

COVID-19 infectious period

A rapid evidence review (update 1)

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Main messages

- This review (search to 4 September 2023) is an update of a previous rapid review (search to 26 January 2023), and identifies and summarises global evidence on coronavirus (COVID-19) Omicron variant infectious period in all settings (82 studies from the previous review (<u>1 to 82</u>) and 111 studies from this update (<u>83 to 195</u>)).
- The 5 studies that directly examined 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) (<u>1 to 4</u>, <u>83</u>). Three studies suggested that between a third and a half of transmission events occurred before symptom onset in the index case (<u>2</u>, <u>4</u>, <u>83</u>).
- 3. Twenty-one studies measured viral culture positivity and suggested that this was highest in the first 5 days after symptom onset or diagnosis (3, 5 to 13, 84 to 94). A further 16 studies reporting on time to peak viral load (3, 12, 23 to 27, 116 to 125) and 11 studies reporting on viral load over time (6, 23, 76 to 82, 194, 195), suggested that peak viral loads occurred a median or mean of 1 to 5 days after symptom onset.
- 4. The 26 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 1 and 9 days). Generation times of between 1 and 7 days were reported (<u>1</u>, <u>2</u>, <u>14 to 16</u>, <u>19 to 22</u>, <u>83</u>, <u>96</u>, <u>97</u>, <u>100</u>, <u>101</u>, <u>103</u>, <u>105 to 115</u>).
- 5. Nineteen studies measuring incubation period suggested the median or mean incubation period was between 2 and 6 days (2, 4, 14 to 19, 95 to 105).
- 6. One hundred and thirty-five studies were identified measuring time to viral clearance (typically positive to negative COVID-19 test) (10, 12, 13, 25, 27 to 75, 85, 87 to 89,91 to 94, 103, 118, 119, 121, 123 to 193). These suggested that there were substantial differences in viral clearance times between cases in individual studies and populations across studies, although the differences in measurement of time to viral clearance between studies may have contributed to these differences. In general, however, most studies of people in the community estimated the mean or median viral clearance to be around 7 to 11 days (including for the BA.5 sub-lineage and studies up to January 2023). Most studies of people who were hospitalised, immunodeficient, or had chronic health conditions, estimated the mean or median viral clearance to be around 10 to 15 days. Detectable viral load does not necessarily indicate that a case is infectious.
- 7. Overall, the evidence is consistent with the findings from the previous review, suggesting that COVID-19 Omicron variant cases were most infectious around symptom onset and up to 5 days after, but could potentially be infectious for longer, especially for cases that are hospitalised, immunocompromised, or otherwise high risk. Three studies looked at transmission before symptom onset. These suggested that between a third and a half of transmission events occurred before symptom onset in the index case. However, while some studies included substantial numbers of cases, most studies included relatively few cases, and the majority of studies included cases with Omicron variant BA.1 and BA.2, with only a small number of studies reporting evidence from 2023.

Purpose

To identify and summarise evidence relating to the infectious period of COVID-19, including all Omicron sub-lineages and any later variants.

Methods

There was one review question:

1. What is the infectious period of COVID-19, including all Omicron sub-lineages and any later variants?

This is an update to a previous rapid review (search to 26 January 2023) that identified and summarised evidence on the infectious period of Omicron variant coronavirus (COVID-19) (<u>196</u>). The previous review also searched for evidence on the difference in transmission from people with asymptomatic compared with symptomatic COVID-19 infection, but this was not considered in this update of the review. The title and research question have been changed because between 28 August and 3 September 2023 all sequenced COVID-19 cases in England had variants that were sub-lineages of Omicron (excepting 1.2% of sequences that were from SARS-CoV-2 lineages not designated as a variant by the UK Health Security Agency (UKHSA), or the sequence was of insufficient quality to identify the variant) (<u>197</u>). However, new variants may emerge that are not sub-lineages of Omicron, and if necessary, these will be captured in future updates of this review on COVID-19 infectious period.

A rapid review update was conducted to search for primary studies between 26 January 2023 (search date of last review) and 4 September 2023, following streamlined systematic methodologies to accelerate the review process (<u>198</u>). Specifically, 20% of the title and abstract screening was completed in duplicate with the remainder screened by one reviewer, and full text screening and data extraction were performed by one reviewer and checked by another. Full details on the methodology are provided in <u>Annexe A</u>.

Only studies where the majority of the participants in the study were stated to have Omicron or later variants of COVID-19 were included.

Evidence

In total, 193 observational studies looking at different measures of COVID-19 infectious period (described below) were included in this report, 82 studies from the previous review (<u>1 to 82</u>) and 111 studies from this update (<u>83 to 195</u>). As per the protocol for this review, as all the data extracted was descriptive rather than analytical, risk of bias in studies was not assessed. Studies excluded at full text screening are listed in <u>Annexe B</u> with reasons for exclusion.

Infectious period is difficult to measure directly, so studies reporting on related measures were also included. The studies included in the original review were all still relevant for the review question in this update, and therefore no distinction is made between the studies found in the original review and the update.

In total, 5 studies reported directly on transmission period (1 to 4, 83), 21 studies on culture positivity over time (3, 5 to 13, 84 to 94), 19 studies on incubation period (2, 4, 14 to 19, 95 to 105), one study on latent period (4), 26 studies on serial interval and generation time (1, 2, 14 to 16, 19 to 22, 83, 96, 97, 100, 101, 103, 105 to 115), 16 studies on time to peak viral load (3, 12, 23 to 27, 116 to 125), 135 studies on time to viral clearance (10, 12, 13, 25, 27 to 75, 85, 87 to 89, 91 to 94, 103, 118, 119, 121, 123 to 193), and 11 studies on viral load over time (6, 23, 76 to 82, 194, 195). Some studies provided evidence for multiple outcomes. Studies on transmission period provide the most direct evidence for the period of infectiousness, other studies provide more indirect evidence by looking at outcomes that are related to transmission and infectiousness, such as viral load. Additionally, a detectable viral load does not necessarily indicate that a case is infectious. 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 (typically above 5,000 people) studies conducted in the UK, and studies of more recent Omicron sub-lineages (BA.3 and later) are individually summarised, whereas the remainder of studies are jointly summarised. The approximate size of the largest jointly summarised study is reported at the start of each section. Annexe C gives study characteristics of the 198 included studies.

Transmission period

There were 5 included studies (1 to 4, 83) (no preprints) that reported direct evidence for the transmission period of COVID-19. These studies identified index cases and known or likely secondary cases (either through contact tracing (2 to 4, 83) or assuming household clusters were related to an index case in the household (1)) and estimated when transmission was likely to have taken place. These studies provide the most direct evidence for the period of infectiousness.

A summary of studies is given in Table 1a, and study characteristics are given in Table C.1a.

Study variable	Number of studies
Study location	 3 in Europe (excluding the UK) (<u>1</u>, <u>2</u>, <u>83</u>)
	• 1 in China (<u>4</u>)
	 1 in South Korea (<u>3</u>)

Table 1a. Summary of transmission period studies

Study variable	Number of studies
Study design	 1 prospective cohort study (<u>1</u>)
	 2 were retrospective cohort studies (<u>2</u>, <u>3</u>)
	 2 cross-sectional studies (<u>4</u>, <u>83</u>)
Study timeframe	All studies were conducted between December 2021 and May 2022
Omicron sub-	• 3 reported on BA.1 (<u>2 to 4</u>)
lineages	 1 reported on BA.1 and BA.2 (<u>1</u>)
reported	 1 did not report the Omicron sub-lineage (83)

All 5 studies are summarised in detail below.

Summaries of individual studies

An der Heiden and others reported on transmission of COVID-19 Omicron variant BA.1 and BA.2 in 11,512 households in Germany between January 2022 and May 2022 (<u>1</u>). 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 622 index cases and 455 secondary cases in Spain in December 2021 (2). The median transmission period after symptom onset was the day of symptom onset (interquartile range [IQR]: 1 day before to 2 days after symptom onset).

Jung and others reported on transmission of COVID-19 Omicron B.1.1.529 variant in 9 healthcare workers exposed to an identified index case in South Korea between March and April 2022 (3). In total, 3 cases (33%) were diagnosed one day after exposure to the index case. One case (11%) was diagnosed 2 days after exposure, and 5 cases (56%) were diagnosed 3 days after exposure.

Manica and others reported on transmission of COVID-19 Omicron variant in 23,122 cases in Italy in January 2022 (<u>83</u>). The estimated proportion of infections that were caused by symptomatic cases before the onset of their symptoms was 51% (95% credible interval [Crl]: 46% to 56%).

Xin and others reported on transmission of COVID-19 Omicron variant BA.1.1 between 113 pairs of cases in China between January and February 2022 ($\underline{4}$). The estimated proportion of transmissions occurring 4 or more days before symptom onset was 4.4% (95% 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 21 included studies (3, 5 to 13, 84 to 94) (4 of which were preprints (7, 85, 86, 92)) that included evidence on viral culture positivity over time for COVID-19. 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 reverse transcriptase polymerase chain reaction (RT-PCR).

A summary of studies is given in Table 1b, and study characteristics are given in Table C.1b.

Study variable	Number of studies
Study location	• 1 in the UK (<u>10</u>)
	 10 in Asia (<u>3</u>, <u>8</u>, <u>9</u>, <u>11</u>, <u>13</u>, <u>87 to 90</u>)
	 6 in North America (<u>6</u>, <u>7</u>, <u>84 to 86</u>, <u>92</u>)
	 3 in Europe (excluding the UK) (<u>5,12,93</u>)
	• 1 in Brazil (<u>12</u>)
Study design	 18 prospective cohort studies (<u>3</u>, <u>5 to 12</u>, <u>85 to 90</u>, <u>92 to 94</u>)
	 2 retrospective cohort studies (<u>3</u>, <u>91</u>)
	 1 cross-sectional study (<u>5</u>, <u>12</u>)
Study timeframe	All studies were conducted between November 2021 and August 2022, except one that was conducted between April 2022 and February 2023 (<u>92</u>), and another between February and March 2023 (<u>6</u> , <u>8 to 10</u> , <u>13</u>)
Omicron sub-	• 6 reported on BA.1 (<u>3, 5, 12, 90, 92, 93</u>)
lineages	 4 reported on BA.1 and BA.2 (<u>11</u>, <u>87</u>, <u>89</u>, <u>94</u>)
reported	 1 reported on BA.2 and BA.5 (85)
	 1 reported on BA.1, BA.2, BA.4 and BA.5 (<u>91</u>)
	 1 reported on BA.2, BA.5 and XBB (86)
	• 7 did not report the Omicron sub-lineage (<u>6</u> , <u>8 to 10</u> , <u>13</u> , <u>84</u> , <u>88</u>)
	 1 did not report the COVID-19 variant, though was very likely Omicron due to the time period of the study (7)

Table 1b. Summary of viral culture positivity over time studies

The study from the UK (5), and the studies reporting on the BA.5 and XBB sub-lineages (85, 86, 88, 92) are summarised in detail below. 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 32 Omicron BA.1 variant cases in the UK up to January 2022 (5). 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).

Dzieciolowska and others reported the proportion of positive viral cultures on days 5, 7, and 10 of infection in 121 Omicron variant BA.1 (12%), BA.2 (60%), and BA.5 (8%) cases in healthcare workers in Canada between February and March 2023 (85). In total, 87 of 121 cases were positive on day 5 (71.9%, 95% CI: 63.0% to 79.7%), 56 of 120 cases were positive on day 7 (46.7%, 95% CI: 27.5% to 56.0%), and 22 of 121 cases were positive on day 10 of their infection (18.2%, 95% CI: 11.8% to 26.2%).

Edelstein and others reported on the median time to first negative viral culture in 55 cases who received no therapy and 72 cases who received nirmatrelvir and ritonavir (Omicron variant BA.2, BA.5, XBB, and other sub-lineages) in the US from March 2022 (end date not reported) (86). The median time to first negative viral culture was 4 days (IQR: 3 to 6 days) in cases who received no therapy, and 3 days (IQR: 2 to 4 days) in cases who received nirmatrelvir and ritonavir. There were 15 cases who received nirmatrelvir and ritonavir and had virologic rebound, and in this group the median time to final negative viral culture was 14 days (IQR: 13 to 20 days).

Kang and others reported the median duration of viable virus shedding in 40 Omicron variant BA.1 and BA.2 and 42 BA.5 cases in healthcare workers in South Korea between January and August 2022 (<u>88</u>). The median duration of viable virus shedding was 4 days (IQR: 3 to 5 days) for the BA.1 and BA.2 cases, and 2.5 days (IQR: 2 to 3 days) for the BA.5 cases.

Raglow and others reported the proportion of cases with culture positivity of more than 32 days in 150 immunocompromised adult cases (Omicron BA.1 [3%], BA.2 [31%], BA.4 [6%], BA.5 [29%], and unknown Omicron [32%] sub-lineages) in the US between April 2022 and February 2023 (92). In total, 5 of 150 cases (3%) had positive cultures of more than 32 days.

Joint summary of remaining studies

Five studies measured the median time from symptom onset to negative viral cultures $(\underline{3}, \underline{7}, \underline{9})$. Four studies estimated a median time of 4 days, with interquartile ranges varying between 2 or 3 to 5 or 6 days $(\underline{3}, \underline{7})$ and one to 7 days $(\underline{9})$. The remaining study was in cases with haematologic malignancies or solid organ transplants, and the median duration of viable virus shedding was 4 weeks (IQR: 3 to 6 weeks) (<u>87</u>).

The remaining 11 studies reported on the proportion of cases with positive viral cultures on different days after either symptom onset or diagnosis ($\underline{6}, \underline{8}, \underline{10 \text{ to } 13}, \underline{84}, \underline{90}, \underline{91}, \underline{93}, \underline{94}$).

Culture positivity was highest in the first 5 days after symptom onset or diagnosis, with different studies reporting:

- 68% and 100% at day 3 (<u>12</u>)
- 33% (<u>94</u>), 46% (<u>10</u>), and 83% (<u>13</u>) at day 5
- a peak of around 30% at day 4 dropping to 10% at day 5 (11)
- 51.5% and 86.5% at day one falling to 18.2% and 32.4% at day 5 depending on treatment (<u>12</u>)
- 11.8% at days 0 to one rising to 41.7% at days 2 to 5 (13)

Beyond 5 days after symptom onset or diagnosis, culture positivity fell, with different studies reporting:

- 20% at day 7 after symptom onset (13)
- 52% at day 7, 13.5% at day 10, and 8% at day 14 (8)
- 18.8% at days 6 to 9 (<u>13</u>)

The time from symptom onset or diagnosis to no further positive cultures was variable, with different studies reporting:

- 8 days (<u>13</u>)
- 10 days (<u>6</u>)
- 10 to 14 days (<u>13</u>)
- 13 days (<u>6</u>)
- 14 days (<u>93</u>)
- at least 15 days (<u>94</u>)
- at least 58 days (91) (in cases with haematological malignancies)

Incubation period

There were 19 included studies ($\underline{2}$, $\underline{4}$, $\underline{14 \text{ to } 19}$, $\underline{95 \text{ to } 105}$) (no preprints, one study extracted from abstract only ($\underline{101}$)) that included evidence for the incubation period of COVID-19. 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.

A summary of studies is given in Table 1c, and study characteristics are given in Table C.1c.

Table 1c. Summary of incubation period studies

Study variable	Number of studies
Study location	 1 in the UK (<u>18</u>)
	 13 in Asia (<u>4</u>, <u>15</u>, <u>17</u>, <u>19</u>, <u>96</u>, <u>97</u>, <u>99 to 105</u>)

Study variable	Number of studies
	 5 in Europe (excluding the UK) (<u>2</u>, <u>14</u>, <u>16</u>, <u>18</u>, <u>95</u>)
	 1 in the Faroe Islands (<u>98</u>)
Study design	• 4 prospective cohort studies (<u>14</u> , <u>15</u> , <u>17</u> , <u>96</u>)
	 5 retrospective cohort studies (<u>2</u>, <u>16</u>, <u>18</u>, <u>97</u>, <u>103</u>)
	 10 cross-sectional studies (<u>4</u>, <u>19</u>, <u>95</u>, <u>98 to 102</u>, <u>104</u>, <u>105</u>)
Study timeframe	All studies were conducted between November 2021 and October 2022
Omicron sub-	 6 reported on BA.1 (<u>2</u>, <u>4</u>, <u>17</u>, <u>99</u>, <u>100</u>, <u>105</u>)
lineages	 2 reported on BA.2 (<u>19</u>, <u>96</u>)
reported	 2 reported on BA.1 and BA.2 (<u>15</u>, <u>18</u>)
	 4 reported on BA.5 (<u>101 to 104</u>)
	 5 did not report the Omicron sub-lineage (<u>14</u>, <u>16</u>, <u>95</u>, <u>97</u>, <u>98</u>)

One study from the UK is summarised in detail below (<u>18</u>), along with 4 studies reporting on the BA.5 sub-lineage (<u>101 to 104</u>). The remaining studies typically included fewer than 1,000 cases in total and are jointly summarised below.

Summaries of individual studies

Liu and others reported on the median incubation period of 44 cases with the Omicron variant BA.5.2 in China in October 2022 (<u>101</u>). The median incubation period was estimated to be 2.52 days (IQR: 1.32 to 4.84 days).

Ogata and others reported on the median and mean incubation period of 122 transmission pairs with the Omicron variant BA.5 in Japan between January and August 2022 (<u>102</u>). The mean incubation period was estimated to be 2.6 days (95% CI: 2.5 to 2.8 days, SD: 1.0 day), and the median incubation period was estimated to be 2.5 days (95% CI: 2.5 to 2.7, IQR: 1.9 to 3.2 days, 5th percentile: 1.2 days, 95th percentile: 4.5 days).

Wang and others reported on the median incubation period of 60 cases with the Omicron variant BA.5.2 in China between August and September 2022 (<u>103</u>). The median incubation period was estimated to be 5.7 days (95% Crl: 4.8 to 6.6 days, 95th percentile: 12.8 days).

Ward and others reported on the incubation period of 124,948 cases (116,163 BA.1, 8,785 BA.2 Omicron sub-lineage) in the UK up to February 2022 (<u>18</u>). 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.

Xiong and others reported on the mean incubation period of 600 cases with the Omicron variant BA.5 in China between June and July 2022 (<u>104</u>). The mean incubation period was estimated to be 3.27 days (SD: 1.05 days).

Joint summary of remaining studies

The remaining 14 studies estimated the median (2, 14, 15, 17, 19, 95) or mean incubation period (4, 14, 16, 96, 98, 100), or both (97, 99, 105). The median incubation period was estimated to be between 2 and 5 days with interquartile ranges between 1 and 6 days (2, 14, 15, 17, 19, 95, 97, 99, 105), with one study suggesting the 95th percentile to be around 6 days (99). The mean incubation period was estimated to be between 2 and 5 days (4, 14, 16, 96 to 100, 105), with one study estimating the 95th percentile to be less than 7 days (4), and another study suggesting the incubation period increased with age and 2 to 3 vaccination doses, compared with 0 or 1 vaccination dose (97).

Latent period

One included study reported on the latent period of the COVID-19 (<u>4</u>). 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.

A summary of studies is given in Table 1d, and study characteristics are given in Table C.1d.

Study variable	Number of studies
Study location	• 1 in China (<u>4</u>)
Study design	 1 cross-sectional studies (<u>4</u>)
Study timeframe	All studies were conducted between January 2022 and February 2022
Omicron sub- lineages reported	• 1 reported on BA.1 (<u>4</u>)

Xin and others estimated the latent period of 114 cases with COVID-19 Omicron variant BA.1.1 between January 2022 and February 2022 in China (<u>4</u>). The estimated mean latent period was 3.1 days (95% credible interval [Crl]: 2.8 to 3.5 days), with 95% of cases developing detectable virus levels 5.9 days after infection (95% Crl: 5.3 to 6.8 days).

Serial interval and generation time

There were 26 included studies (1, 2, 14 to 16, 19 to 22, 83, 96, 97, 100, 101, 103, 105 to 115) (2 preprints (20, 112), one study extracted from abstract only as the full study was not available

in English (<u>101</u>)) that included evidence for the serial interval or generation time of COVID-19. 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 (typically from contact tracing studies), this was usually estimated in the same way as for serial interval.

One study reported results specifically for children ($\underline{21}$). A summary of studies is given in Table 1e, and study characteristics are given in <u>Table C.1e</u>.

