Facts about COVID-19

What we know at the moment

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Mark Nichter PhD, MPH[1], Collin Catalfamo, MPH[2]

[1] School of Anthropology, The University of Arizona
[2] Mel and Enid Zuckerman College of Public Health, The University of Arizona

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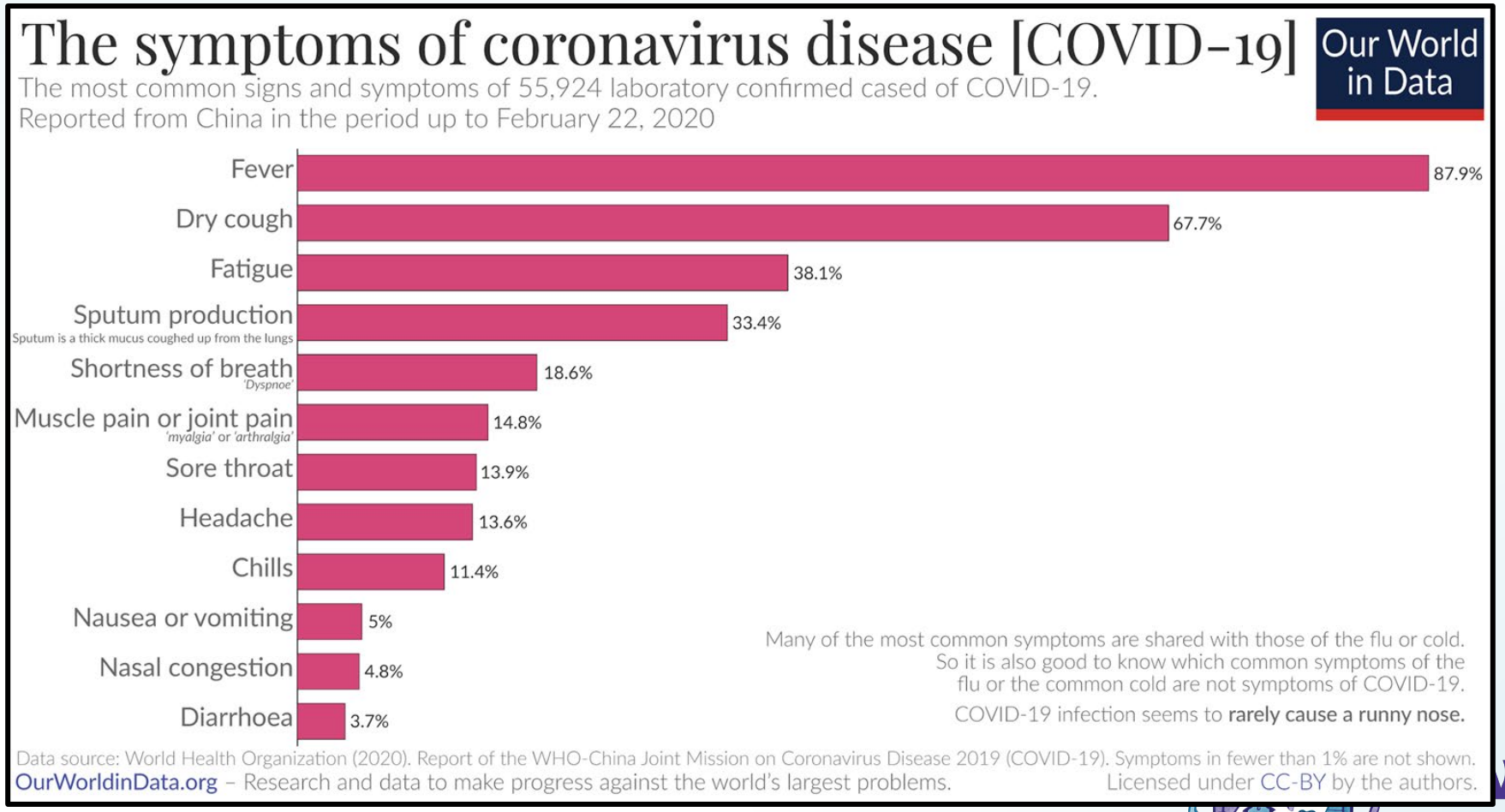
COVID-19

- Coronaviruses cause diseases in mammals and birds. Some cross species to humans causing zoonotic illness.
- In humans they cause respiratory disease. About a quarter of common colds are caused by Coronaviruses. More serious coronavirus diseases include SARS and MERS.
- Why are novel coronaviruses so dangerous?
- Our bodies form antibodies to foreign invaders, such as bacteria or viruses.
    - If we have antibodies from a previous exposure, then we can rapidly ramp up the production of those antibodies if we are infected by that same virus at a later date.
- COVID-19 is a severe respiratory illness caused by the virus named SARS-CoV-2.* It is a novel virus, which means that no one in the world has antibodies to it because no one has ever been infected by it before.

Symptoms vary and mimic other illnesses until severe



MEDICAL NEWS TODAY

COVID-19 vs. Flu vs. Cold

	COVID-19	Flu	Cold
Incubation period	1–14 days	1–4 days	1–3 days
Symptom onset	Gradual	Abrupt	Gradual
Fever	Common	Common	Rare
Cough	Common	Common	Mild to moderate
Fatigue	Common	Common	Sometimes
Runny nose	Sometimes	Sometimes	Common
Nasal congestion	Sometimes	Sometimes	Common
Diarrhea	Sometimes	Sometimes	Rare
Body aches	Sometimes	Common	Slight
Sore throat	Sometimes	Sometimes	Common
Headache	Sometimes	Common	Rare
Loss of appetite	Sometimes	Common	Sometimes
Shortness of breath	Common	Sometimes	Mild
Respiratory issues	Common	Sometimes	Sometimes

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https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html

Symptoms of Coronavirus (COVID-19)

Know the symptoms of COVID-19, which can include the following:

Symptoms can range from mild to severe illness, and appear 2–14 days after you are exposed to the virus that causes COVID-19.

Seek medical care immediately if someone has Emergency Warning Signs of COVID-19

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion
- Inability to wake or stay awake
- Pale, gray, or blue-colored skin, lips, or nail beds, depending on skin tone

This list is not all possible symptoms. Please call your healthcare provider for any other symptoms that are severe or concerning to you.

Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

cdc.gov/coronavirus

CS-317432-A

What are the symptoms and how does it affect my body?

- This video provides an overview of mild, moderate, and severe symptoms, and what is happening to the body during this time:
  - https://www.businessinsider.com/novel-coronavirus-COVID-19-symptoms-day-by-day-2020-3 (covers severity and day to day progression)
- More information on the difference between severity of illness and effects of infection on the body can be found in these videos and at these websites:
  - Mild-moderate-severe symptoms:
    - https://n.pr/3dV9OFH
  - Here's what coronavirus does to the body:
    - nationalgeographic.com/science/2020/02/here-is-what-coronavirus-does-to-the-body
    - https://bit.ly/3gfamYg(good knowledge and recommended practice summary)****

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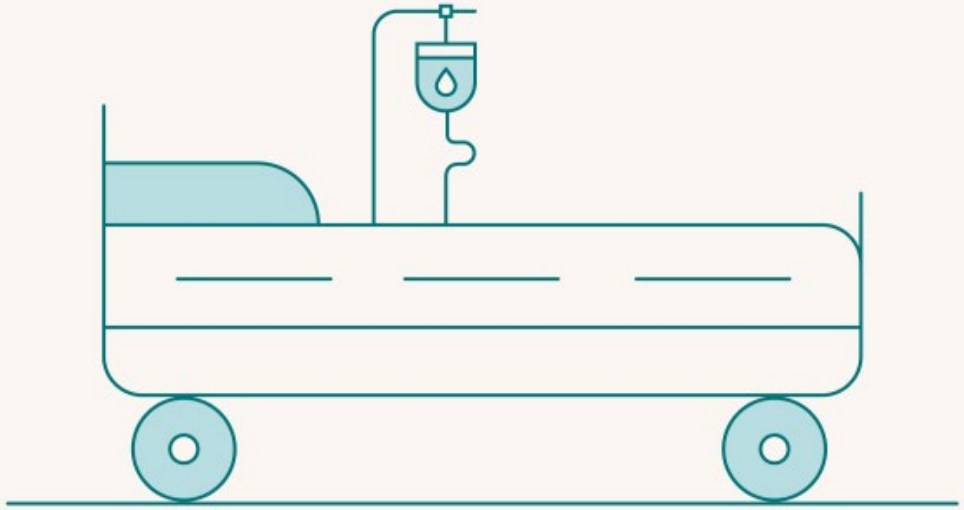
Mild vs. Severe and Critical COVID-19 Cases



81%

of cases are mild (no or mild pneumonia).

14%

of cases are severe (shortness of breath, increased breathing frequency, and/or other symptoms).

5%

of cases are critical (respiratory failure, multiple organ dysfunction or failure, and/or other symptoms).

Source: *China CDC, based on 44,415 confirmed cases in China as of February 11, 2020*

COVID-19 severity: One factor is an uncontrolled inflammatory response

- The immune system works both for us and can in certain instances can work against us
- COVID-19 severity is associated with a cytokine storm known as Cytokine release syndrome (CRS)
- A cytokine storm occurs when a patient's immune system overreacts to the virus and inflicts collateral damage on its own organs
    - CRS is an acute systemic inflammatory syndrome caused by excessive or uncontrolled release of proinflammatory cytokines.
    - When the immune system is fighting pathogens, cytokines signal immune cells such as T-cells and macrophages to travel to the site of infection.
    - Cytokines activate these cells, stimulating them to produce more cytokines.
    - Normally, this feedback loop is kept in check by the body.
    - However, in some instances, the reaction becomes uncontrolled, and too many immune cells are activated in one location.

COVID-19 severity: One factor is an uncontrolled inflammatory response

- Cytokine dysregulation occurs in some virulent influenza infections such as H5N1 (avian flu) and COVID-19
- One reason the elderly are more vulnerable for severe COVID-19 is due to “inflammaging” which refers to cell mediated immune senescence. During ageing low-grade inflammation develops which contributes to the pathogenesis of diseases experienced. It is a possible contributor to a CRS.

Signs of illness may precede actual symptoms: Pay attention to your senses

- Sudden loss of smell and taste have been documented in approximately 30% of confirmed cases before notable symptoms occurred, and in 50-90% of cases when accompanied by other symptoms (depending on study)
- Smell is being piloted as an early indicator of COVID-19 when combined with other symptoms such as fever*
- Self-isolate as soon as you notice loss of smell whether you have other symptoms or not
- Younger patients in particular may demonstrate only a loss of smell or taste, without demonstrating the more commonly recognized coronavirus symptoms of high fever and persistent coughs

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Screening Symptoms for COVID-19

- Businesses have begun screening patrons for symptoms
- Most utilize contactless thermometers to ensure individuals entering the area do not have a fever
  - A small survey from the CDC showed that 96% of positive COVID-19 patients had some sort of cough, fever, or shortness of breath
- Fevers don't tell the whole story
  - Other illnesses may result in a fever
  - Not all COVID-19 patients may exhibit a fever
- Loss of smell may serve as a supplement for temperature checks
  - Even though loss of smell is not the most common symptom, COVID-19 positive individuals were at 6.74 times the odds of reporting loss of smell/taste

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How long does the illness last?

- The period from disease onset to recovery ranges according to severity of disease
  - For mild cases, recovery is approximately 2 weeks
  - For severe/critical cases, recovery is approximately 3-6 weeks; however, some other studies have observed illnesses lasting longer than 6 weeks

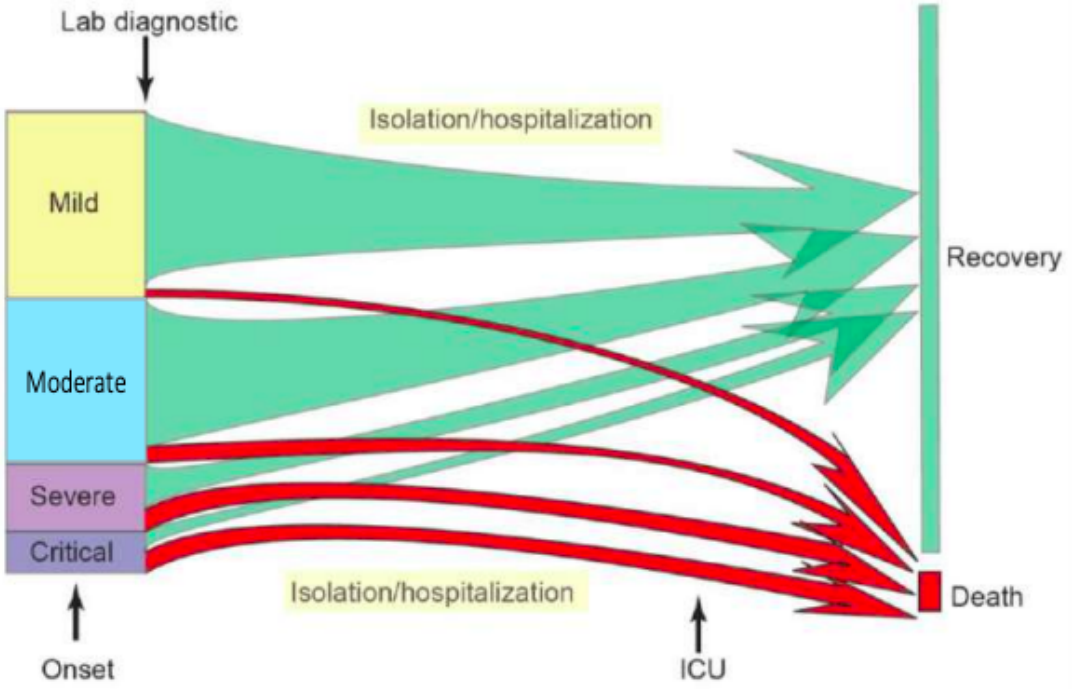

Figure 5. Pattern of disease progression for COVID-19 in China

Note: the relative size of the boxes for disease severity and outcome reflect the proportion of cases reported as of 20 February 2020. The size of the arrows indicates the proportion of cases who recovered or died. Disease definitions are described above. Moderate cases have a mild form of pneumonia.

COVID-19 affects multiple organ systems other than the lungs

- We now know that COVID-19 affects multiple organ systems such as the cardiovascular system, the renal system, the nervous system, and the gastrointestinal system. Some of these symptoms are common among mild illnesses and others appear in patients with severe illness. Some of these effects include:
  - Cardiovascular system: irregular heartbeat, acute cardiac injury, cardiomyopathy (heart muscle damage), and blood clotting
  - Nervous system: headaches, dizziness, fogginess, trouble concentrating, delirium, loss of smell/taste, Guillain-Barre Syndrome, viral encephalitis
  - Renal system: acute kidney injury
  - Gastrointestinal system: abdominal pain, diarrhea, nausea and vomiting, acute liver injury (hepatocellular injury), and altered glucose/lipid metabolism

Long-term effects of COVID-19

- Many recovering COVID-19 patients have reported lingering symptoms long after their initial infection known as PASC (post acute sequalae of COVID-19).
  - In an Italian study, 87% of hospitalized patients still had one or more symptoms two months later; a British study found similar trends.
  - Even those with mild or moderate COVID-19 and were not hospitalized have been found to go one to experience long-term symptoms, with 33% of outpatients still reporting symptoms 6 months later.
  - Another study among a group of COVID-19 with mixed severity of illness observed at least 13.3% of participants still experiencing symptoms 30 days or longer after their initial illness.

