ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

EUCIC EUROPEAN COMMITTEE ON INFECTION CONTROL

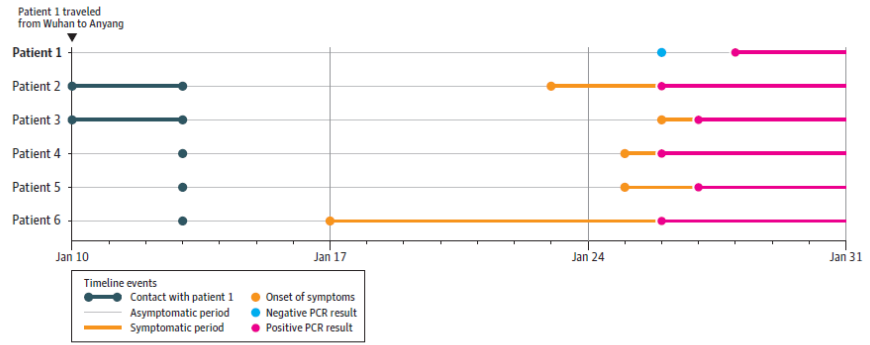
The current literature in Infection Prevention and Control COVID-19

Read for you!

By Gabriel Birgand

Presumed Asymptomatic Carrier Transmission of COVID-19

Figure. Timeline of Exposure to the Asymptomatic Carrier of the Novel Coronavirus That Causes COVID-19 in a Familial Cluster



PCR indicates polymerase chain reaction test for the coronavirus disease 2019 (COVID-19) nucleic acid.

Table. Summary of Laboratory Examination Results of the Familial Cluster Infected With the Novel Coronavirus That Causes Coronavirus Disease 2019

	Reference range	Patient 1[a]	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
C-reactive protein, mg/L	0.0-4.0	0.69	217.17	10.14	66.07	14.9	202.03
Eosinophils, $\times 10^9$/L	0.02-0.52	0.02	0	0.01	0	0	0
Eosinophil ratios, %	0.4-8	0.40	0	0.30	0	0.10	0
Lymphocytes, $\times 10^9$/L	1.1-3.2	1.55	0.53	1.65	0.91	0.46	0.69
Lymphocyte ratios, %	20-50	27.50	6.70	35.90	27.70	13.30	7.40
Neutrophils, $\times 10^9$/L	1.8-6.3	3.62	6.89	2.64	2.10	2.89	8.21
Neutrophil ratios, %	40-75	63.90	86.40	57.40	64.00	84.10	87.00
White blood cell count, $\times 10^9$/L	3.9-9.9	5.65	7.97	4.59	3.29	3.44	9.43

[a] Asymptomatic.

- Familial cluster of 5 patients with fever and respiratory symptoms and 1 asymptomatic family member
- RT-PCR tests for COVID-19 nucleic acid performed using nasopharyngeal swabs
- Patient 1 (presumed asymptomatic carrier),
  - 20 y-o woman, initially met with patients 2 and 3 on January 10. On January 13, she accompanied 5 relatives (patients 2 through 6) to visit another hospitalized relative. February 11, she had no symptomes,
  - RT-PCR testing were negative on January 26, positive on January 28, and negative on February 5 and 8
- Patients 2 to 6 developed COVID-19.
  - Four were women, and ages ranged from 42 to 57 years.
  - None of the patients been in contact with any other people who had traveled toWuhan (except patient 1).
- Patients 2 to 5
  - Developed fever and respiratory symptoms between January 23 and January 26 and were hospitalised the same day.
  - All patients had RT-PCR test results positive for COVID-19 within 1 day.
  - Patient 6 developed fever and sore throat on January 17 and went to the local clinic for treatment. There was no report of COVID-19 at the clinic. Her symptoms improved over the next few days but worsened on January 24, when she was admitted to the hospital and confirmed to have COVID-19 on January 26.
  - Two patients developed severe pneumonia; the other infections were moderate.

Yan Bai JAMA 21 February 2020

Air, Surface Environmental, and Personal Protective Equipment Contamination by SARS-CoV-2 From a Symptomatic Patient

- 3 patients at the dedicated SARS-CoV-2 outbreak center in Singapore in airborne infection isolation rooms
  - Surface environmental samples taken at 26 sites, anterooms and bathrooms (12 air exchanges per hour)
    - Samples were collected on 5 days over a 2-week period.
    - One patient's room was sampled before routine cleaning and 2 patients' rooms after routine cleaning.
    - Twice-daily cleaning of high-touch areas was done using 5000ppmof sodium dichloroisocyanurate. The floor was cleaned daily using 1000 ppm of sodium dichloroisocyanurate.
  - PPE samples from study physicians exiting the patient rooms
  - Air sampling was done on 2 days in the room and anteroom and outside the room
  - RT-PCR targeting RNA-dependent RNA polymerase and E gen, Cycle threshold values, quantified viral load

Table 1. Sampling Time Points in Relation to Patient Illness and Clinical Cycle Threshold Values

Patient	Days of illness when samples were collected	Presence of symptoms during sampling	Symptoms	Disease severity[a]	Before/after routine cleaning	Cycle threshold value from clinical samples[b]
A	4, 10	Yes, both days	Cough, fever, shortness of breath	Moderate	After	31.31 (day 3); 35.33 (day 9)
B	8, 11	Yes on day 8; asymptomatic on day 11	Cough, fever, sputum production	Moderate	After	32.22 (day 8); not detected (day 11)
C	5	Yes	Cough	Mild	Before	25.69 (day 4)

[a] Disease severity was considered moderate if there was lung involvement (opacities on chest radiograph) and severe if patient required supplemental oxygen therapy.

[b] Clinical samples were either nasopharyngeal swabs or sputum samples if patient could produce sputum. The most recent result prior to the environmental sampling was recorded. Cycle threshold refers to the number of cycles required for the fluorescent signal to cross the threshold in reverse transcriptase–polymerase chain reaction; a lower cycle threshold value indicates a higher viral load.

- All **air samples were negative**.
- Patient A: **All surface samples negative**.
- Patient B : **All surface samples negative**.
- Patient C: positive results
  - 13 (87%) of 15 room sites (including air outlet fans), 3 (60%) of 5 toilet sites (toilet bowl, sink,anddoor handle), Anteroom and corridor samples were negative.
  - 2 positive stool samples for SARS-CoV-2 on RT-PCR despite not having diarrhea.
  - Greater viral shedding, with a cycle threshold value of 25.69 in nasopharyngeal samples compared with 31.31 and 35.33 in patients A and B
- Only 1 PPE swab, from the surface of a shoe front, was positive. All other PPE swabs were negative.

- Toilet bowl and sink samples were positive: viral shedding in stool could be a potential route of transmission.
- Post-cleaning samples negative: current decontamination measures are sufficient.

SeanWei Xiang Ong JAMA 27 February 2020

Detection of SARS-CoV-2 in Different Types of Clinical Specimens

- Biodistribution of SARS-CoV-2 among different tissues of inpatients with COVID-19)
- 1070 specimens collected from 205 patients with COVID-19, mean age 44 years, 68% male
- Most of the patients presented with fever, dry cough, and fatigue; 19% of patients had severe illness

Figure. Severe Acute Respiratory Syndrome Coronavirus 2 Distribution and Shedding Patterns Among 20 Hospitalized Patients

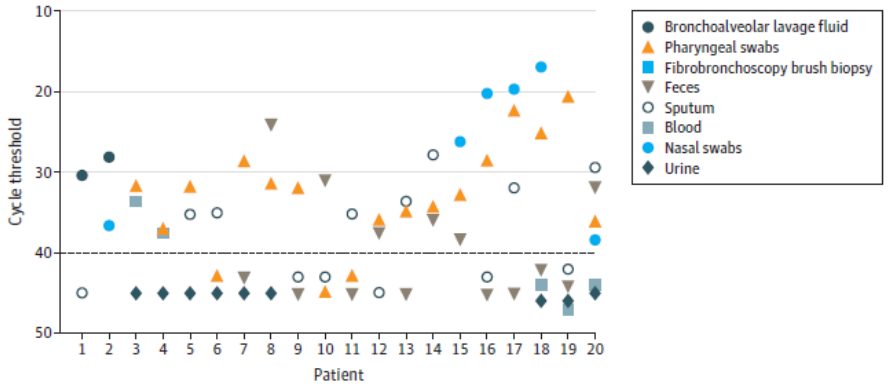


Table. Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

Specimens and values	Bronchoalveolar lavage fluid (n = 15)	Fibrobronchoscope brush biopsy (n = 13)	Sputum (n = 104)	Nasal swabs (n = 8)	Pharyngeal swabs (n = 398)	Feces (n = 153)	Blood (n = 307)	Urine (n = 72)
Positive test result, No. (%)	14 (93)	6 (46)	75 (72)	5 (63)	126 (32)	44 (29)	3 (1)	0
Cycle threshold, mean (SD)	31.1 (3.0)	33.8 (3.9)	31.1 (5.2)	24.3 (8.6)	32.1 (4.2)	31.4 (5.1)	34.6 (0.7)	ND
Range	26.4-36.2	26.9-36.8	18.4-38.8	16.9-38.4	20.8-38.6	22.3-38.4	34.1-35.4	
95% CI	28.9-33.2	29.8-37.9	29.3-33.0	13.7-35.0	31.2-33.1	29.4-33.5	0.0-36.4	

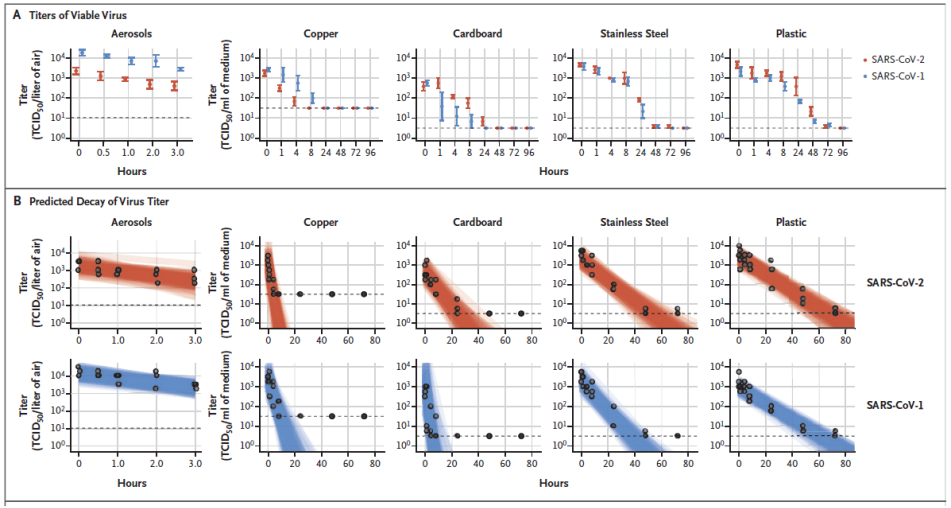
WenlingWang JAMA 11 March 2020

The NEW ENGLAND JOURNAL of MEDICINE

EUCIC
EUROPEAN COMMITTEE ON INFECTION CONTROL

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1

- Aerosol and surface stability of SARS-CoV-2 and SARS-CoV-1
  - Aerosols (<5 µm) containing SARS-CoV-2 or SARS-CoV-1 were generated with the use of a three-jet Collison nebulizer and fed into a Goldberg drum to create an aerosolized environment.
  - Inoculum of CT between 20 and 22, similar to those observed in respiratory samples
  - 10 experimental conditions in five environmental conditions (aerosols, plastic, stainless steel, copper, and cardboard).



