

# An Insight into Coronavirus: A Global Pandemic of the 21<sup>st</sup> Century

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**Abstract:** On March 11, 2020, World Health Organization (WHO) declared COVID-19 as a global pandemic. As of April 2020, COVID-19 has swept across 199 countries infecting more than a half a million people and killing more than 30,000. Recent reports have shown an exponential increase in the number of cases day-by-day with highest number of reported cases in United States of America followed by Italy, Spain, China and other countries. This article attempts to enlighten a concise review on COVID-19- coronavirus, mechanism of action, modes of transmission and preventive measures. The objective of this review is to bring an awareness amongst common people.

**Keywords:** COVID-19, novel coronavirus, SARS-CoV-2, MERS-CoV, SARS-CoV, pandemic

## 1. Introduction

An infection in early 2020 spread throughout the world, across 199 countries<sup>1</sup>, like a wildfire. Affecting more than half a million people and killing an estimate of more than 30,000 people worldwide<sup>2</sup>, the pandemic of 2020 is nearing to be called the next tidal wave of death after the 1918 Spanish Flu pandemic.

A severe acute respiratory syndrome (SARS) associated Coronavirus disease 2019 (COVID-19) caused by a novel coronavirus (SARS-CoV-2) is a contagious febrile respiratory disease that spreads from person-to-person<sup>3</sup>. On 31<sup>st</sup> December 2019, health officials in Wuhan, China identified an unusually high number of pneumonia-related cases with an unknown cause<sup>1</sup>. On further investigation, these cases were linked to Huanan Seafood Market in Wuhan that was famous for the sale of bushmeat alongside other wild animals. Genome sequencing of the virus isolated from the infected patient confirmed the virus to be zoonotic<sup>4</sup> with a 70% similarity of the genetic sequence to SARS-CoV, a zoonotic virus that first emerged in Foshan, China in 2002 causing a cluster with 774 deaths<sup>4</sup>-<sup>6</sup>. Another such similar zoonotic virus is the Middle-East respiratory syndrome coronavirus (MERS-CoV) that emerged in 2012 in Saudi Arabia claiming 858 lives<sup>6</sup>.

The impact of the global outbreak of diseases associated with Coronavirus dates back since the beginning of the 21<sup>st</sup> century- SARS-CoV in 2003 and MERS-CoV in 2012<sup>4</sup>-<sup>6</sup>. SARS-CoV, SARS-CoV-2 and MERS-CoV have been predominantly predicted to stem from Bats and circulate in a range of animals. From these animals, the virus can spillover into humans. This can be due to factors ranging from mutations in the virus or an increase contact with these animals. SARS-CoV is suspected to be transmitted from Civet Cats and MERS-CoV is suspected to be transmitted from Camels<sup>1</sup>. The origin of SARS-CoV-2 is suggested to be from Pangolin but still remains under investigation. To date, no vaccines or drugs have yet been approved with proven efficacy against the prevention of coronavirus spillovers in human.

## 2. What is SARS-CoV2?

Coronaviruses are a large group of viruses. Like all other Coronaviruses that affect the respiratory system, SARS-CoV2 is a single stranded RNA virus that was first identified by experts in Wuhan, China by isolating the virus strain from three infected people who reported pneumonia<sup>4</sup>, [7]-<sup>9</sup>. The term "virus" is derived from a Latin word which means poison and outlines a minute infectious agent. The term "corona" was coined in 1968 by a group of scientists due to its crown-like shape which reflects the corona of the sun, under the microscope<sup>10</sup>, [11]. The structure of a Coronavirus (Fig 1) consists of 30 kilobase RNA as their genetic material that is surrounded by a lipid envelope. The envelope has large distinctive club-shaped crown-like projections or spikes. These spikes are made up of glycoprotein (S protein). The virus consists of membrane proteins (M protein) that are responsible for the shape of the virus and envelope proteins (E protein). Inside the envelope are nucleocapsid (N protein). The fifth structural protein in the virus is the Hemagglutinin Esterase protein (HE protein) that are known to cause clumping in RBCs<sup>10</sup>, [12]-<sup>14</sup>.

