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

July 2021

By Gabriel Birgand

30/07/2021

nature

Untangling introductions and persistence in COVID-19 resurgence in Europe

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- **Objectives:** to build a phylogeographic model to evaluate how newly introduced lineages contributed to the COVID-19 resurgence in Europe.
- **Methods:** Model informed using genomic, mobility and epidemiological data from 10 European countries.

Results:

- Google mobility data predictor of spatial diffusion whereas air transportation data and SCI offered no predictive value
- More viral import than export events for Switzerland, Norway, the Netherlands and Belgium
- France, Italy and Spain are characterized by a relatively high viral export during the first wave
- UK and Germany, the viral flow in and out of the country was initially relatively balanced
- Introductions in UK benefited for successful onward transmission with a considerable fraction originating from Spain reflecting the spread of B.1.177/20A

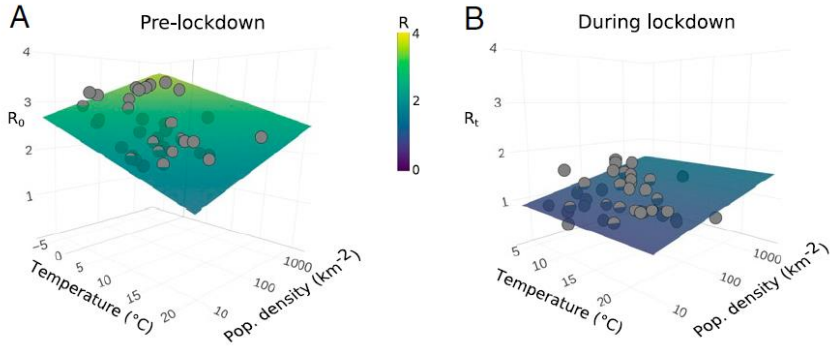
- Travel policies may be a key consideration for viral dissemination and resurgence in 2020,and spread of variants
- Well-coordinated European strategies will therefore be required

Fig. 2 | Posterior estimates for the relative importance of lineage introduction events in 10 European countries and their association with incidence. We report three summaries (posterior mean and 95% HPD intervals) for each country: the ratio of unique introductions over the total number of unique persisting lineages and unique introductions between June 15th and August 15th, 2020 (p_1), the ratio of descendant lineages from these unique introduction events over the total number of descendants circulating on August 15th, 2020 (p_2), and the ratio of descendant taxa from these unique introductions over the total number of descendant taxa sampled after August 15th, 2020 (p_3) (cfr. Extended Data Figure 4). The dot sizes are proportional to: (1) the total number of unique lineage introductions identified between June 15th and August 15th, 2020, (2) the total number of lineages inferred on August 15th, 2020, and (3) the total number of descendant tips after August 15th, 2020.

Philippe Lemey Nature
https://doi.org/10.1038/s41586-021-03754-2

Temperature and population density influence SARS-CoV-2 transmission in the absence of nonpharmaceutical interventions

- **Objectives:** To investigate the role of environment in the transmission of SARS-CoV-2 by incorporating environmental factors into an existing epidemiological framework globally and US
- **Methods:** Correlates of transmission across US states using comparative regression and integrative epidemiological



R0 is affected by the environment, but the impact of lockdown is greater.
A: Temperature has a negative effect on R0 at state level in the United States, while population density has a positive effect
B: The effects of temperature and population density are much weaker in the mobility-restricted data

When considering population density alone, R0 is overestimated in cold states and underestimated in warm states.

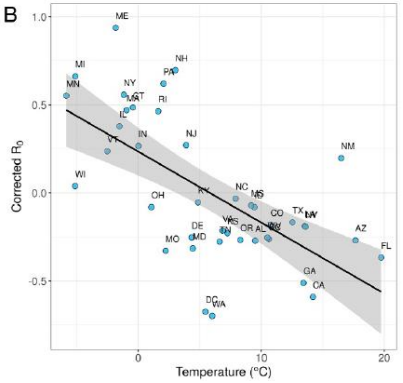


Table 1. Population (Pop) density and temperature are drivers of R_0 at state level in the United States, but the effect of lockdown is greater

	Coefficient	SE	*t* value	*p* value
(Intercept)	2.41	0.050	48.4	< 0.001*
Temperature	−0.30	0.048	−6.13	< 0.001*
Pop density	0.19	0.045	4.20	< 0.001*
Lockdown	−1.29	0.072	−17.8	< 0.001*
Temperature contrast	0.30	0.075	3.92	< 0.001*
Pop density contrast	−0.07	0.064	−1.09	0.28

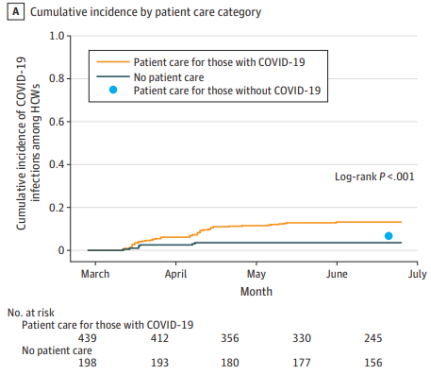
After accounting for population density, there is a significant effect of temperature upon *R*0

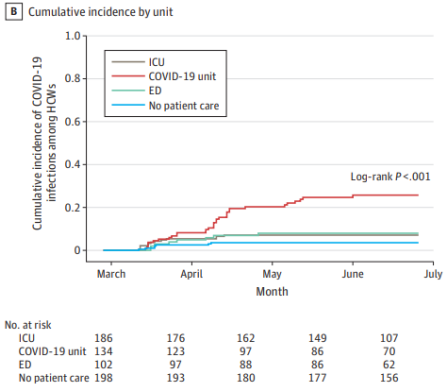
- Both population density and daily weather may play a role in the transmission of SARS-CoV-2.
- When stringent public policy measures are in place, the transmission effects of environmental drivers are negligible.

