

COVID-19 Rapid Briefing*

COVID-19 Update from SAHMRI

18 January 2022

Infectiousness and isolation of COVID-19 positive cases

Key points

- There is evidence that COVID-19 positive cases are heterogenous in their infectivity and some continue to have the potential to infect others up to 10 days post symptom onset.
- A study from Japan [1] demonstrated that positive samples in viral cultures are significantly reduced at 7 days post symptom onset, suggesting low infectivity from this point for most cases.
 - These results support a strategy of 7 days isolation combined with a negative rapid antigen test (RAT) result on or after day 7. The UK has recently changed from 10 isolation days to 7 isolation days plus 2 consecutive negative RAT results 24 hours apart, starting from day 6, to mitigate risk from false negative RAT results.
- A pre-print UK modelling study [3] of risk associated with various isolation strategies demonstrated that 31.4% (23.9-38.2%) of cases will be released while infectious when following a 5-day isolation strategy. This risk reduces to 5.1% when following a 10-day isolation strategy. A 10-day isolation or 2 negative tests (24 hours apart from day 6) corresponds with 6.2% of cases released while infectious.
- A pre-print US observational study [5] of 537 people found that infections with the Omicron variant, relative to Delta infections, feature lower peak viral loads and shorter clearance times, but similar proliferation times and clearance rates (e.g. clearance phase for Omicron was 5.35 days (95% CI 4.78-6.00) compared to 6.23 days for delta (95%CI 5.43-7.17)). However, it remains unclear whether the Omicron variant follows a different trajectory to Delta due to confounding from vaccination status and the higher rates of younger people having Omicron.

EVIDENCE

- Torjesen [1], BMJ News, published 13 Jan 2022
 - Data from Japan suggests that patients with the Omicron variant of COVID-19 shed the virus for longer after symptoms emerge. Preliminary data suggests that the amount of viral RNA is highest 3-6 days after diagnosis or symptom onset (Study reported below [2])
 - Isolation period for people testing positive for COVID-19 was recently cut from 10 to 7 days in England if two lateral flow test returned negative results on days 6 and 7. The UK has so far resisted calls to reduce the isolation period to 5 days.
- National Institute of Infectious Diseases [2] Japan – not peer reviewed
 - In Japan, individuals infected with SARS-CoV-2 are hospitalised and are released from medical facilities after two consecutive negative tests by nucleic acid amplification or antigen quantification methods.
 - Study examined the duration of infectious virus shedding in Omicron cases: A total of 83 respiratory specimens from 21 cases (19 vaccinees and 2 unvaccinated cases; 4 asymptomatic and 17 mild cases) had PCR and virus isolation tests.
 - The date of specimen collection for diagnosis or symptom onset was defined as day 0. The amount of viral RNA was highest on 3-6 days after diagnosis or 3-6 days after symptom onset, and then gradually decreased over time, with a marked decrease after 10 days since diagnosis or symptom onset.
 - The positive virus isolation results showed a similar trend as the viral RNA amount, and no infectious virus in the respiratory samples was detected after 10 days since diagnosis or symptom onset (Table). These findings suggest that vaccinated Omicron cases are unlikely to shed infectious virus 10 days after diagnosis or symptom onset.

Days since diagnosis			
	Number and percentage of viral RNA positive samples n (%)	Number and percentage of virus isolation positive samples n (%)	Number and percentage of virus isolation positive in viral RNA positive samples n (%)
0 ~ 2 days	20/21 (95.2)	2/21 (9.5)	2/20 (10.0)
3 ~ 6 days	14/17 (82.4)	7/17 (41.2)	7/14 (50.0)
7 ~ 9 days	17/18 (94.4)	2/18 (11.1)	2/17 (11.8)
10 ~ 13 days	4/15 (26.7)	0/15 (0)	0/4 (0)
After 14 days	5/12 (41.7)	0/12 (0)	0/5 (0)
Days since symptom onset (symptomatic cases)			
-1 ~ 2 days	15/16 (93.8)	2/16 (12.5)	2/15 (13.3)
3 ~ 6 days	8/8 (100)	4/8 (50.0)	4/8 (50.0)
7 ~ 9 days	16/16 (100)	3/16 (18.8)	3/16 (18.8)
10 ~ 13 days	7/12 (58.3)	0/12 (0)	0/7 (0)
After 14 days	4/10 (40.0)	0/10 (0)	0/4 (0)
Days since positive test (asymptomatic cases)			
0 ~ 5 days	6/6 (100)	3/6 (50.0)	3/6 (50.0)
6 ~ 9 days	3/4 (75.0)	0/4 (0)	0/3 (0)
After 10 days	1/10 (10)	0/10 (0)	0/1 (0)

