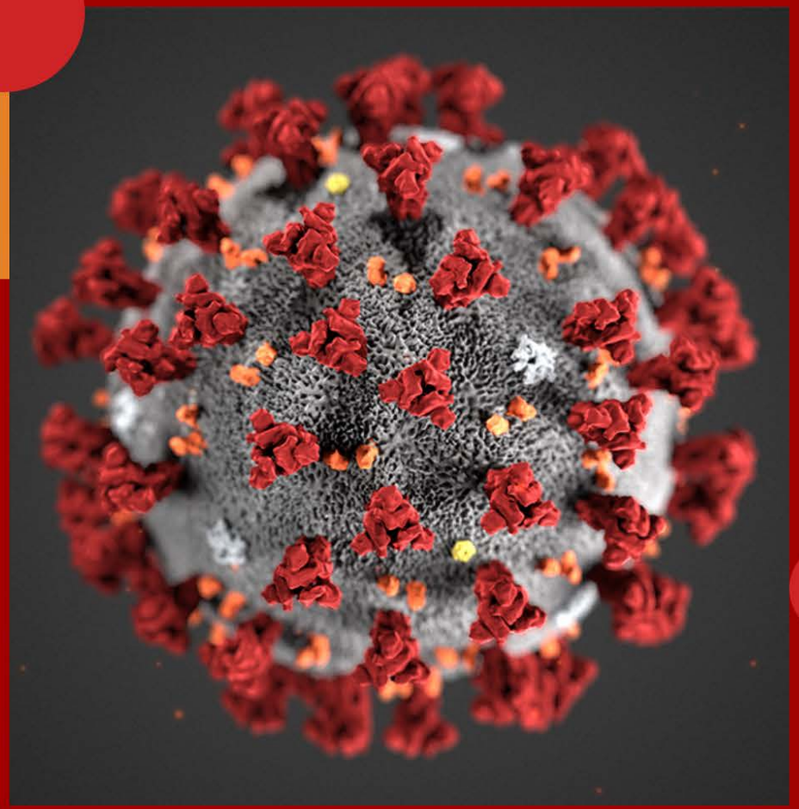
SARS-CoV-2 Modes of Transmission and Related IPC Measures



July 7, 2020

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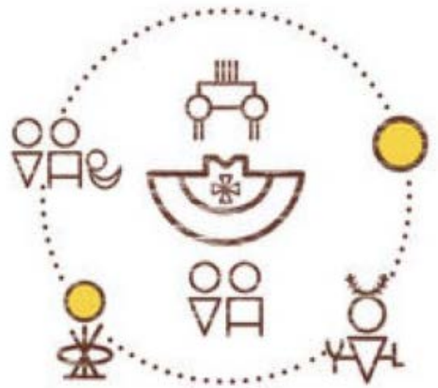
Territorial Acknowledgement



ii' taa'poh'to'p

Source: https://www.ucalgary.ca/indigenous

I acknowledge the traditional territories of the Blackfoot and Treaty 7 peoples including the Siksika, Piikuni, Kainai, Tsuut’ina, and Stoney Nakoda First Nations. Calgary is also home to the Metis Nation of Alberta, Region III.

Sorting the Message

- Mainstream media and social media in **total overdrive**
- First major pandemic in the "modern age" of **instant social messaging**
- Lots of "papers" now published online before even reviewed
- "Science" may be correct but may jump to premature or incorrect conclusions or be incomprehensible; some will never be published
- Even in top quality peer-viewed journals the articles may be premature / over interpreted / incomplete and without necessary limitations
- Many letters and short reports
- Authors/reviewers/journals immense pressure to be **fast and first**
- **Be careful and use your critical appraisal skills and common sense**

The New York Times | https://nyti.ms/2Nb7vDe

Scientists Take Aim at Another Coronavirus Study in Major Journal

A report on masks relied on unfounded assumptions, researchers charged, and the authors were permitted to choose their own reviewers.

By Apoorva Mandavilli

June 18, 2020

A group of leading scientists is calling on a journal to retract a paper on the effectiveness of masks, saying the study has "egregious errors" and contains numerous "verifiably false" statements.

The scientists wrote a letter to the journal editors on Thursday, asking them to retract the study immediately "given the scope and severity of the issues we present, and the paper's outsized and immediate public impact."

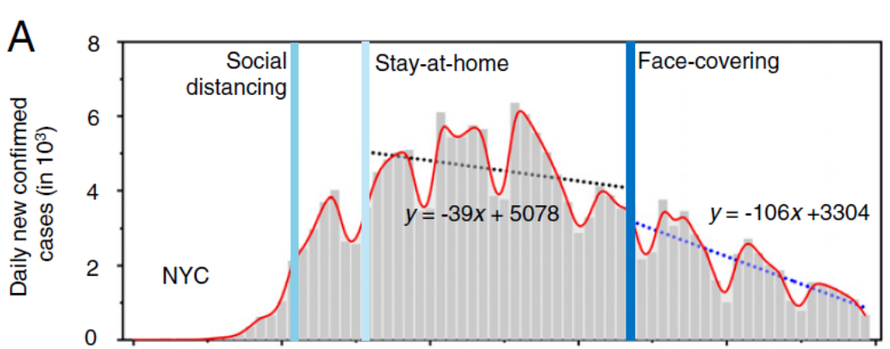
The letter follows heated criticism of two other major coronavirus studies in May, which appeared in the New England Journal of Medicine and The Lancet. Both papers were retracted amid concerns that a rush to publish coronavirus research had eroded safeguards at prestigious journals.

The study now under fire was published on June 11 in the journal Proceedings of the National Academy of Sciences. The senior author is Mario Molina, who won the Nobel Prize in Chemistry in 1995, with two other scientists, for finding a link

Identifying airborne transmission as the dominant route for the spread of COVID-19

Renyi Zhang[a,b,1], Yixin Li[b], Annie L. Zhang[c], Yuan Wang[d], and Mario J. Molina[e,1]

[a]Department of Atmospheric Sciences, Texas A&M University, College Station, TX 77843; [b]Department of Chemistry, Texas A&M University, College Station, TX 77843; [c]Department of Chemistry, College of Natural Sciences, The University of Texas at Austin, Austin, TX 78712; [d]Division of Geological and Planetary Sciences, California Institute of Technology, Pasadena, CA 91125; and [e]Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, CA 92093



Basic Viral Facts

- The SARS-CoV-2 causes COVID-19 infection.
- Single strand RNA virus in coronavirus family named from its morphology
- Only a few coronaviruses cause human illness (mostly **respiratory** such as colds but also serious respiratory infections SARS and MERS)
- It is a respiratory virus (predominant route contact /droplet transmission)
- Uses human ACE 2 receptor(angiotensin converting enzyme 2)
- **High affinity** for receptor on respiratory cells vs. SARS-CoV-1 (? few viruses needed for infection)

