



Multiple non-patient related SARS

5.1.2e

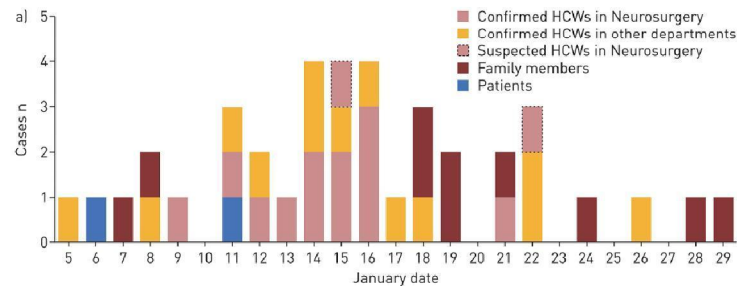
MD PhD
AIOS MMB AUMC / RIVM IDS

05-01-2021



Nosocomial infections are common for other coronaviruses

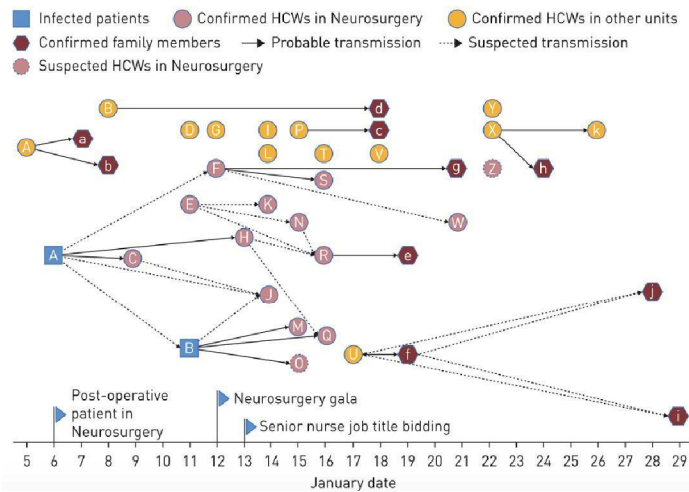
- In MERS-CoV nearly 50% of new cases was due to nosocomial spread.
- Also described in January 2020 in Wuhan, China for SARS-CoV-2 including spread to family members



Wang et al. Nosocomial outbreak of COVID-19 pneumonia in Wuhan, China Eur Respir J 2020; 55: 2000544

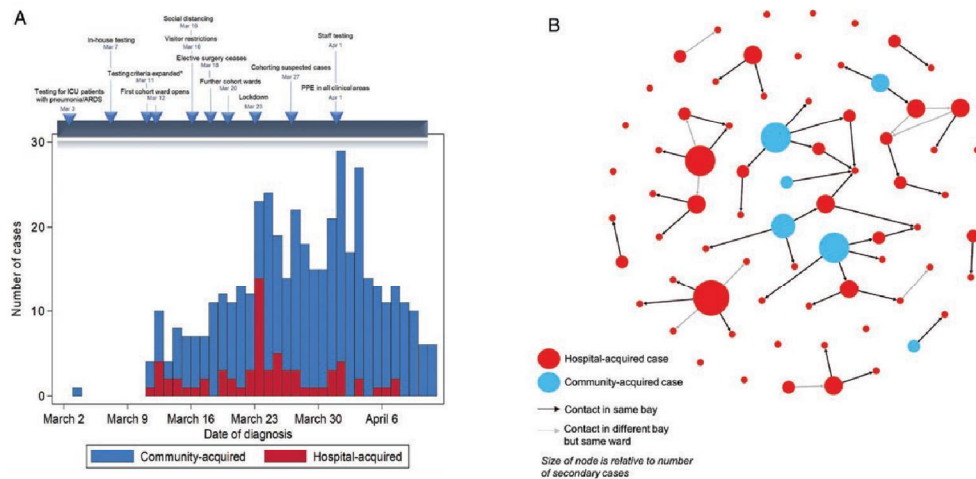


Also infection of family members





Nosocomial transmission in teaching hospital in England



Nearly 15% of cases were due to nosocomial transmission

Rickman et al. Nosocomial Transmission of Coronavirus Disease 2019: A Retrospective Study of 66 Hospital-acquired Cases in a London Teaching Hospital *CID* 2020;XX(X):1-4