Long-term effects of COVID-19

- Many “long-haulers” (those experiencing these long-term symptoms) start feeling better in their fourth or fifth month, but recovery is tentative, variable, and not guaranteed
- Individuals have reported symptoms ranging from insomnia, chronic fatigue and brain fag to muscle aches, shortness of breath and skin rashes.
    - Long-term effects were observed following the severe acute respiratory syndrome (SARS) pandemic in 2003. In one Hong Kong study, 27% of SARS survivors were found to meet chronic fatigue syndrome criteria several years after acquiring SARS

Long haulers – A few observations

- It is estimated that at least 10 % percent of those infected have long-term symptoms
- Longer haulers included a mix of relativity young, healthy people as well as older individuals.
- Long haulers include those who only suffered mild disease
  - Long haulers are not just patients who spend significant time in an ICU. Such patients —whether battling an infection or recovering from a stroke- often require further treatment after they are released, because they suffer from post–intensive care syndrome, often characterized by weakness and cognitive problems.
  - Many long haulers who only suffered from mild symptoms when ill with COVID , had no known preconditions
- The vast majority of long-haulers test negative for COVID-19, despite lingering symptoms.
- There have been reports of long haulers' symptoms greatly being reduced after vaccination

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Younger adults and stroke

- There have been reports of adults experiencing strokes while sick with COVID-19 coming out of the Netherlands and US.
  - Strokes are usually more common in the elderly; however, these patients with COVID-19 are presenting with symptoms of strokes as young as 30 years of age.
- This is due to blood clot formation while sick with the infection. Researchers are not positive as to what is causing these blood clots to form and travel to the brain.
  - Young adults who experience symptoms of COVID-19 should monitor themselves for neurological symptoms.
  - If you start to experience weakness/numbness on one half of your body/face, trouble walking, trouble speaking, or difficulty concentration, contact EMS immediately.

How does COVID-19 spread

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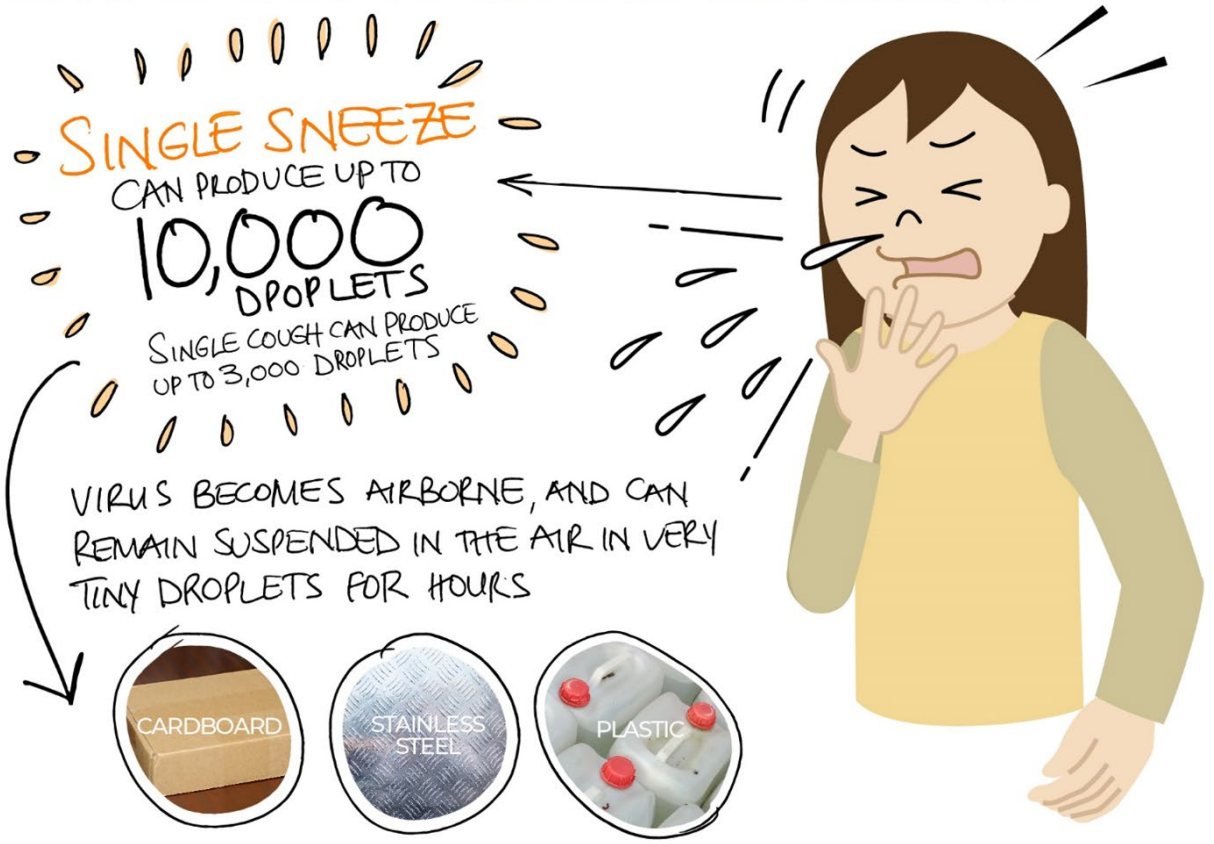
The primary route is airborne transmission

- The primary route through which the virus infects you is through your nose or mouth via inhaling viral droplets from an infected person
  - This can be from talking, coughing, or sneezing.
- This virus has cell receptors for lung cells but has also been observed to infect other tissues like the organs of your gastrointestinal system and nervous system, among others.
  - The eye is also a potential site for virus transmission.
- You are at risk if you are close to a person (less than 6ft) who has the infection whether they are showing symptoms or not

COVID-19 PANDEMIC

How is the virus transmitted?



If the droplets land on surfaces, the virus may survive for as long as 24 hours on cardboard and up to 3 days on stainless steel and plastic, according to a recent study.

Source: AL JAZEERA | Last updated: 11:30 GMT, March 24, 2020

@AJLabs ALJAZEERA

The virus can remain in the air in aerosol form for some time and travel beyond 6 feet in closed spaces

- Research suggests that the virus may remain in the air for minutes up to three hours, depending on environmental conditions *
- The virus can also travel beyond 6 feet in places with poor ventilation
    - For example: A Chinese, 48-seat bus study found that the virus infected people in a closed environment with air-conditioning up to 15 feet, suggesting that in some environments the transmission distance of this coronavirus exceeds the commonly recognized safe distance of 6 feet.

Spread from smaller microdroplets as aerosols is also a source of concern

- Because aerosols are smaller, they contain much less virus than droplets do.
  - But because they are lighter, they can linger in the air for hours, especially in the absence of fresh air.
- In a crowded indoor space, a single infected person can release enough aerosolized virus over time to infect many people
- The person does not have to be coughing or sneezing, but just talking loudly
  - Some super-transmitters of viruses do so without doing any of the above for reasons that are not yet clear

Transmission thru contact with infected surfaces

- The primary mode of COVID-19 transmission is through inhalation of respiratory droplets.
  - This is why masks are so important!
- Surfaces can also be a mode of transmission, but this is far less likely.
  - The chance of transmission through inanimate surfaces is relatively small, and only in instances where an infected person coughs or sneezes on the surface, and someone else touches that surface soon after the cough or sneeze (within 1-2 hours)
    - In this case, you acquire the infection by touching your nose, mouth, or eyes after touching an object/surface that has been contaminated with viral droplets
- Studies have been conducted that show how long the virus stays alive on surfaces
  - Presence of the virus does not mean you will catch COVID-19 from touching these surfaces. Just because the virus can survive on a surface, does not mean it can be transmitted that way
  - It is always best to wash one's hands to be sure transmission does not take place this way.

How long the new coronavirus can live on surfaces

SURFACE	LIFESPAN OF COVID-19 VIRUS
Paper and tissue paper**	3 hours
Copper*	4 hours
Cardboard*	24 hours
Wood**	2 days
Cloth**	2 days
Stainless steel*	2–3 days
Polypropylene plastic*	3 days
Glass**	4 days
Paper money**	4 days
Outside of surgical mask**	7 days

*At 69.8 to 73.4°F (21 to 23 °C) and 40% relative humidity **At 71°F and 65% relative humidity

Source: New England Journal of Medicine*; The Lancet Microbe**

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Transmission patterns

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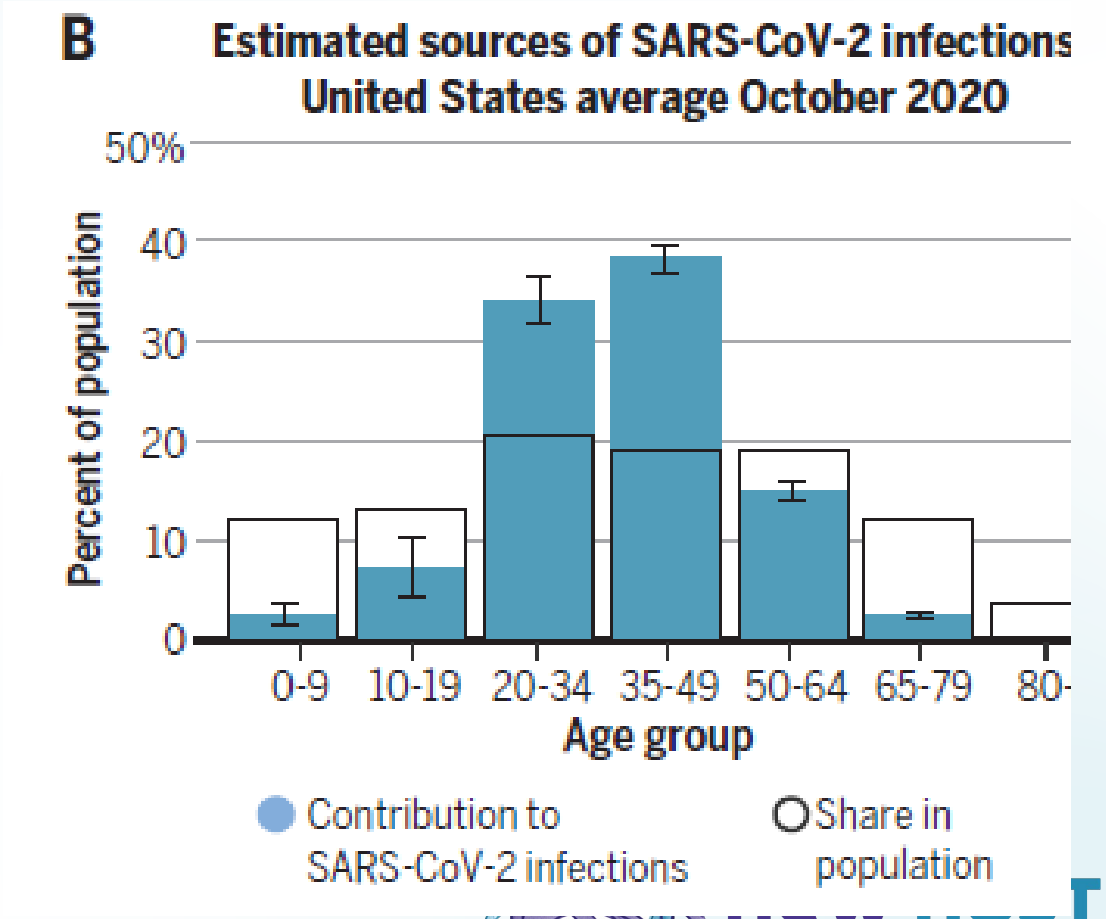
Transmission patterns

- The World Health Organization (WHO) uses the following categories to describe transmission patterns
- Sporadic cases refers to a small number of cases (one or more) that are either imported or detected locally
- Clusters of cases refers to cases that are clustered in time, geographic location and or by common exposures;
- Community transmission refers to larger outbreaks of local transmission that can be defined through different approaches, including big numbers of cases not linkable to transmission chains and multiple unrelated clusters in several areas.

Which age group is most responsible for COVID 19 transmission

- SARS-CoV-2 transmission is sustained primarily from age groups 20 to 49
- They have the most contacts with other adults aged 20 and above, who are more susceptible to COVID-19 than younger individuals
- Trend of increasing mobility and attending social gatherings with larger groups, often without wearing masks
- Among those getting vaccinated, returning to normal behavior right after their first shot thinking they are now immune, when they are not



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Household clusters of COVID-19 cases

- SARS-CoV-2 is more transmissible in households than related coronaviruses SARS and MERS
- Older individuals (aged ≥60 years) are the most susceptible to household transmission of SARS-CoV-2.
- Family clusters became the main mode of human-human transmission in China
  - The estimated secondary attack rate among household contacts was 12·4% (95% CI 9·8–15·4) when household contacts were defined on the basis of close relatives and 17·1% (13·3–21·8) when household contacts were defined on the basis of residential address.
  - Compared with the oldest age group (≥60 years), the risk of household infection was lower in the youngest age group (<20 years; odds ratio [OR] 0·23 [95% CI 0·11–0·46]) and among adults aged 20–59 years (OR 0·64 [95% CI 0·43–0·97]).
  - Notably, greater infectivity occurred during the incubation period than during the symptomatic period, although differences were not statistically significant (OR 0·61 [95% CI 0·27–1·38]).

Household contacts and disease transmission

- A study of 59,073 contacts of 5,706 coronavirus disease (COVID-19) index patients reported in South Korea (January 20 – March 27, 2020) found that *
  - Of 10,592 household contacts, 11.8% had COVID-19.
  - Of 48,481 non-household contacts, 1.9% had COVID-19.
- A US based study conducted early on in the pandemic likewise found infection rates for symptomatic household contacts in the United States to be 10.5% (95% CI 2.9%–31.4%), significantly higher than for non-household contacts**
  - A Mass General Brigham study reported a similar 10.1% infection rate
- Rates were higher for contacts of children than adults.
  - The study took place in the middle of mitigation and therefore might characterize transmission dynamics during school closure and child isolation
- Given high rates of preventive behavior the study illustrated that use of personal protective measures and social distancing reduces the likelihood of transmission.

Household clusters: how often is a child the first case

- In the China study, adult household contacts were suspected or confirmed to have COVID-19 infection before the study child in 79% (31/39) of cases.
  - The study child developed symptoms before any other household contact in only 8% (3/39) of households.
- In a similar international study of COVID-19 transmission in 31 household clusters from China, Singapore, South Korea, Japan, and Iran, the investigators found that a child was the first (index) case in only three of the 31 (9.7%) household clusters investigated.
  - However, because children are less likely to be symptomatic, they may also be less likely to be identified as the “index” case during a contact tracing investigation and therefore their role in transmission could be underrecognized
  - This study was also conducted during school closures, so it is likely that the children were less likely to have been exposed first due to remaining physically distant at their homes.