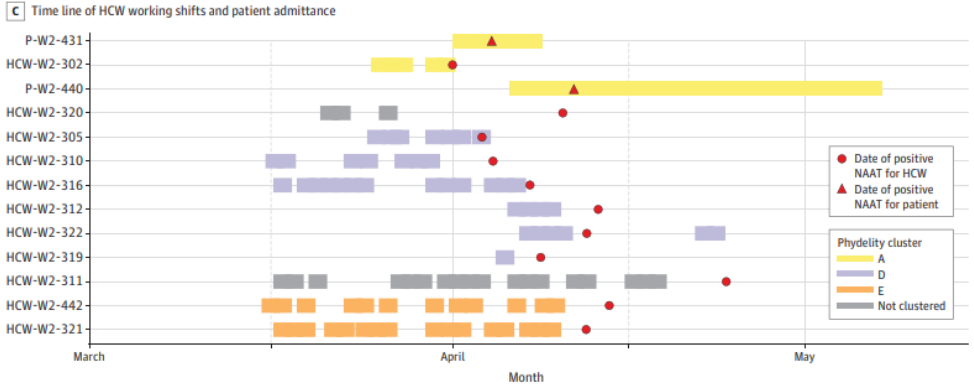
Thomas P. Smith PNAS
https://doi.org/10.1073/pnas.2019284118

Serologic Surveillance and Phylogenetic Analysis of SARS-CoV-2 Infection Among Hospital Health Care Workers

- **Objectives:** To determine how often and in what manner nosocomial SARS-CoV-2 infection occurs in HCW groups with varying exposure to patients with COVID-19.
- **Methods:** 4 weekly measurements of SARS-CoV-2–specific antibodies + questionnaires from March 23 to June 25, 2020, + phylogenetic & epidemiologic transmission analyses / Netherlands







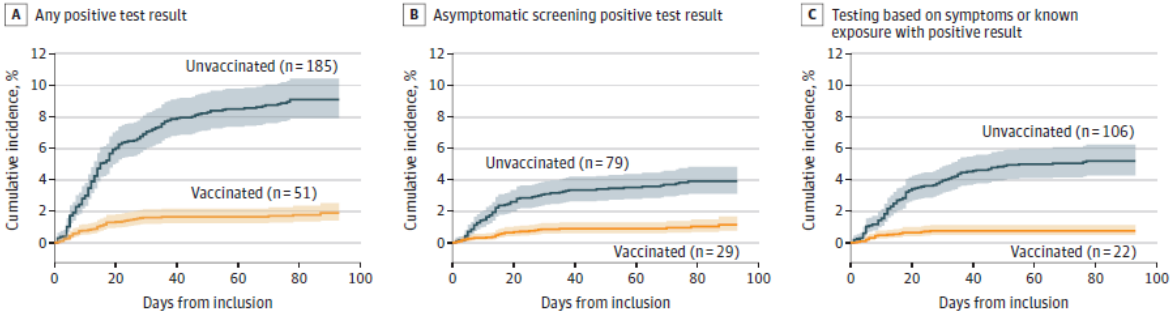
- Overall risk was largely associated with a substantially increased risk among HCWs on regular-care COVID-19 wards
- Infection rates among HCWs working in ICUs & EDs were similar to HCWs working in non–COVID-19 care.
- Phylogenetic + epidemiologic data identified **transmission clusters comprising only HCWs**, consistent with HCW-to-HCW transmission on COVID-19 wards, while **no evidence of patient-to-HCW transmission was found**.

Jonne J. Sikkens JAMA open
doi:10.1001/jamanetworkopen.2021.18554

Asymptomatic and Symptomatic SARS-CoV-2 Infections After BNT162b2 Vaccination in a Routinely Screened Workforce

- **Objectives:** to evaluated association between vaccination and reduction in symptomatic disease.
- **Methods:** March 2020 to march 2021, St Jude Children's Research Hospital initiated routine, test-based screening of asymptomatic workers

Figure. Cumulative Incidence of COVID-19 Against SARS-CoV-2 Infections After the First Dose



A total of 2165 unvaccinated employees and 3052 vaccinated employees were included. A, Any SARS-CoV-2 infection among St Jude employees during follow-up. B, Asymptomatic infections identified through routine asymptomatic screening; SARS-CoV-2 cases through testing based on the presence of symptoms or known COVID-19 exposure were treated as competing risks. C, Positive results via testing based on the presence of symptoms or known COVID-19 exposure; positive results from asymptomatic screening were treated as competing risks. Shaded areas are 95% CIs.

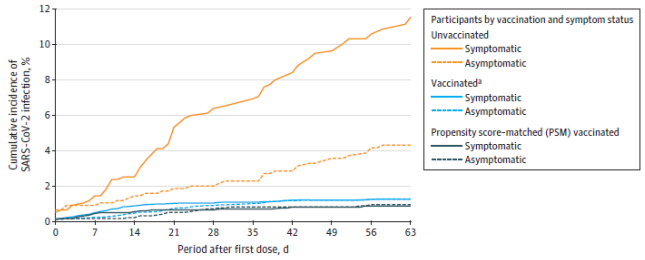
Association between vaccination with BNT162b2 in hospital employees and a decreased risk of symptomatic and asymptomatic infections with SARS-CoV-2.

