




COVID-19

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Introduction

Corona virus is caused by a novel, enveloped single-stranded RNA virus, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Corona virus first appeared in Wuhan China in December of 2019 with presumed zoonotic origin. Since then, the World Health Organization (WHO) have declared a global health emergency as COVID-19 continues to spread world wide. COVID-19 has shown to infect the human lungs, showing a ground glass appearance on imaging. Each and every case of COVID-19 varies from patient to patient which may include a mild, moderate, or severe reaction. As of April 10th 2020, there are 1,684,833 confirmed cases, 375,499 recovered patients, and 102,136 deaths worldwide.

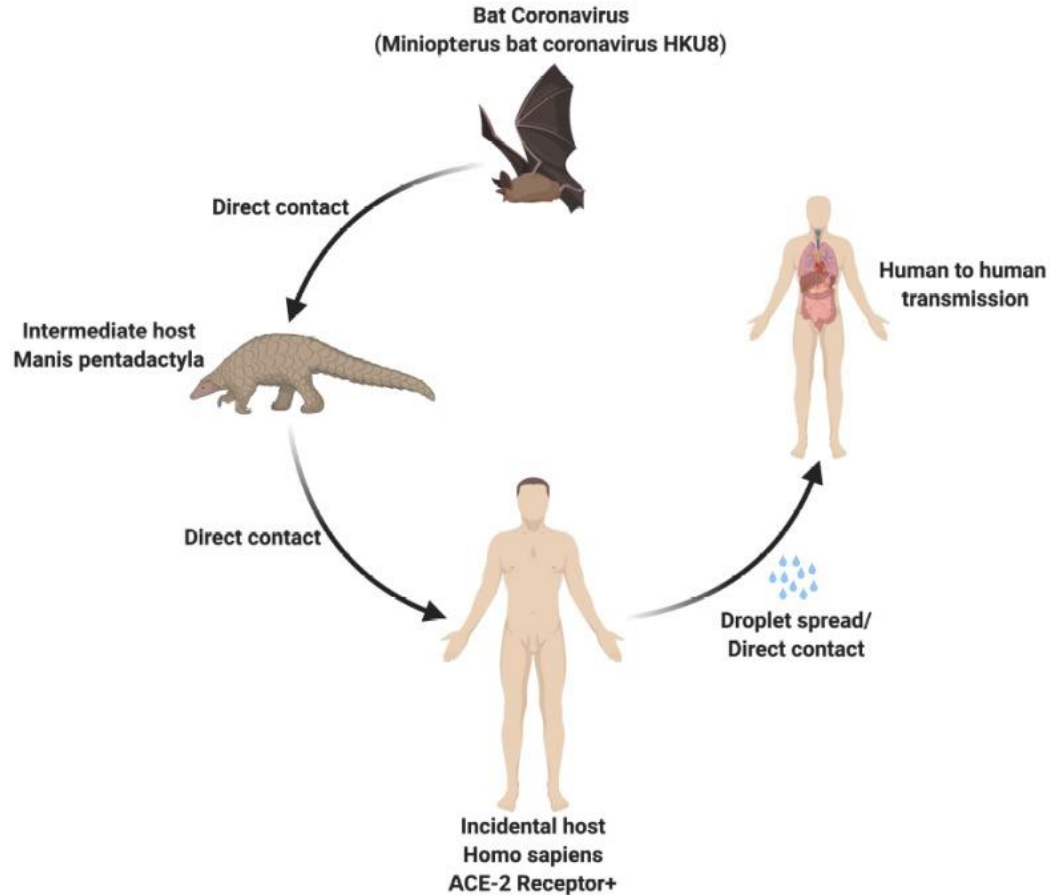


Origin

- SARS-CoV-2 appears to have been a zoonotic infection that has adapted to humans.
 - Origin is uncertain although bats implicated.
 - Genetic analysis shows a great similarity to bat SARS-like coronavirus (genus *Betacoronavirus*, subgenus *Sarbecovirus*)

