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COVID-19

Lessons We Should Have Learned

COLLECTED ESSAYS

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Essay One: The Risk in Perspective

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COVID-19

The Risk in Perspective

Kenneth P. Green

COVID-19: A new risk emerges into the human domain

In the last quarter of 2019, a semi-novel risk entered the human biological ecosystem, and simultaneously, the human public policy ecosystem. That semi-novel risk was COVID-19, a previously unknown variant of coronavirus capable of infecting, sickening, and killing otherwise healthy human beings.¹ In late 2019 COVID-19 began to spread through the Earth's human population from its origination point somewhere in the vicinity of the city of Wuhan, China.

To say that the reaction of the human policy ecosystem to the risk of COVID-19 was both extreme, haphazard, and historically unprecedented would be an understatement. Actions proposed, promoted, mandated, and enforced to modify the risks posed by COVID-19 to individuals and to society as a whole were orders of magnitude more intrusive than any other risk-intervention policies ever promoted, proposed, or implemented by governments in the past. This was a truly radical, global intervention by governments to control a novel biological risk.



Should you think that hyperbole, here's a partial list of the mandated actions:

- Wash your hands frequently;
- Social distance: Stay 6 feet (2 meters) apart from other persons;
- Wear a mask at all times in public;
- Self-isolate—"stay home; stay safe"²;
- Forgo international travel (travel bans were almost universally in place);
- Don't travel outside your immediate area (international and interprovincial borders were closed);
- Shut down "unnecessary" businesses;
- Shut down necessary businesses—schools, nursing homes, non-COVID medical facilities, and hospital wings;
- Respect the ban on social gatherings (with notable exceptions);
- Get tested/show proof of testing;
- Get a vaccine;
- Get boosters as soon as available.

The wildly diverging impacts and likely effectiveness, or ineffectiveness, of these various strategies on COVID-19 suggest an equally wild divergence in the understanding of COVID-19 itself—its

size, mass, shape, physical nature, potential interactions, exposure, viral uptake, established infection, reproduction, shedding of virus particles, and so on. It would

take a full textbook to unpack it all, which we don't have space for here, but perhaps we can put some of those risks and risk-management strategies in perspective to help make sense of COVID-19 public policies: what was suggested, what was mandated, what was rational, and what was irrational.

First, let's talk about the physical scale of the COVID-19 virus by comparing its size with other objects with which we are more familiar, and considering the likelihood of various COVID-19 protective measures working.



Figure 1, courtesy of the World Economic Forum (2020), helps visualize the relative size of a particle of COVID-19 as it compares to other microscopic (and some macroscopic) organisms and objects. The figure shows that at 1.0-1.5 microns (or millionths of a meter) the COVID-19 particle size is



Figure 1: The relative size of particles. Source: World Economic Forum, 2020.

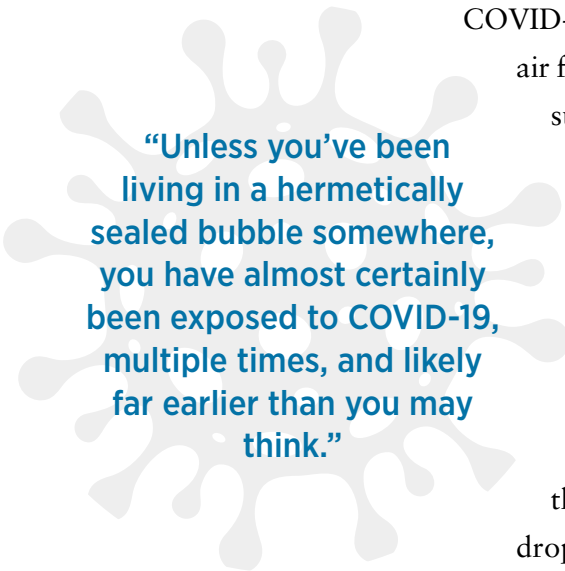
quite small on the relative scale of things: one-tenth the size of a common bacterium, and in fact, only five times larger than the T4 bacteriophage, a virus that infects bacteria. The virus’s size is a serious consideration in any discussions about masking and social distancing since physical particle size is the critical determinant of whether or not either of those activities will modify the risk of one’s exposure to COVID-19. Unfortunately, we don’t have the space to get into the biological details of precisely how COVID-19 operates biochemically/bio-mechanically/reproductively/evolutionarily.

The key point of figure 1 is to help the reader get an intuitive feel for the relative sizes of COVID compared to other agents that we might wish to control as an element of our local environment.