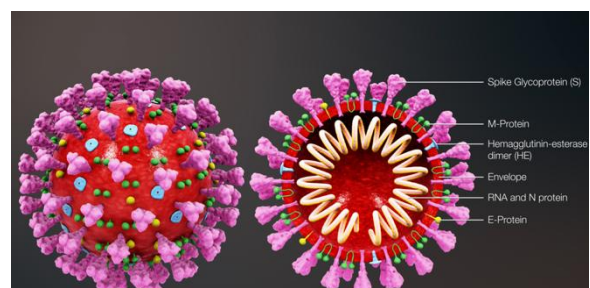


Figure 1: Structure of a Coronavirus<sup>[10]</sup>

## 3. Mechanism of Action

The virus gets attached to its host species by means of its spikes. The S protein in the spikes binds to a receptor, which acts like a doorway, in a human cell. This causes a fusion between the viral and host membranes<sup>[12]</sup>-<sup>[14]</sup>. Because COVID-19 is a respiratory disease, for most patients this means that the infection will start and end with their

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lungs<sup>[15]</sup>. As per the reports from WHO, this can happen in three distinctive phases- replication of the virus, hyperactivity in the immune system and pulmonary destruction. According to previous reports, not all patients who are affected undergo the three phases. Statistics state that only ~25% of SARS affected people undergo pulmonary destruction. This largely includes people with preexisting conditions<sup>[15]-[17]</sup>.

After being exposed to the virus, it can take as few as 2 or as many as 14 days for the symptoms to develop. This is because the virus takes times to multiply. During the process of multiplication, the virus gives rise to new viruses by replicating its genetic information and causing a cell burst in the host, releasing many virus particles and affecting other cells<sup>[16]</sup>. During the early days of infection, the virus invades the lung cells in the respiratory pathway (Fig 2). The respiratory pathway consists of small hair-like projection called cilia which are covered with a thin layer of mucus that keeps infection away from the lungs and makes sure the organs don't dry out. The cilia are responsible to move around and to keep the airways clear by removing debris and moving the mucus from bronchial tubes up into the throat. Invasion of coronavirus into the respiratory pathway specifically can damage the cilia thus making the mucus more viscous. When cells get infected, they die and shed off adding to the debris thus hindering the body's ability to keep things out of the lungs and trachea<sup>[15], [16]</sup>. The inflammation causes damage in the lungs and this damage leads to an excessive inflammation. This cycle continues until there's no healthy tissue left. The inflammation can also explain the reason behind the virus causing a dry cough along with dyspnea and phlegm production. In case of milder and moderate version of the infection, there are chances of recovery after Phase I. For infected people who have pre-existing conditions, the common symptoms can escalate to Acute Respiratory Distress Syndrome (ARDS)<sup>[16], [17]</sup>.

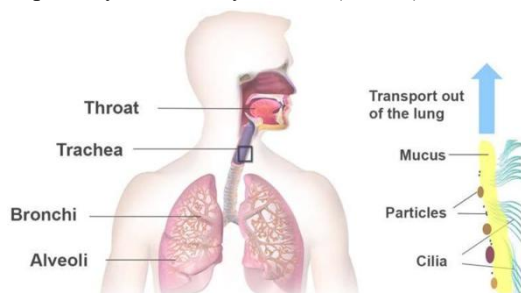


Figure 2: Simple Illustration of a human lung<sup>[16]</sup>

Coronavirus and many viruses including the Influenza virus, commonly known as the Flu virus, that goes around every year, affect humans causing death due to ARDS. ARDS is an illness that preliminary happens due to fluid and debris buildup in lungs. This part is where Phase II kicks in. Inflammation builds up a flood of non-specific immune cells in the host. These cells are originally meant to keep the lungs clean by targeting the infected area only. These immune cells usually isolate the infected cells and kill them to repair the lungs from the damage caused by the infection. But sometimes, the immune system tends to go overboard, and this is when they start killing anything that comes in their path. This is when the healthy tissues in the host fall prey to the immune cells. About 30-40% of the total ARDS

