

Evidence Review Table presentation

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Please note, that although funding to OHCOW is from the Ontario government, the views of the presentation do not necessarily reflect the position of the Ontario government.

Chu, Schünemann et al. (June 1/20)

“Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis.” Lancet (June 1, 2020)

Funding: World Health Organization

- 15 page article with 48 pages of supplementary appendix
- Holger Schünemann and his McMaster colleagues originally proposed the “rapid review” process:
 - Schünemann HJ, Hill S, Kakad M, Vist G, Bellamy R, Stockman L, Wisloff T, Del Mar C, Shindo N, Fukuda K, Hayden F, Uyeki T, Farrar Yazdanpanah Y, Zucker H, Beigel J, Chotpitayasunondh T, Hien TT, Ozbay B, Sugaya N, Oxman, AD. “Transparent Development of the WHO Rapid Advice Guidelines.” PLoS Medicine 4(5):e119, 2007 <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0040119>
 - Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ. “GRADE: An Emerging Consensus on Rating Quality of Evidence and Strength of Recommendations.” BMJ 26;336(7650):924-6, 2008 <https://pubmed.ncbi.nlm.nih.gov/18436948/>

PHO critique

“This meta-analysis does not provide conclusive evidence of benefit of N95 respirators compared to surgical masks for non-AGMPs for healthcare workers caring for COVID-19 patients. ”

- How much evidence is needed to warrant a change? an RCT
- Effectively, there can't be enough evidence to warrant better protection because it is difficult to organize a large enough RCT to provide conclusive evidence in the middle of a pandemic
- Given the multi-dimensional nature of infection transmission and the issue of compliance assessment, it is doubtful that a large scale high quality RCT can ever be implemented in reality especially under pandemic conditions
- This level of evidence is practically unachievable (e.g. John Snow and the cholera epidemic in London)

Other reviews:

- Results are “all over the map”
- The one thing they all agree on is that the quality of the evidence is weak
- Weak evidence gives the authors the latitude to interpret their results according to their prior biases

1	Seale et al (2009) - A review of medical masks and respirators for use during an influenza pandemic
2	bin-Reza et al (2012) -The use of masks and respirators to prevent transmission of influenza - a systematic review of the scientific evidence
3	Smith et al (2016) - Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection - a systematic review and meta-analysis
4	Offeddu et al (2017) - Effectiveness of masks and respirators against respiratory infections in healthcare workers - a systematic review and meta-analysis
5	Saunders-Hastings et al (2017) - Effectiveness of personal protective measures in reducing pandemic influenza transmission - A systematic review and meta-analysis
6	Long et al (Mar 13 2020) - Effectiveness of N95 respirators versus surgical masks against influenza - A systematic review and meta-analysis
7	Jefferson et al (Mar 30 2020) - Physical interventions to interrupt or reduce the spread of respiratory viruses. Part 1 - Face masks, eye protection and person distancing - systematic review and meta-analysis
8	Garcia Godoy et al (Mar 31 2020) - Facial protection for healthcare workers during pandemics - a scoping review
9	Bartoszek et al (Apr 4 2020) - Medical Masks vs N95 Respirators for Preventing COVID-19 in Health Care Workers A Systematic Review and Meta-Analysis of Randomized Trials
10	Brainard et al (Apr 6 2020) - Facemasks and similar barriers to prevent respiratory illness such as COVID-19 - A rapid systematic review
11	Liang et al (Apr 7 2020) - Efficacy of face mask in preventing respiratory virus transmission - a systematic review and meta-analysis
12	Iannone et al (Apr 11 2020) - The need of health policy perspective to protect Healthcare Workers during COVID-19 pandemic. A GRADE rapid review on the N95 respirators effectiveness.
13	Chu et al (Jun 1 2020) - Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis

Example: Bartoszko et al (Apr 4 2020)

“Low certainty evidence suggests that medical masks and N95 respirators offer similar protection against viral respiratory infection including coronavirus in health care workers during non-aerosol generating care. Preservation of N95 respirators for high-risk, aerosol generating procedures in this pandemic should be considered when in short supply.”

- The last statement does not follow from the evidence, it is an interpretation based on the authors biases – this is advice that goes beyond the evidence

Argument from discomfort: Noise protection analogy

- Used to stuff cotton in our ears to protect against noise (about 10 dB protection)
- Then came foam ear plugs (not as comfortable as cotton) – in the lab they reduced noise by 25-30 dB
- However when we measured the protection factor in the field, the noise reduction was only about 7-15 dB
- So what do we do? Statistically no different than cotton, so, go back to cotton?
- Response: education, training, supervision, supports, etc., but only a few more decibels, nowhere near the lab's level of protection
- Double up protection when noise levels warrant it (plugs with muffs over top)

“COVID-19 – What We Know So Far About... Routes of Transmission (Apr 28/20)”

“Airborne Transmission

There is currently no evidence that COVID-19 is transmitted through the airborne route. As more epidemiological data emerge on cases globally, information is becoming available that suggest that airborne transmission is not occurring:”

1. WHO China Joint Mission on COVID-19 report
2. “An article describing the active follow-up of individuals exposed to first ten cases of COVID-19 in the United States describes secondary transmission only to close household contacts.”
3. “Healthcare workers caring for COVID-19 patients in other jurisdictions, including British Columbia, have not acquired COVID-19 while using Droplet and Contact Precautions recommended in the province (Weeks).”
4. “The lack of transmission to passengers seated nearby cases who have travelled on airplanes, does not support an airborne transmission route of COVID-19 (Schwartz et al.).”
5. “Studies have inconsistently detected virus in air sampling”
6. An investigation of a COVID-19 outbreak in a restaurant in Guangzhou, China

<https://www.publichealthontario.ca/-/media/documents/ncov/wwksf-routes-transmission-mar-06-2020.pdf?la=en>

1. Report of the WHO-China Joint Mission

“Routes of transmission

COVID-19 is transmitted via droplets and fomites during close unprotected contact between an infector and infectee. Airborne spread has not been reported for COVID-19 and it is not believed to be a major driver of transmission based on available evidence; however, it can be envisaged if certain aerosol-generating procedures are conducted in health care facilities.” (page 8, WHO (Feb 28 2020) - Report of the WHO-China Joint Mission)

- no evidence supplied
- no references at all in the document

the reference to this report in the PHO document is argument based on an **appeal to authority**

Diagnosis and treatment plan of Corona Virus Disease 2019 (6th edition)

“2.2. Route of transmission

COVID-19 is mainly transmitted by droplets and contact. Aerosol transmission is possible when people have prolonged exposure to high concentrations of aerosols in relatively closed spaces.”

- released mid-February two weeks before the Joint Commission’s Report was released
- widely reported in the media (especially in China)

Human-to-human transmission

- Chinese authorities and the WHO kept saying until mid-January, that there was “no evidence” for human-to-human transmission (suggested animal-to-human transmission from the Wuhan wet market)
- Criteria for human-to-human transmission:
 1. Household close contact (but couldn't household members also have animal-to-human contact if the animal was brought home?)
 2. HCW infections
- Essentially, the HCW's are the “canaries in the cage” for infection control – if they are being infected, then we know there is human-to-human transmission

2. First 10 cases in the US:

- How many cases now in the US? 2,000,000 as of yesterday?
- Here we are in June, and, because there were no HCW's infected among the first 10 cases, and, because they were deemed to occur during "household contact", therefore, there is no airborne transmission
- Now, after 2,000,000 cases, we have at least 300,000 US HCW's infected, how does that change the conclusion?
- Why does "household contact" exclude aerosol transmission?

