HARTMANN

LOOKING BACK AND AHEAD

Past and future challenges in infection prevention

HSC Symposium 2023

Lessons learned from the pandemic -
Experiences of a tertiary hospital in Germany

Prof. Dr. Johannes Knobloch

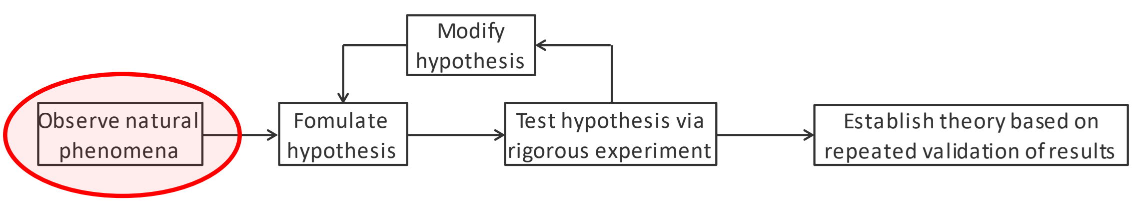
Lessons learned from the pandemic
Experiences of a tertiary care hospital in Germany

Prof. Dr. med. Johannes K. Knobloch

Universitätsklinik um Hamburg-Eppendorf

Science in pandemics

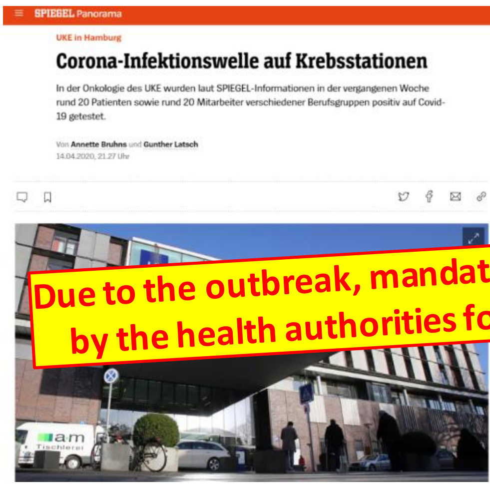
The SCIENTIFIC METHOD



The strongest impact of lessons learnt comes from outbreaks and other transmission events

Modified after Jorge Cham, 2006, phdcomics.com

Consequences of a SARS-CoV-2 Outbreak


SPIEGEL Panorama

UKE in Hamburg

Corona-Infektionswelle auf Krebsstationen

In der Onkologie des UKE wurden laut SPIEGEL-Informationen in der vergangenen Woche rund 20 Patienten sowie rund 20 Mitarbeiter verschiedener Berufsgruppen positiv auf Covid-19 getestet.

Von Annette Bruhns und Gunther Latsch
14.04.2020, 21.27 Uhr


SPIEGEL Panorama

Schlamperei am UKE

Wie sich eine ganze Krebsstation mit dem Virus infizierte

Sars-CoV-2 kann einen überall erwischen - sogar auf der Hochsicherheitsstation der Hamburger Uniklinik. Insider berichten von gravierenden Fehlern.

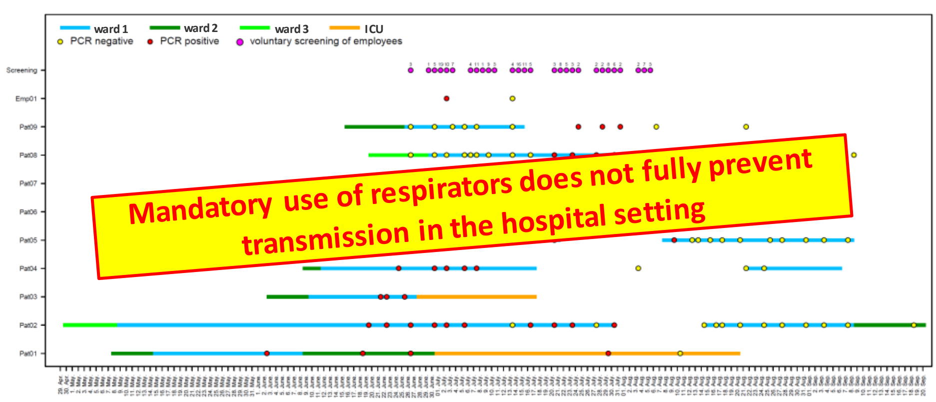
Von Annette Bruhns, Jürgen Dahlkamp und Gunther Latsch
17.04.2020, 14.25 Uhr

Due to the outbreak, mandatory respirator wearing was imposed by the health authorities for all oncologic wards in April 2020

https://www.spiegel.de/panorama/coronavirus-hamburg-universitaetsklinikum-eppendorf-infektionswelle-auf-krebs-stationen-a-6754218c-39c0-4206-ac52-60bf387b0feb
https://www.spiegel.de/panorama/corona-ausbruch-am-uke-in-hamburg-wie-sich-eine-ganze-krebsstation-mit-dem-virus-infizierte-a-00000000-0002-0001-0000-000170518564

Outbreaks despite PPE usage 1

Parainfluenza Virus 3 outbreak during maximum prevention measures



Mandatory use of respirators does not fully prevent transmission in the hospital setting

Universal respirator use (?)