The risk of exposure to COVID-19 viral particles

Amazingly enough, explaining the risk of exposure to COVID-19 viral particles is simple, though generally denied or ignored by governments and most public health authorities. However, your risk of exposure to COVID-19 (once it has achieved a minimally sustainable population within its human hosts, something that happened long before it was ever manifest) is essentially 1 (ie., 100 percent). Unless you’ve been living in a hermetically sealed bubble somewhere, you have almost certainly been exposed to COVID-19, multiple times, and likely far earlier than you may think.) As has indeed happened (Wernau, 2022). This is simply the nature of microscopic and sub-microscopic life—it is, essentially, everywhere. You may think the air your home is clear and clean, and filtered and pure,

for example. But leave some moist bread out on your kitchen counter for a few days, and see what happens. The result is yeast or fungi, which are much larger organisms than COVID-19.



“Unless you’ve been living in a hermetically sealed bubble somewhere, you have almost certainly been exposed to COVID-19, multiple times, and likely far earlier than you may think.”

COVID-19 can stay airborne as microscopic aerosols floating on the air for several hours (at diminishing potency), or can lie about on surfaces and remain viable for nine days (Kampf et al., 2020). Again, unless, somehow, you were in a biological containment facility somewhere, the risk that you’d be exposed to (and probably infected by) COVID-19 is 100 percent. This is not new knowledge; it was known early on despite all the talk about mucus droplets being the primary risk of concern (a convenient, enabling belief that allowed for the illusion of safety for people who wore masks—even though the masks have pore sizes far larger than the airborne aerosol droplets rich with active COVID-19 particles) (Morawska and Cao 2020; Jarvis, 2020).

Risk of infection or re-transmission

Note that the risk of infection or re-transmission is not the same as the risk of exposure to COVID-19 virus particles. But what is the risk that the exposure will translate into infection? That is, what is the risk of disease establishment and contagion? The earliest estimates of COVID-19 risk—at least, those that emerged in the Anglosphere early in 2020, came out of the MRC Centre for Global Infection Disease Analysis, at Imperial College, London.³

Report 3: Transmissibility of 2019-nCoV (one of several that developed identifying terms for the virus) established the first widely known estimate of COVID-19 transmissibility (or contagion risk). Based on data from Wuhan, China, the research team of Neil M. Ferguson et al.⁴ estimated that, “each case infected 2.6 (uncertainty range: 1.5-3.5) other people up to 18th January 2020, based on an analysis combining our past estimates of the size of the outbreak in Wuhan with computational modelling of potential epidemic trajectories” (Ferguson et al., 2020a). This transmissibility value, called R_0 , (spoken “R-naught”), represents the basic reproductive rate of the virus (Ferguson, et al., 2020a).

For a good lay discussion of R_0 in the context of COVID-19, the reader might find it salutary to refer to the 2020 paper “ R_0 : How Scientists Quantify the Intensity of an Outbreak Like Coronavirus and Its Pandemic Potential” by Joseph Eisenberg, Professor and Chair in Epidemiology at the University

of Michigan. As Eisenberg explains, if R_0 is less than 1, the disease will die out in a population because on average an infectious person will transmit to fewer than one other susceptible person. On the other hand, if R_0 is greater than 1, the disease will spread.

Clearly, the first estimates of COVID-19 transmissibility put the risk of its spread through the human population significantly higher than zero. For comparison, table 1 (extracted from Eisenberg’s paper) shows the R_0 values of other contagious diseases that should be familiar to the reader.

Table 1: Reproduction Number (R_0) of Several Well-Known Human Viral Diseases

DISEASE	REPRODUCTION NUMBER R_0
Ebola, 2014	1.51 to 2.53
H1N1 Influenza, 2009	1.46 to 1.48
Seasonal Influenza	0.9 to 2.1
Measles	12 to 18
MERS	around 1
Polio	5 to 7
SARS	<1 to 2.75
Smallpox	5 to 7
SARS-CoV-2 (causes COVID-19)	1.5 to 3.5

Source: Eisenberg, 2020.

As table 1 shows, COVID-19 is moderately contagious when compared to other infectious diseases that we already manage as a society. It is somewhat more contagious than the common seasonal flu, but compared to the vast human infectious disease threats of the past and present: polio, smallpox, and measles... the risk of COVID-19 is nowhere near to being of the same magnitude.