cases are fatal due to more damage caused by the immune system. In critical cases, it leads to a respiratory failure, which is phase III, thus demanding advanced life support in the patients. The treatment for ARDS includes supplemental oxygen and mechanical ventilation. Due to the failure of lungs to provide oxygen to the body, the objective for advanced life support is to provide the necessary oxygen to the blood stream. In the case where this treatment fails, the lungs by this time are too flooded to provide any oxygen into the blood stream. This is the main cause of most of the deaths due to COVID-19<sup>[14], [15]</sup>. Alternatively, when an infected person survives this phase, there is a high possibility of a permanent lung damage in the patient. SARS has a history of punching holes in the patient by giving them a honey-comb effect. The honey-comb effect has been observed in people who have been affected with SARS-CoV-2. Early studies have indicated death in critical patients within 14-19 days<sup>[15]</sup>.

#### 4. Modes of Transmission

Coronaviruses are known to cause respiratory and sometimes, gastrointestinal infections. COVID-19, the disease caused by SARS-CoV-2, has been associated with severe respiratory ailments. The most common symptoms associated with COVID-19 are fever, cough, myalgia (muscle pain), dyspnea (difficulty in breathing) and fatigue<sup>[7], [8]</sup>. A noteworthy observation is that Coronavirus infections have been more prevalent in the winter<sup>[14]</sup>.

WHO, Center for Disease Control and Prevention (CDC) and many other sources suggest the novel coronavirus to spread through person-to-person contact or coming in contact with a contaminated surface or object. This can be correlated to various modes of transmission. Person-to-person contact is claimed to be the prime mode of transmitting the virus. If an infected person sneezes or coughs without covering their mouth, there's a potential spray over of infected respiratory droplets which can very likely come in contact with a nearby person, similar to how other respiratory virus spread. The virus was also isolated from other body fluids and feces. Another mode of transmission is if a person comes in contact with any surface, object or item that has virus on it. The main point of entry is if an individual who has come in physical contact with the virus touches their nose or mouth which gives the virus a potential entry to the respiratory system. Although reports suggest that a person who has contracted the virus is at a peak of being contagious when they start showing symptoms, there's still a high probability that an infected person may still be able to pass the virus even before they show any symptoms<sup>[18]-[20]</sup>.

Recent studies and reports also warn that there might be a possibility of community transmission. Community transmission is described as the spread of the virus in an area or population through a source that is unknown<sup>[19], [21]-[23]</sup>.

#### 5. Preventive measures

Countries across the globe have now executed a variety of strategies to combat transmission of the novel coronavirus

and to alleviate the effects of COVID-19. Because there are no vaccines or therapeutics yet available to prevent further spreading of COVID-19<sup>[25]</sup>, the only ways we can adapt to are the ones mentioned below:

### 5.1. Avoid being exposed to the virus

Social distancing, the act of staying away from other people, forms a key component of avoiding exposure to the virus. Staying home as much as possible is the safest way to avoid the pandemic<sup>[24], [25]</sup>. Because coronavirus spreads mainly through respiratory droplets, limiting exposure to other people is a safe way to protect yourself. You may consider a person to be healthy but there could be a high possibility of the person being asymptomatic but still a carrier of the virus<sup>[18]-[20], [24], [25]</sup>.

### 5.2. Wearing a face mask ONLY if you are sick

WHO and CDC suggest wearing a face mask only if you are sick<sup>[25]-[26]</sup>. This may include common cold, coughing, sneezing. This is very important to avoid transmitting the infection to other people around you or contaminating surfaces and objects that may come in contact with other people. If you are healthy, wearing a face mask is only essential if you are taking care of a person who has been suspected to be affected with COVID-19. Unnecessary use of facemasks may cause a shortage of supply to the people who are really in need. This includes health care providers caring for the infected and people who are actually infected<sup>[24]-[26]</sup>.