Li Tang JAMA
doi:10.1016/S0140-6736(21)00448-7

Association Between Vaccination With BNT162b2 and ncidence of Symptomatic and Asymptomatic SARS-CoV-2 Infections Among Health CareWorkers

- **Objectives:** To estimate the association of vaccination with the Pfizer-BioNTech BNT162b2 vaccine with symptomatic and asymptomatic SARS-CoV-2 infections among HCW
- **Methods:** single-center, retrospective cohort study conducted at a tertiary medical center in Tel Aviv, Israel. between December 20, 2020, and February 25, 2021.

Figure 3. Cumulative Incidence of SARS-CoV-2 Infection Among Vaccinated, Propensity Score–Matched Vaccinated, and Unvaccinated Participants Screened for SARS-CoV-2 Infection



No. at risk										
Unvaccinated	757	743	731	713	698	693	678	664	654	645
Vaccinated with first dose[a]	5953	5790	5640	766	79	28	21	12	8	4
Vaccinated with second dose[a]	0	90	0	4775	5370	5238	5093	4816	4322	3082
PSM vaccinated with first dose	2141	2098	2047	310	32	9	7	4	3	1
PSM vaccinated with second dose	0	0	0	1686	1926	1846	1777	1636	1425	970

Data are the cumulative incidence of symptomatic and asymptomatic SARS-CoV-2 cases after the first dose of the vaccine in the unvaccinated cohort (n = 757), in the original vaccinated cohort (n = 5953), and in the propensity score–matched vaccinated cohort (n = 2141). Additional information appears in eFigure 2 in the Supplement.

[a] Unadjusted for propensity score.

Table 2. Observed Incidence Rate Ratios of Symptomatic and Asymptomatic SARS-CoV-2 Infection[a]

		Vaccinated				Unvaccinated[b]				Incidence rate ratio (95% CI)[c]		
Vaccination status	Subgroup	No. of cases	No.	Surveillance time, person-days	Incidence rate per 100 000 person-days[c]	No. of cases	No.	Surveillance time, person-days	Incidence rate per 100 000 person-days[c]	Unadjusted[d]	Adjusted[e]	*P* value
Original cohort												
Fully vaccinated[f]	Symptomatic	8	5372	168 571	4.7	38	696	25 359	149.8	0.03 (0.01-0.07)	0.03 (0.01-0.06)	<.001
	Asymptomatic	19			11.3	17			67.0	0.17 (0.09-0.32)	0.14 (0.07-0.31)	<.001
Late fully vaccinated[g]	Symptomatic	2	5036	95 689	2.1	23	675	15 726	146.3	0.01 (0-0.06)	0.02 (0-0.06)	<.001
	Asymptomatic	4			4.2	11			69.9	0.06 (0.02-0.19)	0.06 (0.02-0.22)	<.001
Partially vaccinated[h]	Symptomatic	31	5761	117 389	26.4	37	741	15 091	245.2	0.11 (0.07-0.17)	0.11 (0.06-0.17)	<.001
	Asymptomatic	37			31.5	8			53.0	0.59 (0.28-1.28)	0.64 (0.31-1.51)	.27
Propensity score–matched adjusted cohort												
Fully vaccinated[f]	Symptomatic	2	1916	57 274	3.5	38	696	25 359	149.8	0.02 (0.01-0.10)	0.02 (0-0.07)	<.001
	Asymptomatic	4			7.0	17			67.0	0.10 (0.04-0.31)	0.09 (0.03-0.25)	<.001
Late fully vaccinated[g]	Symptomatic	1	1748	31 645	3.2	23	675	15 726	146.3	0.02 (0-0.16)	0.02 (0-0.10)	<.001
	Asymptomatic	2			6.3	11			69.6	0.09 (0.02-0.41)	0.09 (0.01-0.35)	.002
Partially vaccinated[h]	Symptomatic	4	2085	42 414	9.4	37	741	15 091	245.2	0.04 (0.01-0.11)	0.03 (0.01-0.09)	<.001
	Asymptomatic	11			25.9	8			53.0	0.49 (0.20-1.22)	0.48 (0.19-1.26)	.12

[a] Participants with fewer than 7 days of follow-up or who contracted SARS-CoV-2 less than 7 days after the first vaccine dose were not included in this analysis (Figure 2).

[b] The surveillance period used corresponded to the period used for the vaccinated participants (ie, 28, 42, or 7-28 days after the beginning of follow-up, which was set as December 20, 2020).

[c] When estimating incidence rates and incidence rate ratios of symptomatic infection, asymptomatic cases were censored on the day of case confirmation (and vice versa).

[d] Indicates the ratio of incidence rates in each group.

[e] Calculated using Poisson regression as detailed in the Methods section.

[f] Included those with data for longer than 7 days after the second dose to the end of follow-up.

[g] Included those with data for longer than 21 days after the second dose to the end of follow-up.

[h] Included those with data for days 7 to 28 after first dose.

BNT162b2 vaccine compared with no vaccine was associated with a significantly lower incidence of symptomatic and asymptomatic SARS-CoV-2 infection more than 7 days after the second dose.

