Good News – Bad news

Updated April 27,2020:

Early estimates were that the R_0 of the SARS-Cov-2 infection was around 2.8. Thus disease is easily transmitted. This disease is transmitted through exposure to respiratory aerosols and droplets as well as direct contact.

(see https://www.drcharleslewis.com/uploads/1/3/1/1/131169625/aerosol_transmission of_sars-cov.pdf for explanation of aerosol transmission)

COVID-19 has a long disease course, which gives ample time for an infected person to spread the infection, and those infected are thought to shed the virus particles in high numbers especially in the early phases of the infection and perhaps there is shedding of the virus even when the infected person does not have symptoms. Those with mild symptoms and adequate immune response continue to shed the infectious particles for about one week into symptomatic disease.[1]

Thus, this virus is well adapted to causing a pandemic. That is not good news.

A mathematical modeling of disease spread in China, and in particular in Wuhan, gives estimates that 86.2 percent of all cases went undocumented, and that only 13.8% of cases were reported. It is assumed that these cases were either mild or asymptomatic. This modeling also estimates that these unreported cases were only 55% as likely to transmit the disease to other persons. These people were still infectious, but each on average only infected about half as many other persons as did the documented cases. Using these estimates, the study estimates that these undocumented cases (and presumably mild or asymptomatic cases) accounted for 79% of all disease spread. This is because there were so many more unreported than reported cases.[2]

Undocumented cases may result from a lack of any symptoms, insignificant symptoms, or fear of internment. In Wuhan, there was good reason to avoid hospitals and interment facilities where it was rumored there were insufficient bathroom facilities, no medications, insufficient food, and no privacy. Thus many cases may have been symptomatic, but hiding their condition at home. If the disease progressed, they may have then sought hospitalization, or at the peak of the crisis, perhaps perished at home. I don't think we have reliable information on this.

While in part a function of culture and environment, the overall R_0 of SARS-CoV-2 is around 2.8. This study suggests that undocumented cases have a R_0 55% that of reported cases, but made up the lion's share of those transmitting the disease. It does make sense that someone who is coughing, has a longer disease course, and has a higher viral load is more likely to spread the disease than someone with mild infection. This suggests an R_0 around 2.5 for undocumented cases and an R_0 about 4.5 for documented cases, if I got the math right.

Another study from Shenzhen, China looked at the infection rates among close contacts and household contacts. In this city there were many fewer cases and contacts were traced as a public health measure to blunt the spread of the disease. Three hundred ninety one cases and 1286 close contacts were identified. Among the cases, there were three deaths at the time of

publication an average recovery time was 21 days. Traveling companions were 7 times more likely, and household contacts were 6 times more likely to develop COVID-19 than were other close contacts. Children were just as likely to become infected as adults.

Only 15% of household contacts became infected. The observed reproductive number was 0.4. [3] Wait?! How can the R_o be 0.4 for household contacts and 0.47 for traveling companions? Remember that most homes in China are small. People can hardly isolate themselves at home from their families. If the R_o is less than 1.0, how could this disease have ever spread?

This early data suggested that most cases must be asymptomatic or trivial. The rates of unreported cases in Wuhan were estimated to be 86% of all cases, but perhaps people there hid their disease. In Shenzhen there was case-contact tracing and 85% of household contacts were unaffected. Two different situations, with the same outcome.

(Note: The RT-PCR testing used early during this outbreak had a sensitivity rate of 30 to 50% - so these data may also underestimate the number of persons actually infected. Improved RT-PCR testing now has a sensitivity rate of about 60 - 70%. This however does not change the death rate, or likely the severe infection case rate.) (Yes 30 to 40% of those with the infection will have a false positive RT-PCR test. Risk of false negative testing would be lower during peak viral reproduction in the nasal cavity and higher earlier or later in the infections course.)