- SARS-CoV-2 remained viable in aerosols throughout 3 hours, with a reduction similar SARS-CoV-1 = 90%
- SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours = reduction of 99,9% after 24 hours
- Stability kinetics of SARS-CoV-1 were similar (from 103.4 to 100.7 TCID50 per milliliter after 72 hours on plastic and from 103.6 to 100.6 TCID50 per milliliter after 48 hours on stainless steel).
- On copper, no viable SARS-CoV-2 was measured after 4 hours and no viable SARS-CoV-1 was measured after 8 hours.
- On cardboard, no viable SARS-CoV-2 was measured after 24 hours and no viable SARSCoV-1 was measured after 8 hours

Conclusion: aerosol and fomite transmission of SARS-CoV-2 is plausible, since the virus can remain viable and infectious in aerosols for hours and on surfaces up to days

Neeltje van Doremalen NEJM 17 March 2020

THE LANCET
Infectious Diseases

Prolonged presence of SARS-CoV-2 viral RNA in faecal samples

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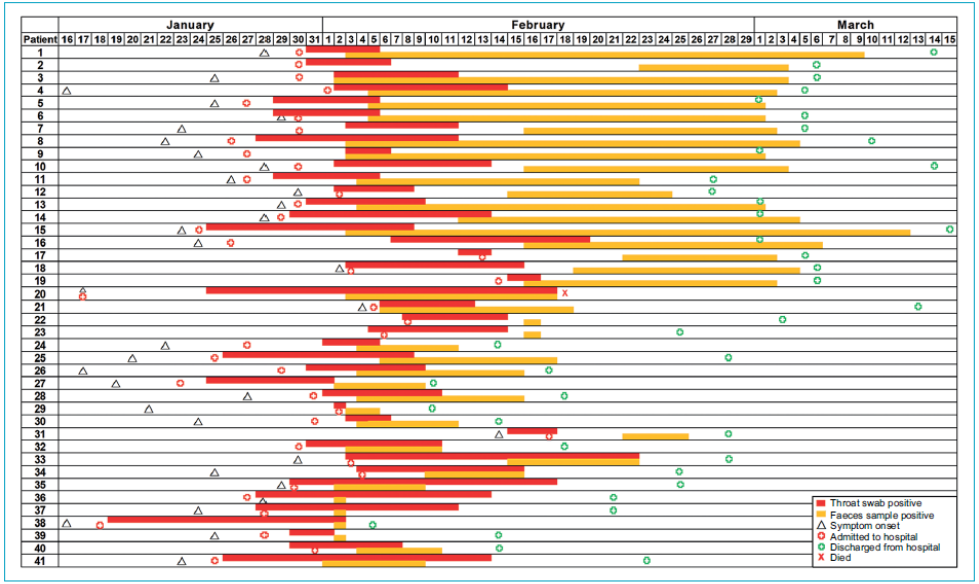

Figure: Timeline of results from throat swabs and faecal samples through the course of disease for 41 patients with SARS-CoV-2 RNA positive faecal samples, January to March, 2020

- Jan 16 and March 15, 2020, 98 patients.
  - Respiratory and faecal samples from 74 (76%) patients.
  - 33 (45%) of 74 patients faecal negative for SARS CoV-2 RNA, and respiratory positive until 15·4 days (SD 6·7) from symptom .
  - 41 (55%) of 74 patients faecal samples positive for SARS-CoV-2 RNA, respiratory positive for a mean of 16·7 days (SD 6·7) and faecal samples remained positive for a mean of 27·9 days (10·7) after first symptom onset
  - Patient 1 had positive faecal samples for 33 days continuously after the respiratory samples became negative, Patient 4 tested positive for SARS-CoV-2 RNA in their faecal sample for 47 days after first symptom onset
- Gastrointestinal symptoms not associated with faecal sample viral RNA positivity (p=0·45);
- Disease severity not associated with extended duration of faecal sample viral RNA positivity (p=0·60);
- Antiviral treatment positively associated with the presence of viral RNA in faecal samples (p=0·025;

Yongjian WuLID 19 March 2020

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Infectious Diseases

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Viral dynamics in mild and severe cases of COVID-19

- 76 patients from Jan 21 to Feb 4, 2020, confirmed to have COVID-19 at the time of admission by RT-PCR.
- Viral loads of their nasopharyngeal swab samples estimated with the DCt method (Ctsample – Ctref).
- 46 (61%) individuals classified as mild cases and 30 (39%) classified as severe cases
- DCt values of severe cases were significantly lower than those of mild cases
- Mean viral load of severe cases was around **60 times higher** than that of mild cases, suggesting that higher viral loads might be associated with severe clinical outcomes
- DCt values of severe cases remained **significantly lower for the first 12 days after onset** than those of corresponding mild cases
- Mild cases were found to have an **early viral clearance**, with 90% of these patients repeatedly testing negative on RT-PCR by day 10 post-onset.
- All severe cases still tested positive at or beyond day 10 post onset.

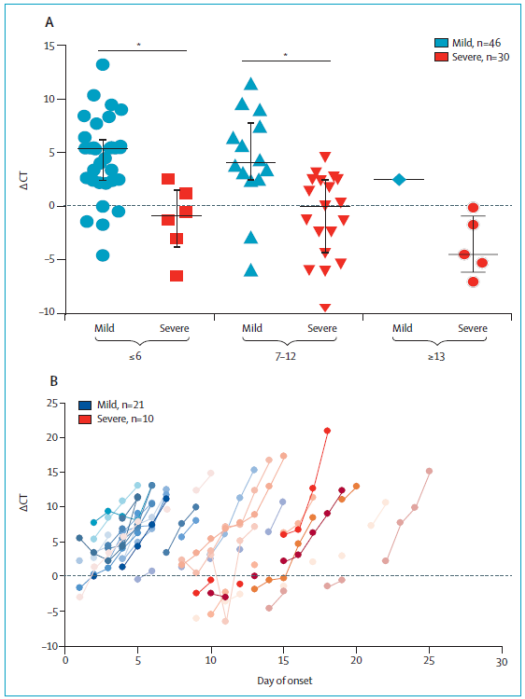

Figure: **Viral dynamics in patients with mild and severe COVID-19**
(A) ΔCT values (Ct_{sample}-Ct_{ref}) from patients with mild and severe COVID-19 at different stages of disease onset. Median, quartile 1, and quartile 3 are shown. (B) ΔCT values of serial samples from patients with mild and severe COVID-19. COVID-19=coronavirus disease 2019. *p<0·005.

Yang Liu LID 19 March 2020

nature

Virological assessment of hospitalized patients with COVID-2019

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Objectives: To detail virological analysis of nine cases, providing proof of active virus replication in upper respiratory tract tissues.

Methods: Uses samples taken during the clinical course in the hospital, as well as from initial diagnostic testing before admission.

Results:

- No discernible differences in viral loads or detection rates when comparing naso- vs. oropharyngeal swabs
- Analyze 1st paired swab and sputum samples taken on the same occasion from seven patients between 2 and 4 days post-onset.
  - In two cases, swab samples had clearly higher virus concentrations than sputum samples, as indicated by a difference greater than 3 in threshold cycle (Ct) value. The opposite was true in two other cases, while the remaining 5 cases had similar concentrations in both sample types.
- Virus isolated during the 1st week of symptoms from 16.66% in swabs, 83.33% in sputum samples,
- No isolates were obtained from samples taken after day 8 in spite of ongoing high viral loads.
- Virus isolation from stool samples was never successful
- These data indicate active replication of SARS-CoV-2 in the throat during the first 5 days after symptoms onset.
- Viral RNA concentrations were very high in initial samples.
- Sputum RNA concentrations declined more slowly, with a peak during the first week of symptoms
- Stool RNA concentrations were also high. Courses of viral RNA concentration in stool seemed to reflect courses in sputum in many cases
- In only one case, independent replication in the intestinal tract seemed obvious from the course of stool RNA excretion (Figure 2D). Whereas symptoms mostly waned until the end of the first week (Table 2), viral RNA remained detectable in throat swabs well into the second week. Stool and sputum samples remained RNA-positive over three weeks in six of the nine patients, in spite of full resolution of symptoms.
- Seroconversion in 50% of patients occurred by day 7, and in all by day 14 (Figure 1D). No viruses were isolated after day 7.

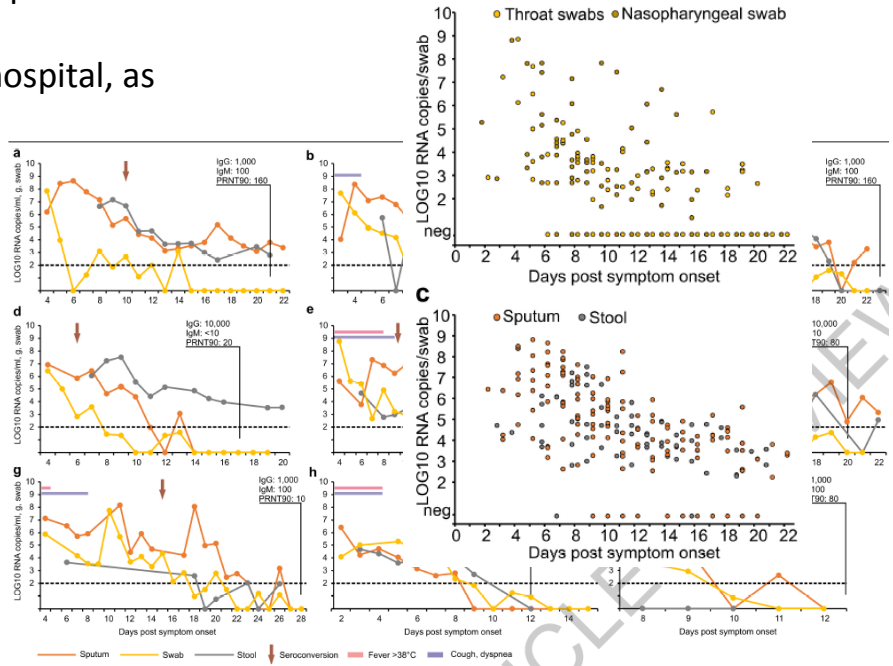

Fig. 2 | Viral load kinetics, seroconversion and clinical observations in individual cases. Panels A to I correspond to cases #1, #2, #3, #4, #7, #8, #10, #14, and #16 in Böhmer et al.[11] Dotted lines, limit of quantification. Experiments were performed in duplicate and the data presented are means of results obtained by two laboratories independently.

Roman Wölfel Nature 1 April 2020

THE LANCET
Microbe

Stability of SARS-CoV-2 in different environmental conditions

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- Measured the stability of SARS-CoV-2 at different temperatures.
  - SARS-CoV-2 in virus transport medium incubated for up to 14 days and then tested for its infectivity
  - Virus highly stable at 4°C (only around a 0·7 log-unit reduction of infectious titre on day 14)
  - Virus sensitive to heat: incubation temperature increased to 70°C, the time for virus inactivation was reduced to 5 mins.
- Stability of this virus on different surfaces.
  - 5 µL droplet of virus culture pipetted on a surface and left at room temperature (22°C) with a relative humidity of around 65%.
  - Objects soaked with 200 µL of virus transport medium for 30 mins to elute the virus
  - No infectious virus recovered from printing and tissue papers after a 3-hour incubation, whereas no infectious virus could be detected from treated wood and cloth on day 2
  - No infectious virus could be detected from treated smooth surfaces on day 4 (glass and banknote) or day 7 (stainless steel and plastic).
  - Detectable level of infectious virus could still be present on the outer layer of a surgical mask on day 7
- Virucidal effects of disinfectants
  - adding 15 µL of SARS-CoV-2 culture to 135 µL of various disinfectants at working concentration
  - With the exception of a 5-min incubation with hand soap, no infectious virus could be detected after a 5-min incubation at room temperature (22°C)

A) Temperature*

Time	Virus titre (Log $TCID_{50}$/mL)									
	4°C		22°C		37°C		56°C		70°C	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
1 min	N.D.	N.D.	6.51	0.27	N.D.	N.D.	6.65	0.1	5.34	0.17
5 mins	N.D.	N.D.	6.7	0.15	N.D.	N.D.	4.62	0.44	U	-
10 mins	N.D.	N.D.	6.63	0.07	N.D.	N.D.	3.84	0.32	U	-
30 mins	6.51	0.27	6.52	0.28	6.57	0.17	U	-	U	-
1 hr	6.57	0.32	6.33	0.21	6.76	0.05	U	-	U	-
3 hrs	6.66	0.16	6.68	0.46	6.36	0.19	U	-	U	-
6 hrs	6.67	0.04	6.54	0.32	5.99	0.26	U	-	U	-
12 hrs	6.58	0.21	6.23	0.05	5.28	0.23	U	-	U	-
1 day	6.72	0.13	6.26	0.05	3.23	0.05	U	-	U	-
2 days	6.42	0.37	5.83	0.28	U	-	U	-	U	-
4 days	6.32	0.27	4.99	0.18	U	-	U	-	U	-
7 days	6.65	0.05	3.48	0.24	U	-	U	-	U	-
14 days	6.04	0.18	U	-	U	-	U	-	U	-