The scenario may be changing in the US with children being the first case in the household to get ill

- Now, as more coronavirus variants have begun to dominate, and seniors gain protection from vaccines, children who are returning to school and engaging in sports may play a larger role in household transmission .
- Infectious disease experts are watching to see if COVID-19 starts to spread in a pattern similar to influenza, with children becoming infected first and bringing the infection home to their parents.
- In Michigan, for example, cases have been rising in February - April 2021 with the biggest rise among children aged 10-19
  - Incidence in this age group has more than doubled.
  - Cases among younger children — infants through 9-year-olds — have also increased by > 230%

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Those who live in multigenerational households are at an increased risk

- Multigenerational households, especially among those poor with limited house space, are at high risk to infection especially if one or more members must work outside the home in a service-related job where they are routinely exposed to the public , and/or a child is attending school
- This is especially true for households where someone is > 65 years of age and /or has a precondition like hypertension, diabetes, COPD, or an immune disorder.
- In the USA this includes >25% of minority group households, groups that have the highest rates of COVID-19 prevalence
- At present data on COVID-19 cases within such households is limited and scant resources have been allocated to isolate those testing positive from family members if they do not have the wherewithal to do so

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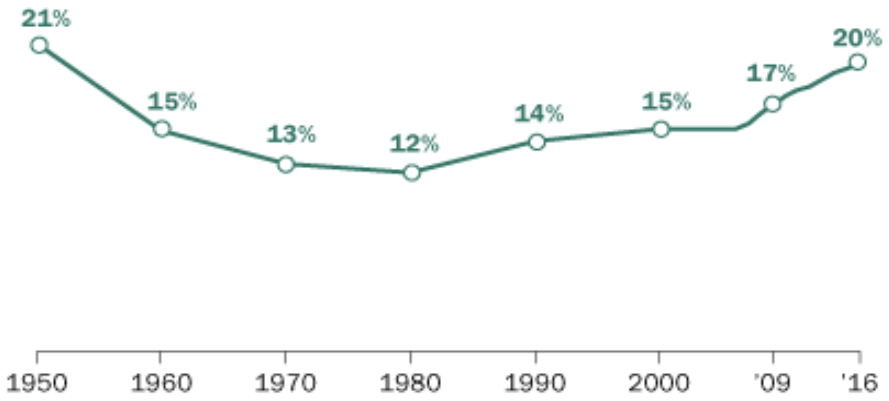
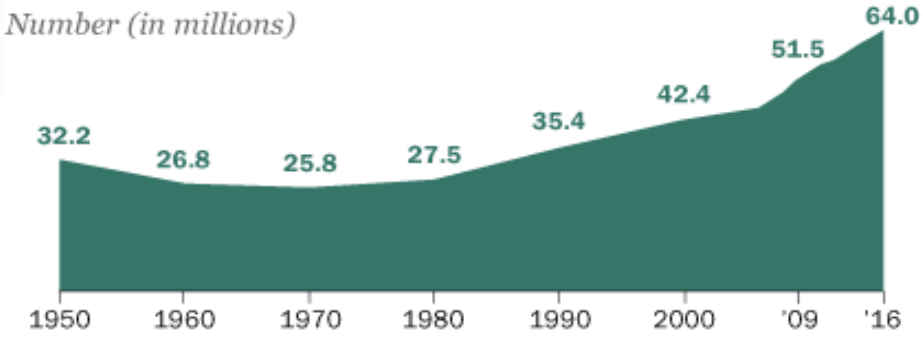
One-in-five Americans live in a multigenerational household

% of population in multigenerational households



Number (in millions)



Note: Multigenerational households include at least two adult generations or grandparents and grandchildren younger than 25.
Source: Pew Research Center analysis of 1950-2000 decennial censuses and 2006-2016 American Community Survey (IPUMS).

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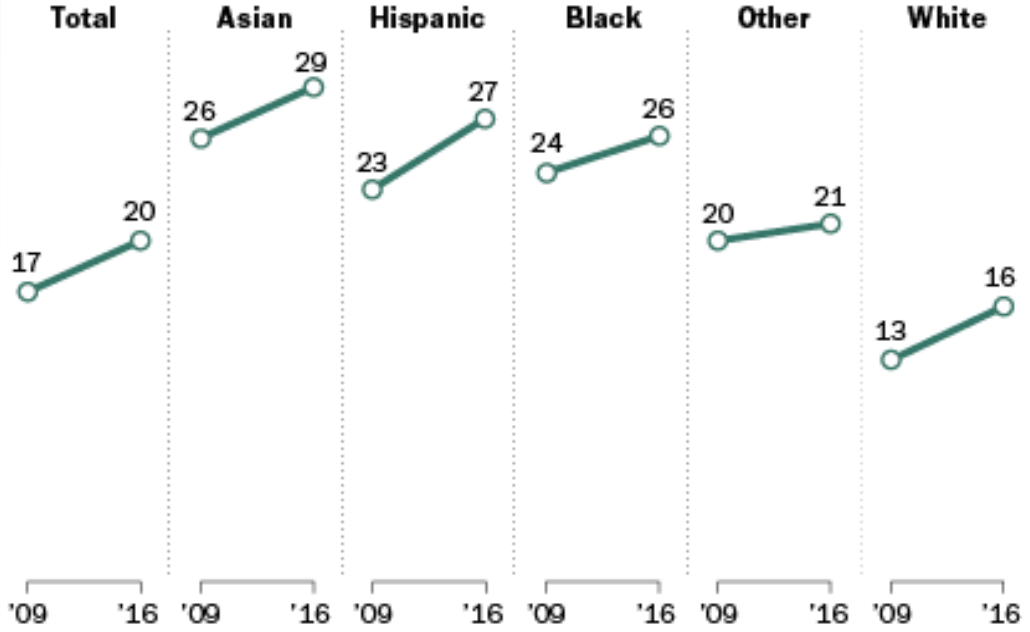
Whites less likely than other racial and ethnic groups to live in multigenerational households

% of population in multigenerational households



Note: Multigenerational households include at least two adult generations or grandparents and grandchildren younger than 25. Hispanics are of any race. Asians include Pacific Islanders. Whites, blacks and Asians are single-race only and include only non-Hispanics. "Other" includes non-Hispanics in remaining single-race groups or multiracial groups.
Source: Pew Research Center analysis of 2009 and 2016 American Community Surveys (IPUMS).

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Bottom line

- **Household transmission is common.**
- If you work in an environment of risk, you need to adopt precautions, so you do not bring the virus home to family members, especially those with preexisting conditions or older than 65 years of age.
- This is especially true for health care workers.
- More resources need to be allocated to enabling those with limited means to isolate if they test positive or are ill to protect other household members
  - Multigenerational households are an immediate priority
  - Testing and tracing without isolation does little to break the chain of transmission

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Incubation and disease transmission

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Asymptomatic & mildly symptomatic in relation to disease transmission

- The CDC currently estimates that 40% of infections are asymptomatic
- Several studies have shown that people without symptoms are causing substantial amounts of infection.
  - More than 43,000 people in China had tested positive without immediate symptoms by the end of February and were quarantined
  - Of the 135 people in the Tianjin cluster, between 62% and 77% contracted the infection from someone who was pre-symptomatic.
  - Between 48% and 66% of the 91 people in the Singapore cluster contracted the infection from someone who was pre-symptomatic.
  - Iceland is attempting to test its entire small population and has the means to do so. It has reported that so far 50% of all cases identified are asymptomatic.
- Physical Distancing is important!
- Those who are 60+ must physically distance themselves from youth, someone you know, even your grandchild may be asymptomatic
- Engage in safe forms of social interaction with loved ones and friends such as sociality through social media, video chatting, and phone calls

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Incubation period

- 4 to 6* days appears to be the median amount of time, but the range is much larger with some studies suggesting up to 24 days***.

- Existing data suggests that about 97.5 percent of people who develop symptoms of COVID-19 infection will do so within 11.5 days of exposure.

- The researchers estimate that for every 10,000 individuals quarantined for 14 days, only about 101 would develop symptoms after being released from quarantine.**

When are you most contagious if you have a mild to moderate illness

- In COVID-19 peak shedding occurs from the upper airways early on in the infection which makes for a virus much harder to contain than another coronavirus like SARS (where peak shedding occurs deep in the lungs) *
- At peak shedding, people with COVID-19 are emitting more than 1,000 times more virus than was emitted during peak shedding of SARS infection
- Research suggests that peak shedding for COVID-19 occurs before you feel ill. This emphasizes the importance of precautionary measures and helps explains why this is much harder to contain than previous coronavirus outbreaks like SARS and MERS.

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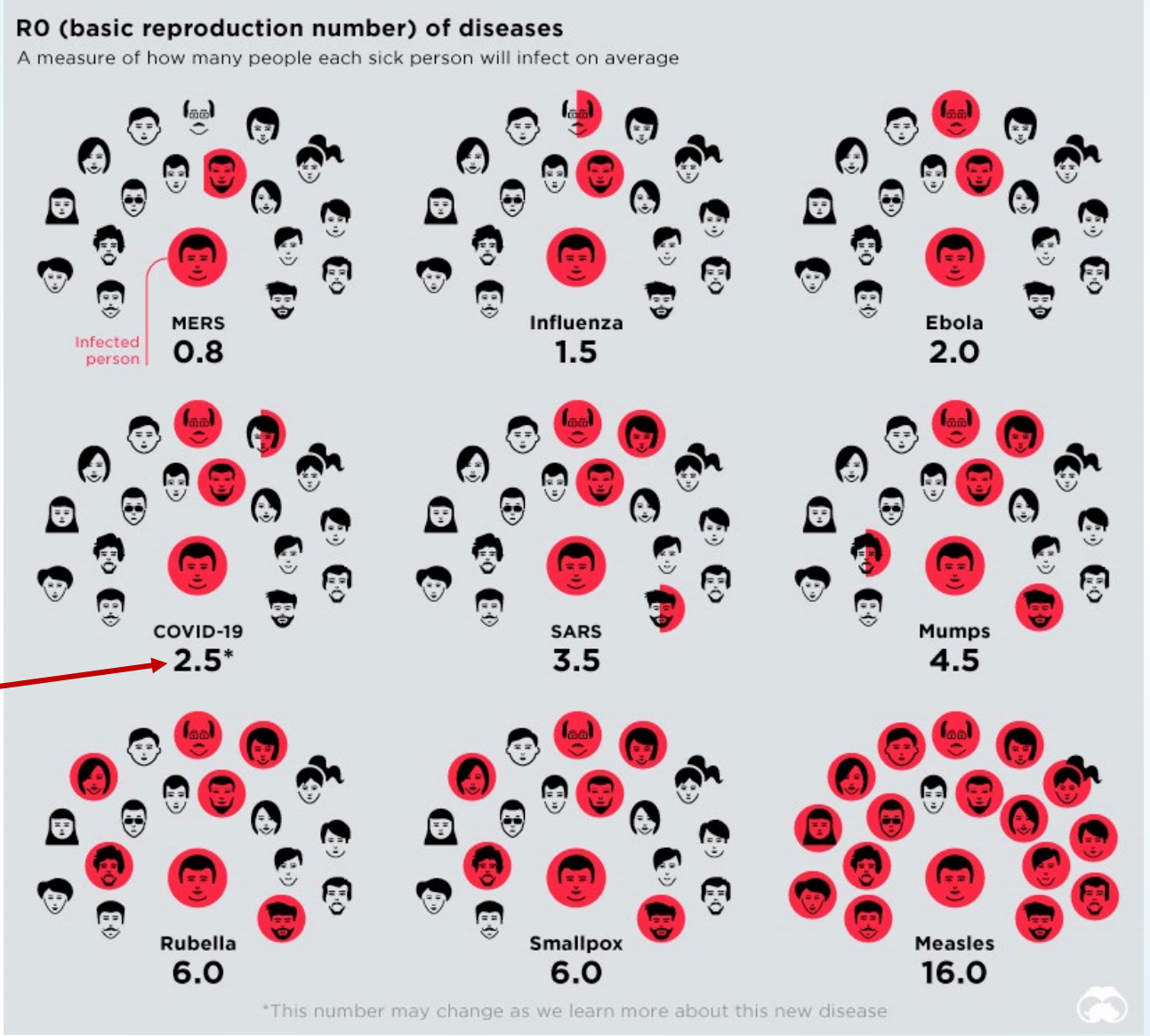
How many people will a sick person infect?

Current studies suggest that a person with COVID-19 will infect between 2-3 additional persons without the use of preventative measures, but the range of estimates is around 2-6.5.*

These estimates are likely to change as we progress in the pandemic, and will vary regionally depending on how strict restrictions are



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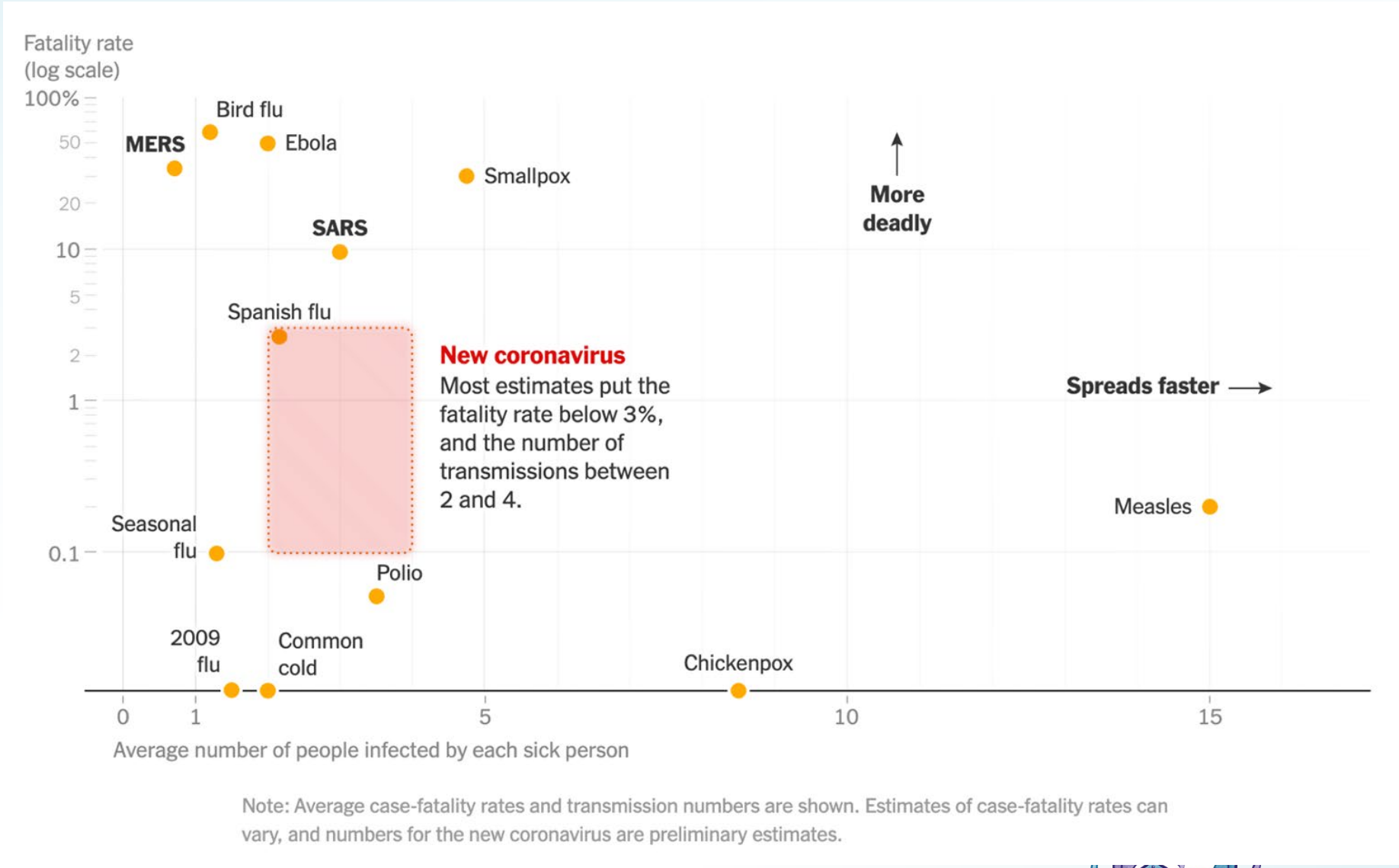

Note: Average case-fatality rates and transmission numbers are shown. Estimates of case-fatality rates can vary, and numbers for the new coronavirus are preliminary estimates.

How long do people shed the virus and how does this relate to being contagious?

- Presence of the virus does not necessarily indicate level of infectiousness. What do we know so far ?
  - Wuhan data: Median duration of viral shedding was 20.0 days (IQR 17.0–24.0) in survivors. The longest observed duration of viral shedding in survivors was 37 days
- A small but important German study found that people with mild infections can still test positive by throat swabs for days and even weeks after their illness.*
  - However, those only mildly sick are most likely not still infectious by about 10 days after they start to experience symptoms, and moderately sick by days 10-11.
  - The scientists could not grow viruses from throat swabs or sputum specimens after day 8 of illness from people who had mild infection.
- Notably, researchers have found very high levels of virus emitted from the throat of patients from the earliest point in their illness—when people are generally still going about their daily routines.

Does a high viral load or infectious dose make COVID-19 worse?