Early analysis of SARS-CoV-2 genetic drift in Washington State, suggested that the virus began circulating in the community around January 15th and that by March 2nd, there were an estimated 570 cases.[4] Yet there were few severe cases identified at that time and almost all isolated to a single nursing home with high risk patients. It was estimated that there should have been hundreds of thousands of cases in the U.S. as of March 23rd, yet there were about only 26,747 confirmed cases reported at this time.

The data above suggest that 85% of the cases of this disease are asymptomatic or nearly asymptomatic.

Data from Gangelt Germany, where randomized antibody testing for SARS-CoV-2 was done in a in a town with an early outbreak, suggested that about 15% of the population had formed antibodies to the virus at the time of testing. However among the estimated 1900 infections, there were 44 deaths; giving a 2.3 percent infection fatality rate, including asymptomatic cases. That was not very hopeful.

On April 13, a letter in the new England Journal of Medicine reported that one-in-eight pregnant women coming into hospital in Net York at the height of the epidemic tested positive for SARS-CoV-2 on RT-PCR testing, but most were asymptomatic. Between March 22nd and April 4th, 2020, 215 women arrived at hospital for delivery; 33 tested positive, and 4 of these women had symptoms including fever. Twenty-nine women had no symptoms. This data suggest a 12% symptomatic disease rate.[5] If we apply a 70% detection rate because of the low sensitivity of the test method, the symptomatic disease rate might be as low as 9 percent.

If this population is reflective of the city as a whole, it also suggests that during this period, 15% of the population of New York had current SARS-CoV-2 infections during this period. Thus, this

data suggests that the immune population is considerably higher than 15%, as this number only reflects current infections and not those that had recovered or tested false negative.

On April 16th, it was reported that 655 crew members on the aircraft carrier Theodore Roosevelt tested positive, but that only 213 of these showed any symptoms. That is just less than one-in-three. If we assume that the RT-PCR test is about 70% sensitive, that suggests that the denominator (true positive) current viral infection number would be about 936, giving a 23% rate of symptomatic disease among those currently infected.[6] There was one death of a 41 year-old officer. More recently was reported that 955 of 4200 crew members have tested positive. Without antibody testing, the number of those already infected and resolved is not apparent.

Both sailors and pregnant women are largely healthy young persons with an average age likely to be around 25. Thus, they may not represent the risk seen among typical adult populations.

UPDATE April 24, 2020

We now have decent sized sample from which we can make some estimates as to the virulence of COVID-19 in the general population. This data comes from New York, where the outbreak has been severe. The New York Times and other outlets report some statistics from a study in which a random IgG and IgM testing was been done, both in the city of New York and throughout New York state. The study likely over-estimates the rate slightly, as the randomly selected individuals were people grocery shopping, and these individuals may be in more "circulation" and thus at higher risk than people that shop less frequently or go out less. Grocery shopping is sort of a treat – as it is an excuse to go out during a lock-down. Nevertheless, the test of 3000 individuals allows for some estimates.

The report found that 21% of randomly tested individuals in New York City (NYC) tested positive for antibodies to the virus. Thus with population of 8.4 million city residents, this gives an estimate that 1,764,000 NYC residents has already experience the viral infection and recovered by the time the testing was done. The paper reported that 13.9 percent randomly tested persons in New York State tested positive. With a population of 19.5 million residents, that gives an estimate of 2.71 million cases in the state. Only 3.6% of those living in upstate New York had immunity. At the time of the survey, there were 269,000 confirmed cases and 15,740 deaths.[7]

If one assumes that every significant case is tested, then *only one in 10 people experience significant disease* from a SARS-CoV-2 infection. This number would likely include among the nine insignificant cases those that tested false negative. This attack rate is similar to the results from other studies. New York City has an unusual population distribution with a high number of young adults, as many young adults move to NYC for work. This should be expected to lower the symptomatic disease rate and population mortality rates for COVID-19, as there should be somewhat more young healthy adults as a percent of the population as compared to most cities.

