NOTE: Instructor version with Tables 2 and 3 filled

Case Study: To Mask or Not to Mask

That is the Scientific Question

On Friday afternoon, three college friends – Tom, Jamie, and Ben – decide to meet at 7 PM at The Proudest Monkey, a bar & grill on Northgate, that is always packed with more than 25 people at that time. However, because of the SARS-CoV-2 pandemic, Tom is having second thoughts about the decision to go to a crowded place - particularly one indoors with limited ability to social distance. Tom, a biology major, suspects his friends may be unaware of the risk, so he asks them to join him in a Zoom meeting to discuss his hesitancy.

Tom: Hi guys, I do not think hanging out in a crowded place like the Proudest Monkey is wise during this pandemic. I think it is too risky given the speedy spread of SARS-CoV-2 virus.
Jamie: What is the SARS-CoV-2 virus? I thought the pandemic was COVID-19.
Tom: COVID-19 is the disease and SARS-CoV-2 is the virus that causes it.
Ben: I know that and understand some viruses can make you sicker than others, but I am unsure how they are different.
Tom: Some viruses have a DNA genome like we do and some have an RNA genome. Even with the DNA and RNA based viruses there are differences. Thus, a system called the Baltimore classification is used to group the different types. Here, I have it in **Table 1.**

TABLE 1

I	Double-stranded DNA	mRNA is transcribed directly from the DNA template	*Herpes simplex* (herpesvirus)
II	Single-stranded DNA	DNA is converted to double-stranded form before RNA is transcribed	*Canine parvovirus* (parvovirus)
III	Double-stranded RNA	mRNA is transcribed from the RNA genome	Childhood gastroenteritis (rotavirus)
IV	Single stranded RNA (+)	Genome functions as mRNA	Common cold (picornavirus)
V	Single stranded RNA (-)	mRNA is transcribed from the RNA genome	Rabies (rhabdovirus)
VI	Single stranded RNA virus with reverse transcriptase	Reverse transcriptase makes DNA from the RNA genome; DNA is then incorporated in the host genome; mRNA is transcribed from the incorporated DNA	Human immunodeficiency virus (HIV)

SARS-CoV-2 is a class IV single stranded positive-sense RNA virus just like the flu influenza virus. The milder symptoms of COVID-19 and flu are very similar and thus can be confusing. However, COVID-19 has a much higher infectivity and mortality rate, and emerging research indicates potentially serious lasting health impacts such as structural changes to the heart[1].

Jamie: Really??? I thought that COVID-19 was no worse than the flu.
Ben: I've also heard that, but I think it is a misconception causing people to doubt the seriousness of COVID-19. Isn't that correct?
Tom: Yes, many misconceptions exist about the virus causing COVID-19 and the pandemic. For example, many people wrongly claim that COVID-19 is not harmful to younger populations and will "disappear" in warm weather. We read a story in our class about COVID-19 "*COVID-19 pandemic and the fool's errand of pseudoscience-based decision-making*" that addressed commonly held misconceptions many people have about it. For more examples, you should read that story, but specific to the wrongly held idea that COVID-19 is no different than the flu, see if you can fill in the information in **Table 2.** Try it for a few minutes on your own.

NOTE: Instructor version with Tables 2 and 3 filled

TABLE 2: *Comparison of SARS-CoV-2 virus and Influenza virus (flu)* [2,3,4,5,6,7,8,9,10,11,12,13]

Characteristics	**SARS-CoV-2 virus (COVID-19)**	**Influenza virus (flu)**
Hosts and intermediate hosts	humans, origin: bats intermediate host unknown[2]	humans, origin: birds | intermediate hosts: birds, pigs, horses, other animals depending upon virus[3]
Hosts and intermediate hosts	epithelial cells of respiratory tract, GI tract, kidney, and also infects blood vessels[4]	epithelial cells of respiratory tract
Nucleic acid type & advantages/disadvantages	single stranded RNA, mutate frequently, can bypass transcription, more errors by RNA polymerase if transcribed[5]	single stranded RNA, mutate frequently, can bypass transcription, more errors by RNA polymerase if transcrbed
Viral transmissibility (R_0)	2.5 (estimated)[6]	1.3 (mean)[7]
Incubation period[8]	4-12 days	2 days
Symptoms[9]	fever, cough, shortness of breath, fatigue, headache, loss of smell and or taste and more	fever, cough, shortness of breath, fatigue, headache, runny nose, and more
Infections that are asymptomatic	40%[6]	5.2% - 35.5%[10]
Infectiousness of asymptomatic individuals relative to symptomatic	75%[6]	not significant[11]
% of transmission occurring prior to symptom onset	50%[6]	not significant[11]
Case fatality rate[12,13]	on 9/2/2020: US: ~3.0%, worldwide: avg 3-4% range: 0-29%	<0.01%