Risk of morbidity and mortality

In February 2020, the Ferguson team published its first estimates of the COVID-19 *severity* risk in *Report 4: Severity of 2019 Novel Coronavirus (nCoV)* (Ferguson, 2020b). (Remember, the previous report was on *transmissivity*, or “can you catch it?” This report was on “*how serious will it be if I catch it?*”) Report 4 was later published in the journal *Lancet*. The risk value discussed in Report 4, the “Case Fatality Ratio (CFR)” was immediately controversial, because it was based on early data out of China, which was not considered trustworthy.

In Report 4, Ferguson et al. looked at three groups of infected people at the time: those detected in Hubei, China, those detected in travelers outside of mainland China, and those detected in passengers being repatriated to China from Germany and Japan. Using the three groups of data, Ferguson et al. estimated the overall CFR in all infections (asymptomatic or symptomatic) to be approximately 1 percent (95 percent confidence interval 0.5-4 percent).



And in fact, this estimate was quite accurate. As of this writing, some 2.5 years out, according to the World Health Organization's COVID-19 dashboard, "Globally, as of 5:33 pm CEST, 8 July 2022, there have been 551,226,298 confirmed cases of COVID-19, including 6,345,595 deaths, reported to WHO." Again, the math is fairly simple: $6.3M/551.2M = 1$ percent. The US CFR from COVID-

19 (again, as of this writing) is running at $(1M/87.2M = 1.15$ percent). The Canadian CFR from COVID-19 is estimated at $41,932/3,935,490 = 1.07$ percent.

For the more detail-minded, these are the estimated case fatality ratios from a literature review conducted in 2021 published in the *Journal of Preventive Medicine and Hygiene* that looks at 39 studies published in the prior year (2020). The research team of Alimohamadi et al. calculated (rephrased from study) that:

- The overall pooled CFR of COVID-19 was 10.0 percent (95 percent confidence interval: 8.0-11.0 percent); $P < 0.001$; $I^2 = 99.7$);
- The pooled CFR of COVID-19 in the general population was 1.0 percent (95 percent confidence interval: 1.0-3.0 percent); $P < 0.001$; $I^2 = 94.3$);
- The pooled CFR in hospitalized patients was 13.0 percent (95 percent confidence interval: 9.0-17.0 percent); $P < 0.001$, $I^2 = 95.6$);
- The pooled CFR in patients admitted in intensive care unit (ICU) was 37.0 percent (95 percent confidence interval: 24.0-51.0 percent); $P < 0.001$, $I^2 = 97.8$); and
- The pooled CFR in patients older than 50 years was 19.0 percent (95 percent confidence interval: 13.0-24.0 percent); $P < 0.001$; $I^2 = 99.8$) (Alimohamadi et al., 2021).

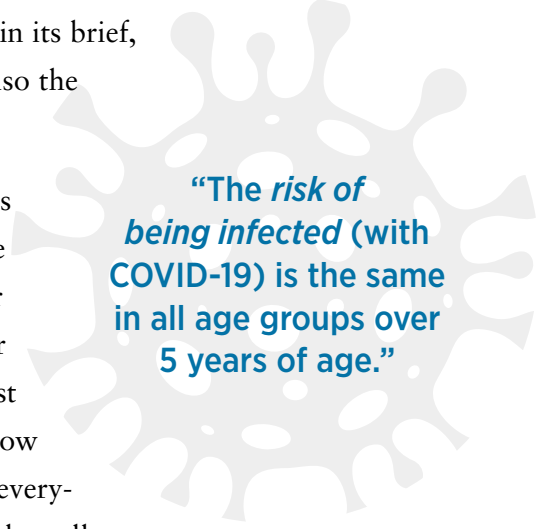
Risk stratification by age

The case fatality ratios discussed above were (primarily) population-wide values, not stratified by age, which, in the case of COVID-19, hides a large amount of important information that would let an average person understand his or her individual risk.

Table 2, which comes from the US Centers for Disease Control (CDC), illuminates how the risk of infection, hospitalization, and death from COVID-19 vary by age group (CDC, 2022).

Table 2 is perhaps the most useful data available for an individual wishing to assess the various risks to his or her health posed by COVID-19. The 18 to 29-year-old cohort is used as the baseline risk level because, as the CDC observes, “it has accounted for the largest cumulative number of COVID-19 cases compared to other age groups.” The CDC does not say so in its brief, but one assumes that this is the case because that age group is also the most highly active in just about all social aspects.