lost in translation

Deutsch (erkannt) ⇄ Englisch (US) Glossar

Maske | Mask

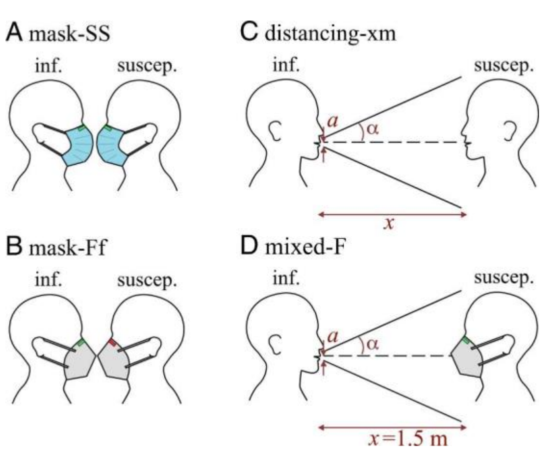
Studies on "universal masking" were often misinterpreted in Germany as continuous/mandatory use of respirators

Alternativen:

Mouth-nose protector
Mouth-nose guard
Mouth and nose protection

medical mask
surgical mask

Universal respirator use (?)



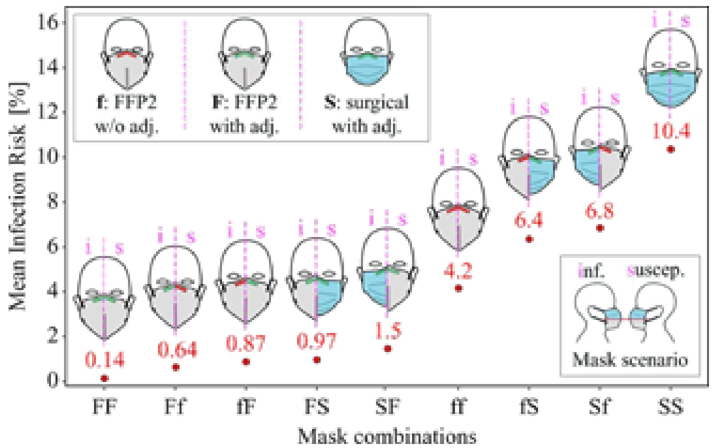
Given these assumptions, the total absorbed dose by the susceptible individual can be calculated as follows:

$$\mu_k(t) = \int_{d_{0,min}(k)}^{d_{0,max}(k)} \mathrm{d}\phi \int_0^{t_{exp}} \mathrm{d}t \times \overbrace{n_{I,k}(\phi,t)\, f_d\,(\phi, \lambda_I(t), w(\phi,t), t)}^{\text{infec. particle conc. in breath. zone of susceptible}} \times \overbrace{[q_{P,ex}P_{ex}(\phi,\lambda_I(t)) + q_{L,ex}L_{ex}(\phi,\lambda_I(t))]}^{\text{total outward leakage } (TOL)} \times \overbrace{[q_{P,in}P_{in}(\phi, w(\phi,t), \lambda_S(t)) + q_{L,in}L_{in}(\phi, w(\phi,t), \lambda_S(t))]}^{\text{total inward leakage } (TIL)} \times \overbrace{D_{rt}(\phi, w(\phi,t), \lambda_S(t))}^{\text{intake\&deposition eff. susc. resp. tract}} \overbrace{\lambda_S(t)}^{\text{susc. inhalation rate}}, \quad [3]$$

Gholamhossein Bagheri et al. PNAS 2021;118:49:e2110117118

Universal respirator use (?)

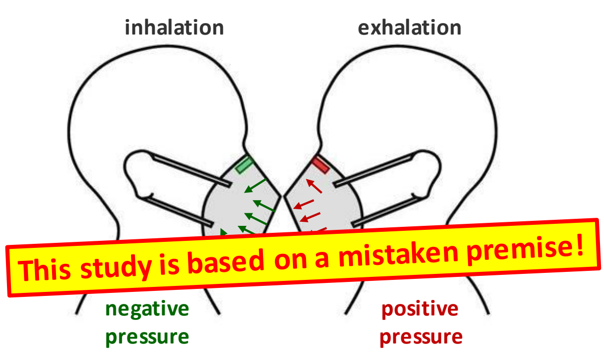
Mittleres Infektionsrisiko in Maskenszenarien mit verschiedenen Maskenkombinationen für eine Dauer von 20 min.



Gholamhossein Bagheri et al. PNAS 2021;118:49:e2110117118

Universal respirator use (?)

For the lack of a reliable measurement method on human subjects and since data from the literature are inconclusive, we assume the *TOL* to be the same as *TIL* (see *Total inward leakage* and *Total outward leakage* for more details).



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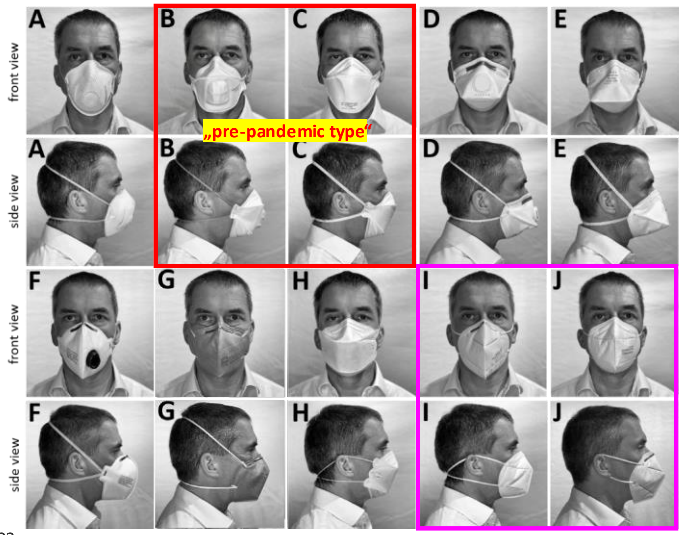
Universal respirator use (?)



dominant in Germany after a period of PPE shortage

Knobloch et al., J Hosp Infect, 2023

Universal respirator use (?)

