



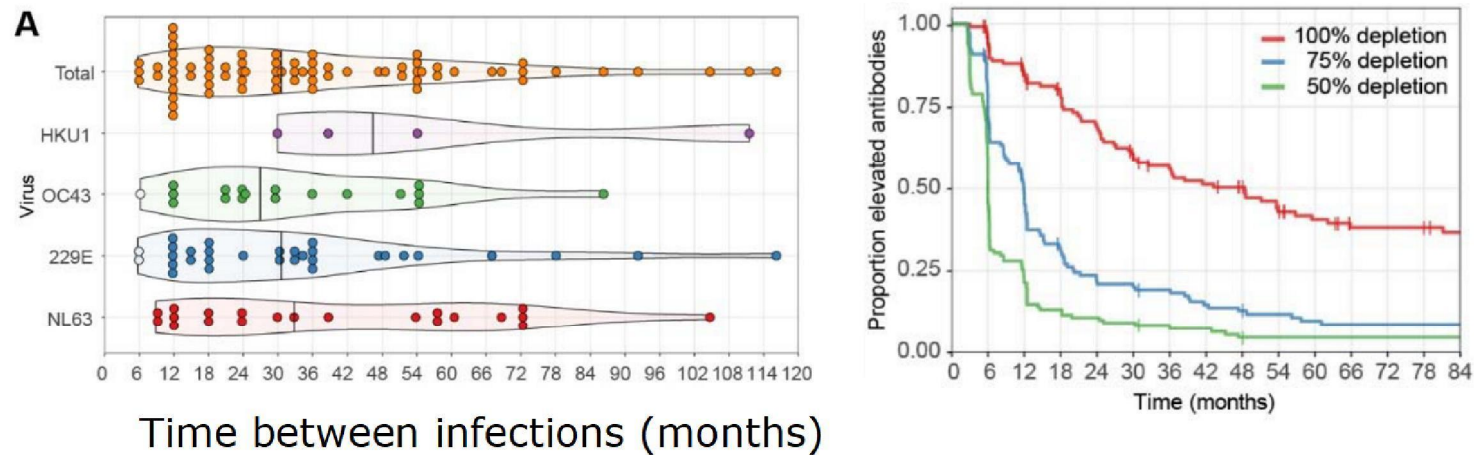
SARS-CoV-2 reinfo

5.1.2e

08-09-2020



Coronavirus reinfections are a common event

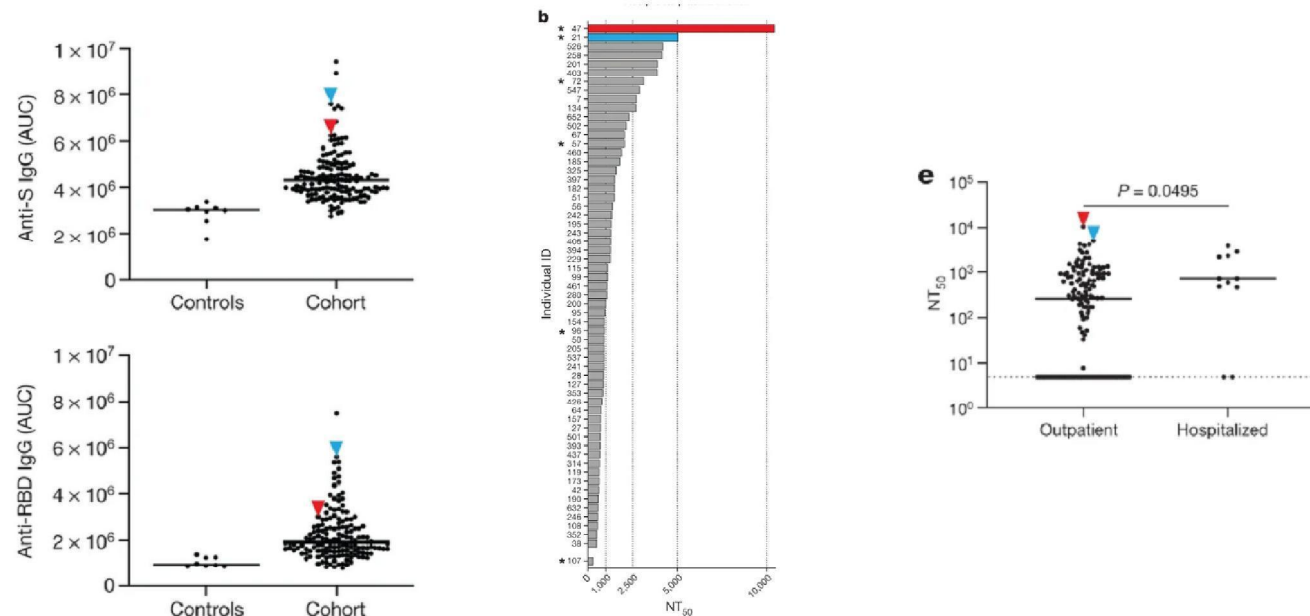


In seasonal coronaviruses reinfections occur as early as 6 months after initial infection, in part due to waning immunity.



Are antibodies elicited after infection sufficiently neutralizing?

People who recover from SARS-CoV-2 infection appear to have low levels of neutralizing antibodies.





SARS-CoV-2 reinfection in Hong Kong

CORONA-ONDERZOEK

NOS NIEUWS · BINNENLAND · MA 24 AUGUSTUS, 16:51 · AANGEPAST MA 24 AUGUSTUS, 17:48

Onderzoekers Hongkong: voor het eerst herbesmetting met corona vastgesteld

Herbesmetting

Ook bij ons: coronapatiënten na genezing opnieuw besmet

25 augustus 2020 00:42