3. No HCW's in BC infected

- In the earlier edition (Mar 6/20) of the PHO document, the citation for this claim was a newspaper article stating that no BC healthcare workers had been infected (on Mar 10th it was announced that first two BC HCW's were confirmed to be infected)
- It was anticipated that this item would be dropped in the revision of the PHO document – astonishingly it was not!
- The reference was changed to a different newspaper article (Mar 3/20) but it states a similar case: “Ontario is the only province recommending airborne precautions. B.C. uses droplet precautions and none of the COVID-19 cases there have spread to health-care workers.”, and: “But the evidence shows that droplet precautions are sufficient at protecting workers from infection. For instance, B.C. hospital workers who are treating COVID-19 patients have been using droplet precautions since the outbreak began and, so far, none has contracted the infection.”

Since this is no longer the case, if we use the same logic that “if no HCW's are infected, then the protection used is adequate”, one would assume the reverse is now would hold: “if HCW's are infected, then the protection used is inadequate”

4. Lack of transmission during travel

- A single citation of the absence of transmission

logical fallacy: the absence of evidence is not evidence for the absence

from the NY Times this week (re: asymptomatic transmission):

“Some experts said that when the W.H.O. uses the phrase “there is no evidence” to indicate uncertainty, it is in fact conveying certainty about the absence of a phenomenon.

Dr. Van Kerkhove conceded that point.”

<https://www.nytimes.com/2020/06/09/health/coronavirus-asymptomatic-world-health-organization.html?referringSource=articleShare>

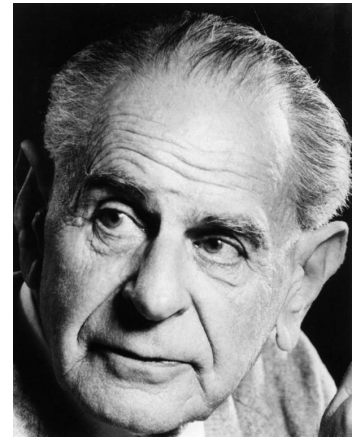
- Since that time (and prior) papers have reported transmission during travel (Yang et al (Mar 30, 2020) “*In-flight Transmission Cluster of COVID-19: A Retrospective Case Series*”), and some have been suppressed (Luo et al (Feb 18 2020) “*An epidemiological investigation of 2019 novel coronavirus diseases through aerosol-borne transmission by public transport*”).

5. Inconsistent air sampling results:

- Initially (Mar 6/20) papers were cited which stated that no (not quite none) virus could be measured in the air around patients – this was cited as proof that the virus was not transmitted by air
- Later there were other reports published that virus was found in air samples – now the inconsistency of the results is put forward as evidence that the virus is not airborne
- This is an example of the problem with the verification approach to scientific reasoning (c.f. Karl Popper)
- The problem can be illustrated with the premise: “all swans are white” – a million observations of white swans verifying this premise cannot counter the evidentiary weight a single observation of a black swan
- The Nebraska study (the only North American one) is completely ignored (Santarpia et al (Mar 26 2020) “Transmission Potential of SARS-CoV-2 in Viral Shedding Observed at the University of Nebraska Medical Center”) – selection bias
- BTW: Houlihan et al (Jun 9 2020) “SARS-CoV-2 virus and antibodies in front-line Health Care Workers in an acute hospital in London - preliminary results from a longitudinal study” (has a nice literature review of studies to date that measured COVID virus in the air and on surfaces)

Karl Popper

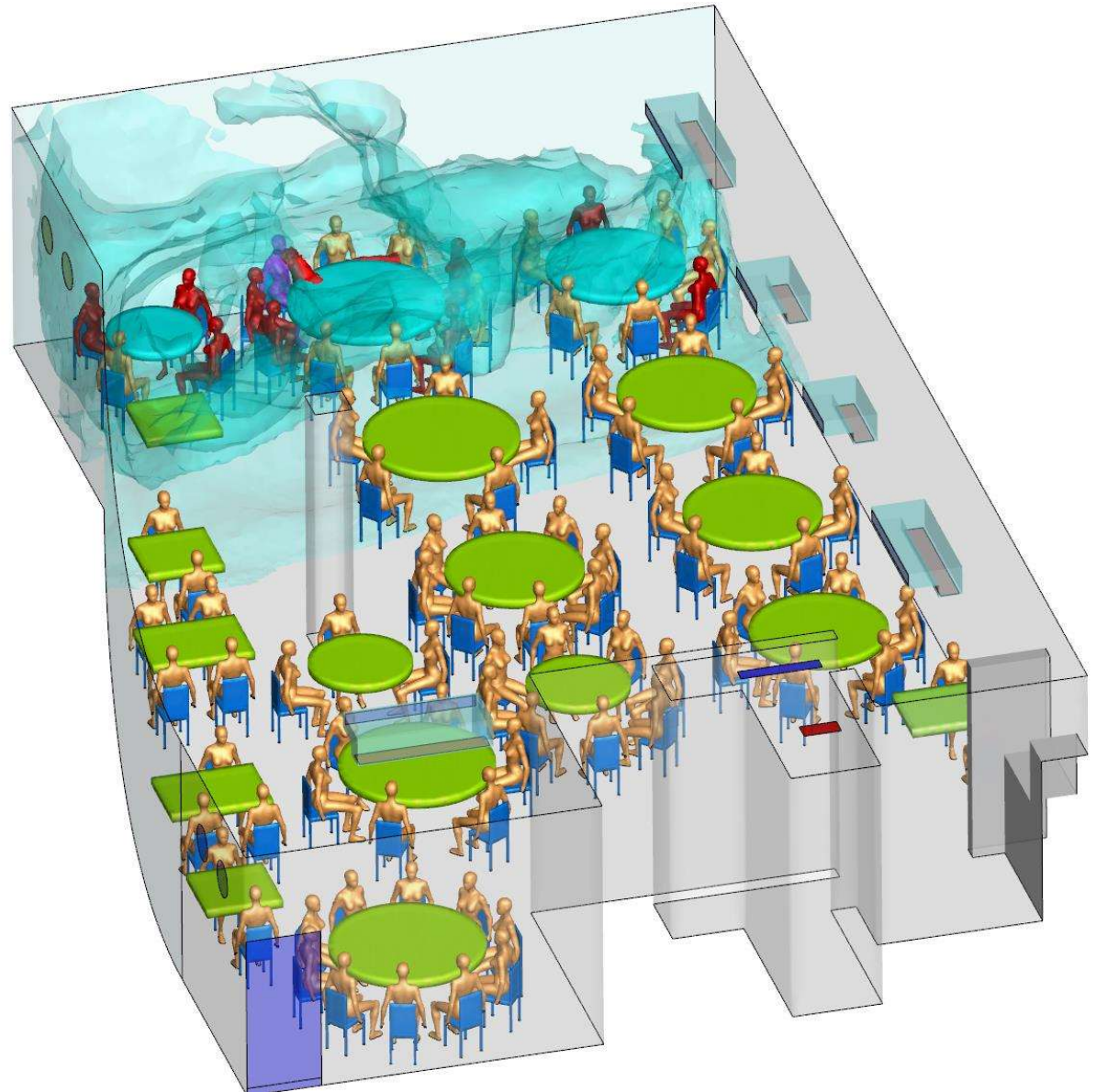
- Falsifiability as the criteria for testable scientific knowledge – verification can never prevail
- If every piece of evidence can be interpreted as supporting a theory then the theory is not falsifiable and thus cannot be considered scientific, rather, it becomes dogma
- “All swans are white” – a million observations of white swans verifying this premise cannot counter the evidentiary weight a single observation of a black swan



6. The restaurant in Guangzhou, China

- Lu et al (Apr 2 2020) “COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China, 2020”
 - “We conclude that in this outbreak, droplet transmission was prompted by air-conditioned ventilation. The key factor for infection was the direction of the airflow.”
 - “Our study has limitations. We did not conduct an experimental study simulating the airborne transmission route.”
- PHO review: “A weakness of this report is that the authors did not conduct any aerodynamic testing to support their hypothesis. In addition, the authors focused on potential droplet transmission at the restaurant and did not explore other possibilities, such as indirect transmission of fomites.” PHO Review
- Li et al (Apr 23 2020) “Evidence for probable aerosol transmission of SARS-CoV-2 in a poorly ventilated restaurant”:
 - “We collected epidemiological data, obtained a video record and a patron seating-arrangement from the restaurant, and measured the dispersion of a warm tracer gas as a surrogate for exhaled droplets from the suspected index patient. Computer simulations were performed to simulate the spread of fine exhaled droplets. We compared the in-room location of subsequently infected cases and spread of the simulated virus-laden aerosol tracer. The ventilation rate was measured using the tracer decay method.”
 - In summary, our epidemiologic analysis, onsite experimental tracer measurements, and airflow simulations support the probability of an extended short-range aerosol spread of the SARS-CoV-2 having occurred in the poorly ventilated and crowded Restaurant X on January 24, 2020.
 - Specifically, although close contact and fomite exposure may play a major role in the transmission of SARS-CoV-2, extended short-range aerosol transmission of the virus is possible in crowded and poorly ventilated enclosures. Our study suggests that it is crucial to prevent overcrowding and provide good ventilation in buildings and transport cabins for preventing the spread of SARS-CoV-2 and the development of COVID-19.
- Will this change the PHO’s interpretation?

