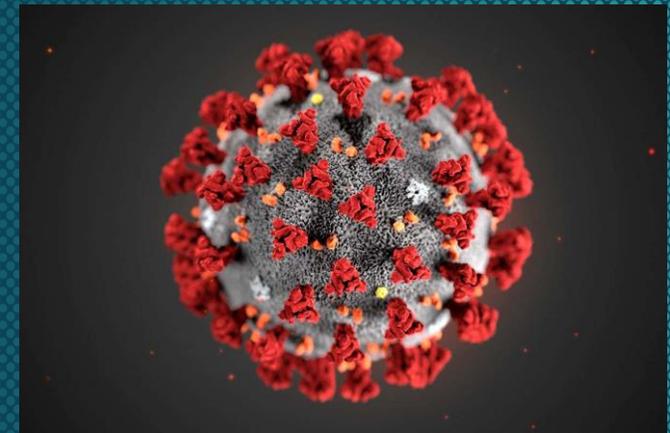


COVID-19 Clinical Update

I-TECH Videoconference July 11, 2020

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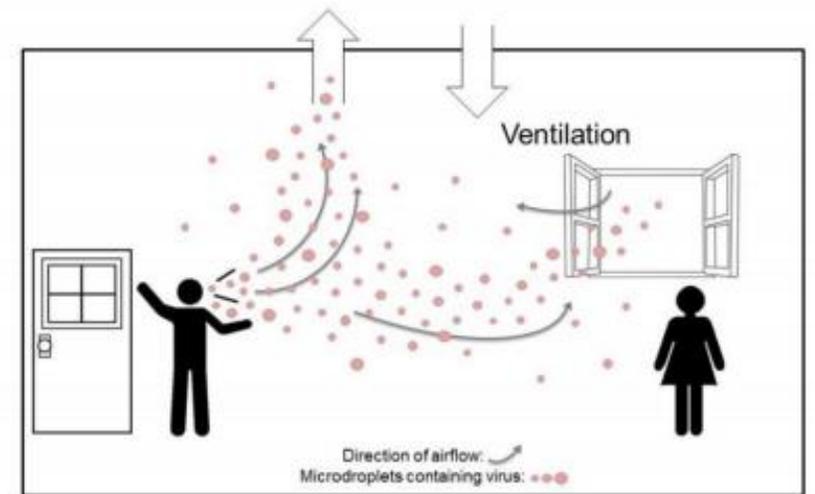
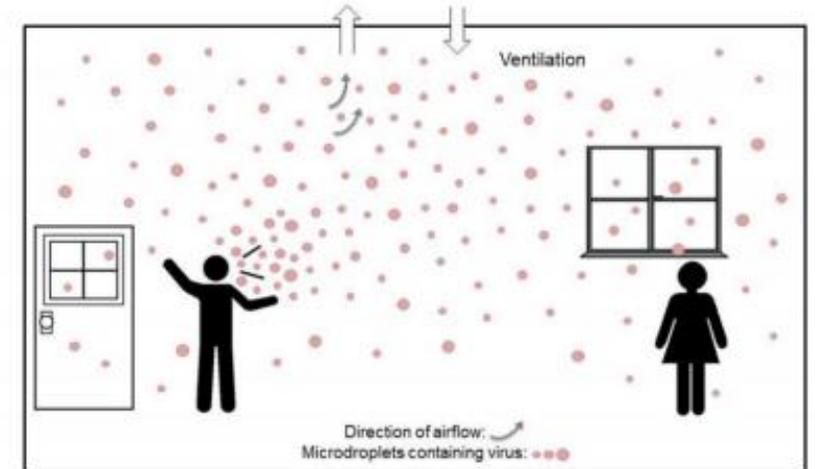
International Training and Education Center for Health

Overview

- Epidemiology – airborne transmission
- Laboratory testing
- New data on COVID-19 treatments – Corticosteroids
 - 1982 clinical trials as of June 8!

Continued Controversy on Airborne COVID-19 Transmission

- Letter advocating action to avert airborne transmission
- Argument
 - Virus released on microdroplets during exhalation, talking & coughing
 - Some data from SARS-CoV-1 suggesting airborne transmission
 - Other respiratory viruses show viable airborne virus (flu, MERS)
 - At least one study of SARS-CoV-1 suggest airborne transmission
- Action
 - ↑ Ventilation - Supply clean outdoor air, minimize recirculating air, particularly in public buildings, workplaces, schools, hospitals, & aged care homes.
 - Airborne infection controls - local exhaust, high efficiency air filtration, and germicidal ultraviolet lights.
 - Avoid overcrowding - public transport and public buildings.