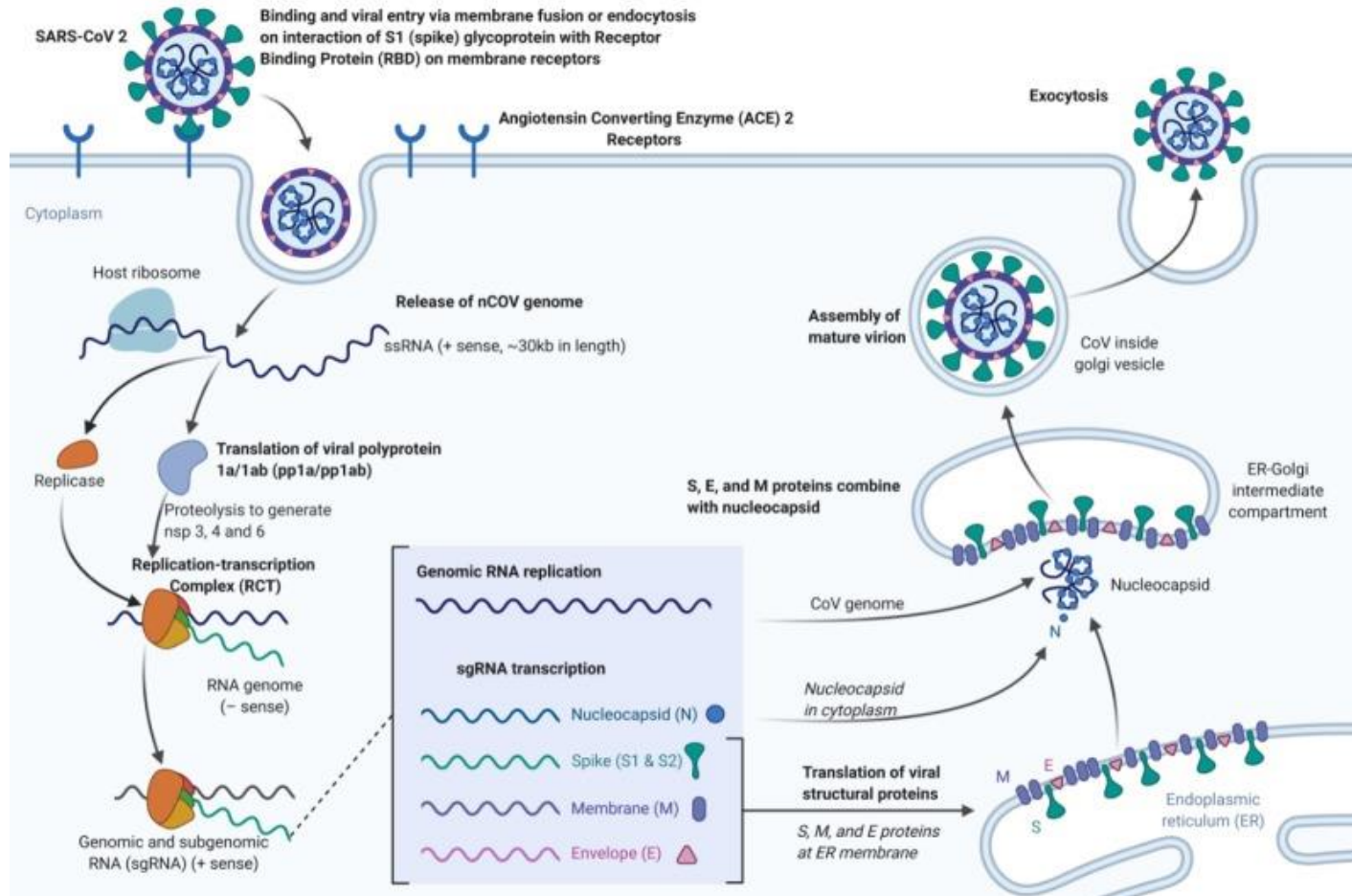


Transmission Cycle of SARS CoV 2



Global pandemic

- A pandemic is a global outbreak of disease. Pandemics happen when a new virus emerges to infect people and can spread between people sustainably. Because there is little to no pre-existing immunity against the new virus, it spreads worldwide.
- The virus that causes COVID-19 is infecting people and spreading easily from person-to-person. On March 11, the COVID-19 outbreak was characterized as a pandemic by the WHO.
- This is the first pandemic known to be caused by a new coronavirus. In the past century, there have been four pandemics caused by the emergence of new influenza viruses. As a result, most research and guidance around pandemics is specific to influenza, but the same premises can be applied to the current COVID-19 pandemic. Pandemics of respiratory disease follow a certain progression outlined in a “Pandemic Intervals Framework.” Pandemics begin with an investigation phase, followed by recognition, initiation, and acceleration phases. The peak of illnesses occurs at the end of the acceleration phase, which is followed by a deceleration phase, during which there is a decrease in illnesses. Different countries can be in different phases of the pandemic at any point in time and different parts of the same country can also be in different phases of a pandemic.



