 6 (data was truncated at day 6). The study also suggested that BA.2 infections had higher Ct values (lower viral loads) than BA.1 infections, cases with reinfections had higher Ct values (lower viral loads) than cases with no known previous infection, and there was no clear difference in Ct values between people with different doses of vaccine.

Choi and others reported on Ct values over time for n=5,187 Omicron variant cases in South Korea in January 2022 (25). Data extracted from a figure suggested Ct values decreased (viral load increased) up to between 3 and 4 days after symptom onset, increased (viral load decreased) to between 12 and 13 days after symptom onset, then decreased again (viral load increased) up to 17 days after symptom onset (data truncated after this).

Joint summary of remaining studies

In the remaining studies, Ct values typically decreased (viral load increased) or remained steady after symptom onset for one (7, 79) or 2 to 3 days (80, 82 to 84), then increased (viral

load decreased), either until the end of testing (7, 79 to 84), or until a slight decrease in Ct values (increase in viral load) between 15 and 17 days for the Omicron BA.2 variant (83). One study also suggested that, for the Omicron BA.2 variant, Ct values increased (viral load decreased) up to one to 3 days after symptom onset, then decreased (viral load increased) up to 7 to 9 days after symptom onset, then increased again (viral load decreased) (82).

Summary

In total, 82 studies provided evidence on different measures of infectious period.

The 3 studies measuring transmission period directly suggested most transmission events happened around symptom onset, with the vast majority of transmission events happening up to 5 days after symptom onset (100% in one study, 81% in another study, not reported in the third study). However, these studies were reasonably small and therefore the results may be imprecise.

The 10 studies measuring viral culture positivity over time suggested that viral culture positivity was highest in the first 5 days after symptom onset or diagnosis before falling, with variable times for all cases to have negative viral cultures (between 8 and 14 days in different studies). Three of the studies were conducted in healthcare workers, 2 in hospitalised patients or care home residents and the remaining studies in community settings. Whilst viral culture positivity results do not provide direct evidence on the risk of transmission, they indicate potential infectivity.

The 8 studies measuring incubation period (exposure to symptom onset) suggested the median and mean incubation period was between 2 and 5 days, with a large UK study estimating a mean incubation period of between 3 and 4 days.

The one study measuring latent period (exposure to detectable viral levels) suggested the mean latent prior was around 3 days, with 95% of cases developing detectable virus levels around 6 days after infection.

The 9 studies measuring serial interval (symptom onset in an index case to symptom onset in a secondary case) and generation time (exposure in an index case to exposure in a secondary case) suggested the median and mean serial interval was between 2 and 4 days (though this can be variable, with interquartile ranges between one and 9 days), and generation times of around 3 days.

The 6 studies measuring time to peak viral load and 9 studies measuring viral load over time (one study reported on both outcomes) suggested peak viral loads occurred a median and mean of 2 to 5 days after symptom onset, and this may be quicker in Omicron BA.2 compared with BA.1 variant cases. Two of the studies were conducted in healthcare workers, one in hospitalised patients and the remaining studies in community settings.

The 53 studies measuring time to viral clearance (typically positive to negative COVID-19 test) suggested that there were substantial differences in viral clearance times between cases and populations, although the differences in measurement of time to viral clearance between studies may have contributed to these differences. In general, however, most studies of the general population estimated viral clearance to take around 7 to 11 days, and most studies of hospitalised, immunodeficient, and other high-risk cases estimated viral clearance to take around 10 to 15 days. Detectable viral load does not necessarily indicate that a case is infectious.

Overall, the evidence suggests that COVID-19 Omicron variant cases were most infectious up to 5 days after symptom onset, but could potentially be infectious for longer, especially if hospitalised, immunocompromised, or otherwise high-risk cases. However, while some studies included substantial numbers of cases, most studies included relatively few cases, and the majority of studies only included Omicron BA.1 and BA.2 variant cases.

Table 1. Studies for infectious period

Acronyms: CI = confidence interval, CrI = credible interval, IQR = interquartile range, RT-PCR = reverse transcriptase polymerase chain reaction, SD = standard deviation

Table 1a. Transmission period

Study	Country, time period	Study type	Participants	Outcome
An der Heiden (3)	Germany, January to May 2022	Prospective cohort	n=11,512 households (Omicron BA.1 and BA.2 variants)	81% of transmission occurred by day 5 of symptom onset in the index case, and 95% of transmission occurred by day 10 of symptom onset in the index case
Del Aguila-Mejia (4)	Spain, December 2021	Retrospective cohort	n=622 index cases, n=455 secondary cases (Omicron BA.1 variant)	Median transmission period after symptom onset: 0 days (IQR: -1 to 2 days)
Xin (5)	China, January to February 2022	Cross-sectional	n=113 pairs of cases (Omicron BA.1.1 variant)	Proportion of transmissions occurring before symptom onset: 33.6% (95% CrI: 24.8% to 42.5%)
				Transmission peaked at symptom onset, all observed transmission events occurring within 5 days after symptom onset

Table 1b. Culture positivity over time

Study	Country, time period	Study type	Participants	Outcome
Boucau (6)	UK, July 2021 to January 2022	Prospective cohort	n=34 cases (Omicron BA.1 variant)	Median time from the first positive RT-PCR to negative culture: 5 days (IQR: 3 to 9 days)
				Median time from the first positive RT-PCR or symptom onset (whichever was earlier) to negative culture: 8 days (IQR: 5 to 10 days)
Bouton (7)	US, November 2021 onwards (end date not stated)	Prospective cohort	n=92 university cases (n=75 Omicron, n=17 Delta)	Culture positive more than 5 days from diagnosis: n=10 (11%)
				Culture positive more than 5 days from symptom onset: n=16 of 92 (17%)
Gilbert (8) (Preprint, conference abstract)	US, November 2021 to March 2022	Prospective cohort	n=54 university cases (variant not stated)	Median time to negative culture: 4 days (IQR: 3 to 5.75 days)
				No statistically significant association between time to negative culture and time since last dose of COVID-19 vaccine (p=0.34)
Jang (9)	South Korea, December 2021	Prospective cohort	n=11 hospitalised cases (Omicron variant)	Last positive viral culture after symptom onset: 8 days
Jung (10)	South Korea, February to March 2022	Prospective cohort	n= 32 healthcare worker asymptomatic and mild cases (Omicron B.1.1.529 variant)	Median time from symptom onset to negative culture: 4 days (95% CI: 3 to 5 days)
				Median time from diagnosis to negative culture: 3 days (95% CI: 3 to 4 days)
Kang (11)	South Korea, February to May 2022	Prospective cohort	n=67 adult cases (Omicron variant)	Median time from symptom onset to negative culture: 4 days (IQR: 1 to 7 days)
Keske (12)	Turkey, January to February 2022	Prospective cohort	n=55 healthcare worker non-severe cases (Omicron variant)	Positive viral cultures (day 5): n=44 of 53 (83%)
				Positive viral cultures (day 7): n=26 of 50 (52%)
				Positive viral cultures (day 10): n=7 of 52 (13.5%)
				Positive viral cultures (day 14): n=4 of 50 (8%)
Kim (13)				Positive viral cultures (day 1, nirmatrelvir and ritanavir group): 51.5%

Study	Country, time period	Study type	Participants	Outcome
	South Korea, October 2021 to May 2022	Prospective cohort	n=33 mild cases (nirmatrelvir and ritanavir group, Omicron BA.1 and BA.2 variants)	Positive viral cultures (day 5, nirmatrelvir and ritanavir group): 18.2%
			n=37 mild cases (supportive care group, Omicron BA.1 and BA.2 variants)	Positive viral cultures (day 1, supportive care group): 86.5%
				Positive viral cultures (day 5, supportive care group): 32.4%
Luna-Muschi (14)	Brazil, January 2022	Prospective cohort	n=30 vaccinated healthcare worker mild cases (Omicron BA.1 variant)	Positive viral culture (day 5 after symptom onset): n=11 of 24 (46%)
				Positive viral culture (day 7 after symptom onset): n=6 of 30 (20%)
				Positive viral culture (day 10 after symptom onset): n=0 of 30 (0%)
Takahashi (15)	Japan, November to December 2021	Retrospective cohort	n=18 asymptomatic and mild cases (Omicron variant)	Positive viral culture (0 to 1 days after diagnosis): n=2 of 17 (11.8%)
				Positive viral culture (2 to 5 days after diagnosis): n=5 of 12 (41.7%)
				Positive viral culture (6 to 9 days after diagnosis): n=3 of 16 (18.8%)
				Positive viral culture (10 to 14 days after diagnosis): n=0 of 17 (0%)
				Positive viral culture (15 days and more after diagnosis): n=0 of 10 (0%)

Table 1c. Incubation period

Study	Country, time period	Study type	Participants	Outcome
Backer (16)	The Netherlands, December 2021 to January 2022	Prospective cohort	n=258 cases (Omicron variant)	Mean incubation period: 3.2 days (95% CrI: 2.9 to 3.6 days), SD: 2.2 days (95% CrI: 1.9 to 2.5 days)
				Median incubation period: 2.8 days (95% CrI: 2.5 to 3.2 days)
Del Aguila-Mejia (4)	Spain, December 2021	Retrospective cohort	n=622 index cases, n=455 secondary cases (Omicron BA.1 variant)	Median incubation period: 3 days (IQR: 1 to 4 days)
Mefsin (17)	Hong Kong, January 2022 to March 2022	Prospective cohort	n=57 cases (Omicron BA.1 variant)	Median incubation period (Omicron BA.1, n=57): 4.38 days (95% CI: 3.88 to 4.87 days)
			n=23 cases (Omicron BA.2 variant)	Median incubation period (Omicron BA.2, n=23, Gamma distribution): 4.27 days (95% CI: 3.29 to 5.02 days)
Park (18) (Preprint)	The Netherlands, November 2021 to January 2022	Retrospective cohort	n=258 cases (Omicron variant)	Mean Incubation period: 4.2 days (95% CI: 3.6 to 4.9 days
Tanaka (19)	Japan, January 2022	Prospective cohort	n=172 cases (BA.1 Omicron variant)	Median incubation period: 2.6 days (95% CI: 2.4 to 2.8 days), IQR: 1.9 days (95% CI: 1.7 to 2.1 days) to 3.5 days (95% CI: 3.2 to 3.9 days)
Ward (20)	UK, May 2020 to February 2022	Retrospective cohort	n=124,948 cases (n=116,163 Omicron BA.1, n=8,785 Omicron BA.2 variant)	Mean incubation period (Omicron BA.1): 3.67 days (95% CrI: 3.61 to 3.72 days), SD: 3.14 days (95% CrI: 3.06 to 3.22 days)
				Mean incubation period (Omicron BA.2): 3.48 days (95% CrI: 3.43 to 3.53 days), SD: 2.90 days (95% CrI: 2.82 to 2.98 days)
				Mean incubation periods did not appear to vary much by age group