Aangepast: 25 augustus 2020 08:49

Ziekenhuis: Mogelijk eerste bewijs van herbesmetting met corona

Onderzoekers in Hongkong melden dat een patiënt die hersteld was van een besmetting met het coronavirus, opnieuw is gediagnostiseerd met een infectie met het virus.

Buitenlandredactie 24-08-20, 20:22 Laatste update: 21:00

Herbesmetting met coronavirus blijkt mogelijk

Tweede infectie In Hongkong, en ook in Nederland en België, is nu bewezen dat iemand opnieuw met Covid-19 besmet kan worden.

Niki Korteweg · 25 augustus 2020 · Leestijd 2 minuten





SARS-CoV-2 reinfection in Hong Kong

33 year old man from Hong Kong

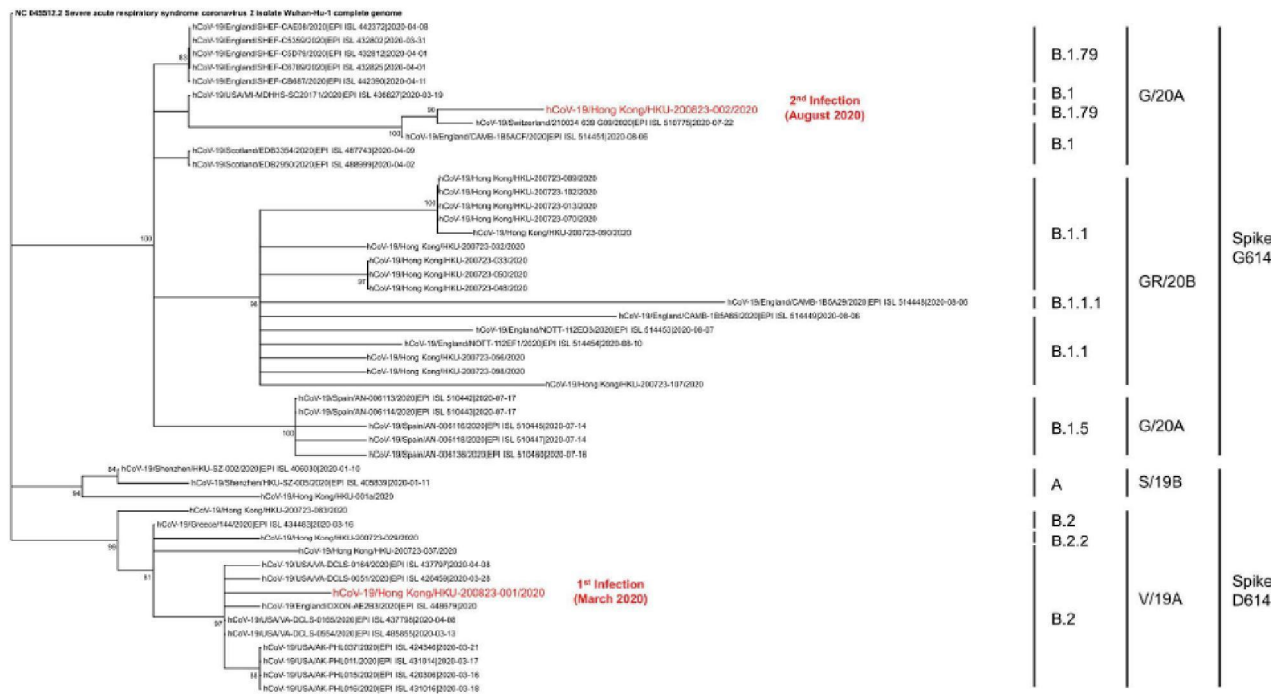
Initial infection with cough, sputum, headache, sore throat and fever. Hospitalized in March 2020, discharged on April 14th.