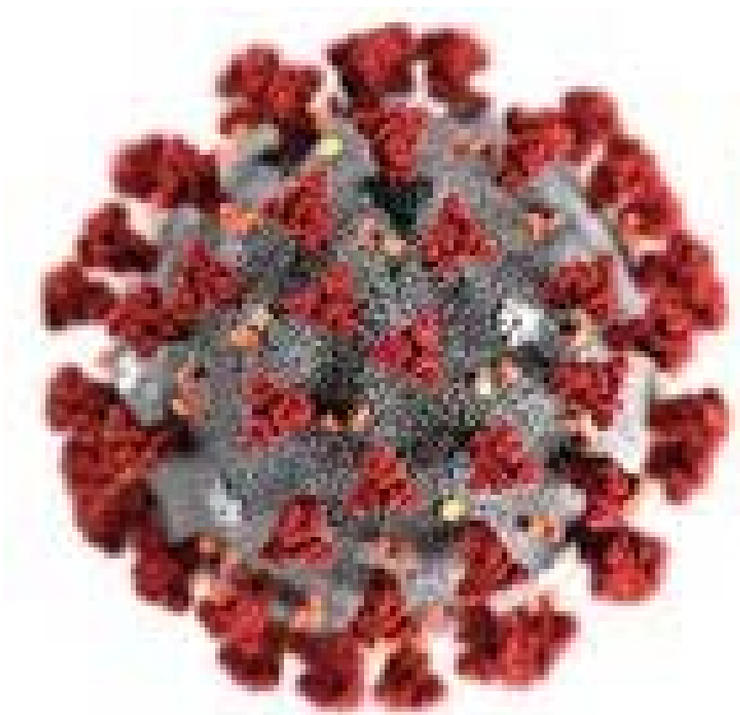
SARS -CoV-2

- SARS-CoV-2 likely originated from Asian bats into intermediary animal host (? the pangolin) and then to humans
- Virus not mutating significantly. So vaccine possible
- IgG and IgM Antibody tests are available: Will be very useful for determining natural history and possible health care staffing
- No one is immune

Natural History in Humans

- Proportion of asymptomatic infections unknown and critical for understanding possible transmission and HCW immunity.
- Estimates range 0-6% but models higher
- Incubation period after exposure likely 2-14 days (median ~5 days)
- 97.5% develop symptoms within 11 days
- Of those diagnosed
  - **80%** have self-limited mainly respiratory illness probably of ~ 14 days duration
  - **15%** have more severe illness requiring medical care +/- hospitalization
  - **5%** go to intensive care +/- ventilation
- Risk in hospitalized is mainly respiratory then multi organ failure requiring ventilation and high risk of death ~ 70% ventilated patients
- Progression risk and rate down pathway below is unclear