Table I
Results of fit tests depending on the shape type of respirators

Type of respirator	Type of fixation	No. of studies	No. of QNFTs	Overall QNFT pass rate[a]	Mean[a] (no. of QNFT/studies)	Median[a] (no. of QNFT/studies)
Three-panel folded respirator (dome shape)	Head straps	15	4625	80.8%	141.5–220.9 (2097/6)	139–200 (28/3)
Rigid respirator (dome shape)	Head straps	20	8234	72.4%	4.8–187.8 (402/10)	5.6–200 (58/5)
Respirator with duckbill shape	Head straps	11	2120	31.6%	29–152.7 (80/4)	21–145 (202/3)
Respirator with coffee filter shape	Head straps	4	3392	30.9%	13.5–110.7 (407/1)	–
Three-panel folded respirator (dome shape)	Ear loops	1	60	8.3%	43 (60/1)	43 (60/1)
Respirator with coffee filter shape	Ear loops	5	162	1.9%	2.2–11.4 (132/4)	3–39 (90/1)

QNFT, quantitative fit test.
[a] Mean/median refers to the indicated values of the fit factors of the individual studies if indicated; the values might not be representative for all studies (details see Supplementary Tables).

Knobloch et al., J Hosp Infect, 2023

Transmission despite adequate protection

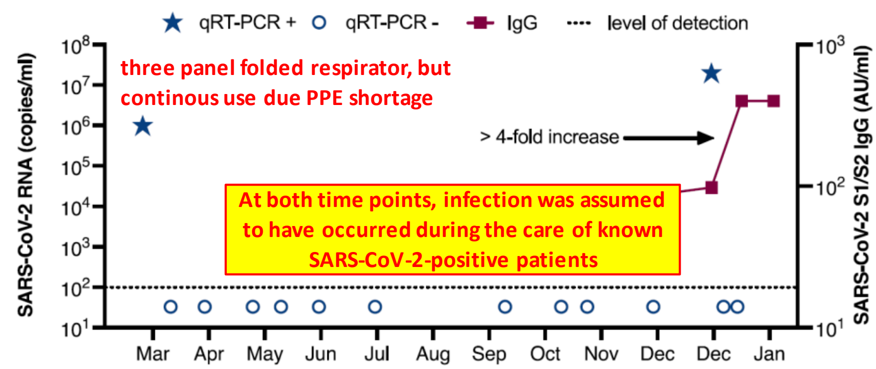


Figure 1. Time course with quantitative detection of SARS CoV-2 RNA [log copies/mL] (blue) and quantitative anti SARS CoV-2 S1/S2 antibody levels [log AU/mL] (red). RNA level was 1×10^6 copies/mL and 2×10^7 copies/mL at first infection and reinfection respectively. Anti-SARS-CoV-2 spike (S1/S2) IgG was 40 IU/mL after first infection and a > 4-fold booster during reinfection was observed (97 AU/mL on 29 December 2020, and >400 AU/mL on 13 January 2021).

Brehm et al., Viruses, 2021; doi: 10.3390/v13040661

UKE HAMBURG Prof. Dr. med. J. Knobloch
Lessons learned from the pandemic

Transmission despite adequate protection

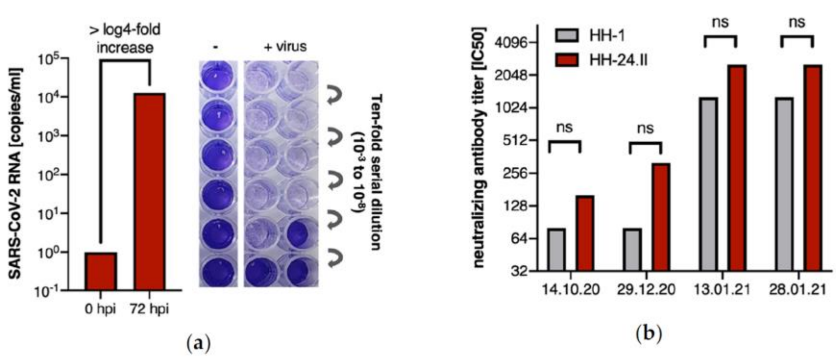


Figure 2. (**a**) Successful isolation of SARS-CoV-2 from swab sample (HH-24.II) reflected by > log4-fold in-crease of viral RNA in the supernatant of Vero cells at 72 h post infection (hpi) detected by qRT-PCR. Quantification of the virus stock produced of the rescued virus in cell culture revealed a TCID50 of 1.57×10^7; (**b**) Virus neutralization assay was performed with serial dilutions of patient sera of one time point before (14 October 2020) and three time points after the reinfection (29 December 2020, 13 January 2021, 28 January 2021) and both the isolated virus of the patient (HH-24.II, red bars) and the HH-1 isolate (gray bars). Neutralizing antibody titers (IC50) were detected at all time points. No significant differences in the neutralizing capacity of the two linages were observed. Between 29 December 2020 and 13 January 2021 a > 4-fold titer increase was observed which reflects a significant increase.