The infection fatality rate (IFR) estimate for New York State is thus 5808 per million infections. (15740 / 2.71M), or around 0.58%, and about one in 172 people that got infected died. The case fatality ratio (CFR), cases being those that were symptomatic enough to seek medical care or testing, is higher; of those with symptomatic infection, 5.8 percent died (15740 / 269,000)

however; some of those cases were not resolved cases, so the CFR may be higher. On the other hand, this number may be too high, as perhaps 30% of RT-PCR tests are false negatives, which would make the denominator larger, but these would likely mostly include those will less severe symptoms or even asymptomatic but worried exposed individuals that requested testing.

These data suggest an infection fatality rate of about 0.6% across the general population.

If we assume that 85% of the population would need to develop immunity before there was sufficient herd immunity to stop the spread of SARS-CoV-2, with 331 million people in the United States, we should then expect 1.63 million deaths from this virus if we fail to control its spread.

We know that the mortality is much higher for the elderly and those with pre-existing disease, thus the IFR for a given individual can be much higher or considerably lower than 0.6 percent.

Using data from New York City,[8] nearly 48% of deaths from COVID-19 are among the elderly.

Age group	% of pop by age (est.)	% COVID deaths by age	Rate ratio	Infections: Death ratio
0 - 17	21	0.04	0.00198	90393
18 - 44	40	4.5	0.1168	1530
45 - 64	24	23.1	1	179
65 - 74	8	24.6	3.195	56
75+	7	47.7	7.080	26

Assuming that everyone has equal chance of exposure and infection, the table above shows an estimate of risk of death by age after adjusting for the population at different ages.

Persons 75 or older are 7 times more likely to die of COVID-19 than are persons aged 45 to 64. Children and teenagers up less than 18 are 500 times less likely to die from COVID are less likely to die from this disease than are middle aged persons. This data provides an estimate that less than one in over 90,000 children under 18 will die if they get infected, but one in 26 persons aged over 75 will die if they get infected.

Overall, using data from New York City, more than 95% of COVID deaths occur in individuals with one or more underlying medical conditions. The underlying medical conditions include diabetes, hypertension, heart disease lung disease, kidney disease, GI/liver disease, cancer, immunodeficiency, and asthma. All pediatric deaths were among children with an underlying condition.

The good news is that if one is young and healthy, risk of death from this disease is not terrifyingly high. Persons aged 18 – 44 with no underlying conditions may have a risk below one-in-7,500 of dying from getting a SARS-CoV2 infection.

The bad news is that 55% of adults have at least one "underlying condition" that increases the risk of COVID-19 death. The really bad news is that if one is a 45 to 64 year-old man with one or more underlying conditions, the risk of death from infection may be as high as one in 30, and by age 65 the risk of death from a SARS-CoV-2 infection for a man with underlying disease may be one in 10. The risk of death increases with age and is higher for men than for women, but the greatest risk determinants are underlying conditions. A 65 to 74 year old man with no underlying conditions appears to be at lower risk than a young adult with an underlying condition. A considerable portion of the risk associated with age can be explained by the fact that as people grow older, they are more likely to have developed chronic disease.

On average, having underlying conditions raises risk of death about 20 times over that of people of the same age with no underlying conditions. The risk is so high because many of these diseases cluster –people often have multiple diagnoses. Having cardiovascular disease raised the risk of mortality in COVID-19 by about 12 times, diabetes about 8 times, hypertension or chronic lung disease by nearly 7 times. Thus, having diabetes and hypertension, on average might increase risk by 15 times, and those with more severe disease or requiring more medications would be at higher risk.

Most people under the age 40 are at very low risk of death from COVID-19. Those that are, are those with underlying conditions. Even those below the age of 50 are at low risk if they have no underlying medical conditions.[9]

These numbers are based on CFR data from New York City, not IFRs. These numbers look not too dissimilar to the Chinese CFRs. This suggests that young healthy people are much more likely to have asymptomatic than are the elderly.