Tom: Were you able to fill in? Here, let me go over it with you. *(Tom helps them fill the table)*

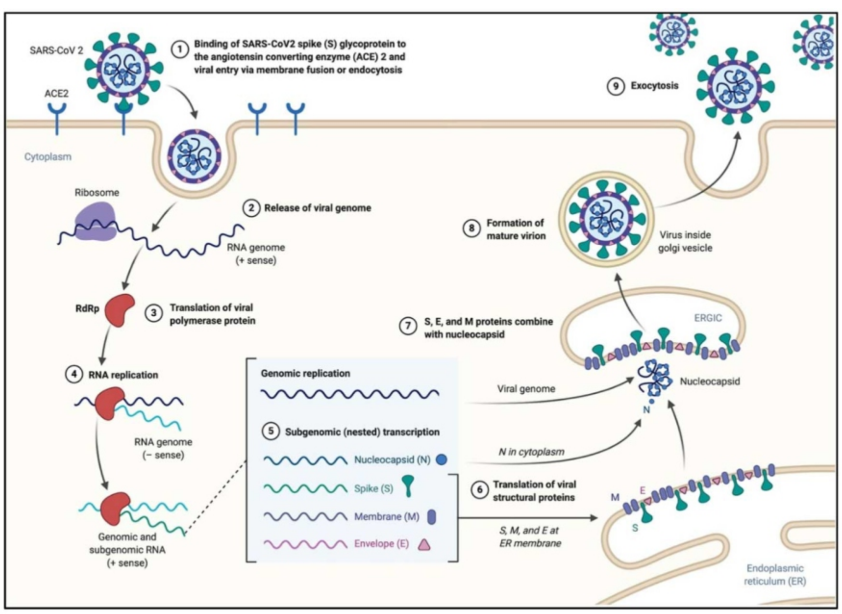
Reviewing the table information ***Ben says****:* They sure seem similar in a lot of ways, but they are different in how fast they spread and their impacts.

Jamie: Yes, that sure is an interesting fact. So Tom, how do these viruses enter our body?

Tom: Let me walk you through the steps of how SARS-CoV2 infects a human body and how its life cycle works shown in **Figure 1.**[14] You guys will be blown away by how small parasitic like entities can cause a havoc in our body.

FIGURE 1

Life cycle of SARS-CoV-2



Step 1: SARS-CoV-2 is recognized by and attaches to the ACE2 protein on the surface of a host cell via the spike glycoproteins in the cell membrane of the virus.
Step 2: SARS-CoV-2 is either engulfed by the host cell (endocytosis) or it fuses with the membrane
Step 3: The original infecting SARS-CoV-2 RNA is released, but remains in the host cytoplasm.
Step 4: A specific section of the original infecting SARS-CoV-2 RNA is translated by ribosomes to make RNA-dependent RNA polymerase (RdRp)
Step 5: The viral RdRp simultaneously makes complete copies of the genomic RNA to be packaged into new virions or virus particles and transcribes specific sections to mRNA as templates for translation from the original RNA genome.
Step 6: The newly synthesized coronavirus viral mRNA is translated into viral proteins like viral proteases, structural proteins, and RdRp using host ribosomes.
Step 7: Many of the newly synthesized viral proteins are processed for packaging into new virions.
Step 8: Partially complete virions are assembled and then bud from the host (exocytosis) taking with them parts of the host membrane that contain spike glycoproteins and other viral membrane proteins.

NOTE: Instructor version with Tables 2 and 3 filled

Jamie: Oh boy! I'm an Engineer and not a Biology major, but I think I get the gist of it.
Ben: Agreed. So, how do these virions or newly formed viruses that exit the host infect another person who is close by?
Tom: Ahh...now you are talking. Based on research, we know the virus is transmitted in three ways. Let me show you **Figure 2.**[15] Once you look at that, try to complete **Table 3** on how each of these are generated, by whom (symptomatic, presymptomatic or asymptomatic) and how and are they spread?

