COVID-19

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As of today, the death toll from SARS-CoV-2 infection is 2.4 million worldwide, and on the rise.

The late ophthalmologist Dr. Li Wienling in Wuhan, China issued early warnings about the Severe Acute Respiratory Syndrome in December 2020. Chinese scientists and doctors confirmed the outbreak; the coronavirus spike protein genome was sequenced - CCUCG-GCGGGCA,and a large hospital was made in record time to contain the spread of the virus. The source of that infection was quickly identified as a novel coronavirus, related to those that had caused outbreaks of Severe Acute Respiratory Syndrome (SARS) from 2002-2004 and Middle East Respiratory Syndrome (MERS) in 2012.

The World Health Organization declared the public health emergency of international concern on 30 January 2020. By March 2020, in the US, there were 30,000 confirmed cases of COVID-19, and by August, 50,000 new cases per day. Today, the number is 27,229,862 total cases and 473,699 COVID - 19 related deaths. The national ensemble predicts that a total of 515,000 to 540,000 COVID-19 deaths will be reported by March 6, 2021. An "ensemble" forecast combines each of the independently developed forecasts into one aggregate forecast to improve prediction over the next four weeks.[1] As of today, according to Worldometers, coronavirus cases:109,180,109, deaths: 2,406,975, recovered: 81,223,069 in 219 countries and territories.[2]

2.4 million people dead, so what went wrong?

The British Medical Journal editorial of Feb 4, 2021 had a scathing remark on this global governance failure – ***COVID-19: Social murder***, ***they wrote***, ***elected, unaccountable and unrepentant.***[3] Four-hundred thousand deaths from COVID-19 in the US, 250,000 in Brazil, 150,000 each in India and Mexico, 100,000 in UK, accounting for half of the world's death toll. "Social murder" may describe the lack of political attention to social determinants and inequities that exacerbate the pandemic. If not murder or a crime against humanity, are we seeing involuntary manslaughter, misconduct in public office, or criminal negligence? Blame goes equally to the media and journalists, whose job was to bring truth to power. It didn't happen.

Living together with bacteria and viruses has not been easy.
In the words of E.O. Wilson, "The history of life on earth has been a history of interaction between living things and their surroundings."[4]

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1 US Centers for Disease Control and Prevention
COVID-19 forecasts: deaths.
Date : Feb. 3, 2021

2 www.worldometers.info/coronavirus
Feb 14, 2021

3 Kamran Abbasi
BMJ 2021: 372:N314

4 Top 180 E.O. Wilson quotes/2021 Edition
https://quotefancy.co,/e-o -wilson-quotes

The first recorded epidemic of Babylon flu happened around 1200 B.C. The Plague of Athens in 429 BC killed 100,000 people; the Antonine Plague in 2nd century claimed five million lives; the 6th century Plague of Justinian another 50 million; and the Black Death or Bubonic Plague of the 14th century wiped out half of Europe's population: 200 million people. The dreaded Spanish flu of 1918-1920 infected 500 million worldwide in four successive waves with the death toll somewhere between 20-50 million. Regarding these numbers on the infection rate and death toll, COVID-19 is number 12.[5]

Like other coronaviruses, SARS-CoV-2 particles are spherical and have proteins called spikes protruding from their surface. These spikes latch onto human cells and then undergo a structural change that allows the viral membrane to fuse with the cell membrane. The viral genes can then enter the host cell to be copied, thereby producing more virus. The spikes bind to receptors on the human cell surface called angiotensin-converting enzyme 2 (ACE2).[6]

The incubation period of coronavirus disease 2019 is believed to extend to 14 days, with a median time of four – five days from exposure to symptomatic onset. In one study 97% of patients developed symptoms within 11.5 days of becoming infected with Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2).[7] COVID-19 is thought to spread mainly through close contact from person to person, including between people who are within six feet of each other. Spread is by respiratory droplets as well as air borne transmission. The virus can survive on the surface from hours to few days with at least 48 hours on stainless steel.

Clinical presentation varies widely, and without a strong clinical suspicion, early diagnosis could be easily missed. Fever, sore throat, myalgia, joint pain, headache, new onset of cough, shortness of breath, loss of smell, and gastrointestinal symptoms are usually early symptoms of illness. Depending on high fever, hypoxemia, and altered mental status, the disease process can be classified as mild, moderate, and severe.

There are two tests available: Nucleic Acid Amplification Tests (NAATs) and antigen tests. Nucleic acid amplification tests are more reliable, but they take longer to get the report and they are expensive. Antigen tests, on the other hand, can be performed as a point of care service since it only takes about 15 minutes for its turnaround time, thereby making it a rapid test. Advantages of rapid test are that they are simple and inexpensive to perform and they have a rapid turnaround time. There are different criteria for when and where to be tested depending on the health facilities and practice. Therefore, frequent testing is key to mitigate the pandemic.