Li et al (Apr 23 2020)
“Evidence for probable
aerosol transmission of
SARS-CoV-2 in a poorly
ventilated restaurant”



How are we doing so far?

Rationale/Evidence:	disposition
1. WHO-China Joint report	<ul style="list-style-type: none">- evidence not provided- appeal to authority
2. no HCW's among 1 st 10 US cases	<ul style="list-style-type: none">- jumping to conclusions (now 300,000+ HCW's)- assumes close-contact excludes airborne
3. no HCW's using droplet precautions infected	<ul style="list-style-type: none">- obviously no longer the case!- actually provides evidence to the contrary
4. lack of transmission during travel	<ul style="list-style-type: none">- "evidence of absence" fallacy- subsequent studies contradict
5. inconsistent air sampling results	<ul style="list-style-type: none">- verification fallacy (black swan)- study selection bias
6. Restaurant in Guangzhou	<ul style="list-style-type: none">- insufficient follow-up- subsequent study contradicts

What about the evidence for droplet transmission?

Literature cited in the PHO document in support of droplet transmission:

1. European Centre for Disease Prevention and Control (ECDCa). Risk assessment: outbreak of acute respiratory syndrome associated with a novel coronavirus, China: first local transmission in the EU/EEA – third update [Internet]. Stockholm: ECDC; 2020 [cited 2020 Feb 12].
2. Imai N, Cori A, Dorigatti L, Baguelin M, Donnelly CA, Riley S, et al. Report 3: Transmissibility of 2019-nCoV [Internet]. London: Imperial College London; 2020 [cited 2020 Apr 22].
3. Schneider E, Bermingham A, Pebody R, Watson JM. SARS, MERS, and other coronavirus infections. In: Heymann DL, editor. Control of communicable diseases manual. 20th ed. Washington, DC: American Public Health Association; 2016.

1. ECDC Risk assessment (Jan 31/20):

- Has been updated since January 31st
 - Only a single mention of the word “droplet”:

“WHO’s interim guidance recommends placement of suspected and confirmed cases in single rooms, implementation of contact and droplet precautions, and airborne precautions when performing aerosol generating procedures or interventions [43-45]. Although there is no evidence of airborne transmission so far, ECDC recommends a cautious approach for all patient contacts, with placement of patients in airborne isolation rooms with negative pressure and use of FFP2 or FFP3 respirators with appropriate fit testing.”
 - The citation recommends the opposite for which it is cited; it merely states that there is a lack of evidence; it does not prey to the “absence of evidence” fallacy as the PHO document does
- note: it invokes the precautionary principle

2. Imai et al - Report 3: Transmissibility of 2019-nCoV (January 25 2020)

- another very “early” document
- there is no mention of word “droplet” at all?!?!?
- again “close contact” is assumed to exclude aerosol transmission

3. APHA textbook on infection control

- Does not mention COVID-19, only SARS and MERS (a criticism the PHO leveled at the McMaster review)
- Experts are still “fighting” over whether SARS and MERS have aerosol transmission

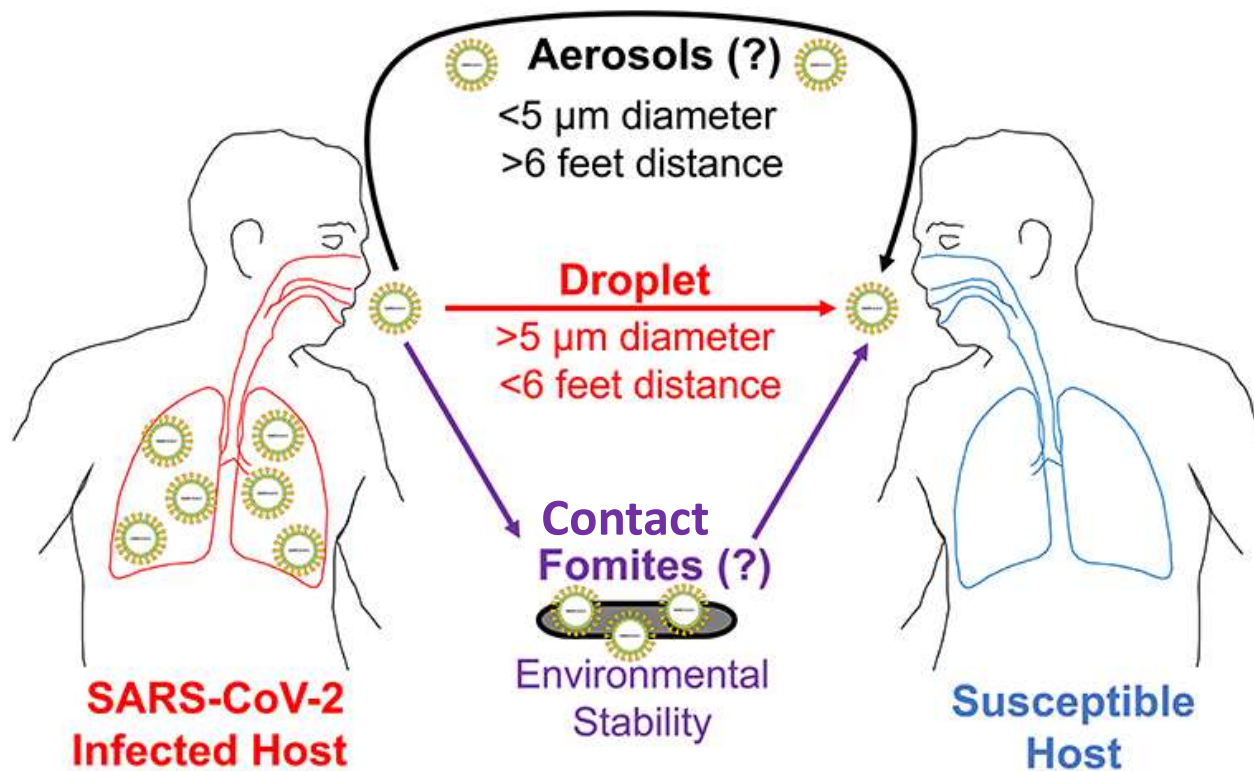
How are we doing so far?