Yoel Angel JAMA
doi:10.1001/jama.2021.7152

AJIC American Journal of Infection Control

Modeling COVID-19 infection risks for a single hand-to-fomite scenario and potential risk reductions offered by surface disinfection

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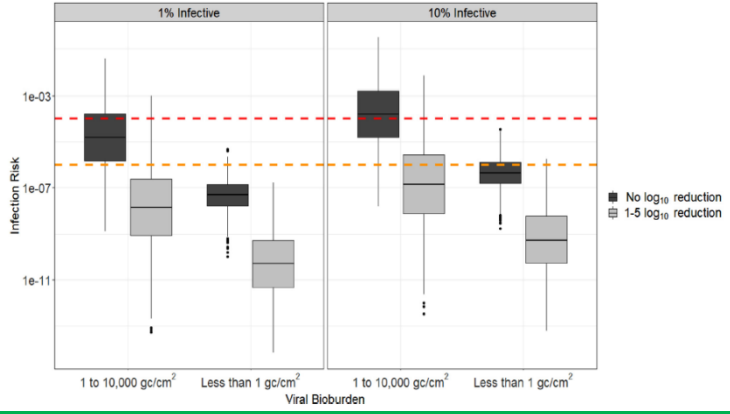
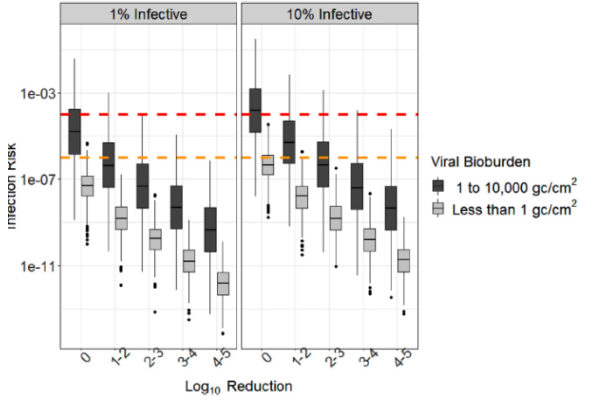
- **Objectives:** to estimate and compare COVID-19 infection risks after single hand-to-fomite-to-mucosal membrane contacts for high and low levels of viral bioburden
- **Methods:** Monte Carlo approach was used to account for variability and uncertainty in the following:
  - transfer efficiencies, fractions of the hand used for surface and face contacts, viral bioburden, disinfection log10 reductions, and surface areas of the hand and of fomites available for contact

Infection risk distributions for low and high surface bioburdens, associated with either no log10 reduction or a 1-5 log10 reduction of bioburden on surfaces, and assuming either 1% or 10% of detected viral genome copies were infectious*.
Red and orange dashed lines represent 1/10,000 and 1/1,000,000 risk targets, respectively



Infection risk distributions for low and high surface bioburdens associated with no log10 reduction or a range of log10 reductions achieved by use of disinfectant* assuming either 1% or 10% of detected viral genome copies were infectious.



Under low viral bioburden conditions, minimal log10 reductions may be needed to achieve risks less than 1:1,000,000. For higher viral bioburden conditions, log10 reductions of more than 2 may be needed to achieve median risks of less than 1:1,000,000

Amanda M. Wilson AJIC
https://doi.org/10.1016/j.ajic.2020.11.013

Environmental contamination in a coronavirus disease 2019 (COVID-19) intensive care unit—What is the risk?

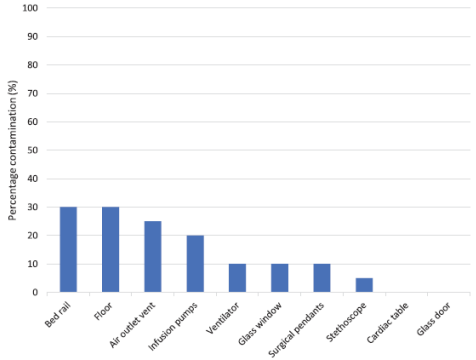
- **Objectives:** to evaluated the extent of environmental contamination by SARS-CoV-2 in an ICU setting
- **Methods:** surface environmental samples collected fromICUpatient rooms and common areas were tested for SARSCoV-2 by polymerase chain reaction (PCR). Select samples from the common area were tested by cell culture.

Table 2. Univariate Logistic Regression Analysis of Factors Associated With Presence of Environmental Contamination

Variable	Environmental Contamination (n=14)	No Environmental Contamination (n=6)	Odds Ratio (95% CI)	*P* Value
Age, median (IQR)	51 (45–64)	55.5 (36–69)	0.999 (0.94–1.06)	.98
Sex, male, no. (%)	11 (78.6)	4 (66.7)		.61
Day of illness, median (IQR)	14 (9–19)	14.5 (11–18)	1.01 (0.87–1.17)	.92
Ventilatory method, no. (%)				
Nil	3 (21.4)	1 (16.7)	Ref	Ref
Mechanical ventilation	4 (28.6)	3 (50)	0.44 (0.03–6.70)	.56
High-flow nasal oxygen	7 (50)	2 (33.3)	1.17 (0.07–18.35)	.91
AGP	2 (14.3)	1 (16.7)	0.83 (0.06–11.42)	.89
Clinical Ct value, median (IQR)	31.72 (26.86–34.72)	31.22 (29.55–32.50)	1.03 (0.83–1.27)	.81

Table 3. Extent of Contamination in ICU Rooms Compared to General Ward Rooms[a,b]