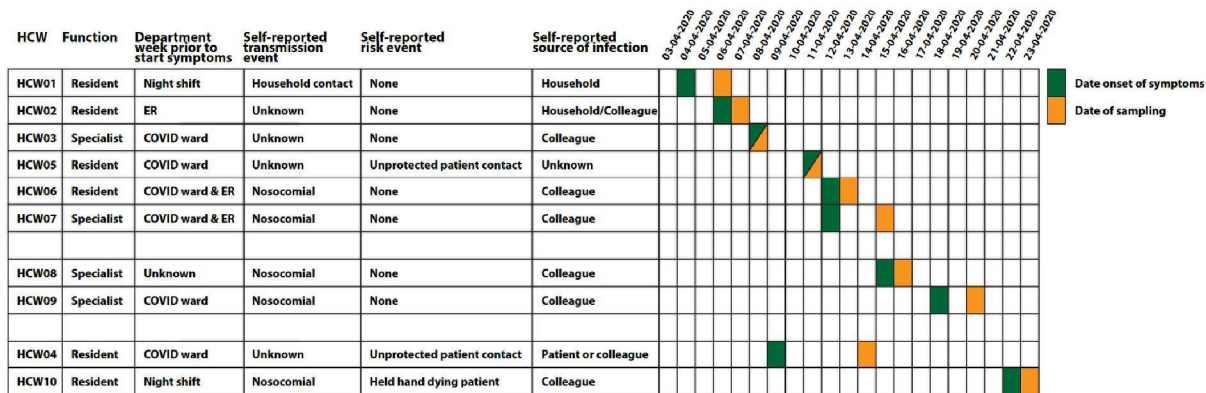
OLVG, located in Amsterdam

- During the first pandemic wave, OLVG was the regional SARS-CoV-2 treatment center.
- At the peak of the first wave: 5 COVID wards and 3 ICU units.
- During April 2020 several internal medicine residents and medical specialists fell ill. All had worked on ER/COVID wards. Testing showed: SARS-CoV-2 positive.
- In total 10 residents/doctors sick.



Epidemiological analysis

- Investigated by infection prevention department. Included review of work schedules, contact patients/colleagues and personal interviews with infected HCWs to identify potential (unknown) risks.

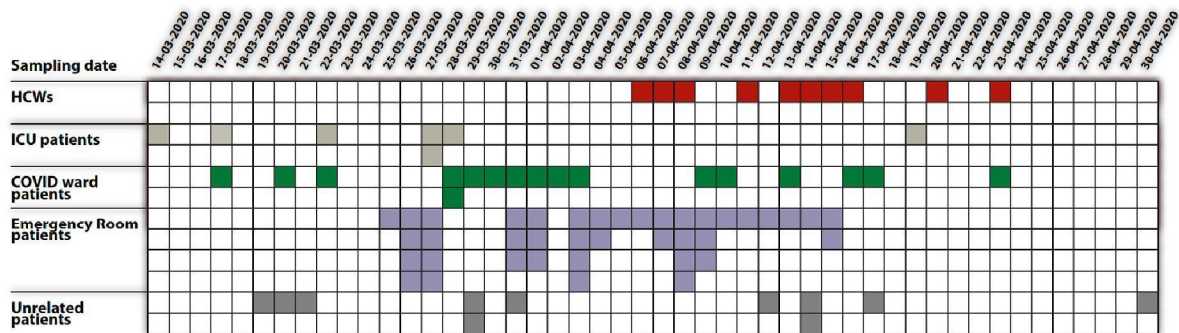




Timeline and selection of samples for sequencing

Subselection of samples based on:

- 1) CT-value <30,
- 2) sampling 2 weeks prior to onset of symptoms of HCW01 and >1 week post onset of symptoms HCW10
- 3) department of sampling





Phylogenetic analysis

From GISAID selected 2484 available Dutch SARS-CoV-2 sequences on October 17th.