COVID-19 and SARS-CoV-2
Infection Prevention and Control



SARS-CoV-2

According to WHO

The disease caused by
Novel Coronavirus, SARS-CoV-2

is now officially called

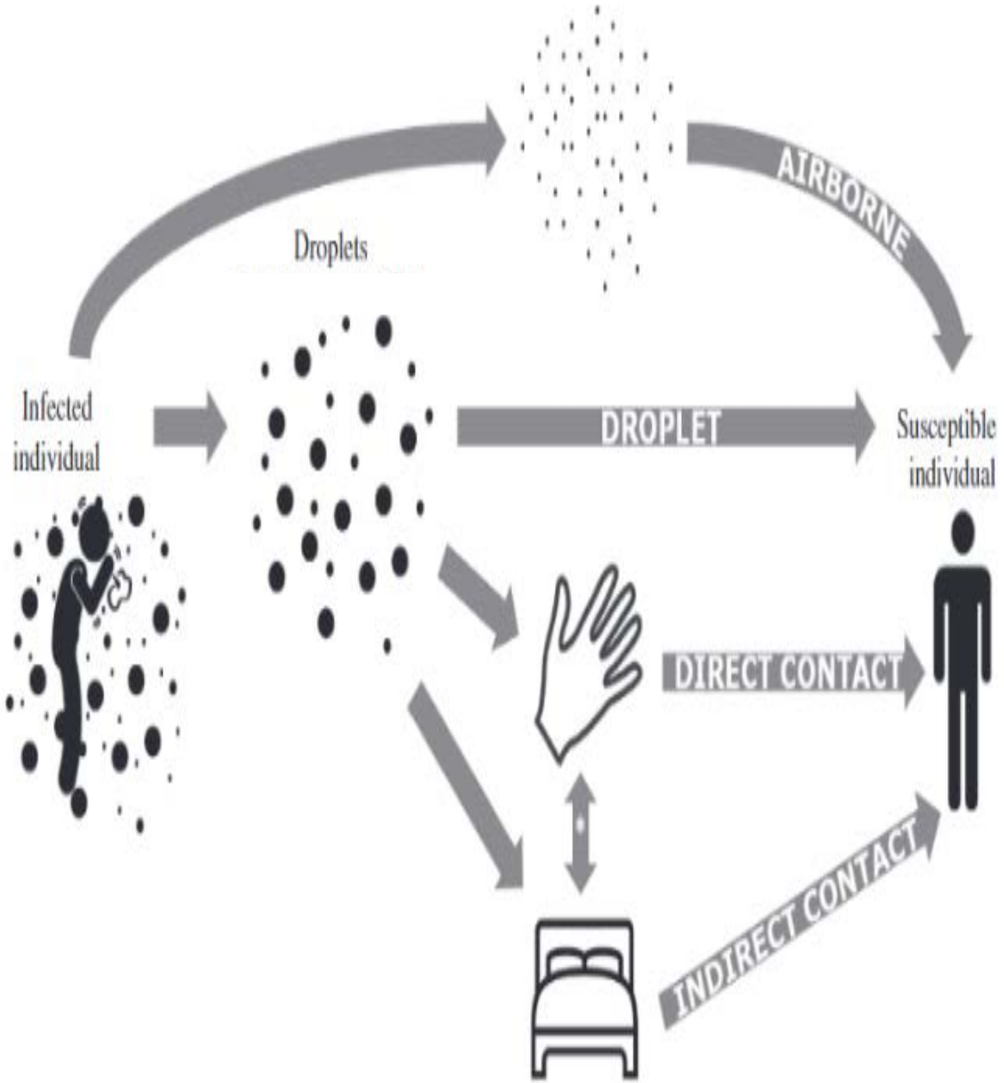
COVID-19

CO - Corona
VI - Virus
D - Disease

www.microbenotes.com

World Health Organization

Transmission Routes



Source: J.A. Otter et al. / Journal of Hospital Infection 92 (2016) 235e250

Transmission Routes

- Droplet and airborne routes create most debate
- Continuum of droplet and airborne routes an important concept
- Particles of a variety of sizes are expelled from the human airway during coughing, sneezing, talking and medical procedures
- Size of these particles and the distance propelled is complex
  - particle sizes variable
  - distance they will be propelled is dependent on the force generated by the individual or the procedure
  - particles may or may not contain the infectious agent
  - infectious agent may or may not be viable
  - concentration of particles affected by many factors: the relative humidity, evaporation level, ,settling velocity, direction of air flow, the number of air changes per hour, temperature, crowding and other environmental factors
- Airborne may be obligate or preferential or opportunistic and refers to particles that stay aloft for minutes or hours (less than 5-10 µm in diameter) and can be carried by air currents over a measurable distance
- Droplet spread refers to large droplets (>5-10um) that fall within 1 metre

Exposure, Transmission and Invasive Infection

- Exposure to microorganisms
- Not all exposures lead to transmission and invasive infection.
- Exposure occurs when a host comes into contact with an infected source or contaminated environment (e.g., inanimate/animate object or respiratory droplets containing the virus)
- Probability of transmission followed by invasive infection →many factors
  - host susceptibility
  - presence of host receptors
  - receptivity of host receptors
  - inoculum
  - pathogen viability
  - virulence
  - effectiveness of the hierarchy of controls

SARS-CoV-2 Detection

Patient specimens

- **BAL** samples (Zhu NEJM) + viral isolation
- **Nasopharyngeal/oropharyngeal** (NP/OP) swabs
  - multiple reports of detection of 2019-nCoV RNA in NP/OP swabs; sensitivity varies 71-100% and depends on operator, timing and site of specimen; specificity near 100%
  - shedding of SARS-CoV-2 RNA over time varies but recent studies elucidating
  - viable virus does not correlate well with RT-PCR positivity depending on timing
  - studies consisently show viable infectious virus gone by Day 7-8
- **Serum**
  - Chan (Lancet 2020) also showed + RT-PCR of serum in one patient
- **Stool**
  - At least 3 studies now found cultivatable virus in stool and one in urine

Wolfel et al Nature. 2020 Apr 1. doi: 10.1038/s41586-020-2196-x.; Bullard J et al Clin infect Dis.https://doi.org/10.1093/cid/ciaa638 Xiao F et al. Sun Infectious SARS-CoV-2 in Feces…. Emerg Infect Dis. 2020;26(8); Wang Wet al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA. 2020;323(18):1843-1844.

SARS-CoV-2 Detection in Cough Samples and the Environment

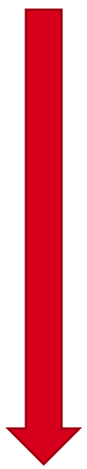
Patient specimens

- **Collection specimens actively infected patients (n= 17 inpatients/6 outpatients to date)**
  - Use of multiple collection techniques using DMEM or UTM for viral culture LKS Virology Institute (Vero cell culture)
  - Collection varies day 1 post onset to > 10 days post illness onset
  - Total 11 patients + to date – all virus + at a **mean of 4** days post onset symptoms
  - Remainder patients mean of **10.3 days** post onset symptoms and all specimens **culture negative**

Unpublished Data: U of Alberta and U of Calgary and ProvLab AB – D Evans, J Lin , J Conly, T Louie, L Ward, L Kiplagat, R Mallot, B Berenger

SARS-CoV-2 Detection in Cough Samples and the Environment

Highest



Lowest and/or no growth

- sputum samples[up to 10^6 pfu/ml; one sample found on a patient's gown]
- saliva specimens [up to 3 x 10^3 pfu/ml]
- cough bags [up to 10^3 pfu/ml]
- hands after coughing into cupped hands [up to 10^2 pfu/ml]
- plastic nasal prongs used for O2 delivery [up to 10^2 pfu/ml]
- no talk or singing bag specimens found +

Unpublished Data: U of Alberta and U of Calgary and ProvLab AB – D Evans, J Lin , J Conly, T Louie, L Ward, L Kiplagat, R Mallot, B Berenger

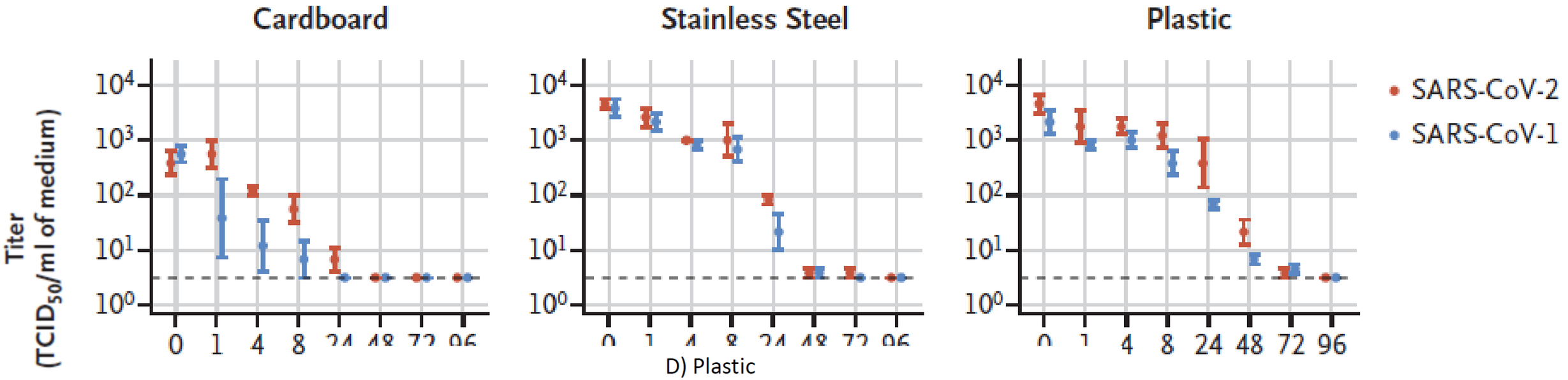
Table I
Persistence of coronaviruses on different types of inanimate surfaces