FIGURE 2
Transmission of SARS-CoV-2

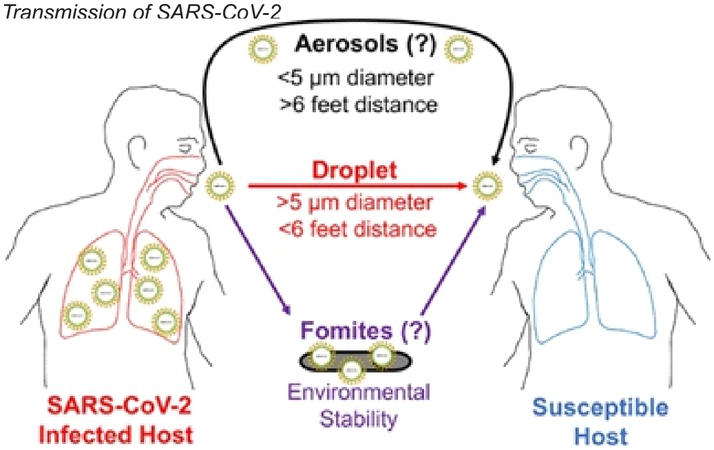


TABLE 3
Characteristics of SARS-CoV-2 transmission

Routes of Transmission	How generated and by whom?	How spread, what distance, and stability?
respiratory droplet transmission - respiratory droplets (particles are >5-10 um in diameter)	human: coughing, sneezing, talking, singing, etc.	direct contact; distances up to or beyond 6 feet
airborne transmission - droplet nuclei or aerosols are <5 um in diameter	human: coughing, sneezing, talking, singing, breathing, etc.	indirect contact; distances farther than 6 feet. Can get caught in airstreams.
fomite transmission - self-inoculation with contaminated secretions	vehicle-borne: virions remain viable on surfaces	indirect contact; farther than 6 feet depending upon duration of stability of environment (could be days)

At the time of writing this case study, scientists are aggressively researching how SARS-CoV2 spreads and, because of emerging research (pre-print and published), some speculate whether six feet physical distancing without protective equipment is enough. A strength of science is that even its most well accepted ideas are open to revision in light of new evidence or reinterpretation of prior evidence. (a) How is the carefully considered revision of scientific knowledge a strength of science? (b) Why is it important that the scientific community adjust their recommendations based on the collective best available evidence, and not isolated studies that have not been carefully vetted or supported by other research? For more information on this topic see the story: *COVID-19 Pandemic and Decision-Making: Waiting for Scientific Certainty is a Fool's Game.*

Jamie: OMG..I remember being sneezed on my face by my roommate earlier. *(Frantic questioning)* Do you think I could have SARS-CoV-2? How will I know? Is there any type of tests or treatment?
Tom: Calm down Jamie. Let us deal with one thing at a time. First, yes you can be tested if you think you were exposed to the virus. There are two FDA approved diagnostics tests being used in the US - molecular assays to detect the genetic material of the SARS-CoV-2 and antigen test to detect proteins that are on the virus surface. At the hospital or designated testing sites, they will take a nasal swab from you that only takes a few seconds and let you know the same day or the next day whether or not you are positive.
Ben: Oh yeah, I think you can get the antibody test done as well, Jamie.
Tom: Actually, Ben, an antibody test looks for antibodies made by the immune system in response to SARS-CoV-2 and is useful to determine if someone had COVID-19 in the past. It is not recommended to determine if someone is currently infected, because the immune system requires weeks to produce antibodies.

Ben: Ah, I see.

Tom: So, to answer Jamie's other question, treatments can relieve symptoms while the body fights the virus. However, there currently is no cure for COVID-19. But, there are several therapeutic approaches under investigation all over the world (See **Figure 3**[16]). Of these, the antiviral drug remdesivir appears the most promising in its development and its efficacy for treating COVID-19. Several other existing medications are being tested for their effectiveness such as the HIV medication lopinavir-ritonavir (Kaletra), the antiviral ribavirin, which is used to treat hepatitis C etc.

Ben: What about vaccines?

Tom: Vaccines are a whole different ball game. Most vaccines take years to develop. However, efforts are underway to develop and test vaccines to COVID-19 on an accelerated timeline.

Jamie: I heard from various folks that we can develop one in matter of days or few months.

Tom: Unfortunately, that is a misconception. The Center for Disease Control and Prevention (CDC) lists six stages for vaccine development, and these take time. Those stages include identifying a potential vaccine; testing in cell cultures and in animal models; clinical testing in humans for safety, effectiveness and dosage; applying for approval; and manufacturing and quality control. All this takes time to ensure a safe and effective vaccine that can be widely distributed. Vaccine development began early in the pandemic in spring 2020. Optimistically, a vaccine could be available by this coming winter or spring. It would be the fastest -development of any vaccine that has been created.