Variable	All ICU Rooms (n=23), No. (%)	All General Ward Rooms (n=27), No. (%)
Day of illness, median (IQR)	14 (9–19)	7 (4–17)
Clinical Ct value, median (IQR)	30.18 (28.45–34.40)	30.40 (22.04–35.24)
Any environmental contamination (at least 1 site)	14 (60.9)	17 (63.0)
No. of sites contaminated, median (IQR)	1 (0–2)	7 (4–17)
% of sites contaminated, median (IQR)	10 (0–20)	14.3 (0–42.9)
	ICU Rooms With Contamination (n=14), No. (%)	General Ward Rooms With Contamination (n=17), No. (%)
No. of sites contaminated, median (IQR)	2 (1–2)	2 (1–5)
% of sites contaminated, median (IQR)	20 (10–20)	28.6 (14.3–62.5)



- Environmental contamination was seen in the ICU, both in patient rooms and common areas. Contamination did not differ depending on the mode of ventilatory support, supporting the safe use of HFNO from an infection control perspective.
- The frequency and extent of contamination in the ICU was lower compared to general ward settings.

Sean Wei Xiang Ong ICHE
doi:10.1017/ice.2020.1278

The interface between COVID-19 and Bacterial Healthcare-Associated Infections

CMI CLINICAL MICROBIOLOGY AND INFECTION

EUCIC EUROPEAN COMMITTEE ON INFECTION CONTROL

- **Objectives:** To review recent data which indicate the occurrence of hospital-onset bacterial infections, including with antibiotic-resistant isolates, in COVID-19 patients.
- **Topics assessed:**
  - Emergence of Reports of Bacterial Infections Related to COVID-19
  - Bacterial Healthcare-Associated Infections in COVID-19 Patients
    - Studies comparing pre- and mid-pandemic periods have reported a higher incidence of some HAIs at specific hospitals since the advent of COVID-19.
  - COVID-19 and Antibiotic-Resistant Healthcare-Associated Infections
    - Many of the bacterial HAIs detected in COVID-19 patients exhibit antibiotic non-susceptibility including multi-drug resistance.
  - Multi-Drug Resistance and Antimicrobial Stewardship
    - It has been proposed that underlying factors for AMR may include the high empiric use of broad-spectrum antibiotics documented in COVID-19 patients.
  - COVID-19 and Infection Prevention and Control
    - COVID-19 measures has been linked to reduced incidence of some bacterial HAIs at certain sites.
    - Further research is required to validate these findings and provide a cost-benefit evidence base for maintenance of intensified IPC measures beyond the COVID-19 pandemic for augmented control of HAIs.

Ronan F. O'Toole CMI
https://doi.org/10.1016/j.cmi.2021.06.001.

Rapid feedback on hospital onset SARS-CoV-2 infections combining epidemiological and sequencing data

- **Objectives:** to describe the performance of the sequence reporting tool (SRT) using COVID-19 Genomics (COG) UK initiative sequence data for HOCI cases collected from Glasgow and Sheffield between February and May 2020
- **Methods:** combines epidemiological and sequence data in order to provide a rapid assessment of the probability of HCAI among HOCI cases (defined as first positive test >48 hours following admission) and to identify infections that could plausibly constitute outbreak events.
- **Results:** 326 HOCIs analysed.
  - Among HOCIs with time-from-admission ≥8 days 60 the SRT algorithm identified close sequence matches from the same ward for 160/244 (65.6%)
  - 61 and in the remainder 68/84 (81.0%) had at least one similar sequence elsewhere in the hospital,
  - 62 resulting in high estimated probabilities of within-ward and within-hospital transmission.
  - For 63 HOCIs with time-from-admission 3-7 days, the SRT probability of healthcare acquisition was 64 >0.5 in 33/82 (40.2%).

SRT described allows rapid feedback on 425 HOCIs that integrates epidemiological and sequencing data to generate a simplified report at 426 the time that sequence data become available.

Oliver T Stirrup eLife
https://elifesciences.org/articles/65828

Clinical Infectious Diseases

The Risk of SARS-CoV-2 Transmission from Patients with Undiagnosed Covid-19 to Roommates in a Large Academic Medical Center

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- **Objectives:** To characterized the incidence and risk factors for SARS-CoV-2 transmission among patients in shared hospital rooms in a large academic medical center.
- **Population:** all patients who tested positive for the first time while in a shared room
  - Roommates exposed: shared a room for ≥15 minutes with an index patient during their infectious window, defined as 48 hours prior to symptom onset (or positive test) until isolation.
  - Exposed roommates tested if remained hospitalized; discharged patients were contacted to offer testing