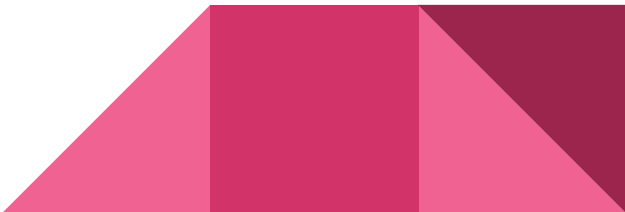
Transmission

- Person to Person Spread

- Through respiratory droplets produced when an infected person coughs, sneezes or talks.
- COVID-19 may be spread by people who are not yet showing symptoms of the disease. Maintaining a good social distance (at least 6ft.) is important to stop the spread of the disease.
- Droplets may hang out in the air up to 3 hours before they fall.

- Contact with contaminated surfaces or objects

- By touching a contaminated surface or object and then touching your face, mouth, nose or even your eyes. Coronavirus can survive for :
 - Up to 4 hours on Copper
 - 24 hours on cardboard
 - 2-3 days on plastic and stainless steel



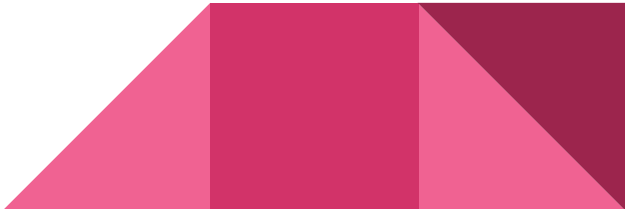
Signs and symptoms

These symptoms may appear 2-14 days after exposure

- Fever
- Cough
- Shortness of breath

When to Seek Medical Attention

If you develop emergency warning signs for COVID-19 get medical attention immediately. Emergency warning signs include:

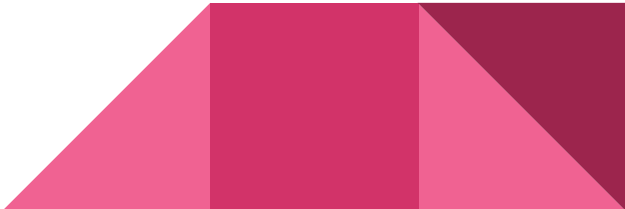
- Trouble breathing
 - Persistent pain or pressure in the chest
 - New confusion or inability to arouse
 - Bluish lips or face
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Clinical Manifestations