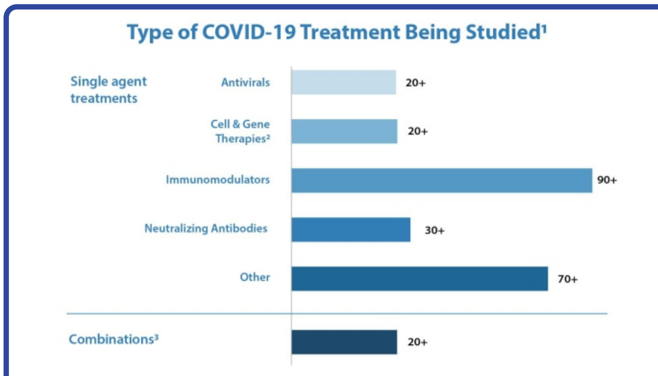


Figure 3. COVID-19 treatments being investigated

Jamie: Oh, then what do we do in the meantime?!

Ben: Is this why we are being bombarded with recommendations to physically distance in public, wear face masks, use eye protection, and wash our hands frequently?

Jamie: But I read online that masks don't actually work and that we shouldn't be required to wear them.

Ben: Well, you're not the first one to question mask-wearing. For instance, during the 1918 Spanish Flu pandemic mask wearing received similar skepticism and resistance despite recommendations from the community of health professionals. This skepticism was fueled by a lack of understanding and wrongly politicizing and rejecting medical experts' guidance. There is an eerie similar resistance to mask wearing today despite scientists' understanding of the spread and prevention of diseases that has drastically improved through much research dating back to the 1800's. Their recommendations to wear masks is based on this historical research and current studies about how SARS-CoV-2 spreads.

Tom: Yeah, once scientists understood that COVID-19 was a respiratory illness caused primarily by the SARS-CoV-2 spreading on the moisture we exhale, the need for public mask wearing became very apparent. Research indicates that most types of masks including N95 and homemade cloth masks significantly reduce the risk of infection when worn appropriately. Research has also demonstrated social distancing of at least two meters (approximately six feet) greatly reduces the chance of infection, although emerging evidence now indicates that six feet may not always be enough[17, 18, 19].

Jamie: Okay then why did the article I read about masks reference a *real* scientific study? It said the virus was too small to be stopped by masks.

Tom: Hmmm what that article could be referring to is the fact that the virus SARS-CoV-2 is 0.06 μm-0.140 μm diameter[20]**,** which is a particle size that could pass through masks intended to prevent disease spread. This was something I saw people talking about on social media. However, we know SARS-CoV-2 is a respiratory disease which requires respiratory droplets or droplet nuclei (i.e., aerosols) for transmission which typically range between 1 μm to 500 μm in diameter with a mean diameter of 10 μm[21]. Coughing and talking produce significant number of droplets and droplet nuclei[22], which masks help prevent from being released into the air. Here is a study that shows how far cough travels. The first image in **Figure 4**[21]**.** shows how far an unimpeded cough can

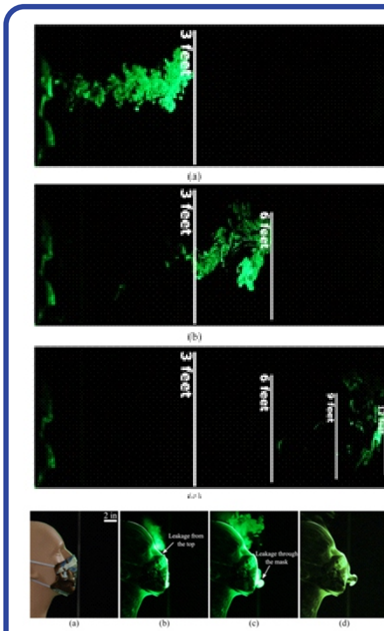


Figure 4. Model or cough unimpeded and impeded with a two-layer cotton mask.

NOTE: Instructor version with Tables 2 and 3 filled

The scientific community's current research on, collective understanding of, and recommendations about SARS-CoV-2 and COVID-19 has its foundations in germ theory established in the late 1800's, and the immense amount of research on diseases conducted since then. However, people often favor emotions, personal preferences, and ideology over well-established scientific knowledge when making decisions. What is the danger with making decisions this way?

Jamie: Wow, it's frustrating how difficult it is to get the right information. I get that science provides the best available understanding of the virus, but I don't have the time or the scientific expertise to read a bunch of scientific articles. How is the average citizen like me, who has little science background, to understand what is good and what isn't? Heck, I've only completed an introductory science course and earned a “C”. That hardly qualifies me to search on the internet judge science results.