- Research has shown that those with severe COVID-19 symptoms often have much higher viral loads than those with minor symptoms.
- We know from influenza that a greater exposure to the virus often causes a more severe illness.
  - However, it is unclear as to whether a greater exposure to the virus for COVID-19 causes more severe symptoms.
  - Its also important to consider patient characteristics, as people with compromised or weakened immune systems due to extreme stress, exhaustion, or other conditions could cause a lower threshold of exposure needed to cause severe symptoms.

Does a decrease in antibodies following infection or vaccination indicate that one has lost their immunity

- As our immune system successfully fights off an infection, a drop in the level of circulating antibodies occurs — this is to be expected when one's immune system is functioning in a healthy manner.
- On a second exposure, immune memory cells (B-cells, T-cells, and "natural killer" cells) are reactivated
- Without re-exposure, protection to a pathogen will decrease through a decrease in antibody and other immune cell protection
    - This is why we have vaccination boosters.
    - A vaccine boosters works to reactivate our immune system's memory so that we retain the protection offered by the first vaccine without having to encounter the pathogen it is for.

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Does a decrease in antibodies following infection or vaccination indicate that one has lost their immunity

- An immediate decrease in antibodies shortly following vaccination does not necessarily translate into a decrease in immunity.
  - Over a longer period of time (6 months later at the earliest), a greater decrease in antibodies occurs and will likely indicate reduced protection to COVID-19
- We still do not know what the minimum level of antibody titers are necessary to prevent COVID-19.

Reinfection

After experiencing COVID-19 or after getting a vaccination

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Reinfection

- As of January 2021, COVID-19 had resulted in more than 100 million cases and over 2 million deaths worldwide. Recent studies have suggested that reinfections are rare and that immunity can last at least six months, however, the degree to which catching COVID-19 confers protection against repeat infection remains poorly understood.
    - Researchers are also investigating whether some cases that appears to be reinfection might actually be reactivation of the virus. I.e. people may almost be completely recovered and then their infection increases again

Reinfection appears to be rare with the initial wild-type COVID-19 strain

- A study in Denmark found that prior infection with COVID-19 protects most people against reinfection, with 0.65% of patients returning a positive PCR test twice during Denmark's first and second waves, compared with 3.27% of people who tested positive after initially being negative.
  - Protection against reinfection remained stable for more than six months.
  - People over the age of 65 were at greater risk of catching COVID-19 again.
    - Although prior infection with COVID-19 protects most people against reinfection, new research has found that people over 65 years of age have a greater risk, with only 47% protection against repeat infection compared to 80% protection for younger people.
  - The findings underline that measures to protect the elderly - including social distancing and vaccinations are essential even if people have already been diagnosed with COVID-19.
- It is important to remember though, the most prevalent variants that are circulating now are NOT the same as what we first encountered at the beginning of the pandemic.

Reinfection and COVID -19 variants

- The strength of the immune response engendered by prior infection with an original strain is not as strong against some of the variants, especially the ones known as P.1 and 501Y.V2.
- A resurgence of COVID-19 in Manaus, Brazil demonstrates that a variant can escape from the immune response generated by infection with prior strains.
  - Manaus experienced an extremely high attack rate during the first wave of the epidemic, such that the city was believed to have reached herd immunity by October 2020.
  - Nevertheless, a major resurgence in December resulted in a second wave that exceeded the size of the first wave.
  - Multiple variants of the virus were detected in Manaus. One of them, referred to as P.1, is six-fold less sensitive than the original strain to an immune response generated by the original strain.
  - Responsiveness to a vaccine-induced immune response is similarly reduced.
  - The big question is whether Manaus's second wave is due to immune escape or waning immunity.

“Super spreader” events

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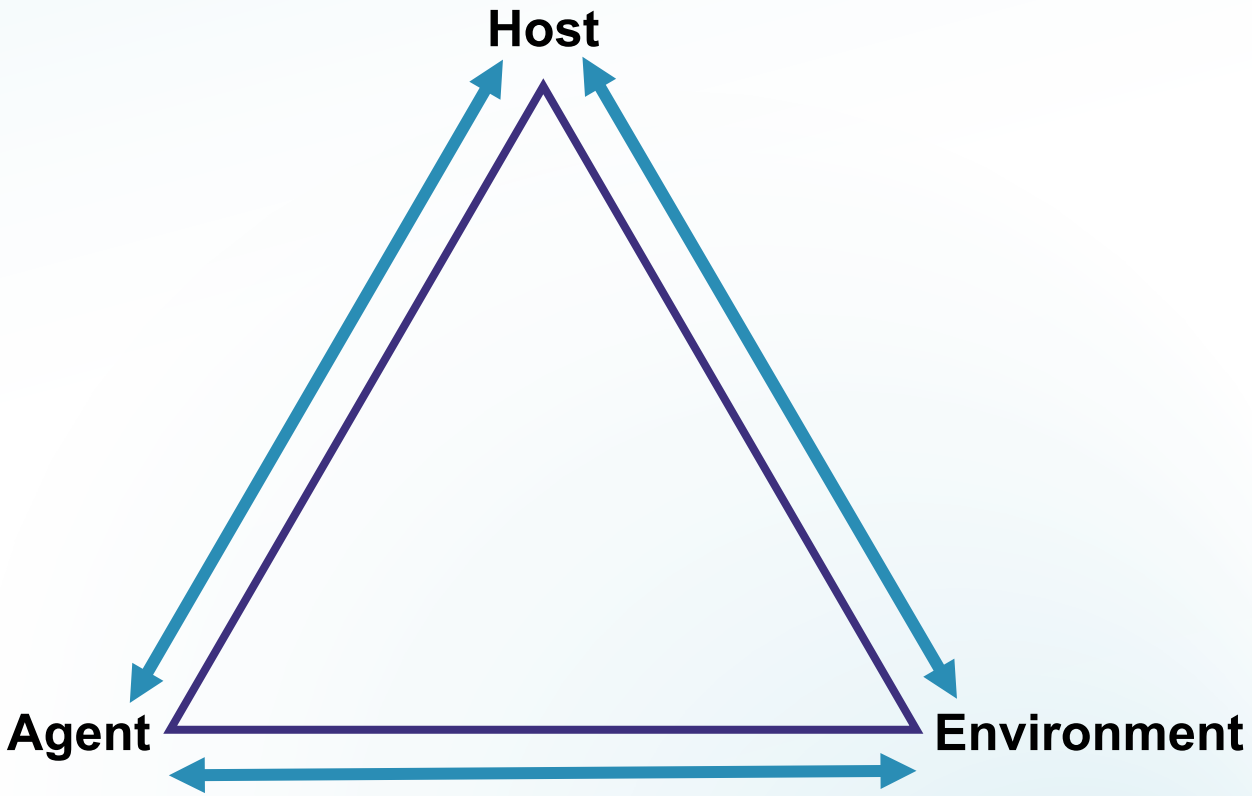
Super-spreader events: looking beyond R0

- A reproductive number R0 is the average number of people who become infected by an infectious person
  - This number while useful can be misleading because it masks the variability of spread from one person to the next. If nine out of 10 people don't pass on a virus at all, while the 10th passes it to 20 people, the average would still be two.
  - Some studies have suggested that 10% of people infected with COVID-19 may be responsible for 80% of all new infections. I.e. most people pass on the virus to very few people, while others end up spreading it to many
    - These individuals are more likely to be pre-symptomatic or asymptomatic
- The instances where these occur are called super-spreader events

Super-spreader events

- A super-spreading event depends as much on circumstance as the biology of an individual who is present (Agent, Host, Environment interaction). In particular:
- Is the individual susceptible to infection? Are the being physically distant? Are they wearing a mask? Are they performing activities that would make them breathe more or harder than usual?
- Is the environment indoors or outdoors? Is there adequate ventilation and air circulation?



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Super-spreader events

- Most super-spreader events occur in scenarios in which the risk of infection is high. For example:
  - at an indoor venue, especially a poorly ventilated one (meaning air is not being exchanged, diluted, or filtered)
  - Where there are lots of people
  - And those people are talking, chanting, singing, or doing other activities that increase the amount of air that they are breathing and how much air they expel.
- Some examples of where super-spreader events have taken place are restaurants, bars, clubs, choir practices, weddings, funerals, cruise ships, nursing homes, prisons, and meatpacking plants.
- In one database of more than 1,200 super-spreader events, only one incident was classified as outdoor transmission. All the rest were events occurring indoors

Examples of super spreader events in 2020

- February 26, 2021 – Biogen leadership conference in Boston with 175 attendees. At least 70 (40%) became ill at the conference.
- March 6-11 – Among 92 church goers in Arkansas during this time, 35 (38%) became ill and 3 died. There were an additional 26 cases linked to the church.
- March 17 – A Skagit County, Washington choir member attended choir practice with 122 members and infected up to 53 (43%) people. 3 were hospitalized, and 2 died.

Bar opening super spreader event : Illinois February 2021

- The opening event of a bar held indoors for an establishment that accommodates approximately 100 persons triggered a COVID-19 outbreak
- Overall, 46 COVID-19 cases were linked to the event, including cases in 26 patrons and three staff members who attended the opening event and 17 secondary cases

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COVID-19 Mortality

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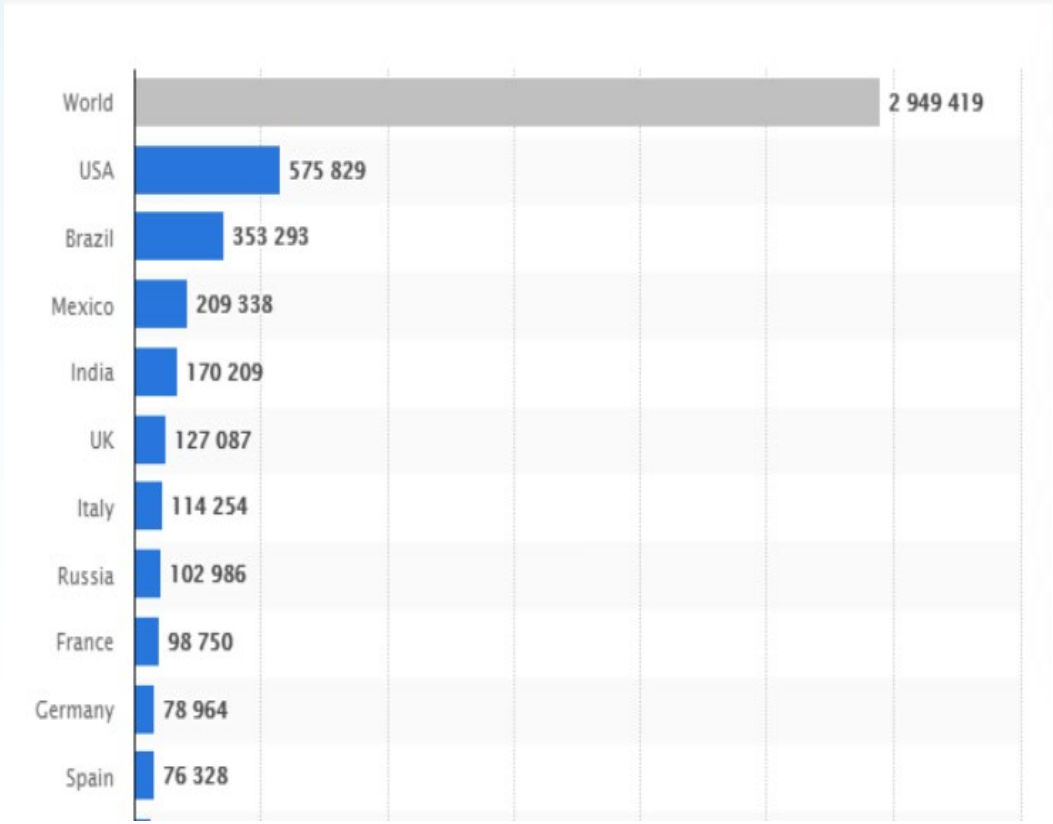
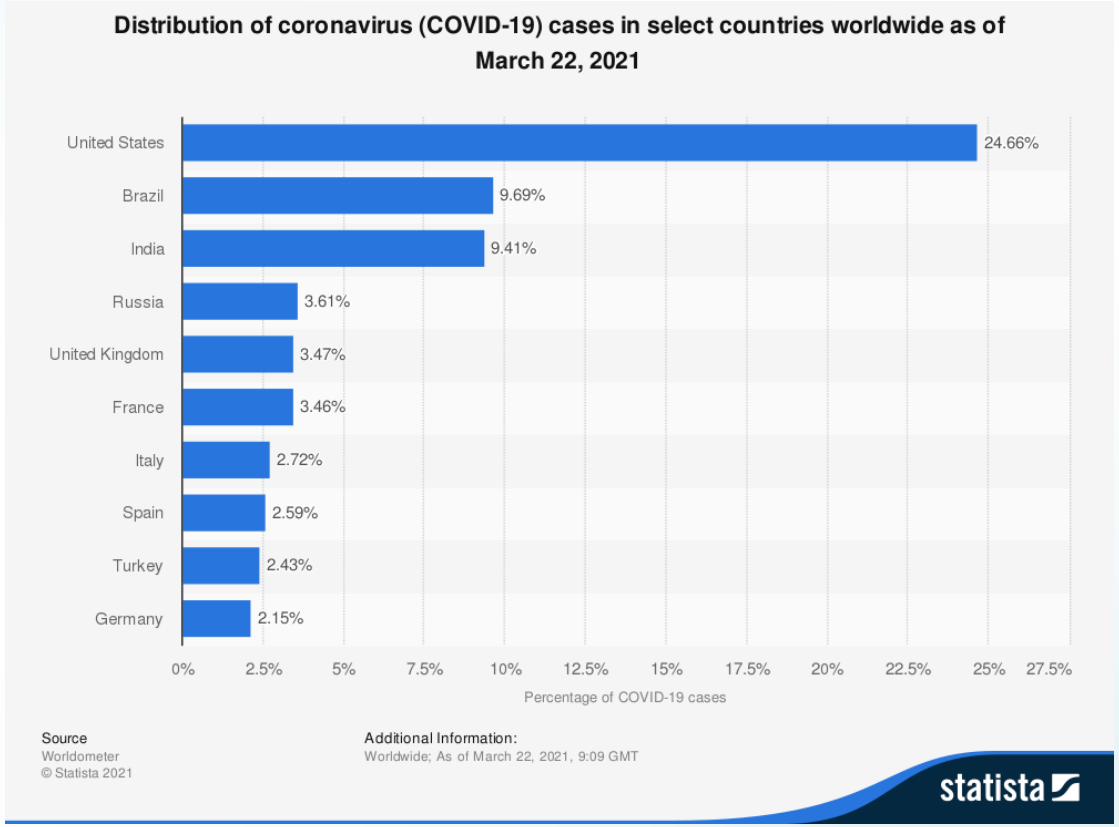
Global COVID-19 deaths : April 12, 2021