- UK Health Security Agency, 22 Dec 2021: [COVID-19 self-isolation changes: scientific summary](#)
 - New Guidance was introduced to enable those who test positive for COVID-19 to reduce their self-isolation period from 10 days to 7 days, for both vaccinated and unvaccinated.
 - It is now advised that self-isolation can end after 7 days provided the individual has 2 consecutive negative lateral flow device (LFD) antigen tests taken 24 hours apart. The first LFD test should be taken no earlier than 6 days after symptoms started, or a positive test result if asymptomatic.
 - Rationale: Synthesis of data from biological studies and international literature reviews addressing periods of infectious virus shedding has been used to inform a recent UKHSA modelling study 1 estimating the impact of different isolation periods.
 - Previous research has shown that during a course of SARS-CoV-2 infection, viral load increases from 1 to 2 days before symptom onset, then peaks at symptom onset and in the first 5 days.
 - Data from the Assessment of Transmission and Contagiousness of COVID-19 in Contacts (ATTACCC) study 4 found that SARS-CoV-2 transmission occurs early during infection and is associated with peak viral loads.
 - Also extended the results of Bays et al [3] (details below) to include a 5-day isolation scenario in the modelled analysis of policy strategies.
 - This study estimated that after 10 full days of self-isolation, 5% of people who tested positive for SARS-CoV-2 are still infectious (Table 1). By comparison, reducing the 10-day isolation period to 7 days with 2 consecutive negative LFD test results from day 6 means an estimated 6% of people are still infectious when ending self-isolation. The proportion of people estimated to remain infectious 5 days after symptom onset or a positive test is 31%, and at 14 days it is 1%.

Table 1: Output from the model of the effect of the considered scenarios on disease release into the community

Policy	Released infectious (%)	Mean time (in hours) a released person is infectious for
5-day isolation	31.4% (23.9-38.2)	65.6 (57.7-73.3)
7-day isolation	15.8% (11.9-21.0)	62.3 (56.5-69.2)
10-day isolation	5.1% (3.4-7.6)	59.3 (53.5-65.6)
14-day isolation	1.0% (0.6-1.8)	57.1 (51.4-63.1)
10-day isolation, or 1 negative test from day 7	9.2% (6.5-12.8)	61.1 (55.3-67.5)
10-day isolation, or 2 negative tests from day 6	6.2% (4.2-9.0)	60.0 (53.9-66.3)
14-day isolation, or 2 negative tests from day 6	4.1% (2.6-6.0)	61.3 (55.8-67.7)

- Bays [3], medRxiv, 24 Dec 2021, not peer reviewed
 - Main result reported in table 1 above
 - Additional findings:

Table 3: Percentages (rounded to integer) of people who are still infectious after each day according to their disease profile.

	Day														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Still infectious (%)	100	92	75	58	43	31	22	16	11	7	5	3	2	2	1
No longer infectious (%)	0.0	8	25	42	57	69	78	84	89	93	95	97	98	98	99

- The current 10-day isolation period results in the release of 5% of the infected population being released from isolation whilst still being infectious. This reduces to 1% when a 14-day isolation period is considered. In comparison, 10-day isolation including 2 rapid antigen test negative results from day 6, provides a large reduction in excess isolation in return for a minimal cost of releasing those who are still infectious. Under this regime, 6% of people are released infectious. Excess isolation is reduced from 142 hours to 82 hours.

Exploring 10 days isolation

We now look in more detail at when people would be released from isolation and the proportions of those being released correctly and falsely at each step. The breakdown according to the day of release can be seen in Table 5.

Table 5: Breakdown of the “10-day isolation, or 2 negative rapid antigen tests from day 6” policy. The majority of people (79%) are released correctly on day 7. Conversely, there are a significant minority who end their isolation yet are still infectious (4.2%). Intervals are the 2.5 and 97.5 quantiles from the simulations.