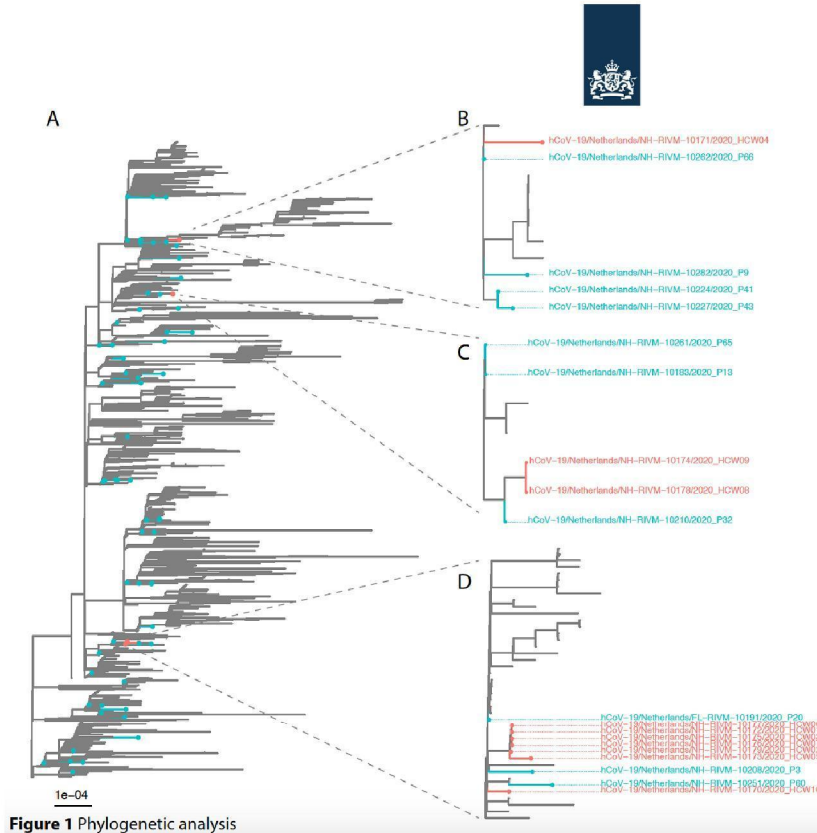
Genetic distance = measure of difference/divergence between 2 genetic sequences

For instance:

Seq1: ATCGT Genetic distance = $1/5 = 0,2$ nt/site

Seq2: GTCGT

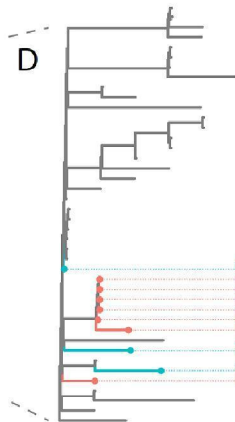
The average evolutionary rate for SARS-CoV-2 is 1 nucleotide change per 2 weeks \rightarrow GD=0,000034 ($3,4 \times 10^{-5}$)



- Diverse set of sequences among patients and HCWs: good representation of total variation in the Netherlands
- 4 separate introductions within the hospital
- 2 clusters with forward transmission among HCW and 2 singleton infections
- No observed transmission from HCWs to patients