Study variable	Number of studies
Study location	• 1 in the UK (<u>106</u>)
	 14 in Asia (<u>15</u>, <u>19 to 21</u>, <u>96</u>, <u>97</u>, <u>100</u>, <u>101</u>, <u>103</u>, <u>105</u>, <u>108</u>, <u>111</u>, <u>113 to</u> <u>115</u>)
	 7 in Europe (excluding the UK) (<u>1</u>, <u>2</u>, <u>14</u>, <u>16</u>, <u>83</u>, <u>109</u>, <u>110</u>)
	 3 in the US (<u>22</u>, <u>107</u>, <u>112</u>)
Study design	• 12 cross-sectional studies (<u>19, 83, 100, 101, 105, 106, 108, 110 to 115</u>)
	 9 prospective cohort studies (<u>1</u>, <u>14</u>, <u>15</u>, <u>20 to 22</u>, <u>96</u>, <u>107</u>, <u>109</u>)
	• 4 retrospective cohort studies (2, <u>16</u> , <u>97</u> , <u>103</u>)
Study timeframe	All studies were conducted between November 2021 and October 2022
Omicron sub-	 9 reported on BA.1 (<u>2</u>, <u>21</u>, <u>100</u>, <u>105</u>, <u>107</u>, <u>110</u>, <u>113 to 115</u>)
lineages	 3 reported on BA.2 (<u>19</u>, <u>96</u>, <u>111</u>)
reported	 4 reported on BA.1 and BA.2 (<u>1, 15, 20, 22</u>)
	 2 reported on BA.5.2 (<u>101</u>, <u>103</u>)
	 1 reported on BA.2.12.1, BA.4 and BA.5 (<u>108</u>)
	 2 reported on BA.1, BA.2, BA.4, and BA.5 (<u>109</u>, <u>112</u>)
	• 5 did not report the Omicron sub-lineage (<u>14</u> , <u>16</u> , <u>83</u> , <u>97</u> , <u>106</u>)

Table 1e. Summary of serial interval and generation time studies

One study included over 11,000 households (<u>1</u>), and another included over 23,000 cases (<u>83</u>), and both are summarised in more detail below, along with the 5 studies reporting on the BA.5 sub-lineage (<u>101</u>, <u>103</u>, <u>108</u>, <u>109</u>, <u>112</u>). 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 11,512 households in Germany between January 2022 and May 2022 (1). 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.

Guo and others reported the mean and median serial interval of 51 transmission pairs with Omicron variant BA.5 COVID-19 in China between May and July 2022 (<u>108</u>). The mean serial interval was estimated to be 2.7 days (SD: 2.5 days), and the median serial interval was estimated to be 2.5 days (95% Crl: 1.9 to 3.2 days).

Hoeve and others reported the median time between positive tests of 3,399 index cases and 1,802 secondary cases with Omicron variant BA.1, BA.2, BA.4 or BA.5 COVID-19 in The Netherlands between July 2021 and August 2022 (<u>109</u>). The median time between positive tests of index and household members was estimated to be 4 days (IQR: 3 to 6 days).

Liu and others reported the median serial interval of 37 cases and median generation time of 21 cases with Omicron variant BA.5.2 COVID-19 in China in October 2022 (<u>101</u>). The median serial interval was estimated to be 2.13 days (IQR: 1.63 to 2.64 days), and the median generation time was estimated to be 1.91 days (IQR: 1.05 to 3.15 days).

Manica and others reported the mean intrinsic and realised household generation times and mean household serial interval of 22,122 cases with Omicron variant COVID-19 in Italy in January 2022 (83). The mean intrinsic generation time was estimated to be 6.84 days (95% CrI: 5.72 to 8.60 days), the mean realised household generation time was estimated to be 3.59 days (95% CrI: 3.55 to 3.60 days), and the mean household serial interval was estimated to be 2.38 days (95% CrI: 2.30 to 2.47 days).

Mellis and others (preprint) reported the mean serial interval of 262 transmission pairs with Omicron variant BA.5 COVID-19 in the US between April 2020 and September 2022 (<u>112</u>). The mean serial interval was estimated to be 3.8 days (95% CI: 3.4 to 4.1 days).

Wang and others reported the mean and median generation interval of 178 transmission pairs with Omicron variant BA.5.2 COVID-19 in China between August and September 2022 (<u>103</u>). The mean generation interval was estimated to be 2.8 days (95% Crl: 2.4 to 3.5 days, SD: 3.7 days), which increased to 4.3 days (95% Crl: 2.6 to 6.9 days) when adjusting for truncation, and the median generation interval was estimated to be 1.4 days (95% Crl: 1.1 to 1.9 days, 95th percentile: 10.4 days).

Joint summary of remaining studies

Of the remaining studies, 6 reported on estimated median serial interval (2, 15, 19, 22, 106, 107), 12 reported on estimated mean serial interval (14, 16, 20, 21, 96, 97, 100, 110 to 114), 3 reported on both the mean and median serial interval (105, 108, 115), and 2 reported on the median generation time (15) or mean forward generation interval (16). The median serial interval was estimated to be between 2 and 4 days, the interquartile ranges between 1 and 9 days (2, 15, 19, 22, 105 to 108, 115), with one study suggesting little difference between

Omicron BA.1 and BA.2 sub-lineages (<u>15</u>). The mean serial interval was estimated to be between 2 and 5 days (<u>14</u>, <u>16</u>, <u>20</u>, <u>21</u>, <u>96</u>, <u>97</u>, <u>100</u>, <u>105</u>, <u>108</u>, <u>110 to 115</u>), with one study suggesting child index cases may have shorter serial intervals (3.0 days) than adult index cases (5.0 days) (<u>21</u>). Both the median generation time and mean forward generation interval were estimated to be around 3 days (<u>15</u>, <u>16</u>). In the one study reporting on child cases, the mean serial interval was estimated to be 3.0 days, compared with 5.0 days for adults (<u>21</u>).

Time to peak viral load

There were 16 included studies (<u>3</u>, <u>12</u>, <u>23 to 27</u>, <u>116 to 125</u>) (5 preprints (<u>27</u>, <u>116</u>, <u>117</u>, <u>119</u>, <u>122</u>)) that included evidence for time to peak viral load of COVID-19 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 cycle threshold (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.

A summary of studies is given in Table 1f, and study characteristics are given in Table C.1f.

Study variable	Number of studies
Study location	• 1 in the UK (<u>122</u>)
	• 6 in Asia (<u>23, 118, 121, 123 to 125</u>)
	 5 in the US (<u>25</u>, <u>27</u>, <u>116</u>, <u>117</u>, <u>119</u>)
	 1 in Australia (<u>120</u>)
	• 1 in Brazil (<u>12</u>)
	 1 in Canada (<u>26</u>)
	• 1 in Spain (<u>24</u>)
Study design	• 8 prospective cohort studies (<u>12</u> , <u>26</u> , <u>27</u> , <u>117</u> , <u>120 to 122</u> , <u>124</u>)
	• 6 retrospective cohort studies (<u>23 to 25</u> , <u>119</u> , <u>123</u> , <u>125</u>)
	 2 cross-sectional studies (<u>116</u>, <u>118</u>)
Study timeframe	All studies were conducted between January 2020 and April 2023
Omicron sub-	 4 reported on BA.1 (<u>12</u>, <u>25 to 27</u>)
lineages reported	 3 reported on BA.2 (<u>120</u>, <u>121</u>, <u>123</u>)
	 2 reported on BA.1 and BA.2 (<u>24</u>, <u>119</u>)
	 1 reported on BA.1, BA.2, BA.4, BA.4/5, BA.5, and Delta (<u>122</u>)
	• 1 reported on BF.7 (<u>125</u>)
	• 4 did not report the Omicron sub-lineage (23, <u>117</u> , <u>118</u> , <u>124</u>)

Table 1f. Summary of time to peak viral load studies

Study variable	Number of studies
	• 1 did not report the COVID-19 variant, but was very likely the Omicron
	variant due to the time period of the study (<u>116</u>)

One study from the UK (<u>122</u>), and one study that included over 5,000 cases (<u>23</u>), are both summarised in more detail below, as are the studies reporting on the BF.7 sub-lineage (<u>125</u>) and the study reporting up to April 2023 (<u>116</u>). The remaining studies typically 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 5,187 Omicron variant cases in South Korea in January 2022 (23). The results suggested the peak viral load occurred 2.4 days (95% CI: 2.2 to 2.5 days) after symptom onset.

Frediani and others (preprint) reported median time to peak viral load for 621 Omicron variant cases in the US between April 2022 and April 2023 (<u>116</u>). The median time to peak viral load after symptom onset was estimated to be 4 days.

Townsley and others (preprint) reported the time from symptom onset to peak viral load for 460 Omicron variant BA.1 (39%), BA.2 (31%), BA.4 (1.5%), BA.4/5 (1.5%), BA.5 (12%) and Delta (15%) infections across 433 cases in the UK between January 2021 and September 2022 (122). The time from symptom onset to peak viral load was reported to be 2 to 5 days.

Zhang and others reported time to peak viral load for 370 hospitalised Omicron variant BF.7 cases aged under 80 years and 110 hospitalised Omicron variant BF.7 cases aged 80 years and over in China between November and December 2022 (<u>125</u>). The viral load was highest on day 3 after a positive test for cases aged under 80 years, and highest on day 2 after a positive test for cases aged over.

Joint summary of remaining studies

The remaining 12 studies estimated the median (<u>118</u>, <u>123</u>) or mean time to peak viral load (<u>12</u>, <u>24 to 27</u>, <u>119</u>, <u>120</u>, <u>124</u>), or a range of times to peak viral load (<u>117</u>, <u>121</u>).

The studies suggested the time to peak viral load was between 1 and 5 days (<u>12</u>, <u>24 to 27</u>, <u>117</u> to <u>121</u>, <u>123</u>, <u>124</u>). Three studies suggested the Omicron variant BA.2 may have a shorter mean time to peak viral load (1 to 3 days) (<u>24</u>, <u>120</u>, <u>123</u>), and one study suggested 87% of cases reached peak viral load by 5 days, and that viral dynamics were similar regardless of vaccination status, but male cases, and cases with underlying health conditions, were slower to reach their peak viral load (<u>124</u>).

Time to viral clearance

There were 135 included studies (10, 12, 13, 25, 27 to 75, 85, 87 to 89, 91 to 94, 103, 118, 119, 121, 123 to 193) (22 preprints (27, 32, 34, 35, 37, 52, 53, 55, 56, 58, 64, 92, 119, 130, 133, 140, 145, 147, 150, 162, 179, 199)) that included evidence for time to viral clearance of COVID-19 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 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.

Ten studies reported specifically on children, all of whom were hospitalised, immunodeficient, other high-risk cases, or in a clinical trial (<u>62</u>, <u>65 to 67</u>, <u>129</u>, <u>130</u>, <u>153</u>, <u>154</u>, <u>174</u>, <u>187</u>).

A summary of studies is given in Table 1g, and study characteristics are given in Table C.1g.

Study variable	Number of studies
Study location	 1 in the UK (<u>140</u>) 78 in China (<u>31, 32, 37, 38, 41 to 46, 49 to 53, 56, 57, 59 to 70, 72 to 75, 103, 121, 125, 129, 131, 133, 135, 138, 139, 142, 143, 146, 148 to 150, 100, 100, 100, 100, 100, 100, 100,</u>
	 <u>155, 163, 165, 170 to 174, 176 to 188, 190, 193, 199 to 201</u>) 23 in Europe (excluding the UK) (<u>10, 28, 30, 33, 36, 47, 54, 55, 93, 94, 127, 130, 132, 134, 144, 157 to 159, 162, 164, 192, 202, 203</u>) 10 in the US (25, 27, 24, 25, 20, 40, 22, 440, 420, 444, 447, 450, 404)
	 18 in the US (25, 27, 34, 35, 39, 40, 92, 119, 136, 141, 147, 156, 161, 166, 168, 169, 175, 189) 12 in Asia (excluding China) (3, 13, 48, 58, 71, 87 to 89, 91, 126, 145, 160)
	 3 in South America (<u>12</u>, <u>29</u>, <u>167</u>) 1 in Jordan (<u>137</u>) 1 in Saudi Arabia (<u>128</u>)
Study design	 66 prospective cohort studies (<u>10</u>, <u>12</u>, <u>27 to 31</u>, <u>34 to 36</u>, <u>39 to 42</u>, <u>44</u>, <u>45</u>, <u>47</u>, <u>51</u>, <u>52</u>, <u>54 to 56</u>, <u>61</u>, <u>63</u>, <u>65</u>, <u>70</u>, <u>72</u>, <u>74</u>, <u>87 to 89</u>, <u>92 to 94</u>, <u>121</u>, <u>126</u>, <u>127</u>, <u>129</u>, <u>131</u>, <u>133</u>, <u>134</u>, <u>136</u>, <u>137</u>, <u>144</u>, <u>146</u>, <u>150 to 153</u>, <u>157</u>, <u>159</u>, <u>163</u>, <u>164</u>, <u>166</u>, <u>169</u>, <u>171</u>, <u>172</u>, <u>174 to 176</u>, <u>181</u>, <u>185</u>, <u>187</u>, <u>201 to 203</u>), 16 of which were randomised controlled trials or quasi to experimental studies but reported here as prospective cohort studies as the randomisation process did not affect the extracted data (<u>29</u>, <u>30</u>, <u>44</u>, <u>52</u>,
	<u>56, 61, 126, 131, 133, 137, 163, 164, 171, 174, 181, 187</u>)

Table 1g. Summary of time to viral clearance studies

Study variable	Number of studies
	 65 retrospective cohort studies (3, 13, 25, 32, 33, 37, 38, 43, 46, 48 to 50, 53, 57 to 60, 62, 64, 66 to 69, 71, 73, 75, 91, 103, 119, 125, 128, 130, 132, 135, 138 to 140, 142, 143, 145, 148, 149, 154 to 156, 158, 160, 162, 165, 170, 173, 177 to 180, 182 to 184, 186, 188 to 190, 193, 199, 200) 4 cross to sectional studies (147, 161, 167, 192) 2 case series (141, 168)
Study timeframe	Most studies were conducted between March 2022 and January 2023, though some were conducted earlier, and 2 were conducted up to February and April 2023 (<u>92</u> , <u>162</u>)
Omicron sub- lineages reported	 12 reported on BA.1 (12, 25, 27, 47, 91, 93, 124, 134, 141, 161, 167, 175) 40 reported on BA.2 (37, 38, 43, 44, 49, 52, 53, 55, 58 to 60, 62, 65 to 71, 74, 75, 121, 123, 129, 142, 143, 152 to 155, 165, 170, 172, 173, 176 to 178, 181, 183, 186) 8 reported on BA.1 and BA.2 (36, 87, 94, 119, 132, 140, 157, 168) 3 reported on BA.5 (42, 103, 145) 1 reported on BF.7 (125) 2 reported on BA.1, BA.2 and BA.5 (85, 88) 1 reported on BA.1, BA.2, BA.4, and BA.5 (92) 54 did not report the Omicron sub-lineage (10, 13, 28, 30 to 35, 39 to 41, 45, 46, 48, 50, 51, 54, 56, 57, 61, 63, 64, 72, 73, 89, 118, 127, 128, 131, 135, 139, 144, 146 to 151, 156, 158 to 160, 162, 163, 166, 171, 180, 182, 184, 185, 187, 188, 191) 13 did not the COVID-19 variant, though due to the time period of the studies these were very likely Omicron variant (29, 126, 130, 133, 136 to 138, 164, 169, 174, 179, 189, 190)

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 <u>Table C.1g</u>. 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.

Five studies reported results where the majority of cases were infected with the Omicron BA.5 (42, 88, 103, 145) and BF.7 (125) sub-lineages, and 7 studies included over 20,000 cases (with likely substantial overlap in cases between these studies), and all are individually summarised below (49, 68, 69, 146, 149, 178, 185). 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

Ikeda and others reported the proportion of cases with RT-PCR positivity after 21 and 42 days after symptom onset for 46 cases with haematologic disease (80% Omicron variant BA.5) between January 2022 and January 2023 in Japan (<u>145</u>). In total, 17 cases (36.9%) had RT-PCR positivity for 21 days or more, and 6 cases (13.0%) had RT-PCR positivity for 42 days or more.

Kang and others reported the median duration of genomic and subgenomic ribonucleic acid (RNA) RT-PCR positivity in 42 healthcare worker cases with the Omicron variant BA.5COVID-19 between January and August 2022 in South Korea (88). The median duration of genomic RNA RT-PCR positivity was estimated to be 7 days, and the median duration of subgenomic RNA RT-PCR positivity was estimated to be 5 days (all data extracted from a figure).

Li and others reported the duration of viral shedding (Ct value of less than 35 on a nucleic acid test) for 27 cases with COVID-19 Omicron variant BA.5 and n=51 cases with Omicron variant BA.2 in August 2022 in China (42). Of the 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.

Wang and others reported the mean time from exposure to the start of viral shedding and the mean viral shedding duration for 709 cases with Omicron variant BA.5.2 COVID-19 between August and September 2022 in China (103). The mean time from exposure to the start of viral shedding was estimated to be 3.3 days (95% CrI: 3.0 to 3.6 days, 95th percentile: 8.9 days, and asymptomatic cases and cases aged 0 to 15 years had longer periods from exposure to viral shedding. The mean viral shedding period was estimated to be 6.7 days (95% CrI: 6.4 to 7.1 days, 95th percentile: 13.7 days), and asymptomatic cases and cases aged 16 to 65 years had longer mean viral shedding periods.

Zhang and others reported the median time to a negative RNA test for 480 hospitalised cases with Omicron variant BF.7 COVID-19 between November and December 2022 in China (125). For 130 hospitalised cases under 45 years of age, the median time to a negative RNA test (ORF1ab) was 9 days (range: 4 to 26 days). For 112 hospitalised cases between 45 and 59 years of age, the median time to a negative RNA test (ORF1ab) was 9 days (range: 7 to 23 days). For 128 hospitalised cases between 60 and 79 years of age, the median time to a negative RNA test (ORF1ab) was 11 days (range: 6 to 24 days). For 110 hospitalised cases over 80 years of age, the median time to a negative RNA test (ORF1ab) was 11.5 days (range: 6 to 39 days).

The following 7 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 (<u>49</u>, <u>68</u>, <u>69</u>, <u>146</u>, <u>149</u>, <u>178</u>, <u>185</u>).

Kang and others reported the median viral shedding time for 55,111 asymptomatic and mild cases with likely Omicron variant BA.2 COVID-19 between April and May 2022 in China (<u>146</u>). The median viral RNA shedding time was estimated to be 7 days (IQR: 5 to 9 days).

Li and others reported the median duration of RNA test positivity for 23,145 cases with likely Omicron variant BA.2 COVID-19 in April 2022 in China (<u>149</u>). The median duration of RNA test positivity was 5 days (IQR: 4 to 7 days).

Pei and others reported the time between first positive and first negative RT-PCR test for 198,262 asymptomatic and mild cases with likely Omicron variant BA.2 COVID-19 between March and May 2022 in China (<u>49</u>). 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 33,896 cases with comorbidities.

Yin and others reported the time between first positive and first negative RT-PCR test for 199,590 asymptomatic or mild cases with Omicron variant BA.2 COVID-19 between March and May 2022 in China (<u>68</u>). The mean time from illness onset to negative RT-PCR test was 7.17 days (SD: 3.42 days).

Yin and others reported the median duration of viral shedding 214,592 cases with Omicron variant BA.2 COVID-19 between March and May 2022 in China (<u>178</u>). The median duration of viral shedding was estimated to be 7 days (IQR: 5 to 10 days) and was smaller for cases aged 18 to 29 years (median = 6 days, IQR: 4 to 9 days) than cases aged 80 years and older (median = 10 days, IQR: 6 to 13 days).

Ying-Hao and others reported the time between first positive and first negative RT-PCR test for 25,168 asymptomatic or mild cases with Omicron variant BA.2 COVID-19 between April and May 2022 in China (<u>69</u>). The median time from first positive to first negative RT-PCR test was 6 days (IQR: 4 to 9 days).

Zhong and others reported the men time to a negative test for 38,565 cases with likely Omicron variant BA.2 COVID-19 between April and May 2022 in China (<u>185</u>). The mean time to a negative test was estimated to be 7.0 days (SD: 2.6 days) for 16,826 cases with a body mass index (BMI) of 18.5 to 24 kg/m², 7.2 days (SD: 2.7 days) for 19,978 cases with a BMI of 24 to 27.5 kg per m², and 7.4 days (SD: 2.6 days) for 1,761 cases with a BMI of 24 to 27.5 kg per m². Additionally, the mean time to a negative test was estimated to be 7.1 days (SD: 2.6 days) for 34,057 cases without diabetes, and 7.4 days (SD: 2.6 days) for 4,535 cases with diabetes.

Joint summary of remaining studies: cases from the general population

In total, 61 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 (25, 27 to 29, 34, 35, 38, 39, 44, 48, 55, 56, 58, 59, 61 to 63, 70, 71, 88, 89, 118, 119, 121, 123, 124, 130 to 135, 138, 139, 142, 143, 150 to 156, 160, 163, 165, 170 to 174, 177, 180, 182 to 184, 186 to 188, 190, 191).

