Breakthroughs that change patients' lives

Introduction to SARS-CoV-2 and COVID-19

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Cell and Gene Therapy Products 2020

June 8, 2020

2009 influenza H1N1 pandemic- Transmissible but not severe

Estimating the Burden of 2009 Pandemic Influenza A (H1N1) in the United States (April 2009–April 2010)

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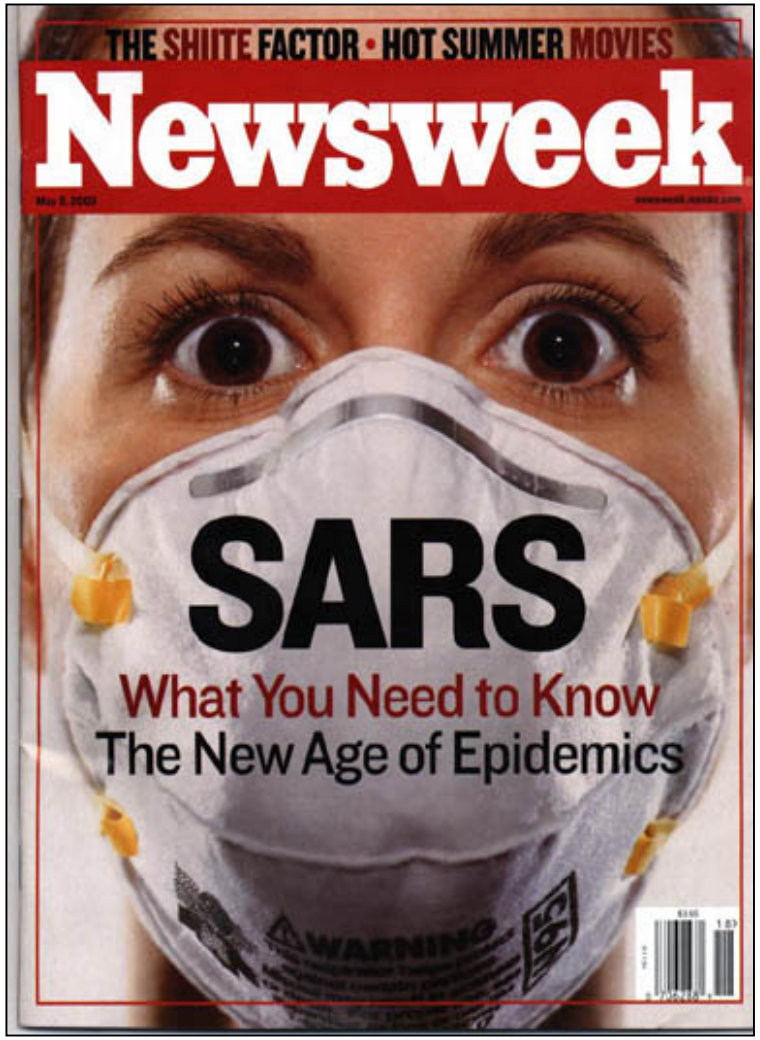
- Spread rapidly worldwide
- Not possible to contain
- Estimated 61 million cases in the United States first year of pandemic
- 12,500 deaths (less than for seasonal influenza)

Shrestha,SS et al. CID 2011;52:S75-S82.

SARS and MERS- Severe but not highly transmissible



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

2014 MERS-CoV Outbreak in Jeddah — A Link to Health Care Facilities

Ikwo K. Oboho, M.D., Sara M. Tomczyk, P.H.N., M.Sc., Ahmad M. Al-Asmari, M.D., Ayman A. Banjar, M.D., M.P.H., Hani Al-Mugti, M.D., Muhannad S. Aloraini, M.D., Khulud Z. Alkhaldi, M.D., Emad L. Almohammadi, M.D., Basem M. Alraddadi, M.D., Susan I. Gerber, M.D., David L. Swerdlow, M.D., John T. Watson, M.D., and Tariq A. Madani, M.D.