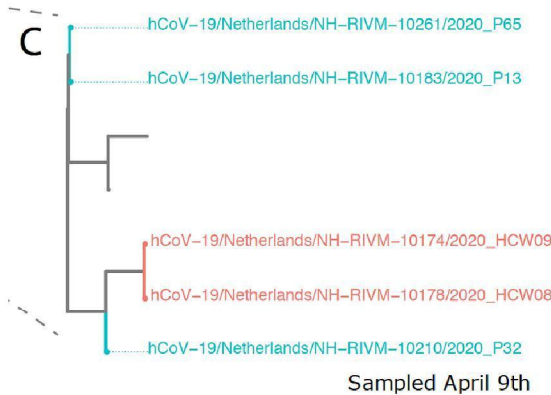
Cluster 1: 6 HCW



HCW	Function	Department week prior to start symptoms	Self-reported transmission event	Self-reported risk event	Self-reported source of infection	03-24-2020	04-01-2020	04-08-2020	04-15-2020	04-22-2020	05-06-2020	05-13-2020	05-20-2020	05-27-2020	06-03-2020	06-10-2020	06-17-2020	06-24-2020	07-01-2020	07-08-2020	07-15-2020	07-22-2020	07-29-2020	08-05-2020	08-12-2020	08-19-2020	08-26-2020	09-02-2020	09-09-2020	09-16-2020	09-23-2020	09-30-2020	10-07-2020	10-14-2020	10-21-2020	10-28-2020	11-04-2020	11-11-2020	11-18-2020	11-25-2020	12-02-2020	12-09-2020	12-16-2020	12-23-2020	12-30-2020	01-06-2021	01-13-2021	01-20-2021	01-27-2021	02-03-2021	02-10-2021	02-17-2021	02-24-2021	03-02-2021	03-09-2021	03-16-2021	03-23-2021	03-30-2021	04-06-2021	04-13-2021	04-20-2021	04-27-2021	05-04-2021	05-11-2021	05-18-2021	05-25-2021	06-01-2021	06-08-2021	06-15-2021	06-22-2021	06-29-2021	07-06-2021	07-13-2021	07-20-2021	07-27-2021	08-03-2021	08-10-2021	08-17-2021	08-24-2021	08-31-2021	09-07-2021	09-14-2021	09-21-2021	09-28-2021	10-05-2021	10-12-2021	10-19-2021	10-26-2021	11-02-2021	11-09-2021	11-16-2021	11-23-2021	11-30-2021	12-07-2021	12-14-2021	12-21-2021	12-28-2021	01-04-2022	01-11-2022	01-18-2022	01-25-2022	02-01-2022	02-08-2022	02-15-2022	02-22-2022	02-29-2022	03-06-2022	03-13-2022	03-20-2022	03-27-2022	04-03-2022	04-10-2022	04-17-2022	04-24-2022	05-01-2022	05-08-2022	05-15-2022	05-22-2022	05-29-2022	06-05-2022	06-12-2022	06-19-2022	06-26-2022	07-03-2022	07-10-2022	07-17-2022	07-24-2022	07-31-2022	08-07-2022	08-14-2022	08-21-2022	08-28-2022	09-04-2022	09-11-2022	09-18-2022	09-25-2022	10-02-2022	10-09-2022	10-16-2022	10-23-2022	10-30-2022	11-06-2022	11-13-2022	11-20-2022	11-27-2022	12-04-2022	12-11-2022	12-18-2022	12-25-2022	01-01-2023	01-08-2023	01-15-2023	01-22-2023	01-29-2023	02-05-2023	02-12-2023	02-19-2023	02-26-2023	03-05-2023	03-12-2023	03-19-2023	03-26-2023	04-02-2023	04-09-2023	04-16-2023	04-23-2023	04-30-2023	05-07-2023	05-14-2023	05-21-2023	05-28-2023	06-04-2023	06-11-2023	06-18-2023	06-25-2023	07-02-2023	07-09-2023	07-16-2023	07-23-2023	07-30-2023	08-06-2023	08-13-2023	08-20-2023	08-27-2023	09-03-2023	09-10-2023	09-17-2023	09-24-2023	10-01-2023	10-08-2023	10-15-2023	10-22-2023	10-29-2023	11-05-2023	11-12-2023	11-19-2023	11-26-2023	12-03-2023	12-10-2023	12-17-2023	12-24-2023	12-31-2023	01-07-2024	01-14-2024	01-21-2024	01-28-2024	02-04-2024	02-11-2024	02-18-2024	02-25-2024	03-04-2024	03-11-2024	03-18-2024	03-25-2024	04-01-2024	04-08-2024	04-15-2024	04-22-2024	04-29-2024	05-06-2024	05-13-2024	05-20-2024	05-27-2024	06-03-2024	06-10-2024	06-17-2024	06-24-2024	07-01-2024	