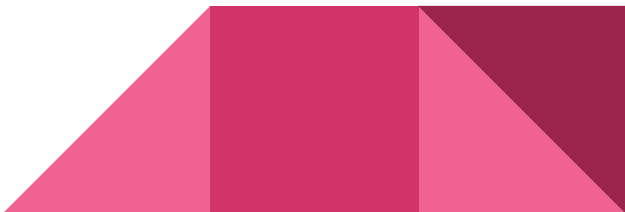
- Mild disease: non-pneumonia and mild pneumonia; this occurred in 81% of cases.
- Severe disease: dyspnea, respiratory frequency $\geq 30/\text{min}$, blood oxygen saturation (SpO_2) $\leq 93\%$, $\text{PaO}_2/\text{FiO}_2$ ratio or P/F [the ratio between the blood pressure of the oxygen (partial pressure of oxygen, PaO_2) and the percentage of oxygen supplied (fraction of inspired oxygen, FiO_2)] < 300 , and/or lung infiltrates $> 50\%$ within 24 to 48 hours; this occurred in 14% of cases.
- Critical disease: respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or failure (MOF); this occurred in 5% of cases.

Who is most at risk?

Based on our current knowledge, those who are at a high risk for becoming seriously ill from COVID-19 are:

- People aged 65 and older
 - People who live in nursing homes, group homes, and long-term care facilities
 - People with chronic lung diseases
 - People with moderate to severe asthma
 - People who are immunocompromised
 - People with severe obesity with a BMI ≥ 40
 - People with diabetes
 - People with chronic kidney disease who are undergoing dialysis
 - People with liver disease
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Diagnostics

- Reverse transcription-polymerase chain reaction (rRT-PCR) nasopharyngeal swab
 - This is the most commonly used test, often seen at “Drive Thru” testing sites
 - Antibody testing
 - Recently approved by the FDA, detects IgM antibodies several days after initial infection
 - Viral culture
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Diagnostics

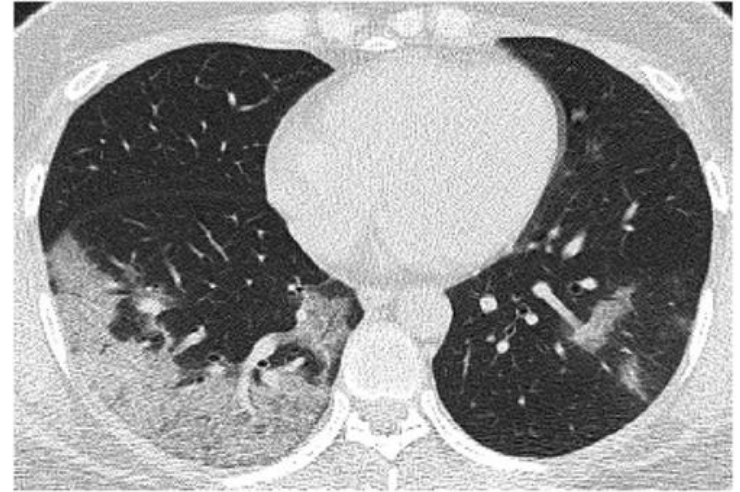
- Lab Values:

- Leukopenia, leukocytosis, lymphopenia
- Elevated lactate dehydrogenase, D-dimer, and ferritin levels

- Imaging

- CT Scan

- Peripheral distribution (80%)
- Ground-glass opacity (91%)
- Fine reticular opacity (56%)
- Vascular thickening (59%)
- Central and peripheral distribution (14%)
- Pleural effusion (4.1%)
- Lymphadenopathy (2.7%)



- Chest x-ray

- Consolidation (47%)
- Ground-glass opacity (33%)
- Severity of findings peaked 10-12 days after symptom onset