B) Surfaces*

Time	Virus titre (Log $TCID_{50}$/ml)									
	Paper		Tissue paper		Wood		Cloth		Glass	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
0 min	4.76	0.10	5.48	0.10	5.66	0.39	4.84	0.17	5.83	0.04
30 mins	2.18	0.05	2.19	0.17	3.84	0.39	2.84	0.24	5.81	0.27
3 hrs	U	-	U	-	3.41	0.26	2.21#	-	5.14	0.05
6 hrs	U	-	U	-	2.47	0.23	2.25	0.08	5.06	0.31
1 day	U	-	U	-	2.07#	-	2.07#	-	3.48	0.37
2 days	U	-	U	-	U	-	U	-	2.44	0.19
4 days	U	-	U	-	U	-	U	-	U	-
7 days	U	-	U	-	U	-	U	-	U	-

Time	Banknote		Stainless steel		Plastic		Mask, inner layer		Mask, outer layer	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
0 min	6.05	0.34	5.80	0.02	5.81	0.03	5.88	0.69	5.78	0.10
30 mins	5.83	0.29	5.23	0.05	5.83	0.04	5.84	0.18	5.75	0.08
3 hrs	4.77	0.07	5.09	0.04	5.33	0.22	5.24	0.08	5.11	0.29
6 hrs	4.04	0.29	5.24	0.08	4.68	0.10	5.01	0.50	4.97	0.51
1 day	3.29	0.60	4.85	0.20	3.89	0.33	4.21	0.08	4.73	0.05
2 days	2.47	0.23	4.44	0.20	2.76	0.10	3.16	0.07	4.20	0.07
4 days	U	-	3.26	0.10	2.27	0.09	2.47	0.28	3.71	0.50
7 days	U	-	U	-	U	-	U	-	2.79	0.46

Alex W H Chin Lancet Microbe 3 April 2020

Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study

- To estimated the viral loads in more than 3000 samples collected from 96 patients infected with SARS-CoV-2, and analysed the temporal change in viral loads and the correlation between viral and severity
- 3497 respiratory, stool, serum, and urine samples were collected
- The median duration of virus in stool (22 days, interquartile range 17-31 days) was significantly longer than in respiratory (18 days, 13-29 days; P=0.02) and serum samples (16 days, 11-21 days; P<0.001). The median duration of virus in the respiratory samples of patients with severe disease (21 days, 14-30 days) was significantly longer than in patients with mild disease (14 days, 10-21 days; P=0.04).

Table 2 | Detection of severe acute respiratory syndrome coronavirus 2 in patients with mild or severe disease at different stages after symptom onset in different sample types. Values are numbers affected/number tested (%) unless stated otherwise

		Weeks since onset of symptoms				
Sample types	After admission	1	2	3	4	P values
All patients:						
Respiratory	96/96 (100)	42/44 (95)	74/90 (82)	64/89 (72)	31/57 (54)	<0.001
Stool	55/93 (59)	9/23 (39)	28/59 (47)	32/71 (45)	20/57 (35)	0.54
Serum	39/95 (41)	5/36 (14)	20/85 (23)	19/85 (22)	5/55 (9)	0.12
Urine	1/67 (1)	0/15 (0)	1/53 (2)	0/21 (0)	0/19 (0)	NC
Mild disease:						
Respiratory	22/22 (100)	11/12 (92)	15/21 (71)	9/19 (47)	4/9 (44)	0.04
Stool	13/22 (59)	2/7 (29)	8/16 (50)	10/17 (59)	5/9 (56)	0.62
Serum	6/22 (27)	0/9 (0)	3/19 (16)	2/17 (12)	0/8 (0)	0.67
Urine	0/19 (0)	0/3 (0)	0/15 (0)	0/7 (0)	0/3 (0)	NC
Severe disease:						
Respiratory	74/74 (100)	31/32 (97)	59/69 (86)	55/70 (79)	27/48 (56)	<0.001
Stool	42/71 (59)	7/16 (44)	20/43 (47)	22/54 (41)	15/48 (31)	0.49
Serum	33/73 (45)	5/27 (19)	17/66 (26)	17/68 (25)	5/47 (11)	0.20
Urine	1/48 (2)	0/12 (0)	1/38 (3)	0/14 (0)	0/16 (0)	NC

NC=not calculable.

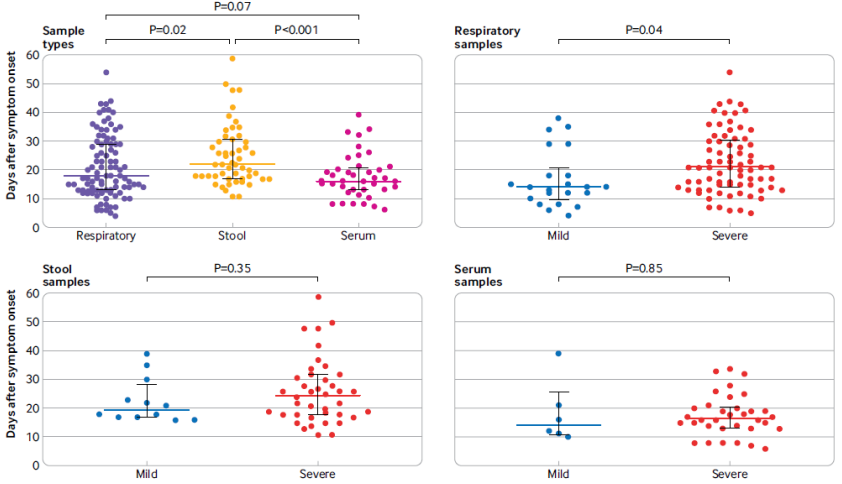
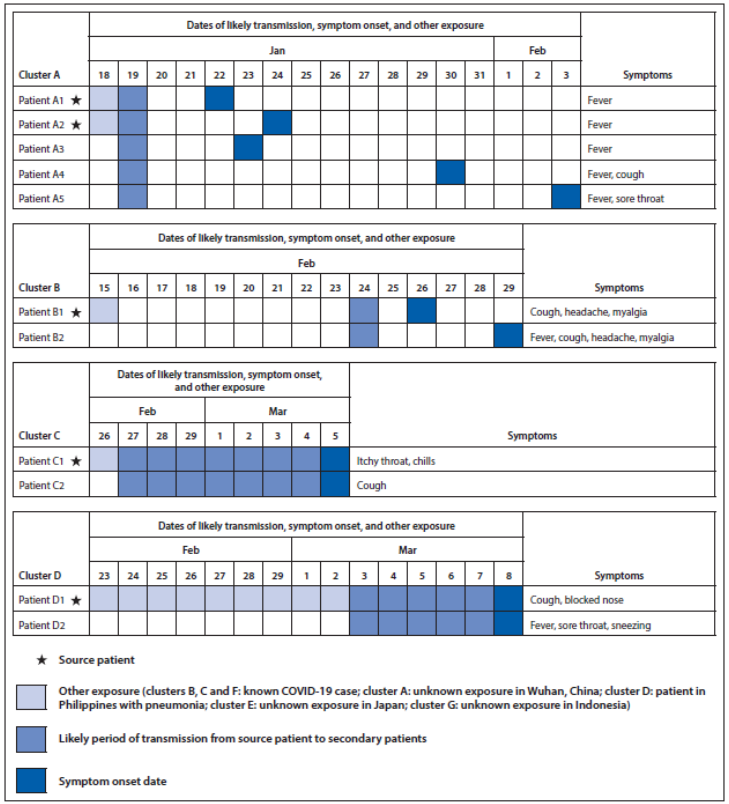


Fig 1 | Duration of detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by sample types and disease severity. Coloured bars represent medians and black bars represent interquartile ranges

Shufa Zheng, BMJ 6 April 2020

Presymptomatic Transmission of SARS-CoV-2
Singapore, January 23–March 16, 2020

- Presymptomatic transmission was defined as the transmission of SARS-CoV-2 from an infected person (source patient) to a secondary patient before the source patient developed symptoms
- Seven COVID-19 epidemiologic clusters in which presymptomatic transmission likely occurred were identified
- In the four clusters for which the date of exposure could be determined, presymptomatic transmission occurred 1–3 days before symptom onset in the presymptomatic source patient.
- Among the 243 cases of COVID-19 reported in Singapore as of March 16, 157 were locally acquired; 10 of the 157 (6.4%) locally acquired cases are included in these clusters and were attributed to presymptomatic transmission.
- 12.6% of transmissions could have occurred before symptom onset in the source patient



Wycliffe E. Wei MMWR 10 April 2020

nature medicine

Temporal dynamics in viral shedding and transmissibility of COVID-19

EUCIC
EUROPEAN COMMITTEE ON INFECTION CONTROL

- Objectives: Comparison of clinical data on virus shedding with separate epidemiologic data on incubation periods and serial intervals between cases
- 94 patients with laboratory-confirmed COVID-19
  - 61/93 (66%) were moderately ill, none were classified as ‘severe’ or ‘critical’ on hospital admission
  - 414 throat swabs collected from symptom onset up to 32 days after onset
- High viral loads soon after symptom onset, which then gradually decreased towards the detection limit at about day 21.
- Serial interval: mean of 5.8 days (95% CI, 4.8–6.8 days) and a median of 5.2 days (95% CI, 4.1–6.4 days)
- Infectiousness started from 2.3 days (95% CI, 0.8–3.0 days) before symptom onset and peaked at 0.7 days (95% CI, −0.2–2.0 days) before symptom
  - Proportion of presymptomatic transmission (area under the curve) was 44% (95% CI, 25–69%). Infectiousness was estimated to decline quickly within 7 days. Sensitivity analysis: infectiousness from 1 to 7 days before symptom onset, infectiousness was shown to peak at 0–2 days before symptom onset, and the proportion of presymptomatic transmission ranged from 46% to 55%.
  - Viral shedding may begin 2 to 3 days before the appearance of the first symptoms.
  - Virus was detected for a median of 20 days (up to 37 days among survivors) after symptom onset but infectiousness may decline significantly 8 days after symptom onset, as live virus could no longer be cultured

Xi He Nature 15 April 2020

nature medicine

Temporal dynamics in viral shedding and transmissibility of COVID-19

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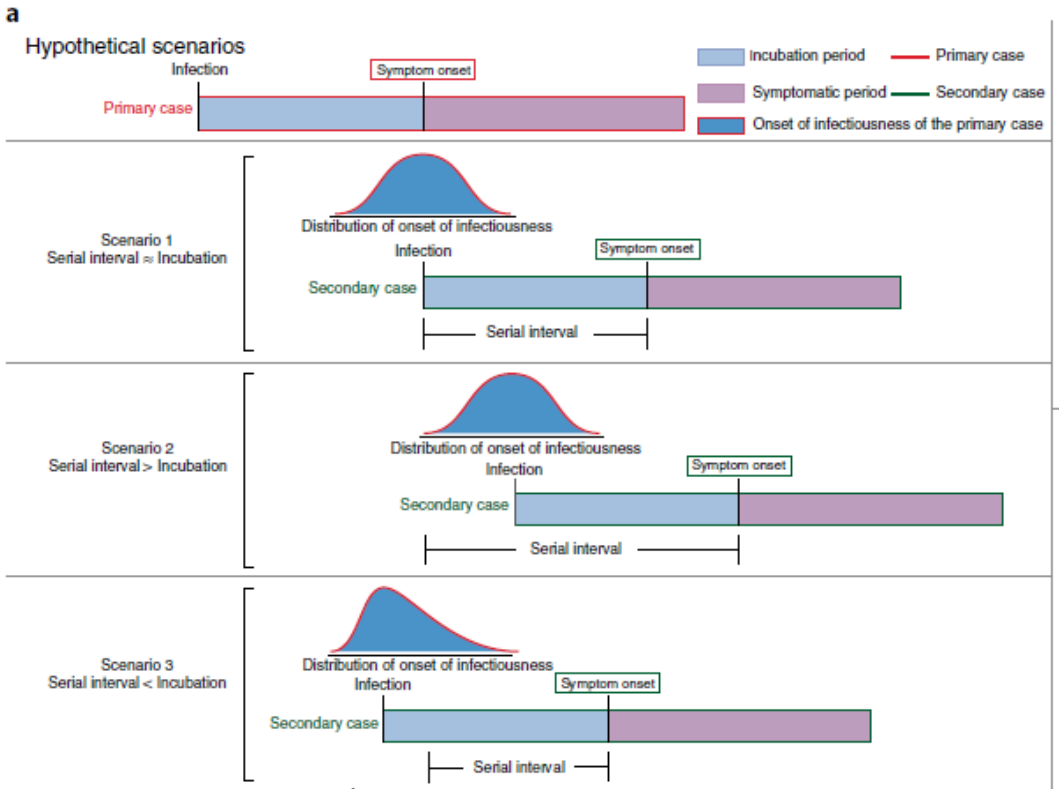