07-08-2024	07-15-2024	07-22-2024	07-29-2024	08-05-2024	08-12-2024	08-19-2024	08-26-2024	09-02-2024	09-09-2024	09-16-2024	09-23-2024	09-30-2024	10-07-2024	10-14-2024	10-21-2024	10-28-2024	11-04-2024	11-11-2024	11-18-2024	11-25-2024	12-02-2024	12-09-2024	12-16-2024	12-23-2024	12-30-2024	01-06-2025	01-13-2025	01-20-2025	01-27-2025	02-03-2025	02-10-2025	02-17-2025	02-24-2025	03-02-2025	03-09-2025	03-16-2025	03-23-2025	03-30-2025	04-06-2025	04-13-2025	04-20-2025	04-27-2025	05-04-2025	05-11-2025	05-18-2025	05-25-2025	06-01-2025	06-08-2025	06-15-2025	06-22-2025	06-29-2025	07-06-2025	07-13-2025	07-20-2025	07-27-2025	08-03-2025	08-10-2025	08-17-2025	08-24-2025	08-31-2025	09-07-2025	09-14-2025	09-21-2025	09-28-2025	10-05-2025	10-12-2025	10-19-2025	10-26-2025	11-02-2025	11-09-2025	11-16-2025	11-23-2025	11-30-2025	12-07-2025	12-14-2025	12-21-2025	12-28-2025	01-04-2026	01-11-2026	01-18-2026	01-25-2026	02-01-2026	02-08-2026	02-15-2026	02-22-2026	02-29-2026	03-06-2026	03-13-2026	03-20-2026	03-27-2026	04-03-2026	04-10-2026	04-17-2026	04-24-2026	05-01-2026	05-08-2026	05-15-2026	05-22-2026	05-29-2026	06-05-2026	06-12-2026	06-19-2026	06-26-2026	07-03-2026	07-10-2026	07-17-2026	07-24-2026	07-31-2026	08-07-2026	08-14-2026	08-21-2026	08-28-2026	09-04-2026	09-11-2026	09-18-2026	09-25-2026	10-02-2026	10-09-2026	10-16-2026	10-23-2026	10-30-2026	11-06-2026	11-13-2026	11-20-2026	11-27-2026	12-04-2026	12-11-2026	12-18-2026	12-25-2026	01-01-2027	01-08-2027	01-15-2027	01-22-2027	01-29-2027	02-05-2027	02-12-2027	02-19-2027	02-26-2027	03-05-2027	03-12-2027	03-19-2027	03-26-2027	04-02-2027	04-09-2027	04-16-2027	04-23-2027	04-30-2027	05-07-2027	05-14-2027	05-21-2027	05-28-2027	06-04-2027	06-11-2027	06-18-2027	06-25-2027	07-02-2027	07-09-2027	07-16-2027	07-23-2027	07-30-2027	08-06-2027	08-13-2027	08-20-2027	08-27-2027	09-03-2027	09-10-2027	09-17-2027	09-24-2027	10-01-2027	10-08-2027	10-15-2027	10-22-2027	10-29-2027	11-05-2027	11-12-2027	11-19-2027	11-26-2027	12-03-2027	12-10-2027	12-17-2027	12-24-2027	12-31-2027	01-07-2028	01-14-2028	01-21-2028	01-28-2028	02-04-2028	02-11-2028	02-18-2028	02-25-2028	03-04-2028	03-11-2028	03-18-2028	03-25-2028	04-01-2028	04-08-2028	04-15-2028	04-22-2028	04-29-2028	05-06-2028	05-13-2028	05-20-2028	05-27-2028	06-03-2028	06-10-2028	06-17-2028	06-24-2028	07-01-2028	07-08-2028	07-15-2028	07-22-2028	07-29-2028	08-05-2028	08-12-2028	08-19-2028	08-26-2028	09-02-2028	09-09-2028	09-16-2028	09-23-2028	09-30-2028	10-07-2028	10-14-2028	10-21-2028	10-28-2028	11-04-2028	11-11-2028	11-18-2028	11-25-2028	12-02-2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Cluster 2: 2 HCW



3 days between onset of symptoms of HCWs.