Study	Country, time period	Study type	Participants	Outcome
Wei (21) (Preprint)	China, April 2022	Cross-sectional	n=52 cases (Omicron BA.2 variant)	Median incubation period: 4.4 days (IQR: 3.1 to 6.0 days, 95th percentile: 8.3 days)
Xin (5)	China, January to February 2022	Cross-sectional	n=114 cases (Omicron BA.1.1 variant)	Mean incubation period: 3.8 days (95% CrI: 3.5 to 4.1 days), 95th percentile: 6.2 days (95% CrI: 5.7 to 6.9 days)

Table 1d. Latent period

Study	Country, time period	Study type	Participants	Outcome
Xin (5)	China, January to February 2022	Cross-sectional	n=114 cases (Omicron BA.1.1 variant)	Mean latent period: 3.1 days (95% CrI: 2.8 to 3.5 days), 95th percentile: 5.9 days (95% CrI: 5.3 to 6.8 days)

Table 1e. Serial interval and generation time

Study	Country, time period	Study type	Participants	Outcome
Ali (22) (Preprint)	Hong Kong, January to February 2022	Prospective cohort	n=229 case pairs (n=204 cases pairs Omicron, n=25 case pairs Delta variant)	Mean serial interval (all cases): 3.6 days (95% CrI: 3.5 to 3.7 days), SD: 3.4 days (95% CrI: 3.3 to 3.5 days)
			n=30 case pairs (Omicron BA.1 variant)	Mean serial interval (Omicron BA.1): 3.3 days, SD: 2.0 days
			n=174 case pairs (Omicron BA.2 variant)	Mean serial interval (Omicron BA.2): 3.6 days, SD: 1.8 days
An der Heiden (3)	Germany, January to May 2022	Prospective cohort	n=11,512 households (Omicron BA.1 and BA.2 variants)	Mean serial interval (Omicron): 3.61 days (95% CI: 3.56 to 3.66 days)
				Mean serial interval (Omicron BA.1): 3.88 days (95% CI: 3.79 to 3.97 days)
				Mean serial interval (Omicron BA.2): 3.39 days (95% CI: 3.30 to 3.49 days)
Backer (16)	The Netherlands, December 2021 to January 2022	Prospective cohort	n=480 household case pairs (Omicron variant)	Mean serial interval (household case pairs): 3.0 days (SD: 2.3 days)
Del Aguila-Mejia (4)	Spain, December 2021	Retrospective cohort	n=622 index cases, n=455 secondary cases (Omicron BA.1 variant)	Median serial Interval: 4 days (IQR: 3 to 6 days)
Kim (23)	South Korea, November to December 2021	Prospective cohort	n=73 case pairs (Omicron variant)	Mean serial interval: 3.78 days (95% CrI: 3.02 to 4.54 days), SD: 3.33 days (95% CrI: 2.56 to 4.09 days)
				Mean serial interval (child index cases): 3.0 days
				Mean serial interval (adult index cases): 5.0 days
Mefsin (17)	Hong Kong, January 2022 to March 2022	Prospective cohort	n=57 cases (Omicron BA.1 variant)	Median generation time (Omicron BA.1, n=45): 2.38 days (95% CI: 2.01 to 2.80 days)
				Median serial Interval (Omicron BA.1, n=30): 3.15 days (95% CI: 2.49 to 3.92 days)
			n=23 cases (Omicron BA.2 variant)	Median serial Interval (Omicron BA.2, n=13, Gamma distribution): 2.52 days (95% CI: 1.68 to 3.55 days)
Park (18) (Preprint)	The Netherlands, November 2021 to January 2022	Retrospective cohort	n=258 cases (Omicron variant)	Mean serial interval: 3.1 days (95% CI: 2.9 to 3.3 days)
				Mean forward generation interval: 3.0 days (95% CI: 2.7 to 3.2 days)

Study	Country, time period	Study type	Participants	Outcome
Wei (21) (Preprint)	China, April 2022	Cross-sectional	n=234 transmission pairs (Omicron BA.2 variant)	Median serial interval: 4.0 days (IQR: 1.4 to 6.5 days)
Weil (24)	US, December 2021 to February 2022	Prospective cohort	n=37 university clusters (Omicron BA.1 and BA.2 variants)	Median serial interval: 2 days (IQR: 1 to 9 days)

Table 1f. Time to peak viral load

Study	Country, time period	Study type	Participants	Outcome
Choi (25)	South Korea, January 2022	Retrospective cohort	n=5,187 (Omicron variant)	Peak viral load after symptom onset: 2.4 days (95% CI: 2.2 to 2.5 days)
De Michelena (26)	Spain, February to March 2022	Retrospective cohort	n=130 cases (Omicron BA.1 variant)	Time to peak viral load (Omicron BA.1): 3 to 5 days
			n=147 cases (Omicron BA.2 variant)	Time to peak viral load (Omicron BA.2): 1 day
Hay (27)	US, December 2021 to January 2022	Retrospective cohort	n=878 cases (Omicron BA.1 variant) (number of cases not split by vaccination status)	Mean time to peak viral load (proliferation time, fully or partially vaccinated cases): 3.6 days (95% CrI: 3.3 to 4.0 days)
				Mean time to peak viral load (proliferation time, booster vaccinated cases): 4.0 days (95% CrI: 3.8 to 4.3 days)
Kandel (28)	Canada, December 2021 to January 2022	Prospective cohort	n=41 adult cases (Omicron BA.1 variant)	Mean time from symptom onset to peak viral load: 2.97 days
				Mean time from first positive test to peak viral load: 2.89 days
Luna-Muschi (14)	Brazil, January 2022	Prospective cohort	n=30 vaccinated healthcare worker mild cases (Omicron BA.1 variant)	Time from symptom onset to lowest Ct value: 5 days
Sikka (29) (Preprint)	US, February 2021 to January 2022	Prospective cohort	n=37 cases (Omicron BA.1 variant)	Average time to peak viral load: 1.97 days

Table 1g. Time to viral clearance

Study	Country, time period	Study type	Participants	Outcome
Anastasiou (30) (Preprint)	Germany, January 2022	Prospective cohort	n=72 cases (Omicron variant)	Median time to negative test: 7 days (IQR: 2 to 14 days)
				Median time to Ct value above 30: 7 days (IQR: 2 to 8 days)
Cabral (31) (Preprint)	Brazil, January to May 2022	Prospective cohort (RCT)	n=143 mild cases (variant not stated)	Mean time to first negative RT-PCR test (AZVUDINE group): 5.55 days, SD: 0.45 days (estimated from figure)
			n=138 mild cases (variant not stated)	Mean time to first negative RT-PCR test (placebo group): 8.27, SD: 0.59 days (estimated from figure)
Cegolon (32)	Italy, February to March 2022	Prospective cohort (RCT)	n=50 symptomatic or mild cases (Tonimer Lab Panthexyl 800 group, Omicron variant)	Viral shedding time of 7 or more days (Tonimer Lab Panthexyl 800 group): n=33 of 50 (66%)
			n=58 symptomatic or mild cases (control group, Omicron variant)	Viral shedding time of 7 or more days (control group): n=52 of 58 (89%)

Study	Country, time period	Study type	Participants	Outcome
Chen (33)	China, March to May 2022	Prospective cohort	n=847 hospitalised cases (Omicron variant)	Median viral shedding time: 13 days (IQR: 10 to 16 days)
				Viral shedding time was longer for older cases (p=0.037) and cases with chronic kidney disease stage 4 to 5 (p<0.001) or heart conditions (p=0.030), and shorter for cases with full or booster vaccinations (p=0.001)
Chen (34) (Preprint)	China, August to October 2022	Retrospective cohort	n=166 hospitalised cases (Azvudine group, Omicron variant)	Median time from treatment to first negative RT-PCR (Azvudine group): 5 days (IQR: 1 to 7 days)
			n=41 hospitalised cases (control group, Omicron variant)	Median time from treatment to first negative RT-PCR (control group): 6 days (IQR: 5 to 7 days)
Colaneri (35)	Italy, December 2021 to May 2022	Retrospective cohort	n=49 mild and moderate cases with hematologic malignancies (Omicron variant)	Median duration of viral load (untreated): 15 days
				Median duration of viral load (treated with Remdesivir): 21 days
				Median duration of viral load (treated with Sotrovimab): 17 days
				Median duration of viral load (treated with Molnupiravir): 17 days
Cosimi (36) (Preprint)	US, January to February 2022	Prospective cohort	n=40 cases (Omicron variant)	Median time from COVID-19 diagnosis or start of symptoms (whichever came first) to first negative rapid antigen test: 9 days
Dai (37) (Preprint)	US, March to May 2022	Prospective cohort	n=11 cases (Nirmatrelvir-Ritonavir treated, Omicron variant)	Median time from first positive test (diagnosis) to last positive RT-PCR (Ct value less than 35) (Nirmatrelvir-Ritonavir treated): 4 days
			n=25 cases (not treated, Omicron variant)	Median time from first positive test (diagnosis) to last positive RT-PCR (Ct value less than 35) (not treated): 7 days
Gliga (38)	Germany, January to February 2022	Prospective cohort	n=43 immunodeficient cases (Omicron BA.1 and BA.2 variants)	Proportion of cases with viral shedding 21 days after starting sotrovimab (immunodeficient): n=12 of 43 cases (27.9%)
			n=14 immunocompetent cases (Omicron BA.1 and BA.2 variants)	Proportion of cases with viral shedding 21 days after starting sotrovimab (immunocompetent): n=1 of 14 cases (7.1%)
Guo (39) (Preprint)	China, March to May 2022	Retrospective cohort	n=470 hospitalised cases with chronic kidney disease (Omicron BA.2 variant)	Median time to negative RT-PCR test (cases with chronic kidney disease): 13 days (IQR: 8 to 18 days)
			n=1,508 hospitalised cases without chronic kidney disease (Omicron BA.2 variant)	Median time to negative RT-PCR test (cases without chronic kidney disease): 10 days (IQR: 7 to 14 days)
Hay (27)	US, December 2021 to January 2022	Retrospective cohort	n=878 cases (Omicron BA.1 variant) (number of cases not split by vaccination status)	Mean time to negative RT-PCR test (fully or partially vaccinated cases): 6.2 days (95% CrI: 5.8 to 6.6 days)
				Mean time to negative RT-PCR test (booster vaccinated cases): 8.4 days (95% CrI: 8.0 to 8.7 days)
Hua (40)	China, July 2022	Retrospective cohort	n=225 adult cases (Omicron BA.2.38 variant)	Median duration of viral shedding: 11.0 days (IQR: 9.0 to 13.0 days)
				No statistically significant difference in duration of viral shedding between unvaccinated, fully vaccinated and booster vaccinated cases (p=0.85)
Keske (12)	Turkey, January to February 2022	Prospective cohort	n=55 healthcare worker non-severe cases (Omicron variant)	Positive RT-PCR (day 5): n=53 of 55 (96.4%)
				Positive RT-PCR (day 7): n=48 of 55 (87.3%)
				Positive RT-PCR (day 10): n=41 of 55 (74.5%)