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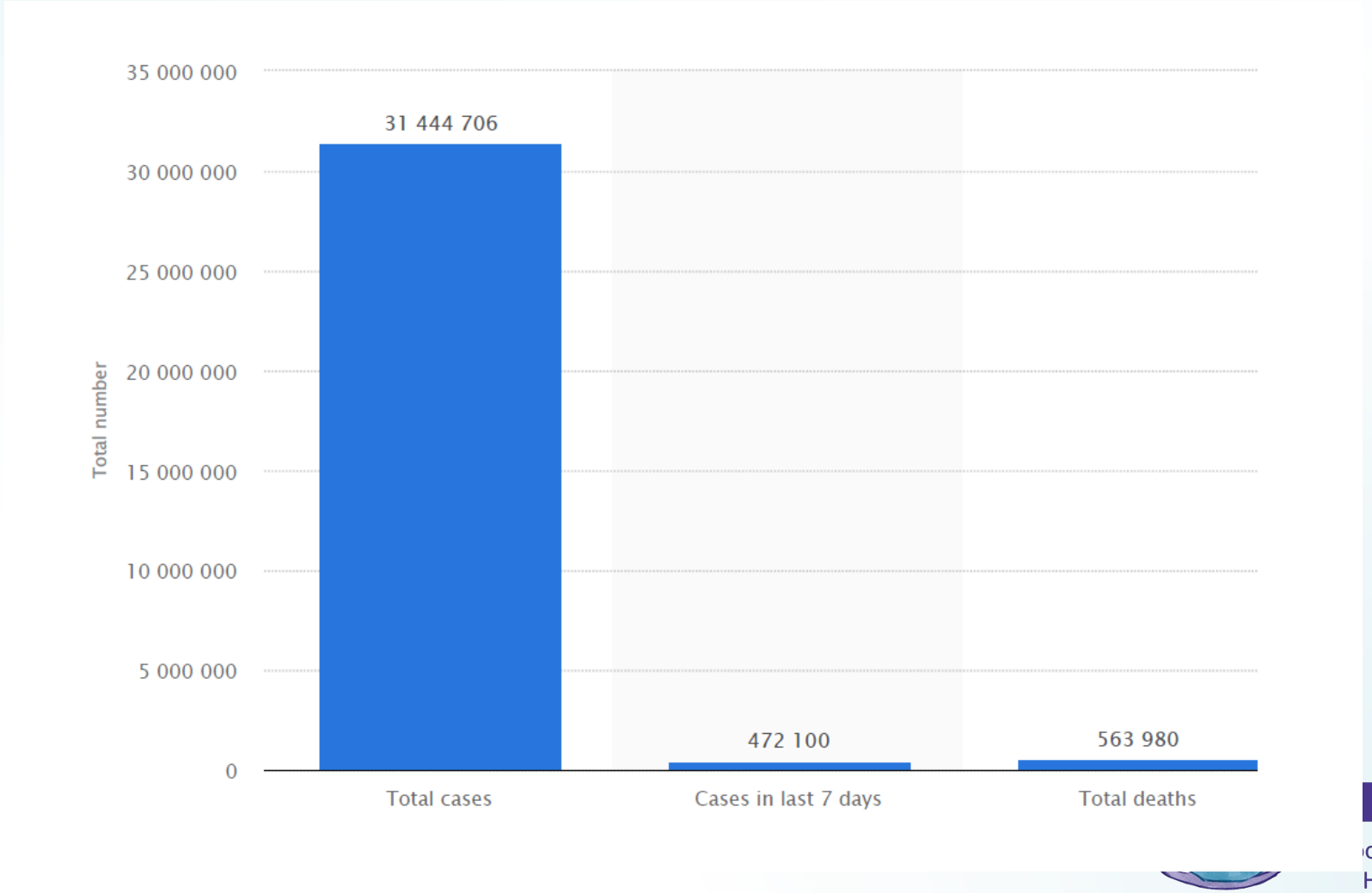
Total number of U.S. coronavirus (COVID-19) cases and deaths as of April 18, 2021



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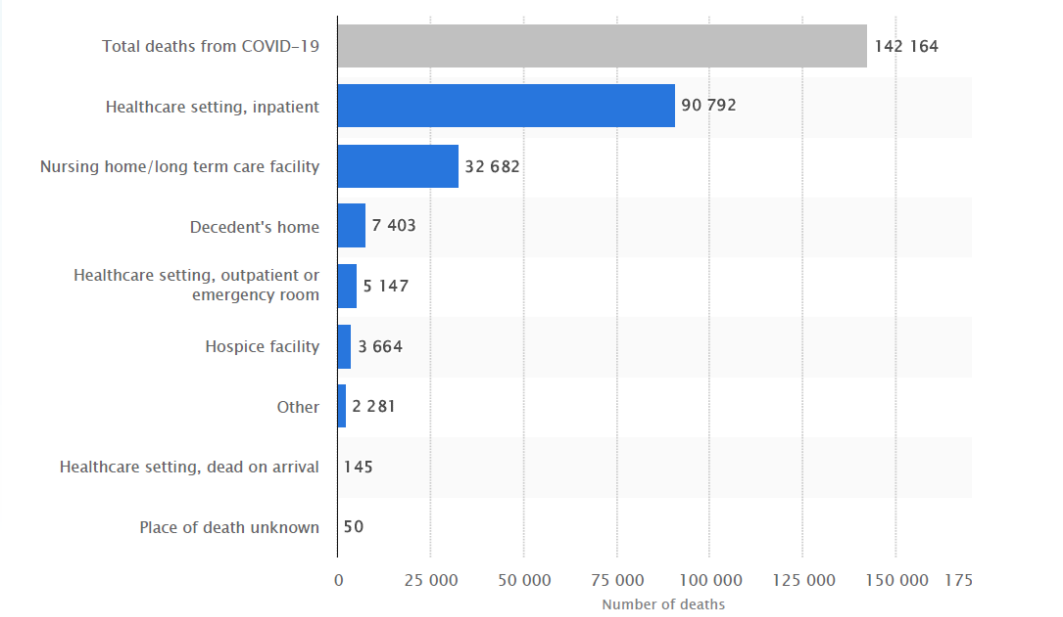
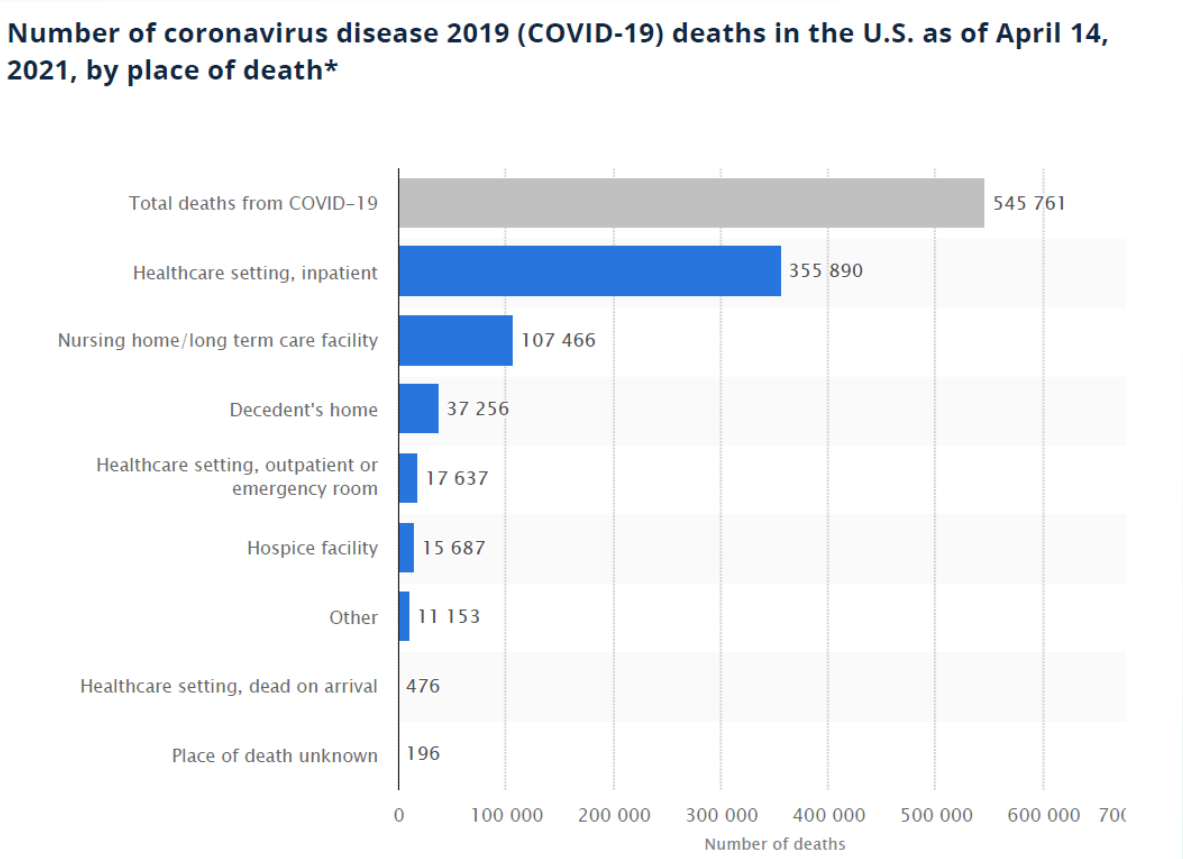
Where are COVID-19 patients dying in the USA ?



In the US, as of 08/05/2020



In the US, as of 04/14/2021

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Morbidity and Mortality by age

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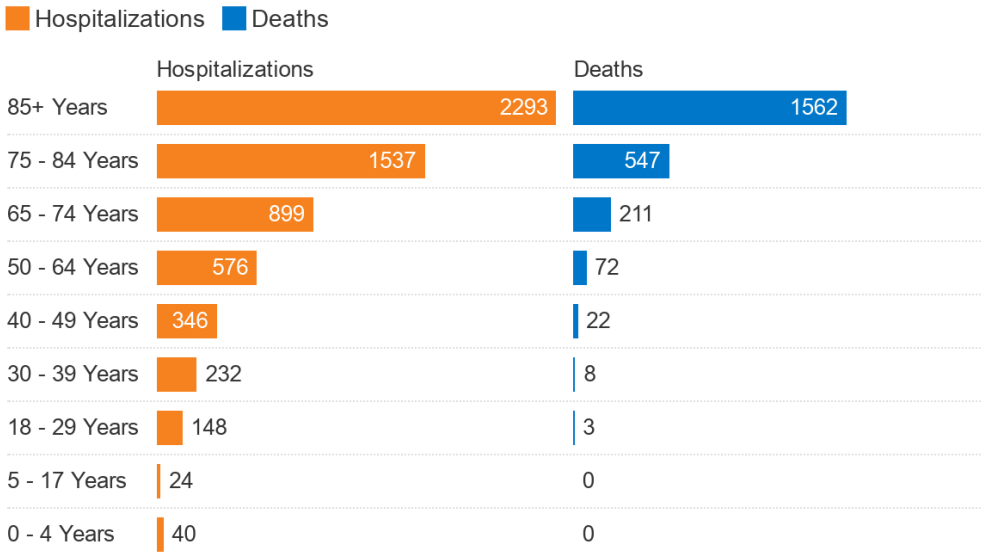
Who is affected most severely in the US?

- Those who are at greatest risk of death due to COVID-19 are:
  - Those 75+ years of age
  - Those with chronic illness like heart disease, diabetes, lung disease, or who are smokers
- Those who are younger than 30 years are the least at risk of death from COVID-1
- Children and adolescents have a low likelihood of experiencing severe illness.

Figure 1

The Rate of COVID-19 Hospitalizations and Deaths Increases with Age

Cumulative Hospitalizations and Deaths per 100,000, by Age Group



SOURCE: CDC COVID Data Tracker: retrieved 2/4/2021; CDC COVID-19 Associated Hospitalization Surveillance Network (COVID-NET) for the week ending January 23, 2021. Population estimates from 2019 US Census Bureau. Census estimates are for the non-institutional population.

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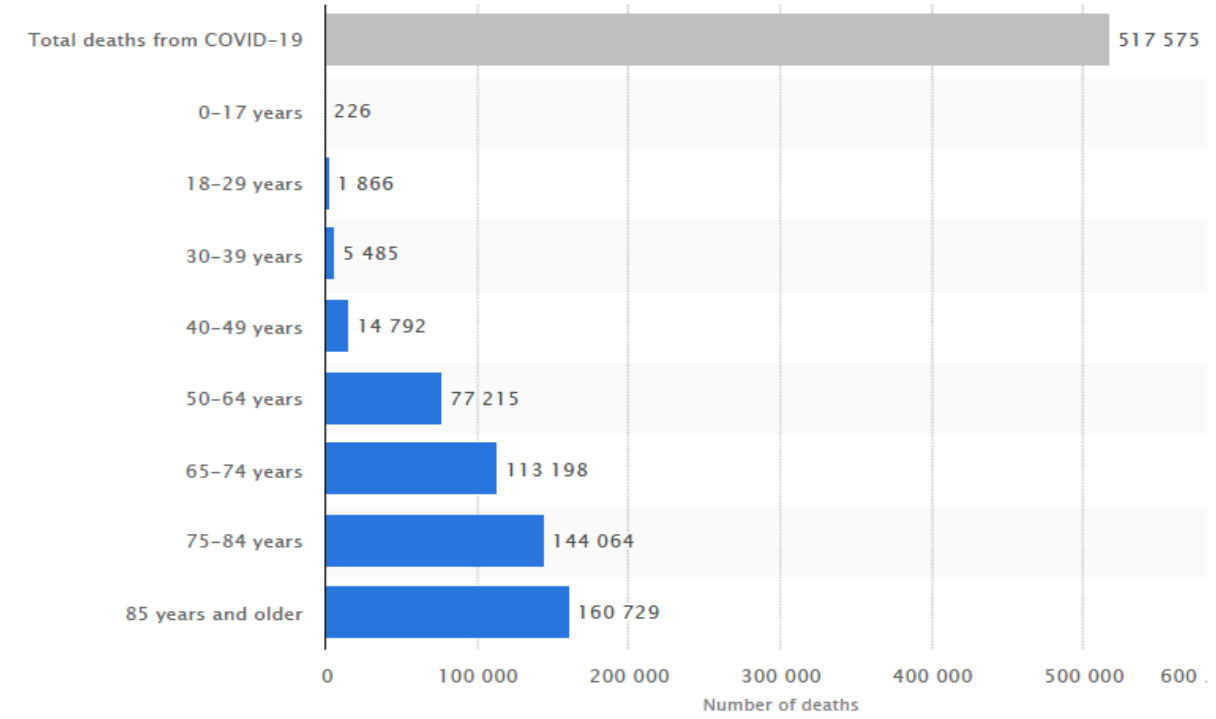
Total number of deaths by age

Number of coronavirus disease 2019 (COVID-19) deaths in the U.S. as of March 17, 2021, age*