Brehm et al., Viruses, 2021; doi: 10.3390/v13040661

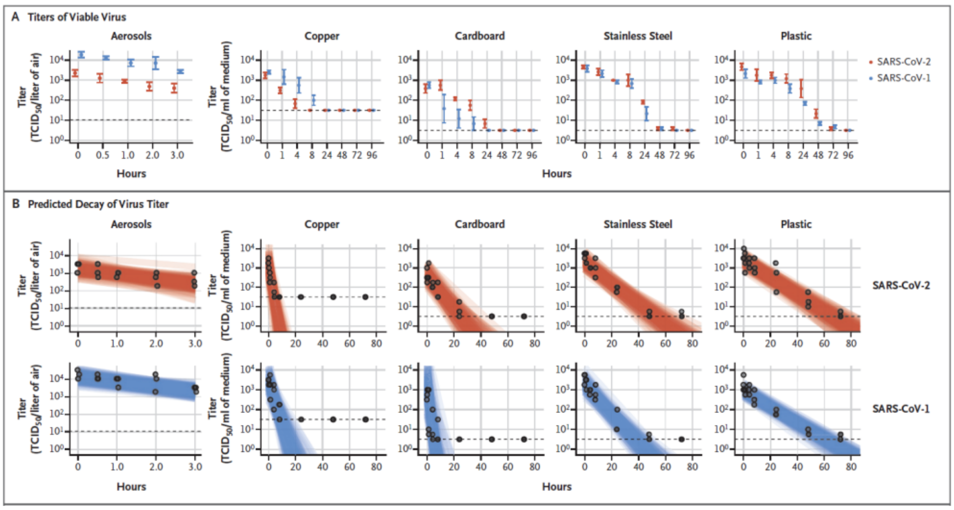
Lessons learned

- The use of a suitable PPE must be sufficiently trained (fit test)
- Not everything that calls itself a respirator also offers adequate protection
- In our hospital, respirators with ear loops were banned from use again
- In case of continuous use, the protection may fail during the wearing period, even with well-trained personnel using high quality respirators

A typical argument during outbreaks:

"It was definitely not the medical staff. It was certainly the cleaning staff who didn't clean properly."

What role do inanimate surfaces play in transmission?



van Doremalen, N., et al. 2020, NEJM

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Lessons learned from the pandemic

What role do inanimate surfaces play in transmission?

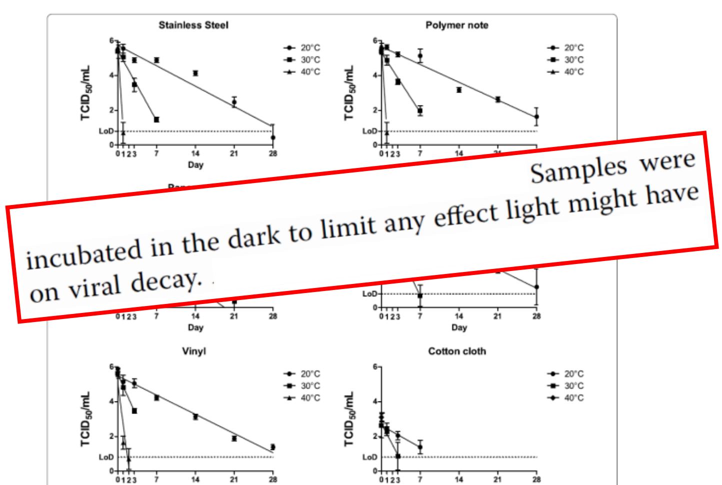


Fig. 1 Recovery of infectious SARS-CoV-2 for all surfaces and temperatures over time, $TCID_{50}$ data is plotted in log_{10} intervals. No infectious virus was recovered at 24 h at 40 °C for cotton cloth. LoD (limit of detection) is recorded as 0.8 Log_{10} $TCID_{50}$

Riddell, S., et al. 2020, Virology Journal

What role do inanimate surfaces play in transmission?

Table 1. Summary of studies reviewed: setting, study aims and methodology.

Study no.	Authors	Country	Setting	Location	Aim	Air sampling method	Air sampling strategy	Surface sampling method	Definition of positive in RT-PCR analysis	Genes analysed
1	Bloise *et al.* (2020)	Spain	Hospital Universitario La Paz, Madrid	Microbiology laboratory used for SARS-CoV-2 diagnosis	D	—	—	WHO	Any of the three genes Ct <39	ORF1ab, N, and S genes
2	Cai *et al.* (2020)	China	Tongji Hospital, Tongji Medical College, Wuhan	Four temporary COVID-19 ICU wards	D	DF	U	WHO	Ct ≤38 (not clear whether just one gene or both)	ORF1a/b and RdRp genes
3	Cheng *et al.* (2020)	Hong Kong	Queen Mary Hospital	Patients hospitalized singly in airborne infection isolation rooms	A	GF	T	Dry	Not clear	RdRp and helicase (Hel)
4	Chia *et al.* (2020)	Singapore	National Centre for Infectious Diseases, Singapore	Three airborne infection isolation rooms in the ICU and 27 rooms in the general ward	A	Im	AP + AB	OW	Positive detection was recorded as long as amplification was observed in at least one assay	ORF1ab and E genes
6	Di Carlo *et al.* (2020)	Italy	Electric bus line in Chieti		D	GF	AB	OW	At least two genes with Ct <37	ORF1ab, N, and S genes
8	Guo *et al.* (2020)	China	ICU and General COVID ward in Huoshenshan Hospital, Wuhan	ICU	D	WC	O	WHO	Either gene had Ct <40 (weak positive) or both (strong positive)	ORF1ab and nucleocapsid protein (NP) gene

Conclusions: The reliability of the reported data is uncertain. The methods used for measuring SARS-CoV-2 and other respiratory viruses in work environments should be standardized to facilitate more consistent interpretation of contamination and to help reliably estimate worker exposure.