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 3 to 29 days, though 35 of the 61 studies estimated mean or median viral clearance to be around 7 to 11 days in at least one of the reported groups (25, 27 to 29, 34, 35, 38, 48, 55, 58, 61, 70, 71, 89, 119, 121, 123, 131, 132, 134, 138, 150, 152, 154 to 156, 163, 165, 171 to 174, 183, 187, 190).

There were 29 studies that included 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 (10, 12, 13, 30, 40, 43, 60, 85, 93, 126, 128, 131, 134, 136, 137, 147, 148, 155 to 157, 161, 164, 166 to 169, 174, 181, 189). As with the studies above, many of these studies did not specify the outcome and different time periods were reported on, making comparison between studies difficult. However, 16 studies reported the proportion of positive tests at day 7 (10, 12, 13, 30, 40, 43, 60, 85, 93, 128, 131, 157, 168, 174, 181, 189), which varied between 2.8% and 100%, with 5 studies reporting positive test proportions between 87% and 100% (10, 12, 13, 30, 93). Additionally, one study reported on cases with persistent COVID-19 infections, with positive cases at 26 and 56 days after infection (140), and another study reported that the proportion of cases with viral clearance of more than 21 days was 47% (148).

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

In total, 33 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 (31 to 33, 37, 41, 45 to 47, 50, 51, 53, 54, 57, 64 to 67, 72 to 75, 87, 91, 92, 127, 129, 144, 158, 159, 162, 175, 176, 179). 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, with the mean or median time to viral clearance viral clearance to take around 10 to 15 days in at least one of the reported groups (31, 33, 37, 46, 47, 50, 51, 53, 54, 64, 65, 67, 73 to 75, 92, 129, 158, 159).

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 (<u>37</u>, <u>64</u>, <u>73</u>, <u>176</u>).

Additionally, 6 studies that included 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 (<u>36</u>, <u>52</u>, <u>94</u>, <u>127</u>, <u>141</u>, <u>158</u>). One study reported that 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 (<u>36</u>). A second study reported that 31.1% of cases had a negative RT-PCR test within 7 days of entry into the study (<u>52</u>). A third study reported that 36.7% of cases tested positive at 21 days after diagnosis, 25% at 28 days, and 10% at 42 days (<u>127</u>). A fourth study reported on 3 cases with durations of infections greater than 4 weeks, 12 weeks, and 4 months (<u>141</u>). A fifth study reported cases were still positive up to 159 days after diagnosis (<u>158</u>). A sixth study reported that 84% and 55% of adult high-risk non-hospitalised immunocompromised cases were RT-PCR positive on days 5 and 15 after symptom onset (<u>94</u>).

Ten studies reported specifically on children, all of whom were hospitalised, immunodeficient, other high-risk cases, or in a clinical trial (62, 65 to 67, 129, 130, 153, 154, 174, 187). The results were similar to those above, with a mean or median time to viral clearance ranging from 5 to 23 days, and 6 of the 10 studies estimated viral clearance to take around 10 to 15 days in at least one of the reported groups (65, 67, 129, 130, 154, 187).

Viral load over time

There were 11 included studies (<u>6</u>, <u>23</u>, <u>76 to 82</u>, <u>194</u>, <u>195</u>) (3 preprints (<u>76</u>, <u>81</u>, <u>82</u>)) that included evidence for the viral load over time for COVID-19 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.

A summary of studies is given in Table 1h, and study characteristics are given in Table C.1h.

Study variable	Number of studies
Study location	• 2 in the UK (<u>76</u> , <u>81</u>)
	 3 in Europe (excluding the UK) (<u>78</u>, <u>80</u>, <u>194</u>)
	• 4 in Asia (<u>23, 77, 82, 195</u>)
	• 2 in the US (<u>6</u> , <u>79</u>)
Study design	 7 prospective cohort studies (<u>6</u>, <u>78 to 81</u>, <u>194</u>, <u>195</u>)
	3 retrospective cohort studies (<u>23</u> , <u>77</u> , <u>82</u>)
	 1 cross-sectional study (<u>76</u>)
Study timeframe	All studies reporting study dates were conducted between November 2021 and July 2022, though one did not report a study date, but was registered in March 2022 (<u>194</u>)
Omicron sub- lineages reported	• 2 reported on BA.1 (<u>79, 82</u>)
	• 1 reported on BA.2 (<u>77</u>)
	 4 reported on BA.1 and BA.2 (<u>76</u>, <u>78</u>, <u>80</u>, <u>81</u>)
	 1 reported on BA.5 (<u>195</u>)
	 3 did not report the Omicron sub-lineage (<u>6</u>, <u>23</u>, <u>194</u>)

Table 1h. Summary of viral load over time studies

One study from England including over a million cases (<u>76</u>) and a study from South Korea including over 5,000 cases (<u>23</u>) 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 1,212,234 cases (1,083,976 BA.1, 128,258 BA.2 Omicron sub-lineages) in England between December 2021 and January 2022 (<u>76</u>). 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 5,187 Omicron variant cases in South Korea in January 2022 (23). 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 (<u>6</u>, <u>77</u>) or 2 to 3 days (<u>78</u>, <u>80 to 82</u>), then increased (viral load decreased), either until the end of testing (<u>6</u>, <u>77 to 82</u>, <u>194</u>, <u>195</u>), or until a slight decrease in Ct values (increase in viral load) between 15 and 17 days for the BA.2 sub-lineage (<u>81</u>). One study also suggested that, for BA.2 sub-lineage, 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) (<u>80</u>).

Summary

In total, 193 studies provided evidence on different measures of infectious period.

The 5 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 remaining studies). There was also evidence that between a third and a half of transmission from the index case was before symptom onset. However, these studies were reasonably small and therefore the results may be imprecise, and no studies directly measuring transmission period looked at cases beyond May 2022.

Twenty-one studies measuring viral culture positivity over time suggested that viral culture positivity was highest in the first 5 days after symptom onset or diagnosis, with variable times until all cases have negative viral cultures (between 8 and 15 days in different studies, higher in cases with virologic rebound and immunocompromised cases [median of 4 weeks in one study, at least 58 days in another]). A recent study conducted between February and March 2023 suggested 72% of cases had positive viral cultures on day 5, 47% on day 7, and 18% on day 10 of their infection. Whilst viral culture positivity results do not provide direct evidence on the risk of transmission, they indicate potential infectivity.

The 19 studies measuring incubation period (exposure to symptom onset) suggested the median and mean incubation period was between 2 and 6 days (including for the BA.5 sublineage), with a large UK study estimating a mean incubation period of between 3 and 4 days. None of these studies looked at cases beyond October 2022.

One study measured latent period (exposure to detectable viral levels) and suggested the mean latent prior was around 3 days, with 95% of cases developing detectable virus levels around 6 days after infection, looking at cases in January and February 2022.

The 26 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, including for the BA.5 sub-

lineage), and generation times of between one and 7 days. None of the studies looked at cases beyond October 2022.

The 16 studies measuring time to peak viral load and 11 studies measuring viral load over time suggested peak viral loads occurred a median and mean of one to 5 days after symptom onset (including for the study conducted between April 2022 and April 2023). The studies suggest that this may be quicker in BA.2 compared with BA.1 sub-lineage cases. For the BF.7 sub-lineage, the viral load was highest on day 3 after a positive test for cases aged under 80 years, and highest on day 2 after a positive test for cases aged 80 years and over. The timing of peak viral load does not necessarily indicate the point of highest infectiousness.

One hundred and thirty-five studies measured time to viral clearance (typically positive to negative COVID-19 test) and 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 the mean or median viral clearance to be around 7 to 11 days (including for the BA.5 sub-lineage and studies up to January 2023), and most studies of hospitalised, immunodeficient, and other high-risk cases estimated the mean or median viral clearance to be around 10 to 15 days. Detectable viral load does not necessarily indicate that a case is infectious.

Overall, and consistent with the findings from the previous review, the evidence suggests that COVID-19 Omicron variant cases were most infectious up to 5 days after symptom onset. Some cases could potentially be infectious for longer, especially those that are hospitalised, immunocompromised, or otherwise high-risk. However, while some studies looked directly at COVID-19 transmission or included substantial numbers of cases, most studies looked indirectly at COVID-19 transmission and included relatively few cases. The majority of studies also looked at Omicron BA.1 and BA.2 sub-lineage cases, with little evidence from 2023.

Inequalities

Many studies looked at time to viral clearance in hospitalised, immunodeficient, and other highrisk cases, suggesting on average a longer time to viral clearance than cases in the general population. Some of these studies also looked at viral clearance in hospitalised, immunodeficient, and other high-risk children, suggesting a similar viral clearance time in children and adults.

There was little other 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 (excepting hospitalised, immunodeficient, and other high-risk cases when looking at viral clearance). As such, it was not possible to examine other inequalities in this report.

Limitations

The source of evidence in this review included peer-reviewed and preprint articles. An extensive search of other sources (such as websites of public health organisations) was not conducted. 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.

In total, 33 of the 193 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 it is limited to evidence for COVID-19 Omicron and later variants, 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. This means that the results of studies cannot be interpreted in the knowledge of the study quality, so poorer quality studies may be over-interpreted. The data extractions and narrative summaries were conducted by one reviewer and checked by another. As a result, studies or relevant information may have been missed.

Evidence gaps

There was a reasonable amount of evidence for most of the different measures of infectious period. However, only 5 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 sub-lineages, and few studies were conducted in 2023, which may limit generalisability to the current circulating COVID-19. There was also limited evidence specifically for children.

Conclusion

In total, 193 studies provided evidence on different measures of the COVID-19 infectious period. The 5 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, and potentially between a third or a half of transmission events occurring before symptom onset in the index case. The 21 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 16 studies reporting on time to peak viral load and 11 studies reporting on viral load over time suggested that peak viral loads occurred a median or mean of 1 to 5 days after symptom onset.

The 26 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 1 and 9 days), and generation times of between one and 7 days. The 19 studies measuring incubation period suggested the median or mean incubation period was between 2 and 6 days.

The 135 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 the mean or median viral clearance to be around 7 to 11 days (including for the BA.5 sub-lineage and studies up to January 2023), and most studies of hospitalised, immunodeficient, and other high-risk cases estimated the mean or median viral clearance to be around 10 to 15 days. Detectable viral load does not necessarily indicate that a case is infectious.

Despite relatively few studies of recent Omicron sub-lineages (such as BA.5) and studies conducted in 2023, the results of these studies were similar to studies of prior variants and studies conducted before 2023.

Overall, the evidence suggests that COVID-19 cases were most infectious up to 5 days after symptom onset, but could potentially be infectious for longer, especially for cases that are hospitalised, immunocompromised, or otherwise high-risk. However, while some studies included substantial numbers of cases, most studies included relatively few cases, and the majority of studies included Omicron BA.1 and BA.2 sub-lineage cases, with little evidence from 2023.

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Annexe A. Protocol

Review question

There is one review questions:

1. What is the infectious period of Omicron variant coronavirus (COVID-19)?

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

This is an update to a previous rapid review (search to 26 January 2023) that identified and summarised evidence on the infectious period of Omicron variant coronavirus (COVID-19) (<u>196</u>). The previous review also searched for evidence on the difference in transmission from people with asymptomatic compared with symptomatic COVID-19 infection, but this will not be considered in this update.

Inclusion and exclusion criteria are shown in Table A.1.

	Included	Excluded
Population	All	Animals
Settings	All settings	
Context		
Intervention or exposure	Omicron variant COVID-19 (any sub- lineage)	Other infectious diseases
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 incubation period	
Language	English	
Date of publication	25 January 2023 to 4 September 2023	
Study design	 controlled trials (including randomised controlled trials, cross-over trials, and 	 systematic or narrative reviews
		 case reports (of single cases)

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
	 quasi-experimental studies, amongst others) observational studies (including cohorts, case controls, and cross- sectional studies, amongst others) 	 guidelines opinion pieces modelling studies laboratory studies ecological studies
Publication type	Published and preprint	

Identification of studies

We will search OVID Medline, OVID Embase, and preprint servers (medRxiv, bioRxiv, aRxiv, and Research Square, via COVID-19 portfolio) for studies published between 25 January 2023 (date of last search) and 4 September 2023.

Screening

Screening on title and abstract will be undertaken in duplicate by 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information will include country, setting, study design, 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 will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

Risk of bias of analytical studies will be 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 will be assessed by one reviewer and checked by a second. Risk of bias in descriptive studies will not be assessed.

Synthesis

A narrative synthesis will be written to describe the results from this review.

Variations across populations and subgroups, for example cultural variations or differences between ethnic or social groups will be considered, where evidence is available.

Search strategy

Search strategy Ovid Medline ALL (25 January to 4 September 2023)

- 1 exp SARS-CoV-2/ (158692)
- 2 exp COVID-19/ (237548)
- 3 (corona* adj1 (virus* or viral*)).tw,kw,kf. (6403)
- 4 (CoV not (Coefficien* or "co-efficien*" or covalent* or Covington* or covariant* or covarianc* or "cut-off value*" or "cutoff value*" or "cutoff volume*" or "cutoff volume*" or "combined optimi?ation value*" or "central vessel trunk*" or CoVR or CoVS)).tw,kw,kf. (127187)
- 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. (389374)
- 6 exp COVID-19 Vaccines/ (22911)
- 7 exp COVID-19 Testing/ (11564)
- 8 or/1-7 (397160)
- 9 ((Transmis* or transmit*) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (14465)
- 10 (Infectious* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (6038)
- 11 (Contagio* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (330)
- 12 (Isolation adj3 (duration* or time or length* or period*)).tw,kw,kf. (3771)
- 13 (shed* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (3616)
- 14 Virus Shedding/ (4216)
- 15 (PCR positiv* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (461)
- 16 (Viral proliferat* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (6)
- 17 cycl* threshold*.tw,kw,kf. (2709)
- 18 CT value*.tw,kw,kf. (5122)
- 19 (peak* adj1 (vir* load* or vir* concentration)).tw,kw,kf. (405)
- 20 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (38501)
- 21 8 and 20 (5541)
- 22 (Viral Load/ or exp Disease Transmission, Infectious/) and exp Time/ (9432)
- 23 COVID-19/tm and exp Time/ (305)
- 24 8 and 22 (292)
- 25 21 or 23 or 24 (5980)
- 26 limit 25 to dt=20230125-20230904 (647)

Search strategy Ovid Embase (25 January to 4 September 2023)

- 1 exp severe acute respiratory syndrome coronavirus 2/ (99455)
- 2 coronavirus disease 2019/ (342630)

- 3 experimental coronavirus disease 2019/ (21)
- 4 (corona* adj1 (virus* or viral*)).tw,kw. (6367)
- 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. (127357)
- 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. (432068)
- 7 COVID-19 Testing/ (7758)
- 8 exp SARS-CoV-2 vaccine/ (39224)
- 9 or/1-8 (465750)
- 10 ((Transmis* or transmit*) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (16059)
- 11 (Infectious* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (7734)
- 12 (Contagio* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (330)
- 13 (Isolation adj3 (duration* or time or length* or period*)).tw,kw,kf. (4721)
- 14 (shed* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (4073)
- 15 virus shedding/ (10324)
- 16 (PCR positiv* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (607)
- 17 (Viral proliferat* adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. (7)
- 18 cycl* threshold*.tw,kw,kf. (3503)
- 19 CT value*.tw,kw,kf. (8147)
- 20 (peak* adj1 (vir* load* or vir* concentration)).tw,kw,kf. (625)
- 21 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (52315)
- 22 (exp virus load/ or exp disease transmission/) and (time/ or time factor/) (2511)
- 23 9 and 21 (7797)
- 24 22 or 23 (10268)
- 25 limit 24 to dc=20230125-20230904 (1283)

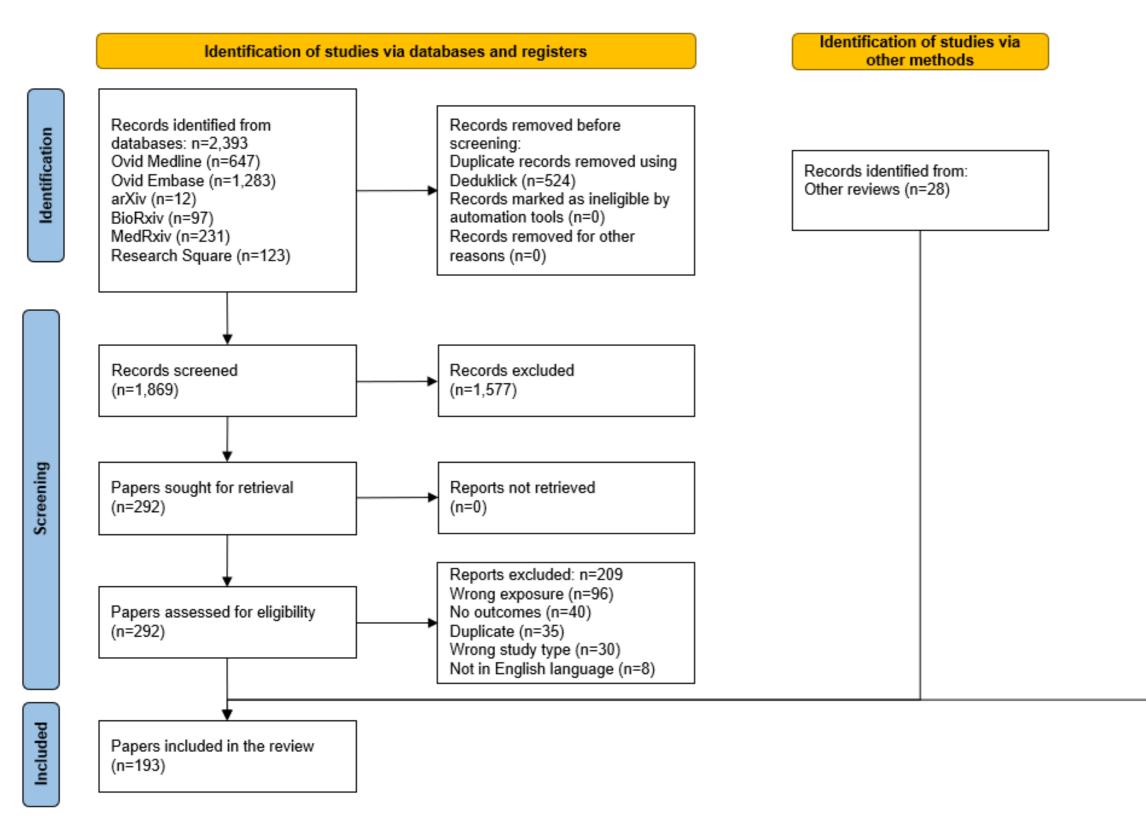
Search strategy for COVID-19 portfolio

Search will be carried out on 4 September 2023, date limited from 25 January 2023.

("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") Results downloaded separately from preprint servers as follows:

ArXiv: 12 results BiorXiv: 97 results MedrXiv: 231 results Research Square: 123 results

Figure A.1. PRISMA diagram



Identification of studies from previous review

Records identified from previous review (n=82)

Text version of Figure A.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 198 studies.

From identification of studies via databases and registers, n=2,393 records identified databases:

- Ovid Medline (n=647)
- Ovid Embase (n=1,283)
- arXiv (n=12)
- BioRxiv (n=97)
- MedRxiv (n=231)
- Research square (n=123)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=524)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=1,869 records screened, of which n=1,577 were excluded, leaving n=292 papers sought for retrieval, all of which were retrieved.

Of the n=292 papers assessed for eligibility, n=209 reports were excluded:

- wrong exposure (n=96)
- no outcomes (n=40)
- duplicate (n=35)
- wrong study type (n=30)
- not English language (n=8)

From identification of studies via other methods, n=28 studies were identified from other reviews.

From identification of studies from previous review, n=82 records were identified.

Overall, n=193 papers included in the review.