Type of surface	Virus	Strain / isolate	Inoculum (viral titer)	Temperature	Persistence	Reference
Steel	MERS-CoV	Isolate HCoV-EMC/2012	10^5	20°C	48 h	[21]
				30°C	8–24 h	
	TGEV	Unknown	10^6	4°C	≥ 28 d	[22]
				20°C	3–28 d	
				40°C	4–96 h	
	MHV	Unknown	10^6	4°C	≥ 28 d	[22]
				20°C	4–28 d	
				40°C	4–96 h	
	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Aluminium	HCoV	Strains 229E and OC43	5×10^3	21°C	2–8 h	[24]
Metal	SARS-CoV	Strain P9	10^5	RT	5 d	[25]
Wood	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
Paper	SARS-CoV	Strain P9	10^5	RT	4–5 d	[25]
	SARS-CoV	Strain GVU6109	10^6	RT	24 h	[26]
			10^5		3 h	
			10^4		< 5 min	
Glass	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Plastic	SARS-CoV	Strain HKU39849	10^5	22°-25°C	≤ 5 d	[27]
	MERS-CoV	Isolate HCoV-EMC/2012	10^5	20°C	48 h	[21]
				30°C	8–24 h	
	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
	SARS-CoV	Strain FFM1	10^7	RT	6–9 d	[28]
	HCoV	Strain 229E	10^7	RT	2–6 d	[28]
PVC	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Silicon rubber	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Surgical glove (latex)	HCoV	Strains 229E and OC43	5×10^3	21°C	≤ 8 h	[24]
Disposable gown	SARS-CoV	Strain GVU6109	10^6	RT	2 d	[26]
			10^5		24 h	
			10^4		1 h	
Ceramic	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Teflon	HCoV	Strain 229E	10^3	21°C	5 d	[23]

MERS = Middle East Respiratory Syndrome; HCoV = human coronavirus; TGEV = transmissible gastroenteritis virus; MHV = mouse hepatitis virus; SARS = Severe Acute Respiratory Syndrome; RT = room temperature.