Using this data for planning: Until there are effective vaccines for SARS-CoV-2, those at high risk for COVID-19 morbidity and mortality should continue social distancing, including from low-risk family members. Society should accommodate, by helping those at high risk remain protected, have higher-risk working age adults work from home. For example, young, low-risk of serious outcome teachers should be encouraged to work with children that are too young to do school work online, while higher-risk teachers can be assigned to work online with high school level students.

If this disease had a lower R_0 and was easier to tamp down with a few weeks of social distancing, I would suggest not reopening society until the disease was rare. This has not happened. I now however, recommend a limited reopening, allowing low-risk young people that do not live with high-risk individuals to return to most work and to many social activities. Let them go back to work, just avoiding high risk situations and high risk individuals.

Even being careful and using masks, many children and low-risk adults would likely develop natural immunity to the virus over the coming months. This would help develop herd immunity in the community that would then lower the risk of spread to moderate risk individuals, and then help stem the spread to the high-risk individuals as the R_0 falls below 1.0. Return to opening should be gradual – beginning with very low risk households, with everyone using

personal protection for most indoor activities such as shopping. Depending on the activity and risk to others in the environment, low-risk individuals could forego masks in some situations. For example if working in a closed team with other low risk individuals that were unlikely to carry the infection to higher risk individuals.

Even though IgG immunity testing is not proven to provide protection from the virus, or long-term protection, and thus is not favored by the WHO, I consider it to be of sufficient probability of at least short-term immunity, that one-year immunity cards could be useful for personnel working with high risk patients such as in nursing homes. In this document (https://www.drcharleslewis.com/system-for-certification-of-immunity.html) I recommend a certification that is color coded so that it will be easily identified for the time period of the certificate.

Allowing the young to acquiesce to the virus comes with the risk of the virus mutating to an even more pernicious form. However, the risk is lower than just reopening society and allowing the virus to replicate in those with less ability to control its proliferation, and thus higher risk of spreading a mutated form.

Type of Exposure:

After a two choir practice in Washington State in early March 2020, in which none of the participants were known to be ill, and no one was sneezing or coughing, there was an extremely high disease transmission rate. Of 56 persons at the practice, 45 were diagnosed with COVID-19. Allowing for a single likely asymptomatic carrier, this means that 45 of 55 persons developed symptomatic disease.[10] This 78% symptomatic disease rate is much higher than the typical 15% symptomatic disease rate that generally occurs with this disease. Two members of the choir died; a 4.4% case fatality rate and a *3.6% percent exposure mortality rate*. This is an extremely high symptomatic case rate and exposure mortality rate compared to what typically occurs with community spread. Another COVID-19 “super-spreader” event occurred in South Korea when a 61 year-old woman in South Korea infected at least 37 people[11] at church in which loud singing of hymns was encouraged as an important part of the religious service.[12]

In both these cases, people were exposed to singing in a closed area. I hypothesize that an asymptomatic person with a current SARS-CoV-2 infection of the nasal and pharyngeal mucosa can aerosolize infected particles during singing, when the larynx, covered with infectious particles vibrates at high velocity under high pressure creating small particle that can go deep into the lungs. Additional risk occurs as other singers take deep oral inhalations. This permits direct alveolar contagion. I suggest that this is a much more dangerous route of infection for this disease. In contrast, most community spread is from larger droplets that are inhaled through the nose and get trapped on the nasal mucosa. Here it can proliferate, but be exposed to the dendritic immune cells. Additionally, the virus particles in the mucous layer get swallowed, may be inactivated by stomach acid, and then are presented to the gastro intestinal immune surveillance.

Limited data suggests that aerosols exposure may be a considerably more deadly route of exposure for SARS-CoV-2. Aerosols exposure appears to impart a higher rate of symptomatic infection and may cause a higher case fatality rate. Aerosol spread may explain the increased risk observed on cruise ships, the aircraft carrier, among medical personnel in hospitals, and churches.

Thus the risk of symptomatic infection and mortality may be considerably higher when exposure is to small aerosols to the lung rather than large particles that are captured by the nose.