### 5.3. Cleaning and Disinfecting

In spite of taking major precautionary measures, it is still impossible to control what your hands can touch. Washing hands is suggested to be more effective than anything else to control the infection<sup>[25]-[28]</sup>. The use of soap has been used for cleaning purposes and is usually thought as a gentle substance. But this can prove very dangerous for micro-organisms.

The structure of a molecule of soap has two distinct ends- a hydrophilic end, which loves water and a hydrophobic end, which hates water and prefers binding to fats or oil<sup>[27]</sup>. The envelop of coronavirus is made up of lipid, a fat-like substance<sup>[12], [14], [27], [28]</sup>. The use of soap and water together creates soap molecules called micelles. The hydrophobic tails in micelles bind to the lipid envelop layer in the virus and disrupts the virus apart, trapping virus particles including the spikes<sup>[27], [28]</sup>. As per CDC and WHO reports, washing hands for 20 seconds is the most effective.

Apart from soap, use of alcohol-based disinfectants that contain 70% ethanol act in a similar manner. Using 100% ethanol is found to be less effective than using a mixture of ethanol and water. This is because ethanol helps in denaturing the protein, but protein denaturation takes place more rapidly in presence of water. Hence, disinfectants that contain 70-80% ethanol should be preferred<sup>[25], [27], [29]</sup>. Use of EPA- registered household disinfectants like dilute bleach (5 tablespoon per gallon) or as per manufacturer's

instruction is also known to be effective against COVID-19<sup>[25]</sup>.

### 5.4. Food related considerations

The transmission of coronavirus through food is still an exploratory point. As per WHO, CDC and FDA reports, there is still no evidence of the virus being spread through any kind of food or food packaging<sup>[30]</sup>. Reports from previous outbreaks from coronavirus suggest that there is a negligible probability for the transmission to occur through any food. However, there are concerns regarding the ability of these viruses to endure on raw foods coming from animal origin<sup>[31]</sup>.

Previous studies and reports on SARS and MERS, that have assessed the viability and survivability of coronavirus, have suggested that the virus is very stable at freezing temperatures. The virus has a survivability of up to 24 months at a temperature of -20 °C and can remain viable at 4 °C for up to 72 hours. The persistence of the virus combined with different parameters such as light, humidity and temperature may vary.

In order to avoid any food-borne transmission, proper hygiene and food safety guidelines should be followed. Any consumption of raw meat/animals, raw milk or undercooked food should be avoided. These viruses are known to be destroyed at a temperature of 70 °C, which is the temperature used to cook food usually<sup>[30], [31]</sup>.

### 5.5. Stay informed and do not panic

There has been a plethora of information on coronavirus that is easily available. The most important thing at this point is to stay informed and know what is best for yourself and your family. Following CDC, WHO and local health department is most logical because they have the most up-to-date information<sup>31</sup>.

## 6. Risk factors

Since the first report of SARS-CoV-2 in Wuhan, China, there have been many on-going studies to ascertain the risk factors associated with COVID-19. In this article, the authors try to shed light on some of the risk factors with the information gathered from a few of these studies. However, the authors also wish to indicate since there has been an increase on the daily reported cases for COVID-19, this data is only partly accurate based on the articles reviewed until April 1, 2020.

### 6.1. Age

According to a new study delineated in Los Angeles Times<sup>[32]</sup> based on the severity of COVID-19, the rate of mortality amongst infected people varies greatly depending on age- 0.06% for age in 20s versus 8.6% for age in 70s and 13.4% for those in 80s. The statistics for this group are based on ~70,000 people whose cases were confirmed between January 1, 2020 and February 11, 2020<sup>[32], [33]</sup>. Based on currently available information, it is suggested that people in the older age group are predominantly susceptible

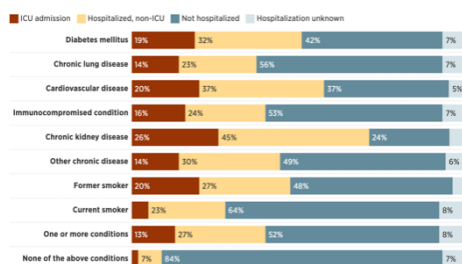
to developing ARDS, unfortunately leading to death, owing to their poor immune response<sup>[25], [34]</sup>.