Study	Country, time period	Study type	Participants	Outcome
				Positive RT-PCR (day 14): n=23 of 55 (41.8%)
Kojima (41)	US, December 2021	Prospective cohort	n=734 cases (Omicron variant)	Duration of RT-PCR positivity: 14.3 days (SD: 7.0 days)
Lefferts (42)	US, January to February 2022	Prospective cohort	n=564 symptomatic cases (Omicron variant)	Positive rapid antigen test (5 days since symptom onset): n=142 of 179 (79.3%)
				Positive rapid antigen test (6 days since symptom onset): n=80 of 121 (66.1%)
				Positive rapid antigen test (7 days since symptom onset): n=74 of 111 (66.7%)
				Positive rapid antigen test (8 days since symptom onset): n=39 of 93 (41.9%)
				Positive rapid antigen test (9 days since symptom onset): n=26 of 60 (43.3%)
			n=165 asymptomatic cases (Omicron variant)	Positive rapid antigen test (5 days since positive test): n=18 of 58 (31.0%)
				Positive rapid antigen test (6 days since positive test): n=11 of 45 (24.4%)
				Positive rapid antigen test (7 days since positive test): n=1 of 33 (3.0%)
				Positive rapid antigen test (8 days since positive test): n=4 of 19 (21.1%)
				Positive rapid antigen test (9 days since positive test): n=1 of 10 (10.0%)
Li (43)	China, March to April 2022	Prospective cohort	n=175 hospitalised adult cases (nirmatrelvir and ritonavir started 5 or fewer days after symptom onset group, Omicron variant)	Median time from first positive to negative RT-PCR test (nirmatrelvir and ritonavir started 5 or fewer days after symptom onset group): 10 days (IQR: 7 to 12 days)
			n=83 hospitalised adult cases (nirmatrelvir and ritonavir started more than 5 days after symptom onset group, Omicron variant)	Median time from first positive to negative RT-PCR test (nirmatrelvir and ritonavir started more than 5 days after symptom onset group): 15 days (IQR: 11 to 21 days)
			n=224 hospitalised adult cases (untreated group, Omicron variant)	Median time from first positive to negative RT-PCR test (untreated group): 17 days (IQR: 12 to 21 days)
Li (45)	China, April to May 2022	Retrospective cohort	n=6,134 hospitalised asymptomatic and mild cases (Omicron BA.2 variant)	Time to negative test (7 or fewer days): n=1,249 of 6,134 (20.4%)
				Time to negative test (8 to 15 days): n=3,832 of 6,134 (62.4%)
				Time to negative test (16 or more days): n=1,059 of 6,134 (17.2%)
Li (44)	China, June to August 2022	Prospective cohort	n=51 cases (Omicron BA.2 variant)	Time to negative test (7 days or more, Omicron BA.2): 54.38%
				Time to negative test (10 days or more, Omicron BA.2): 21.92%
				Time to negative test (14 days or more, Omicron BA.2): 4.51%
			n=27 cases (Omicron BA.5 variant)	Time to negative test (7 days or more, Omicron BA.5): 96.30%
				Time to negative test (10 days or more, Omicron BA.5): 88.89%
				Time to negative test (14 days or more, Omicron BA.5): 48.15%
Liu (46)	China, April to May 2022	Prospective cohort (quasi-experimental)	n=40 hospitalised asymptomatic, mild, and moderate cases (nasal irrigation group, Omicron BA.2.2 variant)	Time to negative test (nasal irrigation group): 17.58 days (SD: 7.31)

Study	Country, time period	Study type	Participants	Outcome
			n=40 hospitalised asymptomatic, mild, and moderate cases (conventional treatment group, Omicron BA.2.2 variant)	Time to negative test (conventional treatment group): 29.10 days (SD: 3.70)
Lu (47)	China, April to May 2022	Prospective cohort	n=1,337 hospitalised cases aged over 60 years (Omicron variant)	Median time from first positive nucleic acid test to first negative test: 9 days (IQR: 6 to 12 days)
				Viral shedding time was shorter in cases who were fully vaccinated or boosted (p<0.0001), cases receiving paxlovid (p=0.003), and cases with mild compared with severe or critical COVID-19 (p=0.047)
Luna-Muschi (14)	Brazil, January 2022	Prospective cohort	n=30 vaccinated healthcare worker mild cases (Omicron BA.1 variant)	RT-PCR positivity (day 7 after symptom onset): n=30 of 30 (100%)
				RT-PCR positivity (day 10 after symptom onset): n=29 of 30 (97%)
				RT-PCR positivity (day 14 after symptom onset): n=17 of 30 (57%)
Ma (48)	China, up to June 2022 (start date not stated)	Retrospective cohort	n=14 liver transplant cases (Omicron variant)	Time from first positive to first negative RT-PCR test (7 days or fewer): n=3 of 14 (21.4%)
				Time from first positive to first negative RT-PCR test (8 to 14 days): n=4 of 14 (28.6%)
				Time from first positive to first negative RT-PCR test (more than 14 days): n=7 of 14 (50.0%)
				Median time from first positive to first negative RT-PCR test: 14 days
Martin-Blondel (49)	France, January to May 2022	Prospective cohort	n=140 mild or moderate cases at high risk of severe COVID-19 (Sotrovimab group, Omicron BA.1 variant)	Median time to negative RT-PCR test (Sotrovimab group, Omicron BA.1): 12.5 days (95% CI: 10.5 to 14 days)
			n=10 mild or moderate cases at high risk of severe COVID-19 (Nirmatrelvir group, Omicron BA.1 variant)	Median time to negative RT-PCR test (Nirmatrelvir group, Omicron BA.1): 5 days (95% CI: 1 to 12.5 days)
			n=43 mild or moderate cases at high risk of severe COVID-19 (Sotrovimab group, Omicron BA.2 variant)	Median time to negative RT-PCR test (Sotrovimab group, Omicron BA.2): 10.5 days (95% CI: 8 to 12.5 days)
			n=49 mild or moderate cases at high risk of severe COVID-19 (Nirmatrelvir group, Omicron BA.2 variant)	Median time to negative RT-PCR test (Nirmatrelvir group, Omicron BA.2): 4 days (95% CI: 4 to 9 days)
Okumura (50)	Japan, November to December 2021	Retrospective cohort	n=11 cases (Omicron variant)	Time for Ct values to become greater than 30: 6.0 days (95% CI: 4.2 to 7.3 days)
				Time for Ct values to become greater than 35: 10.6 days (95% CI: 9.5 to 11.9 days)
				Time for Ct values to become greater than 40: 15.1 days (95% CI: 13.6 to 17.6 days)
				Time for Ct values to become greater than 45: 19.7 days (95% CI: 17.3 to 23.7 days)
Pei (51)	China, March to May 2022	Retrospective cohort	n=198,262 asymptomatic and mild cases (likely Omicron BA.2 variant)	Median time from first positive to first negative RT-PCR test: 8.29 days (IQR: 5.33 to 11.27 days)

Study	Country, time period	Study type	Participants	Outcome
			n=33,896 asymptomatic and mild cases with comorbidities (likely Omicron BA.2 variant)	Median time from first positive to first negative RT-PCR test (cases with comorbidities): 9.29 days (IQR: 6.33 to 12.28 days)
Shao (52)	China, April to May 2022	Retrospective cohort	n=4 asymptomatic hospitalised cases (Omicron variant)	Median time to negative RT-PCR (asymptomatic cases): 9 days (IQR: 8.0 to 10.5 days)
			n=180 mild hospitalised cases (Omicron variant)	Median time to negative RT-PCR (mild cases): 10 days (IQR: 8.0 to 12.5 days)
			n=41 moderate hospitalised cases (Omicron variant)	Median time to negative RT-PCR (moderate cases): 13 days (IQR: 10.0 to 15.0 days)
			n=1 severe hospitalised cases (Omicron variant)	Time to negative RT-PCR (n=1 severe case): 15 days
Shen (53)	China, March 2022	Prospective cohort	n=60 hospitalised non-severe cases (VV116 treated group, Omicron variant)	Time from first positive to first negative nucleic acid test (VV116 treated group): 9.92 day (95% CI: 9.06 to 10.77 days)
			n=76 hospitalised non-severe cases (untreated group, Omicron variant)	Time from first positive to first negative nucleic acid test (untreated group): 11.13 days (95% CI: 10.22 to 12.04 days)
Shi (54) (Preprint)	China, April to May 2022	Prospective cohort (RCT)	n=91 hospitalised asymptomatic and mild cases (Liushen Pill treated group, Omicron BA.2 variant)	Negative RT-PCR test within 7 days of allocation (Liushen Pill treated group): n=44 of 91 (48.35%)
			n=90 hospitalised asymptomatic and mild cases (control group, Omicron BA.2 variant)	Negative RT-PCR test within 7 days of allocation (control group): n=28 of 90 (31.11%)
Sikka (29) (Preprint)	US, February 2021 to January 2022	Prospective cohort	n=37 cases (Omicron BA.1 variant)	Median time to RT-PCR clearance: 9.5 days
Sun (55) (Preprint)	China, April 2022	Retrospective cohort	n=100 hospitalised asymptomatic cases (Omicron BA.2.2.1 variant)	Median time from first positive test to cessation of viral shedding (asymptomatic cases): 10 days (IQR: 9 to 11 days)
			n=274 hospitalised mild cases (Omicron BA.2.2.1 variant)	Median time from first positive test to cessation of viral shedding (mild cases): 10 days (IQR: 9 to 12 days)
Takahashi (15)	Japan, November to December 2021	Retrospective cohort	n=18 asymptomatic and mild cases (Omicron variant)	Positive RT-PCR test (0 to 1 days after diagnosis): n=17 of 17 (100%)
				Positive RT-PCR test (2 to 5 days after diagnosis): n=11 of 12 (91.7%)
				Positive RT-PCR test (6 to 9 days after diagnosis): n=16 of 16 (100%)
				Positive RT-PCR test (10 to 14 days after diagnosis): n=12 of 17 (70.6%)
				Positive RT-PCR test (15 days and more after diagnosis): n=3 of 10 (30.0%)
Tillman (56)	Germany, study period not stated	Prospective cohort	n=20 vaccinated adult chronic dialysis mild cases (Omicron variant)	Mean time from diagnosis to negative RT-PCR test: 13 days

