Let's Talk About COVID-19: Part I

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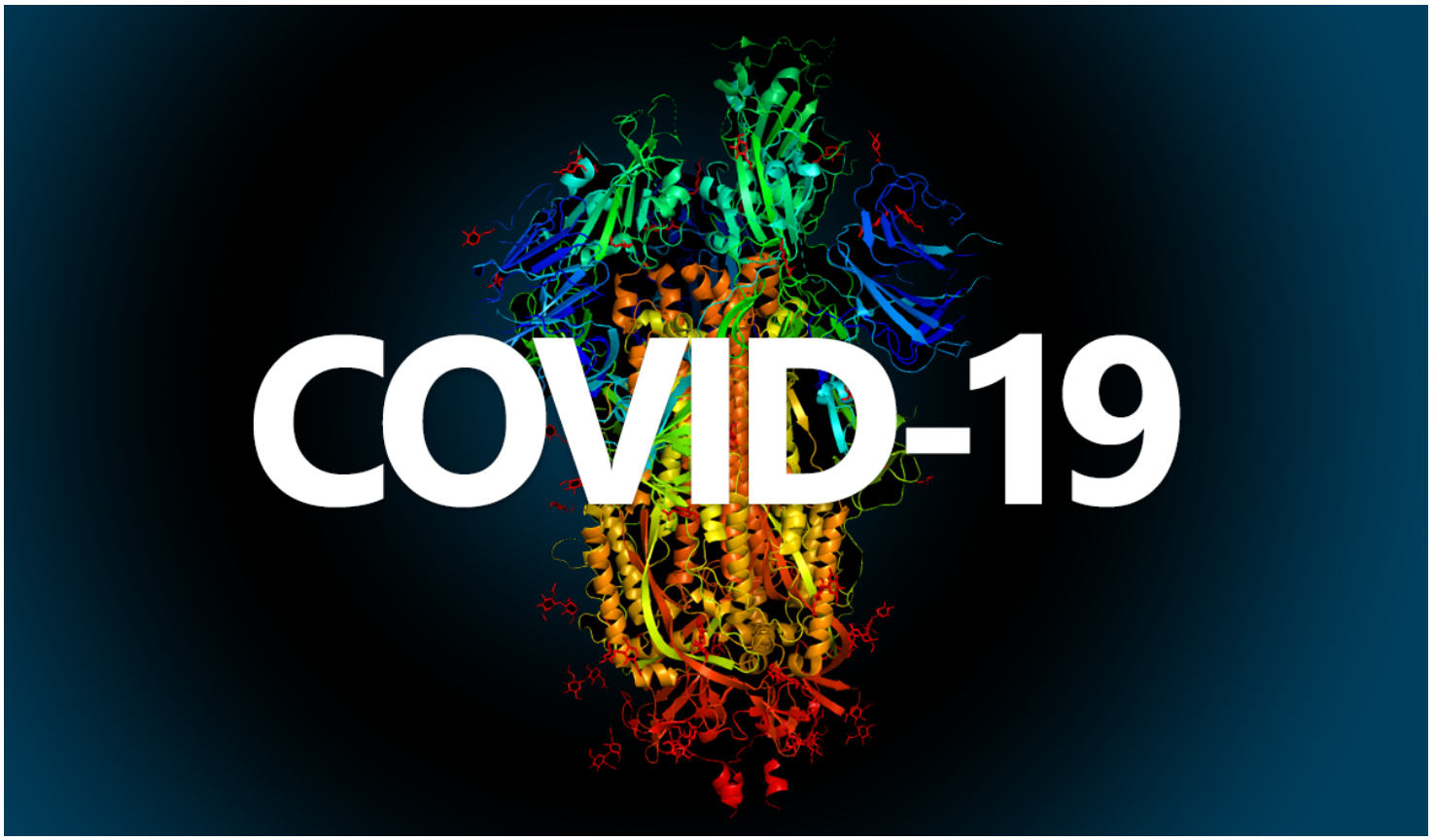
Severe acute respiratory syndrome coronavirus 2 (aka SARS-CoV-2) is the virus responsible for Coronavirus Disease 2019, more commonly known as COVID-19. COVID-19 has affected all of our lives and it's all the news can talk about these days. However, in this world of misinformation, I wanted to provide a bit of insight into what we do and do not know about this pandemic and what that means for us all long term. In this post, I will address some of the pathogen statistics, new scientific developments, and where you can go to get data if you want to do your own analysis.