## 6.2. Gender

Just like older age group is a major risk factor for COVID-19, some studies mention how the disease is taking a higher toll on males<sup>[35], [36]</sup>. As of April 1, 2020, Italy remains to be the country that has reported highest number of deaths, followed by Spain<sup>[3]</sup>. While the probability of infection between male and female still remains under investigation, studies based of Italy, China and some other countries suggest that fatality rate amongst males is higher than females. This observation can be correlated to genetic, behavioral or biological significance. According to scientific experts, females have a more robust and heightened immune system<sup>[35], [36]</sup>. Genetic make-up and endocrinesystem are another prime factors of consideration.

## 6.3. Underlying or pre-existing conditions

Although age and gender have been loosely associated with risk factors for COVID-19, a major risk factor to be considered is any person with a pre-existing condition irrespective of their age or gender<sup>[25]</sup>(Fig 3).



**Figure 3:** Coronavirus patients with Underlying Medical Conditions at a greater risk<sup>[41]</sup>

According to CDC, people with chronic lung disease, severe heart conditions, chronic kidney or lung disease and people with diabetes fall under the umbrella term<sup>[25], [38]</sup>. Fig 3 is a cumulative statistic based on ~7,000 infected patient cases that were statistically analyzed in a report. The report doesn't include statistics from people who died due to these underlying conditions<sup>[41]</sup>.

Infections have always imposed threat on Diabetic patients. Both Type I and Type II diabetes can increase risk of morbidity thus increasing the risk of contracting the virus<sup>[25], [39]</sup>. This has been statistically observed in reports from China<sup>[41]</sup>. Some diabetes patients have damage to their circulatory system, which makes these diabetics experience delayed healing. When a body is prone to inflammation due to uncontrolled blood sugar, the immune system is slowed down<sup>[39]</sup>.

Lung disease could include illness associated with asthma, bronchitis, cystic fibrosis, chronic obstructive pulmonary disease (COPD) and many others. Cardiovascular disease can include congenital heart defects and blockages in arteries and blood vessels that could lead to a stroke or heart attacks. A recent article describes the potential impact of coronaviruses on Cardiovascular system<sup>[39], 41]</sup>.

Apart from this, people who are immunocompromised, having impaired immune system, are also under a risk. This may include people who have undergone an organ transplant or cancer therapy. People who smoke or have an history of prolonged use of corticosteroids or any other medications that weaken immune system are also at a higher risk<sup>[25], [38], [41]</sup>.

## References

- [1] Coronavirus disease (COVID-19) Pandemic, World Health Organization, 2020. Retrieved on March 29, 2020 <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- [2] COVID-19 Coronavirus Pandemic, Worldometer, 2020. Retrieved on March 29, 2020 <https://www.worldometers.info/coronavirus/>
- [3] Coronavirus Disease 2019 (COVID-19), Centers for Disease Control and Prevention, 2020. Retrieved on March 26, 2020 <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/summary.html>
- [4] Hui, David S.; I Azhar, Esam; Madani, Tariq A.; Ntoumi, Francine et al, The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China, *International Journal of Infectious Diseases*. Elsevier BV. **91**: 264–266, 2020
- [5] Hui, David S et al, Severe Acute Respiratory Syndrome: Historical, Epidemiologic, and Clinical Features, *Infectious Disease Clinics of North America*, **33**:4: 869–889, 2019
- [6] Walls, A C et al, Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein, *Cell*, 2020
- [7] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 29 January 2020
- [8] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 7 Feb 2020.
- [9] Epidemiological group of emergency response mechanism of new coronavirus pneumonia in Chinese Center for Disease Control and Prevention. Epidemiological characteristics of new coronavirus pneumonia [J / OL]. *Chinese Journal of Epidemiology*, 2020,41.
- [10] A Ranjan, Coronavirus Symptoms and prevention explained through Medical Animation, *Scientific Animations*, February 2020 <https://www.scientificanimations.com/coronavirus-symptoms-and-prevention-explained-through-medical-animation/>
- [11] Coronavirus: A Glossary of Terms to Help You Understand the Unfolding Crisis, *TIME, Health: COVID-19*, Retrieved on March 30, 2020 <https://time.com/5798684/coronavirus-glossary-definitions/>
- [12] Fehr, A.R. and Perlman S., Coronaviruses: An Overview of Their Replication and Pathogenesis, *Methods Mol Biol*. 2015; 1282: 1–23