Rationale/Evidence:	disposition
1. ECDC Risk assessment (Jan 31/20)	<ul style="list-style-type: none">- lack of evidence declared (PP invoked)- cited to support a conclusion which is contrary to citation's authors' conclusion
2. Imai et al - Transmissibility of 2019-nCoV (Jan 25/20)	<ul style="list-style-type: none">- "droplet" not mentioned- assume "close contact" excludes aerosol transmission ("begging the question" fallacy)
3. APHA text on infection control	<ul style="list-style-type: none">- published prior to COVID- lack of air transmission for SARS & MERS in scientific dispute- appeal to authority

Coughs & sneezes review:

- 23 citations – when you actually read the citations the majority indicate that aerosol transmission is an important phenomenon to consider for infection control
- Using evidence to shore up a position which contradicts the original author's interpretation
- As per Karl Popper; if every piece of evidence can be interpreted as supporting a theory, then it is not falsifiable and as such cannot be considered testable scientific theory

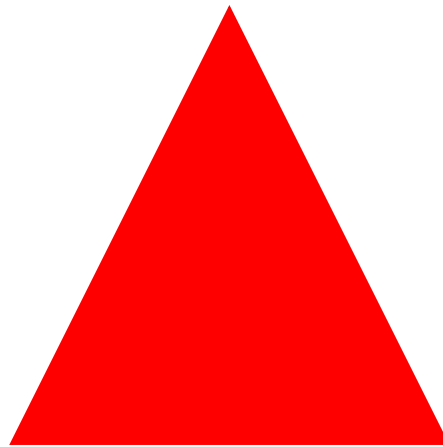
3 main modes of transmission



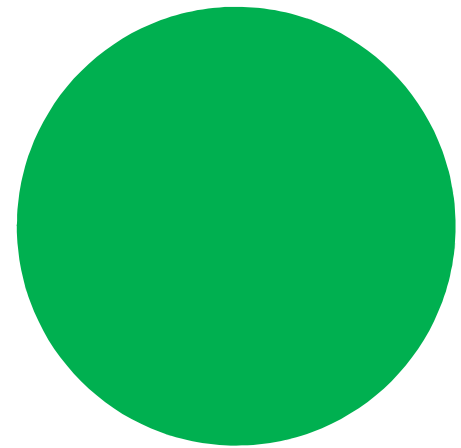
3 main modes of transmission



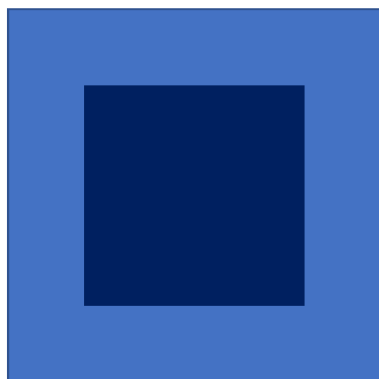
droplet



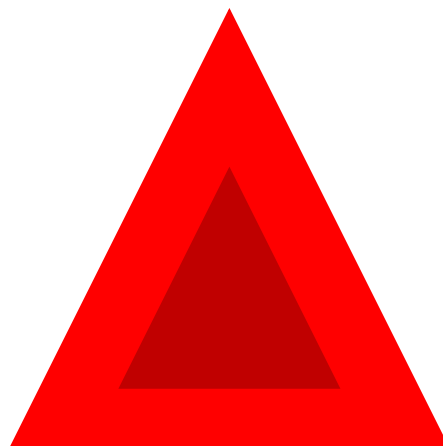
airborne



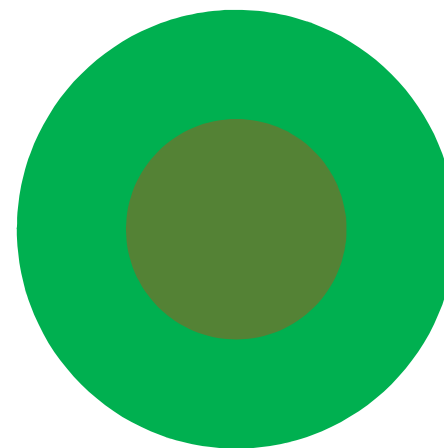
contact



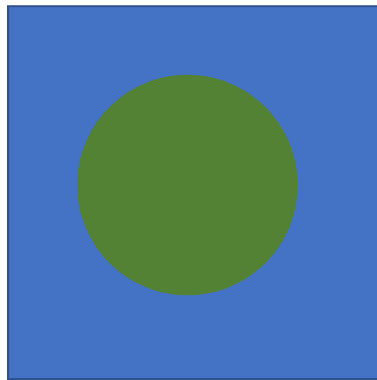
droplet



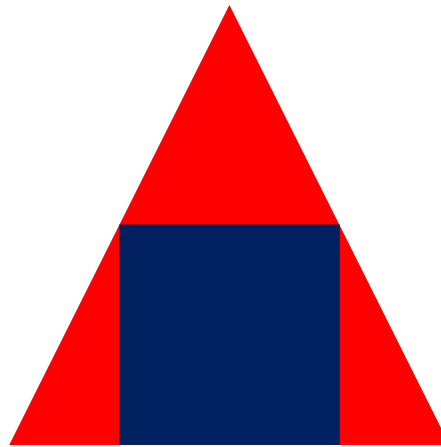
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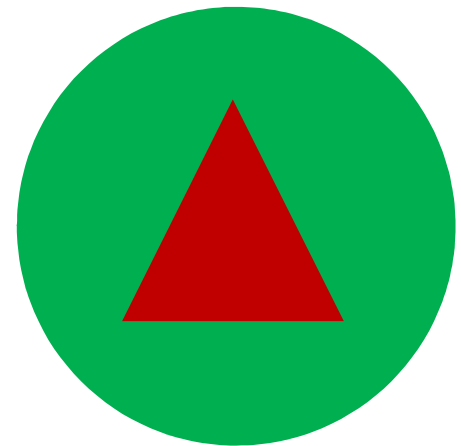
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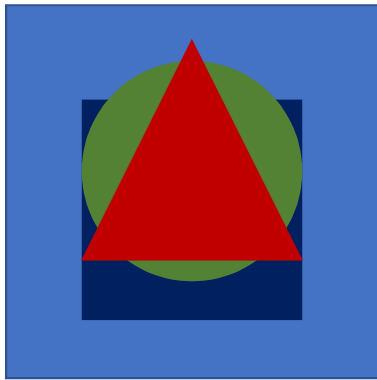
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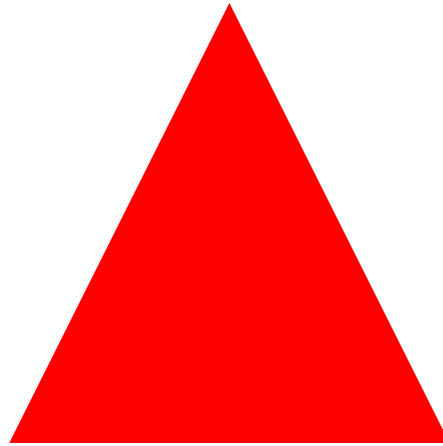
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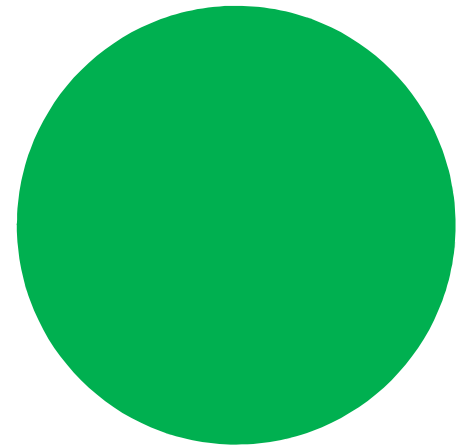
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droplet