During second episode was asymptomatic after travelling from Spain to Hong Kong via United Kingdom. Found positive (Ct-value 26,7) during airport entry screening. Admitted to hospital: CRP 8,6.

Serology (IgG) negative 1 day after admission second episode. Seroconversion at day 5 after admission.



SARS-CoV-2 reinfection in Hong Kong



Difference of 23 nucleotides. In first episode also truncation of ORF8.



Timeline case 1

80 year old man with history of COPD, obesity, CHD, prostate carcinoma

16-03 erysipelas lower right leg

20-03 to 03-04 admitted to hospital for erysipelas treatment

12-04 readmitted due worsening of leg wound and low oxygen saturation. CRP 104. X-thorax: no infiltrates. **PCR nose/throat swab: positive (Ct 15)**. O2 treatment and supportive care. Not intubated.

20-04 discharged from hospital

02-05 complaints of increased drowsiness

04-05 readmitted to hospital due to renal dysfunction, pneumonia and *C.difficile* infection. PCR nose/throat swab: negative.

05-05 admitted to ICU. **PCR on lower airways material: positive (Ct 27)**

07-05 discharged from ICU

09-05 PCR sputum: negative

15-05 discharged to recovery care centre



Timeline case 2

60 year old man with no relevant medical history

07-04 presented with abdominal pain and progressive dyspnea

14-04 admitted to hospital. X-thorax: bilateral infiltrates.

PCR nose/throat swab: positive (Ct 26). O2 treatment and supportive care. No intubation

17-04 discharge from hospital

19-04 readmitted with progressive dyspnea. PCR nose/throat: negative.

20-04 admitted in ICU, required ventilation

24-04 multiple lung embolisms

26-04 broncho-alveolar lavage PCR positive (CT 26)

12-05 galactomannan positive and treated for pulmonary aspergillosis

09-06 discharge from ICU



Timeline case 3

82 year old male with history of diabetes, hypertension, CHD, obesity, gout, gonartrosis. Living in long term care facility with a private room.

01-04 presented with fever, less approachable/communicative, general malaise, mild coughing, no respiratory distress. Patient room placed in isolation

02-04 PCR nose/throat swab: positive.

09-04 moved to in-house COVID19 isolation unit

12-04 fever and decubitus treated with amoxicillin/clavulanic acid (augmentin)