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5 Wikipedia

6 Novel Coronavirus Structure Reveals Targets for Vaccines and Treatments, National Institutes of Health, March 3, 2020

7 Centers for Disease Control and Prevention
Coronavirus Disease (COVID-19): Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19) June 2, 2020

Upper and lower respiratory tract infections including COVID -19 pneumonia are usual. It has affected every organ system, but particularly the lungs. Due to hyperinflammatory changes, cytokine storm, hypercoagulable state, thromboembolism such as pulmonary embolism have been widespread. That is the reason why anticoagulation is started early with critically or severely ill individuals. Changes in mental status and stroke-like symptoms are due to leakage of fibrinogen from the vascular lining in addition to thromboembolism. These stroke-like changes have been seen in MRI of the brain and olfactory nerves that explain the symptoms of anosmia. Abnormal liver function tests, myocarditis, and worsening of acute pancreatitis have also been reported.

Diabetes mellitus, chronic lung disease, congestive heart disease, autoimmune disease, and old age are classified as high-risk factors for contracting this illness. Morbid obesity is an independent risk factor. Those who have dementia, independent from all of the above comorbidities, are twice more likely to get this disease while potentially dying from a severe form of it. For black people, the risk is three times more likely.

Long-term health consequences of COVID-19, though, remain uncertain because it is a new disease. Nonetheless, clinicians are observing persistent severe symptoms and substantial end-organ dysfunction. The terms “long haulers,” “long Covid,” and “post-acute Covid” have been used for patients suffering from shortness of breath, fatigue, and depression. Post-acute COVID-19 is defined as the presence of symptoms extending beyond three weeks from the initial onset of symptoms with chronic COVID-19 extending beyond 12 weeks. Specific organ dysfunction has been reported involving primarily the heart, lungs, and brain. Pathogenesis is thought to be due to direct tissue invasion by the virus, profound inflammation and cytokine storm, related immune system damage, hypercoagulable state, or a combination of these factors.

Myocardial injury, cardiac arrhythmias, congestive heart failure are a few of the common complications following severe acute COVID-19. Diminished diffusion capacity of the lung and respiratory muscle strength have been documented. Headache, vertigo, and chemosensory dysfunction (anosmia and ageusia) are the most common long-term side effects. Stroke, encephalitis, Guillain Barre syndrome, seizures, mood swings, and “brain fog” are serious but uncommon complications. However, there is an even greater risk of depression, anxiety, post traumatic stress disorder, and substance use disorder among people recovering from COVID-19. Longer-ranging longitudinal observational studies and clinical trials will be critical to elucidate the durability and depth of health consequences attributable to COVID-19 and how these may compare with other serious illness.[8]

The treatment part has been daunting, and there is a lack of effective treatment for every stage of the illness. The living systemic review and network analysis is a cumulative synthesis that is updated regularly as new evidence becomes available. This review is part of the BMJ Rapid Recommendations project, a collaborative effort from the MAGIC Evidence Ecosystem Foundation (www.magicproject.org) and the BMJ. After screening 20,228 titles and abstracts and 370 full texts, 130 unique randomized controlled trials from 118 publications were identified that evaluated drug treatments as of December 3, 2020. Eighty-five randomized trials have been published that evaluated

8 Long -term Health Consequences of COVID-19
Drs Carlos del Rio MD, Lauren F Collins,MD and Preeti Malani,MD
JAMA, November 3, 2020, Vol 324, Number 17, page 1723-1724

drug treatments.[9] Of the 130 included drug trials, the three most commonly studied drugs were hydroxychloroquine, followed by corticosteroids, and lopanavir/ritonavir.
This is the list of the drugs that are included in the trials: azithromycin, colchicine, favipiravir, hydroxychloroquine, hydroxychloroquine+ azithromycin, interferon gamma, interferon kappa+treefoil factor 2, lopinavir/ritonavir, nitazoxanide, rhG-CSF, remdesivir, tocilizumab, and umifenovir.

None of the above drugs increased the rate of viral clearance. It did not have any impact on the length of hospital stay either. The length of ICU stay was shortened by three to five days for those who received corticosteroids. Corticosteroids and remdisivir, however, did not reduce the duration of mechanical ventilation.