Notice that the *risk of being infected* is the same in all age groups over 5 years of age. Some might find this surprising though the only surprise from a biological perspective is that children under five don’t even seem to let the virus get enough of a toehold in their bodies to register as an actual infection (the virtue of a truly robust immune system, one supposes). That all of the other age groups show the same risk of infection is simply a reflection of the fact that everyone has, essentially, the same cellular and immune structures that allow



“The risk of being infected (with COVID-19) is the same in all age groups over 5 years of age.”

Table 2: Risk for COVID-19 Infection, Hospitalization, and Death By Age Group

AGE GROUP RATE RATIOS COMPARED TO 18- TO 29-YEAR-OLDS ¹									
Rate compared to 18-29 years old ¹	0-4	5-17	18-29	30-39	40-49	50-64	65-74	75-84	85+
Cases ²	1x	1x	Reference group	1x	1x	1x	1x	1x	1x
Hospitalization ³	1x	<1x	Reference group	2x	2x	3x	5x	8x	15x
Death ⁴	<1x	<1x	Reference group	4x	10x	25x	60x	140x	340x

All rates are relative to the 18 to 29 years age group. This group was selected as the reference group because it has accounted for the largest cumulative number of COVID-19 cases compared to other age groups. Sample interpretation: Compared with ages 18 to 29 years, the rate of death is four times higher in ages 30 to 39 years, and 330 times higher in those who are ages 85 years and older. (In the table, a rate of 1x indicates no difference compared to the 18 to 29 years age group.)

Notes

- 1 Rates are expressed as whole numbers, with values less than 10 rounded to the nearest integer, two-digit numbers rounded to nearest multiple of five, and numbers greater than 100 rounded to two significant digits.
- 2 Includes all cases reported by state and territorial jurisdictions (through September 11, 2022 accessed on September 12, 2022). The denominators used to calculate rates were based on the 2019 Vintage population.
- 3 Includes all hospitalizations reported through COVID-NET (from March 1, 2020 through September 3, 2022, accessed on September 12, 2022). Rates were standardized to the 2000 US standard COVID-NET catchment population.
- 4 Includes all deaths in National Center for Health Statistics (NCHS) provisional death counts (through September 7, 2022 accessed on September 12, 2022). The denominators used to calculate rates were based on the 2019 Vintage population.

Source: National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases; US Centers for Disease Control and Prevention: <https://www.cdc.gov/coronavirus/2019-ncov/COVID-data/investigations-discovery/hospitalization-death-by-age.html#print>

COVID-19 to enter and infect one's cells. Because COVID-19 is a small virus capable of airborne transmission, virtually everyone will be (and likely has been many times) exposed to COVID-19 particles in the environment.

But as the second row of table 2 makes clear, the *risk of being badly sickened* by the infection is not uniform across age groups. The older one is, the higher the risk that the severity of one's COVID-19 infection will result in hospitalization and, ultimately, death. As the table shows, the risk of a severe COVID-19 infection (requiring hospitalization) is five times higher for someone between age 65 and 74 than it is for an 18 to 29-year-old. That risk climbs to 8 times higher for people between 75 and 85, after which it peaks at 10-fold above the average for an infected person.

Finally, when it comes to the *risk that COVID-19 will kill you*, the age stratification is extreme. One's risk of death from COVID-19 infection if one is over 75 years of age is more than a full order of magnitude higher than the risk to someone between 40 and 49 years old.

Table 2 makes it quite clear that discussing COVID-19 risks devoid of age-stratification is terribly misleading.

Risk with co-morbidities

One of the more controversial elements of COVID-19 risk involves the initial conditions of the person that is infected: that is, there's a distinct difference apparent in the severity of COVID-19 infections of people (regardless of age) who are basically in good health compared with those who have what the US health insurance industry used to call "pre-existing conditions," such as obesity, asthma, diabetes, or the presence of any number of other diseases.



The question about this issue in popular discussion usually took the form of “we know people are getting COVID-19 and dying, but is it the virus that's killing them, or ‘just’ the pre-existing conditions that had them on course for death being sped up a bit?”