Covariate	Transmission+ (N=12)	Transmission- (N=19)	OR (95% CI)	p-value
Exposed Patients				
Median Age	64 (56-80)	69 (54-72)	-	0.90
Female Sex	8 (66.7%)	5 (26.3%)	5.6 [1.2-27.1]	0.03[d]
Non-White Race	6 (50.0%)	2 (10.5%)	8.5 [1.3-54.1]	0.02[d]
Exposure Duration ≥18 Hours[a]	8 (66.7%)	9 (47.4%)	2.2 [0.5-10.0]	0.30[d]
Lung Disease	2 (16.7%)	2 (10.5%)	1.7 [0.2-14.0]	0.63
Heart Failure	2 (16.7%)	3 (15.8%)	1.1 [0.2-7.5]	0.95
Cancer or Immunosuppression	3 (25.0%)	5 (26.3%)	0.9 [0.2-4.9]	0.94
Obesity	2 (16.7%)	3 (15.8%)	1.1 [0.2-7.5]	0.95
Chronic Kidney Disease	2 (16.7%)	2 (10.5%)	1.7 [0.2-14.0]	0.63
Location by Window	7 (58.3%)	8 (42.1%)	1.9 [0.4-8.3]	0.39
Index Patients[b]				
PCR Cycle Threshold Value ≤21[a]	11 (91.7%)	7 (36.8%)	18.9 [2.0-179]	<0.01[d]
Nebulizer Use or Other Aerosol-Generating Procedure[c]	3 (25.0%)	0 (0%)	-	-
Cough, Dyspnea, or Tachypnea	5 (41.7%)	2 (10.5%)	6.1 [0.9-39.0]	0.047[d]
Delirium	1 (8.3%)	2 (10.5%)	0.8 [0.1-9.6]	0.84

- 31 roomates with ≥1 documented test ≥3 days post-exposure were included in the analysis.
- Median duration of exposure: 18 hours (IQR 12-47 hours),
- Tested a median 2 times (range 1-4) during the 14-day post-exposure
- 12/31 (39%) exposed roommates tested positive
- infection incidence of 0.1% (12/11,290) among all patients in shared rooms
- Median interval from hospital admission until positive test 9.5 days (7.8-12).

Importance of isolating and testing all patients exposed to roommates with SARS-CoV-2, including those who have been discharged
Consistent with near-range airborne rather than droplet transmission.
Contact with shared surfaces such as sinks, door handles, or bathrooms, and staff intermediaries

Abraar Karan CID
https://doi.org/10.1093/cid/ciab564

Clinical Infectious Diseases

COVID-19 Outbreak Associated with a SARS-CoV-2 P.1 Lineage in a Long-Term Care

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- **Objectives:** To report an outbreak due to a P.1 variant in a LTCH in Canada.
- **Methods:** Epidemiological analysis, environmental samplings, and whole genome sequencing (WGS) were performed for a hospital outbreak.

Roles (residents/staff) and outcome	Number (attack rate as %) by vaccine status		Total‡ (vaccinated & unvaccinated)	Vaccine effectiveness§ (95% CI)
	Fully vaccinated*	Unvaccinated†		
Residents	**(n = 48)**	**(n = 12)**	**60**	-
SARS-CoV-2 infection	19 (39.6)	11 (91.7)	29	52.5 (26.9-69.8)
Symptomatic	11 (22.9)	9 (75.0)	20	66.3 (33.8-82.1)
Severe illness¶	6 (12.5)	7 (58.3)	13	78.6 (47.9-91.2)
Staff	**(n = 43)**	**(n = 40)**	**85**	-
SARS-CoV-2 infection	4 (9.3)	11 (27.5)	15	66.2 (2.3-88.3)
Symptomatic	4 (9.3)	5 (12.5)	9	25.6 (-157-78.5)
Severe illness¶	0	0	0	-

- April 10th: an asymptomatic unvaccinated staff member worked in the home
- April 18th: 2 fully vaccinated residents exposed to staff member developed new onset cough.
- Next 24 days: 31 residents and 22 staff tested positive for SARS-CoV-2.
- Resident attack rates: 18/32, 0/29, 12/31 and 1/32 on the 2nd-5th floors, respectively.
- Staff attack rates: 12/57, 0/30, 3/44, and 1/39 on resident floors, and 4/53 in administrative/service areas.
- 29 residents and 14 staff had specimens where both N501Y and E484Y mutation
- 20 specimens underwent WGSand all all were SARS-CoV-2 lineage P.1
- 6/19 fully vaccinated resident cases had severe illness:
- 7/12 unvaccinated resident cases had severe illness

Despite 81% of residents being fully vaccinated, an outbreak of COVID-19 due to a SARS-CoV-2 P.1variant occurred in this LTCH

Chantal Williams CID
https://doi.org/10.1093/cid/ciab617

Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples

- **Objectives:** To examine the relationship between age and neutralizing antibody titers against the early SARS-CoV-2 USA-WA1/2020 strain and the P.1 variant of concern after 2 doses of the BNT162b2 vaccine
- **Methods:**
  - SARS-CoV-2 spike receptor-binding domain-specific antibody levels measured by enzyme-linked immunosorbent assays.
  - SARS-CoV-2 50% neutralizing titers determined by focus reduction neutralization tests (FRNT50) using live clinical isolates of the original SARS-CoV-2 strain (USA-WA1/2020) and the P.1 variant.