	Day 6	Day 7	Day 8	Day 9	Day 10	End of isolation
New false releases	0 [0 - 0]	1.0 [0.6 - 1.5]	0.5 [0.3 - 0.7]	0.3 [0.2 - 0.5]	0.2 [0.1 - 0.3]	4.2 [2.5 - 6.4]
New true release	0 [0 - 0]	79.0 [73.2 - 84.2]	6.0 [5.0 - 7.0]	4.3 [3.4 - 5.3]	2.9 [2.1 - 3.7]	1.6 [1.1 - 2.2]
Previously released	0 [0 - 0]	0.0 [0.0 - 0.0]	80.0 [74.1 - 84.9]	86.5 [81.6 - 90.4]	91.2 [87.3 - 94.0]	N/A
Still in isolation	100 [100 - 100]	20.0 [15.1 - 25.9]	13.5 [9.6 - 18.4]	8.8 [6.0 - 12.7]	5.8 [3.7 - 8.6]	N/A

We can see that most people (79%) will be released on day 7 of their isolation. Only 6% of people will make it to the full 10 days of isolation. However, the majority of those who made it to day 10 would still need to isolate for even longer.

- Conclusions: Within the bounds of current UK guidance, taking rapid antigen tests from day 6, and requiring 2 consecutive negative tests 24 hours apart, a regime is generated that would release 79% of people correctly on day 7, with 6% of people requiring to stay in isolation until day 10. The total percentage of people released whilst still infectious will be approximately equivalent whereas the excess isolation time will drop from 6 days to 3 days. Note that it is key to this regimen that people should not end isolation early without the two negative rapid antigen tests as there is significant risk that they will still be infectious.
- Mahase [4], BMJ News, 30 Dec 2021
 - What are the isolation rules in different countries?
 - In the US, new rules mean that people have to isolate for only five days, while in the UK they have to isolate for 10 days unless they have negative lateral flow tests on days 6 and 7, at which point they can stop isolating.12
 - In France and Japan the isolation period is 10 days, while in New Zealand it is 10 days if the person is fully vaccinated (including 72 hours free of symptoms) but 14 days if they are unvaccinated (again including 72 hours free of symptoms). Germany, Jordan, and Brazil are following the World Health Organization's recommended 14 day isolation period.
 - Is it safe to reduce the self-isolation period from 14 days?
 - Michael Ryan, Executive Director of the WHO Health Emergencies Programme, called the changes "judgment calls" made to deal with Covid-19 cases while minimising the impact on people's social, economic, and educational lives.
 - Speaking at a press conference on 29 December 2021, he said that most people would incubate and show symptoms or be positive within the first six days of becoming infected. The chances of transmitting the disease after that are lower, although still a risk.
 - Has Omicron changed anything?
 - The US Centers for Disease Control and Prevention certainly thinks so. In its five day isolation announcement it said that the change from 10 days was motivated by evidence that most Omicron transmission occurred one to two days before the onset of symptoms and in the two to three days thereafter.4
 - However, Ryan warned against countries changing rules on the basis of early data. He said, "The data is not certain because we're dealing with a very limited number of studies and a limited number of individuals. We're also talking mainly about younger people. Maybe younger people have a shorter duration than older, but we just don't know. So, we need to be very careful with interpreting these data".
 - "But I think the most important thing at this moment is that we need to be careful about changing tactics and strategies immediately on the basis of what we're seeing in early data."
- Hay [5], 14 Jan 2022, medRxiv, not peer reviewed
 - We sought to describe SARS-CoV-2 Omicron variant viral dynamics in individual infections. To do so, we collected and analysed a longitudinal set of 10,324 SARS-CoV-2 viral samples obtained from 537 participants as part of the occupational health program of the National Basketball Association (NBA) between July 5th, 2021, and January 10th, 2022.
 - The cases used in this analysis include 107 infections with Delta and 97 with Omicron (49 confirmed by sequencing + 48 suspected by S-gene target failure).
 - Individual viral trajectories from Omicron infection demonstrated substantial heterogeneity, though all individuals were RT-PCR negative by day 15 post detection (Fig. 1A). All individuals exhibited Ct values <30 at some point in their infection, and by day 11 post detection all tested individuals had Ct values ≥30.
 - Overall, Omicron infections featured a mean duration of 9.87 days (95% CI 8.83-10.9) relative to 10.9 days (95% CI 9.41-12.4) for Delta infections. The peak viral RNA based on Ct values was lower for Omicron infections than for Delta infections (Ct 23.3, 95% CI 22.4-24.3 for Omicron; Ct 20.5, 95% CI 19.2-21.8 for Delta) and the clearance phase was shorter for Omicron infections (5.35 days, 95% CI 4.78-6.00 for Omicron; 6.23 days, 95% CI 5.43-7.17 for Delta), though the rate of clearance was similar (3.13 Ct/day, 95% CI 2.75-3.54 for Omicron; 3.15 Ct/day, 95% CI 2.69-3.64 for Delta).
 - Conclusions: It was found that infections with the Omicron variant, relative to Delta infections, feature lower peak viral loads and shorter clearance times, but similar proliferation times and clearance rates. However, these differences may be attributable to factors beyond inherent variant