1 nucleotide difference between P32 and both HCW.

However, no direct contact between patient P32 and HCWs.

Possibly transmission via unsampled (asymptotically) infected HCW.

Again, both HCWs had contact during prolonged work shift meetings.

HCW	Function	Department week prior to start symptoms	Self-reported transmission event	Self-reported risk event	Self-reported source of infection	03-04-2020	04-04-2020	05-04-2020	06-04-2020	07-04-2020	08-04-2020	09-04-2020	10-04-2020	11-04-2020	12-04-2020	13-04-2020	14-04-2020	15-04-2020	16-04-2020	17-04-2020	18-04-2020	19-04-2020	20-04-2020	21-04-2020	22-04-2020	23-04-2020	
HCW08	Specialist	Unknown	Nosocomial	None	Colleague																						
HCW09	Specialist	COVID ward	Nosocomial	None	Colleague																						



Conclusion

4 separate introductions in the HCWs, 2 resulting in forward nosocomial transmission clusters

- Large cluster (n=6) possibly initiated from household contact, no relation to any patient sample
- Small cluster (n=2) most likely initiated by a patient followed by HCW to HCW transmission possibly via an unsampled (asymptomatic) HCW

Transmission among HCWs most likely due to prolonged shift change handover meetings in confined spaces without PPE or social distancing

Changes were made in policy: advocated early and rapid testing of HCWs and promote strict adherence to social distancing measures within the hospital among HCWs.



Acknowledgements

OLVG

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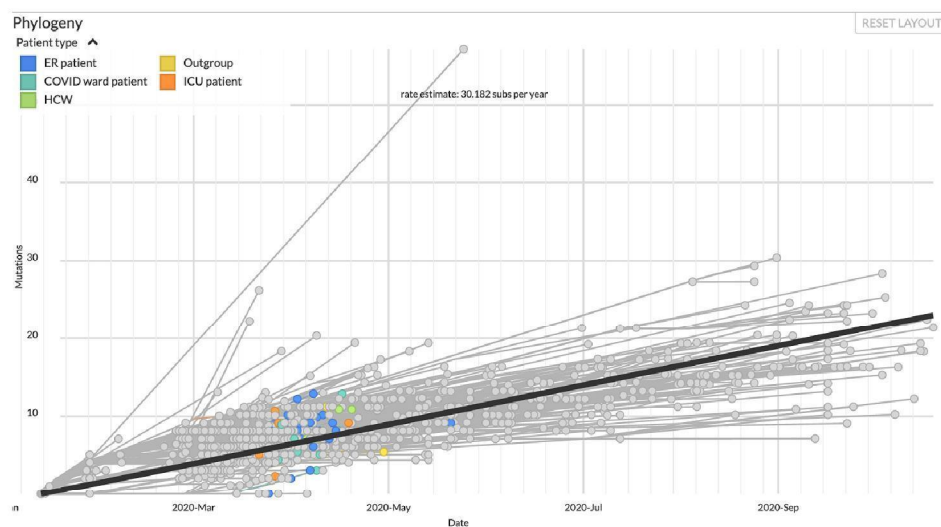
- All submitting and originating laboratories providing data to GISAID



Questions?



Molecular clock time-based tree



Average 10 mutations compared to Wuhan-1 reference. All sequences match contemporary variants from the first pandemic wave.



Nosocomial transmission

WHO definition

"An infection acquired in hospital by a patient who was admitted for a reason other than that infection (1). An infection occurring in a patient in a hospital or other healthcare facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility (2)."

<https://www.who.int/csr/resources/publications/drugresist/en/whocdscsreph200212.pdf>