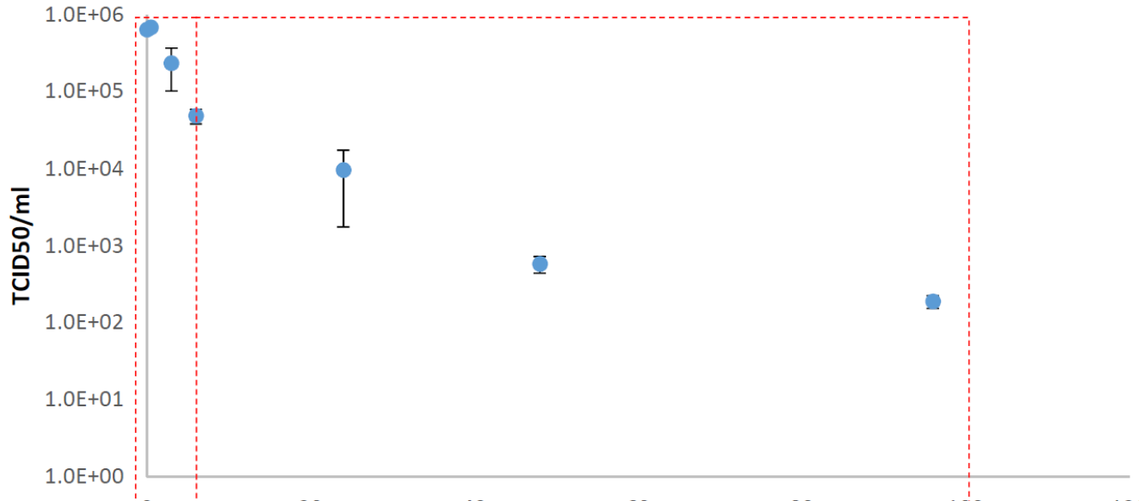
Kampf G et al J Hosp Inf 2020

Survival SARS-CoV-2

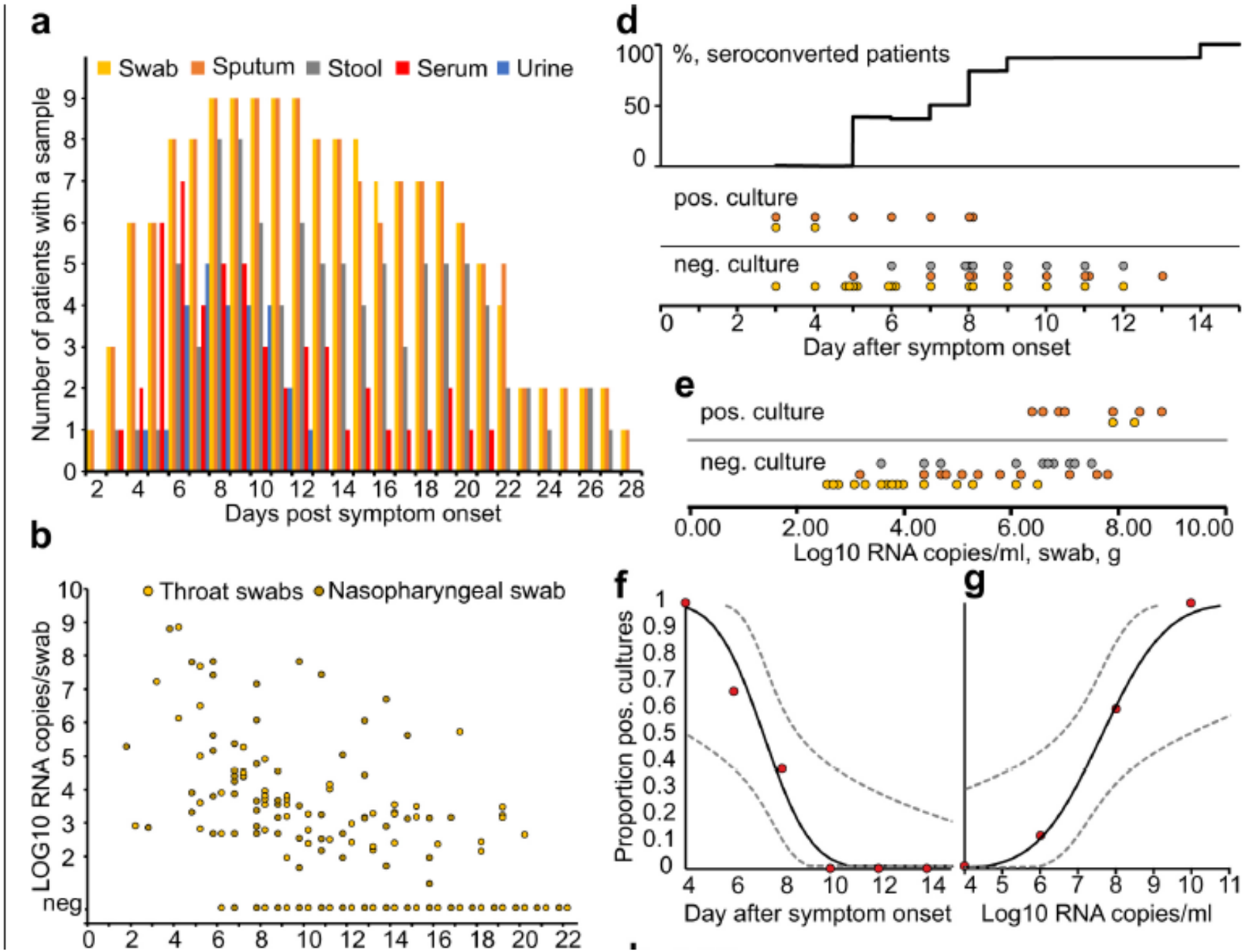


D) Plastic

Van Doremalen N et al. N Engl J Med.2020 Apr 16;382(16):1564-1567

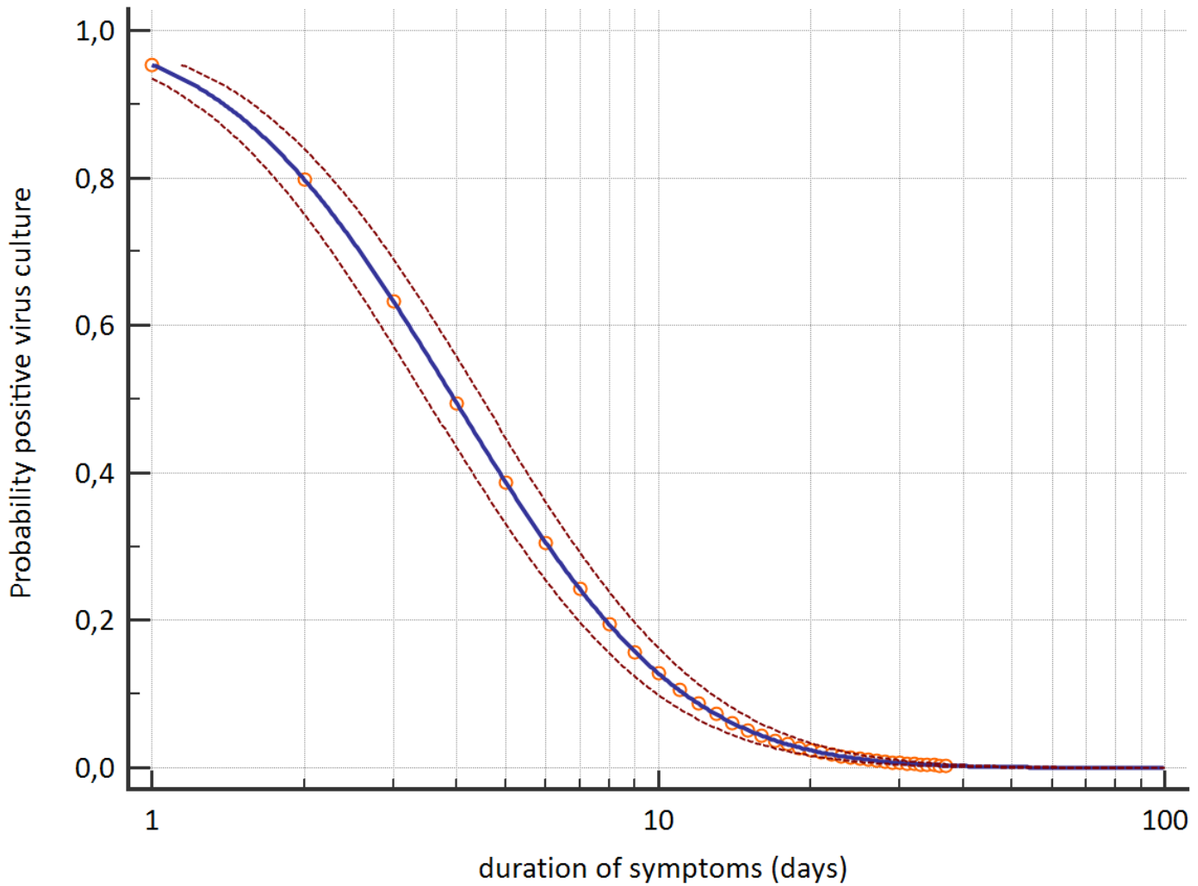


Supplement to: Chin A W H, Chu J T S, Perera M R A, et al. Stability of SARS-CoV-2 in different environmental conditions. *Lancet Microbe* 2020; published online April 2. https://doi.org/10.1016/S2666-5247(20)30003-3.