characteristics. Importantly, it did not control for prior immune history 12, which could partially explain the lower peak viral concentrations and shorter clearance times for Omicron infections given that vaccination and infection were more prevalent during the emergence of Omicron. This may be particularly relevant in this population, with uptake of booster vaccination doses occurring after most Delta infections and before most Omicron infections. Analyses of these data stratifying individuals by number of prior vaccinations and infections are ongoing.

- CDC 14 Jan 2022 [Interim Guidance](#)
 - Mild, symptomatic and asymptomatic: Isolation can end at least 5 days after symptom onset/positive test and for those with symptoms after fever ends for 24 hours and symptoms are improving, if the person can continue to properly wear a well-fitted mask around others for 5 more days post-isolation.
 - Moderate and severe illness requires isolation for at least 10 days, moderately or severely immunocompromised people may have a longer infectious period so isolation should extend to at least 20 days.
 - Rationale <https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine-isolation-background.html> :
 - Data, including a review of 113 studies from 17 countries, show that most SARS-CoV-2 transmission occurs early in the course of infection [2,3]. Infectiousness peaks around one day before symptom onset and declines within a week of symptom onset, with an average period of infectiousness and risk of transmission between 2-3 days before and 8 days after symptom onset [2,3]. These data are from studies of prior SARS-CoV-2 variants, including Delta.
 - The science is evolving, particularly for the Omicron variant, and some reports suggest that compared with previous variants, Omicron has a shorter incubation period (2-4 days) [4-6].
 - Preliminary data suggest that the Omicron variant is up to three times more infectious than the Delta variant [14].
 - **It is important to wear a well-fitting mask after day 5 because modelling data suggest that close to one-third of persons remain infectious after day 5 and can potentially transmit the virus [16].**
 - The recommendations reflect the societal impact (e.g., critical infrastructure and staffing shortages) and the latest science on disease severity and when and for how long a person is maximally infectious. CDC will continue to evaluate these recommendations as more data become available.

References

1. Torjesen I. Covid-19: Peak of viral shedding is later with omicron variant, Japanese data suggest BMJ 2022; 376 :o89. [doi:10.1136/bmj.o89](https://doi.org/10.1136/bmj.o89)
2. National Institute of Infectious Diseases. Active epidemiological investigation on SARS-CoV-2 infection caused by Omicron variant (Pango lineage B.1.1.529) in Japan: preliminary report on infectious period. 5 Jan 2022. <https://www.niid.go.jp/niid/en/2019-ncov-e/10884-covid19-66-en.html>
3. Bays, Declan, Timothy Whiteley, Matt Pindar, Johnathon Taylor, Brodie Walker, Hannah Williams, Thomas J. R. Finnie, and Nick Gent. "Mitigating Isolation: The Use of Rapid Antigen Testing to Reduce the Impact of Self-Isolation Periods," December 24, 2021. <https://doi.org/10.1101/2021.12.23.21268326>.
4. Mahase E. Covid-19: Is it safe to reduce the self-isolation period? BMJ. 2021. 375:n3164 [doi:10.1136/bmj.n3164](https://doi.org/10.1136/bmj.n3164)
5. Hay, James A., Stephen M. Kissler, Joseph R. Fauver, Christina Mack, Caroline G. Tai, Radhika M. Samant, Sarah Connelly, et al. "Viral Dynamics and Duration of PCR Positivity of the SARS-CoV-2 Omicron Variant". January 14, 2022. <https://doi.org/10.1101/2022.01.13.22269257>.

Suggested Citation

Dono J, Wesselingh S Infectiousness and isolation of COVID-19 positive cases. COVID-19 Rapid Evidence Briefing. Adelaide, Australia. South Australian Health and Medical Research Institute (SAHMRI). 18 Jan 2022.