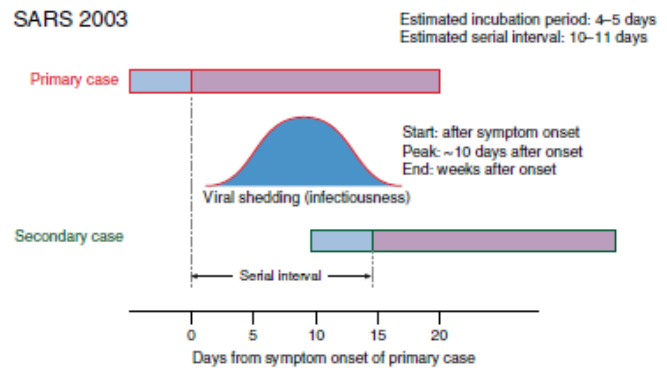

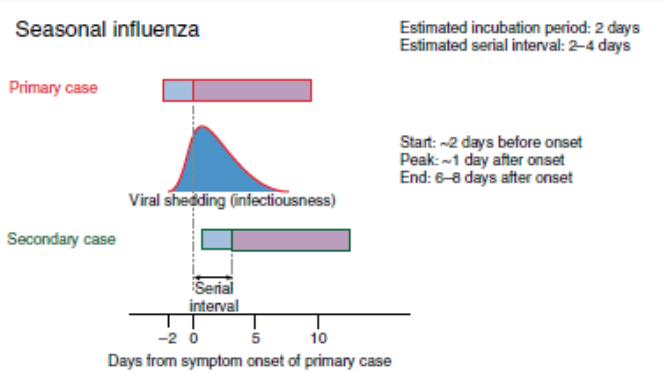

Xi He Nature 15 April 2020

The Journal of Infectious Diseases

Airborne or droplet precautions for health workers treating COVID-19?

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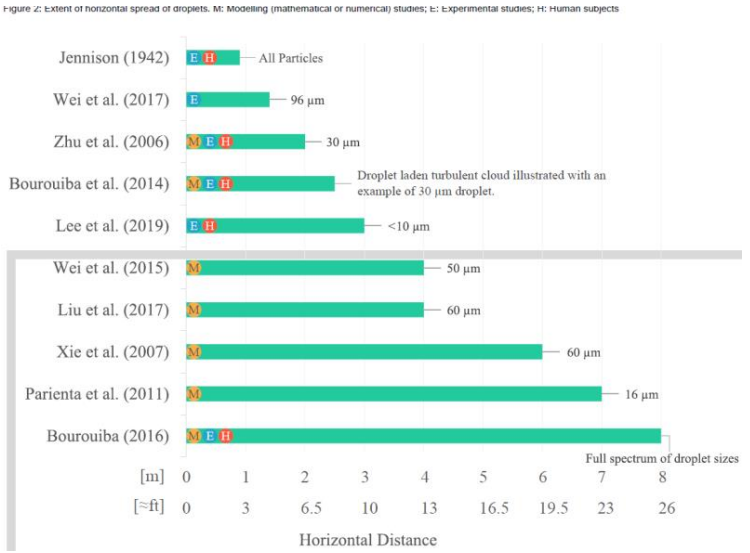
- Objective: to review the evidence for horizontal distance travelled by droplets and the guidelines issued by the WHO, US CDC and ECDC on respiratory protection for COVID-19.
- 10 studies: Seven out of ten studies are based on modelling
- Available data do not support the 1 – 2 m (≈3 – 6 ft) rule of spatial separation.
  - 8/10 studies on horizontal droplet distance showed droplets travel more than 2 m (≈6 ft), in some cases more than 8 meters (≈26 ft).
  - Several studies of SARS-CoV-2 support aerosol transmission and one study documented virus at a distance of 4 meters (≈13 ft) from the patient.
- Evidence suggests infections cannot neatly be separated into the dichotomy of droplet versus airborne transmission routes. Available studies also show that SARS-CoV-2 can be detected in the air, 3 hours after aeroslisation.
- Relative humidity plays an important role in the evaporation of the droplets and the distance a droplet can travel
- The weight of combined evidence supports airborne precautions for the occupational health and safety of health workers treating patients with COVID-19.



Prateek Bahl JID 16 April 2020

Symptom Screening at Illness Onset of Health Care PersonnelWith SARS-CoV-2 Infection in King County, Washington

- Assessment of symptoms at onset of COVID-19 among HCP and evaluated current screening criteria for identifying COVID-19 cases early in illness course.
- 48 HCP interviewed :
  - Median age was 43 years (range, 22-79 years); 37 (77.1%) were female.
  - Most of the HCP (37 [77.1%]) performed direct patient care
  - 23 (47.9%) had chronic medical conditions.
  - 22 health care settings including long-term care facilities (24 [50.0%]), outpatient clinics (13 [27.1%]), and acute care hospitals (6 [12.5%]).
- Most common initial symptoms were: Cough (24 [50.0%]), fever (20 [41.7%]), andmyalgias (17 [35.4%])
- 8(16.7%) did not report fever, cough, shortness of breath, or sore throat at symptom onset; among this group, the most common symptoms were chills, myalgia, coryza, and malaise.

Figure. Symptom Screening Combination for Health Care Personnel With Coronavirus Disease 2019 at Illness Onset (N = 48)

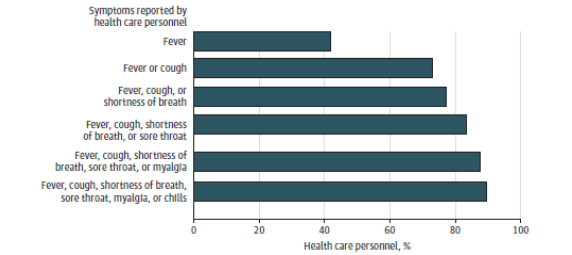


Table. Clinical Course and Outcomes of Health Care Personnel With Confirmed SARS-CoV-2 Infection–King County, Washington

	No. (%)		
	Total health care personnel (N = 48)	Onset with fever, cough, shortness of breath, or sore throat (n = 40 [83.3%])	Onset without fever, cough, shortness of breath, or sore throat (n = 8 [16.7%])
Initial symptoms			
Cough	24 (50.0)	24 (60.0)	0
Fever[a]	20 (41.7)	20 (50.0)	0
Myalgias	17 (35.4)	15 (37.5)	2 (25.0)
Headache	8 (16.7)	7 (17.5)	1 (12.5)
Chills	7 (14.6)	5 (12.5)	2 (25.0)
Sore throat	7 (14.6)	7 (17.5)	0
Coryza	6 (12.5)	4 (10.0)	2 (25.0)
Shortness of breath	5 (10.4)	5 (12.5)	0
Malaise	5 (10.4)	3 (7.5)	2 (25.0)
Diarrhea	3 (6.3)	3 (7.5)	0
Voice hoarseness	2 (4.2)	1 (2.5)	1 (12.5)
Anorexia	1 (2.1)	1 (2.5)	0
Nausea/vomiting	1 (2.1)	1 (2.5)	0
Abdominal pain	1 (2.1)	0	1 (12.5)
Symptoms over illness course			
Cough	42 (87.5)	36 (90.0)	6 (75.0)
Fever[a]	36 (75.0)	32 (80.0)	4 (50.0)
Myalgias	29 (60.4)	25 (62.5)	4 (50.0)
Headache	20 (41.7)	17 (42.5)	3 (37.5)
Chills	16 (33.3)	14 (35.0)	2 (25.0)
Diarrhea	16 (33.3)	13 (32.5)	3 (37.5)
Shortness of breath	15 (31.3)	13 (32.5)	2 (25.0)
Malaise	14 (29.2)	9 (22.5)	5 (62.5)
Sore throat	12 (25.0)	10 (25.0)	2 (25.0)
Coryza	10 (20.8)	8 (20.0)	2 (25.0)
Nausea/vomiting	8 (16.7)	6 (15.0)	2 (25.0)
Anorexia	3 (6.3)	3 (7.5)	0
Voice hoarseness	2 (4.2)	1 (2.5)	1 (12.5)
Abdominal pain	1 (2.1)	0	1 (12.5)
Outcomes			
Hospitalized	3 (6.3)	3 (7.5)	0
Intensive care unit admission	0	0	0
Death	0	0	0
Worked while symptomatic[b]	31 (64.6)	27 (67.5)	4 (50.0)
Days worked while symptomatic, median (range)	2 (1-10)	2 (1-10)	2.5 (1-5)
Days from symptom onset to resolution of all symptoms, median (range)	10 (1-21)	10 (1-21)	4 (3-18)

Eric Chow JAMA 17 April 2020

Positive RT-PCR Test Results in Patients Recovered From COVID-19

- 1 hospitalized patient and 3 patients (all medical personnel) quarantined at home with COVID-19 evaluated RT-PCR (throat swabs) to determine if they could return to work.
- Criteria to meet for hospital discharge or discontinuation of quarantine:
  - normal temperature lasting longer than 3 days,
  - resolved respiratory symptoms,
  - substantially improved acute exudative lesions on chest computed tomography (CT) images, and (
  - 2 consecutively negative RT-PCR test results separated by at least 1 day.
- Among patients:
  - 3 with fever, cough, or both occurred at onset. One patient was initially asymptomatic and underwent thin section CT due to exposure to infected patients. All patients had positive RT-PCR test results and CT imaging showed ground-glass opacification or mixed ground-glass opacification and consolidation.
  - Antiviral treatment: 75mg of oseltamivir taken orally every 12 hours for the 4 patients. For 3 of the patients, all clinical symptoms and CT imaging abnormalities resolved.
- All 4 patients had 2 consecutive negative RT-PCR test results. The time from symptom onset to recovery ranged from12 to 32 days.
- After hospital discharge or discontinuation of quarantine,
  - RT-PCR tests repeated 5 to 13 days later and all were positive.
  - 3 repeat RT-PCR tests performed over the next 4 to 5 days and all were positive.
  - additional RT-PCR test was performed using a kit from a different manufacturer and the results were also positive for all patients.
  - The patients continued to be asymptomatic by clinician examination and chest CT findings showed no change from previous images.
  - They did not report contact with any person with respiratory symptoms. No family member was infected.

Lan Lan JAMA 21 April 2020

Antibody responses to SARS-CoV-2 in patients with COVID-19

- 285 patients with COVID-19 from three designated hospitals; 70 had sequential samples available
  - IgG : 100% approximately 17–19 days after symptom onset,
  - IgM : peak of 94.1% approximately 20–22 days after symptom onset
- First 3 weeks after symptom onset: increases in IgG and IgM antibody titers
  - IgM showed a slight decrease in the >3-week group compared to the ≤3-week group
- 63 patients followed up until discharge. Serum samples collected at 3-day intervals.
  - Seroconversion rate was 96.8% (61/63) over the follow-up period.
  - median day of seroconversion for both IgG and IgM was 13 days post symptom onset.
    - Synchronous seroconversion of IgG and IgM (nine patients),
    - IgM seroconversion earlier than that of IgG (seven patients)
    - IgM seroconversion later than that of IgG (ten patients)
- No association between plateau IgG levels and the clinical characteristics of the patients
- Criteria for the confirmation of MERS-CoV infection suitable for most patients with COVID- 19.
- Collection of the first serum sample as early as possible is required for some patients to meet these criteria, because 12.2% (5/41) of the patients had already plateaued in IgG titer within 7 days of symptom onset
- For patients not sampled during the ideal window, repeated serological tests would be needed to confirm an antibody response to SARS-CoV-2 infection.