My recent research focuses on more common pathogens like *E. coli* superbugs or malaria, though I worked on MERS (another coronavirus) in 2016. My colleagues and I published the research paper Spread of Middle East Respiratory Coronavirus: Genetic versus Epidemiological Data in the Online Journal of Public Health Informatics. What's interesting about this work is that we highlighted the discrepancies between transmission data shown from phylogenetics versus what the World Health Organization's (WHO) Disease Outbreak News was reporting. Though this research was published in May 2017, the presence of conflicting or incomplete data still haunts us today with this current outbreak.

I'm working with my fellow data and AI specialists at BlueGranite on using multiple COVID-19 data sources together to paint a more complete picture of the disease. This includes a chatbot to help state and local governments respond to COVID-19 questions and other work coming soon. To start, I thought I would get everyone up to speed on this virus itself and what efforts are being done to combat it.



Pictured: 3D Structure of SARS-CoV-2 Spike (S) Protein [5]

Disclaimer: Do not take this blog post as medical advice.
Consult your physician before treating yourself or others for this disease.

A Little History

Coronaviruses are not new nor are they necessarily rare. The most common strains in the *Coronavirinae* subfamily only affect mammals like bats, cats, and camels (oh my!), though there are 7 strains known to affect humans, including some that cause common human colds. In fact, most of us have lived through two other coronavirus-based epidemics, obfuscated under the names Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) in 2002 and 2012, respectively. Note that SARS-CoV-2 is not a direct descendant of SARS. This is a bit confusing, but it is named this way due to shared genomic properties from SARS and because they share a common ancestor.

Epidemiology

What makes SARS-CoV-2 interesting is the diversity in its pathogenicity. That is, how differently it affects people. Today, according to the CDC, the reported overall mortality rate for COVID-19 sits at somewhere between 1.8% and 3.4%, but this varies drastically based on other factors like age and existing conditions [1].

Country	Number of Cases	Mortality Rate
USA	51,914	1.30%
Canada	1,739	1.44%
Mexico	370	1.08%
UK	8,081	5.22%

Italy	69,176	9.86%
China	81,848	4.02%
Source: WHO COVID-2019 situation report 65 (Data as of March 25, 2020) [2]		

In the initial report from the Chinese CDC following the Wuhan outbreak, there are a lot of statistics that are still being reported [3]. For example, "The virus affects men more than women." from the report that there is a 2.9% mortality rate in men vs. 1.7% in women. Statistically speaking, there is a lot of bias in the sampling of infected individuals, which may be skewing these percentages. In this example, ~30% of the individuals tested in this study work in the service or farming industries, which may be male-dominated jobs, therefore making the gender breakdown of those tested unrepresentative of the general population.

A problem with many of the reports on this disease is in the lack of broad testing. We see a mortality rate and severity reports based only on a population of individuals that are already experiencing symptoms (plus a couple of celebrities and politicians that got their hands on a test). We think that far more individuals may be infected, but have little to no symptoms. If this is true, this reduces these severity and mortality statistics tremendously, but increases the prevalence numbers.

From Testing to Treatments

It's no secret that one of the hurdles we in the US are working through (aside from the lack of masks and ventilators) is the lack of testing kits. Current existing tests work by swabbing the back of the nasal cavity and then sending this swab off to a lab for manual processing by technicians using reagents to positively identify the presence of the virus. This can take days, which is a huge diagnosis bottleneck in understanding the spread and prevalence of this disease. (Not to mention the accuracy of this method isn't exactly ideal either.)

In other diseases (including malaria, strep, the flu, and MERS), rapid diagnostic tests have been developed that allow for test results to come back in minutes or hours. These tests operate in a similar manner to at-home pregnancy tests in that a small blood or fluid sample is taken and there are proteins (or other chemicals) that bind to a particular target in the sample and can give a quick and accurate result. This is a current push by a couple of research groups that are racing to develop an accurate test and get it out to market quickly.