Additional Information

Show source

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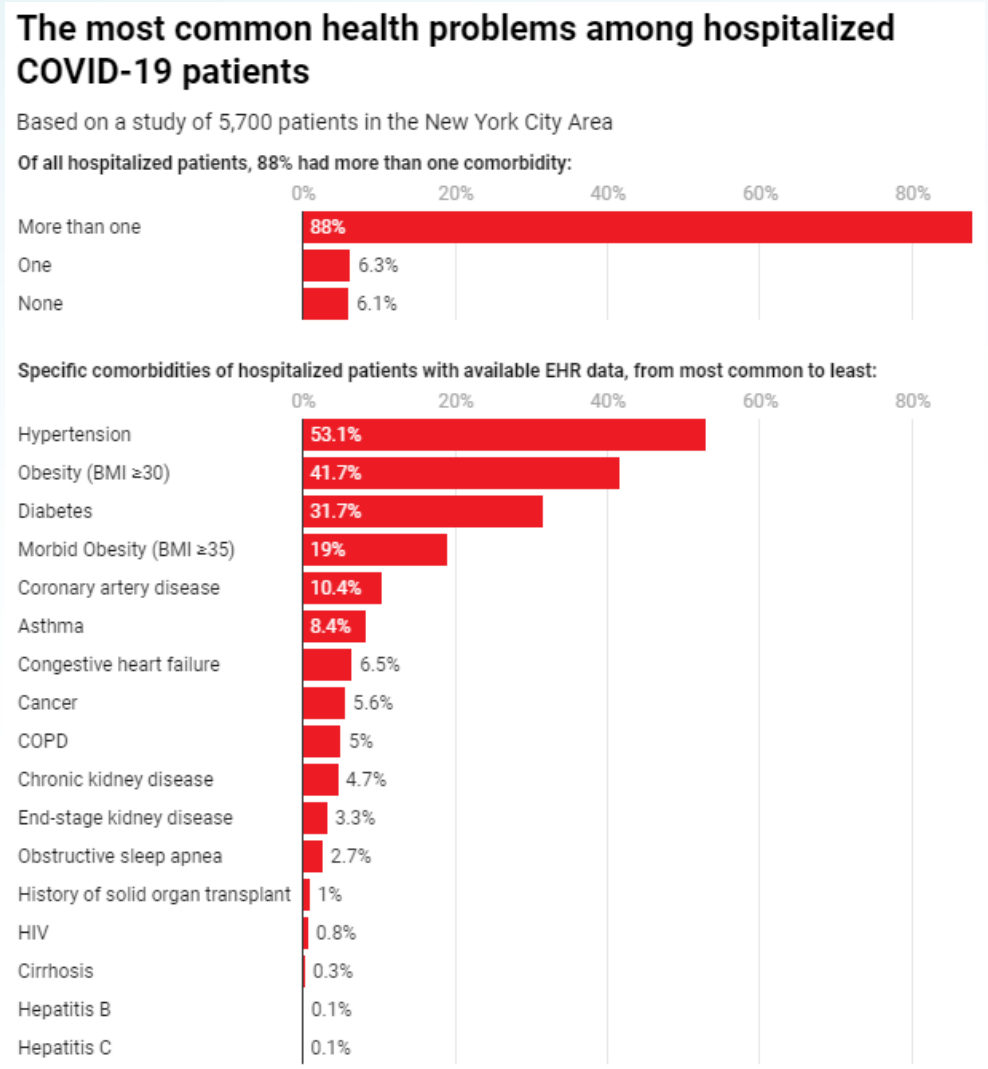
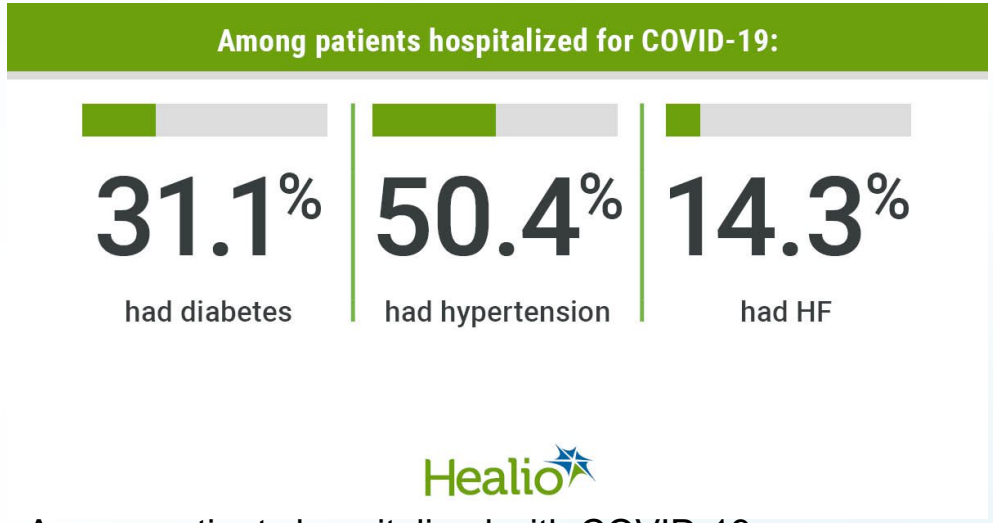
Comorbidity by hospitalized cases of COVID-19





Among patients hospitalized with COVID-19, approximately half had hypertension.

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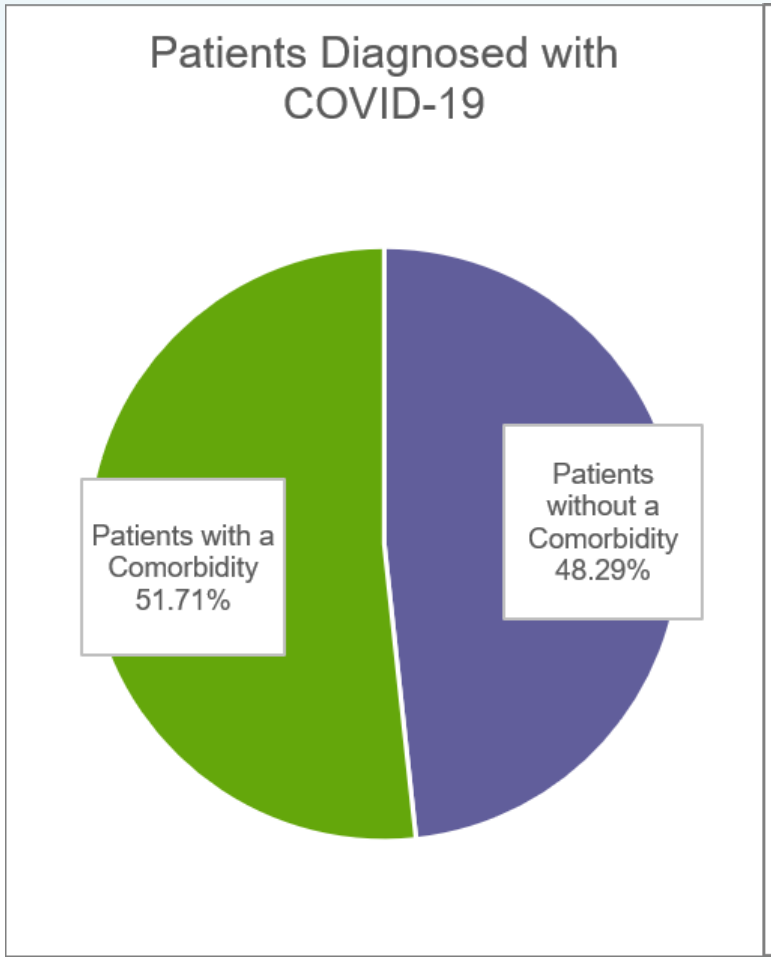

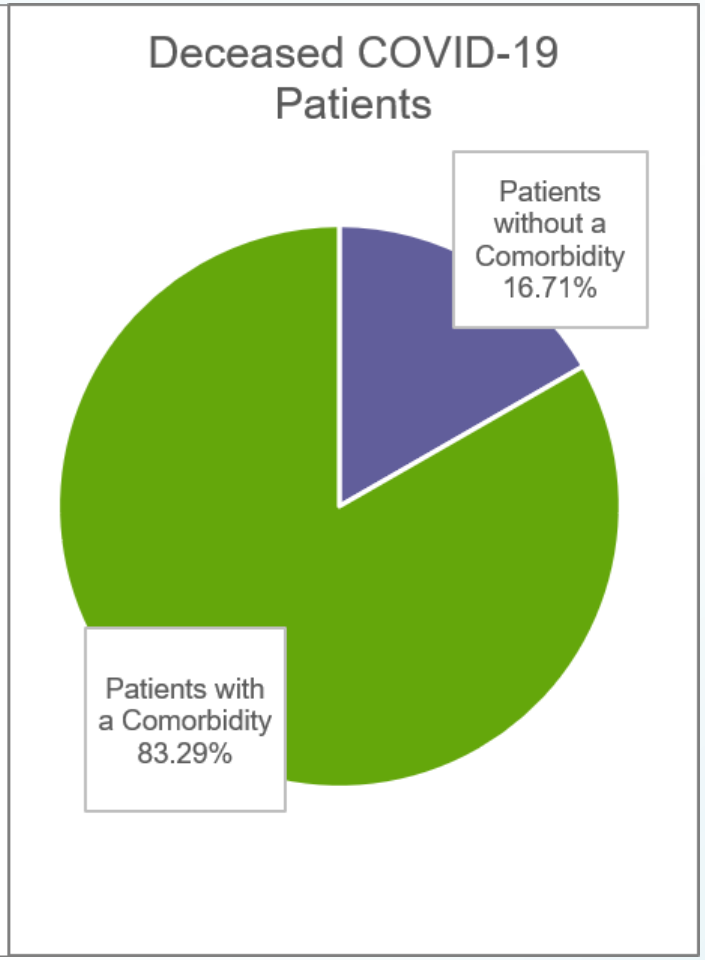

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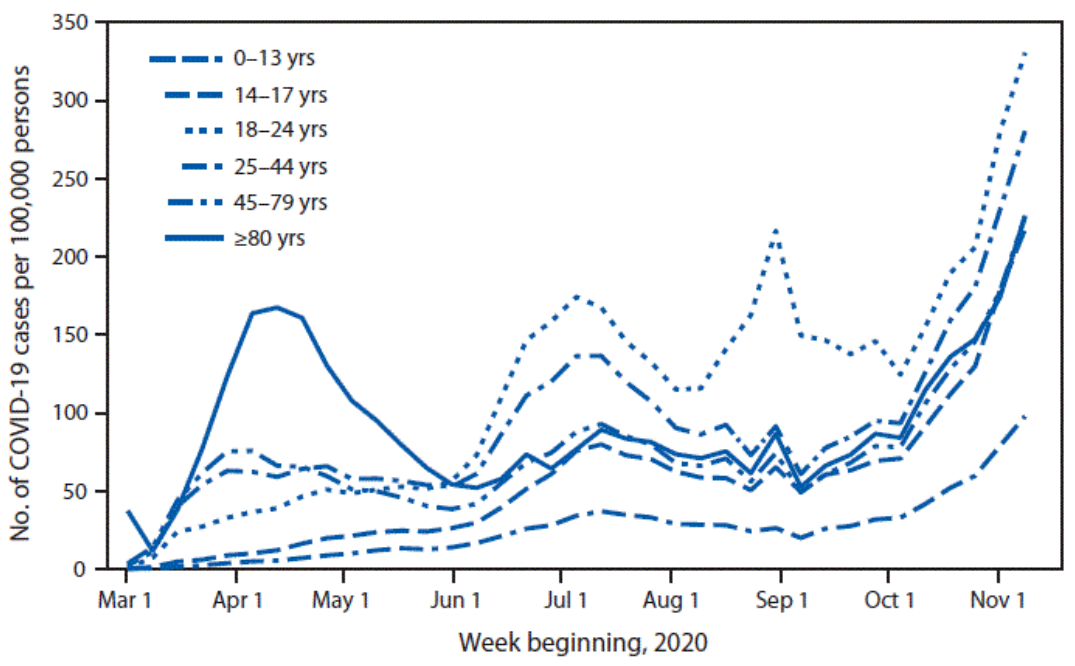
Incidence of cases by age group

- Those between 18 and 45 years of age constitute a greater share of new cases of COVID-19
  - those 65 and older are at greater risk of death from COVID-19.
- The median age of COVID-19 cases in the United States appears to be decreasing. Is this due to changing epidemiology or changing surveillance?
- Vaccination patterns will also influence this scenario



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Cases of severe COVID-19 by age may shift in response to the distribution of variants like P.1

- April 8, 2021 : Most of Brazil's COVID-19 patients in ICUs last week were under 40
- It is not entirely known why younger patients are now being hospitalized with COVID-19 but it is strongly suspected that his is connected to the P1 variant
- The variant is spreading rapidly and has been recently identified in the USA

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Morbidity and Mortality by Gender

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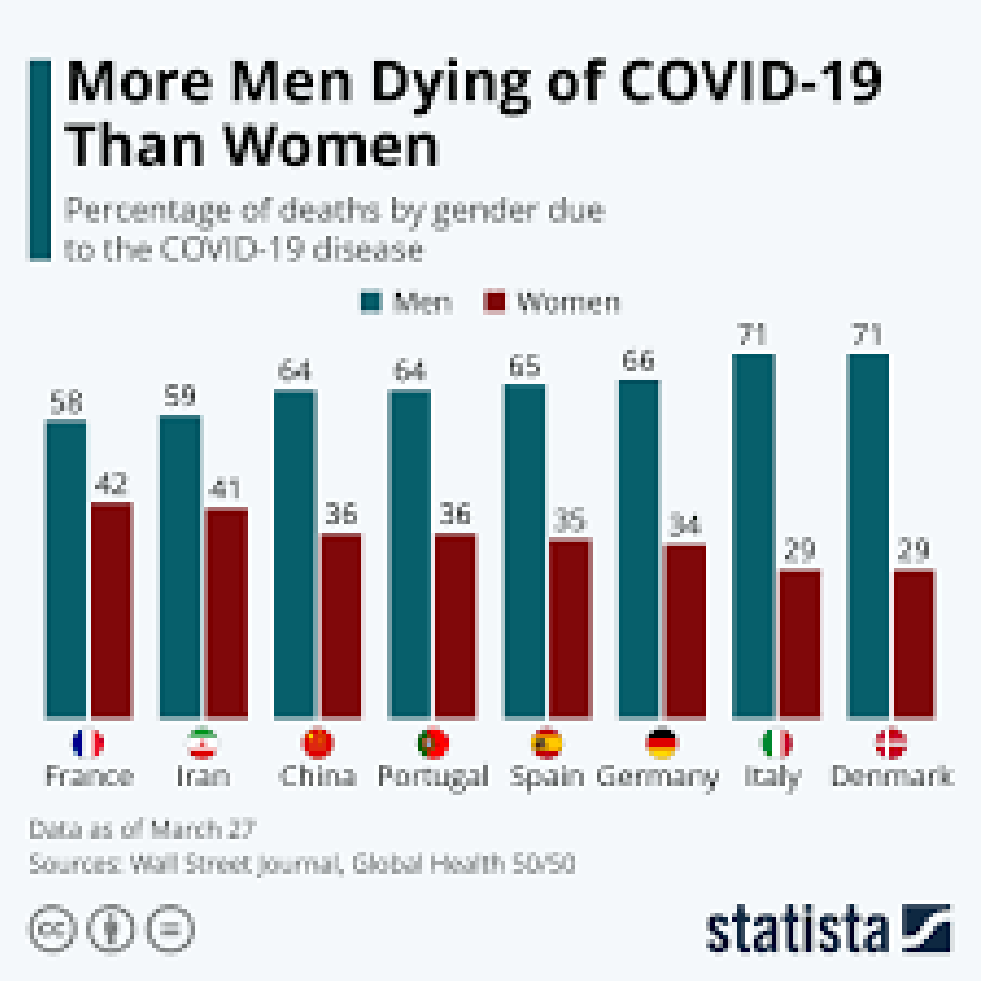
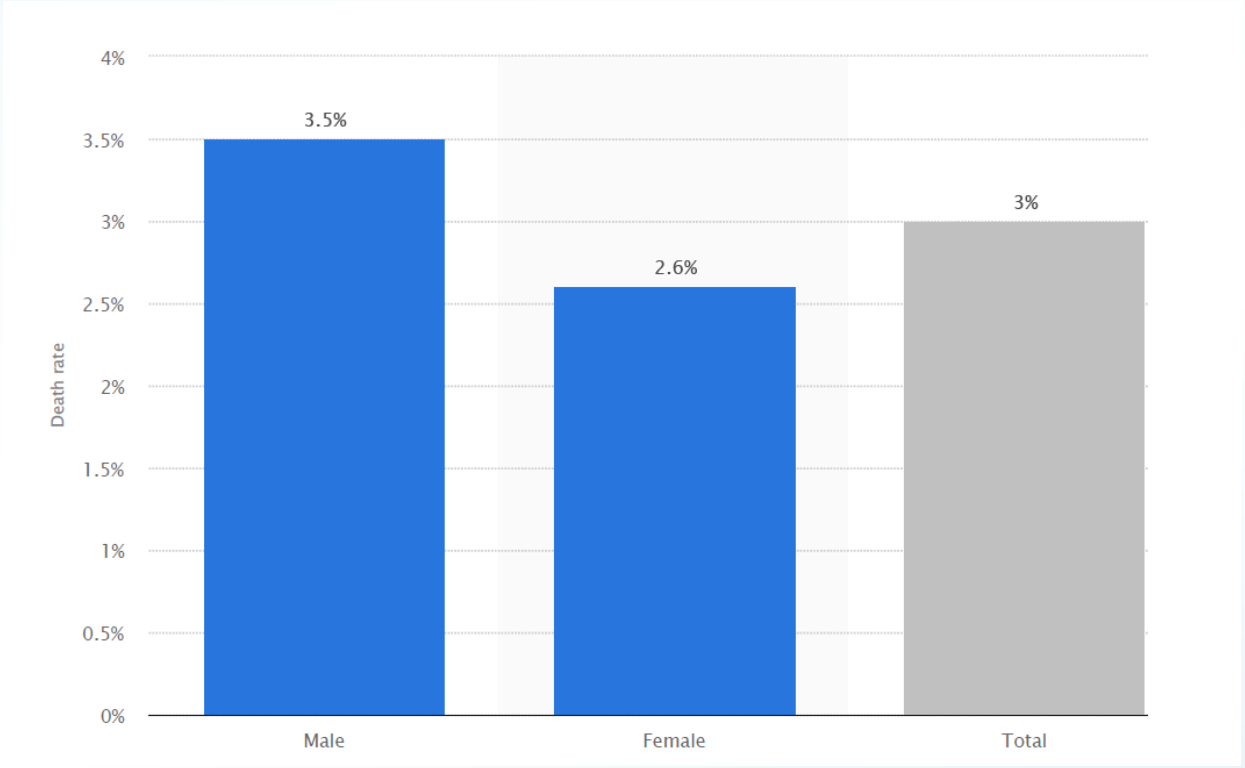
Mortality and hospitalization by gender

- Global data indicate higher COVID-19 case fatality rates among men than women. Most countries with available data indicate a male to female case fatality ratio higher than 1·0, ranging up to 3·5 in some cases
  - In China, 2.8 percent of men died from the virus compared with 1.7 percent of women. The median age of the fatal cases among women was five years older than among men*
  - In Italy , the mortality rate is twice as high among men as it is among women in every age group **
- However, the COVID-19 case fatality rate is higher in women than men in a few countries
  - In India, the COVID-19 case fatality rate among men is 2·9% and 3·3% among women.
  - Previous research from India indicates marked sex differences in access to health services, with women being less likely to be admitted to hospital
  - Case fatality rates in Nepal, Vietnam, and Slovenia are also higher among women than men.