Study	Country, time period	Study type	Participants	Outcome
Van der Veer (57) (Preprint)	The Netherlands, November 2021 to February 2022	Prospective cohort	n=142 healthcare worker cases (Omicron BA.1 variant)	Median time from first positive to first negative RT-PCR test (Omicron BA.1): 12 days (IQR: 10 to 15 days)
			n=37 healthcare worker cases (Omicron BA.2 variant)	Median time from first positive to first negative RT-PCR test (Omicron BA.2): 11 days (IQR: 10 to 13 days)
Wei (58) (Preprint)	China, May to July 2022	Prospective cohort (RCT)	n=94 asymptomatic or mild adult cases (120mg Cepharanthine group, Omicron variant)	Mean time from randomisation to first negative RT-PCR test (120mg Cepharanthine group): 4.70 days (95% CI: 4.11 to 5.30 days)
			n=102 asymptomatic or mild adult cases (60mg Cepharanthine group, Omicron variant)	Mean time from randomisation to first negative RT-PCR test (60mg Cepharanthine group): 4.15 days (95% CI: 3.65 to 4.65 days)
			n=85 asymptomatic or mild adult cases (placebo group, Omicron variant)	Mean time from randomisation to first negative RT-PCR test (placebo group): 4.58 days (3.89 to 5.26 days)
Weng (59)	China, April to May 2022	Retrospective cohort	n=82 hospitalised mild or moderate cases aged over 60 years (Paxlovid group, Omicron variant)	Median time from first positive test to second negative test (Paxlovid group): 16.5 days (IQR: 13 to 20 days)
			n=81 hospitalised mild or moderate cases aged over 60 years (control group, Omicron variant)	Median time from first positive test to second negative test (control group): 20 days (IQR: 17 to 22 days)
Wu (60) (Preprint)	Hong Kong, February to July 2022	Retrospective cohort	n=1,084 mild to moderate cases aged 0 to 18 years (Omicron BA.2 variant)	Median time from symptom onset to RT-PCR Ct value of over 33 (aged 0 to 18 years, mild to moderate cases): 10.4 days (IQR: 8.9 to 11.9 days)
			n=807 mild to moderate cases aged 19 to 64 years (Omicron BA.2 variant)	Median time from symptom onset to RT-PCR Ct value of over 33 (aged 19 to 64 years, mild to moderate cases): 11.6 days (IQR: 9.3 to 13.7 days)
			n=487 mild to moderate cases aged 65 to 74 years (Omicron BA.2 variant)	Median time from symptom onset to RT-PCR Ct value of over 33 (aged 65 to 79 years, mild to moderate cases): 13.6 days (IQR: 11.3 to 16.3 days)
			n=682 mild to moderate cases aged 80 years and older (Omicron BA.2 variant)	Median time from symptom onset to RT-PCR Ct value of over 33 (age 80 years and over, mild to moderate cases): 15.6 days (IQR: 12.7 to 17.9 days)
			n=12,669 symptomatic cases (Omicron BA.2 variant)	The time from symptom onset to RT-PCR Ct value of over 33 was shorter for vaccinated cases ($p<0.001$), younger cases ($p<0.001$), and cases with milder infections
Wu (61)	China, March 2022	Retrospective cohort	n=129 vaccinated asymptomatic or mild cases (likely Omicron BA.2 variant)	Mean time from first positive RT-PCR test to RT-PCR Ct value above 35 (vaccinated): 12.6 days (SD: 3.4 days)
			n=13 unvaccinated asymptomatic or mild cases (likely Omicron BA.2 variant)	Mean time from first positive RT-PCR test to RT-PCR Ct value above 35 (unvaccinated): 14.8 days (SD: 4.7 days)

Study	Country, time period	Study type	Participants	Outcome
Xu (62)	China, April 2022	Retrospective cohort	n=13,162 asymptomatic or mild cases (Omicron BA.2.2 variant)	Negative RT-PCR test by 7 days: n=5,437 of 13,162 (41.3%)
				Negative RT-PCR test by 14 days: n=12,482 of 13,162 (94.8%)
Xu (65)	China, April to May 2022	Prospective cohort	n=413 adult asymptomatic or mild cases (Interferon alpha-2b spray group, Omicron variant)	Median time to negative RT-PCR test (interferon alpha-2b spray group): 11.90 days
			n=458 adult asymptomatic or mild cases (control group, Omicron variant)	Median time to negative RT-PCR test (control group): 12.58 days
Xu (66) (Preprint)	China, April to June 2022	Retrospective cohort	n= 83 hospitalised haemodialysis cases (Omicron variant)	Mean time from first positive to first negative RT-PCR tests (haemodialysis cases): 18.15 days (SD: 6.37 days)
			n=134 hospitalised non-haemodialysis cases (Omicron variant)	Mean time from first positive to first negative RT-PCR tests (non- haemodialysis cases): 11.18 days (SD: 3.52 days)
Xu (63)	China, April to May 2022	Prospective cohort (RCT)	n=1,393 asymptomatic or mild cases (Reyanning group, Omicron variant)	Median time from hospitalisation to negative nucleic acid test (Reyanning group): 6 days (IQR: 3 to 9 days)
			n=1,407 asymptomatic or mild cases (control group, Omicron variant)	Median time from hospitalisation to negative nucleic acid test (control group): 7 days (IQR: 5 to 9 days)
Xu (64)	China, April to June 2022	Retrospective cohort	n=346 child asymptomatic or mild cases (Lianhua Qingwen group, likely Omicron BA.2 variant)	Median time from admission to negative RT-PCR test (Lianhua Qingwen group): 5.0 days (IQR: 3.0 to 7.0 days)
			n=346 child asymptomatic or mild cases (control group, likely Omicron BA.2 variant)	Median time from admission to negative RT-PCR test (control group): 6.0 days (IQR: 5.0 to 8.0 days)
Yan (67)	China, April to May 2022	Prospective cohort	n=5 hospitalised child mild or moderate cases (Paxlovid group, likely Omicron BA.2 variant)	Median time from first positive RT-PCR test or symptom onset (whichever was earlier) to first negative RT-PCR test (Paxlovid group): 9 days (IQR: 9 to 10 days)
			n=30 hospitalised child mild or moderate cases (control group, likely Omicron BA.2 variant)	Median time from first positive RT-PCR test or symptom onset (whichever was earlier) to first negative RT-PCR test (control group): 11 days (IQR: 9 to 12 days)
Yang (68)	China, April to May 2022	Retrospective cohort	n=13 child mild or moderate cases with congenital heart disease (likely Omicron BA.2.2 variant)	Mean duration of viral clearance: 16.4 days (SD: 2.9 days)
Yang (69) (Preprint)	China, March to May 2022	Retrospective cohort	n=603 hospitalised child cases (likely Omicron BA.2.2 variant)	Median time from first positive to first negative RT-PCR test: 12 days (IQR: 9 to 14 days
				Viral shedding time was longer in cases with abnormal defecation and more severe disease, and shorter in vaccinated cases and cases with higher household vaccination rates
Yin (70)	China, March to May 2022	Retrospective cohort	n=199,590 asymptomatic or mild cases (Omicron BA.2 variant)	Mean time from illness onset to negative RT-PCR test: 7.17 days (SD: 3.42 days)

Study	Country, time period	Study type	Participants	Outcome
Ying-Hao (71)	China, April to May 2022	Retrospective cohort	n=25,168 asymptomatic or mild cases (Omicron BA.2 variant)	Median time from first positive to first negative RT-PCR test: 6 days (IQR: 4 to 9 days)
Yu (72)	China, April 2022	Prospective cohort	n=42 asymptomatic cases (Omicron BA.2.2 variant)	Mean time from first positive to first negative nucleic acid test (asymptomatic cases): 9.26 days (SD: 3.16 days)
			n=619 mild cases (Omicron BA.2.2 variant)	Mean time from first positive to first negative nucleic acid test (mild cases): 10.62 days (SD: 2.73 days)
Zee (73)	Hong Kong, February to March 2022	Retrospective cohort	n=422 fully vaccinated healthcare worker cases (likely Omicron BA.2.2 variant)	Mean time to 2 consecutive negative rapid antigen tests: 9.76 days
Zeng (74)	China, January 2022	Prospective cohort	n=355 fully vaccinated hospitalised cases (inactive vaccine, Omicron variant)	Median time from first positive to first negative SARS-CoV-2 RNA test (fully vaccinated with inactive vaccine cases): 17.0 days (IQR: 12.0 to 22.0 days)
			n=14 fully vaccinated hospitalised cases (recombinant vaccine, Omicron variant)	Median time from first positive to first negative SARS-CoV-2 RNA test (fully vaccinated with recombinant vaccine cases): 20.5 days (IQR: 17.8 to 26.3 days)
			n=11 partially vaccinated hospitalised cases (Omicron variant)	Median time from first positive to first negative SARS-CoV-2 RNA test (partially vaccinated cases): 16.0 days (IQR: 9.0 to 25.0 days)
Zhang (75)	China, March to May 2022	Retrospective cohort	n=33 hospitalised haemodialysis mild cases aged 45 to 99 years (Omicron variant)	Mean time from first positive to first negative nucleic acid test (haemodialysis cases): 16.67 days (SD: 5.22 days)
			n=66 hospitalised non-haemodialysis mild cases aged 45 to 99 years (Omicron variant)	Mean time from first positive to first negative nucleic acid test (non-haemodialysis cases): 14.07 days (SD: 5.43 days)
Zhong (76)	China, April to May 2022	Prospective cohort	n=106 hospitalised elderly cases (Paxlovid group, likely Omicron BA.2.2 variant)	Mean time from first positive to first negative nucleic acid test (Paxlovid group): 9.32 days (SD: 2.78 days)
			n=36 hospitalised elderly cases (control group, likely Omicron BA.2.2 variant)	Mean time from first positive to first negative nucleic acid test (control group): 11.11 days (SD: 2.67 days)
Zhong (77) (Preprint)	China, from April 2022 (end date not stated)	Retrospective cohort	n=180 hospitalised elderly cases (Omicron BA.2.2 variant)	Mean time from first positive to first negative nucleic acid test: 10 days (IQR: 8 to 12 days)