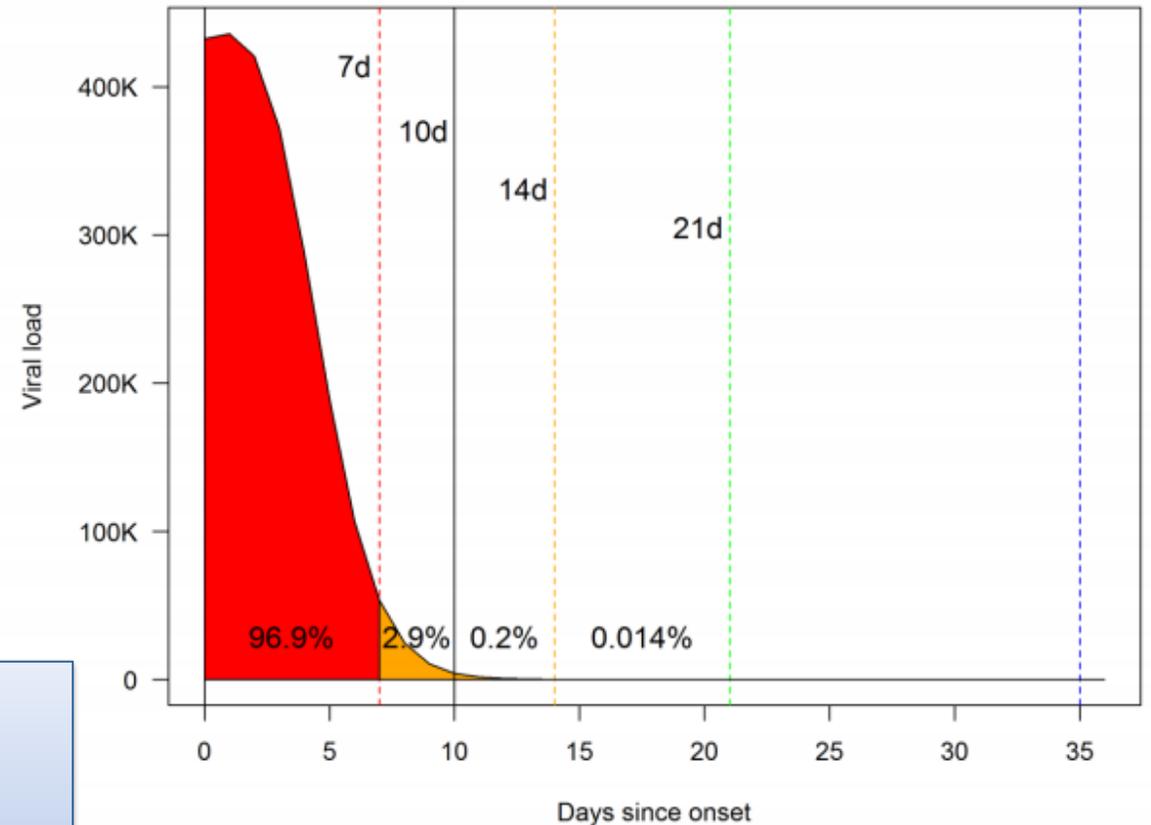
Nasal vs. Nasopharyngeal Specimens

- Design: Prospective cohort study
- Population: 230 non-hospitalized healthcare personnel diagnosed with COVID-19 Cleveland Clinic
- Testing – All tested at least once – 528 tests – Serial testing approach to release from isolation
- Outcome – AUC PCR threshold cycle (cycle at which PCR is 1st positive) to estimate viral load

Implications:

- Supports idea that most transmission emanates from initial week of infection
- Supports current isolation guidelines

Viral load-time curve – Proportion of 30 day area under the curve



Source: Shretha NK CID 2020

Nasal vs. Nasopharyngeal Specimens

| Author | N | Sensitivity NP | Sensitivity Mid-Turbinate* | Sensitivity relative to NP |
|----------|---------------------------------|----------------|----------------------------|----------------------------|
| Tu | 500 (50 COVID19+) | 100% | 96% | |
| Pere | 44 (37 COVID19+) | 100% | 89% | |
| Pinninti | 40 (All COVID19+) Enrollment | 85% | 72% | 85% |
| | 1 Week | 76% | 52% | 68% |