14-04 resolution of pulmonary symptoms

16-04 non-productive cough

20-04 discharged from COVID19 unit to personal room

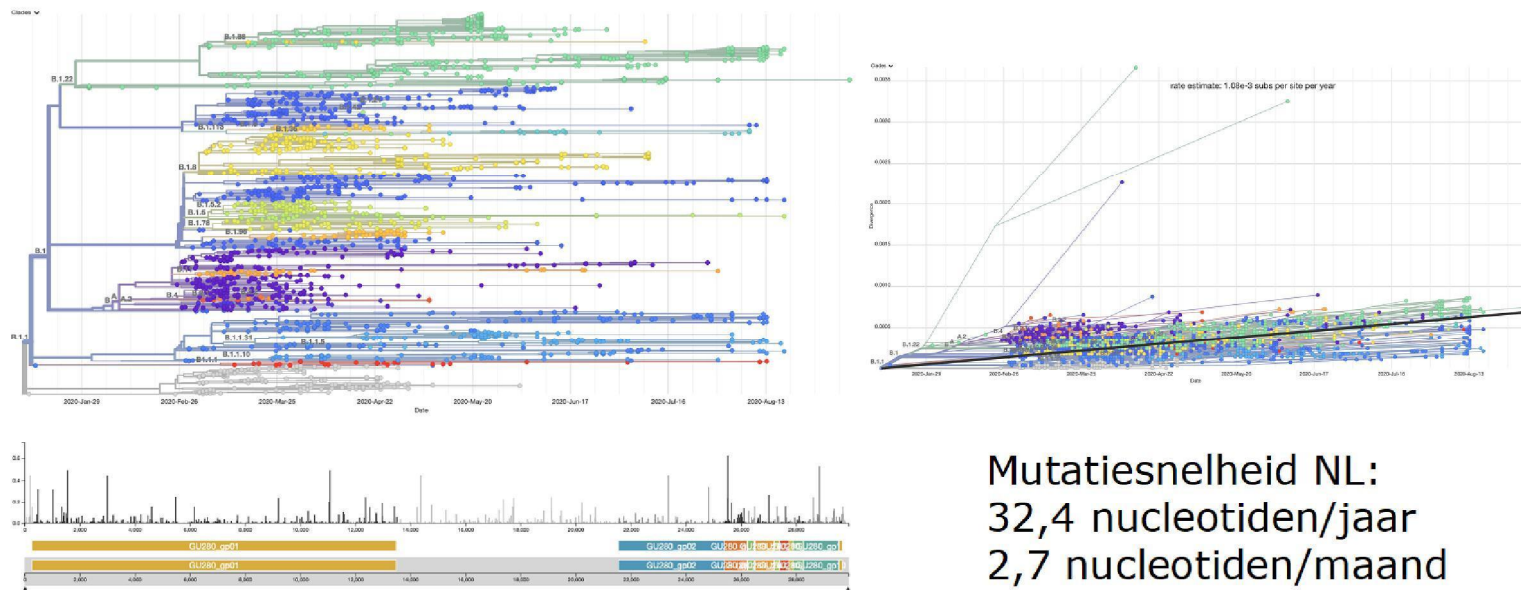
09-06 complaints of increased diarrhea and changed defecation. PCR nose/throat swab: positive. No fever, oxygen saturation 92%. Initially interpreted by local municipal health service as remnant RNA. No contact tracing was performed, 2 week quarantine and care in protective equipment.