I am hopeful that in the coming weeks we will have a better understanding of additional risk factors that raise the risk of developing clinical COVID disease rather than them much more common asymptomatic infection or trivial disease (minor sinus or upper respiratory symptoms) that most people have after exposure.

More work is needed in defining risk factors. Is it the underlying disease alone, or do the medications used by those with these conditions modify disease risk and severity?

Until we have more information, get plenty of sleep, take a zinc supplement and low dose vitamin D daily. Take a deep breath through your nose, get some sunshine if you can get out, watch a comedy, enjoy those around you, and relax, and avoid people singing.

Part 2

Are health care workers at high risk of COVID-19 death?

"The overall case-fatality rate (CFR) was 2.3% (1023 deaths among 44 672 confirmed cases). No deaths occurred in the group aged 9 years and younger, but cases in those aged 70 to 79 years had an 8.0% CFR and cases in those aged 80 years and older had a 14.8% CFR. No deaths were reported among mild and severe cases. The CFR was 49.0% among critical cases. CFR was elevated among those with preexisting comorbid conditions—10.5% for cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6.0% for hypertension, and 5.6% for cancer. Among the 44 672 cases, a total of 1716 were health workers (3.8%), 1080 of whom were in Wuhan (63%). Overall, 14.8% of confirmed cases among health workers were classified as severe or critical and 5 deaths were observed."[5]

Health care workers (HCW) in Wuhan were at high risk of exposure to patients with critical disease.

If we use data from the study above, we find that there were 1018 deaths among 42956 non-HCW cases and 5 deaths among 1716 HCW cases of symptomatic COVID-19. The gives a case fatality rate of 2.37% for non-HCW cases and a case fatality rate of 0.29% for HCW in confirmed disease. The HCW were about eight times less likely to die from this disease than other patients. This is likely a result of them being on average younger and less likely to have chronic disease than the average patient diagnosed with the disease.

We can assume that these worker were more likely to be exposed to the virus and more likely to be diagnosed than the general public. I also think we can assume that HCW provided as good quality care as they were able to, to their fellow HCW. These factors may have affected the case-fatality ratio.

While it is obvious that HCW are highly likely to be exposed to SARS-CoV-2, there is nothing in this data that suggests that health care workers are at increased risk of severe or fatal disease beyond any personal risk factors they may have.

[1] https://www.medrxiv.org/content/10.1101/2020.03.05.20030502v1.full.pdf

[2] Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). Li R, Pei S, Chen B, Song Y, Zhang T, Yang W, Shaman J. Science. 2020 Mar 16. pii: eabb3221. doi: 10.1126/science.abb3221. PMID:32179701
https://science.sciencemag.org/content/early/2020/03/13/science.abb3221

[3] https://www.medrxiv.org/content/10.1101/2020.03.03.20028423v2

[4] https://bedford.io/blog/ncov-cryptic-transmission/

[5] Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. Sutton D, D'Alton m, Goffman D. April 13, 2020 DOI: 10.1056/NEJMc2009316 https://www.nejm.org/doi/full/10.1056/NEJMc2009316

[6] https://www.military.com/daily-news/2020/04/16/hundreds-sailors-carrier-roosevelt-have-covid-19-fewer-half-had-symptoms.html

[7] https://thehill.com/policy/healthcare/494324-27m-new-yorkers-have-had-coronavirus-preliminary-data-shows

[8] https://www1.nyc.gov/assets/doh/downloads/pdf/imm/covid-19-daily-data-summary-deaths-04152020-1.pdf

[9] https://ourworldindata.org/coronavirus#case-fatality-rate-of-covid-19-by-age

[10] https://www.cnn.com/2020/04/01/us/washington-choir-practice-coronavirus-deaths/index.html
[11] https://www.livescience.com/coronavirus-superspreader-south-korea-church.html
[12] https://www.straitstimes.com/asia/east-asia/crazy-auntie-and-secretive-church-at-heart-of-spike-in-s-korea