Annexe B. Full text excludes

Wrong exposure (n=96)

Abosi OJ and others. <u>'A review of extended coronavirus disease 2019 (COVID-19) isolation</u> <u>duration among inpatients in a tertiary-care hospital-lowa, 2020 to 2022</u>. Infection Control and Hospital Epidemiology 2023, pages 1 to 4

Aghbash PS and others. <u>'Dynamic alterations in white blood cell counts and SARS-CoV-2</u> <u>shedding in saliva: an infection predictor parameter</u>'. Frontiers in Medicine 2023: volume 10, page 1208928

Agoti CN and others. <u>'Genomic epidemiology of SARS-CoV-2 within households in coastal</u> Kenya: a case ascertained cohort study'. MedRxiv 2023

Agrawal M and others. <u>'Mucosal and systemic immune dynamics associated with COVID-19</u> outcomes: a longitudinal prospective clinical study'. BioRxiv 2023

Aguareles J and others. <u>'Outcomes and clinical characteristics of the compassionate use of</u> <u>plitidepsin for immunocompromised adult patients with COVID-19</u>'. International Journal of Infectious Diseases 2023: volume 135, pages 12 to 17

Ali DY and others. <u>'Comparable detection of nasopharyngeal swabs and induced sputum</u> <u>specimens for viral nucleic acid detection of suspected novel coronavirus (SARS-Cov-2)</u> <u>patients in Fayoum governorate, Egypt'</u>. Benisuef University Journal of Basic and Applied Sciences Online 2023: volume 12, issue 1, pages 43

Arfijanto MV and others. <u>'Duration of SARS-CoV-2 RNA Shedding Is Significantly Influenced by</u> <u>Disease Severity, Bilateral Pulmonary Infiltrates, Antibiotic Treatment, and Diabetic Status:</u> <u>Consideration for Isolation Period'</u>. Pathophysiology 2023: volume 30, issue 2, pages 186-98

Arya AK and others. <u>'Evaluation of Rapid Antigen Test as a Marker of SARS-CoV-2 Infectivity'</u>. Cureus 2023: volume 15, issue 3, page e36962

Avadhanula V and others. <u>'Longitudinal host transcriptional responses to SARS-CoV-2 infection</u> in adults with extremely high viral load'. NIH COVID Portfolio 2023

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Bendall EE and others. <u>'SARS-CoV-2 genomic diversity in households highlights the challenges</u> of sequence-based transmission inference. mSphere 2022: volume 7, issue 6

Biancofiore A and others. <u>'Remdesivir significantly reduces SARS-CoV-2 viral load on</u> <u>nasopharyngeal swabs in hospitalized patients with COVID-19: A retrospective case-control</u> <u>study'</u>. Journal of Medical Virology 2022: volume 94, pages 2,284 to 2,289

Brailita DM and others. <u>'Prolonged severe acute respiratory coronavirus virus 2 (SARS-CoV-2)</u> <u>viral shedding in lower-respiratory specimens of critically ill patients does not correlate with</u> <u>nasopharyngeal swab results</u>'. Infection Control and Hospital Epidemiology 2023: volume 44, pages 678 to 679

Caillard S and others. <u>'Molecular evolution of the SARS-CoV-2 omicron BA.2 variant in kidney</u> <u>transplant recipients with prolonged viral shedding</u>'. Journal of Infection 2023: volume 86, issue 5, pages 513 to 515

Castro-Balado A and others. <u>'Efficacy and safety of inhaled ethanol in early-stage SARS-CoV-2</u> <u>infection in older adults: a phase II randomized clinical trial</u>. Pharmaceutics 2023: volume 15, issue 2, page 16

Chaudhuri JR and others. <u>'Outcome of COVID-19-associated acute stroke: a study from South</u> <u>India'</u>. Neurology India 2023: volume 71, issue 1, pages 92 to 98

Chopoorian A and others. <u>'Persistence of SARS-CoV-2 in saliva: Implications for late-stage</u> <u>diagnosis and infectious duration</u>'. PLoS ONE 2023: volume 18, issue 3, page e0282,708

Cisse A and others. <u>'Prevalence of COVID-19 at the Wahgnion-Gold mining site in Burkina Faso</u> and use of RT-PCR initial cycle threshold to monitor the dynamics of SARS-CoV-2 load'. African Journal of Clinical and Experimental Microbiology 2023: volume 24, pages 24 to 31

Colado Simao AN and others. <u>'Effect of phthalocyanine oral and nasal antiseptic solutions on</u> <u>the infectivity of SARS-CoV-2 in patients with COVID-19: a randomized controlled trial</u>'. German Medical Science 2023: volume 21, page Doc07

Coplu N and others. <u>'Investigation of the change in antibody Llevels of COVID-19 RT-PCR</u> positive patients over time'. Flora 2023: volume 28, pages 156 to 163

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Crone MA and others. <u>'Rapid emergence of transmissible SARS-CoV-2 variants in mild</u> <u>community cases'</u>. medRxiv 2023

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Annexe C. Study characteristics

Table C.1. Studies for infectious period

Note: References numbered between 1 and 82 are from the previous review, references numbered 83 to 195 are from the updated search Acronyms: CI = confidence interval, CrI = credible interval, Ct = cycle threshold, IQR = interquartile range, RAT = rapid antigen test, RCT = randomised controlled trial, RNA = ribonucleic acid, RT-PCR = reverse transcriptase polymerase chain reaction, SD = standard deviation

Table C.1a. Transmission period

Study	Country, time period	Study type	Participants	Outcome
An der Heiden (<u>1</u>)	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 of by day 10 of symptom onset in the index case
Del Aguila-Mejia (<u>2</u>)	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 o
Jung (<u>3</u>)	South Korea, March to April 2022	Retrospective cohort	n=9 cases (healthcare workers) with an epidemiologic link to an index case and no other epidemiologic links (Omicron B.1.1.529 variant)	n=3 cases (33%) diagnosed 1 day after exposure to index case, n=1 ca exposure, and n=5 cases (56%) diagnosed 3 days after exposure
Manica (<u>83</u>)	Italy, January 2022	Cross- sectional	n=23,122 cases (Omicron variant)	Proportion of infections caused by symptomatic cases before symptom
Xin (<u>4</u>)	China, January to	Cross-	n=113 pairs of cases (Omicron	Proportion of transmissions occurring before symptom onset: 33.6% (95
	February 2022	February 2022 sectional BA.1.1 variant)	BA.1.1 variant)	Transmission peaked at symptom onset, all observed transmission ever symptom onset

Table C.1b. Culture positivity over time

Study	Country, time period	Study type	Participants	Outcome
Boucau (<u>5</u>)	UK, July 2021 to	Prospective	n=34 cases (Omicron BA.1	Median time from the first positive RT-PCR to negative culture: 5 days (IQR: 3 to 9 days)
	January 2022	cohort	variant)	Median time from the first positive RT-PCR or symptom onset (whichever was earlier) to negative culture: 8 days (IQR: 5 to 10 days)
Deyoe (<u>84</u>)	US, April 2020 to January 2022	Cross- sectional	n=3 cases (Omicron variant)	Proportion of cases with viable virus for at least 6 days: n=1 of 3 (33.3%)
Dzieciolowska	Canada, February	Prospective	n=121 cases (healthcare	Positive viral cultures on day 5: n=87 of 121 (71.9%, 95% CI: 63.0 to 79.7%)
BA.2		workers, Omicron BA.1 [11.6%],	Positive viral cultures on day 7: n=56 of 120 (46.7%, 95% CI: 37.5 to 56.0%)	
	BA.2 [60.3%] and BA.5 [8.3%] variants)	Positive viral cultures on day 10: n=22 of 121 (18.2%, 95% CI: 11.8 to 26.2%)		

case, and 95% of transmission occurred

days)

case (11%) diagnosed 2 days after

m onset: 51% (95% Crl: 46% to 56%)

(95% Crl: 24.8% to 42.5%)

vents occurring within 5 days after

Study	Country, time period	Study type	Participants	Outcome	
(Preprint) onwards	US, March 2022 onwards (end date not reported)	nt) onwards (end	Prospective cohort	n=55 cases (no therapy group, Omicron BA.2, BA.5, XBB, other variants)	Median time to first negative viral culture: 4 days (IQR: 3 to 6 days)
			n=72 cases (Nirmatrelvir and Ritonavir group, Omicron BA.2, BA.5, XBB, other variants)	Median time to first negative viral culture: 3 days (IQR: 2 to 4 days)	
			n=15 cases (Nirmatrelvir and Ritonavir group with virological rebound, Omicron BA.2, BA.5, XBB, other variants)	Median time to first negative viral culture: 3 days (IQR: 3 to 4 days)	
			n=40 cases (Nirmatrelvir and Ritonavir group without virological rebound, Omicron BA.2, BA.5, XBB, other variants)	Median time to first negative viral culture: 3 days (IQR: 2 to 4 days)	
			n=15 cases (Nirmatrelvir and Ritonavir group with virological rebound, Omicron BA.2, BA.5, XBB, other variants)	Median time to final negative viral culture: 14 days (IQR: 13 to 20 days)	
2021 onward (end date no	US, November	Prospective	ctive n=92 university cases (n=75	Culture positive more than 5 days from diagnosis: n=10 (11%)	
	2021 onwards (end date not stated)	cohort	Omicron, n=17 Delta)	Culture positive more than 5 days from symptom onset: n=16 of 92 (17%	
Gilbert (<u>7</u>)	US, November	Prospective	n=54 university cases (variant	Median time to negative culture: 4 days (IQR: 3 to 5.75 days)	
(Preprint, conference abstract)	2021 to March 2022	cohort	not stated)	No statistically significant association between time to negative culture ar vaccine (p=0.34)	
Jang (<u>8</u>)	South Korea, December 2021	Prospective cohort	n=11 hospitalised cases (Omicron variant)	Last positive viral culture after symptom onset: 8 days	
Jung (<u>3</u>)	South Korea,	Prospective	n=32 healthcare worker	Median time from symptom onset to negative culture: 4 days (95% CI: 3 to 10 to	
	February to	cohort	asymptomatic and mild cases	Median time from diagnosis to negative culture: 3 days (95% CI: 3 to 4 days	
	March 2022	2	(Omicron B.1.1.529 variant)	Proportion of cases shedding viable virus on day 6 after symptom onset:	
				Proportion of cases shedding viable virus on day 8 after symptom onset:	
Kang (<u>9</u>)	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	
Kang (<u>87</u>)	South Korea, February to April 2022	Prospective cohort	n=41 cases with haematologic malignancies or solid organ	Median duration of viable virus shedding: 4 weeks (IQR: 3 to 6 weeks)	

vs)
70()
7%)
e and time since last dose of COVID-19
: 3 to 5 days) 4 days)
set: 16%
set: 0%
to 7 days)
3)

Study	Country, time period	Study type	Participants	Outcome
			transplantations (Omicron BA.1 and BA.2 variants)	
Kang (<u>88</u>)	South Korea, January to August	Prospective cohort	n=40 cases (healthcare workers, Omicron BA.1 or BA.2 variants)	Median duration of viable virus shedding: 4 days (IQR: 3 to 5 days)
	2022		n=42 cases (healthcare workers, Omicron BA.5 variant)	Median duration of viable virus shedding: 2.5 days (IQR: 2 to 3 days)
Kang (<u>89</u>)	South Korea, February 2021 to	Prospective cohort	n=15 not or partially vaccinated cases (Omicron variant)	Median duration of culture positivity: 4 days (IQR: 2 to 6 days)
	May 2022		n=60 fully vaccinated cases (Omicron variant)	Median duration of culture positivity: 4 days (IQR: 2 to 5 days)
Keske (<u>10</u>)	Turkey, January	Prospective	n=55 healthcare worker non-	Positive viral cultures (day 5): n=44 of 53 (83%)
	to February 2022	cohort	severe cases (Omicron variant)	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%)
				Proportion of cases where the duration of viral shedding was longer tha (19%)
Lee (<u>90</u>)	South Korea, February to April 2022	Prospective		Data extracted from figure: Culture positivity on day 3: n=25 of 37 (67.6)
		ary to April cohort		Culture positivity on day 5: n=0 of 37 (0%)
			n=6 hospitalised cases (control group, Omicron BA.1 and BA.2 variants)	Data extracted from figure: Culture positivity on day 3: n=6 of 6 (100%)
				Culture positivity on day 7: n=3 of 6 (50%)
Kim (<u>11</u>)	South Korea,	ber 2021 to cohort and ritanavir group, Omicron	Positive viral cultures (day 1, nirmatrelvir and ritanavir group): 51.5%	
	October 2021 to		C	Positive viral cultures (day 5, nirmatrelvir and ritanavir group): 18.2%
	May 2022		BA.1 and BA.2 variants)	Positive viral cultures (day 9, nirmatrelvir and ritanavir group): 0%
			n=37 mild cases (supportive	Positive viral cultures (day 1, supportive care group): 86.5%
			care group, Omicron BA.1 and BA.2 variants)	Positive viral cultures (day 5, supportive care group): 32.4%
			DA.2 Valiants)	Positive viral cultures (day 9, supportive care group): 0%
Luna-Muschi (<u>12</u>)	Brazil, January	Prospective	n=30 vaccinated healthcare worker mild cases (Omicron BA.1 variant)	Positive viral culture (day 5 after symptom onset): n=11 of 24 (46%)
	2022	cohort		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%)
Mitsuyuki (<u>91</u>)	Japan, January to April 2022	Retrospective cohort	n=14 patients with haematological malignancies (Omicron BA.1 variant)	One case was culture positive on day 15 after symptom onset, and a see 25 and 58 days after symptom onset
	1		· ·	•

an the duration of symptoms: n=10 of 53
6%)
)
second case was culture positive on days
become case was culture positive on udys

Study	Country, time period	Study type	Participants	Outcome
Raglow (<u>92</u>) (Preprint)	US, April 2022 to February 2023.	Prospective cohort	n=150 immunocompromised adults (Omicron BA.1 [3%], BA.2 [31%], BA.4 [6%], BA.5 [29%], and unknown Omicron [32%] variants)	Proportion of cases with culture positivity of more than 32 days: n=5 of 150 (3%)
Saade (<u>93</u>)	France,	Prospective	n=44 fully vaccinated healthcare	Virus isolated from culture at diagnosis: n=29 of 43 (67.4%)
	November 2021	cohort	worker cases (Omicron variant: BA.1)	Virus isolated from culture on day 7: n=12 of 42 (28.5%)
	to February 2022			Virus isolated from culture on day 14: n=0 of 38 (0.0%)
Takahashi (<u>13</u>) Japan, November	Japan, November	nber Retrospective cohort		Positive viral culture (0 to 1 days after diagnosis): n=2 of 17 (11.8%)
	to December			Positive viral culture (2 to 5 days after diagnosis): n=5 of 12 (41.7%)
2021	2021			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%)
Utzon (<u>94</u>) Denmark,	Prospective	n=29 adult high-risk non-	Culture positivity on day 5 of symptom onset: n=7 of 21 (33%)	
to February 2022 immun (Omicr		hospitalised immunocompromised patients (Omicron BA.1 [41%] and BA.2 [41%] variants)	Culture positivity on day 15 of symptom onset: n=2 of 29 (7%)	

Table C.1c. Incubation period

Study	Country, time period	Study type	Participants	Outcome
Backer (<u>14</u>)	The Netherlands,	Prospective	n=258 cases (Omicron variant)	Mean incubation period: 3.2 days (95% Crl: 2.9 to 3.6 days), SD: 2.2 da
	December 2021 to January 2022	cohort		Median incubation period: 2.8 days (95% Crl: 2.5 to 3.2 days)
Brandal (<u>95</u>)	Norway, November to December 2021	Cross- sectional	n=81 cases (Omicron variant)	Median incubation period: 3 days (IQR: 3 to 4 days)
Chen (<u>96</u>)	China, February to March 2022	Prospective cohort	n=387 cases (Omicron BA.2 variant)	Mean incubation period: 3.6 days (SD: 2.1 days)
Del Aguila-Mejia (<u>2</u>)	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)
Guo (<u>97</u>)		Retrospective cohort	n=649 transmission pairs (Omicron variant)	Mean incubation period: 3.4 days (95% Crl: 2.9 to 4.0 days)

ays (95% CrI: 1.9 to 2.5 days)

Study	Country, time period	Study type	Participants	Outcome
	Hong Kong, January to February 2022		n=162 transmission pairs with 0 to one vaccination doses (Omicron variant)	Mean incubation period: 2.4 days (95% Crl: 1.8 to 3.1 days) Median incubation period: 2.1 days (95% Crl: 1.5 to 2.8 days)
			n=455 transmission pairs with 2 to 3 vaccination doses (Omicron variant)	Mean incubation period: 3.7 days (95% Crl: 3.1 to 4.7 days) Median incubation period: 3.2 days (95% Crl: 2.6 to 3.9 days)
			n=143 transmission pairs aged 18 years and under (unclear if age applies to index case only, Omicron variant)	Mean incubation period: 2.9 days (95% Crl: 2.3 to 2.6 days) Median incubation period: 2.9 days (95% Crl: 2.1 to 4.2 days)
			n=248 transmission pairs aged 19 to 39 years (unclear if age applies to index case only, Omicron variant)	Mean incubation period: 3.3 days (95% Crl: 2.7 to 4.1 days) Median incubation period: 3.3 days (95% Crl: 2.6 to 4.2 days)
			n=204 transmission pairs aged 40 to 64 years (unclear if age applies to index case only, Omicron variant)	Mean incubation period: 3.8 days (95% Crl: 3.1 to 4.9 days) Median incubation period: 3.4 days (95% Crl: 2.7 to 4.6 days)
			n=54 transmission pairs aged at least 65 years (unclear if age applies to index case only, Omicron variant)	Mean incubation period: 3.8 days (95% Crl: 2.9 to 5.5 days) Median incubation period: 4.2 days (95% Crl: 2.8 to 6. days)
Helmsdal (<u>98</u>) Faroe Isl	Faroe Islands,	Cross-	n=21 cases (Omicron variant)	Mean incubation period: 3.24 days (95% CI: 2.87 to 3.60 days, range: 2
	December 2021 sect	sectional		Mean time from exposure to positive test: 3.82 days (95% CI: 3.46 to 4.
Liu (<u>99</u>)		Cross-	n=22 cases (Omicron BA.1	Mean incubation period: 3.5 days (95% CI: 2.5 to 3.8 days), SD: 1.4 day
		sectional	variant)	Median incubation period: 3.3 days (95% CI: 2.4 to 3.7 days), 95th perc days)
Liu (<u>100</u>)	China, January to March 2022	· ·	n=34 transmission pairs (Omicron BA.1 variant)	Mean incubation period: 4.85 days (95% CI: 0 to 9.51) (SD: 2.37 days)
			n=1,064 transmission pairs (Omicron BA.2 variant)	Mean incubation period: 4.17 days (95% CI: 0 to 7.97) (SD: 1.94 days)
Liu (<u>101</u>) (Extracted from abstract only)	China, October 2022	Cross- sectional	n=44 cases (Omicron BA.5.2 variant)	Median incubation period: 2.52 days (IQR: 1.32 to 4.84 days)
Mefsin (<u>15</u>)		Prospective cohort	n=57 cases (Omicron BA.1 variant)	Median incubation period (Omicron BA.1, n=57): 4.38 days (95% CI: 3.8

2 to 6 days)
4.19 days, range: 3 to 5 days)
ays (95% CI: 1.0 to 1.5 days)
rcentile: 6.0 days (95% CI: 4.3 to 6.6
)
)
3.88 to 4.87 days)

Study	Country, time period	Study type	Participants	Outcome
	Hong Kong, January 2022 to March 2022		n=23 cases (Omicron BA.2 variant)	Median incubation period (Omicron BA.2, n=23, Gamma distribution): 4
Ogata (<u>102</u>)	Japan, January to August 2022	Cross- sectional	n=122 transmission pairs (Omicron BA.5 variant)	Mean incubation period: 2.6 days (95% CI: 2.5 to 2.8 days), SD: 1.0 day
				Median incubation period: 2.5 days (95% CI: 2.5 to 2.7), IQR: 1.9 days (95% CI: 3.0 to 3.5 days), 5th percentile: 1.2 days (95% CI: 1.1 to 1.4 d 4.1 to 4.9 days)
			n=68 transmission pairs (Omicron BA.1 variant)	Mean incubation period: 2.9 days (95% CI: 2.6 to 3.2 days), SD: 1.3 day
				Median incubation period: 2.7 days (95% CI: 2.5 to 3.0), IQR: 2.0 days (95% CI: 3.3 to 4.0 days), 5th percentile: 1.2 days (95% CI: 1.0 to 1.5 days) 4.6 to 5.9 days)
Park (<u>16,204</u>)	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 (<u>17</u>)	Japan, January 2022	Prospective cohort	n=172 cases (variant not confirmed)	Median incubation period: 2.6 days (95% CI: 2.4 to 2.8 days), IQR: 1.9 days (95% CI: 3.2 to 3.9 days)
			n=77 cases (confirmed Omicron BA.1 variant)	Median incubation period: 2.8 days (95% CI: 2.5 to 3.1), IQR: 2 days (9 CI: 3.3 to 4.4 days), 5th percentile: 1.3 days (95% CI: 1.0 to 1.6 days), 9 days)
Ward (<u>18</u>)	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 3.7 to 3.22 days)
				Mean incubation period (Omicron BA.2): 3.48 days (95% Crl: 3.43 to 3.4 to 2.98 days)
				Mean incubation periods did not appear to vary much by age group
Wang (<u>103</u>)	China, August to September 2022	Retrospective cohort	n=60 symptomatic cases (Omicron BA.5.2 variant)	Median incubation period: 5.7 days (95% CrI: 4.8 to 6.6 days), 95th period days)
Wei (<u>19,205</u>)	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 percentil
Xin (<u>4</u>)	China, January to February 2022	Cross- sectional	n=114 cases (Omicron BA.1.1 variant)	Mean incubation period: 3.8 days (95% Crl: 3.5 to 4.1 days), 95th perce days)
Xiong (<u>104</u>)	China, June to July 2022	Cross- sectional	n=500 cases (Omicron BA.5 variant)	Mean incubation period: 3.27 days (SD: 1.05 days)
Zeng (<u>105</u>)	Singapore, December 2021 to January 2022	Cross- sectional	n=36 transmission pairs (Omicron BA.1 variant)	Median incubation period: 3 days (IQR: 2 to 4 days)
				Mean incubation period: 2.8 days (95% CI: 0.8 to 7.0 days)