Tom: I agree, the average person is not well-equipped to evaluate complex scientific claims which makes it challenging to make the right decision.

Ben: Even scientists can only speak to the validity of information related to their specific field of research. Science is a social endeavor in which multiple experts and an accumulation of evidence is used to reach consensus. Claims made by a single scientific publication or small research group are not yet well-established. That is why we must rely on the recommendations of large organizations of experts for reliable information.

Jamie: Well, the CDC and WHO all recommend masks, social distancing, and frequent hand-washing.

Tom: They also recommend staying home when possible.

Ben: So what will our decision be?

YOU HELP DECIDE!

If you were Jamie, Tom and Ben, what decision would you make? In your response, provide evidence and reasoning for your decision. Also, consider the case study you read above, your course content and the two stories: *COVID-19 pandemic and decision-making: Waiting for scientific certainty is a fool's game;* and: *COVID-19 pandemic and the fool's errand of pseudoscience-based decision-making.*

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travel at (a) 2.3 s, (b) 11 s, and (c) 53 s. The second image shows how far the same cough travels through a homemade two-layer cotton mask at (b) 0.2 s, (c) 0.47 s, and (d) 1.68 s. Watch this as well https://www.youtube.com/watch?v=_OSz5Gr7gG0[23].

Jamie: But at the beginning of the pandemic, they told us not to buy masks. How are we supposed to trust scientists and health officials if they keep changing their minds?

Ben: Well, a strength of science is that when evidence and reasoning warrants abandoning prior thinking, knowledge will be adjusted accordingly. So science doesn't change without reason, and well-established knowledge is quite durable, but when a new phenomenon arises like with the novel SARS-CoV2 responsible for COVID-19, those who understand how science works should not be surprised that health recommendations have been adjusted as new evidence became available. Early in the COVID-19 pandemic, many health experts referred to social distancing as the primary measure for reducing the risk of infection while more research was needed on how masks might prevent COVID-19. However, an abundance of studies released since then overwhelmingly support masks as an effective way to reduce the spread of respiratory droplets, and subsequent public health and safety recommendations have been changed to reflect our better understanding of how the virus spreads. While changes in science and public health recommendations can appear confusing and erratic to the untrained eye, the evolution of scientific ideas remains a strength of science and natural and crucial part of the process. Waiting for scientific certainty before taking action would be disastrous for decision-making.

See the story: *COVID-19 Pandemic and Decision-Making: Waiting for Scientific Certainty is a Fool's Game* to better understand how a strength of science is that even its most well accepted ideas are open to revision in light of new evidence or reinterpretation of prior evidence.

***Jamie*:** Don't you think scientists might be overreacting to the virus? Many of the scientific models early on in the pandemic ended up being incorrect…

Tom: Well, models are not exact replicas of the phenomena (such as COVID-19 cases and deaths) that they are trying to predict. They make projections based on the best available historical and contemporary evidence, often initially carry a high degree of uncertainty, and are modified as more data is gathered. But models, despite their uncertainty, are especially useful for understanding the plausibility of future situations. Also, few people consider that models are based on a variety of variables. For example, a recent University of Washington Institute for Health Metrics and Evaluation (IHME) model estimates that by December 1st there could be 300,000 COVID-19 related US deaths. However, the model also projected that if 95% of Americans consistently wore masks in public starting August 6th that approximately 70,000 lives would be spared[24]. How many COVID-19 cases will the U.S. have if no one follows social distancing? Unfortunately, these models are often misunderstood by the public, taken out of context, and sometimes manipulated to construct a false narrative or support a political agenda.

See the story: *COVID-19 Pandemic and the Fool's Errand of Pseudoscience-Based Decision-Making* to better understand how pseudoscientific approaches have been used to misrepresent scientific models and the scientists that create them.

Ben: Yeah, sometimes science can be misrepresented in the media and there is a lot of pseudoscience that *sounds* scientific. For instance, people may refer to an isolated study that is out of context or has been discredited, or to someone who appears to be an expert but is not representative of the scientific community studying COVID-19. Scientists rely on the accumulation of evidence and the deliberation between authentic experts in the community to consider a scientific idea and recommendation reliable. Unfortunately, the public usually only sees the outcomes of these deliberations, not the rigorous process of scientific revision. Humans, understandably, turn to friends, family, news media, politicians, etc. to guide their decision-making, but these sources are often at odds with research regarding human health and well-being.

NOTE: Instructor version with Tables 2 and 3 filled

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