In conclusion, corticosteroids probably reduce mortality, mechanical ventilation, and ventilator-free days in patients with severe COVID-19. Whether or not remdesivir has any impact on any outcome remains uncertain. Hydroxychloroquine, lopinavir/ritonavir, and interferon beta may not reduce mortality or mechanical ventilation, and they seem unlikely to have any other benefits. Currently, the effects of most drug interventions are highly uncertain, and no definitive evidence exists other than interventions resulting in important benefits and harms for any outcomes. Post-exposure therapy with hydroxychloroquine did not prevent SARS-CoV-2 infection or symptomatic COVID-19 in healthy people exposed to PCR positive cases. In addition, it did not lower the incidence of transmission.[10] Peripheral treatment including high dose Vitamin D has been touted as an effective approach supported by small trials conducted during this pandemic and is widely prescribed. Recently, treatment with vitamin C and zinc has also fallen out of favor.

Now what?
“We have paleolithic emotions, medieval institutions and god-like technology” - E.O. Wilson, naturalist.

Walter Isaacson, a former editor of TIME magazine, has done a beautiful and eloquent essay on the messenger RNA vaccine, a god-like technology, and the people behind the scenes as well as their ambition and work ethics.

Drs Ugar Sahin, CEO BioNTech and Ozlen Tureci MD, co-founder and its Chief Medical Officer have been working on mRNA since 2008 at their previous venture of curing cancer. When the pandemic was going out of control, both doctors started working on an mRNA vaccine in collaboration with Pfizer. In less than a year, the Pfizer-BioNTech COVID-19 vaccine became the first ever mRNA vaccine available for widespread use. Dr. Katalin Kariko and Dr. Drew Weissman of BioNTech have also been instrumental in achieving this victory. In 2005, they published a study on mRNA, which opened the door to mRNA’s use in vaccines and other therapies.

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9 Drug treatments for COVID-19: living systemic review and network meta analysis
BMJ 2020:370:M2980

10 A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of COVID-19:
Drs O. Mitja, Corbacho-Monne’ and Ubals, and Drs Gonzalez-Beiras and Clotet et.el
for the BCN-PEP-CoV2 Research Group
N Eng J Med 2021:384:417-27
Feb 4, 2021

On the other hand, Moderna, a young company with 800 employees, was working on different cancer treatments using messenger RNA technology. When Stephanie Bancel, CEO of Moderna Therapeutics, and its co-founder Noubar Afeyan grabbed the opportunity, the team took two days to create the RNA sequence that would produce the spike protein, and 41 days later the company shipped its first box to the National Institute of Health to begin its early trials.[11]

There are at least 55 more vaccines in different phases of development, and it is our fervent hope that this holy grail, the vaccines, will ultimately calm this storm. This pandemic has affected every aspect of life that it brought the world to a standstill. On the other hand, we are so proud of this god speed progress in achieving this miracle for mankind, a triumph of science and medicine.

COVID-19 vaccine candidates currently approved or in phase III trials*.

Vaccine (manufacturer)	Type of immune response	Efficacy	Storage	No of vaccines	Status
Killed Whole Virus					
CoronaVac (Sinovac)	IgM/IgG	NA	2-8 degree C	2	Approved countries including China, Turkey, and Brazil
COVAXIN (Bharat Biotech)		NA			Approved in India
BBIBP-CorV (Sinopharm)		NA			Approved in China, & UAE
Purified virus components					
NUX-CoV2373 (Novovax)	IgM/IgG	NA	2-8 degree C	2	Phase III trials
ZF 2001 (Chinese Academy of Sciences)		NA			Phase III trials
Replication-defective virus vector carrying gene(s)					
ChAdOx 1 n CoV-19 (Oxford Astra Zeneca)	IgM/IgG	two full dose 62% one half and one full dose 90%, overall 70.4%	2-8 degree C	1	Approved in UK and by EMA
Ad5-nCoV (CanSino)	IgA, cell mediated	NA			Phase III trials
Sputnik V (Gomaleya Research)		NA			Approved in countries including Russia, Belarus, Argentina
Ad26.C0V2.s (Jansen)		NA			Phase III trials
mRNA based vaccine					
BNT162b2	IgM/IgG	95% in all	-70degree C	2	Approved by FDA and EMA

11 The Miracle Molecule
Walter Isaacson
TIME magazine, Jan 18/Jan 25, 2021

(Pfizer-BioNTech)	IgA, cell mediated immunity	age groups	permanently 2-8 degree C for 5 days		and countries including Canada and UK
mRNA-1273 (Moderna)		94.1%	-20 degree for 6 months, 2-8 degree for 30 da	2	Approved by FDA and EMA in Canada and UK

* All the listed candidates are suitable for people with immunodeficiency, but no efficacy data are currently available for this population. EMA, European Medicines Agency, FDA, US Food and Drug Administration, NA, UAE.