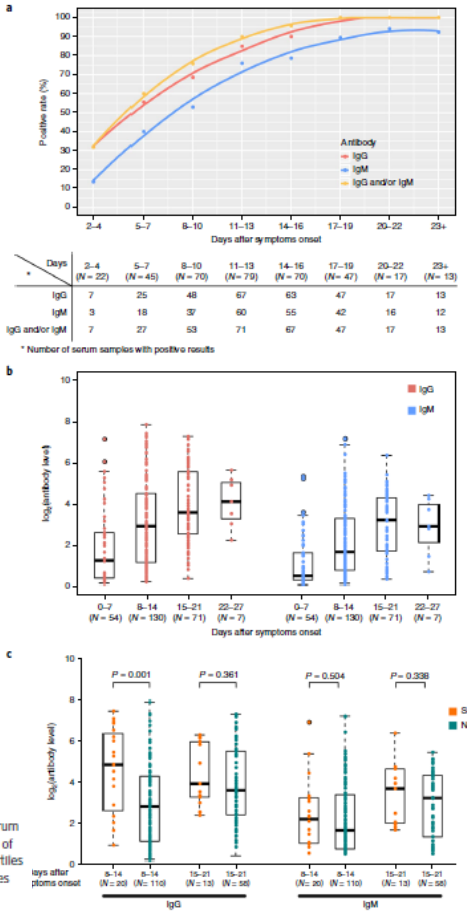


Fig. 1 | Antibody responses against SARS-CoV-2. **a**, Graph of positive rates of virus-specific IgG and IgM versus days after symptom onset in 363 serum samples from 262 patients. **b**, Levels of antibodies against SARS-CoV-2 in patients at different times after symptom onset. **c**, Comparison of the level of antibodies against SARS-CoV-2 between severe and non-severe patients. The boxplots in **b** and **c** show medians (middle line) and third and first quartiles (boxes), while the whiskers show 1.5× the interquartile range (IQR) above and below the box. Numbers of patients (*N*) are shown underneath. *P* values were determined with unpaired, two-sided Mann–Whitney *U*-test.

Quan-Xin Long Nature 29 April

Science

Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2)

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- To assess the full epidemic potential of SARS-CoV-2, we use a model-inference framework to estimate the contagiousness and proportion of undocumented infections in China during the weeks before and after the shutdown of travel in and out of Wuhan
- Mathematical model that simulates the spatiotemporal dynamics of infections among 375 Chinese cities
  - Documented infected individuals with symptoms severe enough to be confirmed, i.e., observed infections;
  - undocumented infected individuals.

- 86% of all infections were undocumented [95% CI: 82–90%] before the 23 January 2020 travel restrictions.
- The transmission rate of undocumented infections per person was 55% the transmission rate of documented infections (95% CI: 46–62%), yet, because of their greater numbers, undocumented infections were the source of 79% of the documented cases.
- a radical increase in the identification and isolation of
- currently undocumented infections would be
- needed to fully control SARS-CoV-2.

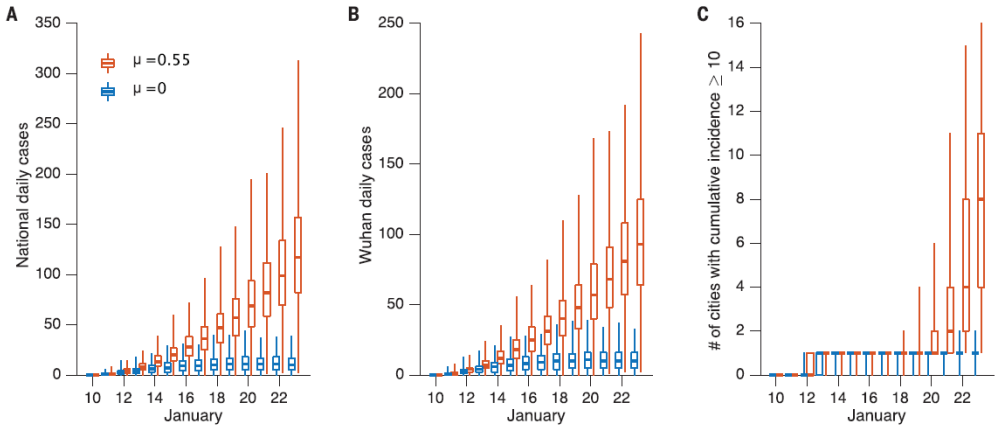
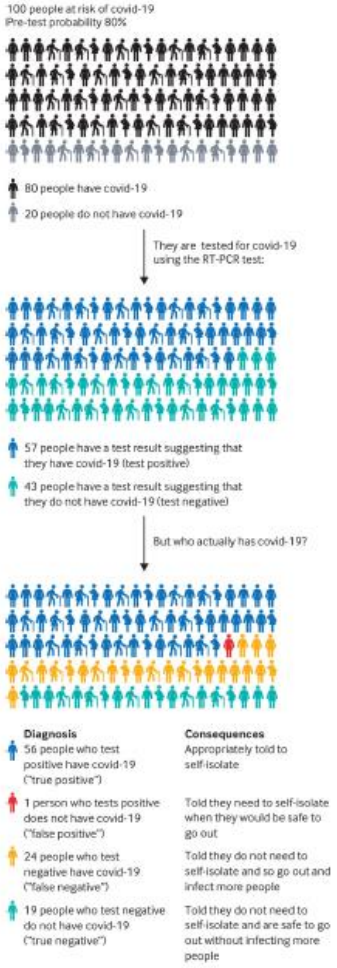


Fig. 2. Impact of undocumented infections on the transmission of SARS-CoV-2. Simulations generated using the parameters reported in Table 1 with μ = 0.55 (red) and μ = 0 (blue) showing daily documented cases in all cities (**A**), daily documented cases in Wuhan city (**B**), and the number of cities with ≥10 cumulative documented cases (**C**). The box and whiskers show the median, interquartile range, and 95% CIs derived from 300 simulations.

Ruiyun Li, Science 1 May 2020

Interpreting a covid-19 test result



1. Estimate a pre-test probability, using knowledge of local rates of covid-19 infection from national and regional data and patients' symptoms and signs, likelihood of alternative diagnoses, and history of exposure to covid-19.
2. Probability on the x axis, one should then trace up to either the upper curve for a positive test result or the lower curve for a negative test result, then trace over to the y axis to read the estimate for post-test probability.
3. Figure 1 shows that the shift in the probability is asymmetric, with a positive test result having a greater impact than a negative test result, owing to the modest sensitivity and negative likelihood ratio of the RNA test.

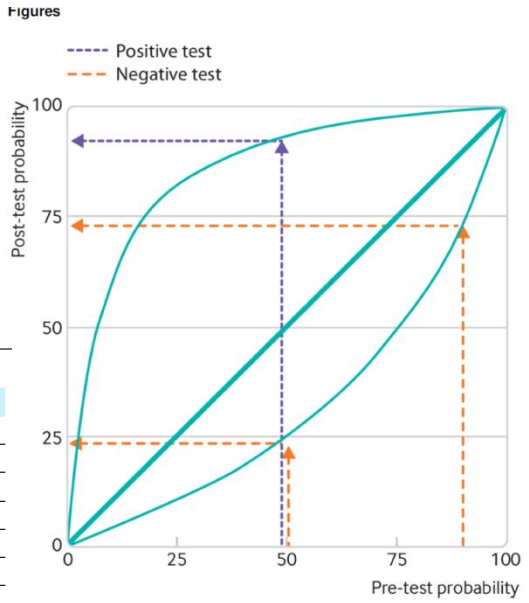


Table 1| **Pre- and post- test probabilities for covid-19 RT-PCR tests, calculations based on a sensitivity of 70% and specificity of 95%**

Pre-test probability	Post-test probability, negative test	Post-test probability, two independently negative tests	Post-test probability positive test
5	1.6	0.5	42
15	5	2	71
25	10	3	82
50	24	9	93
75	49	23	98
90	74	47	99

Pre-test probability is high in someone with typical symptoms of covid-19, an occupational risk of exposure, and working in a high prevalence region, and negative test results can therefore be misleading. Table 1 shows that for a pre-test probability of 90%, someone with a negative test has a 74% chance of having covid-19; with two negative tests this risk is still around 47%.

Jessica Watson BMJ 12 May 2020

THE LANCET
Infectious Diseases

Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays

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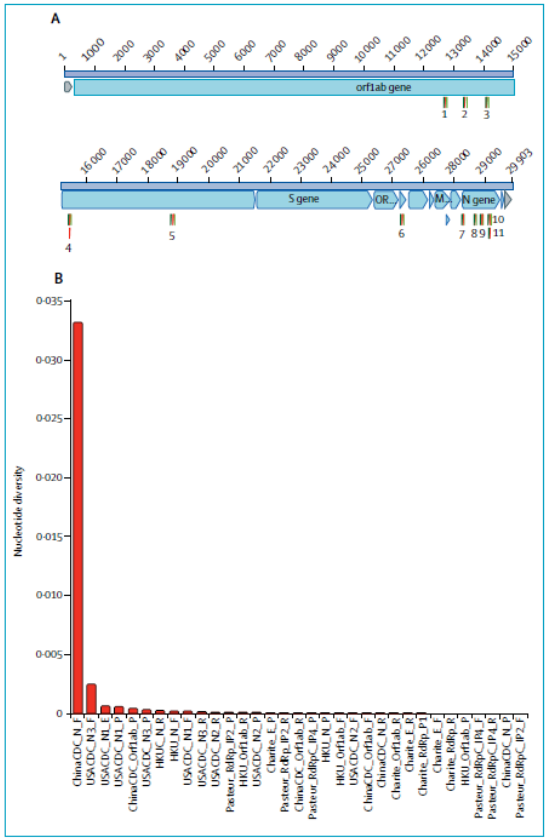
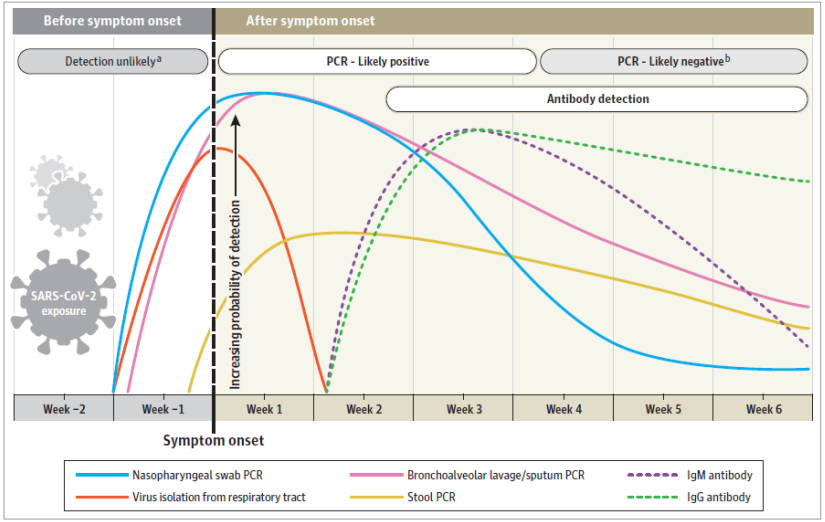


- Analysis of all high coverage SARS-CoV-2 genome sequences (1825 in total) deposited in the Global Initiative on Sharing All Influenza Data (GISAID) database
- We aligned the sequences against the reference sequence obtained from the Wuhan seafood market pneumonia virus isolate, Wuhan-Hu-1 (NC_045512).
- Subsequently, we annotated in the alignments the binding sites of 33 oligonucleotides developed by different centres and shared by WHO for use in the RT-qPCR detection of SARS-CoV-2 from human samples
- 79% (26 of 33) of the primer binding sites used in the RT-qPCR assays were mutated in at least one genome the observation that at least one of the previously designed primers is now likely to be ineffective at detecting up to 14% of the virus variants in circulation strengthens the need to continue optimizing the oligonucleotides in use in assays being developed.