As for prevention and treatments, this is where it gets tricky (and super interesting). There are two main options here: prevention of infection using vaccines or treatment using drug therapies.

Vaccines

Today, a few companies are working on a vaccine for SARS-CoV-2. Two novel approaches you should know about are from Moderna and Inovio. Moderna's work is quite interesting as they are using messenger RNA (mRNA) to help your own immune system learn about a specific viral protein that SARS-CoV-2 uses and enables your body to protect itself against the virus without ever having seen it. (Super cool!)

moderna

Learn more about Moderna's vaccine work here.

Inovio's work is similarly interesting as they are using a DNA injection to invoke the production of customized monoclonal antibodies. Antibodies can serve as ID tags for your immune system to know when something isn't right. So, your immune system can better recognize the coronavirus and get to work on clearing it out. In contrast to traditional vaccines, this also enables your body to prepare for the fight against SARS-CoV-2 without ever having been infected with it.

inovio

Learn more about Inovio's technology platform here.

Note: SARS-CoV-2 is an RNA virus and is expected to mutate quite often (although the data is not sufficient at the moment to get an accurate mutation rate measure). As with yearly flu shots, we should expect continual vaccine updates as the virus will likely change over time.

Treatments

Viruses work by using particular proteins to enter your cells and then reproduce by using the cell's machinery to rapidly make the parts that make up the virus. A good practice to try and stop the virus is to use a combination of drugs that combat multiple different mechanisms.

Example methods:

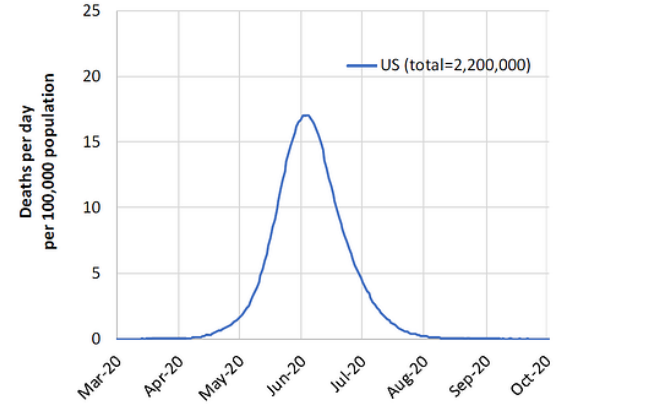
- Stop the virus from attaching to or entering our cells
- Stop the virus from hiding from our immune cells
- Stop the virus from assembling properly in our cells
- Stop our cells from making the viral proteins correctly
- Stop the virus from invoking such a severe response from our bodies (fever, mucus, inflammation, etc.)

Currently, computational biologists (like myself) are working to evaluate proper drug combinations that both reduce the infection while trying to mitigate the likelihood of developing drug resistance. We're working on this by looking at the individual genes that SARS-CoV-2 has and comparing this to treatment pathways that have worked in the past for other viruses.

A Little Hope

In epidemiology, there's a notion of an "inflection point" in the lifespan of a pandemic. When infections begin to spread, they usually spread exponentially up until a certain point where there are not enough individuals for the pathogen to spread to. While we don't know the true number of cases of COVID-19, we do have a decent idea about the number of cases that require medical care. Thus, our social distancing is limiting the spread of the virus.

According to a report by the Imperial College COVID-19 Response Team in London, the US may not reach this inflection point until June '20, but that our isolation practices (social distancing) may be helping tremendously.



Projected deaths per day per 100,000 population in the United States [4].

Flattening the curve isn't the solution to COVID-19, it's just holding off the spread as to not continue to overwhelm our healthcare system. It will be the development and distribution of adequate tests, vaccines, and treatments that will return our lives to normal. In the meantime, stay at home!

	Source	**Link**
[1]	CDC - Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19)	https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm#suggestedcitation
[2]	WHO COVID-19 Situation Reports	https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
[3]	China CDC Weekly - Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases	http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51
[4]	Imperial College London - Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand	https://spiral.imperial.ac.uk/handle/10044/1/77482
[5]	3D Protein Structure of SARS-CoV-2 Spike Protein (from Wrapp et al., PDB: 6VSB)	https://www.rcsb.org/structure/6VSB