In November 2020, the US Food and Drug Administration authorized the use of monoclonal antibody products, bamlanivimab (Lilly), and casirivimab/Imdevimab (Regeneron) to treat outpatient COVID-19.
Monoclonal antibodies are proteins made in the laboratory to mimic the immune system's antibodies when fighting viruses. These neutralizing antibodies are specifically directed against the spike protein present in coronavirus and they are designed to block the virus from entering cells. It may limit the amount of viral load and it is recommended for mild to moderate symptoms of COVID-19 in non-hospitalized patients. It can be given within 10 days of the symptoms starting.

The World Health Organization published "Fair allocation mechanism for COVID -19 vaccines through COVAX Facility" on September 9, 2020. In this document, the WHO proposes that the overarching goals of protecting individuals and health systems and minimizing impacts on societies and economies should drive the allocation process for COVID-19 health products across different countries. Vaccines with broad safety and effectiveness profile would prevent cases of COVID-19 and end the pandemic. The broad goals are:
1. Vaccines: Two billion doses of vaccine fairly distributed by the end of 2021
2. Therapeutics: 245 million treatment courses within 12 months delivered to LMIC (Low Middle Income Countries)
3. Diagnostics: 500 million simple accurate and affordable diagnostic tests used in LMICs by mid-2021
4. Health systems: Help countries use new tools as they become available and supply Personal Protective Equipment (PPE) and oxygen.[12]

Long term care facilities have their unique problems. Life Care Center of Kirkland, Washington had the first encounter resulting in many losses of life. They occurred in a 130-90-30 fashion: 130 residents, 90 SARS CoV 2 infections, and 30 dead. These statistics ran throughout the country. Deep down, the issues were low supply of PPE, inadequate staffing, low-paying jobs, and a fragile population. Front line workers stepped up. Nurses and CNAs (Certified Nursing Assistants) worked fearlessly, extra hours during the day and night. Few got sick, but they came back on day 14. One-third of the lost lives in this country are from "nursing homes" residents and staff. Once lockdown started in March 2020, residents were confined to their rooms for months with little or no social interactions. Families could

12 The Concept of Fair Access and Equitable Allocation of Covid-19 Health Products
WHO: December 6, 2020

not visit for months. Everyone endured. Meanwhile, nursing home survey process continues to function with a punitive tone. Life Care Center of Kirkland received three "immediate jeopardy" deficiencies (with a civil monetary penalty of $611,323).[13]

It is high time that we push for a survey process that not only assesses performance in a no-blame fashion but also facilitates person-centered care and innovations in care delivery while continuing to fairly account for deficient practices and negligence.

Now there is a murmur of re-opening, lifting the lockdown, and welcoming back visitors. This is what *The Delphi* panel had to say. *The Delphi* panel consisted of 21 US and Canadian post-acute and long-term care experts in clinical medicine, administration, and patient care advocacy. The panel made five strong recommendations:

1. maintain strong infection prevention and control precautions
2. facilitate indoor and outdoor visits
3. allow limited physical contact with appropriate precautions
4. assess individual residents' care preferences and level of risk tolerance, and
5. dedicate an essential caregiver and extend the definition of compassionate care visits to include those that promote psycho-social well-being of residents.[14]

Game changer: COVID-19 variants.
The novel coronavirus has mutated to more virulent variants in the UK, Brazil, South Africa, and California. Learning from Brazil, when everyone thought the country had developed herd immunity, the second surge came and it was the variant form, causing another tsunami of infections.
It is predicted that in March 2021, we may have more of the UK variants here. There is always a question of the vaccines being ineffective. That is a chance we take. When the whole country is vaccinated early, there is a chance of overcoming the mutating variants.

Let us continue the basics of preventing the disease.
Masking, social distancing, hand washing, testing and vaccinations.
We are hopeful the good days are ahead, SARS-CoV-2 will become less virulent, vaccines will reach 300 million arms, the economy will flourish, and we will get our life back.

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13 Time for an Upgrade in the Nursing Home Survey Process: A Position Statement from the Society for Post-Acute and Long-Term Care Medicines
Drs Arif Nazir, MD, CMD, FACP, Karl Steinberg, MD, CMD, HMDC et.al
JAMDA- The Journal of Post-Acute and Long-Term Care Medicines

14 Recommendations for Welcoming Back Nursing Home Visitors During the COVID-19 Pandemic: Results of Delphi Panel
Drs Christian Bergman, MD, CMD, Nathan M. Stall MD, Daniel Haimowitz, MD, CMD, Louise Aronson MD,Joanne Lynn MD, Karl Steinberg MD,CMD, Michael Wasserman, MD,CMD
JAMDA December 2020/Vol 21/Number 12, pages 1759-1766