Nuno Sampaio Osório Lancet Infect Dis 28 May 2020

Interpreting Diagnostic Tests for SARS-CoV-2

Figure. Estimated Variation Over Time in Diagnostic Tests for Detection of SARS-CoV-2 Infection Relative to Symptom Onset



Estimated time intervals and rates of viral detection are based on data from several published reports. Because of variability in values among studies, estimated time intervals should be considered approximations and the probability of detection of SARS-CoV-2 infection is presented qualitatively. SARS-CoV-2 indicates severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction.

[a] Detection only occurs if patients are followed up proactively from the time of exposure.

[b] More likely to register a negative than a positive result by PCR of a nasopharyngeal swab.

RT-PCR

- RNA gene targeted: the envelope (env), nucleocapsid (N), spike (S), RNA-dependent RNA polymerase (RdRp), and ORF1 genes.
- Cycle threshold (Ct<40) detectable day 1 of symptoms and **peaks within the first week**. Positivity starts to **decline by week 3** and subsequently becomes undetectable. Viral RNA has been detected by RT-PCR even beyond **week 6** following the first positive test.
- Study of 9 patients: None isolate of virus in culture beyond day 8 of illness onset,
  - CDC: health care workers can return to work, if "at least **3 days** (72 hours) have passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and, at least **10 days** have passed since symptoms first appeared.
- PCR positivity
  - Declines more slowly in sputum and may still be positive after nasopharyngeal swabs are negative.
  - PCR positivity in stool was observed in 55 of 96 (57%) infected patients and remained positive in stool beyond nasopharyngeal swab by a median of 4 to 11 days, but was unrelated to clinical severity.
  - Highest in bronchoalveolar lavage specimens (93%), followed by sputum (72%), nasal swab (63%), and pharyngeal swab (32%)
  - False-negative results mainly occurred due to inappropriate timing of sample collection in relation to illness onset and deficiency in sampling technique, especially of nasopharyngeal swabs

Serology

- Important for patients with mild to moderate illness , and to understand the extent of COVID-19 in the community and to identify individuals who are immune and potentially "protected" from becoming infected.
- Higher levels occur in the second and third week of illness: Begin to increase from the second week of symptom onset, although Ig M and IgG ELISA have been found to be positive even as early as the fourth day after symptom onset
- Study of 140 patients, combined sensitivity of PCR and IgM ELISA was 98.6% vs 51.9% with a single PCR test. During the first 5.5 days, quantitative PCR had a higher positivity rate than IgM, whereas IgM ELISA had a higher positivity rate after day 5.5 of illness.
- Testing of paired serum samples with the initial PCR and the second 2 weeks later can further increase diagnostic accuracy.

Nandini Sethuraman, JAMA 5 June 2020

The NEW ENGLAND JOURNAL of MEDICINE

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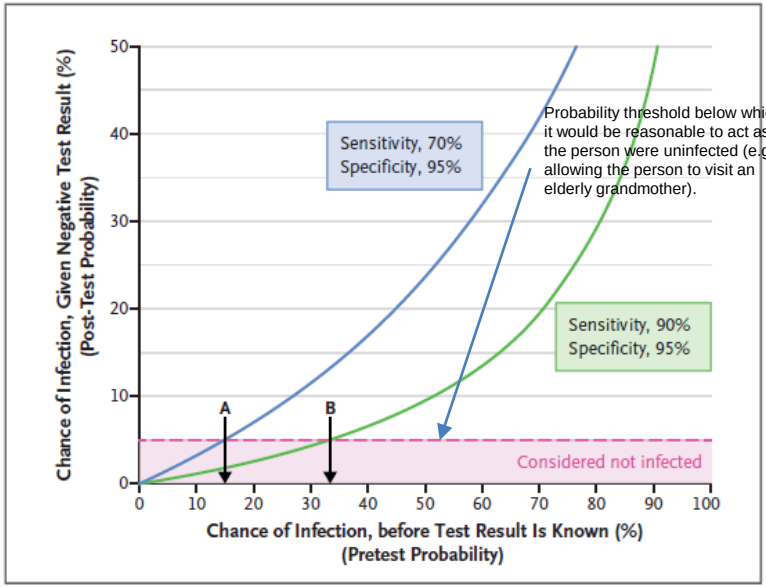
False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications

- Yang et al. 213 patients hospitalized with Covid-19, of whom 37 were critically ill:
  - 205 throat swabs, 490 nasal swabs, and 142 sputum samples
  - Days 1 through 7 after onset of illness, 11% of sputum, 27% of nasal, and 40% of throat samples were deemed falsely negative.
- Zhao et al. 173 hospitalized patients with acute respiratory symptoms and a chest CT "typical" of Covid-19:
  - SARS-CoV-2 detected in at least one respiratory specimen.
  - Antibody seroconversion was observed in 93%.
  - Days 1 through 7 of hospitalization: at least one sample from 67% of patients.
- Systematic review of five studies (not including the Yang and Zhao studies), involving 957 patients ("under suspicion of Covid-19" or with "confirmed cases")
  - False negatives ranged from 2 to 29%. Certainty of the evidence was considered very low
- For a negative test, there are two key inputs:
  - **Pretest probability:** estimate, before testing, of the person's chance of being infected, and test sensitivity.
  - Pretest probability: might depend on local Covid-19 prevalence, SARSCoV- 2 exposure history, and symptoms.
  - At a sensitivity level of 70% , with a pretest probability of 50%, the post-test probability with a negative test would be 23% — far too high to safely assume someone is uninfected.



The blue line represents a test with sensitivity of 70% and specificity of 95%. The green line represents a test with sensitivity of 90% and specificity of 95%. The shading is the threshold for considering a person not to be infected (asserted to be 5%). Arrow A indicates that with the lower-sensitivity test, this threshold cannot be reached if the pretest probability exceeds about 15%. Arrow B indicates that for the higher-sensitivity test, the threshold can be reached up to a pretest probability of about 33%.

Steven Woloshin NEJM 5 June

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals

- Sampled airborne SARS-CoV-2 and its aerosol deposition at 30 sites in two designated hospitals and public areas in Wuhan, to quantify the SARS-CoV-2 copy counts of aerosol samples using droplet digital PCR-based detection method.
- Patient Areas (PAA), with COVID-19 patients (i.e. ICU)
  - Highest concentration in **patient mobile toilet room** (19 copies m-3), which is a temporary single toilet room of approximate 1 m2 in area without ventilation
  - Higher deposition rate was in the hindrance-free corner of the room, approximately 3 m from the patient's bed; in another corner 2 m from the patient's bed and below medical equipment which may have blocked the path of virus aerosol sediments.
- Medical Staff Areas (MSA), the workplaces in the two hospitals exclusively accessed by the medical staff who had direct contact with the patients
  - Low concentration in Renmin Hospital of 6 copies m-3, while higher concentrations in Fangcang Hospital
- Public Areas (PUA), venues open for the general public
  - Very low concentrations of SARS-CoV-2 aerosol (below 3 copies m-3), except for one crowd gathering site about 1 m to the entrance of a department store with customers frequently passing through
- SARS-CoV-2 aerosol mainly resides in two size ranges,
  - Submicron region (dp between 0.25 to 1.0 μm): Patient area in Zone B and C of Fangcang Hospital
    - The source of the submicron peak is the resuspension of virus-laden aerosol from the surface of medical staff protective apparel while they are being removed
  - Supermicron region (dp > 2.5 μm): staff's office, Fangcang Hospital Zone C patient area
    - supermicron virus-laden aerosol and was carried across different areas by the medical staff

Yuan Liu Nature 28 May 2020

EMERGING INFECTIOUS DISEASES®

Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020

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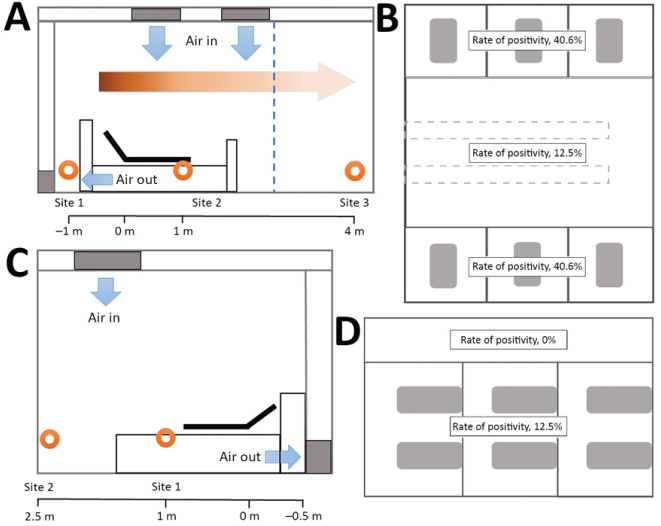
- Swab samples from potentially contaminated objects, indoor air and the air outlets in the ICU (15 patients with severe disease) and General Ward (24 patients with milder disease)
- Almost all surfaces positive results concentrated in the contaminated areas
  - ICU 54/57, 94.7%; GW 9/9, 100%
  - Rate of positivity: 43.5% ICU (54/124), 7.9% in GW (9/114),
    - floor swab samples (ICU 7/10, 70%; GW 2/13, 15.4%)
    - computer mice (ICU 6/8, 75%; GW 1/5, 20%),
    - trash cans (ICU 3/5, 60%; GW 0/8),
    - sickbed handrails (ICU 6/14, 42.9%; GW 0/12),
    - doorknobs (GW 1/12, 8.3%).
  - Half of the samples from the soles of the ICU medical staff shoes tested positive
- Air samples
  - ICU: Positive test results for 35% (14 samples positive/40 samples tested)
  - GW: 12.5% (2/16) of GW samples.
  - Air outlet swab samples also yielded positive test results, with positive rates of 66.7% (8/12) fo 8.3% (1/12) for GWs.
  - Rates of positivity were 35.7% (5/14) near air outlets, 44.4% (8/18) in patients' rooms, and 12.5% (1/8) in the doctors' office area

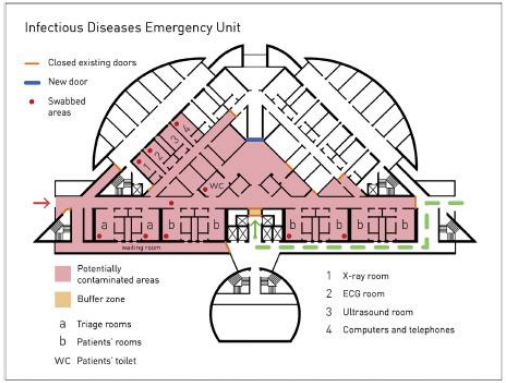


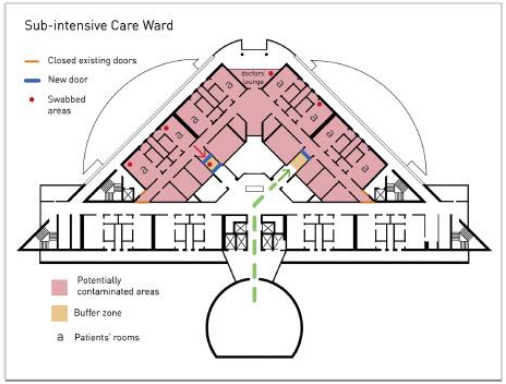
Zhen-Dong Guo EID 7 July 2020

Figure 2. Spatial distribution of severe acute respiratory syndrome coronavirus 2 aerosols in isolation wards of the intensive care unit (ICU) and the general ward at Huoshenshan Hospital, Wuhan, China. A) The air sampling sites in the ICU were distributed in different regions: near the air outlet (site 1), near the patients (site 2), and around the doctors' office area (site 3). Orange circles represent sampling sites; blue arrows represent direction of the fresh air flow; and the graded orange arrow and scale bar indicate the horizontal distance from the patient's head. B) In terms of viral aerosol distribution, the space in the ICU was divided into 2 parts: a high-risk area with a 40.6% rate of virus positivity and a low-risk area with a 12.5% rate of virus positivity. C) The air sampling sites in the general ward were distributed in different regions around the patient (site 1), under the air inlet (site 2), and in the patient corridor. D) In terms of the viral aerosol distribution, the space in the general ward was divided into 2 parts: a high-risk area with a 12.5% rate of virus positivity and a low-risk area with a 0% rate of virus positivity.