12-06 resolution of complaints

18-06 ceased all isolation measures



Phylogeny of Dutch sequences

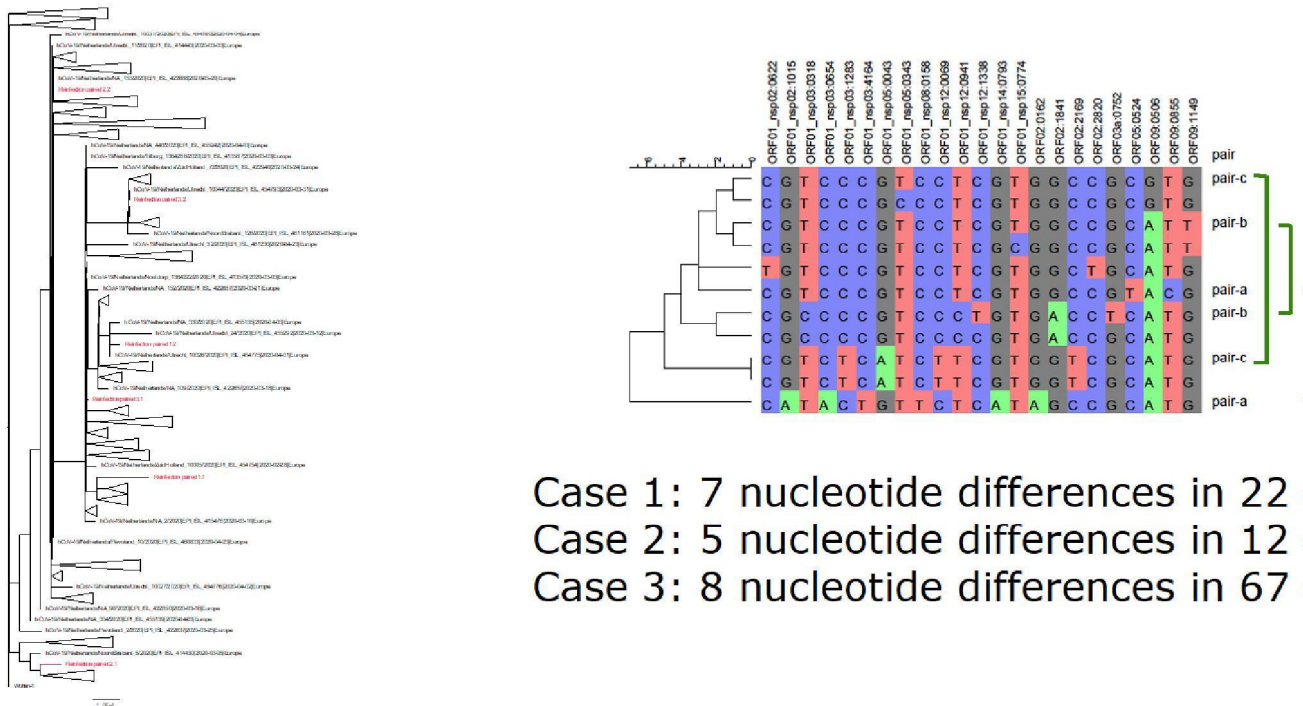


Mutatiesnelheid NL:
32,4 nucleotiden/jaar
2,7 nucleotiden/maand

GISAID (31-08-2020): 2280 Dutch sequences



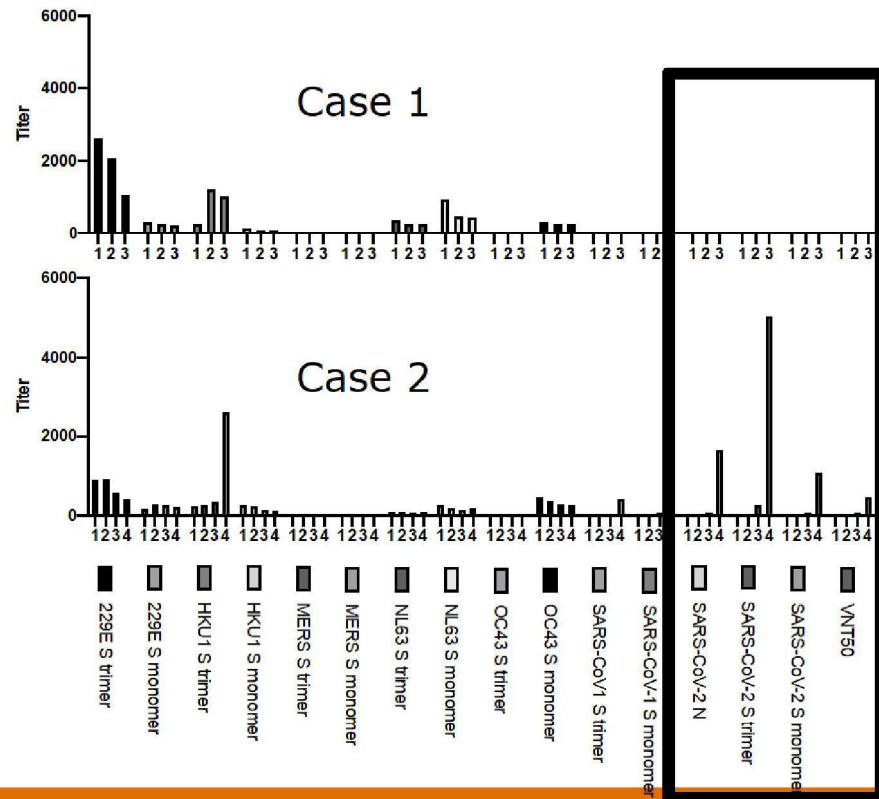
Phylogenetics and SNP differences



Case 1: 7 nucleotide differences in 22 days
 Case 2: 5 nucleotide differences in 12 days
 Case 3: 8 nucleotide differences in 67 days



Coronavirus serology via micro array



For case 1 and 2 sequential sera were available. At the earliest available time point both had no response to SARS-CoV-2 antigens.

Case 2 seroconverted over time with a broad response to multiple SARS-CoV-2 antigens.

For the 3rd patient no sera were available for testing.



Labinf@ct sent on 15-07-2020

Nationwide signaling system by e-mail to all laboratories, municipal health services and relevant clinicians, requesting notification of suspected cases of COVID19 re-infection.