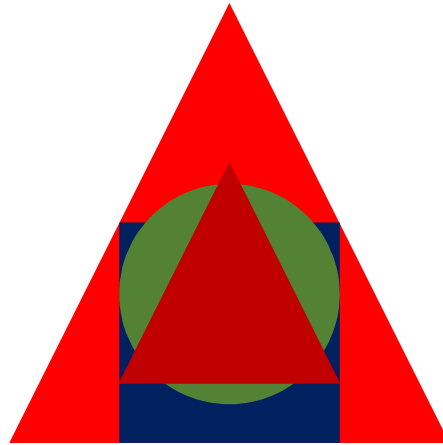
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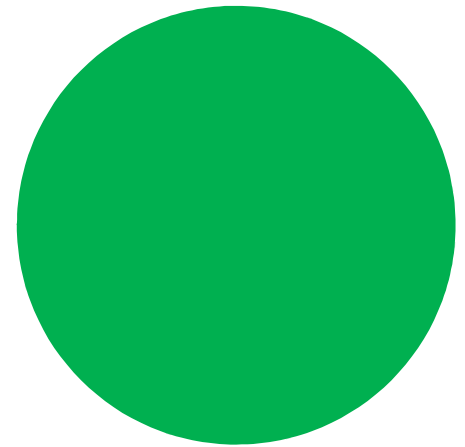
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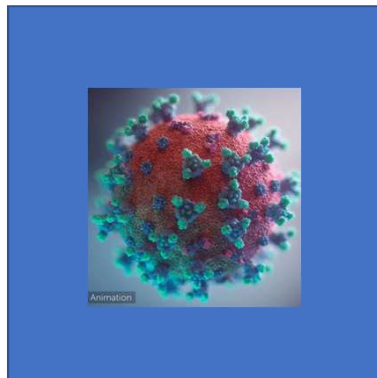
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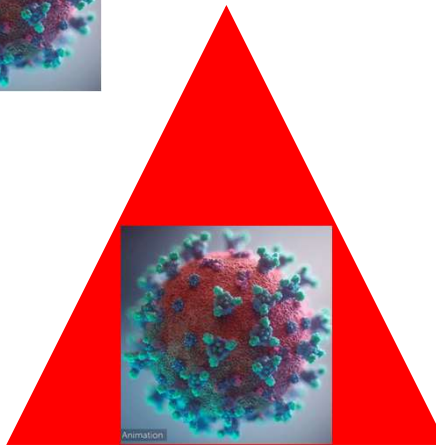
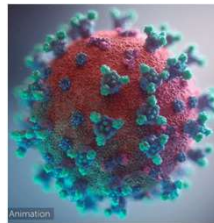
airborne



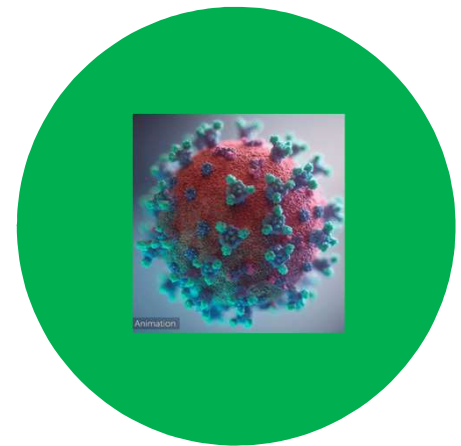
contact



droplet

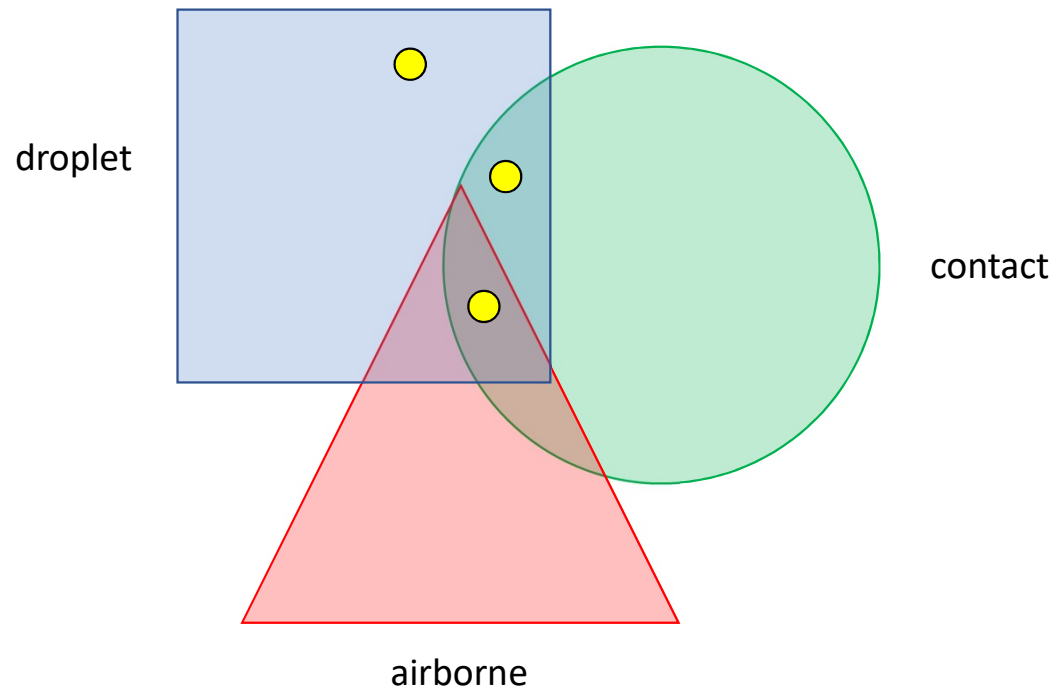


airborne

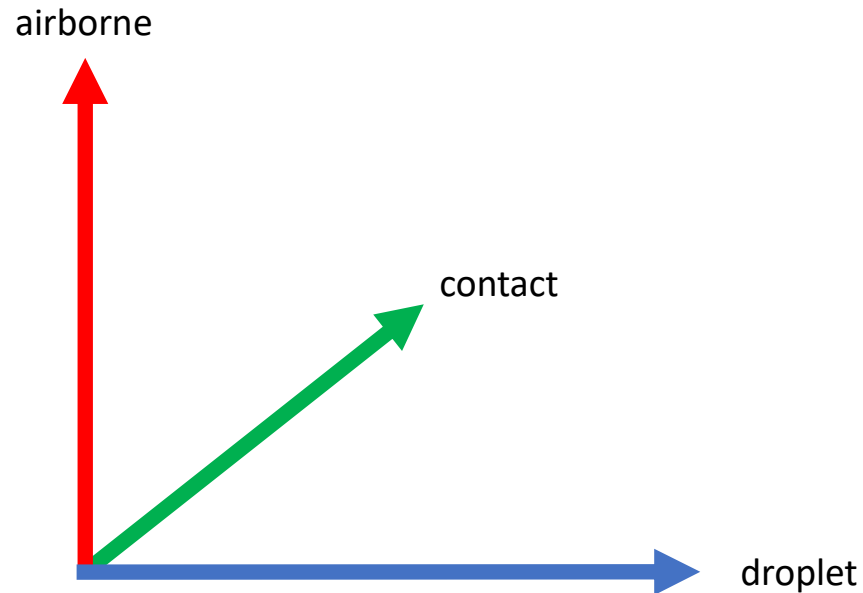


contact

Instead of square peg in a round hole, what if it's a Venn Diagram?



What if it's a 3 dimensional problem?



... a **continuous** set of variables rather than discrete, categorical ones

Distancing – how many meters? (... for how many minutes?)

WHO – 1 m

PHO – 2 m

McMaster study – RR: -0.5/m
aerosol studies – depends ...

