1 SARS-CoV-2

SARS-CoV-2 Was identified and sequenced in 5 weeks

1.1 Death and Illness

Reported 7 million confirmed COVID-indiced deaths worldwide w/ 700 million confirmed cases

Likely 19.1-36 million COVID induced deaths

The US (4% of population) had over 15% of the cases

COVID-19 hospitalizations and death are highly dependent on age

	Hospitalization[1]	Death[2]
0-4 years	4x lower	9x lower
5-17 years	9x lower	16x lower
18-29 years	Comparison Group	Comparison Group
30-39 years	2x higher	4x higher
40-49 years	3x higher	10x higher
50-64 years	4x higher	30x higher
65-74 years	5x higher	90x higher
75-84 years	8x higher	220x higher
85+ years	13x higher	630x higher

Figure 1: COVID-19 hospitalization and death by age

Risk of illness and death from COVID-19 increases due to systemic health and social inequities

Risk of hospitalization affected by other conditions

1. Asthma
2. Hypertension
3. Obesity
4. Diabetes
5. Kidney disease

1.2 Long Covid

A chronic condition that occurs after SARS-CoV-2 infection and is present for at least 3 months

Estimated at 10-30% of non-hospitalized cases, 50-70% of hospitalized cases, and 10-12% of vaccinated cases

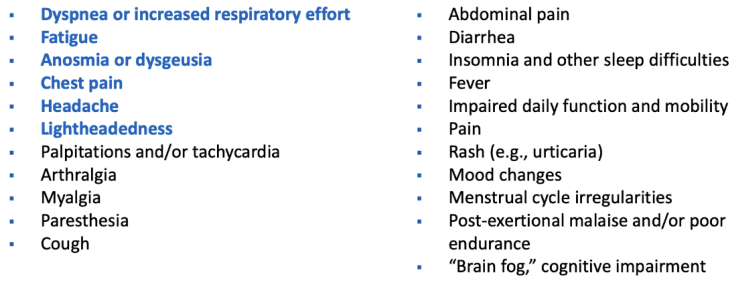

Figure 2: Symptoms of long Covid

Proposed contributing mechanisms:

1. Viral antigen persistence
2. Systemic and tissue-specific inflammation
3. Human herpesvirus reactivation
4. Dysbiosis
5. Microvascular dysfunction
6. SARS-CoV-2-specific and autoreactive immune responses

1.3 Vaccines

SARS-CoV-2 Vaccines are very effective

1. Pfizer-BioNTech and Moderna mRNA vaccine
2. AstraZeneca-Oxford and Covishield chimpanzee-derived adenovirus
3. Johnson & Johnson and Janssen human adenovirus (Ad26)
4. Sinovac and Sinopharm inactivated SARS-CoV-2 virus

Approximately 14 billion doses administered worldwide, preventing 15-20 million deaths

In-vitro transcribed mRNA is formulated into lipid nanoparticle using a cell-free production pipeline

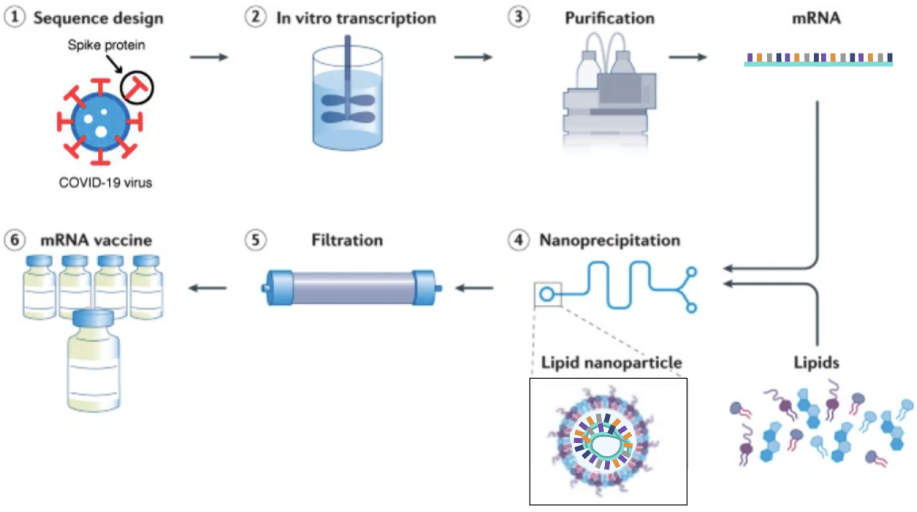

Figure 3: mRNA vaccine formulation

Injected mRNA vaccines are endocytosed by antigen-presenting cells

→ By translating the mRNA into protein in the ribosome, the immune system is stimulated

1.4 Immune Response

1.4.1 Neutralization

Neutralization is one mechanism of antibody function

→ Antibodies attatch to spike proteins, so viruses cannot attatch to host cells

1.4.2 Immune Sensing

RNA from viruses (or vaccines) are recognized by inate sensors, eliciting the release of cytokines

Early attempts at lipid-mRNA particles resulted in low imunogenicity because they looked like viruses and therefore only created inflammation (production of type I interferons)

→ By incorporating modified nucleotides into the mRNA, it strongly reduces the innate immune signaling through decreased activation of TLRs and cytosolic RNA sensors

1.5 New mRNA Vaccines in Development

1. SARS-CoV-2
2. Influenza virus
3. Zika virus
4. HIV

5. RSV
6. Ebola virus
7. Rabies
8. Plasmodium gametocyte (Malaria parasite)

1.6 Vaccine Innovation

Most vaccines take years to develop, but multiple vaccines for SARS-CoV-2 were made within a year

How was this possible?

1. Coronaviruses were already a concern
2. The technology was ready
3. Worldwide collaboration
4. Funding for vaccine research
5. Close collaboration between pharmaceutical companies and governmental agencies
6. Very high infection rate in the population and no difficulty recruiting volunteers