Cherrie, J. W., et al. 2021, Annals of Work Exposures and Health

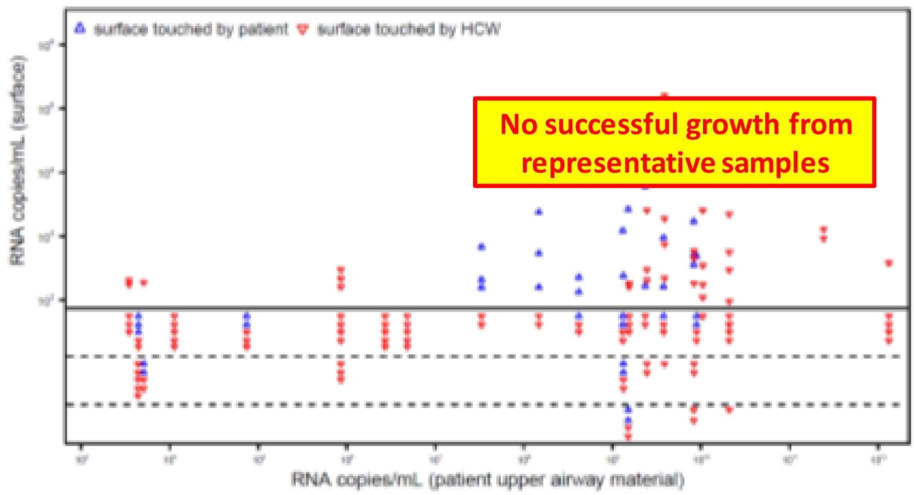
What role do inanimate surfaces play in transmission?

Own investigations:

- Examination of the contamination of the environment with SARS-CoV-2 in the intensive care unit by means of swabbing
  => PCR and cell culture of representative samples with low CT-value
- Artificial contamination of surfaces with four clinical materials with subsequent disinfection
  => PCR and cell culture
- Artificial contamination of surfaces with surrogate virus (phage phi6) with subsequent disinfection
  => PCR and plaque quantification

Knobloch et al. 2022, Int J Environ Res Public Health doi: 10.3390/ijerph192417074

What role do inanimate surfaces play in transmission?



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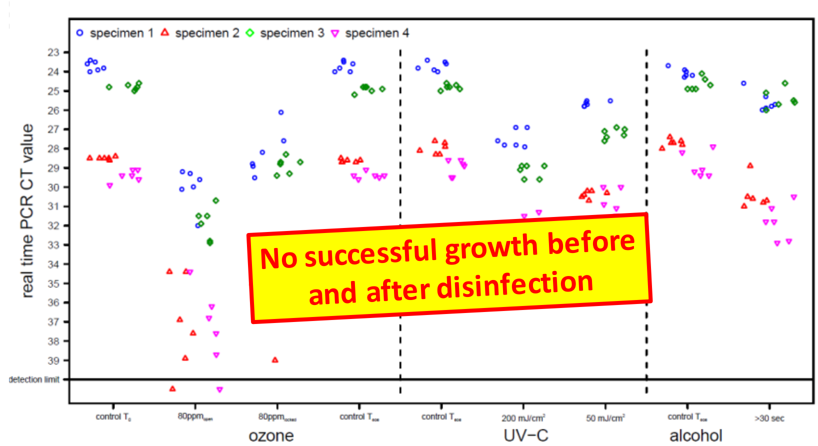

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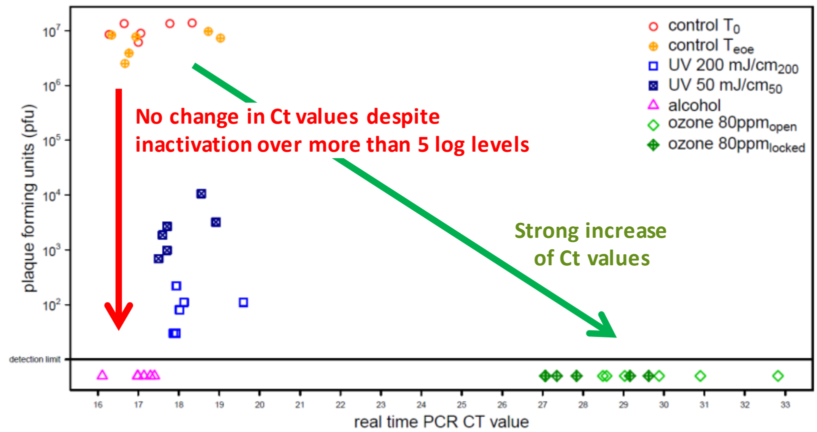

Knobloch et al. 2022, Int J Environ Res Public Health doi: 10.3390/ijerph192417074

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What role do inanimate surfaces play in transmission?

Feature

Workers spray disinfectant on a street in Shijiazhuang, China, in January 2020.

COVID-19 RARELY INFECTS THROUGH SURFACES. SO WHY ARE WE STILL DEEP CLEANING?

– houses, buses, churches, schools and shops – should clean and disinfect surfaces, especially those that are frequently touched. Disinfectant factories worked around the clock to keep up with heavy demand.

But Goldman, a microbiologist at Rutgers New Jersey Medical School in Newark, decided to take a closer look at the evidence around

Lewis D., Nature, 590, 26

What role do inanimate surfaces play in transmission?