SARS-CoV-2 RNA contamination of inanimate surfaces and virus viability in a healthcare emergency unit

- To detect possible SARS-CoV-2 RNA contamination of inanimate surfaces in areas at high risk of aerosol formation by patients with COVID-19
- Surfaces samples with swabs, RT-PCR targeting RNA and E genes, + Virus isolation with Vero E6 cell
- Infectious Disease Emergency Unit, (febrile patients with respiratory symptoms), and infectious disease sub-intensive care ward.
  - Ward surfaces routinely cleaned twice daily with sodium hypochlorite
- 26 swabs collected, performed around 12 noon, approximately 4 hours after cleaning
  - Double room where two patients with CPAP helmets; emergency room, samples from two different rooms with three patients,
  - External surface of the CPAP helmet, the fomite closer to the face.
  - Two samples taken there were positive for SARS-CoV-2 RNA, very low RNA level.
    - Patient 1 treated with CPAP admitted 24 hours before swabbing and had a 10-day history of fever and cough.
    - Patient 2 admitted to the sub-intensive care unit for 3 days and had become symptomatic 12 days earlier.
    - Both patients had a positive nasal swab for SARSCoV-2 RNA on admission and both had pneumonia.
  - 24 samples, taken farther from the patient, were SARS-CoV-2 RNA negative.
- 26 samples inoculated onto Vero E6 cells: None induced a cytopathic effect on day 7 of culture. Supernatants collected on day 7 tested by real-time RT-PCR were all negative.





Marta Colaneri CMI 9 May 2020

Clinical Infectious Diseases

The natural history and transmission potential of asymptomatic SARS-CoV-2 infection

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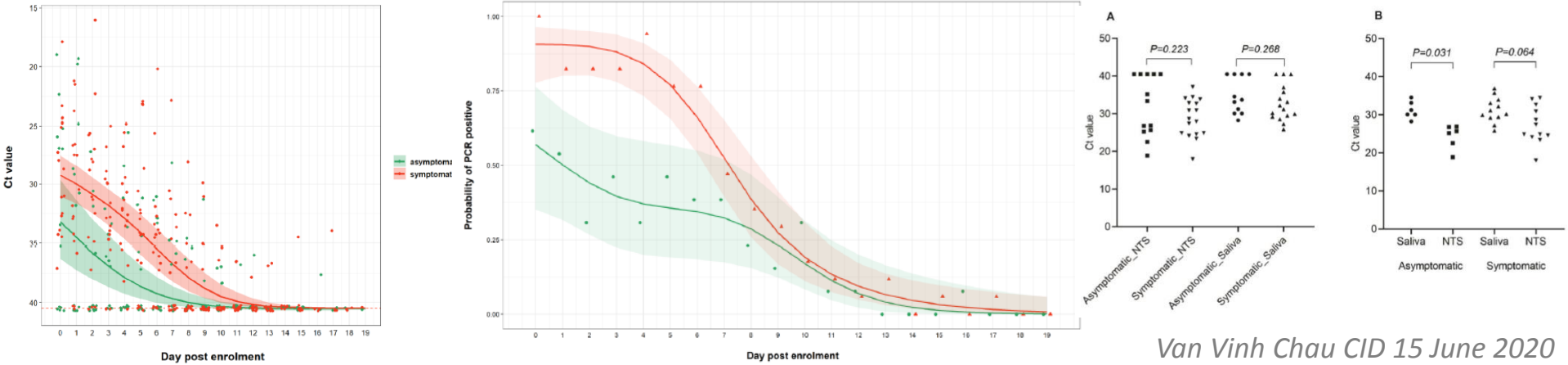
- To compare the duration of viral detection and abundance in the respiratory tract, including saliva, of asymptomatic and mildly symptomatic patients, and assess their ability to transmit the virus to others.
- Between March 10th and April 4th, 2020, 14,000 quarantined people were tested for SARS-CoV-2
  - For viral-load associated analysis, in the absence of quantitative RT-PCR results, we use cycle threshold (Ct) values as surrogates
- 49 people had a positive test, accounting for 96% (49/51) of all reported cases in HCMC during the same period.
  - 30 (30/33, 91%) agreed to participate in the clinical study



Van Vinh Chau CID 15 June 2020

Clinical Infectious Diseases

Characterization of an asymptomatic cohort of SARS-COV-2 infected individuals outside of Wuhan, China

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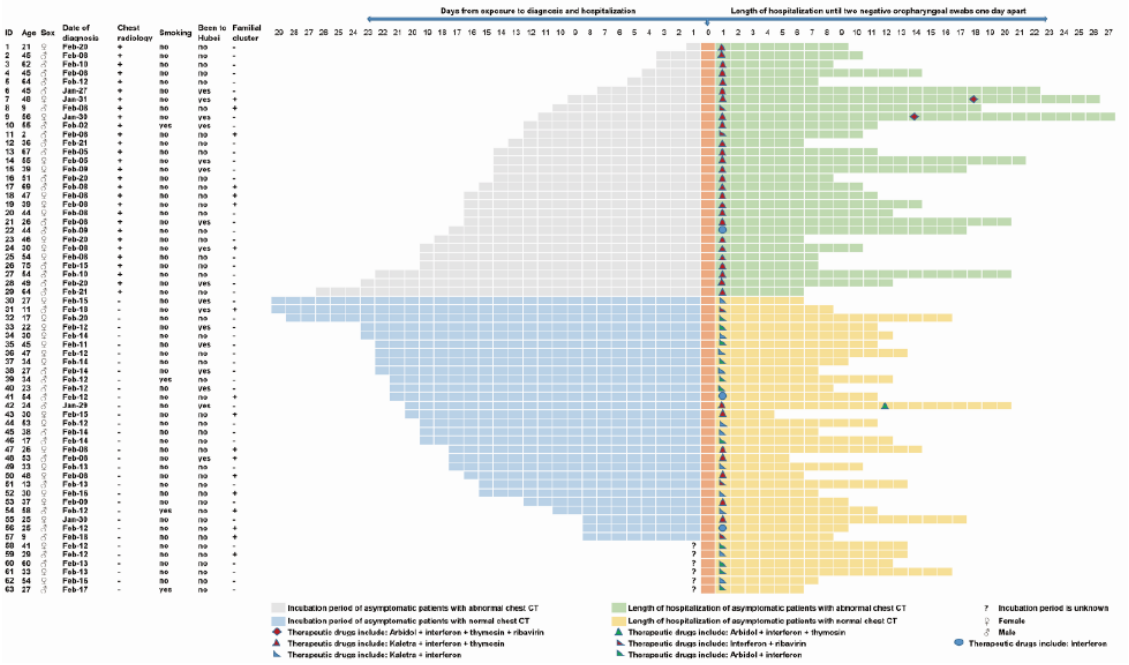
- Objective: to document the characteristics of asymptomatic infections and identify factors associated with asymptomatic infection, enabling the formulation of corresponding strategies and control measures.

- Results:
  - 279 RT-PCR+ contacts of COVID-19 patients
  - 63 (23%) remained asymptomatic until discharge; 29 had abnormal and 34 had normal chest CT findings
  - Mean latency between close contact and diagnosis was 16.0 days, with a maximum of 29 days.
  - 18 of the 63 asymptomatic cases (28.6%) had infection associated with familial clustering

A portion of these asymptomatic individuals, with and without abnormal chest CT scans, were capable of transmitting the virus to others.

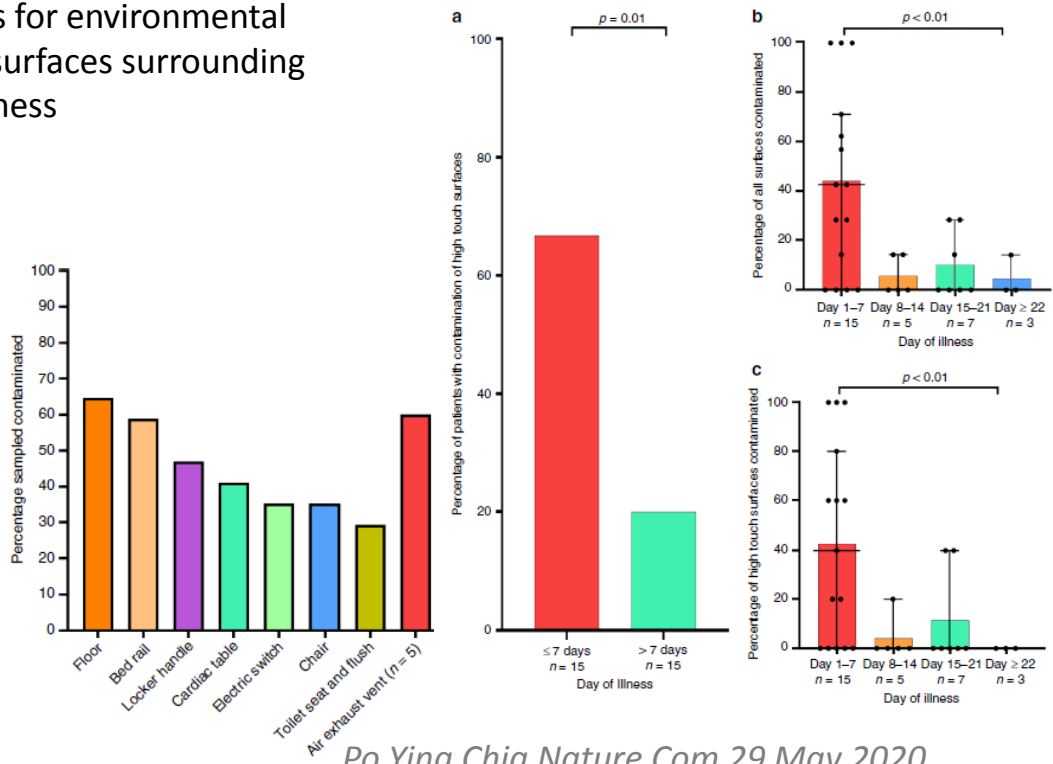


Yubo Wang CID 17 June 2020

Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients

Objective: To identify potential patient-level risk factors for environmental contamination by SARS-CoV-2 by sampling the air and surfaces surrounding hospitalized COVID-19 patients at different stages of illness

- Results
  - Seven patients (23%) asymptomatic at the time of environmental sampling, and 23 symptomatic patients
  - Environmental sampling in three airborne infection isolation rooms (AIIRs) in the ICU and 27 AIIRs in the general ward.
    - the floor was most likely to be contaminated (65%), followed by the air exhaust vent (60%, n = 5), bed rail (59%), and bedside locker (47%) (Fig. 1). Contamination of toilet seat and automatic toilet flush button was detected in 5 out of 27 rooms, and all 5 occupants had reported gastrointestinal symptoms within the preceding 1 week of sampling.
    - environmental surface contamination was higher
    - in week 1 of illness
  - Air sampling in three of the 27 AIIRs in the general ward
    - Air samples from two (66.7%) of three AIIRs tested positive for SARS-CoV-2, in particle sizes >4 μm and 1–4 μm in diameter



Po Ying Chia Nature Com 29 May 2020

Annals of Internal Medicine

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Prevalence of Asymptomatic SARS-CoV-2 Infection

Table. Summary of SARS-CoV-2 Testing Studies

Cohort	Tested, *n*	SARS-CoV-2 Positive, *n* (%)	Positive but Asymptomatic, *n* (%)	Notes*
Iceland residents (6)	13 080	100 (0.8)	43 (43.0)	R
Vo', Italy, residents (7)	5155	102 (2.0)	43 (42.2)	R, L
Diamond Princess cruise ship passengers and crew (8)	3711	712 (19.2)	331 (46.5)	–
Boston homeless shelter occupants (9)	408	147 (36.0)	129 (87.8)	–
New York City obstetric patients (11)	214	33 (15.4)	29 (87.9)	L
U.S.S. *Theodore Roosevelt* aircraft carrier crew (12)	4954	856 (17.3)	~500 (58.4)	E
Japanese citizens evacuated from Wuhan, China (2)	565	13 (2.3)	4 (30.8)	L
Greek citizens evacuated from the United Kingdom, Spain, and Turkey (14)†	783	40 (5.1)	35 (87.5)	L
Charles de Gaulle aircraft carrier crew (13)	1760	1046 (59.4)	~500 (47.8)	E
Los Angeles homeless shelter occupants (10)	178	43 (24.2)	27 (62.8)	–
King County, Washington, nursing facility residents (15)	76	48 (63.2)	3 (6.3)	L
Arkansas, North Carolina, Ohio, and Virginia inmates (16)	4693	3277 (69.8)	3146 (96.0)	–
New Jersey university and hospital employees (17)	829	41 (4.9)	27 (65.9)	–
Indiana residents (18)	4611	78 (1.7)	35 (44.8)	R
Argentine cruise ship passengers and crew (19)	217	128 (59.0)	104 (81.3)	–
San Francisco residents (29)	4160	74 (1.8)	39 (52.7)	–

E = estimated from incomplete source data; L = longitudinal data collected; R = representative sample.
* A dash indicates that the study did not have a representative sample, collected no longitudinal data, and did not require estimation of missing data.
† Clarified via e-mail communication with coauthor.