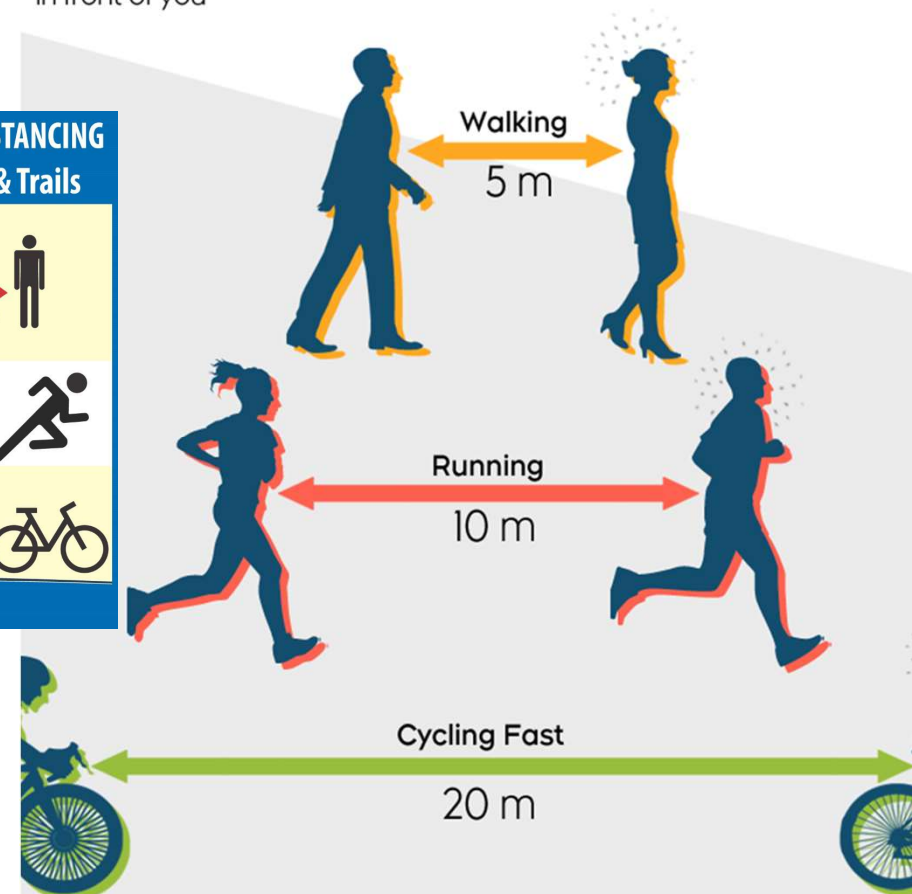
For how long? 10/15/20/30 minutes?
time weighted average (TWA)

Haber's Rule: $\text{dose} \propto \text{concentration} \times \text{time}$

... what about same dose delivered as peaks vs. a stable concentration over time?
(exposure peaks may overwhelm defense mechanisms which can handle a steady dose)

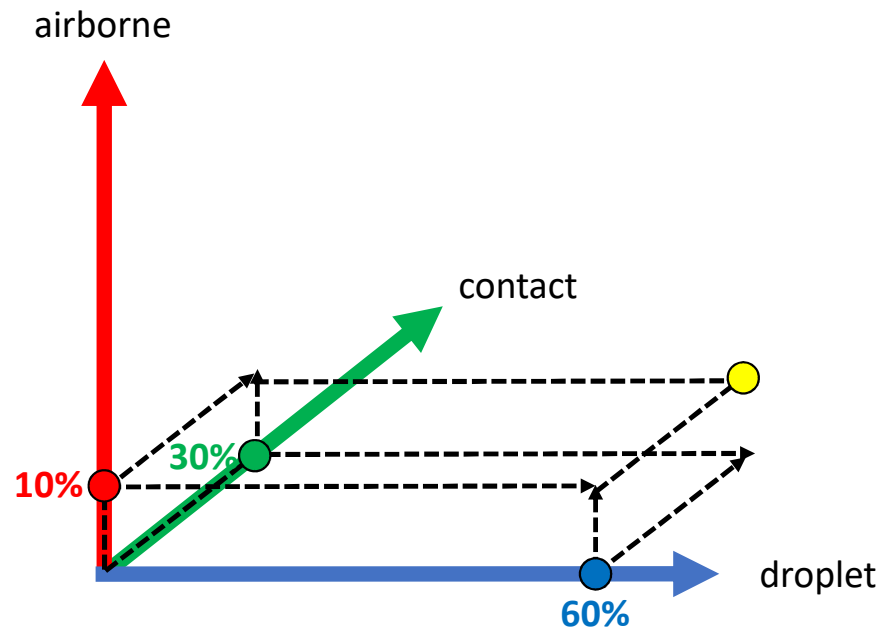
Distancing to avoid slipstreams

To avoid the chance of acquiring droplets from a slipstream, you may want to consider keeping more distance between you and the person in front of you



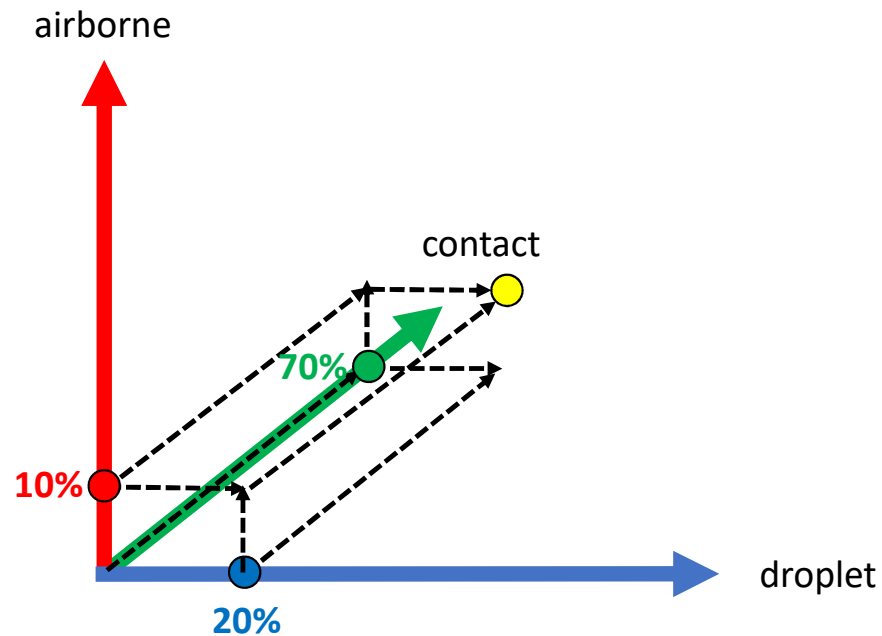
Source: Eindhoven University of Technology
Silhouette Vectors by Freepik.com

What if it's a 3 dimensional problem?



Nicas & Jones (2009)
"Relative Contributions
of Four Exposure
Pathways to Influenza
Infection Risk"

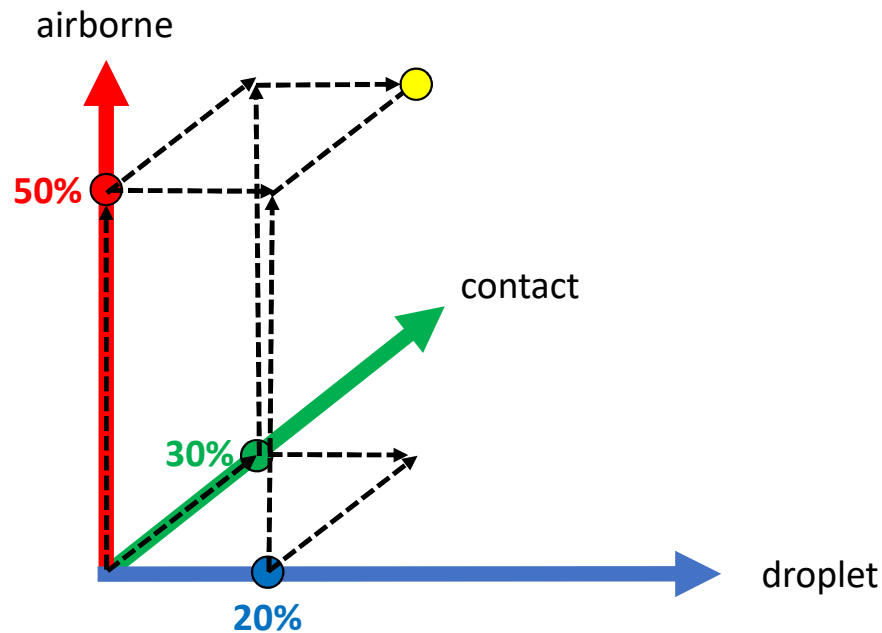
Applying controls changes the relative contributions