Publishing in *Nature* (February 2021), the team of Elezkurta et al. tried to answer this question. They performed autopsies on 26 people who had contracted COVID-19 and subsequently died in hospital in Germany. The study's abstract tells the tale with admirable brevity:

We performed full body autopsies on 26 patients that had died after SARS-CoV-2 infection and COVID-19 at the Charité University Hospital Berlin, Germany, or at associated teaching hospitals. We systematically evaluated causes of death and pre-existing health conditions. Additionally, clinical records and death certificates were evaluated. We report findings on causes of death and comorbidities of 26 decedents that had clinically presented with severe COVID-19. We found that septic shock and multi organ failure was the most common immediate cause of death, often due to suppurative pulmonary infection. Respiratory failure due to diffuse alveolar damage presented as immediate cause of death in fewer cases. Several comorbidities, such as hypertension, ischemic heart disease, and obesity were present in the vast majority of patients. Our findings reveal that causes of death were directly related to COVID-19 in the majority of decedents, while they appear not to be an immediate result of pre-existing health conditions and comorbidities. We therefore suggest that the majority of patients had died of COVID-19 with only contributory implications of preexisting health conditions to the mechanism of death. (Elezkurtaĵ et al., 2021)

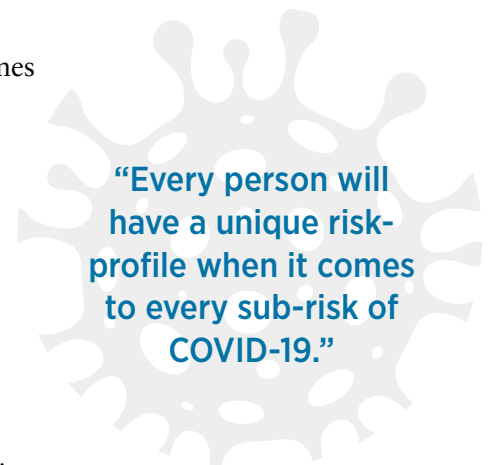
As to whether someone died *from* COVID-19, or merely *with* COVID-19, the answer seems clear: COVID-19 was quite capable of doing the deed all by itself, co-morbidities present or not.

For those interested in exactly what co-morbidities were observed in patients that died with/from COVID-19 in 2020, the CDC has that data available in tabular form at https://www.cdc.gov/nchs/data/health_policy/COVID19-comorbidity-expanded-12092020-508.pdf (CDC, 2020).

Assess your personal risk

Ultimately, every person will have a unique risk-profile when it comes to every sub-risk of COVID-19, from the risk of infection, to the risk of progression to severity, to the risk of hospitalization, to the risk of treatment ineffectiveness, and so on.

Fortunately, the *Economist* has put together a risk-estimation calculator that people can use to assess that individualized risk, the better to make informed choices about how they wish to manage them (Economist, 2022, March 11). As the *Economist* summarizes, “we have built a statistical risk model, using records in the COVID-19 Research Database from 425,000 people in America who tested positive. For any group of unvaccinated people of a given age, sex and mix of comorbidities, our model estimates the share that would be hospitalized or die within 30 days of a COVID-19 diagnosis (COVID-19 Research Database, 2022). As with all statistical models, all caveats apply: the reader is advised to remember that models are not reality, and are often not particularly robust representations of reality. They are, at best, illuminations of what might be reality.



Summary

One lesson that we might draw from humanity's recent experience with COVID-19 is that, to put it mildly, humans are not particularly adept at perceiving, understanding, and rationally acting upon issues involving risk.

This is not surprising, as risk is a slippery concept: it is a matter of probabilities, some large, some small, some independent, some co-dependent, some completely dependent, all acting upon and amidst one another in both time and space. And yet, humans feel compelled to slap a simple number on risks (often using byzantine, opaque, and assumption laden computerized models of risk), and then act as if that number actually reflects some level of reality involving the probability that a given series of events will transpire that will ultimately cause harm. Even though risk estimates reflect no such thing.

COVID-19 was a novel risk to humanity (in recorded history, at any rate), and its toll in human lives and suffering should not be trivialized. At the same time, it should be recognized that humanity's horrendous interpretations of the risks of COVID-19 led to the implementation of draconian, historically novel disease-control policies.



Endnotes

- 1 I note this as a semi-novel risk, as there are four other known coronaviruses that seasonally infect and afflict the human population as a seasonal flu-like virus. For those curious about some of the biology of the coronaviruses, there is a good lay primer available at <https://www.sciencealert.com/coronavirus> (Science Alert, Undated).
- 2 Unless, of course, you're a designated "vital worker."
- 3 For those interested in the early development of COVID-19 risk estimates, Imperial College hosts an archive of its COVID-19 reports from January of 2020 onward (Imperial College, 2020).
- 4 The research teams for the various Imperial College studies headed by Dr. Ferguson varied based on the nature of the study. I will refer to them generically as "Ferguson et al."

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