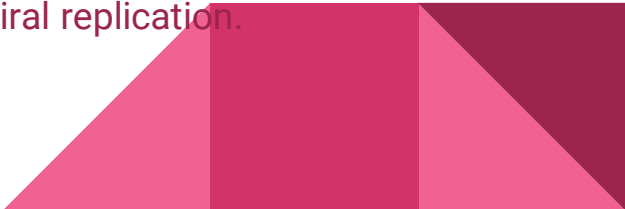


A race to find treatment


- The World Health Organization (WHO) launched an international clinical trial called “Solidarity”. This clinical trial enrolls patients from multiple countries to assess the effectiveness on COVID-19 of four different treatment options against standard of care. Solidarity’s goal is to be able to quickly determine if any of these drugs are successful at slowing the disease progression or improving survival rates. Drugs included in this study are:
 - **Remdesivir**- a drug previously tested as an ebola treatment.
 - **Lopinavir/Ritonavir**- a licensed treatment for HIV
 - **Interferon beta-1a** - used to treat multiple sclerosis
 - **Chloroquine and hydroxychloroquine** - two drugs that are closely related and used to treat malaria and rheumatology conditions.
- Studies are also underway for other ways to target the virus or treat the complications such as
 - Monoclonal antibodies that have been isolated and retrieved from people who have recovered from COVID-19.
 - Blood plasma transfers from people who have recovered from COVID-19.
 - Stem Cells

Therapeutic Options

Although there is no definitive treatment for COVID-19, there are many therapeutic options being used.

- Hydroxychloroquine and Chloroquine
 - Oral prescription drugs that have been used in the past for viral and inflammatory purpose
 - Convalescent Plasma
 - Delivering anti-SARS-CoV-2 convalescent plasma to hospitalized patients with severe or life-threatening COVID-19.
 - Remdesivir
 - An intravenous drug with broad antiviral activity that inhibits viral replication.
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Prevention

- Wash your hands with soap and water for at least 20 seconds
 - If soap and water are not readily available, use hand sanitizer that contains at least 60% alcohol.
 - Avoid touching your face, eyes, nose, and mouth
 - Clean and disinfect frequently touched surfaces daily
 - Cover your mouth and nose with a cloth face cover when around others
 - Cover coughs and sneezes with tissue or the inside of your elbow
 - Wash hands with soap and water for 20 seconds immediately after disposing of tissue
 - Social Distance
 - Stay 6 ft away from others
 - Avoid those who are sick
 - Stay home unless essential
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STOP THE SPREAD OF GERMS

Help prevent the spread of respiratory diseases like COVID-19.

Avoid close contact with people who are sick.



Cover your cough or sneeze with a tissue, then throw the tissue in the trash.



Avoid touching your eyes, nose, and mouth.



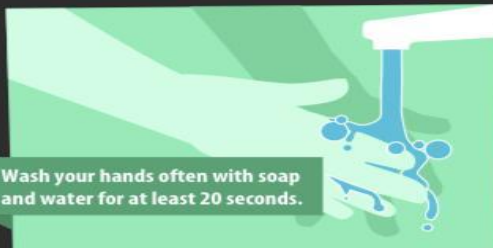
Clean and disinfect frequently touched objects and surfaces.



Stay home when you are sick, except to get medical care.



Wash your hands often with soap and water for at least 20 seconds.

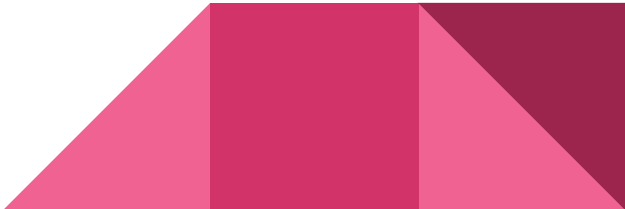


Social and physical distancing

While it may be disappointing to hear that so many sports events, cruises, festivals and other gatherings are being cancelled, there is a public health reason for these measures. These cancellations help stop or slow down the spread of disease allowing the health care system to more readily care for patients over time.

Cancelling events that are likely to draw crowds is an example of **social and physical distancing**. Social distancing is deliberately increasing the physical space between people to avoid spreading illness. Staying at least six feet away from other people lessens your chances of catching COVID-19.