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National Archives exhibition reveals 'Roaring Twenties' reality

21 January 2022

ADOBE STOCK
The decade begin with the nation still reeling from the effects of the deadly Spanish flu pandemic

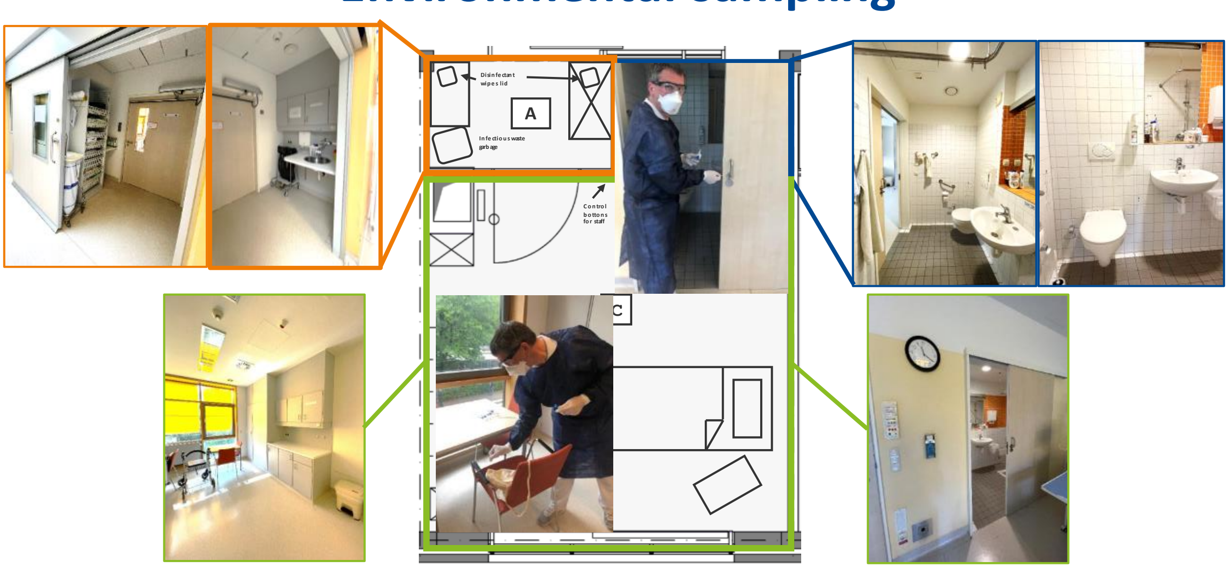
By Aurelia Foster
BBC News

[National Archives exhibition reveals 'Roaring Twenties' reality - BBC News]

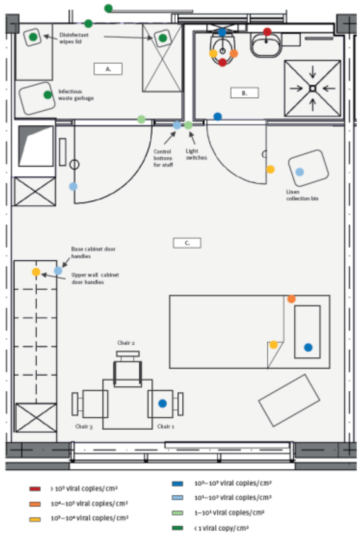
Catching up on missed opportunities

https://www.dw.com/en/monkeypox-who-declares-outbreak-a-global-public-health-emergency/a-62554539

Environmental sampling



What role do inanimate surfaces play in transmission?