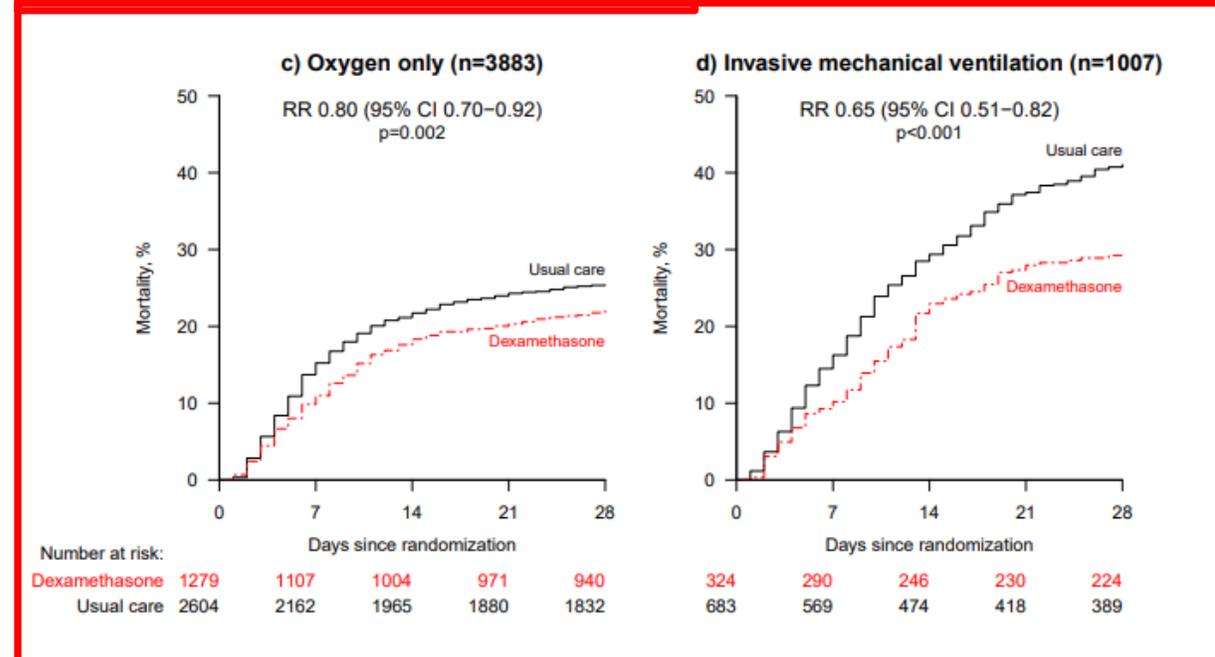
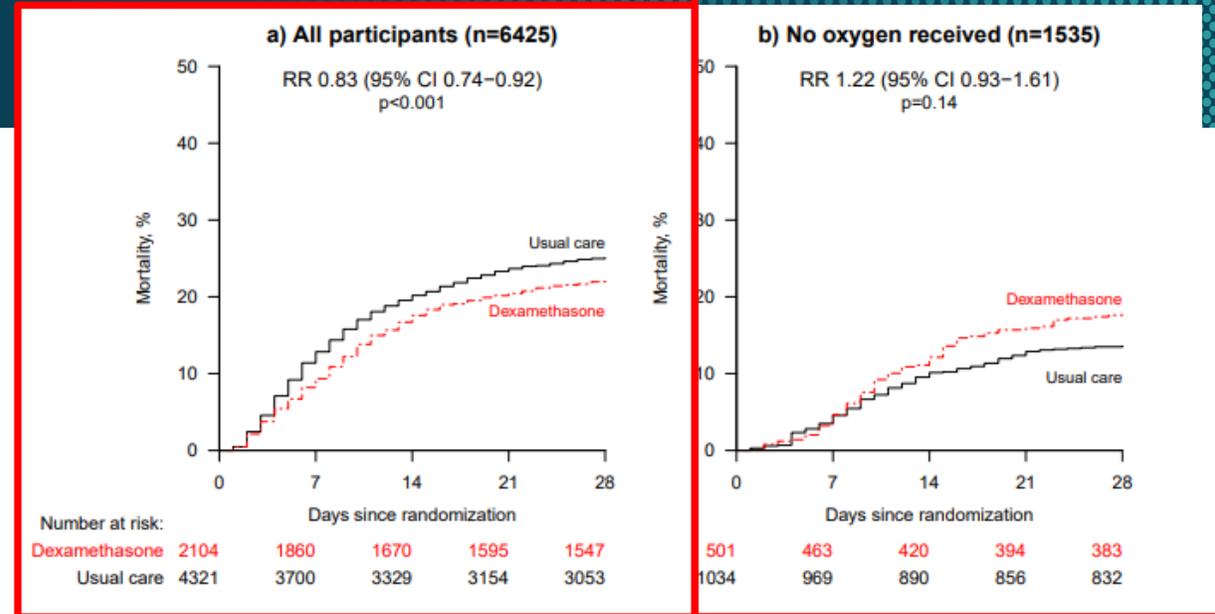
* Self-obtained