Other examples of social and physical distancing that allow you to avoid larger crowds or crowded spaces are:

- Working from home instead of at the office
 - Closing schools or switching to online classes
 - Visiting loved ones by electronic devices instead of in person
 - Cancelling or postponing conferences and large meetings
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Self-quarantine

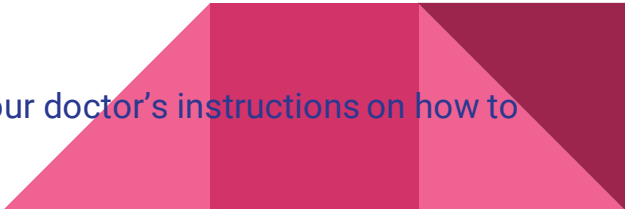
People who have been exposed to the new coronavirus and who are at risk for coming down with COVID-19 might practice **self-quarantine**. Health experts recommend that self-quarantine lasts 14 days. Two weeks provides enough time for them to know whether or not they will become ill and be contagious to other people.

You might be asked to practice self-quarantine if you have recently returned from traveling to a part of the country or the world where COVID-19 is spreading rapidly, or if you have knowingly been exposed to an infected person.

Self-quarantine involves:

- Using standard hygiene and washing hands frequently
- Not sharing things like towels and utensils
- Staying at home
- Not having visitors
- Staying at least 6 feet away from other people in your household

Once your quarantine period has ended, if you do not have symptoms, follow your doctor's instructions on how to return to your normal routine.



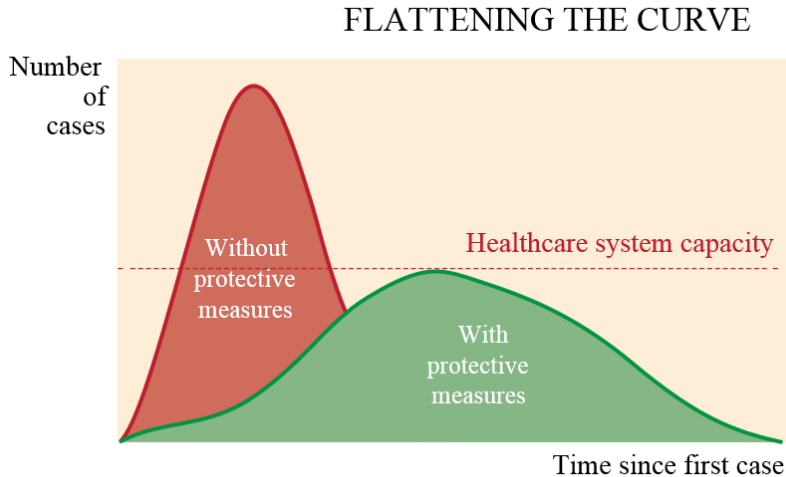
Isolation

For people who are confirmed to have COVID-19, **isolation** is appropriate. Isolation is a health care term that means keeping people who are infected with a contagious illness away from those who are not infected. Isolation can take place at home or at a hospital or care facility. Special personal protective equipment will be used to care for these patients in health care settings.



Flattening the curve

Flattening the curve refers to using protective practices to slow the rate of COVID-19 infection so hospitals have room, supplies and doctors for all of the patients who need care.



The effect on the health care worker

- **Mental Health**

- With limited treatments available, healthcare workers on the front line of this disease are experiencing dying patients at alarming rates. Healthcare workers have also become the main source of support and comfort for these patients in their final moments as policies restricting visitors have been put into place to help contain COVID-19. During these stressful times, many healthcare workers are also in self-isolation to prevent the possible spread of this disease to their families. The lack of human interaction and loneliness during this time coupled with the stressful situations they are facing can have a negative affect on their mental health; possibly leading to depression as well as post traumatic stress disorder.

- **Safety**

- Many hospitals lacked the proper amount of PPE required to protect workers as they help to fight this disease. This left many healthcare workers concerned about the amount of exposure they would be facing as the numbers of positive cases increased steadily. Communities have come together to donate items such as N95 masks, surgical masks, handmade masks, and face shields to local hospitals in our Toledo, Ohio area.