Figure 1. SARS-CoV-2–Specific Antibody Levels

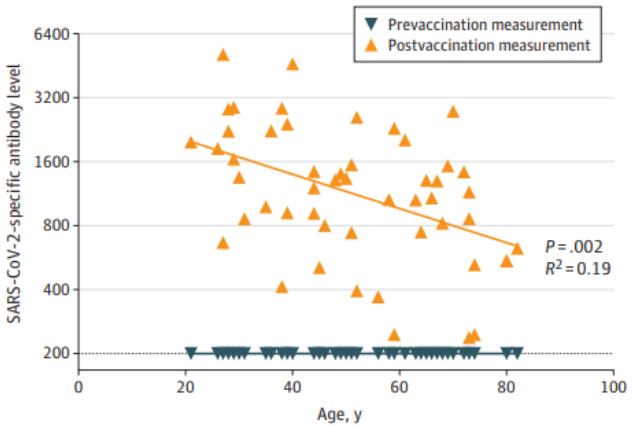
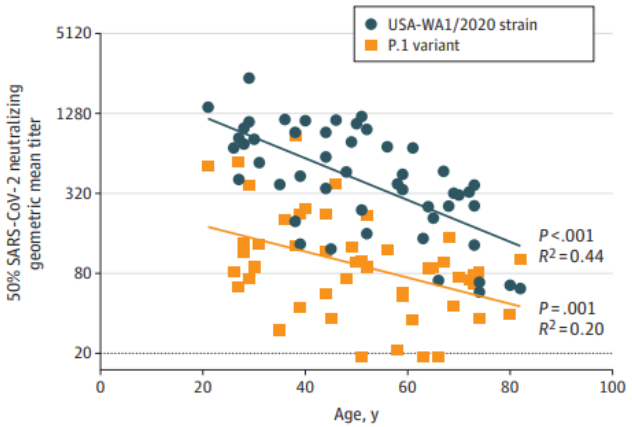


Figure 2. Neutralization of Live SARS-CoV-2 Clinical Isolates



- Initial vaccine-elicited neutralizing antibody titers were negatively associated with age, resulting in a diminished ability to neutralize SARS-CoV-2 in vitro.
- Neutralizing titers against P.1 were reduced across all ages, although the magnitude of the age-dependent difference was smaller.

Timothy A. Bates JAMA
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Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant

- **Objectives:** to estimate the effectiveness of vaccination against symptomatic disease caused by the delta variant or the predominant strain (B.1.1.7, or alpha variant)
- **Methods:** test-negative case–control design

Table 2. Vaccine Effectiveness against the Alpha Variant or *S* Target–Negative Status and the Delta Variant or *S* Target–Positive Status, According to Dose and Vaccine Type.*

Vaccination Status	Test-Negative Status		Alpha Variant or *S* Target–Negative Status			Delta Variant or *S* Target–Positive Status	
	Controls	Cases	Case:Control Ratio	Adjusted Vaccine Effectiveness (95% CI)	Cases	Case:Control Ratio	Adjusted Vaccine Effectiveness (95% CI)
	no.	*no.*		%	*no.*		%
Unvaccinated	96,371	7313	0.076	Reference	4043	0.042	Reference
Any vaccine							
Dose 1	51,470	2226	0.043	48.7 (45.5–51.7)	1493	0.029	30.7 (25.2–35.7)
Dose 2	23,993	143	0.006	87.5 (85.1–89.5)	340	0.014	79.6 (76.7–82.1)
BNT162b2 vaccine							
Dose 1	8,641	450	0.052	47.5 (41.6–52.8)	137	0.016	35.6 (22.7–46.4)
Dose 2	15,749	49	0.003	93.7 (91.6–95.3)	122	0.008	88.0 (85.3–90.1)
ChAdOx1 nCoV-19 vaccine							
Dose 1	42,829	1776	0.041	48.7 (45.2–51.9)	1356	0.032	30.0 (24.3–35.3)
Dose 2	8,244	94	0.011	74.5 (68.4–79.4)	218	0.026	67.0 (61.3–71.8)

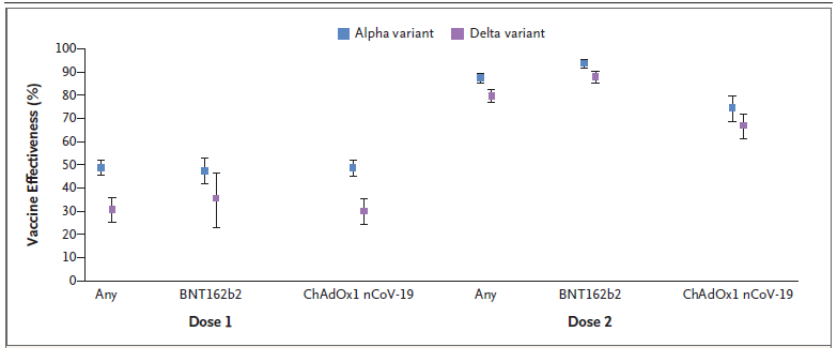

Figure 1. Vaccine Effectiveness against the Alpha and Delta Variants, According to Dose and Vaccine Type.
Shown is the effectiveness of one dose and two doses of the BNT162b2 and ChAdOx1 nCoV-19 vaccines, or either vaccine ("any"), against symptomatic disease with the B.1.1.7 (alpha) or B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2. I bars indicate 95% confidence intervals.

- Only modest differences in vaccine effectiveness were noted with the delta variant as compared with the alpha variant after the receipt of two vaccine doses.
- Absolute differences in vaccine effectiveness were more marked after the receipt of the first dose.

Jamie Lopez Bernal NEJM
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nature REVIEWS

SARS- CoV-2 variants, spike mutations and immune escape

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Box 2 | **Mechanisms of antigenic change**

In common with other virus surface glycoproteins responsible for attachment to host cell-surface receptors, such as influenza virus haemagglutinin and the envelope glycoprotein GP120 of HIV, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein is an important target for neutralizing antibodies. There are various distinct mechanisms by which mutations can alter the antigenic properties of a glycoprotein.