Implications:

- Most studies suggest nasal turbinate swabs as being only slightly less sensitive than NP swabs
- New data demonstrates declining sensitivity with time

Dexamethasone in COVID-19: RECOVERY Trial

- Design: open-label adaptive RCT (control varies)
- Population: Hospitalized patients - 2104 dex arm and 4321 control - in 176 hospitals in the UK
- Intervention: 6mg dexamethasone qd for up to 10 days (discharge) vs. usual care
- Outcome: 28 day mortality



Steroids in COVID-19

- Design: Retrospective cohort study
- Population: 463 hospitalized patients with COVID19 pneumonia and ARDS (64%) or hyperinflammatory syndrome – 396 received steroids
- Intervention: methylprednisolone 1 mg/kg/day (78%) or pulse steroids (250-500mg) median of 3 days (22%) – treatment median 10 days after onset of symptoms
- Outcome: Mortality

| | Survivors | Non-Survivors | OR 95% CI |
|-------------|-----------|---------------|---------------------------|
| No steroids | 51 (76%) | 16 (24%) | 0.51 (0.27-0.96) |
| Steroids | 341 (86%) | 55 (14%) | Adj OR - 0.36 (0.14-0.93) |

Dexamethasone in COVID-19: RECOVERY Trial

- COVID-19 is a biphasic illness
 - Early innate immune response
 - Adaptive immune response – appearance of antibody
- Poor outcomes in SARS-CoV-2 not associated with higher viral burden in the lung at time of death (though VL is higher early on), virus is not frequently found in the blood in symptomatic persons, and hypoxemia develops as viral load in the upper respiratory tract declines – unlike MERS or SARS-CoV-1
- RECOVERY highlights the benefits of steroids in decreasing the immunopathogenesis of COVID19 in the later phase of illness

NIH Guideline: Dexamethasone in COVID-19

June 25, 2020

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends using dexamethasone (at a dose of 6 mg per day for up to 10 days) in patients with COVID-19 who are mechanically ventilated **(AI)** and in patients with COVID-19 who require supplemental oxygen but who are not mechanically ventilated **(BI)**.
- The Panel **recommends against** using dexamethasone in patients with COVID-19 who do not require supplemental oxygen **(AI)**.

NIH Guideline: Dexamethasone in COVID-19

June 25, 2020

- No use of Remdesivir
- Few pediatric or pregnant patients
- Trial occurred in a country with few patients with latent TB or strongyloides – Some data that even short courses of high dose steroids increases the risk of TB reactivation

Table 3. Relationship between the number of glucocorticoid (GC) prescriptions and risk of tuberculosis*

| Exposure | Cases (n = 497) | Controls (n = 1,966) | Crude OR (95% CI) | Adjusted OR† (95% CI) |
|--------------|--------------------|-------------------------|----------------------|--------------------------|
| Nonexposed‡ | 395 | 1,798 | 1.0 (–) | 1.0 (–) |
| 1 Rx GC | 13 | 13 | 4.9 (2.5–9.9) | 3.2 (1.4–7.4) |
| 2–9 Rxs GC | 18 | 12 | 8.4 (3.7–19.1) | 7.0 (2.8–17.5) |
| 10–19 Rxs GC | 9 | 5 | 10.3 (3.1–34.3) | 8.7 (2.2–33.9) |
| ≥20 Rxs GC | 11 | 8 | 6.3 (2.5–15.7) | 4.1 (1.6–11.4) |
| Recent GC | 10 | 10 | 4.6 (1.9–11.3) | 4.2 (1.6–10.8) |
| Past GC | 41 | 120 | 1.7 (1.2–2.5) | 1.4 (0.9–2.2) |