- [13] Holmes, K.V., SARS-Associated Coronavirus, The New England Journal of Medicine, March 2003
- [14] Geller, C., Varbanov, M., Duval, R.E., Human Coronaviruses: Insights into Environmental Resistance and Its Influence on the Development of New Antiseptic Strategies, *Viruses* 2012, 4, 3044-3068; doi:10.3390/v4113044
- [15] McKeever, Amy., Here's what coronavirus does to your body, *Coronavirus Coverage, Science, National Geographic*, February 18, 2020. Retrieved on March 30, 2020 <https://www.nationalgeographic.com/science/2020/02/here-is-what-coronavirus-does-to-the-body/>
- [16] Vogel, V., Reducing the risk of infection, *Medical Express, Diseases, Conditions, Syndromes*, March 13, 2020. Retrieved on March 30, 2020 <https://medicalxpress.com/news/2020-03-infection.html>
- [17] Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19), February 16-20, 2020. Retrieved on March 30, 2020 <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>
- [18] Coronavirus, World Health Organization, 2020. Retrieved on March 29, 2020 [https://www.who.int/health-topics/coronavirus#tab=tab\\_3](https://www.who.int/health-topics/coronavirus#tab=tab_3)
- [19] Coronavirus Disease 2019 (COVID-19), Centers for Disease Control and Prevention, 2020. Retrieved on March 30, 2020 <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html>
- [20] Li, Q. et al, Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia, *The New England Journal of Medicine*, 2020; 382:1199-1207
- [21] Carrigan, D., More COVID-19 cases, more 'community' transmission of virus, *News Center Maine*, March 26, 2020. Retrieved on March 30, 2020 <https://www.newscentermaine.com/article/news/health/coronavirus/more-covid-19-cases-more-community-transmission-of-virus/97-b6278f15-8658-46c9-9211-1281447a4051>
- [22] Leven, S.J., Cambridge Reports First COVID-19 Death, Officials Warn of Further Community Transmission, March 29, 2020. Retrieved on March 30, 2020 <https://www.thecrimson.com/article/2020/3/30/first-cambridge-death-coronavirus/>
- [23] Feely, P., DHHS warn of community transmission as nine new cases confirmed, *New Hampshire Union Leader*, March 17, 2020. Retrieved on March 30, 2020 [https://www.unionleader.com/news/health/dhhs-warns-of-community-transmission-as-nine-new-cases-confirmed/article\\_8bbaac93-e7b5-552d-a59d-c0ace7f505ae.html](https://www.unionleader.com/news/health/dhhs-warns-of-community-transmission-as-nine-new-cases-confirmed/article_8bbaac93-e7b5-552d-a59d-c0ace7f505ae.html)
- [24] Nierenberg, A., How to Protect yourself and Prepare for the Coronavirus, *The New York Times*, March 27, 2020. Retrieved on March 31, 2020 <https://www.nytimes.com/article/prepare-for-coronavirus.html>
- [25] Coronavirus Disease 2019 (COVID-19), Centers for Disease Control and Prevention, 2020. Retrieved on March 31, 2020 <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>
- [26] Coronavirus disease (COVID-19) advice for public: When and how to use masks, *World Health Organization*, 2020. Retrieved on March 30, 2020 <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks>
- [27] Ferris, J., Why Soap Works, *The New York Times*, March 13, 2020. Retrieved on March 31, 2020 <https://www.nytimes.com/2020/03/13/health/soap-coronavirus-handwashing-germs.html>