Coronavirus (COVID-19) death rate in Italy as of April 2021, by gender

As of 3/27/2020

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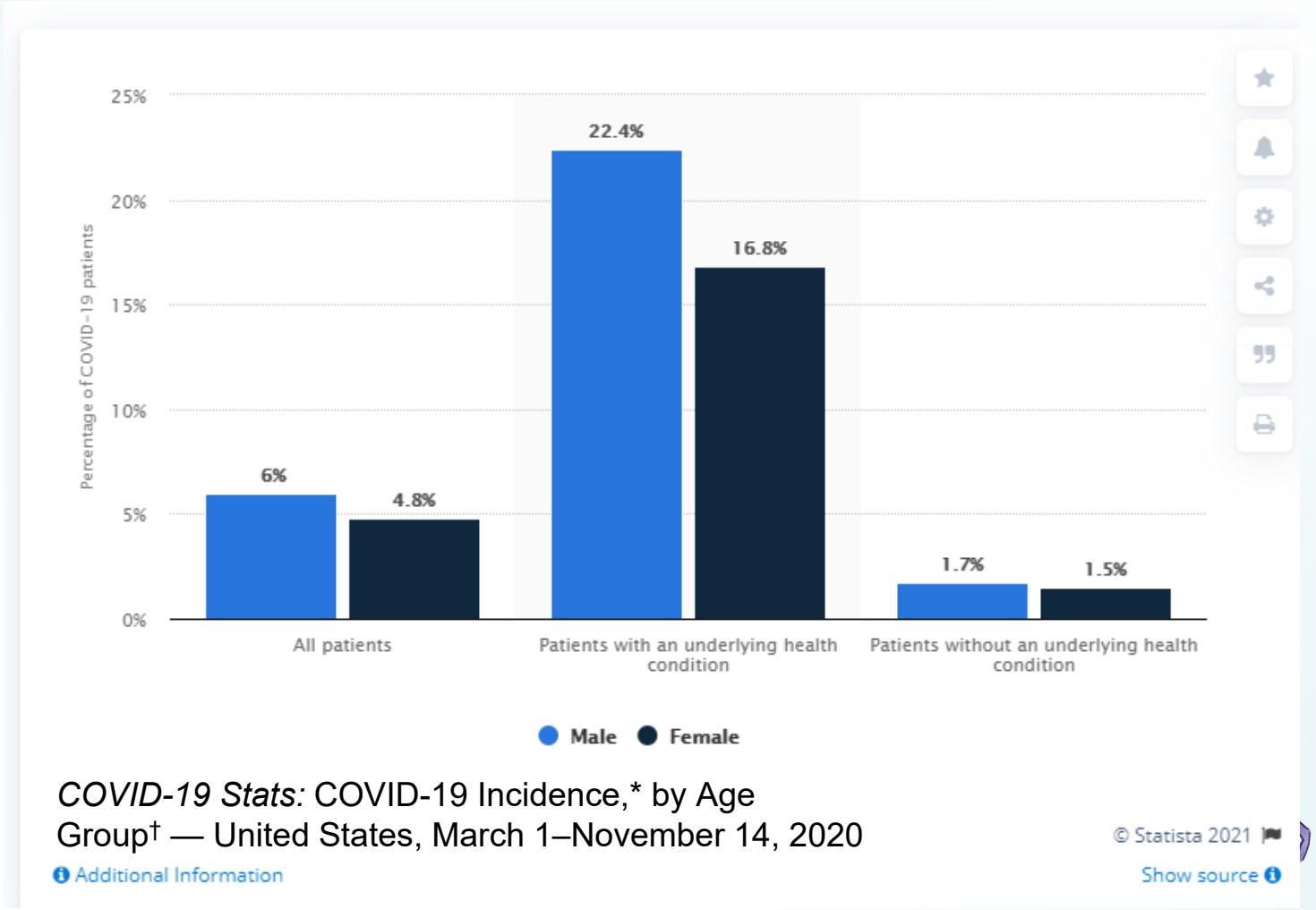
Gender differences in COVID-19 mortality USA



COVID-19 Stats: COVID-19 Incidence,* by Age Group† — United States, March 1–November 14, 2020

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Mortality and hospitalization by gender in the USA

- In the US, hospitalization rate from COVID-19 is slightly higher in men than in women.
- Why?
- Could be many factors
  - Differences in rates of smoking by gender
  - Differences in rates of high blood pressure and heart disease by gender
  - Differences in the way that male and female immune systems respond, and/or as a result of hormonal changes*
    - Differences exist: For example, women tend to have more autoimmune disorders than men
    - Gender differences in the microbiota
  - Differences in medication use

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Morbidity and Mortality by ethnicity

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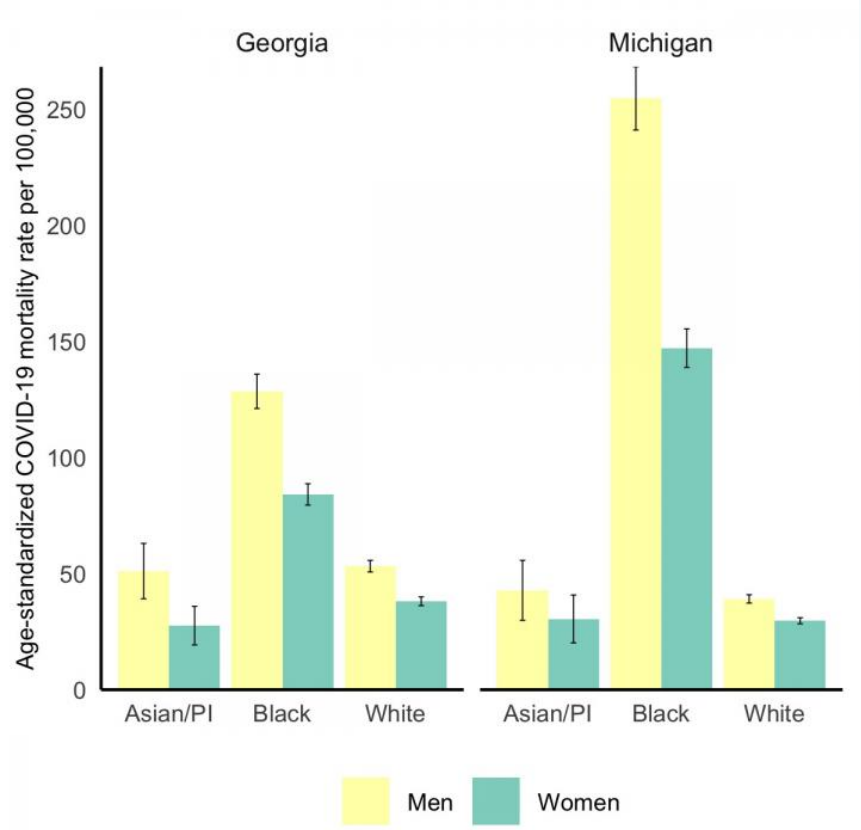
Mortality and hospitalization among race/ethnicity groups

- Members of particular ethnic groups are more at risk due to difficulties in engaging in physical distancing related to housing, intergenerational contact associated with familial responsibility, and occupation, etc. Demographics and overall health status are also risk factors influencing the crude numbers of people hospitalized and dying.
- You have no doubt heard that COVID-19 is an equal opportunity viral threat. This is only partially true. There are social and structural determinants of both disease transmission and prognosis based on access to resources and health care.
    - For example, African Americans in the USA are far more likely to die of COVID-19. Black Chicagoans account for half of all coronavirus cases in the city and more than 70% of deaths, despite making up 30% of the population.

Mortality and hospitalization among race/ethnicity groups



[Black women are dying of COVID-19 at rates higher than men in other racial/ethnic groups]

- Black women have COVID-19 mortality rates that are almost 4 times higher than that of white men and 3 times higher than that of Asian men, as well as higher than white and Asian women.
- Black men have far higher mortality rates than any other sex and racial group, including over 6 times higher than the rate among white men.
- The disparity in mortality rates between Black women and white women is over 3 times the disparity between white men and white women.
- The disparity between Black men and Black women is larger than the disparity between white men and white women.

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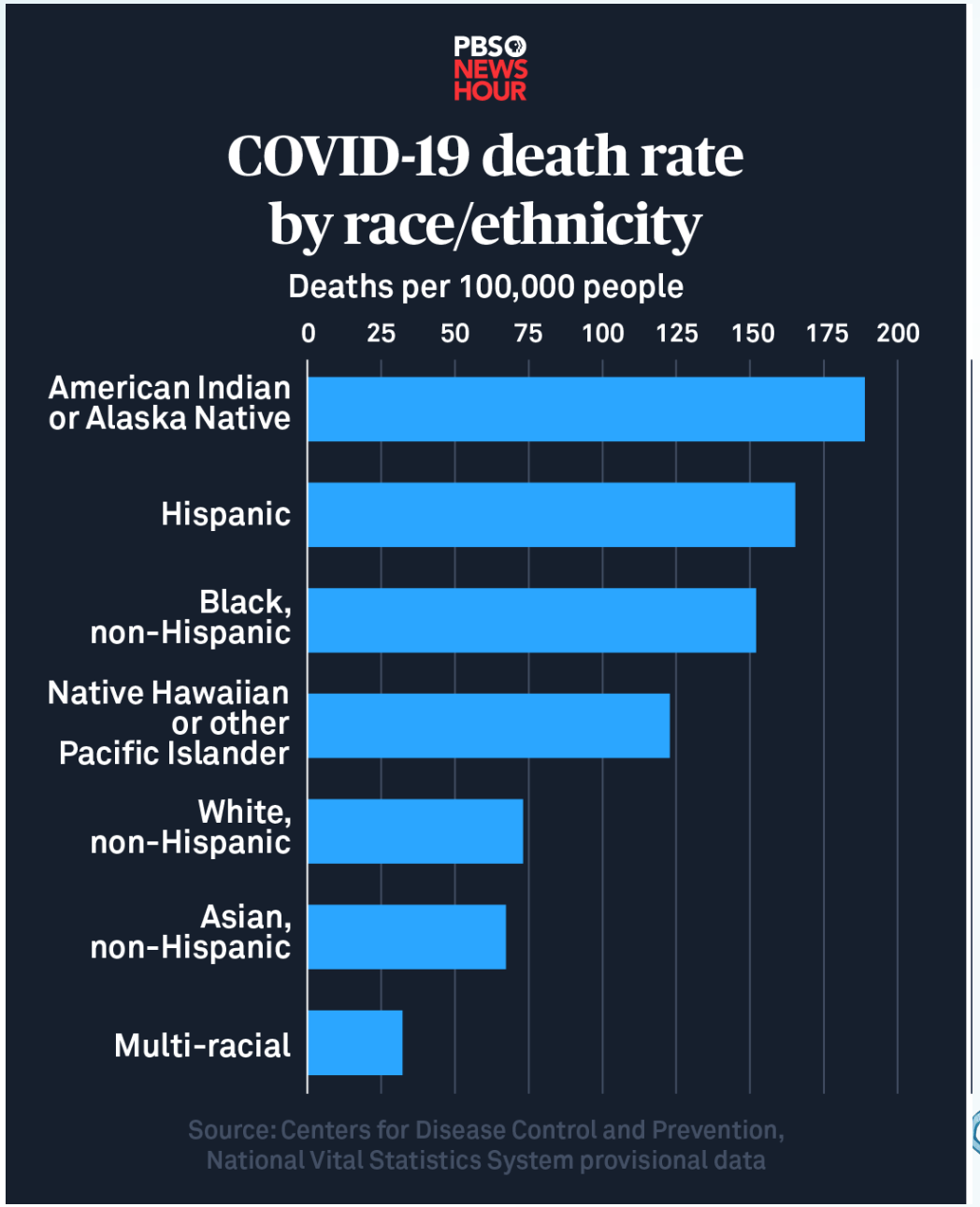