Table 1h. Viral load over time

Study	Country, time period	Study type	Participants	Outcome
Bouton (7)	US, November 2021 onwards (end date not stated)	Prospective cohort	n=92 university cases (n=75 Omicron, n=17 Delta variant)	Data extracted from figure: Ct values increased from day 0 to day 15 after diagnosis (more slowly after day 8), Ct values steady from 3 days before to 1 day after symptom onset, increased from day 1 to day 20 after symptom onset (more slowly after day 9), proportion of positive cultures rose between days 1 and 3 after diagnosis (to about 30% positivity), then reduced to 0 by 8 days after diagnosis (some sporadic

Study	Country, time period	Study type	Participants	Outcome
				positive cultures up to day 15), proportion of positive cultures rose from 1 day before to 4 days after symptom onset (to about 30% positivity), dropped substantially on day 5 (to about 10%), then continued to drop until day 13, with no further positive cultures up to day 20
Choi (25)	South Korea, January 2022	Retrospective cohort	n=5,187 (Omicron variant)	Data extracted from figure: Ct values decreased (viral load increased) up to between 3 and 4 days after symptom onset, increased (viral load decreased) to between 12 and 13 days after symptom onset, then decreased again (viral load increased) up to 17 days after symptom onset (data truncated after this)
Funk (78) (Preprint)	England, December 2021 to January 2022	Cross-sectional	n=1,212,234 cases (n=1,083,976 Omicron BA.1, n=128,258 Omicron BA.2 variant)	Data extracted from figure: Ct values for both Omicron BA.1 and BA.2 decreased from days 0 to 2 since symptom onset, then increased up to day 6 since symptom onset (data truncated at day 6). BA.2 infections had higher Ct values than BA.1 infections, reinfections had higher Ct values than no known previous infections, and there was no clear difference between people with different doses of vaccine.
Li (79)	Hong Kong, January to February 2022	Retrospective cohort	n=104 hospitalised cases (likely Omicron BA.2.2 variant)	Data extracted from figure: The Ct value was lowest (viral load highest) on day 1 after symptom onset, and gradually decreased until 10 days after symptom onset (data truncated after this)
Marking (80) (Preprint)	Sweden, January to February 2022	Prospective cohort	n=60 cases (Omicron BA.1, BA.1.1 and BA.2 variants)	Data extracted from figure: Ct values decreased (viral load increased) up to day 3 from first positive RT-PCR test, then increased (viral load decreased) up to day 15 (data truncated at day 15)
Tassetto (81)	US, July 2021 to March 2022	Prospective cohort	n=33 cases (Omicron BA.1 variant)	Data extracted from figure: Ct values increased from days 2 to 7 after symptom onset (data truncated before day 2), with a decrease in Ct values in days 7 to 9 (data truncated at day 9)
Teyssou (82)	France, December 2021 to May 2022	Prospective cohort	n= 84 cases (Omicron BA.1 variant)	Data extracted from figure: For Omicron BA.1, Ct values decreased (viral load increased) from symptom onset to days 1 to 3 after symptom onset, then increased (viral load decreased) until day 10 after symptom onset (data truncated at day 10)
			n=60 cases (Omicron BA.2 variant)	Data extracted from figure: For Omicron BA.2, Ct values increased (viral load decreased) from symptom onset to days 1 to 3 after symptom onset, decreased (viral load increased) until days 7 to 9 after symptom onset, then increased (viral load decreased) until day 10 after symptom onset (data truncated at day 10)
Townsley (83) (Preprint)	UK, January 2021 to May 2022	Prospective cohort	n=240 cases (Omicron BA.1 and BA.2 variants)	Data extracted from figure: Ct values decreased (viral load increased) up to days 2 and 3 from first symptom onset, then increased (viral load decreased) up to day 15 (data truncated around day 15 for Omicron BA.1 variant cases), then slightly decreased (viral load increased) up to day 17 for Omicron BA.2 variant cases (data truncated at day 17 for Omicron BA.2 variant cases)
Young (84) (Preprint)	Singapore, December 2021	Retrospective cohort	n=87 cases (Omicron B.1.1529 variant)	Data extracted from figure: Ct values decreased (viral load increased) over the first 2 to 3 days of illness, then increased (viral load decreased) until 20 days after illness onset (data truncated at 20 days)

The difference in transmission from people with asymptomatic compared with symptomatic COVID-19 Omicron variant

Evidence

In total, 10 observational studies looking at the difference in COVID-19 transmission between asymptomatic and symptomatic cases were included in this report (5 preprints (55, 85 to 88), one rated as low quality (87), 6 rated as medium quality (55, 86, 88 to 91), and 3 rated as high quality (51, 85, 92)). All studies were identified through the literature search, as no studies of the Omicron variant were found in our previous review (unpublished, search up to 15 March 2022). Three studies reported on the difference in the secondary attack rates (SAR) between asymptomatic and symptomatic index cases (85, 86, 88), while 5 studies reported on differences in viral load (87, 89 to 92) and 2 studies reported on differences in viral shedding time between asymptomatic and symptomatic cases (51, 55).

Five studies were conducted in Asia (51, 55, 88, 90, 91), 3 studies in the US (87, 89, 92), one study in Turkey (85), and one study in Nicaragua (86). While most studies were conducted between December 2021 and June 2022 when the COVID-19 Omicron variant was dominant across the world, other studies started earlier and reported COVID-19 Omicron variant cases separately. All studies were either retrospective (51, 55, 87, 89, 91) or prospective (85, 86, 88, 90, 92) cohort studies.

Table 2 gives study characteristics of the 10 included studies.

Secondary attack rates

Three prospective cohort studies reported the household SAR of asymptomatic and symptomatic COVID-19 Omicron variant index cases (85, 86, 88). Study characteristics are given in Table 2a.

Erik and others (preprint, rated as high quality) reported on the household SAR of COVID-19 (variant not stated) from n=42 index cases and n=112 household contacts in Turkey between August 2021 and February 2022 (85). The results suggested that asymptomatic index cases transmitted COVID-19 substantially less than symptomatic index cases, although imprecision was high (odds ratio [OR] of transmission = 0.12, 95% confidence interval [CI]: 0.02 to 0.77, p=0.03).

Frutos and others (preprint, rated as medium quality) reported on the household SAR of COVID-19 (likely Omicron variant) in n=104 households in Nicaragua between January 2022

and June 2022 (86). The results suggested that symptomatic index cases (SAR = 20%, 95% CI: 17% to 25%) transmitted COVID-19 substantially more than asymptomatic index cases (SAR = 2%, 95% CI: 1% to 8%), although imprecision was again high (relative risk [RR] of transmission = 14.77, 95% CI: 3.12 to 70.03).

Wei and others (preprint, rated as medium quality) reported on the household SAR of COVID-19 (likely Omicron BA.2 variant) from n=236 index cases (including n=67 children) and n=546 adult household contacts in China in April 2022 (88). The results suggested that asymptomatic index cases (SAR = 72.7%, 95% CI: 62.0% to 83.5%) transmitted COVID-19 at a similar rate to symptomatic index cases (SAR = 77.7%, 95% CI: 74.0% to 81.4%, p value for difference = 0.46).

Viral load

Five studies reported the viral loads of asymptomatic and symptomatic COVID-19 Omicron variant cases (87, 89 to 92). Most studies measured Ct (cycle threshold) values with RT-PCR (reverse-transcriptase polymerase chain reaction), which are inversely proportional to viral load, though do not necessarily indicate infectious virus (87, 89 to 91). Study characteristics are given in Table 2b.

Three studies reported similar Ct values or viral loads between asymptomatic and symptomatic cases in the US (87, 89) and China (91), although the number of participants was small in all studies. Wu and others (rated as medium quality) reported similar Ct values (Omicron variant COVID-19) between n=22 asymptomatic (median nasopharyngeal Ct value = 27.8, interquartile range [IQR]: 23.4 to 34.5) and n=339 symptomatic cases (median nasopharyngeal Ct value = 30.5, IQR: 24.5 to 35, p value for difference = 0.19) (91). Kaur and others (conference abstract only, rated as low quality) reported similar viral loads (Omicron variant COVID-19) between n=45 asymptomatic, n=23 pre-symptomatic, and post-infection asymptomatic cases (p value = 0.45) (87). Laitman and others (rated as medium quality) reported similar Ct values (likely Omicron BA.1 variant COVID-19) between n=272 asymptomatic (median Ct value = 22.98, SD: 4.4) and n=552 symptomatic cases (median Ct value = 21.27, SD: 4.2) (89).