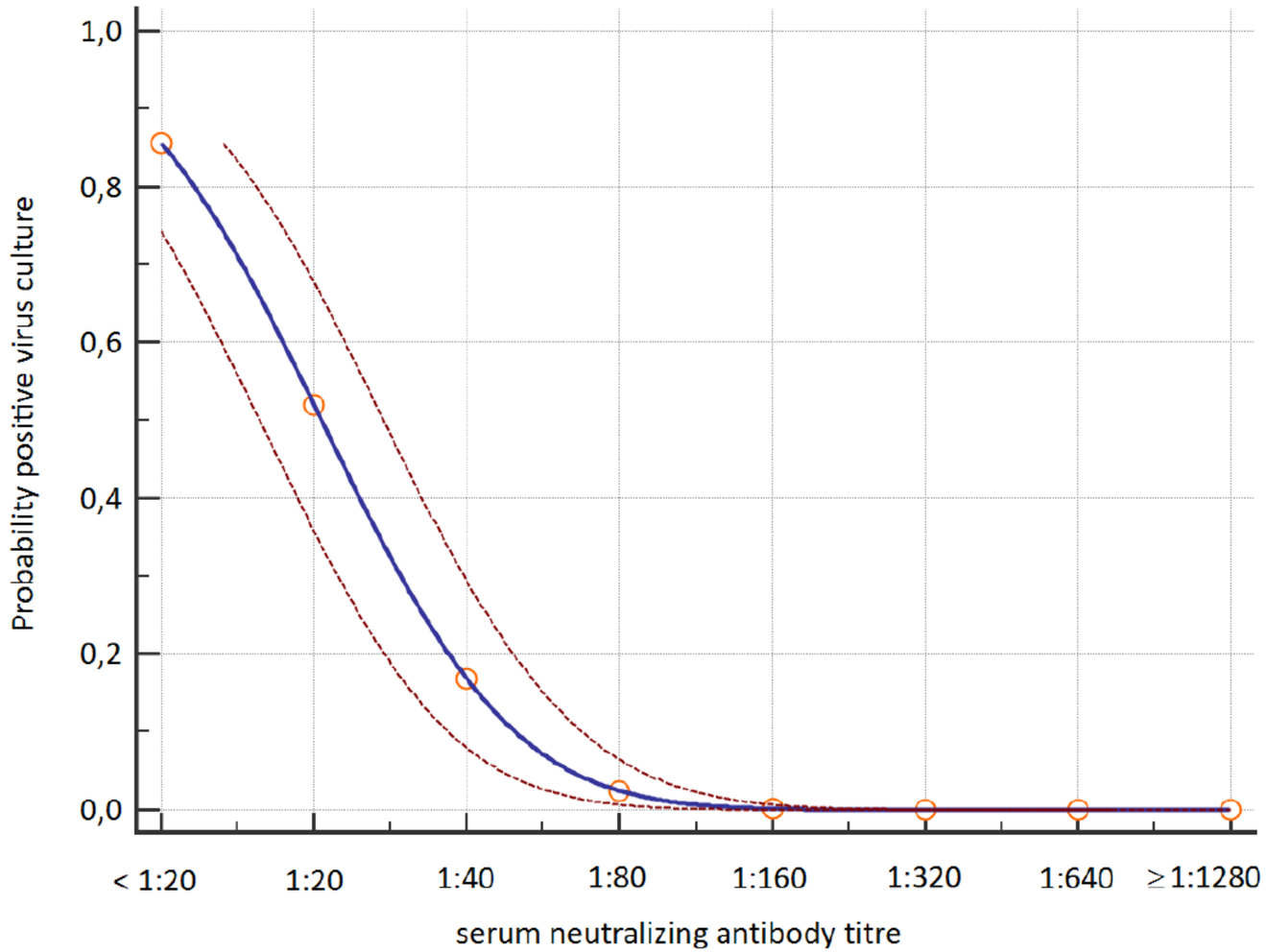


- Virus was readily isolated during the first week of symptoms from a considerable fraction of samples (16.66% in swabs, 83.33% in sputum samples)
- No isolates of virus obtained from samples taken after day 8 in spite of ongoing high viral loads by RT-PCR

Wolfel et al Nature. 2020 Apr 1. doi: 10.1038/s41586-020-2196-x.



Van Kampen et al . Shedding of infectious virus in hospitalized patients with coronavirus disease-2019 (COVID-19): duration and key determinants. medRxiv preprint doi: https://doi.org/10.1101/2020.06.08.20125310.this version posted June 9, 2020.



Van Kampen et al . Shedding of infectious virus in hospitalized patients with coronavirus disease-2019 (COVID-19): duration and key determinants. medRxiv preprint doi: https://doi.org/10.1101/2020.06.08.20125310.this version posted June 9, 2020.

SARS-CoV-1/ MERS-CoV Findings Relevant to IPC in the Clinical Setting

- **Droplet and contact** – multiple studies demonstrated **compliance with gloves, gowns and medical masks or N95s** were adequate to prevent transmission for SARS

- **Major risks** exposure of eye and mucous membranes to **respiratory secretions and AGMPs**, ie intubation (**opportunistic airborne);** no association with contact with urine/stool

- **HCW spread -** associated with **inconsistent or improper PPE use** for SARS/MERS-CoV outbreaks; **Infections in HCWs: 22% and 25%** for SARS and MERS, respectively

- **Risk factors for nosocomial spread** of MERS-CoV in two large outbreaks in Saudi Arabia and South Korea found ER/Ward **overcrowding and sub-optimal control of visitors** were major factors

Seto WH et al Lancet 2003;Raboud J et al Plos One 2010; Jefferson et al Cochrane Rev 2011; Oboho IK et a NEJM 2015;Kim SW CID 2017; Cheng VC et al Antiviral Res 2013; Van Kerkhove MD et al Sci Rep. 2019.

Mode Transmission SARS-CoV-2

- Droplet - contact considered predominant route
  - Consistent with SARS-CoV-1, MERS-CoV
  - Consistent with R_0 of other droplet-contact respiratory viruses
  - WHO-China Joint Mission on COVID-19 in China with 75,465 cases supported person-to-person droplet and fomite transmission
    - 78-85% of the investigated infection clusters occurred within families, with an intra- household 2^0 attack rate of 3-10%, not consistent with airborne transmission where much higher attack rates would have been expected
    - Multiple other reports Korea, Taiwan, US with similar findings

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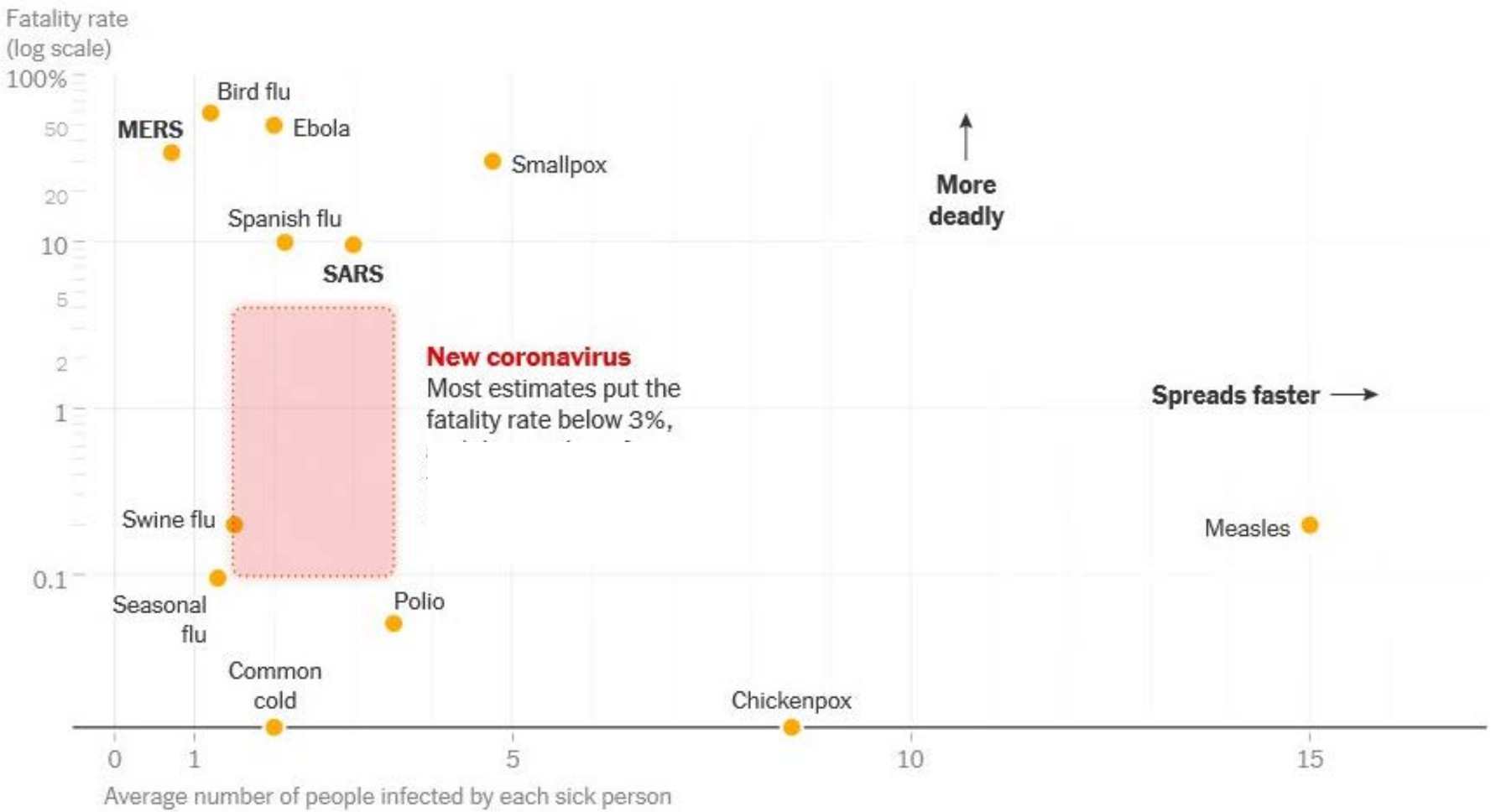
References: WHO- China Joint Mission Report 2020; Scientific Brief: Transmission of SARS-CoV-2: implications for infection prevention precautions, WHO 2020.