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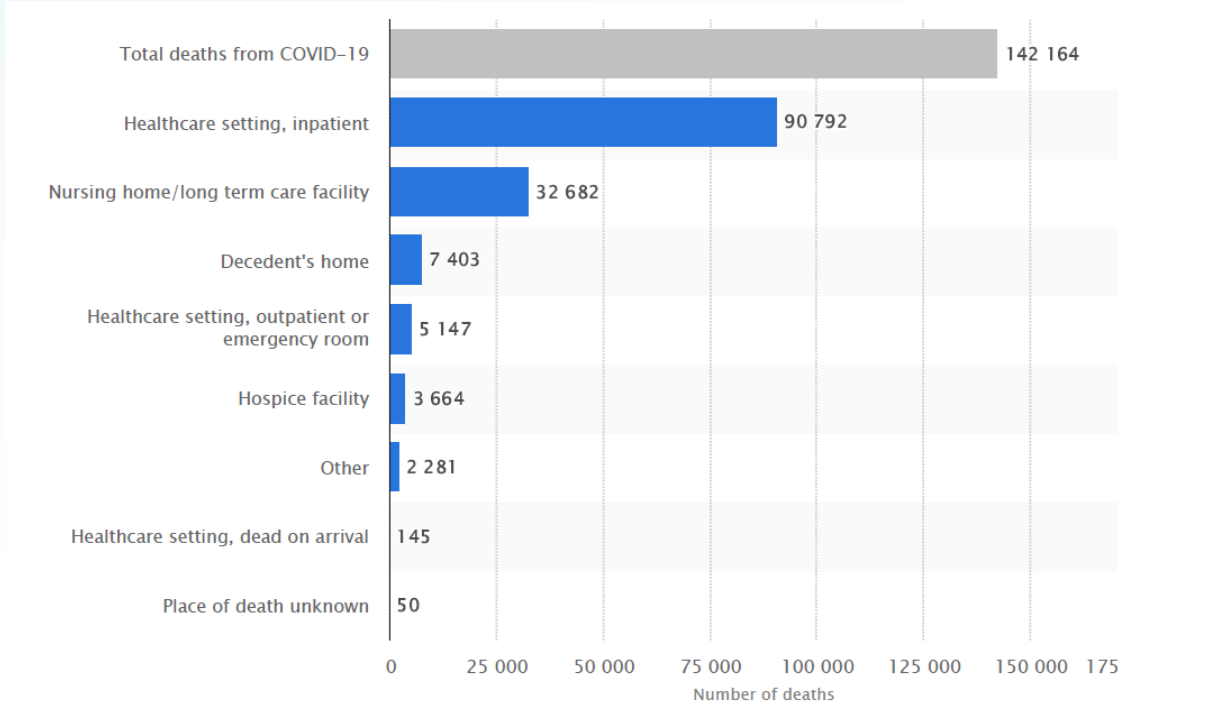
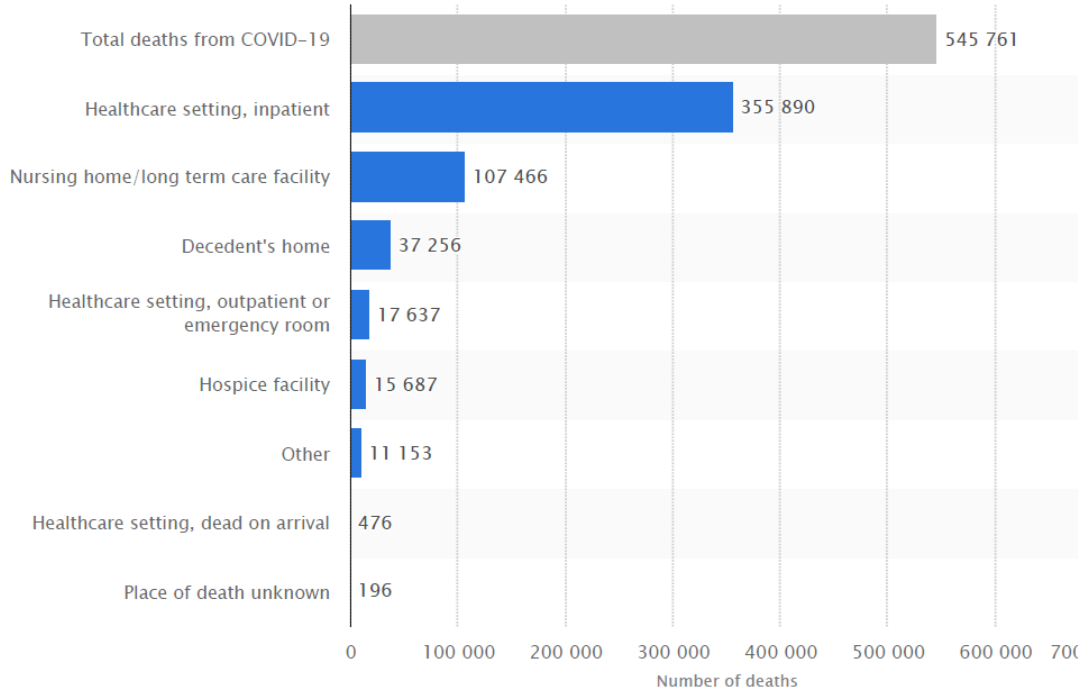
April 8, 2021

Where are COVID-19 patients dying?



In the US, as of 08/05/2020

Number of coronavirus disease 2019 (COVID-19) deaths in the U.S. as of April 14, 2021, by place of death*



In the US, as of 04/14/2021

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COVID-19

Compared to the seasonal flu and other pandemics

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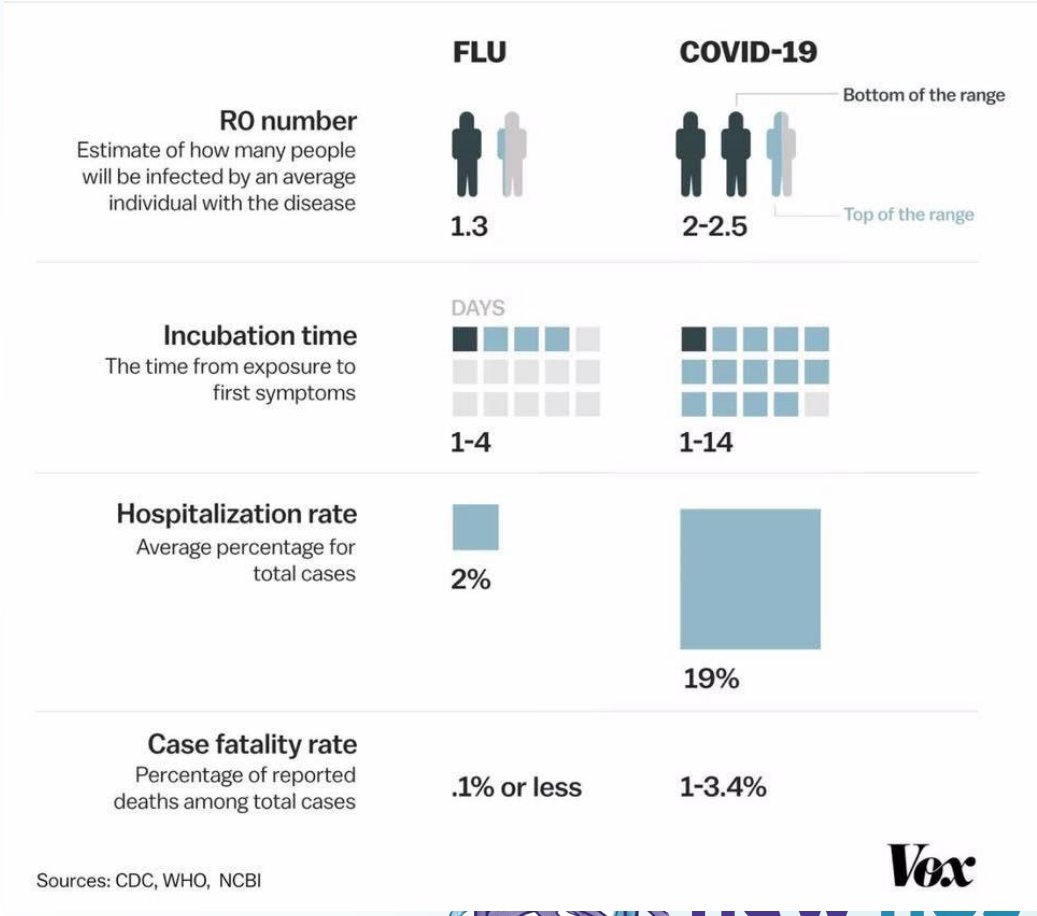
How serious is COVID-19 compared to the “flu”

- While COVID-19 has many of the same symptoms as the flu, **there are some very important differences that make our current COVID-19 pandemic <u>more serious.</u>**

- **Each person with COVID-19 infects 2-3 people on average, and the number of days that a person is contagious before feeling sick is much greater in COVID-19 compared to the flu.**



https://www.vox.com/science-and-health/2020/3/13/21176735/COVID-19-coronavirus-worse-than-flu-comparison

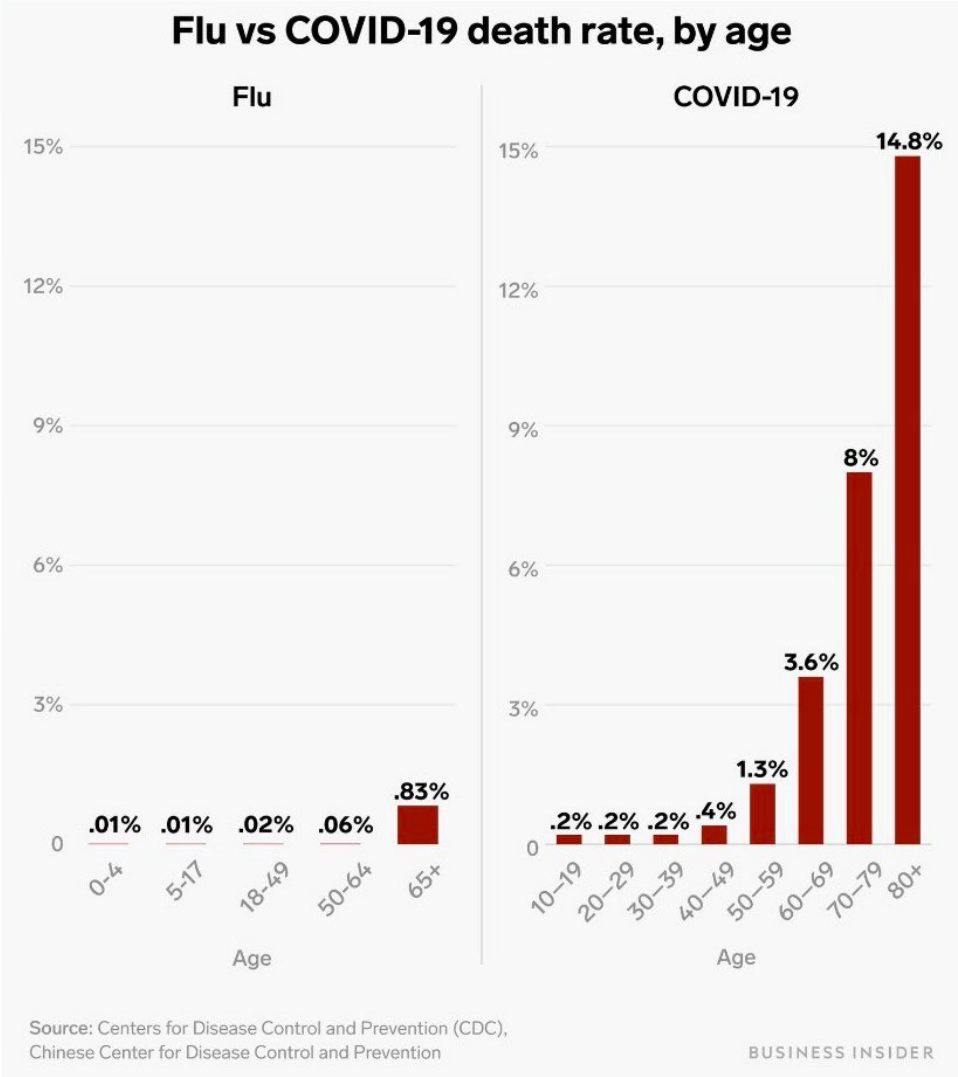
Table. Comparison Between Seasonal Influenza and SARS-CoV-2

Characteristics	Seasonal influenza viruses	SARS-CoV-2
Primary route of transmission	Droplet	Droplet (airborne, fomite, and fecal-oral transmission possible but less important)
Overall infectivity	Less contagious	More contagious
	The basic reproduction number (R_0) of both viruses is highly dependent on NPIs effective in decreasing transmission	
Dynamics of infectivity	Patients are most infectious after symptom onset	Patients are most infectious starting 48 h prior to symptom onset[2]
	Both viruses capable of asymptomatic transmission, but less than during presymptomatic and symptomatic phases	
Incubation period	1-4 d (median, 2 d)	2-14 d (median, 5 d)
Risk factors for severe disease	• Age >65 y and <2 y • Immunosuppression • Pregnancy (through 2 weeks postpartum) • Morbid obesity • Chronic lung disease, cardiac disease, advanced liver disease, chronic kidney disease • Residence in nursing home or long-term care facilities • American Indian/Alaska Native heritage	• Advanced age (risk increases with age) • Male sex • Obesity • Hypertension • Chronic lung disease, cardiac disease, type 2 diabetes, cancer,chronic kidney disease, advanced liver disease • Surgery during incubation period • Residence in nursing home • Structural racism, poverty[3]
Most common clinical manifestations	Fever, chills, headache, myalgias, cough, nasal congestion, sore throat, fatigue	Fever, chills, headache, myalgias, cough, shortness of breath, fatigue, anosmia
	For both viruses, the majority of infections are either subclinical or mild	
Pediatric disease	• Common, especially high risk in children <2 y • Children play a leading role in propagating outbreaks	• Uncommon, with typically mild disease • Multisystem inflammatory syndrome has been observed in children, but is rare • Limited evidence on children as a source of infection
Case-fatality rate	≈0.1%	≈0.25%-3.0%[4]
Dynamics of symptoms	Symptoms typically peak during first 3-7 d of illness	Symptoms can peak during week 2 or 3 of illness
Vaccine	Multiple approved	No vaccine currently licensed
Clinical diagnostics	Nucleic acid amplification and antigen-based assays from respiratory samples	• Nucleic acid amplification and antigen-based assays from respiratory samples • Serologies
Available antiviral agents	• Neuraminidase inhibitors • Cap-dependent endonuclease inhibitors • M2 channel blockers	Nucleoside analogue (remdesivir)

Abbreviations: NPI, nonpharmacologic intervention; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

How serious is COVID-19 compared to the “flu”

- Any suggestion of COVID-19 being just like influenza is false.
- For those aged 20-29 years, the case fatality ratio is around three times higher than that of seasonal influenza in people aged 18-49 years.
- COVID-19 infections are 10 times greater that of the “flu” even in the least effected group of individuals older than 10 years and younger than 40 years of age



How COVID-19 compares to other epidemics

As of June 9th, there have been 173,674,509 global cases of COVID-19 and 3,744,408 deaths

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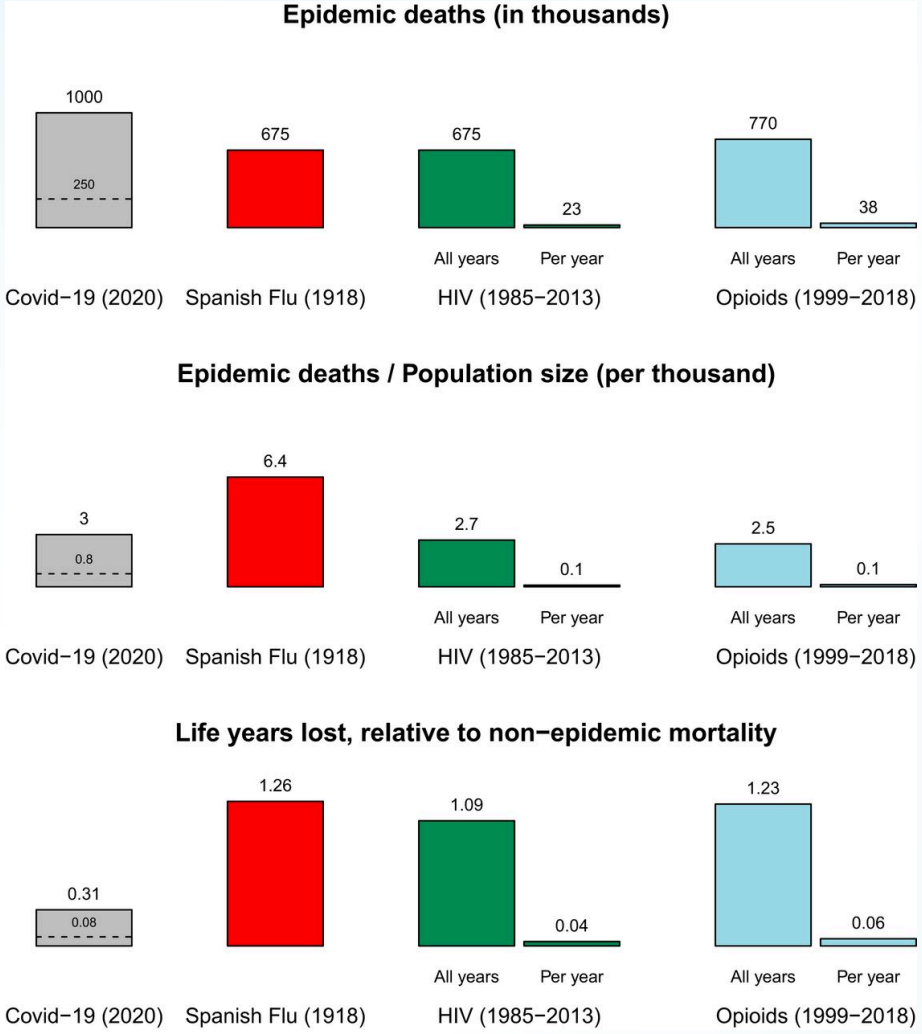
Mortality of COVID-19 scenario compared to past US epidemics according to different measures.



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