: 4.27 days (95% CI: 3.29 to 5.02 days)

days

vs (95% CI: 1.8 to 2.0 days) to 3.2 days days), 95th percentile: 4.5 days (95% CI:

days

vs (95% CI: 1.8 to 2.3 days) to 3.6 days days), 95th percentile: 5.2 days (95% CI:

.9 days (95% CI: 1.7 to 2.1 days) to 3.5

(95% CI: 1.7 to 2.4 days) to 3.8 days (95%), 95th percentile: 5.8 days (4.8 to 7.5

3.72 days), SD: 3.14 days (95% Crl: 3.06

3.53 days), SD: 2.90 days (95% Crl: 2.82

ercentile: 12.8 days (95% Crl: 10.7 to 15.6

ntile: 8.3 days)

rcentile: 6.2 days (95% Crl: 5.7 to 6.9

Study	Country, time period	Study type	Participants	Outcome
Xin (<u>4</u>)	China, January to February 2022	Cross- sectional	n=114 cases (Omicron BA.1.1 variant)	Mean latent period: 3.1 days (95% Crl: 2.8 to 3.5 days), 95th percentile:

Table C.1e. Serial interval and generation time

Study	Country, time period	Study type	Participants	Outcome
Allen (<u>106</u>)	UK, December 2021	Cross- sectional	n=40,123 cases (Omicron variant)	Median serial interval: 3 days (IQR: 2 to 5 days)
Ali (<u>20</u>) (Preprint)	Hong Kong, January to February 2022	anuary to 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% Crl: 3.5 to 3.7 days), SD
			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 (<u>1</u>)	Germany,	Prospective	n=11,512 households (Omicron	Mean serial interval (Omicron): 3.61 days (95% CI: 3.56 to 3.66 days)
	January to May 2022	cohort	BA.1 and BA.2 variants)	Mean serial interval (Omicron BA.1): 3.88 days (95% CI: 3.79 to 3.97 da
				Mean serial interval (Omicron BA.2): 3.39 days (95% CI: 3.30 to 3.49 days
Backer (<u>14</u>)	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)
Bendall (<u>107</u>)	US, June 2021 to January 2022	Prospective cohort	n=55 transmission pairs (Omicron BA.1 variant)	Median serial interval: 3 days
Chen (<u>96</u>)	China, February to March 2022	Prospective cohort	n=387 cases (Omicron BA.2 variant)	Mean serial interval: 3.2 days (SD: 1.7 days)
Del Aguila-Mejia (<u>2</u>)	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)
Guo (<u>108</u>)	China, May to July 2022	Cross- sectional	n=8 transmission pairs (Omicron BA.4 variant)	Mean serial interval: 2.8 days (SD: 2.1 days)
			n=51 transmission pairs (Omicron BA.5 variant)	Mean serial interval: 2.7 days (SD: 2.5 days)
			n=45 transmission pairs (Omicron BA.2.12.1 variant)	Mean serial interval: 4.4 days (SD: 4.3 days)

e: 5.9 days (95% Crl: 5.3 to 6.8 days)
D: 3.4 days (95% Crl: 3.3 to 3.5 days)
days)
days)

Study	Country, time period	Study type	Participants	Outcome
			n=8 transmission pairs (Omicron BA.4 variant)	Median serial interval: 2.2 days (95% Crl: 1.1 to 5.3 days)
			n=51 transmission pairs (Omicron BA.5 variant)	Median serial interval: 2.5 days (95% Crl: 1.9 to 3.2 days)
			n=45 transmission pairs (Omicron BA.2.12.1 variant)	Median serial interval: 2.9 days (95% Crl: 1.7 to 4.8 days)
Guo (<u>97</u>)	Hong Kong, January to	Retrospective cohort	n=1,090 transmission pairs (Omicron variant)	Mean serial interval: 4.4 days (95% Crl: 4.1 to 4.9 days)
	February 2022		n=883 household transmission pairs (Omicron variant)	Mean serial interval: 4.3 days (95% Crl: 3.9 to 4.8 days)
			n=207 non-household transmission pairs (Omicron variant)	Mean serial interval: 4.8 days (95% Crl: 3.9 to 6.1 days)
			n=162 transmission pairs with 0 to 1 vaccination doses (Omicron variant)	Mean serial interval: 2.7 days (95% Crl: 2.1 to 3.4 days)
			n=455 transmission pairs with 2 to 3 vaccination doses (Omicron variant)	Mean serial interval: 4.9 days (95% Crl: 4.2 to 5.9 days)
			n=256 transmission pairs before 1 February epidemic phase (Omicron variant)	Mean serial interval: 5.8 days (95% Crl: 5.2 to 6.5 days)
			n=834 transmission pairs after 1 February epidemic phase (Omicron variant)	Mean serial interval: 2.9 days (95% Crl: 2.6 to 3.1 days)
Hoeve (<u>109</u>)	The Netherlands, July 2021 to August 2022	Prospective cohort	n=3,399 index cases and n=1,802 secondary cases (Omicron BA.1, BA.2, BA.4, and BA.5 variants)	Median time between positive tests of index and household members: 4
Kim (<u>21</u>)	South Korea,	Prospective	n=73 case pairs (Omicron	Mean serial interval: 3.78 days (95% Crl: 3.02 to 4.54 days), SD: 3.33 d
	November to December 2021	cohort	variant)	Mean serial interval (child index cases): 3.0 days
	December 2021			Mean serial interval (adult index cases): 5.0 days
Kremer (<u>110</u>)	Belgium, November to December 2021	Cross- sectional	n=2,161 transmission pairs (Omicron BA.1 variant)	Mean serial interval: 2.75 days (SD: 2.53 days)

4.0 days (IQR: 3 to 6 days)
days (95% Crl: 2.56 to 4.09 days)

Study	Country, time period	Study type	Participants	Outcome
Li (<u>111</u>)	China, May 2022	Cross- sectional	n=21 transmission pairs (Omicron BA.2 variant)	Mean serial interval: 2.89 days (SD: 0.95 days)
Liu (<u>100</u>)	China, January to March 2022	Cross- sectional	n=34 transmission pairs (Omicron BA.1 variant)	Mean serial interval: 3.84 days (95% CI: 0 to 8.37 days)
			n=1,064 transmission pairs (Omicron BA.2 variant)	Mean serial interval: 2.77 days (95% CI: 0 to 5.83 days)
Liu (<u>101</u>) (Extracted from	China, October 2022	Cross- sectional	n=37 cases (Omicron BA.5.2 variant)	Median serial interval: 2.13 days (IQR: 1.63 to 2.64 days)
abstract only)			n=21 cases (Omicron BA.5.2 variant)	Median generation time: 1.91 days (IQR: 1.05 to 3.15 days)
Manica (<u>83</u>)	Italy, January	Cross-	n=23,122 cases (Omicron	Mean intrinsic generation time: 6.84 days (95% Crl: 5.72 to 8.60 days)
	2022	sectional	variant)	Mean realised household generation time: 3.59 days (95% Crl: 3.55 to 3
				Mean household serial interval: 2.38 days (95% Crl: 2.30 to 2.47 days)
Mellis (<u>112</u>) (Preprint)	US, April 2020 to September 2022	Cross- sectional	n=109 transmission pairs (Omicron BA.1 variant)	Mean serial interval: 4.1 days (95% CI: 3.3 to 5.0 days)
			n=180 transmission pairs (Omicron BA.2 variant)	Mean serial interval: 4.6 days (95% CI: 4.2 to 5.0 days)
			n=57 transmission pairs (Omicron BA.4 variant)	Mean serial interval: 4.3 days (95% CI: 3.6 to 5.0 days)
			n=262 transmission pairs (Omicron BA.5 variant)	Mean serial interval: 3.8 days (95% CI: 3.4 to 4.1 days)
Mefsin (<u>15</u>)	Hong Kong,	Prospective cohort	n=57 cases (Omicron BA.1 variant)	Median generation time (Omicron BA.1, n=45): 2.38 days (95% CI: 2.01
	January 2022 to			Median serial Interval (Omicron BA.1, n=30): 3.15 days (95% CI: 2.49 to
	March 2022		n=23 cases (Omicron BA.2 variant)	Median serial Interval (Omicron BA.2, n=13, Gamma distribution): 2.52
Park (<u>16,204</u>)	The Netherlands,	Retrospective	n=258 cases (Omicron variant)	Mean serial interval: 3.1 days (95% CI: 2.9 to 3.3 days)
	November 2021 to January 2022	cohort		Mean forward generation interval: 3.0 days (95% CI: 2.7 to 3.2 days)
Park (<u>113</u>)	South Korea, January 2022	Cross- sectional	n=31 transmission pairs (Omicron BA.1 variant)	Mean serial interval: 2.6 days (SD: 1.9 days)
Shim (<u>114</u>)	South Korea, November 2021 to January 2022	Cross- sectional	n=202 transmission pairs (Omicron BA.1 variant)	Mean serial interval: 4.2 days (95% CI: 3.8 to 4.5 days) (SD: 2.48, 95%
Song (<u>115</u>)				Mean serial interval: 2.9 days (SD: 1.6)

3.60 days)
)
1 to 2.80 days)
to 3.92 days)
2 days (95% CI: 1.68 to 3.55 days)
6 CI: 2.22 to 2.72 days)

Study	Country, time period	Study type	Participants	Outcome
	South Korea, November to December 2021	Cross- sectional	n=12 transmission pairs (Omicron BA.1 variant)	Median serial interval: 3.0 days
Wang (<u>103</u>)	China, August to	Retrospective	n=178 transmission pairs	Mean generation interval: 2.8 days (95% Crl: 2.4 to 3.5 days) SD: 3.7 d
	September 2022	cohort	(Omicron BA.5.2 variant)	Mean generation interval, adjusting for truncation: 4.3 days (95% Crl: 2.
				Median generation interval: 1.4 days (95% Crl: 1.1 to 1.9 days), 95th pedays)
Wei (<u>19,205</u>)	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 (<u>22</u>)	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)
Zeng (<u>105</u>)	Singapore, December 2021	nber 2021 sectional	n=76 transmission pairs (Omicron BA.1 variant)	Median serial interval: 2 days (IQR: 2 to 3 days)
	to January 2022		n=38 transmission pairs (Omicron BA.2 variant)	Median serial interval: 3 days (IQR: 2 to 3 days)
			n=76 transmission pairs (Omicron BA.1 variant)	Mean serial interval: 2.6 days (95% CI: 0.6 to 6.8 days)
			n=38 transmission pairs (Omicron BA.2 variant)	Mean serial interval: 2.6 days (95% CI: 1.0 to 5.1 days)

Table C.1f. Time to peak viral load

Study	Country, time period	Study type	Participants	Outcome
Choi (<u>23</u>)	South Korea, January 2022	Retrospective cohort	n=5,187 cases (Omicron variant)	Peak viral load after symptom onset: 2.4 days (95% CI: 2.2 to 2.5 days)
	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
Frediani (<u>116</u>) (Preprint)	US, April 2022 to April 2023	Cross- sectional	n=621 cases (variant not stated)	Median time to peak viral load after symptom onset: 4 days
Hay (<u>25</u>)	US, December 2021 to January	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 days)
	2022			Mean time to peak viral load (proliferation time, booster vaccinated case

days	(95%	Crl: 3.0	to 4.8	days)
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2.6 to 6.9 days)

percentile: 10.4 days (95% Crl: 8.5 to 13.0

rs) nated cases): 3.6 days (95% Crl: 3.3 to 4.0 nases): 4.0 days (95% Crl: 3.8 to 4.3 days)

Study	Country, time Study type Participants period		Participants	Outcome
Herbert (<u>117</u>) (Preprint)			n=2,086 cases (Omicron variant dominant)	Peak viral load 0 to 2 days after symptom onset
			n=546 cases (Omicron variant dominant)	Peak viral load 5 days after exposure
Jiang (<u>118</u>)	China, May to June 2022	Cross- sectional	n=298 hospitalised cases (Omicron variant)	Median time from first RNA positive to peak viral load: 3 days (IQR: 2 to 5 days)
			n=222 asymptomatic hospitalised cases (Omicron variant)	Median time from first RNA positive to peak viral load: 3 days (IQR: 2 to 5 days)
			n=76 symptomatic hospitalised cases (Omicron variant)	Median time from first RNA positive to peak viral load: 3 days (IQR: 2 to 5 days)
Kandel (<u>26</u>)	Canada,	Prospective	n=41 adult cases (Omicron BA.1	Mean time from symptom onset to peak viral load: 2.97 days
	December 2021 to January 2022	cohort	variant)	Mean time from first positive test to peak viral load: 2.89 days
Kissler (<u>119</u>) (Preprint)	US, March 2020 to July 2022	Retrospective cohort	n=1,400 cases (Omicron BA.1 or BA.2 variants)	Mean time to peak viral load: 4.4 days (95% CI: 3.7 to 5.2 days)
Koutsakos (<u>120</u>)	Australia, study dates not reported	Prospective cohort	n=7 cases (Omicron BA.1 variant)	Mean time between symptom onset and peak viral load: 2.43 days (95% CI: 1.24 to 4.78 days)
			n=10 cases (Omicron BA.2 variant)	Mean time between symptom onset and peak viral load: 1.12 days (95% CI: 0.47 to 2.63 days)
Li (<u>121</u>)	China, August to September 2022	Prospective cohort	n=60 cases (Omicron BA.2.76 variant)	Time from onset to peak viral load: 2 to 3 days
Luna-Muschi (<u>12</u>)	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 (<u>27</u>) (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
Townsley (<u>122</u>) (Preprint)	UK, January 2021 to September 2022	Prospective cohort	n=460 infections across 433 individuals (Omicron BA.1 [39%], BA.2 [31%], BA.4 [1.5%], BA.4/5 [1.5%], BA.5 [12%], and Delta [15%%] variants).	Time from symptom onset to peak viral load: 2 to 5 days
Wong (<u>123</u>)	China, February to July 2022	Retrospective cohort	n=242 cases (Nirmatrelvir and Ritonavir group, Omicron BA2.2 variant dominant)	Median time from start of follow up to peak viral load: 0 days (IQR: 0 to 3 days)

Study	Country, time period	Study type	Participants	Outcome
			n=563 cases (Molnupiravir group, Omicron BA2.2 variant dominant)	Median time from start of follow up to peak viral load: 1 day (IQR: 0 to 3
			n=3,787 (Control group, Omicron BA2.2 variant dominant)	Median time from start of follow up to peak viral load: 1 day (IQR: 0 to 6
Yang (<u>124</u>)	China, January 2020 to April 2022	Prospective cohort	n=1,721 patients (Omicron variant)	Mean time between symptom onset and peak viral load: 3.19 days (95%
				Proportion of cases reaching peak viral load by 5 days: n=1,492 of 1,72
				Viral dynamics were similar regardless of vaccination status, and male conditions, were slower to reach their peak viral load
Zhang (<u>125</u>)	China, November to December 2022	Retrospective cohort	n=370 hospitalised cases aged under 80 years (Omicron BF.7)	Viral load was highest on day 3 after a positive test
			n=110 hospitalised cases aged 80 years and over (Omicron BF.7)	Viral load was highest on day 2 after a positive test

Table C.1g. Time to viral clearance

Study	Country, time period	Study type	Participants	Outcome
Abhyankar (<u>126</u>)	India, March to May 2022	Prospective cohort (RCT)	n=48 cases (Imusil and standard care, variant not stated)	Proportion of cases with positive test at day 4: n=7 of 48 (14.6%)
			n=50 cases (standard care, variant not stated)	Proportion of cases with positive test at day 4: n=18 of 50 (36.0%)
Aiello (<u>127</u>)	Spain, December 2021 to March 2022	Prospective cohort	n=60 cases with high-risk haematological malignancies (Omicron variant)	Median duration of viral shedding: 20 days (IQR: 14 to 28 days)
				Viral shedding 21 days after diagnosis: n=22 (36.7%)
				Viral shedding 28 days after diagnosis: n=15 (25%)
				Viral shedding 42 days after diagnosis: n=6 (10%)
Alshukairi (<u>128</u>)	Saudi Arabia, January to February 2022	Retrospective cohort	n=480 cases (Omicron variant)	Proportion of cases positive on day 7 after diagnosis: n=173 of 480 (36%
Anastasiou	Germany,		n=72 cases (Omicron variant)	Median time to negative test: 7 days (IQR: 2 to 14 days)
(<u>28,192</u>)	January 2022			Median time to Ct value above 30: 7 days (IQR: 2 to 8 days)
Ao (<u>129</u>)	China, April to May 2022	Prospective cohort	n=35 hospitalised child cases (Omicron BA.2.2 variant)	Data extracted from figure: Duration of viral RNA shedding: 13 days (IQR

o 3 days)

6 days)

5% CI: 3.09 to 3.28 days)

721 (86.7%)

e cases, and cases with underlying health

5%) QR: 12 to 16 days)

Study	Country, time period	Study type	Participants	Outcome
			n=10 hospitalised child cases aged less than one year (Omicron BA.2.2 variant)	Data extracted from figure: Duration of viral RNA shedding: 14 days (IQR: 9 to 16 days)
			n=7 hospitalised child cases aged one to 3 years (Omicron BA.2.2 variant)	Data extracted from figure: Duration of viral RNA shedding: 10.5 days (IQR: 10 to 11 days)
			n=8 hospitalised child cases aged 3 to 6 years (Omicron BA.2.2 variant)	Data extracted from figure: Duration of viral RNA shedding: 8.5 days (IQR: 9.5 to 10.5 days)
			n=9 hospitalised child cases aged 6 to 18 years (Omicron BA.2.2 variant)	Data extracted from figure: Duration of viral RNA shedding: 12 days (IQR: 9 to 14 days)
			n=46 parent cases (Omicron BA.2.2 variant)	Data extracted from figure: Duration of viral RNA shedding: 10 days (IQR: 8 to 11 days)
Bernardi (<u>130</u>) (Preprint, conference abstract)	Italy, April to September 2022	Retrospective cohort	n=40 child cases treated with paxlovid (variant not stated)	Mean duration of viral shedding: 12.7 days
Cabral (<u>29</u>) and Brazil, January t da Silva (<u>206</u>) May 2022	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)
Cao (<u>131</u>) China, Ap	China, April to	Prospective cohort (RCT)	n=384 mild to moderate cases (VV116 group, Omicron BA.2.2 variant)	Median time to first negative test: 7.0 days (IQR: 6.0 to 7.0 days)
	May 2022			Proportion of cases with SARS-CoV-2 clearance by day 5: n=186 of 384 (48.4%)
				Proportion of cases with SARS-CoV-2 clearance by day 7: n=288 of 384 (75.0%)
				Proportion of cases with SARS-CoV-2 clearance by day 10: n=337 of 384 (87.8%)
				Proportion of cases with SARS-CoV-2 clearance by day 14: n=364 of 384 (94.8%)
			n=387 mild to moderate cases	Median time to first negative test: 7.0 days (IQR: 6.0 to 7.0 days)
			(paxlovid group, Omicron BA.2.2	Proportion of cases with SARS-CoV-2 clearance by day 5: n=183 of 387 (47.3%)
			variant)	Proportion of cases with SARS-CoV-2 clearance by day 7: n=275 of 387 (71.1%)
				Proportion of cases with SARS-CoV-2 clearance by day 10: n=345 of 387 (89.1%)
				Proportion of cases with SARS-CoV-2 clearance by day 14: n=358 of 387 (92.5%)
Cegolon (<u>30</u>)	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%)