Conversely, 2 studies reported differences in viral loads or Ct values between asymptomatic and symptomatic cases in Japan (90) and the US (92). Suzuki and others (rated as medium quality) reported proportionately higher Ct values (lower viral loads, Omicron BA.1 and BA.2 variant COVID-19) in n=28 asymptomatic compared with n=382 symptomatic cases, for example, 29% of asymptomatic and 46% of symptomatic cases had Ct values of less than 20, but did not test these differences statistically (90). The Heroes-Recover Network and others (rated as high quality) reported higher viral loads (Omicron B.1.1.529 and BA1 variant COVID-19) in n=628 symptomatic (mean viral load = 3.4 $\log_{10}$ copies per µL, standard deviation [SD]: 1.6 $\log_{10}$ copies per µL) compared with n=96 asymptomatic cases (mean viral load = 2.3 $\log_{10}$ copies per µL, SD: 1.8 $\log_{10}$ copies per µL), with a mean difference of 1.2 $\log_{10}$ copies per µL (95% CI: 0.8 $\log_{10}$ copies per µL to 1.6 $\log_{10}$ copies per µL).

Viral shedding time

Two studies reported the viral shedding time (typically time from symptom onset to negative RT-PCR) of asymptomatic and mildly symptomatic COVID-19 Omicron variant cases in China (51, 55). Study characteristics are given in Table 2c.

Pei and others (rated as high quality) reported that the viral shedding time (likely Omicron BA.2 variant) was longer in cases with a mild COVID-19 infection (n=20,504) compared with asymptomatic cases (n=177,758) (OR for viral shedding time of more than 8.3 days, 1.50, 95% CI: 1.46 to 1.55, p<0.001) (51).

Conversely, Sun and others (preprint, rated as medium quality) reported similar viral shedding times (Omicron BA.2.2.1 variant) between n=100 asymptomatic (median viral shedding time = 10 days, IQR: 9 to 11 days) and n= 274 mildly infected cases (median viral shedding time = 10 days, IQR: 9 to 12 days, p value for difference = 0.35) (55).

Summary

Ten studies reported on differences in transmission from people with asymptomatic compared with symptomatic COVID-19 Omicron variant. Three studies compared household SAR of asymptomatic and symptomatic index cases, with 2 studies suggesting more transmission from symptomatic than asymptomatic index cases although imprecision was high, and one study suggesting no clear difference. Five studies compared viral loads (usually using Ct values) between symptomatic and asymptomatic cases, with 3 studies suggesting similar viral loads, and 2 studies suggesting higher viral loads in symptomatic compared with asymptomatic cases. Two studies compared viral shedding times between symptomatic and asymptomatic cases, with one study suggesting similar viral shedding times, and one study suggesting longer viral shedding times in symptomatic compared with asymptomatic cases.

All studies were relatively small, with only one study having more than a few hundred participants (51), which increases the imprecision of the results. The evidence was also limited due to the small number of studies, the variability between studies and differences in results, which limit our ability to draw conclusions.

Table 2. Studies for asymptomatic compared with symptomatic transmission

Acronyms: CI = confidence interval, IQR = interquartile range, OR = odds ratio, RT-PCR = reverse transcriptase polymerase chain reaction, SAR = secondary attack rate, SD = standard

Table 2a. Secondary attack rates (SARs)

Study	Country, time period	Study type	Participants	Definition of symptomatic	Outcome	
Erik (85) (preprint)	Turkey, August 2021 to February 2022	Prospective cohort	n=42 index cases, n=112 household contacts (variant not stated)	Any of: sore throat, runny nose, cough, fever (and other symptoms not listed)	OR for transmission (asymptomatic compared with symptomatic index cases):	0.12 (95% CI: 0.02 to 0.77, p=0.03)
Frutos (86) (preprint)	Nicaragua, January to June 2022	Prospective cohort	n=104 households (likely Omicron variant)	Not stated (daily symptom data collected by staff during visits)	SAR (symptomatic index cases):	0.20 (95% CI: 0.17 to 0.25)
					SAR (asymptomatic index cases):	0.02 (95% CI: 0.01 to 0.08)
					RR for transmission (symptomatic compared with asymptomatic index cases):	14.77 (95% CI: 3.12 to 70.03)
Wei (88) (preprint)	China, April 2022	Prospective cohort	n=236 index cases, n=546 household contacts (likely Omicron BA.2 variant)	Moderate COVID-19 defined as non-severe pneumonia (definitions of mild, severe and critical COVID-19 not stated)	SAR (asymptomatic index case, n=24):	72.7% (95% CI: 62.0% to 83.5%)
					SAR (symptomatic index case, n=212):	77.7% (95% CI: 74.0% to 81.4%)
					p value for difference:	0.46

Table 2b. Viral load

Study	Country, time period	Study type	Participants	Definition of symptomatic	Outcome	
Heroes-Recover Network (92)	US, December 2020 to May 2022	Prospective cohort	n=743 cases (Omicron B.1.1.529 and BA1 variants)	Presence of 1 or more of the following: fever, chills, cough, shortness of breath, sore throat, diarrhoea, muscle aches, or a change in smell or taste	Mean viral load (Asymptomatic, n=96):	2.3 log_{10} copies per µL (SD: 1.8 log_{10} copies per µL)
					Mean viral load (Symptomatic, n=628):	3.4 log_{10} copies per µL (SD: 1.6 log_{10} copies per µL)
					Mean difference in viral load (symptomatic compared with asymptomatic cases):	1.2 log_{10} copies per µL (95% CI: 0.8 to 1.6 log_{10} copies per µL)
Kaur (87) (preprint)	US, December 2021	Retrospective cohort	n=68 cases (Omicron variant)	Not stated	No statistically significant difference in the Ct values of asymptomatic (n=45), pre-symptomatic (n=23), and post-infection asymptomatic cases (p=0.45)	
Laitman (89)	US, December 2021 to January 2022	Retrospective cohort	n=1,935 viral samples (likely Omicron BA.1 variant)	Not stated	Median Ct value (Roche Cobas) (Asymptomatic, n=272):	22.98 (SD: 4.4)
					Median Ct value (Roche Cobas) (Symptomatic, n=552):	21.27 (SD: 4.2)
Suzuki (90)	Japan, December 2021 to February 2022	Prospective cohort	n=410 viral samples (Omicron BA.1 and BA.2 variants)	Not stated	Ct values (asymptomatic, n=28):	Less than 20: n=8 (29%); 20 to 24: n=16 (57%); 25 to 29: n=3 (11%); 30 and above: n=1 (4%)

Study	Country, time period	Study type	Participants	Definition of symptomatic	Outcome	
					Ct values (symptomatic, n=382):	Less than 20: n=175 (46%); 20 to 24: n=164 (43%); 25 to 29: n=25 (7%); 30 and above: n=18 (5%)
Wu (91)	China, January 2022	Retrospective cohort	n=361 cases (Omicron variant)	Patients with one or more of: fever, cough, fatigue, decreased or loss of ability to smell and taste, nasal congestion, runny nose, sore throat, conjunctivitis, myalgia, and diarrhoea	Median nasopharyngeal Ct value (symptomatic, n=339):	30.5 (IQR: 24.5 to 35)
					Median nasopharyngeal Ct value (asymptomatic, n=22):	27.8 (IQR: 23.4 to 34.5)
					p value for difference (nasopharyngeal):	0.19
					Median oropharyngeal Ct value (symptomatic, n=339):	34.5 (IQR: 30 to 37)
					Median oropharyngeal Ct value (asymptomatic, n=22):	33.5 (IQR: 26 to 35)
					p value for difference (oropharyngeal):	0.11

Table 2c. Viral shedding time

Study	Country, time period	Study type	Participants	Definition of symptomatic	Outcome	
Pei (51)	China, March 2022 to May 2022	Retrospective cohort	n=198,262 cases (likely Omicron BA.2 variant)	Not stated	OR of viral shedding time of more than 8.29 days (mild infection [n=20,504] compared with asymptomatic cases [n=177,758]):	1.50 (95% CI: 1.46 to 1.55, p<0.001)
Sun (55) (preprint)	China, April 2022	Retrospective cohort	n=382 cases (Omicron BA.2.2.1 variant)	Moderate COVID-19 defined as onset of fever or respiratory symptoms (or both) and radiographic evidence of pneumonia (not stated, but mild COVID-19 likely symptoms less severe than moderate COVID-19)	Median viral shedding time (asymptomatic, n=100):	10 days (IQR: 9 to 11 days)
					Median viral shedding time (mildly infected, n=274):	10 days (IQR: 9 to 12 days)
					p value for difference:	0.35

Inequalities

There was little evidence available to explore inequalities through variations across populations and subgroups (notably, no included study included cases from more than one country), for example cultural variations or differences between ethnic, social or vulnerable groups. As such, it was not possible to examine inequalities in this report.

Limitations

The source of evidence in this review included peer-reviewed and preprint articles. We did not conduct an extensive search of other sources (such as websites of public health organisations). As with all reviews, the evidence identified may be subject to publication bias, whereby null or negative results are less likely to have been published by the authors, though descriptive studies may be less susceptible to publication bias than other study types.

For infectious period, 24 of the 82 included studies were preprints, and for asymptomatic compared with symptomatic transmission, 5 of the 10 included studies were preprints. In general, preprints should be treated with caution as they have not been peer reviewed or subject to publishing standards and may be subject to change.

In addition, this rapid review is limited by the fact that we were reviewing evidence for the COVID-19 Omicron variant, which caused outbreaks of COVID-19 in different countries. Studies may have been conducted rapidly, with the aim to provide evidence in a timely manner, and this may have impacted on quality, both in term of design (especially limited statistical analyses) and reporting (insufficient detail).

This review was conducted at pace following streamlined methodology. Quality of the descriptive studies was not assessed and only the main characteristics of the studies were extracted. The narrative summary was conducted by one reviewer and checked by another.

Evidence gaps

For infectious period, there was a reasonable amount of evidence for most of the different measures of infectious period. However, only 3 studies measured infectious period directly, and none from the UK. Additionally, the majority of studies included cases with only COVID-19 Omicron BA.1 and BA.2 variant, which may limit generalisability to the current circulating variants.

For asymptomatic compared with symptomatic transmission of COVID-19, only 3 studies directly compared transmission from asymptomatic and symptomatic cases, again with none from the UK. Additionally, as with infectious period, the vast majority of studies included cases with only Omicron BA.1 and BA.2 variant COVID-19, limiting generalisability to the current circulating variants.