ABSTRACT

BACKGROUND

A marked increase in the number of cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection occurred in Jeddah, Saudi Arabia, in early 2014.

Novel coronavirus - Severe and highly transmissible

VIEWPOINT

Preparation for Possible Sustained Transmission of 2019 Novel Coronavirus
Lessons From Previous Epidemics

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Viewpoint page 1131
Audio

Transmissibility and severity are the 2 most critical factors that determine the effect of an epidemic. Neither the 2009 pandemic influenza A(H1N1) virus ([H1N1]pdm09) pandemic or the severe acute respiratory syndrome coronavirus (SARS-CoV) or the Middle East respiratory syndrome coronavirus (MERS-CoV) epidemics had the combination of both high transmissibility and severity. Control strategies are driven by this combination. R_0, the basic reproduction number, is a commonly used measure of transmissibility and is defined as the number of additional persons one case infects over the course of their illness. An R_0 of less than 1 indicates the infection will die out "eventually." An R_0 of greater than 1 indicates the infection has the potential for sustained transmission.

For example, influenza A(H1N1)pdm09, first identified in southern California on April 15, 2009, was highly transmissible. By May 5, 2009, influenza A(H1N1) pdm09 had spread to 41 US states and 21 countries.[1]

In preparing for possible sustained transmission of 2019-nCoV beyond China, applicable lessons from previous experiences with epidemics/pandemics of respiratory viruses should be carefully considered...

controlled. Control was thought to have been possible because a high proportion of cases were severe, making it easier to rapidly identify and isolate infected individuals. In addition, the virus was present at lower levels in upper airway secretions. There was no secondary transmission in the United States from the 8 imported cases, although in Toronto, Canada, a single importation is thought to have led to about 400 cases and 44 deaths. Later estimates of R_0 were less than 1, indicating that SARS-CoV may not have been capable of sustained transmission, especially in the setting of control measures.[4]

Similarly, MERS-CoV appears to have high severity and low transmissibility. Since 2012, MERS-CoV has caused 2494 reported cases and 858 deaths (case-fatality rate, 34%) in 27 countries. MERS-CoV has also caused some rapid outbreaks, mainly in hospitals in Saudi Arabia, Jordan, and South Korea, but estimates of MERS-CoV R_0 are less than 1, and thus far it has been contained.[5]

Can a respiratory virus that is both transmissible and severe be contained? In preparation for an influenza pandemic, the US Department of Health and Human Services' Pandemic Influenza Plan included a combination of nonpharmaceutical (border and school closing, infection control measures) and pharmaceutical (antiviral prophylaxis, vaccines) interventions meant to be used in combination to interrupt or slow influenza transmission. Despite imple-

- Novel coronavirus reported from China in early January
- Paper published two weeks before first US death
- A transmissible virus would be difficult to contain
- Would likely not have adequate ventilators, masks etc.

Effective prevention and control will not be easy if there is sustained transmission and will require the full attention of public health, federal and local governments, the private sector, and every citizen.

Swerdlow DL, Finelli L. JAMA 2020;323:1129-30. Published online February 11, 2020

Origin and evolution of pathogenic coronaviruses

*Jie Cui[1], Fang Li[2] and Zheng-Li Shi[1]**

Abstract | Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are two highly transmissible and pathogenic viruses that emerged in humans at the beginning of the 21st century. Both viruses likely originated in bats, and genetically diverse coronaviruses that are related to SARS-CoV and MERS-CoV were discovered in bats worldwide. In this Review, we summarize the current knowledge on the origin and evolution of these two pathogenic coronaviruses and discuss their receptor usage; we also highlight the diversity and potential of spillover of bat-borne coronaviruses, as evidenced by the recent spillover of swine acute diarrhoea syndrome coronavirus (SADS-CoV) to pigs.