Economic effects

- Within the last three weeks there have been over 16 million Americans seeking unemployment benefits.
 - These are the highest numbers America has seen since The Great Depression
- The Coronavirus Aid, Relief, and Economic Security Act (CARES) provides an estimated \$2 trillion stimulus package to battle the harmful effects of the COVID-19 pandemic.
 - Includes payments to taxpayers as well as bailouts for hard-hit industries to mitigate Covid-19's impact.
- The economic effects of the pandemic are affecting the global economy through three trade channels:
 - Directly through supply chains as reduced economic activity is spread from intermediate goods producers to finished goods producers
 - As a result of a drop overall in economic activity, which reduces demand for goods in general, including imports
 - Through reduced trade with commodity exporters that supply producers, which, in turn, reduces their imports and negatively affects trade and economic activity of exporters.

Managing mental health concerns

- Take breaks from social media and the news
- Meditate, stretch, practice deep breathing
- Get regular exercise
- Eat well-balanced, healthy meals
- Get plenty of sleep
- Avoid the use of alcohol and drugs
- Find activities that you enjoy doing
- Connect with friends and family through phone, text, FaceTime, etc.



Vaccination research

- Creating a safe vaccine for a new illness is no easy feat. Thankfully, rapid progress is being made for a variety of reasons, including China's efforts to sequence the genetic material of Sars-CoV-2 and to share that information with research groups around the world.
- Another factor contributing to the unprecedented speed of development is the fact that coronaviruses were already on the radar of health science researchers. Both SARS and MERS were caused by coronaviruses, and even though vaccines were shelved once those outbreaks were contained, learnings can still be applied to defeating COVID-19.
- One of the most promising leads on a COVID-19 vaccine is mRNA-1273. This vaccine, developed by **Moderna Therapeutics**, is being developed with extreme urgency, skipping straight into human trials before it was even tested in animals. If all goes well with the trials currently underway in Washington State, the company hopes to have an early version of the vaccine ready by fall 2020. The earliest versions of the vaccine would be made available to at-risk groups such as healthcare workers.
- Further down the pipeline are 15 types of subunit vaccines. This method of vaccination uses a fragment of a pathogen, typically a surface protein, to trigger an immune response, teaching the body's immune system how to fight off the disease without actually introducing live pathogens

VACCINES

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Vaccine	Company	Platform	Stage	Description	Location
1. mRNA-1273	 Moderna	RNA	Phase I-First Patient Dosed	First to dose a human in the US. Vaccine consists of a synthetic strand of mRNA designed to elicit an immune response to produce antibodies against SARS-CoV-2	
2. Ad5-nCoV	 CanSino Bio	Non-Replicating Viral Vector	Phase I	Benefits from previous success in the Ebola virus (time to market ~3 years). The vaccine being developed is based on viral vectors (adenoviruses) to deliver antigens to express the SARS-CoV-2 spike protein	
3. ChAdOx1 nCoV-19	 University of Oxford	Non-Replicating Viral Vector	Phase I/II	Enrolling 500+ individuals to test its vaccine candidate, which uses a non-replicating virus to deliver RNA into cells.	
4. LV-SMENP-DC	 Shenzhen Geno-Immune Medical Institute	Lentiviral	Phase I/II	Begun early testing of its vaccine candidate. The vaccine uses a lentiviral vector to deliver Covid-19 minigenes to modify dendritic cells and activate T cells.	
5. BCG Vaccine	Research Group, Netherlands	Live Attenuated Virus (LAV)	Phase II/III	Repurposing the BCG vaccine, originally for TB, to fight SARS-CoV-2 in healthcare workers at high risk of infection. 1,000 individuals will be enrolled across 8 hospitals to receive the vaccine or placebo.	
6. BCG Vaccine	 Murdoch Children's Research Institute	Live Attenuated Virus (LAV)	Phase II/III	The BRACE trial will conduct a randomized, multi-center study of the TB vaccine in 4,000 healthcare workers across Australia.	

*Trial sponsor

Source: FDA, WHO, company websites, news. Available upon request.



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