Conclusion

Infectious period of Omicron variant COVID-19

In total, 82 studies provided evidence on different measures of the Omicron variant COVID-19 infectious period. The 3 studies directly measuring the transmission period suggested most transmission events happened around symptom onset, with the majority of transmission events happening up to 5 days after symptom onset (100% in one study, 81% in another study, not reported in the third study). The 10 studies measuring viral culture positivity also suggested that viral culture positivity was highest in the first 5 days after symptom onset or diagnosis, and the 14 studies reporting on viral load over suggested that peak viral loads occurred a median and mean of 2 to 5 days after symptom onset.

The 9 studies measuring serial interval and generation time suggested the median and mean serial interval was between 2 and 4 days (though this could be variable, with interquartile ranges between one and 9 days), and generation times of around 3 days. The studies measuring incubation period suggested the median and mean incubation period was between 2 and 5 days.

The 53 studies measuring time to viral clearance suggested that there were substantial differences in viral clearance times between cases and populations, although the differences in measurement of time to viral clearance between studies may have contributed to these differences. In general, however, most studies of the general population estimated viral clearance to take around 7 to 11 days, and most studies of hospitalised, immunodeficient, and other high-risk cases estimated viral clearance to take around 10 to 15 days. Detectable viral load does not necessarily indicate that a case is infectious.

Overall, the evidence suggests that COVID-19 Omicron variant cases were most infectious up to 5 days after symptom onset, but could potentially be infectious for longer, especially if hospitalised, immunocompromised, or otherwise high-risk cases. However, while some studies included substantial numbers of cases, most studies included relatively few cases, and the majority of studies only included Omicron BA.1 and BA.2 variant cases.

Asymptomatic compared with symptomatic transmission of Omicron variant COVID-19

In total, 10 studies reported on differences in transmission from people with asymptomatic compared with symptomatic Omicron variant COVID-19. Three studies compared household SARs of asymptomatic and symptomatic index cases, with 2 studies suggesting more transmission from symptomatic than asymptomatic index cases (although imprecision was high), and one study suggesting no clear difference. Five studies compared viral loads (usually

using Ct values) between symptomatic and asymptomatic cases, with 3 studies suggesting similar viral loads, and 2 studies suggesting higher viral loads in symptomatic compared with asymptomatic cases. Two studies compared viral shedding times between symptomatic and asymptomatic cases, with one study suggesting similar viral shedding times, and one study suggesting longer viral shedding times in symptomatic compared with asymptomatic cases.

Overall, the evidence on differences in transmission from people with asymptomatic compared with symptomatic Omicron variant COVID-19 was mixed, with some studies suggesting that symptomatic cases were more likely to transmit Omicron variant COVID-19 than asymptomatic cases and others showing no difference. The lack of precision due to small study samples combined with the variability between studies and the small number of studies limit our ability to draw conclusions.

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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: i) use accelerated methods and may not be representative of the whole body of evidence publicly available; ii) have undergone an internal, but not independent, peer review; and iii) are only valid as of the date stated on the review.

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Annexe A. Methods

This rapid review aimed to answer the following research questions:

1. What is the infectious period of Omicron variant COVID-19?
2. What is the difference in transmission from people with asymptomatic compared with symptomatic Omicron variant COVID-19?

Only studies where the majority of the participants in the study have the Omicron variant of COVID-19 (any sub-lineage) were included.

We have conducted previous (unpublished) reviews looking for rapid and systematic reviews covering the infectious period of COVID-19 (searches to 23 February 2022 and 16 May 2022). However, these could not be used as source of evidence for primary studies as these searches aimed at identifying existing rapid and systematic reviews, these reviews will not be used as a source of evidence. The infectious period primary study search therefore started 1 December 2021, shortly after the start of the Omicron wave.

We also conducted a previous (unpublished) review looking at the difference in transmission of COVID-19 between symptomatic and asymptomatic index cases (search to 15 March 2022). This review was used as a source of evidence up to 15 March 2022.

The review questions for this current review were searched for and reported separately within the same report.

Our rapid review approach follows streamlined systematic methodologies (1). In particular, 10% of the screening on title and abstract were screened in duplicate; full text screening, data extraction and risk of bias assessment were performed by one reviewer and checked by another. The review has been reported according to PRISMA guidelines (93).

Protocol

A protocol was produced a priori.

Inclusion and exclusion criteria

Article eligibility criteria are summarised in Table A.1.

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	All	Animals
Settings	All settings	
Context	COVID-19 pandemic	Other infectious diseases
Intervention or exposure	Omicron variant COVID-19 (any sub-lineage)	
Outcomes	• any measure of infectious period of COVID-19, including live virus culture (for example, from cytopathic effects in cell cultures, and the isolation of live virus from cell cultures), epidemiology and contract tracing, viral RNA shedding, and, if necessary, incubation period • transmission of COVID-19 from people with asymptomatic or symptomatic COVID-19, as measured by secondary attack rates • viral load comparisons between people with asymptomatic and symptomatic COVID-19	
Language	English	
Date of publication	1 December 2021 (infectious period search) and 15 March 2022 (asymptomatic transmission search) to 25 January 2023	
Study design	• Interventional studies • Observational studies (cohorts, case controls and cross-sectional studies)	• systematic or narrative reviews • case reports (of single cases) • guidelines • opinion pieces • modelling studies • laboratory studies • ecological studies
Publication type	Published and preprint	

Identification of studies

Our previous review on the difference in transmission of COVID-19 between symptomatic and asymptomatic index cases was used to identify studies published up to 15 March 2022 (latest search date).

We searched OVID Medline, OVID Embase, and preprint servers (medRxiv, bioRxiv, aRxiv, and Research Square, via COVID-19 portfolio) for studies published after 1 December 2021 (for the infectious period of Omicron variant COVID-19) and 15 March 2022 (for the difference in asymptomatic and symptomatic Omicron variant COVID-19 transmission).

Screening

Screening on title and abstract was undertaken in duplicate by 2 reviewers for at least 10% of the eligible studies (separately for each of the searches), with the remainder completed by one reviewer. Disagreement was resolved by discussion.

Screening on full text was undertaken by one reviewer with a second reviewer checking the excluded full texts, and disagreement resolved by discussion.

If the dominant variant was not stated in a study, participants in studies conducted after 1 December 2022 were considered likely to have Omicron variant COVID-19 (meeting the inclusion criteria for COVID-19 variant), whereas studies not reporting the time period of the study were excluded.

Data extraction

Summary information for each study was extracted and reported in tabular form. Information included country, setting, study design, objective, outcomes measures, participants, study period, results and any relevant contextual data (such as timing or level of community transmission at the time of the study). This was undertaken by one reviewer and checked by a second.

Risk of bias assessment

Risk of bias for analytical studies (studies comparing asymptomatic and symptomatic transmission of COVID-19) was assessed using the quality criteria checklist (QCC) for primary research which assesses the methodological quality of a study. This tool can be applied quickly to most study designs to consider core areas of potential bias. Risk of bias was assessed by one reviewer and checked by a second.

Risk of bias for descriptive studies (studies measuring the infectious period of Omicron variant COVID-19) were not assessed.

Search strategy for infectious period of Omicron variant COVID-19

Search strategy Ovid Medline

1 exp SARS-CoV-2/ (146874)
2 exp COVID-19/ (210509)
3 (corona* adj1 (virus* or viral*)).tw,kw,kf. (5961)
4 (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. (113432)
5 (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. (344396)
6 exp COVID-19 Vaccines/ (19017)
7 exp COVID-19 Testing/ (10360)
8 or/1-7 (352015)
9 ((Transmis* or transmit*) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (13916)
10 (Infectious* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (5806)
11 (Contagio* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (315)
12 (Isolation adj3 (duration* or time or length* or period*)).tw,kw,kf. (3612)
13 (shed* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (3487)
14 Virus Shedding/ (4172)
15 (PCR positiv* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (456)
16 (Viral proliferat* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (6)
17 cycl* threshold*.tw,kw,kf. (2484)
18 CT value*.tw,kw,kf. (4742)
19 (peak* adj1 (vir* load* or vir* concentration)).tw,kw,kf. (384)
20 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (36921)
21 8 and 20 (4990)
22 (Viral Load/ or exp Disease Transmission, Infectious/) and exp Time/ (9404)
23 COVID-19/tm and exp Time/ (304)
24 8 and 22 (291)
25 21 or 23 or 24 (5428)
26 limit 25 to dt=20211201-20230126 (1822)

Search strategy Ovid Embase

1 exp severe acute respiratory syndrome coronavirus 2/ (86769)
2 coronavirus disease 2019/ (309119)
3 experimental coronavirus disease 2019/ (18)
4 (corona* adj1 (virus* or viral*)).tw,kw. (6270)

5 (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. (115399)
6 (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. (388908)
7 COVID-19 Testing/ (6418)
8 exp SARS-CoV-2 vaccine/ (29066)
9 or/1-8 (415212)
10 ((Transmis* or transmit*) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (15531)
11 (Infectious* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (7489)
12 (Contagio* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (313)
13 (Isolation adj3 (duration* or time or length* or period*)).tw,kw,kf. (4573)
14 (shed* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (3981)
15 virus shedding/ (9802)
16 (PCR positiv* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (606)
17 (Viral proliferat* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (7)
18 cycl* threshold*.tw,kw,kf. (3344)
19 CT value*.tw,kw,kf. (7645)
20 (peak* adj1 (vir* load* or vir* concentration)).tw,kw,kf. (606)
21 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (50254)
22 (exp virus load/ or exp disease transmission/) and (time/ or time factor/) (2479)
23 9 and 21 (7127)
24 22 or 23 (9570)
25 limit 24 to dc=20211201-20230126 (3062)

Search strategy for COVID-19 portfolio

Search will be carried out on 26 January 2023, date limited from 1 December 2021.