droplet precautions

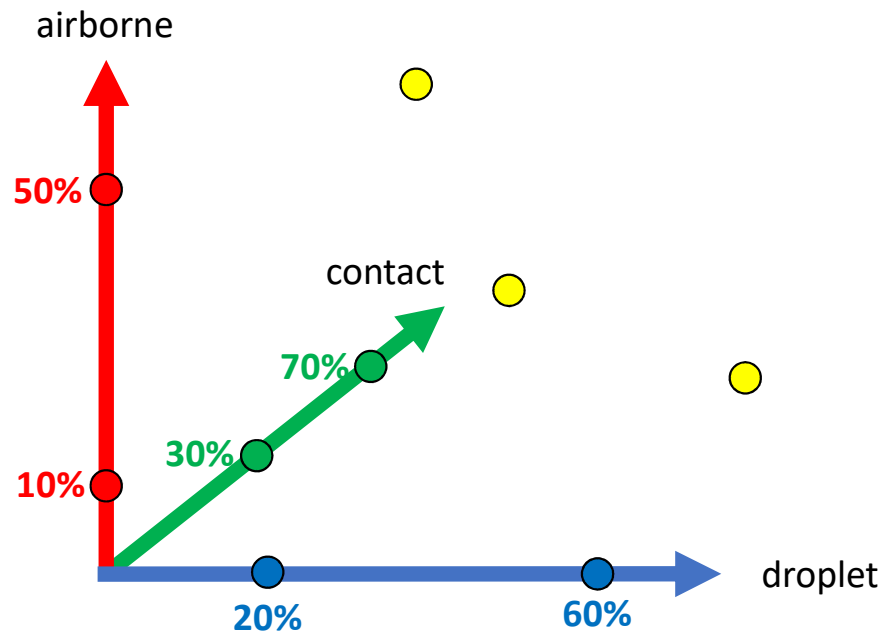


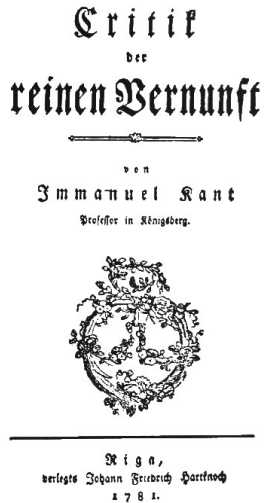
Certain conditions are recognized as contributing to aerosol transmission



super-spreader
crowding
patients not wearing mask the right way
poor ventilation
AGMP's

Different relative proportions of transmission under varying circumstances



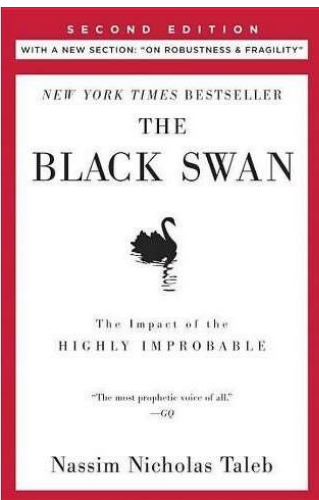


Immanuel Kant

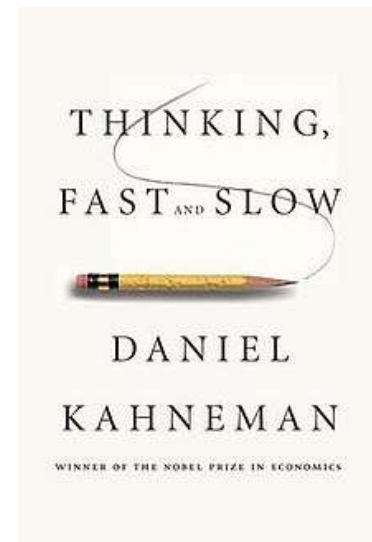
– categories of the mind



- Critique of Pure Reason (1781)
- Categories of our conceptual system (mind)
- Our minds cannot contain the fullness of reality, we are confined by the categorical nature of our thoughts and reasoning (he listed 12 categories)
- Empirical correspondence of our categories with the evidence collected



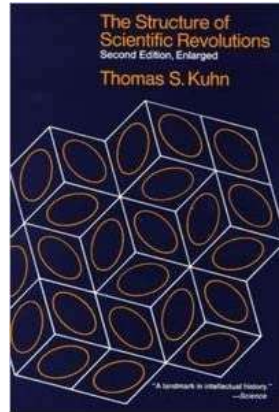
Kahneman & Taleb



- Our brains are wired to take short cuts which can lead us to illogical/irrational conclusions which we can avoid with more deliberate slow thinking (but which takes more effort)
- A system that is entrenched in dogma, cannot react to an anomalous event (seeing a black swan for the first time)

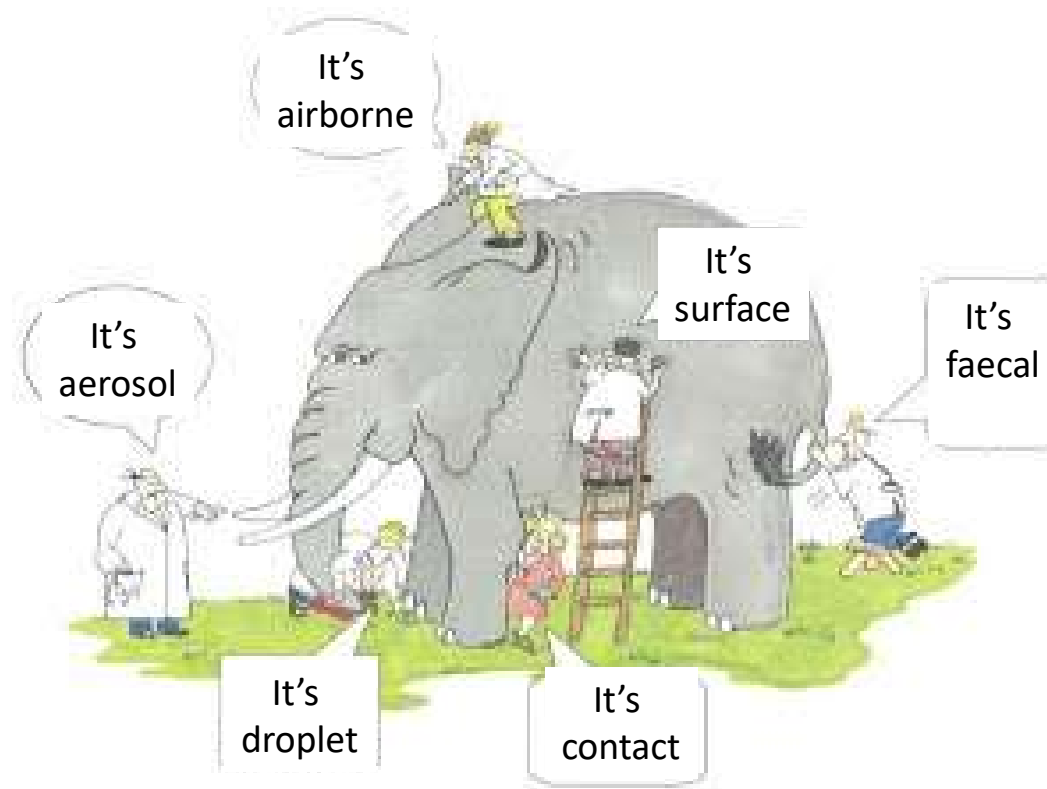


Thomas Kuhn – The Structure of Scientific Revolutions



- “Normal” science operating within the accepted paradigm
- Anomalous observations that don’t fit within the dominant paradigm
- Sudden or gradual “paradigm shift” due to the inadequacy of the old paradigm to explain the anomalous findings
- Current situation – intersection of paradigms causing confusion:
 - IPC (3 categories of transmission)
 - H&S (precautionary principle)
 - Occupational hygiene (measuring air and surface exposures)
 - Aerosol science (particle dynamics, settling, surface stability, CFD modelling)
 - Cognitive/Behavioural science (why don’t people wear their PPE properly?)