- [28] Goodman, B., The power of hand-washing to prevent coronavirus, *WebMD Health news*, March 6, 2020. Retrieved on March 30, 2020 <https://www.webmd.com/lung/news/20200306/power-of-hand-washing-to-prevent-coronavirus>
- [29] Infection Control, Centers for Disease Control and Prevention, 2020. Retrieved on March 31, 2020 <https://www.cdc.gov/infectioncontrol/guidelines/disinfection/disinfection-methods/chemical.html>
- [30] Wadyka, S., Common Questions About Coronavirus and the Food You Eat, *Consumer Reports*, March 30, 2020. Retrieved on March 31, 2020 <https://www.consumerreports.org/food-safety/coronavirus-common-questions-about-the-food-you-eat-food-safety/>
- [31] Coronavirus diseases 2019 (COVID-19) Situation Report, *World Health Organization*, February 21, 2020. Retrieved on March 31, 2020 [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200221-sitrep-32-covid-19.pdf?sfvrsn=4802d089\\_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200221-sitrep-32-covid-19.pdf?sfvrsn=4802d089_2)
- [32] Kaplan, K., New coronavirus death rate estimates show how sharply the risk rises with age, *Los Angeles Times*, March 31, 2020. Retrieved on April 1, 2020 <https://www.latimes.com/science/story/2020-03-31/coronavirus-death-rate-estimates-show-risk-rising-sharply-with-age>
- [33] Verity, R. et al, Estimates of the severity of coronavirus disease 2019: a model-based analysis, *Lancet Infect Dis*, 2020
- [34] Wu C, Chen X, Cai Y, et al. Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med*. Published online March 13, 2020. doi:10.1001/jamainternmed.2020.0994
- [35] Guzman, J., Coronavirus appears to be more fatal in men than women, *Changing America, The Hill*, March 19, 2020. Retrieved on March 31, 2020 <https://thehill.com/changing-america/well-being/prevention-cures/488507-coronavirus-appears-to-be-more-fatal-in-men-than>
- [36] Why the new coronavirus may kill more men than women, *Advisory Board*, February 25, 2020. Retrieved on April 1, 2020 <https://www.advisory.com/daily-briefing/2020/02/25/men-coronavirus>
- [37] Young, A. Coronavirus: Why do more men die of Covid-19 than women, *France 24*, March 31, 2020. Retrieved on March 31, 2020 <https://www.france24.com/en/20200331-coronavirus-why-do-more-men-die-of-covid-19-than-women>

- [38] What 'Underlying Factors' Put People at Higher Risk for Severe Coronavirus Cases, Coronavirus, NBC New York, March 18, 2020. Retrieved on March 31, 2020 <https://www.nbcnewyork.com/news/coronavirus/what-underlying-factors-put-people-at-higher-risk-for-severe-coronavirus-cases/2332144/>
- [39] Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. JAMA Cardiol. Published online March 27, 2020. doi:10.1001/jamacardio.2020.1286
- [40] Basile, L.M., How to prepare for the Coronavirus with diabetes, Endocrine Disorders, Endocrine Web, March 31, 2020. Retrieved on April 1, 2020 <https://www.endocrineweb.com/conditions/diabetes/diabetes-covid-19>
- [41] Avril, T. and Purcell D., How much diabetes, smoking and other risk factors worsen your Coronavirus odds, The Philadelphia Inquirer, March 31, 2020. Retrieved on April 1, 2020 <https://www.inquirer.com/health/coronavirus/coronavirus-underlying-conditions-heart-lung-kidney-cdc-20200331.html>