Study	Country, time period	Study type	Participants	Outcome
			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%)
Chen (<u>31</u>)	China, March to	Prospective	n=847 hospitalised cases	Median viral shedding time: 13 days (IQR: 10 to 16 days)
	May 2022	cohort	(Omicron variant)	Viral shedding time was longer for older cases ($p=0.037$) and cases with ($p<0.001$) or heart conditions ($p=0.030$), and shorter for cases with full or
Cegolon (<u>132</u>)	Italy, Feburary to May 2022	Retrospective cohort	n=111 high-risk outpatient cases with comorbidities (standard of care group, Omicron BA.1 and BA.2 variants)	Median time from first positive to first negative RT-PCR or antigenic test:
			n=57 high-risk outpatient cases with comorbidities (Sotrovimab group, Omicron BA.1 and BA.2 variants)	Median time from first positive to first negative RT-PCR or antigenic test:
			n=116 high-risk outpatient cases with comorbidities (Molnupiravir group, Omicron BA.1 and BA.2 variants)	Median time from first positive to first negative RT-PCR or antigenic test:
			n=102 high-risk outpatient cases with comorbidities (Nirmatrelvir with Ritonavir group, Omicron BA.1 and BA.2 variants)	Median time from first positive to first negative RT-PCR or antigenic test:
			n=111 high-risk outpatient cases with comorbidities (standard of care group, Omicron BA.1 and BA.2 variants)	Mean time from first positive to first negative RT-PCR or antigenic test: 13
			n=57 high-risk outpatient cases with comorbidities (Sotrovimab group, Omicron BA.1 and BA.2 variants)	Mean time from first positive to first negative RT-PCR or antigenic test: 16
			n=116 high-risk outpatient cases with comorbidities (Molnupiravir group, Omicron BA.1 and BA.2 variants)	Mean time from first positive to first negative RT-PCR or antigenic test: 1
			n=102 high-risk outpatient cases with comorbidities (Nirmatrelvir with Ritonavir group, Omicron BA.1 and BA.2 variants)	Mean time from first positive to first negative RT-PCR or antigenic test: 10

n chronic kidney disease stage 4 to 5 or booster vaccinations (p=0.001)
t: 11 days (IQR: 8 to 15 days)
t: 10 days (IQR: 14 to 19 days)
t: 8 days (IQR: 11 to 14 days)
t: 7 days (IQR: 7 to 12 days)
13.0 days (SD: 7.7 days)
16.5 days (SD: 10.5 days)
11.7 days (SD: 5.2 days)
10.2 days (SD: 4.4 days)

Study	Country, time period	Study type	Participants	Outcome
Chen (<u>32</u>)	Chen (<u>32</u>) China, August to		n=166 hospitalised cases	Median time from treatment to first negative RT-PCR: 5 days (IQR: 1 to 7 days)
(Preprint)	October 2022	cohort	(Azvudine group, Omicron variant)	Median time from first positive to first negative RT-PCR test: 9 days (IQR: 7 to 11 days)
			n=41 hospitalised cases (control group, Omicron variant)	Median time from treatment to first negative RT-PCR: 6 days (IQR: 5 to 7 days)
				Median time from first positive to first negative RT-PCR test: 8 days (IQR: 7 to 13 days)
Chen (<u>133</u>) (Preprint)	China, April to May 2022	Prospective cohort	n=368 mild cases (control group, variant not stated)	Median time from first day of admission to first negative NAAT test: 5 days (IQR: 4 to 6 days)
			n=390 mild cases (ZhengQi group, variant not stated)	Median time from first day of admission to first negative NAAT test: 4 days (IQR: 2 to 6 days)
Colaneri (<u>33</u>)	Italy, December	Retrospective	n=49 mild and moderate cases	Median duration of viral load (untreated): 15 days
	2021 to May 2022	cohort	with hematologic malignancies (Omicron variant)	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 (<u>34</u>) (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 (<u>35</u>) (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
Dewald (<u>134</u>)	Germany,	Prospective	n=10 cases with middle to high	Mean time from symptom onset to Ct value of 30: 8 days
	January 2022	cohort	viral loads and double vaccinated (Omicron BA.1 variant)	Proportion with Ct value of at least 30 at day 9 after symptom onset: 79.4%
			n=22 cases with middle to high	Mean time from symptom onset to Ct value of 30: 9 days
			viral loads and received booster vaccine (Omicron BA.1 variant)	Proportion with Ct value of at least 30 at day 9 after symptom onset: 54.2%
Dong (<u>135</u>)	China, March to June 2022	Retrospective cohort	n=653 mild cases (Pupingqinghua group, Omicron variant)	Median viral load shedding time (from admission after treatment to 3 consecutive negative COVID-19 test results): 5.0 days (IQR: 5.0 to 7.0 days)
			n=220 mild cases (Lianhuaqingwen group, Omicron variant)	Median viral load shedding time (from admission after treatment to 3 consecutive negative COVID-19 test results): 5.0 days (IQR: 4.0 to 7.0 days)

Study	Country, time period	Study type	Participants	Outcome
Dzieciolowska	Canada, February	Prospective	n=121 cases (healthcare	Proportion of cases positive on RT-PCR (day 5): n=112 of 120 (93.3%)
(<u>85</u>) (Preprint)	to March 2023	cohort	workers, Omicron BA.1 [11.6%],	Proportion of cases positive on RT-PCR (day 7): n=107 of 120 (89.1%)
			BA.2 [60.3%], and BA.5 [8.3%] variants)	Proportion of cases positive on RT-PCR (day 10): n=74 of 120 (61.2%)
				Proportion of cases positive on RAT (day 5): n=97 of 119 (81.5%)
				Proportion of cases positive on RAT (day 7): n=75 of 117 (64.1%)
				Proportion of cases positive on RAT (day 10): n=40 of 117 (34.2%)
Earnest (<u>136</u>)	US, January to	Prospective	n=177 cases (variant not stated)	Proportion of cases positive on RAT (day 5): 47%
	February 2022	cohort		Proportion of cases positive on RAT (day 6): 22%
				Proportion of cases positive on RAT (day 7): 8%
				Proportion of cases positive on RAT (days 8 to 13): 1 to 2%
			n=47 cases (last negative RAT 5 to 9 days before diagnosis, variant not stated)	Proportion of cases positive on RAT (day 5): 28%
				Proportion of cases positive on RAT (day 6): 17%
				Proportion of cases positive on RAT (day 7): 6%
				Proportion of cases positive on RAT (days 8 to 9): 2 to 4%
			n=91 cases (last negative RAT 10 or more days before diagnosis, variant not stated)	Proportion of cases positive on RAT (day 5): 26%
				Proportion of cases positive on RAT (day 6): 15%
				Proportion of cases positive on RAT (day 7): 7%
				Proportion of cases positive on RAT (days 8 to 9): 1%
El-Tanani (<u>137</u>)	Jordan, January to March 2022	Prospective cohort (RCT)	n=34 symptomatic cases attending the emergency room (mebendazole group, variant not stated)	Positive RT-PCR (day 5 of treatment): n=2 of 34 (5.9%)
			n=35 symptomatic cases attending the emergency room (control group, variant not stated)	Positive RT-PCR (day 5 of treatment): n=5 of 35 (11.8%)
Feng (<u>138</u>)	China, January to	Retrospective	n=417 hospitalised cases	Median time from admission to negative RT-PCR test: 10 days (IQR: 8 to 12 days)
	March 2022	cohort	(variant not stated)	Proportion of case who had RT-PCR positivity after discharge: n=99 of 417 (23.7%)
Geng (<u>139</u>)	China, April to May 2022	Retrospective cohort	n=25,143 non-severe cases (Omicron variant)	Viral shedding time, 75th quartile: 9 days
Ghafari (<u>140</u>)		Retrospective	-	Persistent infection of more than 26 days (BA.1 lineage): n=97
(Preprint)		cohort	sequences spanning at least 26	Persistent infection of more than 56 days (BA.1 lineage): n=15

•	Country, time period	Study type	Participants	Outcome
Uł	JK, November		days (Alpha, Delta and Omicron	Persistent infection of more than 26 days (BA.2 lineage): n=167
	2020 to August 2022		variants)	Persistent infection of more than 56 days (BA.2 lineage): n=23
•	Germany,	Prospective	n=43 immunodeficient cases	Positive RNA test at day 14 from first positive PCR test: n=1 of 14 (7.1%)
	anuary to ebruary 2022	cohort	(Omicron BA.1 and BA.2 variants)	Positive RNA test at day 21 from first positive PCR test: n=0 of 13 (case up)
			n=14 immunocompetent cases	Positive RNA test at day 14 from first positive PCR test: n=21 of 43 (48.8
			(Omicron BA.1 and BA.2 variants)	Positive RNA test at day 21 from first positive PCR test: n=12 of 43 (27.9
Reiche (<u>141</u>) 20	JS, December 2021 to March 2022		n=1 immunocompromised case (diffuse B-cell lymphoma) with persistent Omicron BA.1 infection (index case)	Duration of infection: more than 12 weeks, first onward transmission estir and 82
			n=1 case of persistent Omicron BA.1 infection (secondary case)	Duration of infection: 4 weeks
			n=1 case of persistent Omicron BA.1 infection (secondary case)	Duration of infection: more than 4 months
· · · · · · · · · · · · · · · · · · ·	China, February o May 2022	Retrospective cohort	n=2,033 asymptomatic, mild or moderate cases (Omicron BA.2.2 variant)	Median time from symptom onset or first positive RT-PCR test (whicheve 13.0 days (IQR: 10.0 to 16.0 days)
`	China, March to Aay 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
			n=1,508 hospitalised cases without chronic kidney disease (Omicron BA.2 variant)	Median time to negative RT-PCR test (cases without chronic kidney disea
\/	China, March to Aay 2022	Retrospective cohort	n=2,938 hospitalised cases (Omicron BA.2 variant)	Median time from first positive to first negative RT-PCR: 12.3 days (IQR:
· · · · · · · · · · · · · · · · · · ·	JS, December	Retrospective cohort	n=878 cases (Omicron BA.1	Mean time to negative RT-PCR test (fully or partially vaccinated cases): 6
	2021 to January 2022		variant) (number of cases not split by vaccination status)	Mean time to negative RT-PCR test (booster vaccinated cases): 8.4 days
Hua (<u>38</u>) Ch	China, July 2022	Retrospective cohort	n=225 adult cases (Omicron	Median duration of viral shedding: 11.0 days (IQR: 9.0 to 13.0 days)
			BA.2.38 variant)	No statistically significant difference in duration of viral shedding between booster vaccinated cases (p=0.85)
Ma Hay (<u>25</u>) 20 20	May 2022 JS, December 2021 to January 2022	cohort Retrospective cohort Retrospective	(Omicron BA.2 variant) n=2,938 hospitalised cases (Omicron BA.2 variant) 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 Mean time to negative RT-PCR test (booster vaccina Median duration of viral shedding: 11.0 days (IQR: 9. No statistically significant difference in duration of vira

%)

e who was positive at day 14 lost to follow

.8%)

.9%)

stimated to have occurred between days 64

ver came first) to first negative RT-PCR test:

se): 13 days (IQR: 8 to 18 days)

sease): 10 days (IQR: 7 to 14 days)

R: 9.3 to 16.3 days)

: 6.2 days (95% Crl: 5.8 to 6.6 days)

ys (95% Crl: 8.0 to 8.7 days)

en unvaccinated, fully vaccinated and

Study	Country, time period	Study type	Participants	Outcome
Huygens (<u>144</u>)	The Netherlands, December 2022 to January 2023	Prospective cohort	n=6 immunocompromised cases (Omicron variant)	Median duration of RT-PCR positivity before nirmatrelvir and ritonavir trea
lkeda (<u>145</u>)	Japan, January	Retrospective	n=46 cases with haematologic	Proportion of cases with RT-PCR positivity for 21 days or more after sym
(Preprint)	2022 to January 2023	cohort	disease (Omicron BA.5 variant [80%])	Proportion of cases with RT-PCR positivity for 42 days or more after sym
Jiang (<u>118</u>)	China, May to June 2022	Cross- sectional	n=1,085 hospitalised cases (Omicron variant)	Median duration of RNA positivity: 13 days (IQR: 11 to 17 days)
			n=766 asymptomatic hospitalised cases (Omicron variant)	Median duration of RNA positivity: 13 days (IQR: 10 to 17 days)
			n=319 symptomatic hospitalised cases (Omicron variant)	Median duration of RNA positivity: 14 days (IQR: 11 to 17 days)
Jung (<u>3</u>)	South Korea, March to April	Retrospective cohort	n=32 cases (healthcare workers) (Omicron B.1.1.529 variant)	Median time from symptom onset to negative conversion of subgenomic days)
	2022			Median time from symptom onset to negative conversion of genomic RN/ 9 days)
Kang (<u>87</u>)	South Korea,	Prospective cohort	n=41 cases with haematologic malignancies or solid organ transplantations (Omicron BA.1 and BA.2 variants)	Median duration of viable subgenomic RNA shedding: 5 weeks (IQR: 4 w
	February to April 2022			Median duration of viable genomic RNA shedding: not reached
Kang (<u>88</u>)	South Korea, January to August 2022	Prospective cohort	n=40 cases (healthcare workers) (Omicron BA.1 and BA.2 variants)	Data extracted from figure: Median duration of subgenomic RNA RT-PCF
			n=42 cases (healthcare workers) (Omicron BA.5 variant)	Data extracted from figure: Median duration of subgenomic RNA RT-PCF
			n=40 cases (healthcare workers) (Omicron BA.1 and BA.2 variants)	Data extracted from figure: Median duration of genomic RNA RT-PCR po
			n=42 cases (healthcare workers) (Omicron BA.5 variant)	Data extracted from figure: Median duration of genomic RNA RT-PCR po
Kang (<u>89</u>)	South Korea, February 2021 to	Prospective n=15 not or partially vaccinated cases (Omicron variant)		Median duration of subgenomic RNA RT-PCR positivity: 9 days (IQR: 8 c
	May 2022		n=60 fully vaccinated cases (Omicron variant)	Median duration of subgenomic RNA RT-PCR positivity: 8 days (IQR: 4 to

reatment: 70 days (range: 20 to 231 days)
mptom onset: n=17 of 46 (36.9%)
mptom onset: n=6 of 46 (13.0%)
c RNA RT-PCR: 5 days (95% CI: 5 to 7
NA RT-PCR: 8 days (95% CI: 7 to more than
weeks to not reached)
CR positivity: 6 days
CR positivity: 5 days
positivity: not reached
positivity: 7 days
days to not reached)
to 18 days)

Study	Country, time period	Study type	Participants	Outcome
			n=15 not or partially vaccinated cases (Omicron variant)	Median duration of genomic RNA RT-PCR positivity: not reached (IQR: 6
			n=60 fully vaccinated cases (Omicron variant)	Median duration of genomic RNA RT-PCR positivity: not reached (IQR: 7
Kang (<u>146</u>)	China, April to May 2022	Prospective cohort	n=55,111 cases (Omicron variant)	Median viral RNA shedding time: 7 days (IQR: 5 to 9 days)
			n=9,649 asymptomatic cases (Omicron variant)	Median viral RNA shedding time: 6 days (IQR: 5 to 8 days)
			n=34,203 asymptomatic to mild cases (Omicron variant)	Median viral RNA shedding time: 7 days (IQR: 5 to 9 days)
			n=11,259 mild cases (Omicron variant)	Median viral RNA shedding time: 7 days (IQR: 5 to 9 days)
Keske (<u>10</u>)	Turkey, January		n=55 healthcare worker non- severe cases (Omicron variant)	Positive RT-PCR (day 5): n=53 of 55 (96.4%)
	to February 2022			Positive RT-PCR (day 7): n=48 of 55 (87.3%)
				Positive RT-PCR (day 10): n=41 of 55 (74.5%)
				Positive RT-PCR (day 14): n=23 of 55 (41.8%)
Kojima (<u>39</u>)	US, December 2021	Prospective cohort	n=734 cases (Omicron variant)	Duration of RT-PCR positivity: 14.3 days (SD: 7.0 days)
Kissler (<u>119</u>) (Preprint)	US, March 2020 to July 2022	Retrospective cohort	n=1,400 cases (Omicron BA.1 and BA.2 variants)	Mean viral clearance time: 5.1 days (95% CI: 4.6 to 5.7 days)
			n=159 cases with prior infection history (Omicron BA.1 and BA.2 variants)	Mean viral clearance time: 4.9 days (95% CI: 4.5 to 5.3 days)
			n=1,241 cases without prior infection history (Omicron BA.1 and BA.2 variants)	Mean viral clearance time: 7.2 days (95% CI: 6.8 to 7.5 days)
Landon (<u>147</u>) (Preprint)	US, January 2022	Cross- sectional	n=260 cases (healthcare workers) (Omicron variant)	Proportion of positive tests on days 5 to 10: n=107 of 260 (41%)
Lee (<u>148</u>)	China, January 2022 to April 2022	Retrospective cohort	n=200 hospitalised cases (Omicron variant)	Proportion of cases with slow viral clearance (defined as more than 21 day undetectable in 2 consecutive samples within 72 hours): n=94 of 200 (47)
Lefferts (<u>40</u>)	US, January to	Prospective	n=564 symptomatic cases	Positive rapid antigen test (5 days since symptom onset): n=142 of 179 (
	February 2022	cohort	(Omicron variant)	Positive rapid antigen test (6 days since symptom onset): n=80 of 121 (6
				Positive rapid antigen test (7 days since symptom onset): n=74 of 111 (60
				Positive rapid antigen test (8 days since symptom onset): n=39 of 93 (41.

6 days to not reached)
7 days to not reached)
days for the Ct values rising to at least 30 or 7%)
(79.3%)
66.1%)
66.7%)
1.9%)

Study	Country, time period	Study type	Participants	Outcome
				Positive rapid antigen test (9 days since symptom onset): n=26 of 60 (43.3%)
			n=165 asymptomatic cases	Positive rapid antigen test (5 days since positive test): n=18 of 58 (31.0%)
			(Omicron variant)	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 (<u>41</u>)	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 (<u>43</u>)	China, April to	Retrospective	n=6,134 hospitalised	Time to negative test (7 or fewer days): n=1,249 of 6,134 (20.4%)
	May 2022	cohort	asymptomatic and mild cases (Omicron BA.2 variant)	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 (<u>42</u>)	China, June to	Prospective cohort	n=51 cases (Omicron BA.2 variant)	Time to negative test (7 days or more, Omicron BA.2): 54.38%
	August 2022			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%
Li (<u>149</u>)	China, April 2022	Retrospective cohort	n=23,145 cases (Omicron variant)	Median duration of RNA test positivity: 5 days (IQR: 4 to 7 days)
Li (<u>121</u>)	China, August to September 2022	Prospective cohort	n=27 booster vaccinated cases (Omicron BA.2.76 variant)	Median time between onset and negative test: 8 days (IQR: 7 to 11 days)
			n=23 fully vaccinated cases (Omicron BA.2.76 variant)	Median time between onset and negative test: 8 days (IQR: 7 to 10 days)
			n=10 partially vaccinated cases (Omicron BA.2.76 variant)	Median time between onset and negative test: 12 days (IQR: 7 to 13 days)

Study	Country, time period	Study type	Participants	Outcome
Li (<u>150</u>) (Preprint)	China, November 2022 to January 2023	Prospective cohort (controlled trial)	n=12 high risk healthy cases (A8G6 nasal spray group, Omicron variant)	Median duration of RNA positivity: 6.5 (IQR: 5.0 to 7.2)
			n=151 high risk healthy cases (control group, Omicron variant)	Median duration of RNA positivity: 7.0 (IQR: 4.0 to 7.0)
Lin (<u>151</u>)	China, April to May 2022	Prospective cohort	n=77 hospitalised mild cases (sleep duration less than 6 hours, Omicron variant)	Mean time to virus clearance: 14.96 days (SD: 0.44 days)
			n=193 hospitalised mild cases (sleep duration at least 6 hours, Omicron variant)	Mean time to virus clearance: 13.94 days (SD: 0.28 days)
Liu (<u>44</u>)	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)
			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.
Liu (<u>152</u>)	China, March to May 2022	to Prospective cohort	n=42 elderly (over 60 years) cases (Omicron BA.2 variant)	Median viral shedding time: 13 days (IQR: 9 to 15 days)
			n=26 elderly (over 60 years) cases (molnupiravir group, Omicron BA.2 variant)	Median viral shedding time: 11 days (IQR: 8 to 14.5 days)
			n=16 elderly (over 60 years) cases (standard care group, Omicron BA.2 variant)	Median viral shedding time: 14 days (IQR: 12.25 to 16.5 days)
Liu (<u>153</u>)	China, April to May 2022	Prospective cohort	n=20 non-severe child (3 to 13 years) cases (routine group, Omicron BA.2.2 variant)	Mean time to negative nucleic acid test: 22.46 days (SD: 7.10 days)
			n=20 non-severe child (3 to 13 years) cases (isotonic saline group, Omicron BA.2.2 variant)	Mean time to negative nucleic acid test: 17.25 days (SD: 4.16 days)
			n=20 non-severe child (3 to 13 years) cases (hypertonic saline group, Omicron BA.2.2 variant)	Mean time to negative nucleic acid test: 16.98 days (SD: 2.80 days)