How SARS-CoV-2 spread compares to other viruses



Basic reproductive number (R_0)
the average number of individuals infected by a case over the infectious period, in a fully susceptible population.
Most major studies of COVID-19 suggest it is falling into a range of 2.20 -2.68 Korea and Italy of 2.60 (based on initial case growth)

Li Q et al N Engl J Med. 2020 Mar 26;382(13):1199-1207; Wu JT Lancet. 2020 Feb 29;395(10225):689-697
Zhynag Z et al. Int J Infect Dis. 2020 Apr 22. pii: S1201-9712(20)30259-9.

Reports against/for Airborne Transmission for CoVs

- 41 HCW exposure over 10 minutes within 2 meters to a COVID-19 patient during multiple AGMPs, 85% surgical masks and no transmission events
- COVID-19 + who was nursed in an open cubicle of a general ward before the diagnosis was made and 76 tests 52 contacts, some without PPE and no transmissions
- No evidence of COVID-19 transmission to passengers seated around a COVID+ passenger long flight

References:; Ng K et al Ann Int Med.16 Mar 2020; Wong SC-Y. J Hosp Inf 2020; :Schwartz K et al. CMAJ 24 March 2020;

- Amoy Garden outbreak Sars-CoV-1 > 300 residents possible aerosol event vs rats
- Report of a bus transmission 4.5 meters distance in Chinese report (translated) – **now retracted**
- Outbreak in air-conditioned (AC) restaurant China with 10 persons with 1 meter distance between tables along flow of air from the AC
- Experimental laboratory study with 3-jet Collison nebulizer creating aerosol of viable SARS-CoV-2
- Systematic review of droplet dispersion but mainly modelling studies; no clinical settings or epidemiologic data

References: Yu IT et al N Engl J Med. 2004 Apr 22;350(17):1731-9; Luo Y et al. Pract Prev Med. 2020-03-05. Lu J et al. MMWR 26:7 July 2020; Van Doremalen N et al. N Engl J Med.2020 Apr 16;382(16):1564-1567; Bahl P et al. JID 2020;XX:1–8

Reports against/for Airborne Transmission for CoV-2 (partial review of 14 studies to date)

- SARS-CoV-2 (RT-PCR) in 1/13 (7.7%) environmental samples but 0/8 air samples collected 10 cm from the patient's chin in Hong Kong
- SARS-CoV-2 (RT-PCR) in 17/22 (77%) environmental samples but 0/5 air sample sites including beside the patient collected in Singapore
- None/10 air samples for SARS-CoV-2 (RT-PCR) with samplers with fresh DMEM 2 to 5 m away from the patient (severely ill)

Cheng V, et al. ICHE 2020; Ong SW, et al. JAMA 2020; Faridi S et al. Science of The Total Environment 2020

- SARS-CoV-2 (RT-PCR) in 20/37 air samples at 1-113 copies/m^3 highest ICU – multiple areas hospital
- SARS-CoV-2 (RT-PCR) in 126/163 samples (77.3%) collected in this study, 0 to 1.75 copies/µL and air samples 2.86 copies/L including outside pt rooms**; no viable virus** cultivated in any of the 163 samples
- SARS-CoV-2 (RT-PCR) high touch surface contamination was shown in 10/15 (66.7%) rooms 1840 to 3380 RNA copies per m^3 ; **viabilty not done**

References: Liu Y et al Nature Med. 2004 Apr 27; Santarpia JL et al 2020 medRxiv preprint; Chia PY, 2020, medRxiv preprint

Lack of Evidence to Support Airborne Transmission in Clinical Settings

- Alberta Health Services Calgary
- > 5000 cases and > 160 inpatient admissions
- Use PHAC recommendations with surgical mask as component of PPE all COVID wards – gowns/gloves, goggles or face shields plus HH
- **NO transmission events** in 5544 continuous person hours HCW exposure to 132 inpatient COVID + pts on medical wards
- Workup 5 symptomatic HCWs exposing 72 patients (no masking in 66 exposures) and other HCWs (Ct values of 10-30) and prolonged intense contact < 1 metre and > 15 min but excellent hand hygiene– no transmission events – Calgary, Canada
- Consistent with multiple other reports in the literature – Hong Kong, Italy, Germany

Conly J. Unpublished. Mponponsuo J et al Submitted . Wong SC et al. Risk of nosocomial transmission of coronavirus disease 2019: an experience in a general ward setting in Hong Kong . J Hosp Inf 2020.Durante –Mangoni E et al. Low rate of severe acute respiratory syndrome coronavirus 2 spread among health-care personnel using ordinary personal protection equipment in a medium-incidence setting. CMI 2020. Wendt R et al . Comprehensive investigation of an in-hospital transmission cluster of a symptomatic SARS-CoV-2-positive physician among patients and healthcare workers in Germany. ICHE 2020.