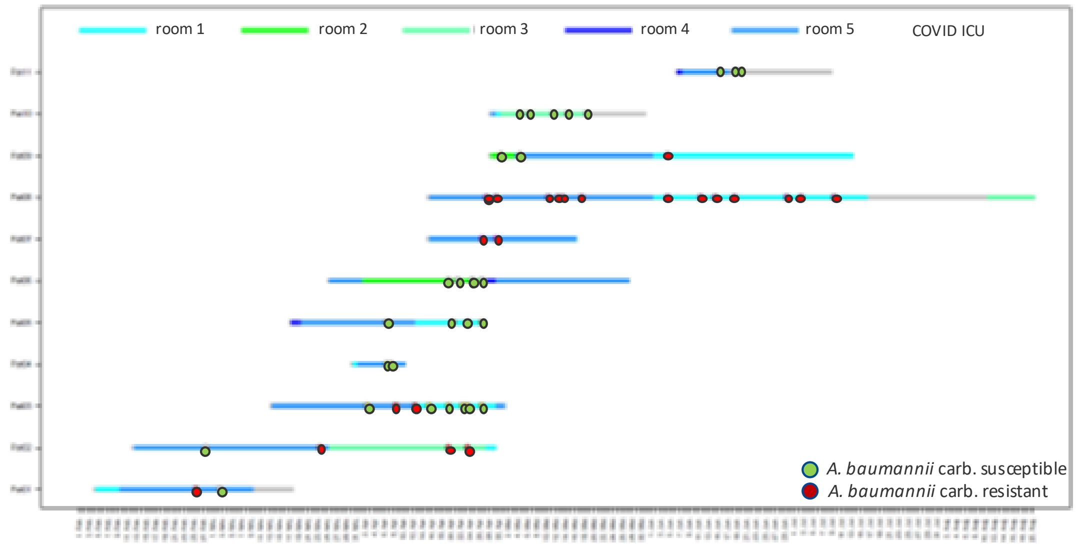
Location	Patient 1		Patient 2	
	Number of viral copies	Number of viral copies per cm²	Number of viral copies	Number of viral copies per cm²
Patient's room				
Bathroom door handle, patient room side	**1.9×10^5**	1.6×10^3	**6.8×10^4**	5.7×10^2
Upper wall cabinet door handles	**1.6×10^5**	1.3×10^3	n. d.	n. d.
Chair seat surface	**5.8×10^4**	5.8×10^2	**1.4×10^5**	1.4×10^3
Second anteroom door, patient room side	**1.1×10^4**	88	n. d.	n. d.
Lid of the dirty linen collection bin	**1.0×10^5**	84	n. d.	n. d.
Intercom control buttons for staff in patient room	2.2×10^2	11	**4.2×10^2**	21
Base cabinet door handles	1.3×10^3	10	n. d.	n. d.
Light switches	**6.3×10^2**	8	**56**	2
Armrests chair	n. d.	n. d.	**1.0×10^5**	2.1×10^2
Window handle	n. d.	n. d.	**2.7×10^5**	6.8×10^2
Mobile phone touch display	n. d.	n. d.	1.5×10^4	1.5×10^2
Light switch bathroom	n. d.	n. d.	**3.8×10^4**	1.5×10^3
Handles of empty wardrobe	n. d.	n. d.	**32**	‹1
Patient's bathroom				
Tap control lever	**4.8×10^6**	2.4×10^5	**1.1×10^5**	5.5×10^3
Seating surface toilet seat front in the middle	**2.5×10^6**	1.3×10^5	**1.5×10^4**	7.5×10^2
Seating surface toilet seat left	2.1×10^5	1.0×10^4	**2.6×10^4**	1.3×10^3
Seating surface toilet seat right	1.2×10^5	5.9×10^3	**2.6×10^4**	1.3×10^3
Bathroom door handle, bathroom side	**4.9×10^4**	4.1×10^2	**3.1×10^5**	2.6×10^3
Toilet flush control buttons	**6.8×10^4**	3.4×10^2	**1.6×10^5**	8.0×10^2
Soap dispenser operating lever	n. d.	n. d.	**1.7×10^6**	4.7×10^4
Anteroom				
Second anteroom door, anteroom side	**4.6×10^2**	4	**‹10**	‹1
First anteroom door, anteroom side	**2.4×10^2**	‹1	3.3×10^2	3
Infectious waste garbage can handle	**‹10**	‹1	n. d.	n. d.
Disinfectant wipes lid 1	‹10	‹1	n. d.	n. d.
Disinfectant wipes lid 2	‹10	‹1	n. d.	n. d.
Switch for electronic door opener	n. d.	n. d.	**‹10**	‹1
Lid of the dirty linen collection bin	n. d.	n. d.	‹10	‹1
Handles cabinets worktop top	n. d.	n. d.	‹10	‹1
Ward corridor				
First anteroom door, corridor side	**‹10**	‹1	**‹10**	‹1
Fabrics				
Mattress cover with visible soiling	**1.7×10^6**	1.7×10^4	n. d.	n. d.
Comforter cover with visible soiling	**2.3×10^5**	1.2×10^3	n. d.	n. d.
Patient shirt middle of the bottom	**4.9×10^4**	4.9×10^2	n. d.	n. d.
Pillowcase without visible soiling	**6.2×10^4**	3.1×10^2	n. d.	n. d.
Towel in bed to protect the bed sheet	n. d.	n. d.	**1.0×10^7**	1.0×10^5
Pillowcase used to cover cooling packs	n. d.	n. d.	**1.6×10^6**	8.0×10^3
Personal protective equipment (PPE)				
Glove of the examiner after contact with fabrics	**3.8×10^4**	2.7×10^2	**1.1×10^6**	7.9×10^3

Nörz et al., Eurosurveillance, 2022, DOI: 10.2807/1560-7917

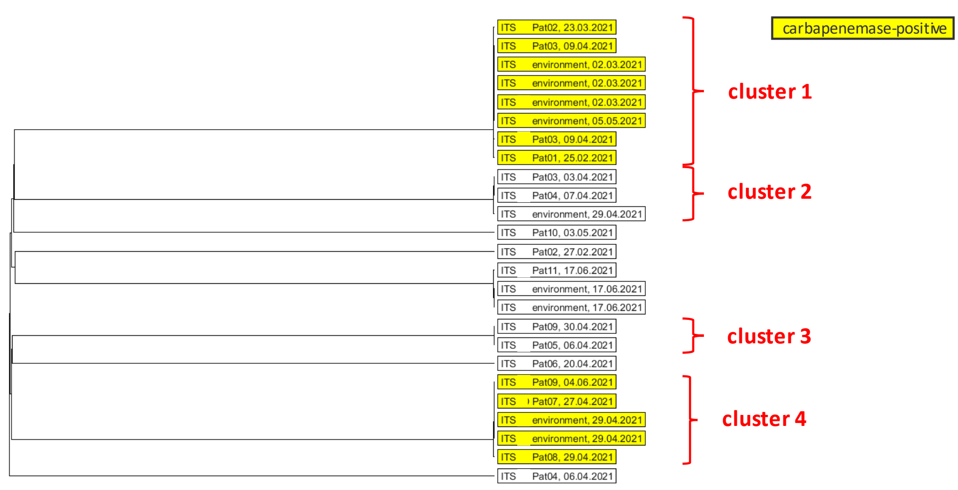
Lessons learned

- SARS-CoV-2 transmission by contact with surfaces is unlikely
- PCR methods are not suitable for estimating the infectivity of inanimate surfaces
- We should not always blame everything on "the cleaners“ in the case of transmission events
- Dermal viral replication (Mpox) leads to significantly higher environmental contamination