8.70)	

Study	Country, time period	Study type	Participants	Outcome
Liu (<u>154</u>)	China, March to May 2022	Retrospective cohort	n=2,620 hospitalised child (under 18 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 11.0 days (SD: 4.2 days)
			n=664 hospitalised child (under 3 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 12.6 days (SD: 3.8 days)
			n=601 hospitalised child (3 to 5 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 10.7 days (SD: 3.7 days)
			n=663 hospitalised child (6 to 11 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 10.3 days (SD: 3.9 days)
			n=692 hospitalised child (12 to 17 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 10.5 days (SD: 4.7 days)
			n=1,011 asymptomatic hospitalised child (under 18 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 11.6 days (95% CI: 11.1 to 12.1 days)
	hosp year	n=1,609 symptomatic hospitalised child (under 18 years) cases (Omicron BA.2.2 variant)	Mean duration of viral shedding: 10.0 days (95% CI: 9.7 to 10.3 days)	
Lu (<u>45</u>)	China, April to	Prospective	n=1,337 hospitalised cases aged	Median time from first positive nucleic acid test to first negative test: 9 da
	May 2022	/ 2022 cohort	over 60 years (Omicron variant)	Viral shedding time was shorter in cases who were fully vaccinated or bo (p=0.003), and cases with mild compared with severe or critical COVID-1
Lu (<u>155</u>)	China, February to June 2022	Retrospective cohort	n=14,991 cases (Omicron BA.2 variant)	Median duration of viral shedding: 12 days (IQR: 8 to 15 days)
			n=731 cases (aged 3 to 17 years, Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 13 days)
			n=4,420 cases (aged 18 to 39 years, Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 14 days)
			n=4,998 cases (aged 40 to 59 years, Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 14 days)
			n=3,529 cases (aged 60 to 79 years, Omicron BA.2 variant)	Median duration of viral shedding: 13 days (IQR: 9 to 16 days)

days (IQR: 6 to 12 days)

boosted (p<0.0001), cases receiving paxlovid 0-19 (p=0.047)

Study	Country, time period	Study type	Participants	Outcome
			n=1,313 cases (aged at least 80 years, Omicron BA.2 variant)	Median duration of viral shedding: 16 days (IQR: 11 to 20 days)
			n=7,458 female cases (Omicron BA.2 variant)	Median duration of viral shedding: 12 days (IQR: 9 to 15 days)
			n=7,533 male cases (Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 15 days)
			n=11,315 cases with co- morbidities (Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 14 days)
			n=3,676 cases without co- morbidities (Omicron BA.2 variant)	Median duration of viral shedding: 14 days (IQR: 10 to 17 days)
			n=4,603 incompletely vaccinated cases (Omicron BA.2 variant)	Median duration of viral shedding: 13 days (IQR: 10 to 17 days)
			n=4,430 fully vaccinated cases (Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 14 days)
			n=5,958 booster vaccinated cases (Omicron BA.2 variant)	Median duration of viral shedding: 11 days (IQR: 8 to 14 days)
			n=14,991 cases (Omicron BA.2 variant)	Proportion of cases with a negative test by day 7: 17.9% (95% CI: 19.1%
			n=14,991 cases (Omicron BA.2 variant)	Proportion of cases with a negative test by day 14: 71.6% (95% CI: 70.8%
Luna-Muschi	Brazil, January	Prospective	n=30 vaccinated healthcare	RT-PCR positivity (day 7 after symptom onset): n=30 of 30 (100%)
(<u>12</u>)	2022	cohort	worker mild cases (Omicron	RT-PCR positivity (day 10 after symptom onset): n=29 of 30 (97%)
			BA.1 variant)	RT-PCR positivity (day 14 after symptom onset): n=17 of 30 (57%)
Ma (<u>46</u>)	China, up to June	Retrospective	n=14 liver transplant cases	Time from first positive to first negative RT-PCR test (7 days or fewer): n=
	2022 (start date	cohort	(Omicron variant)	Time from first positive to first negative RT-PCR test (8 to 14 days): n=4 c
	not stated)			Time from first positive to first negative RT-PCR test (more than 14 days)
				Median time from first positive to first negative RT-PCR test: 14 days
Mack (<u>156</u>)	US, December	Retrospective	n=173 fully vaccinated adult cases (Omicron variant)	Median time to first negative RT-PCR: 7 days (IQR: 5 to 9 days)
	2021	cohort		Negative RT-PCR (on or before day 5): n=53 of 173 (31%)
				Negative RT-PCR (on or before day 6): n=79 of 173 (46%)
				Negative RT-PCR (on or before day 10): n=146 of 173 (84%)

% to 20.4%)
% 10 Z0.4%)
3% to 72.3%)
n=3 of 14 (21.4%)
of 14 (28.6%)
s): n=7 of 14 (50.0%)

Study	Country, time period	Study type	Participants	Outcome
Martin-Blondel (<u>47</u>)	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):
			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)
			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)
			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)
Mazzotta (<u>157</u>)	totta (<u>157</u>) Italy, December 2021 to March		n=378 cases (Omicron BA.1 variant)	Proportion of cases positive on day 7: n=31 of 378 (8.20%)
	2022		n=143 cases (Omicron BA.2 variant)	Proportion of cases positive on day 7: n=4 of 143 (2.80%)
Mikulska (<u>158</u>)	Italy, March 2021 to July 2022	Retrospective cohort	n=301 mild or moderate cases with haematological malignancies who cleared the infection (Omicron variant dominant)	Median time from diagnosis to first negative swab: 14 days (range: 1 to 1
			n=not reported (monoclonal antibodies group, Omicron variant dominant)	Median time from diagnosis to first negative swab: 12 days (range: 1 to 1
			n=not reported (antivirals group, Omicron variant dominant)	Median time from diagnosis to first negative swab: 20 days (range: 3 to 1
Minoia (<u>159</u>)	Italy, February to September 2022	Prospective cohort	n=82 outpatient cases with haematological malignancy and treated with Molnupiravir or Nirmatrelvir and Ritonavir (Omicron variant)	Median duration of viral shedding: 12 days (IQR: 7 to 22 days)
Mitsuyuki (<u>91</u>)	Japan, January to April 2022	Retrospective cohort	n=14 patients with haematological malignancies (Omicron BA.1 variant)	Median time to Ct value above 30: 22 days

1): 12.5 days (95% CI: 10.5 to 14 days)
1): 5 days (95% CI: 1 to 12.5 days)
2): 10.5 days (95% CI: 8 to 12.5 days)
2): 4 days (95% CI: 4 to 9 days)
112 days)
104 days)
159 days)

Study	Country, time period	Study type	Participants	Outcome
Murakami (<u>160</u>)	Japan, March 2021 to January 2023	Retrospective cohort	n=85 hospitalised cases (Omicron variant)	Mean time from symptom onset to Ct value above 35: 22.3 days (SD: 11
Nelson (<u>161</u>)	US, January 2022	Cross- sectional	n=408 student cases (Omicron BA.1 variant)	Proportion of positive tests on days 5 to 9: n=128 of 408 (31.4%)
Okumura (<u>48</u>)	Japan, November	Retrospective	n=11 cases (Omicron variant)	Time for Ct values to become greater than 30: 6.0 days (95% CI: 4.2 to 7
	to December 2021	cohort		Time for Ct values to become greater than 35: 10.6 days (95% CI: 9.5 to
	2021			Time for Ct values to become greater than 40: 15.1 days (95% CI: 13.6 to
				Time for Ct values to become greater than 45: 19.7 days (95% CI: 17.3 to
Orth (<u>162</u>)	Germany, March	Retrospective	n=144 cases at risk of severe COVID-19 due to immunodeficiency or 3 more other risk factors (Omicron variant)	Median time from initiation of treatment to negative RT-PCR: 8.0 days (IC
(Preprint)	to April 2023	cohort		Positive RT-PCR (day 21): n=21 of 144 (14.6%)
			n=81 cases aged less than 65 years, at risk of severe COVID- 19 due to immunodeficiency or 3 more other risk factors (Omicron variant)	Positive RT-PCR (day 21): n=17 of 81 (21.0%)
			n=63 cases aged at least 65 years, at risk of severe COVID- 19 due to immunodeficiency or 3 more other risk factors (Omicron variant)	Positive RT-PCR (day 21): n=4 of 63 (6.3%)
			n=99 male cases at risk of severe COVID-19 due to immunodeficiency or 3 more other risk factors (Omicron variant)	Positive RT-PCR (day 21): n=13 of 99 (31.1%)
			n=45 female cases at risk of severe COVID-19 due to immunodeficiency or 3 more other risk factors (Omicron variant)	Positive RT-PCR (day 21): n=8 of 45 (17.8%)
		n=123 cases with immunodeficiency (Omicron variant)	Positive RT-PCR (day 21): n=21 of 123 (17.1%)	

11.0 days)
o 7.3 days)
to 11.9 days)
6 to 17.6 days)
3 to 23.7 days)
(IQR: 6.0 to 15.3 days)

Study	Country, time period	Study type	Participants	Outcome
			n=21 cases without immunodeficiency (Omicron variant)	Positive RT-PCR (day 21): n=0 of 21 (0.0%)
			n=41 cases with haematological malignancies (Omicron variant)	Positive RT-PCR (day 21): n=11 of 41 (26.8%)
			n=103 cases without haematological malignancies (Omicron variant)	Positive RT-PCR (day 21): n=10 of 103 (9.7%)
			n=10 cases with history of allogenic bone marrow transplantation (Omicron variant)	Positive RT-PCR (day 21): n=4 of 10 (40.0%)
			n=134 cases without history of allogenic bone marrow transplantation (Omicron variant)	Positive RT-PCR (day 21): n=17 of 134 (12.7%)
			n=76 cases with history of sold organ transplantation (Omicron variant)	Positive RT-PCR (day 21): n=9 of 76 (11.8%)
			n=68 cases without history of solid organ transplantation (Omicron variant)	Positive RT-PCR (day 21): n=12 of 68 (17.6%)
			n=105 fully vaccinated cases (Omicron variant)	Positive RT-PCR (day 21): n=13 of 105 (12.4%)
			n=27 not fully vaccinated cases (Omicron variant)	Positive RT-PCR (day 21): n=6 of 27 (22.2%)
Pan (<u>163</u>)	China, December 2022	Prospective cohort (RCT)	n=27 mild to moderate severity cases (leflunomide group, Omicron variant)	Median time from diagnosis to 2 consecutive negative antigen detection to 9.5 days)
			n=30 mild to moderate severity cases (control group, Omicron variant)	Median time from diagnosis to 2 consecutive negative antigen detection to 12.0 days)
Pantazopoulos (<u>164</u>)	Greece, June to December 2022	Prospective cohort (RCT)	n=28 cases (hypertonic seawater group, variant not reported)	Negative RT-PCR (day 14): n=17 of 28 (60.7%)
			n=28 cases (control group, variant not reported)	Negative RT-PCR (day 14): n=9 of 28 (32.1%)

on tests or RT-PCR tests: 7.0 days (IQR: 6.0 on tests or RT-PCR tests: 9.0 days (IQR: 7.5

Study	Country, time period	Study type	Participants	Outcome
Pei (<u>49</u>)	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 (I
			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 on 12.28 days)
Qiu (<u>165</u>)	China, August 2022	Retrospective cohort	n=15 cases (Nirmatrelvir and Rotonavir group, Omicron BA.2.76 variant)	Median time to Ct value above 40: 9 days (range: 4 to 21 days)
			n=43 cases (control group, Omicron BA.2.76 variant)	Median time to Ct value above 40: 14 days (range: 6 to 22 days)
Raglow (<u>92</u>)	US, April 2022 to	Prospective	n=150 immunocompromised	Median time to last positive RT-PCR test: 9 days (IQR: 2 to 26 days)
(Preprint)	February 2023.	cohort	adults (Omicron BA.1 [3%], BA.2 [31%], BA.4 [6%], BA.5 [29%], and unknown Omicron [32%] variants)	Proportion of cases positive on RT-PCR for at least 21 days: n=38 of 150
				Proportion of cases positive on RT-PCR for at least 56 days: n=5 of 150
			n=18 cases with B cell dysfunction (Omicron variant)	Median time to last positive RT-PCR test: 11 days (IQR: 3 to 44 days)
			n=59 cases with solid organ or hematopoietic stem cell transplant (Omicron variant)	Median time to last positive RT-PCR test: 16 days (IQR: 4 to 29 days)
			n=5 cases with acquired Immune deficiency syndrome (Omicron variant)	Median time to last positive RT-PCR test: 32 days (IQR: 20 to 33 days)
			n=23 cases with malignancy (Omicron variant)	Median time to last positive RT-PCR test: 9 days (IQR: 3 to 27 days)
		n=45 cases with autoimmune and autoinflammatory conditions (Omicron variant)	Median time to last positive RT-PCR test: 4 days (IQR: 0 to 9 days)	
Saade (<u>93</u>)	France,	Prospective	n=44 fully vaccinated cases	Positive RT-PCR (day 7): 90.4%
	November 2021 to February 2022	cohort	(healthcare workers, Omicron BA.1 variant)	Positive RT-PCR: (day 14): 44.7%
Selby (<u>166</u>)	US, January 2022	Prospective cohort	n=57 mild or asymptomatic cases (healthcare workers, Omicron variant)	RT-PCR positivity 5 to 8 days from initial symptoms or positive test: n=55
Shao (<u>50</u>)	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

(IQR: 5.33 to 11.27 days)
comorbidities): 9.29 days (IQR: 6.33 to
50 (25%)
) (3%)
5 of 57 cases (96%)
3.0 to 10.5 days)

Study	Country, time period	Study type	Participants	Outcome
			n=180 mild hospitalised cases (Omicron variant)	Median time to negative RT-PCR (mild cases): 10 days (IQR: 8.0 to 12.5
			n=41 moderate hospitalised cases (Omicron variant)	Median time to negative RT-PCR (moderate cases): 13 days (IQR: 10.0 t
			n=1 severe hospitalised cases (Omicron variant)	Time to negative RT-PCR (n=1 severe case): 15 days
Shen (<u>51</u>)	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 g days)
			n=76 hospitalised non-severe cases (untreated group, Omicron variant)	Time from first positive to first negative nucleic acid test (untreated group days)
Shi (<u>52</u>) (Preprint)	China, April to May 2022	o 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 gro
			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
Sikka (<u>27</u>) (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 (<u>53</u>) (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 (asympt
			n=274 hospitalised mild cases (Omicron BA.2.2.1 variant)	Median time from first positive test to cessation of viral shedding (mild ca
Takahashi (<u>13</u>)	Japan, November	Retrospective	n=18 asymptomatic and mild	Positive RT-PCR test (0 to 1 days after diagnosis): n=17 of 17 (100%)
	to December	cohort	cases (Omicron variant)	Positive RT-PCR test (2 to 5 days after diagnosis): n=11 of 12 (91.7%)
	2021			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
Theaux (<u>167</u>)	Argentina, July	Prospective	n=24 cases (Omicron BA.1	Proportion of cases positive days 11 to 15: n=2 of 25 (8%)
	2021 to February 2022	cohort	variant)	Proportion of cases positive days 16 to 19: n=0 of 25 (0%)

2.5 days)

0 to 15.0 days)

group): 9.92 day (95% CI: 9.06 to 10.77

up): 11.13 days (95% CI: 10.22 to 12.04

group): n=44 of 91 (48.35%)

s of 90 (31.11%)

nptomatic cases): 10 days (IQR: 9 to 11 days)

cases): 10 days (IQR: 9 to 12 days)

%)

0.0%)

Study	Country, time period	Study type	Participants	Outcome
Tillman (<u>54</u>)	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
Tsao (<u>168</u>)	US, January to		n=248 student athlete cases	RAT positive (day 7): n=67 of 248 (27%)
	May 2022	Case series	(Omicron BA.1 and BA.2 variants dominant)	RAT positive (day 8): n=40 of 76 (53%)
				RAT positive (day 9): n=28 of 43 (65%)
Van der Veer (<u>55</u>) (Preprint)	The Netherlands, November 2021	Prospective cohort	n=142 healthcare worker cases (Omicron BA.1 variant)	Median time from first positive to first negative RT-PCR test (Omicron BA
	to February 2022		n=37 healthcare worker cases (Omicron BA.2 variant)	Median time from first positive to first negative RT-PCR test (Omicron BA
Utzon (<u>94</u>)	Denmark,	Prospective	n=29 adult high-risk non-	RT-PCR positivity on day 5 of symptom onset: n=21 of 25 (84%)
	December 2021 to February 2022		hospitalised immunocompromised patients (Omicron BA.1 [41%] and BA.2 [41%] variants)	RT-PCR positivity on day 15 of symptom onset: n=16 of 29 (55%)
Wagester (<u>169</u>)	US, January to April 2022	Prospective cohort	n=1,023 cases (healthcare workers, variant not stated)	Negative antigen test (day 5): n=161 of 1023 (15.7%)
Wang (<u>170</u>)	China, March 2022	Retrospective cohort	n=376 paediatric cases (Omicron BA.2.2 variant dominant)	Mean duration of Ct value less than 35: 11.7 days (SD: 3.7 days, range: 3
Wang (<u>103</u>)	China, August to September 2022		n=709 cases (Omicron BA.5.2 variant)	Mean time from exposure to the start of viral shedding: 3.3 days (95% Cr days (95% Crl: 8.1 to 9.8 days)
				Asymptomatic cases, and cases aged 0 to 15 years, had longer mean pe
				Mean viral shedding period: 6.7 days (95% Crl: 6.4 to 7.1 days), 95th per days)
				Asymptomatic cases, and cases aged 16 to 65 years, had longer mean v
Wang (<u>171</u>)	China, April to May 2022	-	n=667 hospitalised mild cases (Longyizhengqi granule group, Omicron variant)	Mean time of nucleic acid positivity: 10.7 days (SD: 3.54 days)
			n=2,576 hospitalised mild cases (conventional treatment group, Omicron variant)	Mean time of nucleic acid positivity: 14.2 days (SD: 4.26 days)
Wei (<u>56</u>) (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 Cep 4.11 to 5.30 days)

BA.1): 12 days (IQR: 10 to 15 days) BA.2): 11 days (IQR: 10 to 13 days) e: 3 to 25 days) Crl, 3.0 to 3.6 days), 95th percentile: 8.9 periods from exposure to viral shedding percentile: 13.7 days (95% Crl: 12.7 to 14.7 viral shedding periods. Cepharanthine group): 4.70 days (95% CI:

Study	Country, time Study type period		Participants	Outcome		
			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 (<u>57</u>)	China, April to May 2022	Retrospective cohort	n=163 mild or moderate cases (Omicron variant)	Median viral shedding time: 18 days (IQR: 15 to 21 days)		
			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)		
Wong (<u>123</u>)	Wong (<u>123</u>) Hong Kong, Retrospector February to July 2022		n=242 cases (Nirmatrelvir and Ritonavir group, Omicron BA.2.2 variant dominant)	Median time from start of follow up to Ct value above 30: 8 days (IQR: 3 to 14 days)		
			n=563 cases (Molnupiravir group, Omicron BA.2.2 variant dominant)	Median time from start of follow up to Ct value above 30: 11 days (IQR 7 to 17 days)		
			n=3,787 (Control group, Omicron BA.2.2 variant dominant)	Median time from start of follow up to Ct value above 30: 10 days (IQR: 4 to 17 days)		
Wu (<u>58</u>) (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)		

Study	Country, time period	Study type	Participants	Outcome
			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 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 shorte cases (p<0.001), and cases with milder infections
Wu (<u>59</u>)	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
			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
Wu (<u>172</u>)	China, March to May 2022	Prospective cohort	n=4,443 participants (Omicron BA.2 variant)	Median viral shedding time of 8 days (IQR: 6.0 to 10.0 days), 96.1% did r days
			n=1,345 fully vaccinated (Omicron BA.2 variant)	Median viral shedding time of 8 days (IQR: 6.0 to 10.0 days), 95.5% did r days
			n=2,397 booster vaccinated (Omicron BA.2 variant)	Median viral shedding time of 8 days (IQR: 6.0 to 10.0 days), 96.7% did r days
			n=701 not fully vaccinated (Omicron BA.2 variant)	Median viral shedding time of 9 days (IQR: 7.0 to 10.0 days), 94.7% did r days
Wu (<u>173</u>)	China, March to May 2022	Retrospective cohort	n=3,364 symptomatic and asymptomatic cases (Omicron BA.2.2 variant dominant)	Mean time to viral clearance (2 consecutive negative RT-PCR tests): 10.0
			n=1,481 asymptomatic cases (Omicron BA.2.2 variant dominant)	Mean time to viral clearance (2 consecutive negative RT-PCR tests): 8.8
			n=1,326 mild severity cases (Omicron BA.2.2 variant dominant)	Mean time to viral clearance (2 consecutive negative RT-PCR tests): 11.
			n=479 moderate severity cases (Omicron BA.2.2 variant dominant)	Mean time to viral clearance (2 consecutive negative RT-PCR tests): 12.4
			n=78 severe cases (Omicron BA.2.2 variant dominant)	Mean time to viral clearance (2 consecutive negative RT-PCR tests): 12.0
Xu (<u>60</u>)	China, April 2022	Retrospective	n=13,162 asymptomatic or mild	Negative RT-PCR test by 7 days: n=5,437 of 13,162 (41.3%)
		cohort	cases (Omicron BA.2.2 variant)	Negative RT-PCR test by 14 days: n=12,482 of 13,162 (94.8%)