Principles of IPC Strategies associated with Health Care for Suspected COVID-19

1. Ensuring triage, early recognition, and source control (isolating patients with suspected COVID-19)
2. Applying standard precautions for all patients
3. Implementing empiric additional precautions (**droplet and contact** and, whenever applicable e. g. AGPs, airborne precautions) for suspected cases of COVID-19
4. Implementing administrative controls
5. Using environmental and engineering controls

https://www.who.int/publications/i/item/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125

Ensuring Triage, Early Recognition, and Source Control

- Encourage HCWs to have a **high level of clinical suspicion**
- Establish a well-equipped **triage station** at the entrance to the facility, supported by trained staff
- Institute the use of screening questionnaires according to the updated case definition; refer to the Global Surveillance for human infection with coronavirus disease (COVID-19) for case definitions
- Post signs in public areas reminding symptomatic patients to alert HCWs

Applying Standard Precautions for all Patients

- Ensure that all patients **cover their nose and mouth** with a tissue or elbow when coughing or sneezing
- Offer a **medical mask to patients** with suspected COVID-19 while they are in waiting/public areas or in cohorting rooms
- Perform **hand hygiene after contact** with respiratory secretions
- Hand hygiene includes either cleansing hands with an alcohol-based hand rub or with soap and water
- Alcohol-based hand rubs are preferred if hands are not visibly soiled
- Wash hands with soap and water when they are visibly soiled

Implementing Empiric Additional Precautions

- **Contact and droplet** precautions
  - Gloves, gowns, medical masks, eye protection
  - Donning and doffing appropriately
  - Requires education for HCW populations
  - Single use or dedicated equipment
  - Limit visitors
  - Refrain touching face/mask/eyes
  - Disinfect high touch surfaces
- **Airborne** precautions for **aerosol-generating procedures**
  - Well ventilated room
  - Use a particulate respirator at level of a NIOSH-certified N95 or (EU) standard FFP2, or equivalent

Alberta Health Services

Infection Prevention and Control

Putting on (Donning) Personal Protective Equipment (PPE)

1 HAND HYGIENE

A Using an alcohol-based hand rub is the preferred way to clean your hands.

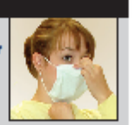
B If your hands look or feel dirty, soap and water must be used to wash your hands.

2 Gown

A Make sure the gown covers from neck to knees to wrist.

B Tie at the back of neck and waist.

3a Procedure/Surgical mask

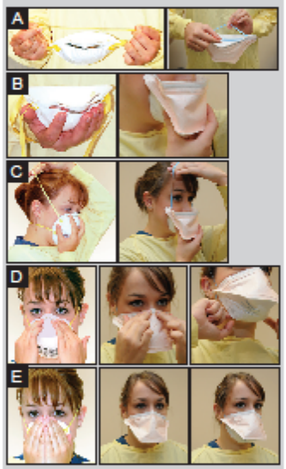


- Secure the ties or elastic around your head so the mask stays in place.
- Fit the moldable band to the nose bridge. Fit snugly to your face and below chin.

3b N95 respirator

There are different styles of N95 respirators (pictured below). They include: a) molded cup, b) duckbill, c) flat-fold and d) v-fold

All styles have the same basic steps for donning; molded cup and duckbill are pictured below. Refer to the manufacturer for specific donning instructions.



A Pre-stretch both top and bottom straps before placing the respirator on your face.

B Cup the N95 respirator in your hand.

C Position the N95 respirator under your chin with the nose piece up. Secure the elastic band around your head so the N95 respirator stays in place.

D Use both hands to mold the metal band of the N95 respirator around the bridge of your nose.

E Fit check the N95 respirator.

4 Eye protection or face shields

- Place over the eyes (or face).
- Adjust to fit.

5 Gloves

- Pull the cuffs of the gloves over the cuffs of the gown.

May 2014

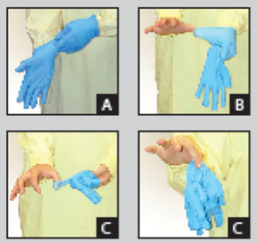
www.albertahealthservices.ca

Alberta Health Services

Infection Prevention and Control

Taking off (Doffing) Personal Protective Equipment (PPE)

1 Gloves



A Grasp the outside edge of the glove near the wrist and peel away from the hand, turning the glove inside-out.

- Hold the glove in the opposite gloved hand.

B Slide an ungloved finger or thumb under the wrist of the remaining glove.

C Peel the glove off and over the first glove, making a bag for both gloves.

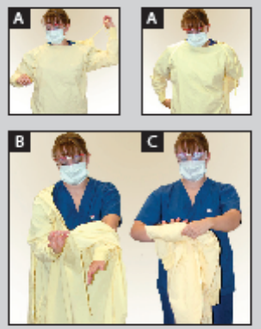
- Put the gloves in the garbage.

2 HAND HYGIENE

A Using an alcohol-based hand rub is the preferred way to clean your hands.

B If your hands look or feel dirty, soap and water must be used to wash your hands.

3 Gown



A Carefully unfasten ties.

B Grasp the outside of the gown at the back of the shoulders and pull the gown down over the arms.

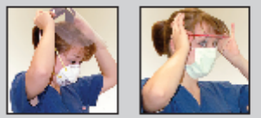
C Turn the gown inside out during removal.

- Put in hamper or, if disposable, put in garbage.

4 HAND HYGIENE

- Clean your hands. (See No. 2)
- Exit the patient room, close the door and clean your hands again.

5 Eye protection or face shield



- Handle only by headband or ear pieces.
- Carefully pull away from face.
- Put reusable items in appropriate area for cleaning.
- Put disposable items into garbage.

6 Mask or N95 respirator

- Bend forward slightly and carefully remove the mask from your face by touching only the ties or elastic bands.
- Start with the bottom tie, then remove the top tie.
- Throw the mask in the garbage.

There are different styles of N95 respirators but all styles have the same basic steps for doffing.

7 HAND HYGIENE

- Clean your hands. (See No. 2)

May 2014

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Images; AHS Donning and Doffing

Administrative Measures related to Health Care Workers

- Provision of **adequate training** for HCWs
- Ensuring an adequate patient-to-staff ratio
- Establishing a surveillance process for acute respiratory infections potentially caused by COVID-19 virus among HCWs
- Ensuring that HCWs and the public understand the
- Importance of promptly seeking medical care
- Monitoring HCW compliance with standard precautions and providing mechanisms for improvement

Using Environmental and Engineering Controls

- Address basic infrastructure of the health care facility[14] and aim to ensure adequate ventilation
- Maintain **adequate environmental** cleaning
- **Separation** of at least 1 metre between all patients
- Ensure that **cleaning and disinfection** procedures are followed consistently and correctly
- Manage laundry, food service utensils and medical waste in accordance with safe routine procedures

Questions

- Spectrum COVID “app”