Amino acid substitutions that alter the epitope

A change in the biophysical properties of an epitope residue directly diminishes antibody binding. For example, the neutralizing antibody 4A8 forms salt bridges with spike protein residues K147 and K150, and therefore substitutions at these residues are likely to inhibit binding. The E484K amino acid substitution has received attention for its effect on monoclonal antibodies and convalescent plasma neutralizing activity. Its position has been described as belonging to the footprint of several antibodies, and a change in charge caused by replacement of a glutamate residue with a lysine residue has the potential to diminish antibody binding.

Increasing receptor-binding avidity

Substitutions that individually increase receptor-binding affinity can shift the binding equilibrium between glycoprotein and neutralizing antibodies in favour of a higher-avidity interaction between glycoprotein and the cellular receptor[102]. The spike amino acid substitution N501Y, which increases ACE2-binding affinity[19], has been described as emerging in individuals treated with convalescent plasma, potentially as a means of immune escape.

Changes in glycosylation

Glycans are bulky sugar molecules that may shield epitopes from antibody binding. N-linked glycans are typically prominent in glycan shielding of virus surface glycoprotein epitopes[39], although O-linked glycans can also contribute[103]. A substitution can introduce an additional N-linked glycosylation motif. The acquisition of epitope-masking glycans during the evolution of human influenza viruses is well described[104].

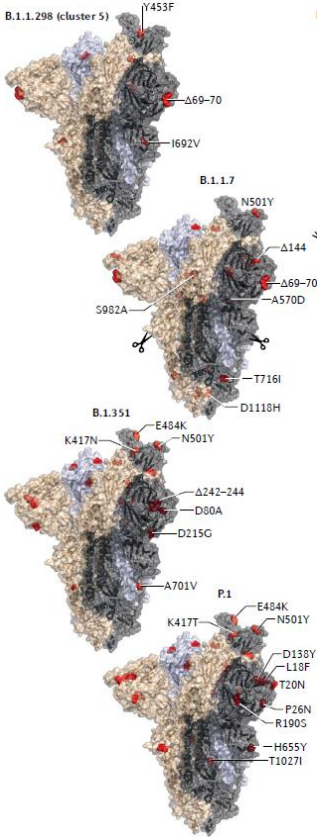
Deletions and insertions

The deletion or insertion of residues has the potential to alter epitope conformation, diminishing antibody binding. Several deletions in the spike amino-terminal domain (NTD) that affect recognition by neutralizing antibodies have been described[41,42]. In laboratory experiments, a multiresidue insertion in the spike NTD has been described as emerging and contributing to escape from polyclonal antibodies in convalescent plasma[41].

Allosteric structural effects

Similarly to deletions or insertions, an amino acid substitution outside an epitope footprint may affect antibody binding by changing the protein conformation in such a way that an epitope is altered or differently displayed. In the spike NTD, changes to disulfide bonds are thought to reduce binding by multiple monoclonal antibodies through this mechanism[39].

- Prediction of the mutational pathways by which a virus such as SARS- CoV-2 will evolve is extremely challenging.
- Tracking the emergence of these viruses flagged as potential antigenically significant variants will help to guide the implementation of targeted control measures and further laboratory characterization.
- An important part of this process will be the preparation of updated vaccines tailored to emerging antigenic variants that are maximally cross- reactive against all circulating variants.

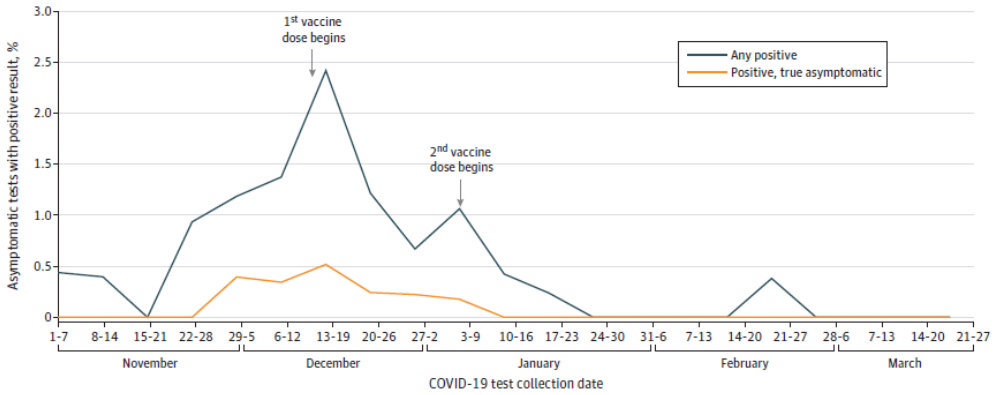


William T. Harvey Nature Rev
https://doi.org/10.1038/s41579-021-00573-0

Asymptomatic and Symptomatic COVID-19 Infections Among Health Care Personnel Before and After Vaccination

- **Objectives:** to evaluated COVID-19 rates before and after HCP vaccination.
- **Methods:** cohort study of HCP at University of California Irvine (UCI) Health, COVID-19 cases, both symptomatic and asymptomatic, before and after mRNA vaccination (Pfizer, Moderna)

Figure 2. Percentage of Health Care Personnel Who Tested Positive for COVID-19 Using the Asymptomatic Testing Pathway



Most health care personnel who tested positive using the asymptomatic testing pathway reported symptoms consistent with COVID-19 (81% [34 of 42]). Asymptomatic cases

Rapid and sustained decline in both COVID-19 symptomatic and asymptomatic infections following HCP vaccination in a region experiencing high rates of COVID-19 disease nationally in the 2020 to 2021 winter season.

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