Daniel P. Oran Ann of Int Med 3 June 2020

nature medicine

Respiratory virus shedding in exhaled breath and efficacy of face masks

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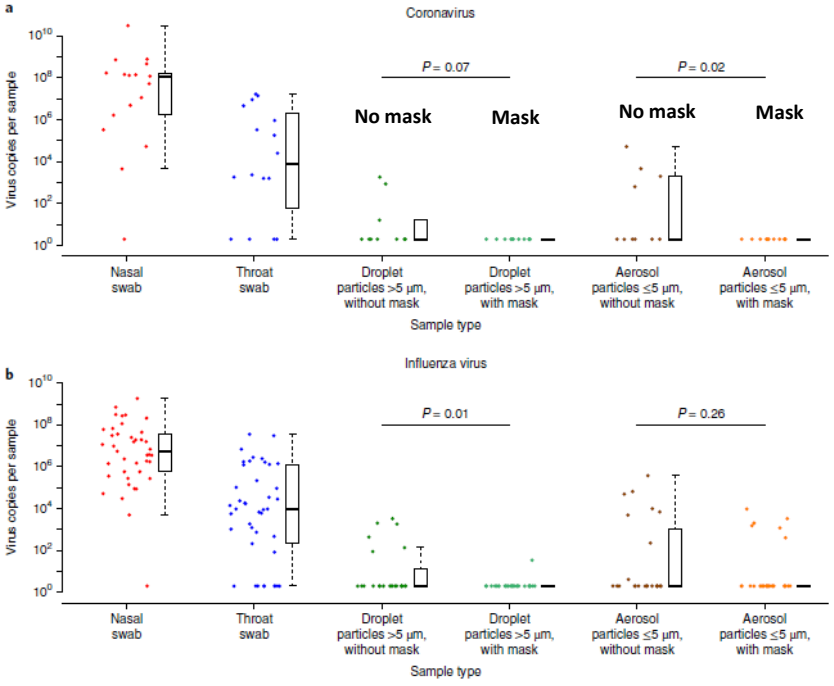
- Objective: To explore the importance of respiratory droplet and aerosol routes of transmission by quantifying the amount of respiratory virus in exhaled breath of participants with masks
- Results: 123 participants, 111 (90%) were infected by human (seasonal) coronavirus (n = 17), influenza virus (n = 43) or rhinovirus (n = 54)

Table 1b | Efficacy of surgical face masks in reducing respiratory virus frequency of detection and viral shedding in respiratory droplets and aerosols of symptomatic individuals with coronavirus, influenza virus or rhinovirus infection

	Droplet particles >5 µm			Aerosol particles ≤5 µm		
Virus type	Without surgical face mask	With surgical face mask	*P*	Without surgical face mask	With surgical face mask	*P*
	Detection of virus					
	No. positive/no. total (%)	No. positive/no. total (%)		No. positive/no. total (%)	No. positive/no. total (%)	
Coronavirus	3 of 10 (30)	0 of 11 (0)	0.09	**4 of 10 (40)**	**0 of 11 (0)**	**0.04**
Influenza virus	**6 of 23 (26)**	**1 of 27 (4)**	**0.04**	8 of 23 (35)	6 of 27 (22)	0.36
Rhinovirus	9 of 32 (28)	6 of 27 (22)	0.77	19 of 34 (56)	12 of 32 (38)	0.15
	Viral load (log_{10} virus copies per sample)					
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
Coronavirus	0.3 (0.3, 1.2)	0.3 (0.3, 0.3)	0.07	**0.3 (0.3, 3.3)**	**0.3 (0.3, 0.3)**	**0.02**
Influenza virus	**0.3 (0.3, 1.1)**	**0.3 (0.3, 0.3)**	**0.01**	0.3 (0.3, 3.0)	0.3 (0.3, 0.3)	0.26
Rhinovirus	0.3 (0.3, 1.3)	0.3 (0.3, 0.3)	0.44	1.8 (0.3, 2.8)	0.3 (0.3, 2.4)	0.12

P values for comparing the frequency of respiratory virus detection between the mask intervention were obtained by two-sided Fisher's exact test and (two-sided) *P* values for mask intervention as predictor of log_{10} virus copies per sample were obtained by an unadjusted univariate Tobit regression model, which allowed for censoring at the lower limit of detection of the RT-PCR assay, with significant differences in bold. Undetectable values were imputed as 0.3 log_{10} virus copies per sample. IQR, interquartile range.



Surgical face masks could prevent transmission of human coronaviruses and influenza viruses from symptomatic individuals.

Nancy H. L. Leung Nature Med May 2020

Cochrane Library
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Barriers and facilitators to healthcare workers' adherence with guidelines for respiratory infectious diseases

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EUROPEAN COMMITTEE ON INFECTION CONTROL

- 36 relevant studies and sampled 20 of these studies for our analysis.
  - 10 from Asia, four from Africa, four from Central and North America and two from Australia.
  - Experiences of nurses, doctors and other healthcare workers when dealing with SARS, H1N1, MERS, TB, or seasonal influenza.
- HCW felt
  - unsure to adhere when guidelines were long and ambiguous or did not reflect national or international guidelines.
  - overwhelmed because local guidelines were constantly changing.
  - motivated to follow the guidance because of fear of infecting themselves or their families, or because they felt responsible for their patients
  - A lack of isolation rooms, anterooms and shower facilities was a problem.
  - minimising overcrowding, fast-tracking infected patients,
  - restricting visitors, and providing easy access to handwashing facilities.
  - A lack of PPE, and equipment that was of poor quality, was a serious concern for healthcare workers and managers. They also pointed to the need to adjust the volume of supplies as infection outbreaks continued.
  - diFicult to use masks and other equipment when it made patients feel isolated, frightened or stigmatised.
  - masks and other equipment uncomfortable to use

Factors tied to the guideline itself and how it is communicated, support from managers, workplace culture, training, physical space, access to and trust in personal protective equipment, and a desire to deliver good patient care.

Houghton Cochrane Database of Systematic Reviews 2020

Face Masks Against COVID-19: An Evidence Review

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1. Do asymptomatic or presymptomatic patients pose a risk of infecting others?
2. Would a face mask likely decrease the number of people infected by an infectious mask wearer?

there is laboratory-based evidence that household masks have some filtration capacity in the relevant droplet size range, as well some efficacy in blocking droplets and particles from the wearer

3. Are there alternative face covers that will not disrupt the medical supply chain, e.g. homemade cloth masks?
4. Will wearing a mask impact the probability of the wearer becoming infected themselves?
5. Does mask use reduce compliance with other recommended strategies, such as physical distancing and quarantine?

near-universal adoption of non-medical masks when out in public, in combination with complementary public health measures could successfully reduce effective-R to below 1.0, thereby stopping community spread.

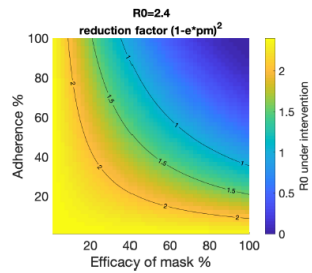

Fig. 1. Impact of public mask wearing under the full range of mask adherence efficacy scenarios. The color indicates the resulting reproduction number R_0 an initial R_0 of 2.4 (7).

Jeremy Howard PNAS 10 April 2020

Use of personal protective equipment against coronavirus disease 2019 by healthcare professionals in Wuhan, China: cross sectional study

Objective: To examine the protective effects of appropriate personal protective equipment for frontline healthcare professionals who provided care for patients with coronavirus disease 2019 (covid-19).

- 420 healthcare professionals included in this study consisted of 116 doctors and 304 nurses
- participants were equipped with standardised personal protective equipment, including protective suits, masks, gloves, goggles, face shields, and gowns
- no evidence was found of infection in any of the 420 participants as shown by negative test results for nucleic acids and specific IgM or IgG antibodies.

Table 2 | Personal protective equipment provided to study participants for prevention of covid-19

	Ward*			AGP† exposure	
Personal protective equipment	Intensive care units	Regular wards	No covid-19 contact area	AGPs	Non-AGPs
Mask:					
N95 respirator	+	+	-	+	+
Surgical mask	+	+	+	+	+
Medical suit	+	+	-	+	+
Isolation gown	+	+	-	+	+
Apron	-	-	-	+	-
Gloves	+	+	-	+	+
Eye protection	+	+	-	+	+
Hair cover	+	+	-	+	+

AGP=aerosol generating procedure; covid-19=coronavirus disease 2019.
*Overlap existed between the different wards.
†Powered air purifying respirator used when performing tracheal intubation.

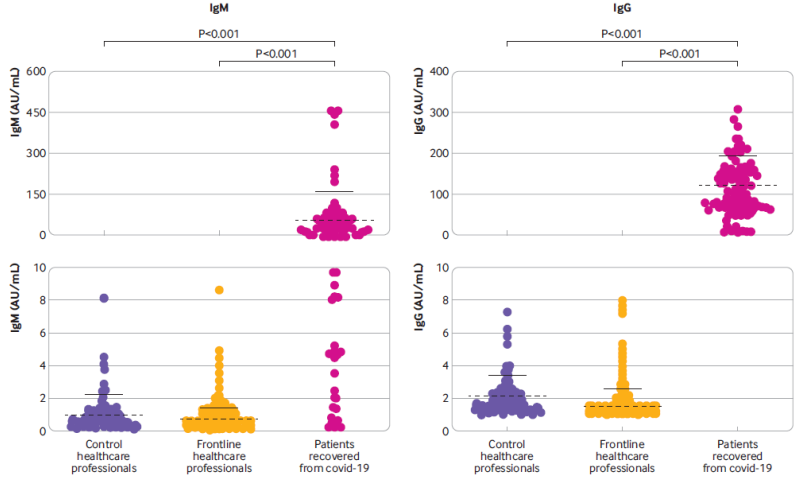

Fig 1 | Serological response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Concentrations of SARS-CoV-2 specific IgM and IgG antibodies in serum samples of healthcare professionals who had been exposed to coronavirus disease 2019 (covid-19) in Wuhan were quantified by chemiluminescence immunoassay (n=420). Serum samples from healthcare professionals without covid-19 exposure were used as negative controls (n=77). Serum samples from patients who had recovered from covid-19 were used as positive controls (n=80). Data are expressed as mean±standard deviation. Reference specified by manufacturer (<10 AU/mL)

Despite being at high risk of exposure, healthcare professionals who were appropriately protected did not contract infection or develop protective immunity against SARS-COV-2.

Min Liu BMJ 2 June 2020

Thank you

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