Reporting criteria:

- Patients with a first COVID19 episode with a positive PCR or first clinical episode from a household with a previous PCR-positive case
- OR
- A second clinical episode with symptoms matching COVID19 and a positive PCR and symptom-free interval of at least 8 weeks



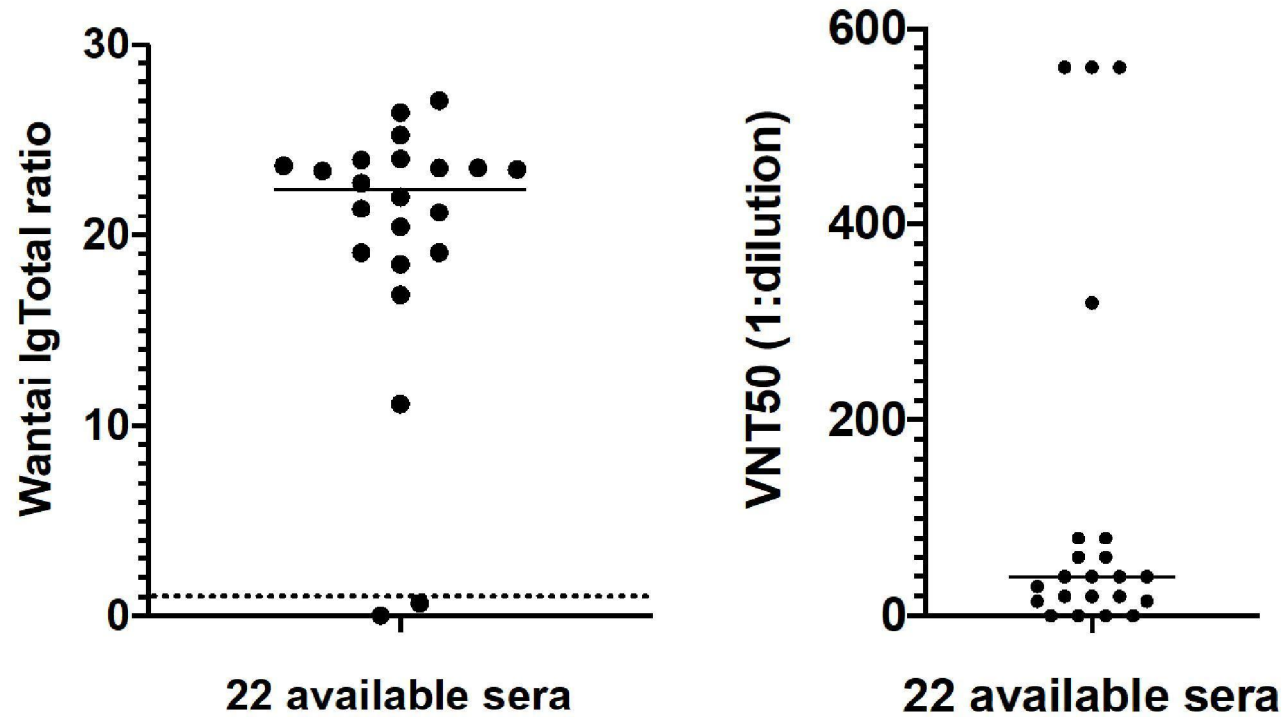
Reported reinfection

As of 31st of August 2020

- 38 reported cases of possible reinfection
- 22 possible cases had available materials
- 15 of 22 cases had >8 weeks of symptom-free period
- 5 of 22 cases did not report symptoms of <8 weeks symptom-free period
- 2 of 22 cases dates of symptom onset unknown



Serology and virus neutralization





Conclusions

- In total three sequencing confirmed reinfection cases in The Netherlands
- 2 of the 3 described cases had short intervals between reinfections, but no adequate virus neutralization capabilities were observed suggesting lack of protective antibodies after the initial infection
- For the third case no serology could be performed as no samples were available
- In 22 clinically reported suspected reinfection cases lack or very low level neutralizing antibodies were observed in 82% (18/22) of cases. Findings comparable to Robbiani et al.



Discussion & questions

- What is the most accurate genetic cutoff to distinguish reinfection from prolonged shedding?
- Is the SARS-CoV-2 evolutionary rate within (immunocompromised) hosts comparable to the evolutionary rate between hosts?
- Is the clinical spectrum different in the second episode?
- Is there evidence of subsequent transmission? What is the level of viral load/shedding and is the shedding duration shorter?



Acknowledgements