80 years and over, mild to moderate cases):

rter for vaccinated cases (p<0.001), younger

35 (vaccinated): 12.6 days (SD: 3.4 days)

35 (unvaccinated): 14.8 days (SD: 4.7 days)

not have detectable viral shedding after 14

0.07 days (95% CI: 9.77 to 10.36 days)

8.89 days (SD: not reported)

1.07 days (SD: not reported)

2.44 days (SD: not reported)

2.69 days (SD: not reported)

Study	Country, time period	Study type	Participants	Outcome
Xu (<u>63</u>)	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):
			n=458 adult asymptomatic or mild cases (control group, Omicron variant)	Median time to negative RT-PCR test (control group): 12.58 days
Xu (<u>64</u>) (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 (haemodialys
			n=134 hospitalised non- haemodialysis cases (Omicron variant)	Mean time from first positive to first negative RT-PCR tests (non- haemoo
Xu (<u>61</u>)	China, April to May 2022		n=1,393 asymptomatic or mild cases (Reyanning group, Omicron variant)	Median time from hospitalisation to negative nucleic acid test (Reyanning
			n=1,407 asymptomatic or mild cases (control group, Omicron variant)	Median time from hospitalisation to negative nucleic acid test (control gro
Xu (<u>62</u>)	China, April to June 2022		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
			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
Xu (<u>174</u>)	China, April to	Prospective	n=214 children aged one to 17	Median time to 2 consecutive negative tests: 5 days (IQR: 5 to 6 days)
	May 2022	cohort (RCT)	years (oral Reyanning plus standard care, variant not stated)	Proportion of cases with 2 consecutive negative tests (day 3): 32.7%
				Proportion of cases with 2 consecutive negative tests (day 7): 75.2%
			n=217 children aged one to 17	Median time to 2 consecutive negative tests: 7 days (IQR: 6 to 7 days)
			years (standard care, variant not stated)	Proportion of cases with 2 consecutive negative tests (day 3): 21.2%
				Proportion of cases with 2 consecutive negative tests (day 7): 60.8%
Yan (<u>65</u>)	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 (whicheve (Paxlovid group): 9 days (IQR: 9 to 10 days)

: 11.90 days

ysis cases): 18.15 days (SD: 6.37 days)

nodialysis cases): 11.18 days (SD: 3.52 days)

ng group): 6 days (IQR: 3 to 9 days)

roup): 7 days (IQR: 5 to 9 days)

en group): 5.0 days (IQR: 3.0 to 7.0 days)

6.0 days (IQR: 5.0 to 8.0 days)

ver was earlier) to first negative RT-PCR test

Study	Country, time period	Study type	Participants	Outcome
			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 (whicheve (control group): 11 days (IQR: 9 to 12 days)
Yan (<u>191</u>)	China, April to June 2022	Retrospective cohort	n=73 cases (nirmatrelvir and ritonavir group, Omicron variant)	Median duration of viral shedding: 5 days (IQR: 3 to 10 days)
			n=122 cases (control group, Omicron variant)	Median duration of viral shedding: 13 days (IQR: 10 to 17 days)
Yan (<u>175</u>)	US, December 2021 to January 2022	Prospective cohort	n=156 hospitalised patients with hematologic malignancy and who received sotrovimab (Omicron BA.1 variant)	Median time to viral clearance for n=62 of 156 who cleared the virus by th (range: 8 to 133 days)
Yan (<u>176</u>)	China, April to June 2022	Prospective cohort	n=171 patients with kidney dysfunction (likely Omicron BA.2.2 variant)	Mean duration of viral shedding: 15.79 days (SD: 9.57 days)
			n=109 mild to moderate cases of COVID-19 with kidney dysfunction (likely Omicron BA.2.2 variant)	Mean duration of viral shedding: 16.80 days (SD: 9.99 days)
			n=62 severe to critical cases of COVID-19 with kidney dysfunction (likely Omicron BA.2.2 variant)	Mean duration of viral shedding: 14.41 days (SD: 8.86 days)
			n=342 patients without kidney dysfunction (likely Omicron BA.2.2 variant)	Mean duration of viral shedding: 11.21 days (SD: 6.33 days)
			n=311 mild to moderate cases of COVID-19 without kidney dysfunction (likely Omicron BA.2.2 variant)	Mean duration of viral shedding: 10.78 days (SD: 6.14 days)
			n=31 severe to critical cases of COVID-19 without kidney dysfunction (likely Omicron BA.2.2 variant)	Mean duration of viral shedding: 14.19 days (SD: 6.89 days)
Yang (<u>66</u>)	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)

ver was earlier) to first negative RT-PCR test
the end of the study period: 62.5 days

Study	Country, time period	Study type	Participants	Outcome
Yang (<u>67,193</u>)	China, March to	Retrospective cohort	n=603 hospitalised child cases	Median time from first positive to first negative RT-PCR test: 12 days (IQF
	May 2022		(likely Omicron BA.2.2 variant)	Viral shedding time was longer in cases with abnormal defecation and mo vaccinated cases and cases with higher household vaccination rates
			n=373 hospitalised children	Proportion of cases with 2 consecutive negative tests (day 7): 3.5%
			aged under 3 years (likely	Proportion of cases with 2 consecutive negative tests (day 14): 73.2%
			Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 21): 98.7%
			n=107 hospitalised children,	Proportion of cases with 2 consecutive negative tests (day 7): 14.0%
			aged between 3 and 5 years	Proportion of cases with 2 consecutive negative tests (day 14): 83.2%
			(likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 21): 97.2%
			n=96 hospitalised children, aged	Proportion of cases with 2 consecutive negative tests (day 7): 25.0%
			between 6 and 11 years (likely	Proportion of cases with 2 consecutive negative tests (day 14): 86.5%
			Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 21): 99.0%
			n=27 hospitalised children, aged	Proportion of cases with 2 consecutive negative tests (day 7): 30.0%
			between 12 and 17 years (likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 14): 85.2%
				Proportion of cases with 2 consecutive negative tests (day 21): 88.9%
			n=24 hospitalised asymptomatic children (likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 7): 54.2%
				Proportion of cases with 2 consecutive negative tests (day 14): 95.8%
				Proportion of cases with 2 consecutive negative tests (day 21): 100%
			n=399 hospitalised children with mild COVID-19 infection (likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 7): 9.8%
				Proportion of cases with 2 consecutive negative tests (day 14): 78.4%
				Proportion of cases with 2 consecutive negative tests (day 21): 98.7%
			n=179 hospitalised children with	Proportion of cases with 2 consecutive negative tests (day 7): 8.9%
			moderate COVID-19 infection (likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 14): 73.7%
			(likely Officion BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 21): 96.6%
			n=1 hospitalised children with	Proportion of cases with 2 consecutive negative tests (day 7): 0%
			severe COVID-19 infection	Proportion of cases with 2 consecutive negative tests (day 14): 0%
			(likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 21): 0%
			n=522 hospitalised unvaccinated	Proportion of cases with 2 consecutive negative tests (day 7): 7.7%
			children (likely Omicron BA.2.2	Proportion of cases with 2 consecutive negative tests (day 14): 75.1%
			variant)	Proportion of cases with 2 consecutive negative tests (day 21): 97.9%
				Proportion of cases with 2 consecutive negative tests (day 7): 33.3%

QR: 9 to 14 days)						
nore severe disease, and shorter in						

Study	Country, time period	Study type	Participants	Outcome
			n=12 hospitalised children with	Proportion of cases with 2 consecutive negative tests (day 14): 75.0%
			one dose of vaccine (likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 21): 100%
			n=69 hospitalised children with 2	Proportion of cases with 2 consecutive negative tests (day 7): 34.8%
			doses of vaccine (likely Omicron BA.2.2 variant)	Proportion of cases with 2 consecutive negative tests (day 14): 95.7%
				Proportion of cases with 2 consecutive negative tests (day 21): 98.6%
Yang (<u>177</u>)	China, April to June 2022	Retrospective cohort	n=445 hospitalised patients (Omicron BA.2 and BA.2.2 variant)	Median duration of viral shedding: 13 days (range: 1 to 47 days)
Yang (<u>124</u>)	China, January	Prospective	n=1,721 patients (Omicron	Mean duration of vial shedding after symptom onset: 13.5 days (95% CI:
	2020 to April 2022	cohort	variant B.1.1.529)	Viral dynamics were similar regardless of vaccination status, and male ca asymptomatic cases had slightly faster viral clearance, while cases with u virus clearance
Yin (<u>68</u>)	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.
Yin (<u>178</u>)	China, March to May 2022	Retrospective cohort	n=214,592 cases (Omicron BA.2 variant)	Median duration of viral shedding: 7 days (IQR: 5 to 10 days)
			n=42,379 cases aged 18 to 29 years (Omicron BA.2 variant)	Median duration of viral shedding: 6 days (IQR: 4 to 9 days)
			n=not reported cases aged 80 years and over (Omicron BA.2 variant)	Median duration of viral shedding: 10 days (IQR: 6 to 13 days)
Ying-Hao (<u>69</u>)	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
Yu (<u>70</u>)	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 (asymptom
			n=619 mild cases (Omicron BA.2.2 variant)	Mean time from first positive to first negative nucleic acid test (mild cases
Yu (<u>179</u>) (Preprint, conference abstract)	China, before January 2023	Retrospective cohort	n=16 patients with chronic kidney disease who were administered paxloid within 5 days of symptom onset (variant not stated)	Positive nucleic acid duration: 7 days
			n=19 patients with chronic kidney disease who were administered paxloid after 5	Positive nucleic acid duration: 25 days

CI: 13.32 to 13.67 days)
cases, cases aged 14 years and under, and n underlying health conditions had slower
3.42 days)
R: 4 to 9 days)
matic cases): 9.26 days (SD: 3.16 days)
es): 10.62 days (SD: 2.73 days)

Study	Country, time period	Study type	Participants	Outcome
			days of symptom onset (variant not stated)	
Zee (<u>71</u>)	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 (<u>72</u>)	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 (fu 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 (fu 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 (pa 9.0 to 25.0 days)
Zhang (<u>73</u>)	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 (haemodial
			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-haem days)
Zhang (<u>180</u>)	China, December 2021 to March 2022		n=305 patients with mild COVID- 19 (Omicron variant)	Time between positive to negative RT-PCR test: 12.31 days (SD: 0.37 da
			n=89 patients with moderate COVID-19 (Omicron variant)	Time between positive to negative RT-PCR test: 14.70 days (SD: 0.84 da
Zhang (<u>181</u>)	China, April to May 2022	to Prospective cohort (RCT)	n=91 participants (Liushen pill, Omicron BA.2 variant)	Proportion of cases with negative test (day 7): n=44 of 91 (48.35%)
			n=90 participants (control group, Omicron BA.2 variant)	Proportion of cases with negative test (day 7): n=28 of 90 (31.11%)
Zhang (<u>182</u>)	China, August 2022	Retrospective cohort	n=278 cases (Omicron variant)	Median viral shedding duration: 3 days (IQR: 2 to 6 days)
Zhang (<u>125</u>)	China, November to December	China, November Retrospective cohort	n=130 hospitalised cases under 45 years of age (Omicron BF.7)	Median time to negative RNA test (ORF1ab): 9 days (range: 4 to 26 days
	2022		n=112 hospitalised cases aged between 45 and 59 years (Omicron BF.7)	Median time to negative RNA test (ORF1ab): 9 days (range: 7 to 23 days

fully vaccinated with inactive vaccine cases):
fully vaccinated with recombinant vaccine
partially vaccinated cases): 16.0 days (IQR:
alysis cases): 16.67 days (SD: 5.22 days)
nodialysis cases): 14.07 days (SD: 5.43
days)
days)
/S)
/s)

Study	Country, time period	Study type	Participants	Outcome	
			n=128 hospitalised cases aged between 60 to 79 years (Omicron BF.7)	Median time to negative RNA test (ORF1ab): 11 days (range: 6 to 24 day	
			n=110 hospitalised cases aged over 80 years (Omicron BF.7)	Median time to negative RNA test (ORF1ab): 11.5 days (range: 6 to 39 d	
Zheng (<u>183</u>)	China, March to May 2022	Retrospective cohort	n=31 hospitalised adult cases, treated with Nirmatrelvir and Ritonavir (Omicron BA.2 variant)	Mean time to negative RT-PCR: 13.74 days (SD: 7.45 days)	
			n=7 hospitalised adult cases with BMI at least 25 kg per m ² , treated with Nirmatrelvir and Ritonavir (Omicron BA.2 variant)	Median time to negative RT-PCR test: 8.5 days (IQR: 4 to 12 days)	
			n=24 hospitalised adult cases with BMI under 25 kg per m ² , treated with Nirmatrelvir and Ritonavir (Omicron BA.2 variant)	Median time to negative RT-PCR test: 14.5 days (IQR: 9.5 to 18 days)	
			n=20 hospitalised adult cases with Charlson comorbidity index less than one.	Median time to negative RT-PCR test: 11 days (IQR: 8 to 14.5 days)	
			n=11 hospitalised adult cases with Charlson comorbidity index greater than one.	Median time to negative RT-PCR test: 16 days (IQR: 10 to 24 days)	
Zheng (<u>184</u>)	China, March to April 2022	Retrospective cohort	n=75 participants (Omicron variant)	Median duration of viral shedding: 14 days	
Zhong (<u>74</u>)	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 g	
			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 gro	
Zhong (<u>75</u>)	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 (IC	
Zhong (<u>185,207</u>)	China, April to May 2022	Prospective cohort	n=16,826 cases with BMI from 18.5 to less than 24 kg per m ² (Omicron variant)	Mean time to negative test: 7.0 days (SD: 2.6 days)	

ays)
days)
group): 9.32 days (SD: 2.78 days)
roup): 11.11 days (SD: 2.67 days)
IQR: 8 to 12 days)

Study	Country, time period	Study type	Participants	Outcome
			n=19,978 cases with BMI from 24 to less than 27.5 kg per m ² (Omicron variant)	Mean time to negative test: 7.2 days (SD: 2.7 days)
			n=1,761 cases with BMI equal to or over 27.5 kg per m ² (Omicron variant)	Mean time to negative test: 7.4 days (SD: 2.6 days)
			n=34,057 cases without diabetes (Omicron variant)	Mean time to negative test: 7.1 days (SD: 2.6 days)
			n=4,535 cases with diabetes (Omicron variant)	Mean time to negative test: 7.4 days (SD: 2.6 days)
Zhong (<u>186</u>)	China, March to May 2022	Retrospective cohort	n=230 cases (Omicron BA.2 variant)	Median time to negative nucleic acid test: 17 days (IQR: 14 to 20 days)
Zhou (<u>187</u>)	China, May 2022	Prospective cohort (RCT)	n=126 children (Interferon-a-2b nasal spray, Omicron variant)	Mean viral shedding time: 10.9 days (SD: 3.0 days)
			n=142 children (standard care group, Omicron variant)	Mean viral shedding time: 11.6 days (SD: 3.3 days)
Zhuang (<u>188</u>)	China, May 2022	Retrospective cohort	n=95 patients with nucleic acid Ct fluctuation (Omicron variant)	Mean time to negative test: 14.5 days (SD: 4.6 days)
			n=97 patients without fluctuation (Omicron variant)	Mean time to negative test: 11.8 days (SD: 4 days)
Zigo (<u>189</u>)	US, Febuary to April 2022	Retrospective cohort	n= 4 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 3 of isolation period, from sy
			n= 12 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 4 of isolation period, from sy
			n= 259 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 5 of isolation period, from sy
			n= 121 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 6 of isolation period, from sy
			n= 210 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 7 of isolation period, from sy
			n= 127 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 8 of isolation period, from sy
			n= 91 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 9 of isolation period, from sy
			n= 63 rapid antigen tests from 880 cases (variant not stated)	Proportion of cases with a positive test (day 11 and over of isolation period 11.1%

symptom onset or positive test): 0%

symptom onset or positive test): 33.3%

symptom onset or positive test): 45.6%

symptom onset or positive test): 45.5%

symptom onset or positive test): 47.1%

symptom onset or positive test): 32.3%

symptom onset or positive test): 19.8%

riod, from symptom onset or positive test):

Study	Country, time period	Study type	Participants	Outcome
Zou (<u>190</u>)	China, April to May 2022	Retrospective cohort	n=238 patients with mild COVID- 19 (variant not stated)	Median time to negative test: 11 days (IQR: 8 to 15 days)

Table C.1h. Viral load over time

Study	Country, time period	Study type	Participants	Outcome
Bouton (<u>6</u>)	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 diagnost steady from 3 days before to 1 day after symptom onset, increased from day 1 to after day 9), proportion of positive cultures rose between days 1 and 3 after diagnost to 0 by 8 days after diagnosis (some sporadic positive cultures up to day 15), propulsefore to 4 days after symptom onset (to about 30% positivity), dropped substantiat to drop until day 13, with no further positive cultures up to day 20
Choi (<u>23</u>)	South Korea, January 2022	Retrospective cohort	n=5,187 (Omicron variant)	Data extracted from figure: Ct values decreased (viral load increased) up to betwe increased (viral load decreased) to between 12 and 13 days after symptom onset, up to 17 days after symptom onset (data truncated after this)
Funk (<u>76</u>) (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 increased up to day 6 since symptom onset (data truncated at day 6). BA.2 infection infections, reinfections had higher Ct values than no known previous infections, ar people with different doses of vaccine.
Li (<u>77</u>)	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 a decreased until 10 days after symptom onset (data truncated after this)
Marking (<u>78,208</u>)	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 increased (viral load decreased) up to day 15 (data truncated at day 15)
Sigamani (<u>194</u>)	India, study dates not stated (trial registered March 2022)	Prospective cohort (RCT)	n=34 adult mild to moderate hospitalised cases recruited 3 or fewer days from diagnosis (variant not stated)	Viral load measured on days 1, 3, and 7 after randomisation, and fell over time fro
Tassetto (<u>79</u>)	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 or decrease in Ct values in days 7 to 9 (data truncated at day 9)
Teyssou (<u>80</u>)		Prospective cohort	n= 84 cases (Omicron BA.1 variant)	Data extracted from figure: For Omicron BA.1, Ct values decreased (viral load incl after symptom onset, then increased (viral load decreased) until day 10 after symp

osis (more slowly after day 8), Ct values o day 20 after symptom onset (more slowly gnosis (to about 30% positivity), then reduced oportion of positive cultures rose from 1 day ntially on day 5 (to about 10%), then continued

ween 3 and 4 days after symptom onset, et, then decreased again (viral load increased)

ed from days 0 to 2 since symptom onset, then ctions had higher Ct values than BA.1 and there was no clear difference between

after symptom onset, and gradually

3 from first positive RT-PCR test, then

rom a high on day 1

onset (data truncated before day 2), with a

ncreased) from symptom onset to days 1 to 3 mptom onset (data truncated at day 10)

Study	Country, time period	Study type	Participants	Outcome
	France, December 2021 to May 2022		n=60 cases (Omicron BA.2 variant)	Data extracted from figure: For Omicron BA.2, Ct values increased (viral load decreased after symptom onset, decreased (viral load increased) until days 7 to 9 after symptom decreased) until day 10 after symptom onset (data truncated at day 10)
Townsley (<u>81</u>) (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 increased (viral load decreased) up to day 15 (data truncated around day 15 for Or decreased (viral load increased) up to day 17 for Omicron BA.2 variant cases (data variant cases)
Vila Mendez (<u>195</u>)	Spain, February to July 2022	Prospective cohort (RCT)	n=191 adult cases (Omicron BA.5 variant dominant)	Viral load measured at baseline and on days 4, 7, and 14 after randomisation, and
Young (<u>82</u>) (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 load decreased) until 20 days after illness onset (data truncated at 20 days)

creased) from symptom onset to days 1 to 3 ptom onset, then increased (viral load

s 2 and 3 from first symptom onset, then Omicron BA.1 variant cases), then slightly ata truncated at day 17 for Omicron BA.2

nd fell over time from a high at baseline

rst 2 to 3 days of illness, then increased (viral

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