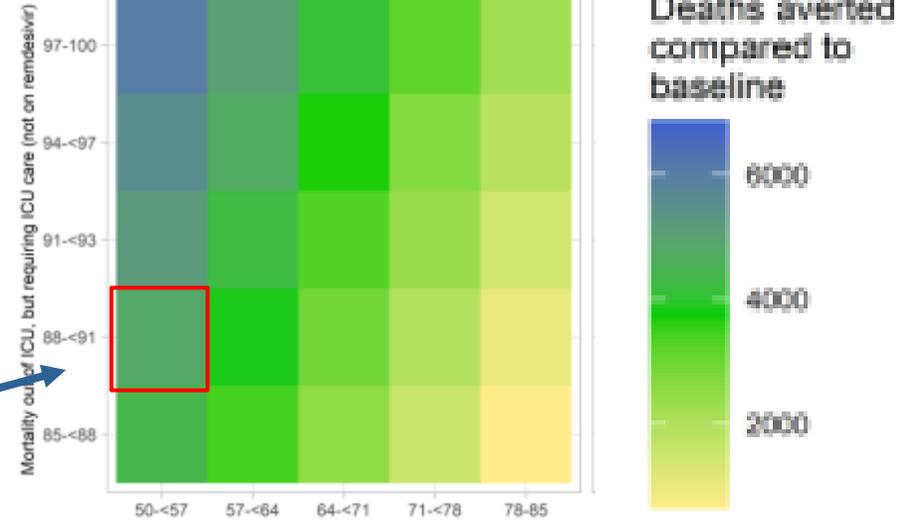
* Values are the number unless otherwise indicated. OR = odds ratio; 95% CI = 95% confidence interval; Rx = number of prescriptions.
 † Adjusted for body mass index, smoking, diabetes, pulmonary diseases, and use of antirheumatic or immunosuppressive agents.
 ‡ Referent.

Remdesivir to Decrease ICU Demand

- Remdesivir decreases ICU time from 15 to 11 days
- Monte Carlo simulation to assess how much remdesivir might affect mortality in South Africa by decreasing ICU stays, thereby increasing capacity
- Study highlights interplay between ICU capacity and drug treatment

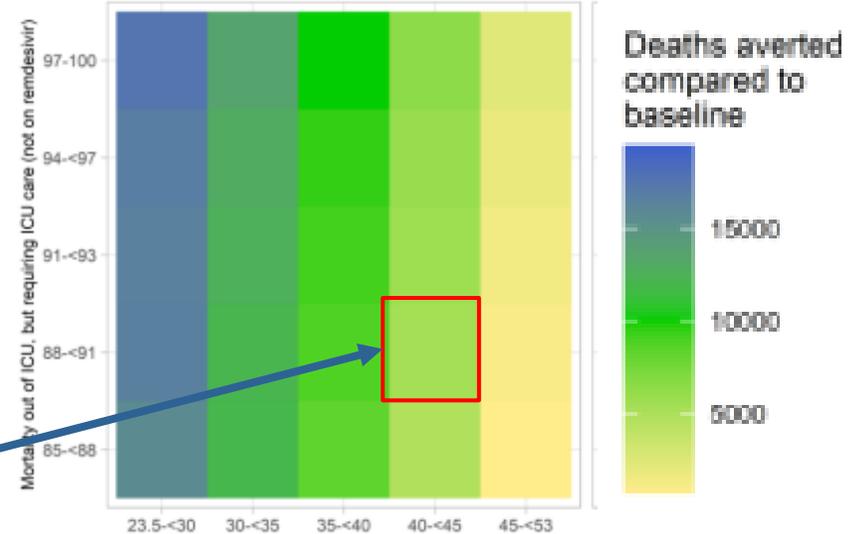
Remdesivir has no direct effect on mortality