Reminds me of the Indian folk story:
the 6 blind people and the elephant



Summary of evidence so far:

- There is some evidence for all the routes of transmission
- Generally the quality evidence is weak to moderate and thus the level of uncertainty is high
- What do we do when the science is in dispute and uncertainty is high?
- Justice Campbell dealt with exactly the same situation and prescribed the precautionary principle
- What about our actual performance – How are we actually doing?
Are HCW's getting infected? Are they dying?

The bottom-line evidence:

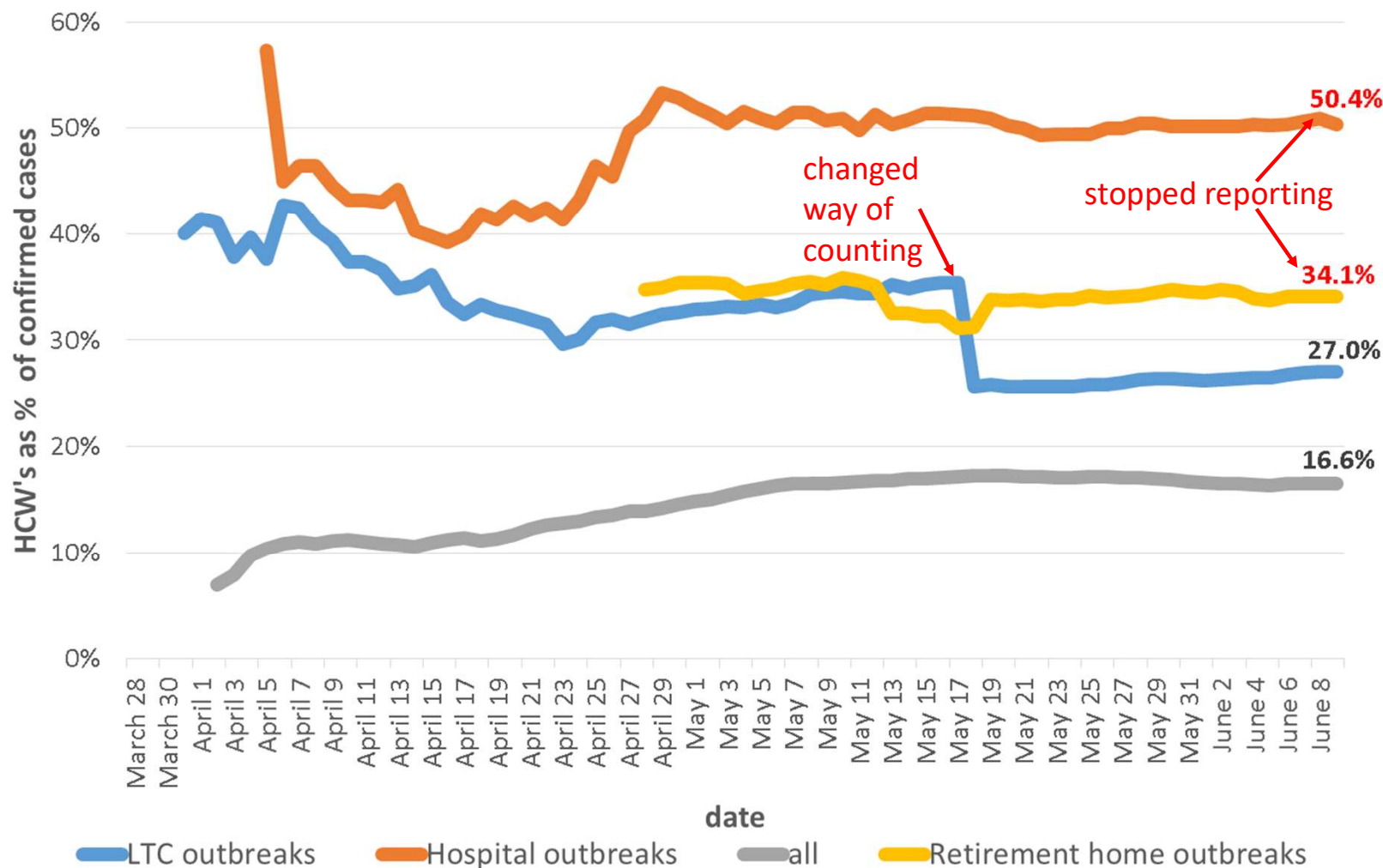
- Human-to-human transmission was accepted when HCW's became infected (the “canaries in the coal mine”)
- Despite all the arguments about transmission, is what we're currently doing working?

In Ontario (as of yesterday):

“Health care worker: 5,210 confirmed cases (16.5%)” – 11 deaths

<https://www.publichealthontario.ca/en/data-and-analysis/infectious-disease/covid-19-data-surveillance/covid-19-data-tool>

Proportion of HCW's as % of Total COVID-19 Cases (to Jun 9/20)



Compared to Ontario's 16.5% (Jun 10/20), China had 4.4%; world average $\approx 6\%$. When China was faced with this kind of situation they stepped up their controls to Ebola type protection and after that had only a single case of infection among over 42,000 healthcare workers

**whatever we're doing –
it's not working!**

This is what they did in China

- Initially HCW's were being infected (up to 20% of people considered positive were HCW's)
- as of Feb 24th, 3387 healthcare workers were infected in China (4.35% of all confirmed cases) and that 23 of them died due to the infection
- What caused the drop in proportion?
- Chang et al (Feb 13 2020) "Protecting health-care workers from subclinical coronavirus infection", report that as of Jan 20th the level of protection for HCW's was raised to level of protection used to prevent infection from bubonic plague and cholera (Class A) – triple layers, N95 with surgical mask over top

<https://www.youtube.com/watch?v=9HsGqQCLzLU>

The **Infectious Diseases Law** governs thirty-seven infectious diseases that are already known, i.e. the statutory infectious diseases. They are classified into three classes requiring the implementation of different preventive and control measures.

There are only two diseases under **Class A**: bubonic plague and cholera.

Class B contains diseases such as SARS, anthrax, AIDS, typhoid, and viral hepatitis.

Class C contains diseases such as influenza, leprosy, mumps, and schistosomiasis. (Art. 3.)

China

Central State Organ Reporting Website

2020年06月12日 星期五

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Announcement

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Announcement of the National Health Commission of the People's Republic of China

Release time: 2020-01-20 Source: CDC

No. 1 of 2020

Approved by the State Council, the announcement is as follows:

1. The pneumonia infected by the new coronavirus is included in the Class B infectious diseases as stipulated in the Law of the People's Republic of China on the Prevention and Control of Infectious Diseases, and the prevention and control measures for Class A infectious diseases are taken.

2. Pneumonia infected by the new coronavirus is included in the management of quarantine and infectious diseases as stipulated in the Law of the People's Republic of China on Frontier Health and Quarantine

Special announcement.

National Health Commission of the People's Republic of China

January 20, 2020

HCW's PPE requirements in Taiwan

	Surgical mask	N-95 mask	glove	Fluid repellant gown	Fluid resistant gown	Goggle/ Shield	Cap
Public area	V						
Out-patient or ER triage	V						
Patient transfer		V	V	V			
Drivers		V	V	V			
EMS		V	V		V	Shield	
Non-infection ward		V	V	V		Goggle	V
Infectious disease ward		V	V		V	Shield	V

From "COVID-19: Protecting Health Care Workers - Lessons from Taiwan and Italy" ACOEM Webinar

https://acoem.my.salesforce.com/sfc/p/#1N000002ArMw/a/3m000000MXqm/1AahxtYyS6ekMunLF9ituWyY.PchZ_i7B6WQcOO0iSs

It can be done!

(but not the way we're doing it now)