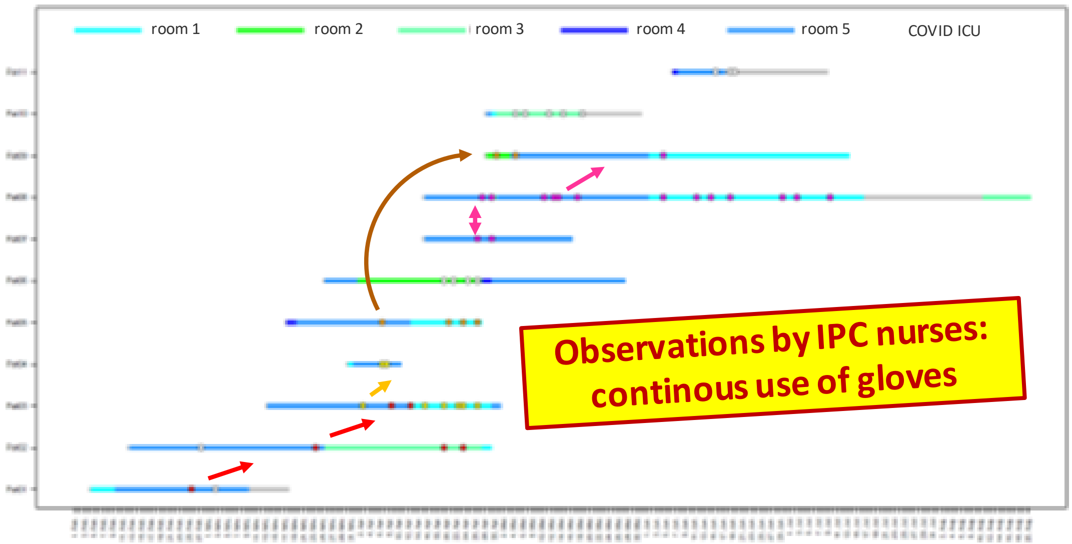
Outbreaks despite PPE usage 2



Outbreaks despite PPE usage 2



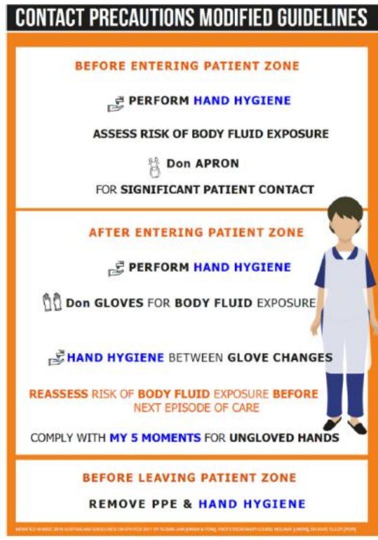
Outbreaks despite PPE usage 2



Basic principles/observations for glove usage

- Gloves only protect against gross contamination (handling of secretions)
- Every moment for hand disinfection is also an indication for changing gloves
- Glove wearing times should be limited as far as possible to protect the skin
- Changing gloves is difficult with wet hands (freshly disinfected or sweaty hands)

Change of glove usage in our hospital



Jain et al., 2019. Am J Infect Control, doi: 10.1016/j.ajic.2019.01.009

Change of glove usage in our hospital

Use of gloves in the care of COVID-19 (+ other pathogens)

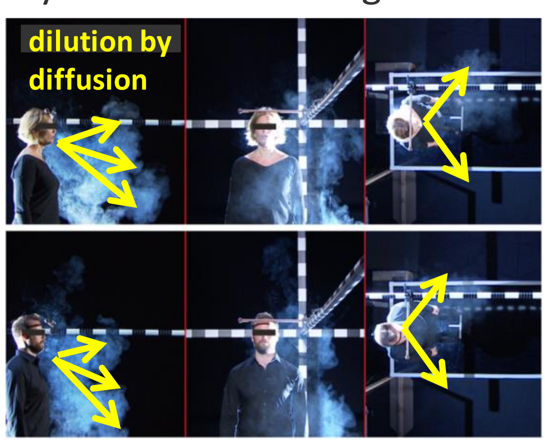
- Gloves must be worn when there is a possibility of gross contamination (handling of secretions).
- Gloves can be dispensed with for other ("dry") activities
- The 5 moments for hand disinfection must be followed
- If staff wish to wear gloves at all times, they must be changed in accordance with the rules

Lessons learned

- Gloves should be used targeted for the prevention of gross contamination and not in general in isolation rooms (except for organisms causing skin infections)
- Rethinking these rules requires a high level of training

My personal opinion (maybe not the truth)

- Viral transmission by aerosols over long distanced is overestimated



Knieburges et al., 2022, J. Exposure Science & Environmental Epidemiology, 32:727–734

My personal opinion (maybe not the truth)

- Viral transmission by aerosols over long distanced is overestimated (dilution by diffusion)
- In the short distance all viral respiratory pathogens can be trans-mitted by droplets and aerosols (in the case of high viral loads)
- Respirators should be applied in a targeted manner depending on the respective situation in care but not mandatory during complete shifts
- Respirators should not be used with the goal of third-party protection

My personal opinion (maybe not the truth)

- Don`t trust CT values for the assessment of infectivity of inanimate surfaces
- Neutralizing Ab detected in serum samples do not predict “sterile immunity” (which can´t be reached for viral respiratory infections)