~3000 lives saved



Remdesivir has a direct effect on mortality

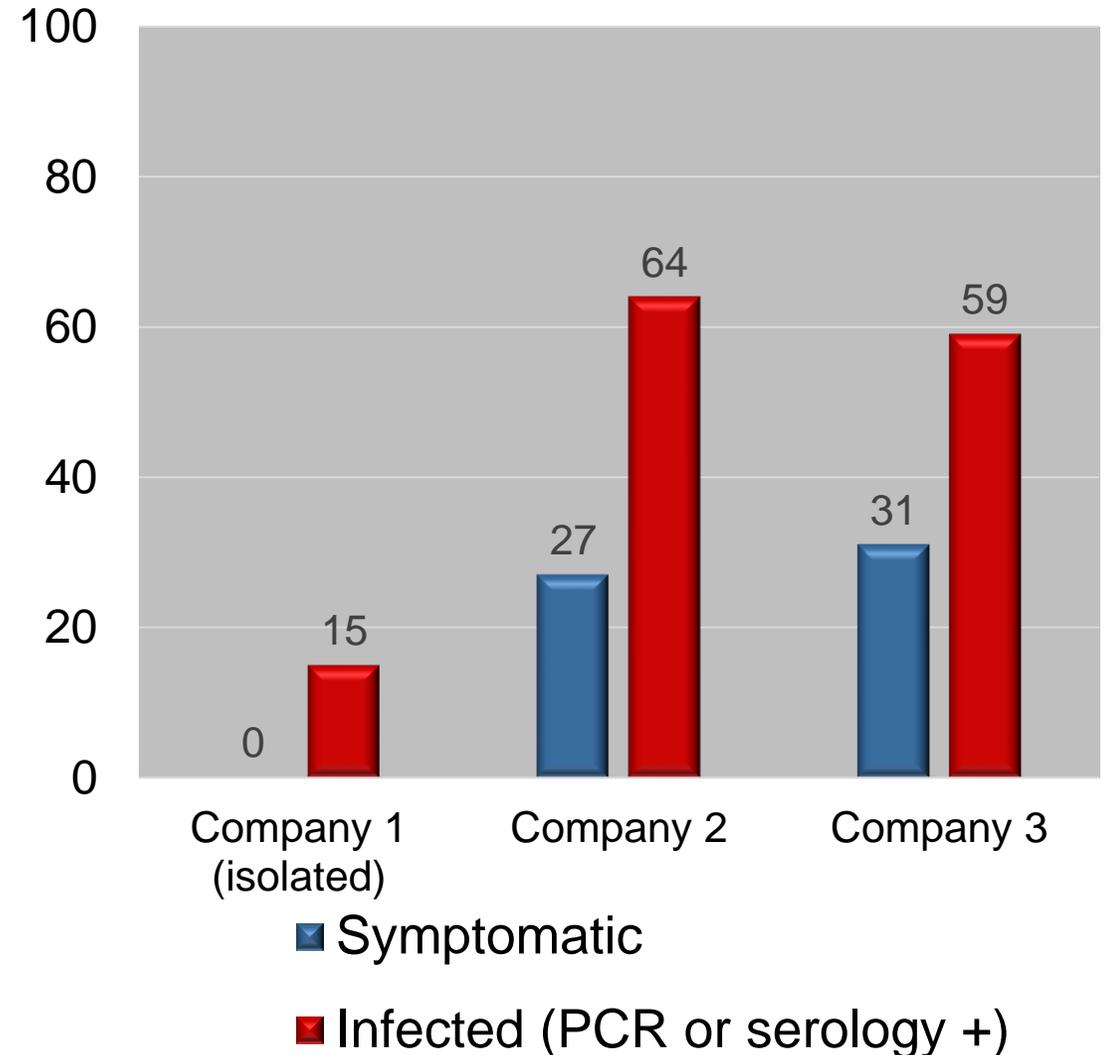
~6000 lives saved



Mortality in ICU

Does Social Distancing Affect the Clinical Course of COVID-19?

- Population - Swiss soldiers presenting for illness + sample of 363 asymptomatic
 - 3 companies
 - Companies 2 & 3 had outbreaks
 - Company 1 - 3km away – outbreak
 - Social distancing & masks after outbreak in companies 2 and 3
- Testing – Nasopharyngeal swabs and sera
- Why?
 - Social distancing, mask wearing & hygiene may shift the route of transmission away from droplets & aerosols to lower inoculum transmission routes (fomites)
 - Higher nasal viral load associated with worse outcomes



Questions and Discussion