(“transmission period”~5 OR “transmission duration”~5 OR “transmission time”~5 “transmission length”~5 OR “transmitted period”~5 OR “transmitted duration”~5 OR “transmitted time”~5 OR “transmitted length”~5 OR “transmissible period”~5 OR “transmissible duration”~5 OR “transmissible time”~5 OR “transmissible length”~5 OR “infectious duration”~5 OR “infectious period”~5 OR “infectious time”~5 OR “infectious time”~5 OR “infectious length”~5 OR “contagious duration”~5 OR “contagious period”~5 OR “contagious time”~5 OR “contagious length”~5 OR “shedding duration”~5 OR “shedding period”~5 OR “shedding time”~5 OR “shedding length”~5 OR “cycle threshold” OR “cycling threshold” OR “CT value”)

Search strategy for the difference in transmission of COVID-19 from people with asymptomatic and symptomatic Omicron variant COVID-19

Search strategy Ovid Medline

1 exp SARS-CoV-2/ (146325)
2 exp COVID-19/ (209172)
3 (corona* adj1 (virus* or viral*)).tw,kw,kf. (5942)
4 (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. (112571)
5 (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. (341602)
6 exp COVID-19 Vaccines/ (18791)
7 exp COVID-19 Testing/ (10322)
8 or/1-7 (349211)
9 transmiss*.tw,kf. (466722)
10 transmit*.tw,kf. (193714)
11 (breakthrough or break through).tw,kf. (27417)
12 viral load*.tw,kf. (39861)
13 viral burden.tw,kf. (1148)
14 viral level*.tw,kf. (370)
15 (shed*1 or shedding).tw,kf. (118634)
16 cytopath* effect*.tw,kf. (8659)
17 Viral Load/ (38565)
18 exp Disease Transmission, Infectious/ (80110)
19 Cytopathogenic Effect, Viral/ (9596)
20 Virus Shedding/ (4169)
21 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (861934)
22 asymptomatic*.tw,kf. (185094)
23 symptomatic*.tw,kf. (217451)
24 pre-symptomatic.tw,kf. (1861)
25 non-symptomatic.tw,kf. (1021)
26 (symptom free or symptom-free).tw,kf. (9086)
27 no symptom*.tw,kf. (11375)
28 with* symptom*.tw,kf. (80153)
29 symptomless.tw,kf. (3072)
30 symptom* status.tw,kf. (1600)
31 exp Asymptomatic Diseases/ (9921)
32 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (431945)

33 8 and 21 and 32 (4684)
34 COVID-19/tm [Transmission] (4798)
35 32 and 34 (559)
36 33 or 35 (4770)
37 limit 36 to dt=20220315-20230126 (984)

Search strategy Ovid Embase

1 exp severe acute respiratory syndrome coronavirus 2/ (86533)
2 coronavirus disease 2019/ (308026)
3 experimental coronavirus disease 2019/ (18)
4 (corona* adj1 (virus* or viral*)).tw,kw. (6298)
5 (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. (114978)
6 (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. (387643)
7 COVID-19 Testing/ (6371)
8 exp SARS-CoV-2 vaccine/ (28834)
9 or/1-8 (413724)
10 transmiss*.tw,kf. (520930)
11 transmit*.tw,kf. (226337)
12 (breakthrough or break through).tw,kf. (39022)
13 viral load*.tw,kf. (62319)
14 viral burden.tw,kf. (1475)
15 viral level*.tw,kf. (499)
16 (shed*1 or shedding).tw,kf. (138850)
17 cytopath* effect*.tw,kf. (9405)
18 exp virus load/ (103317)
19 exp disease transmission/ (235545)
20 cytopathogenic effect/ (10696)
21 virus shedding/ (9776)
22 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (1078321)
23 asymptomatic*.tw,kf. (270074)
24 symptomatic*.tw,kf. (335224)
25 pre-symptomatic.tw,kf. (3247)
26 non-symptomatic.tw,kf. (1593)
27 (symptom free or symptom-free).tw,kf. (12424)
28 no symptom*.tw,kf. (17051)
29 with* symptom*.tw,kf. (122988)
30 symptomless.tw,kf. (2711)
31 symptom* status.tw,kf. (2520)
32 exp asymptomatic disease/ (29248)

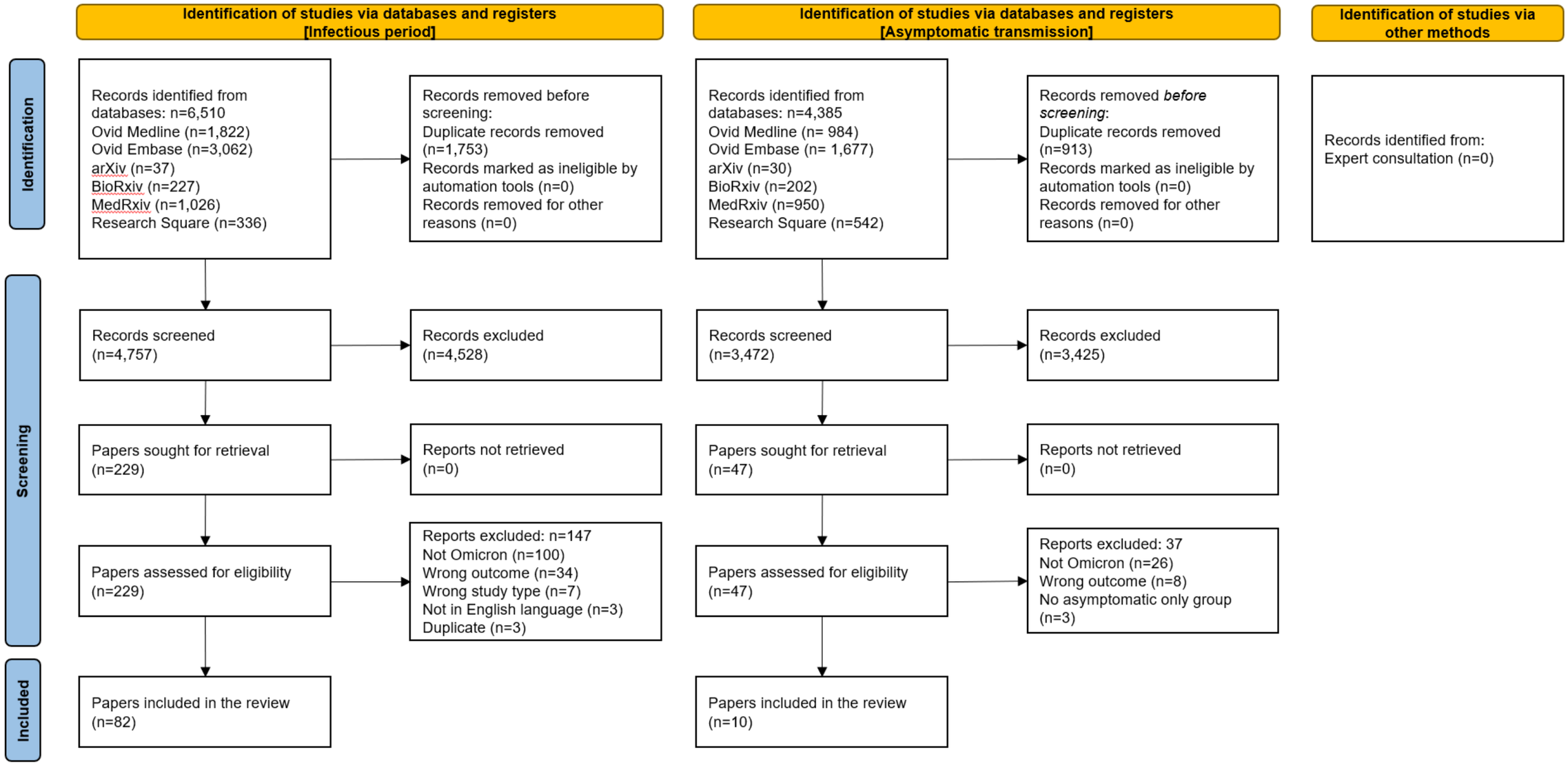
33 asymptomatic carrier/ (1267)
34 asymptomatic transmission/ (114)
35 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 (652094)
36 asymptomatic coronavirus disease 2019/ (1792)
37 22 and 36 (587)
38 9 and 22 and 35 (6837)
39 37 or 38 (6840)
40 limit 39 to dc=20220315-20230126 (1677)

Search strategy for COVID-19 portfolio

Search will be carried out on 26 January 2023, date limited from 15 March 2022.

(transmiss* OR transmit* OR breakthrough OR “break through” OR “viral load*” OR “viral burden” OR “viral level*” OR shed OR sheds OR shedding) AND (asymptomatic* OR symptomatic* OR “pre-symptomatic*” OR “non-symptomatic*” OR “symptom free” OR “no symptom*” OR “with* symptom*” OR symptomless OR “symptom status”)

Figure A.1. PRISMA diagram



Accessible text version of Figure A.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 82 studies for the research question concerning infectious period, and 10 studies for the research question concerning the difference in transmission of COVID-19 from asymptomatic and symptomatic cases.

From identification of studies via databases and registers for the studies on infectious period, n=6,510 records identified from databases:

- Ovid Medline (n=1,822)
- Ovid Embase (n=3,062)
- arXiv (n=37)
- BioRxiv (n=227)
- MedRxiv (n=1,026)
- Research square (n=336)

From these, records removed before screening:

- duplicate records removed (n=1,753)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=4,757 records screened, of which n=4,528 were excluded, leaving n=229 papers sought for retrieval, all of which were retrieved.

Of the n=229 papers assessed for eligibility, n=147 reports were excluded:

- not Omicron (n=100)
- wrong outcome (n=34)
- wrong study type (n=7)
- not English language (n=3)
- duplicate (n=3)

From identification of studies via other methods, n=0 studies were identified from expert consultation.

Overall, n=82 papers included in the review for the research question concerning infectious period.

From identification of studies via databases and registers for the studies on asymptomatic transmission, n=4,385 records identified from databases:

- Ovid Medline (n=984)
- Ovid Embase (n=1,677)
- arXiv (n=30)
- BioRxiv (n=202)
- MedRxiv (n=950)
- Research square (n=542)

From these, records removed before screening:

- duplicate records removed (n=913)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=3,472 records screened, of which n=3,425 were excluded, leaving n=47 papers sought for retrieval, all of which were retrieved.

Of the n=47 papers assessed for eligibility, n=37 reports were excluded:

- not Omicron (n=26)
- wrong outcome (n=8)
- no asymptomatic only group (n=3)

From identification of studies via other methods, n=0 studies were identified from expert consultation.

Overall, n=10 papers included in the review for the research question concerning asymptomatic transmission.

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

UKHSA is an executive agency, sponsored by the Department of Health and Social Care.

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