NATURE REVIEWS | MICROBIOLOGY VOLUME 17 | MARCH 2019

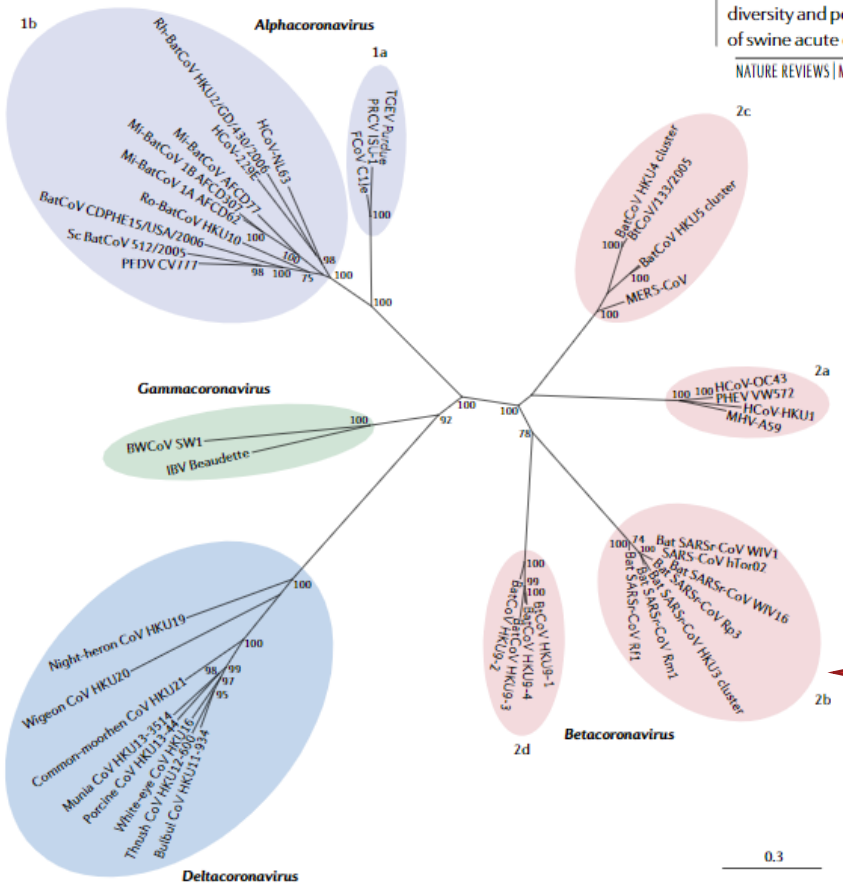


Fig. 3 | **Phylogenetic relationships in the *Coronavirinae* subfamily.** The highly human-pathogenic coronaviruses belong to the subfamily *Coronavirinae* from the family *Coronaviridae*. The viruses in this subfamily group into four genera (prototype or representative strains shown): *Alphacoronavirus* (purple), *Betacoronavirus* (pink), *Gammacoronavirus* (green) and *Deltacoronavirus* (blue). Classic subgroup clusters are labelled 1a and 1b for the alphacoronaviruses and 2a–2d for the betacoronaviruses. The tree is based on published trees of *Coronavirinae*[25,136] and reconstructed with sequences of the complete RNA-dependent RNA polymerase-coding region of the representative coronaviruses (maximum likelihood method under the GTR + I + Γ model of nucleotide substitution as implemented in PhyML, version 3.1 (REF.[137])). Only nodes with bootstrap support above 70% are shown. IBV, infectious bronchitis virus; MERS-CoV, Middle East respiratory syndrome coronavirus; MHV, mouse hepatitis virus; PEDV, porcine enteric diarrhoea virus; SARS-CoV, severe acute respiratory syndrome coronavirus; SARSr-CoV, SARS-related coronavirus.

Human Coronaviruses:

229E *(alpha coronavirus)*
NL63 *(alpha coronavirus)*
OC43 *(beta coronavirus)*
HKU1 *(beta coronavirus)*

SARS-CoV *(beta coronavirus)*
MERS-CoV *(beta coronavirus)*
SARS-CoV-2 *(beta coronavirus)*

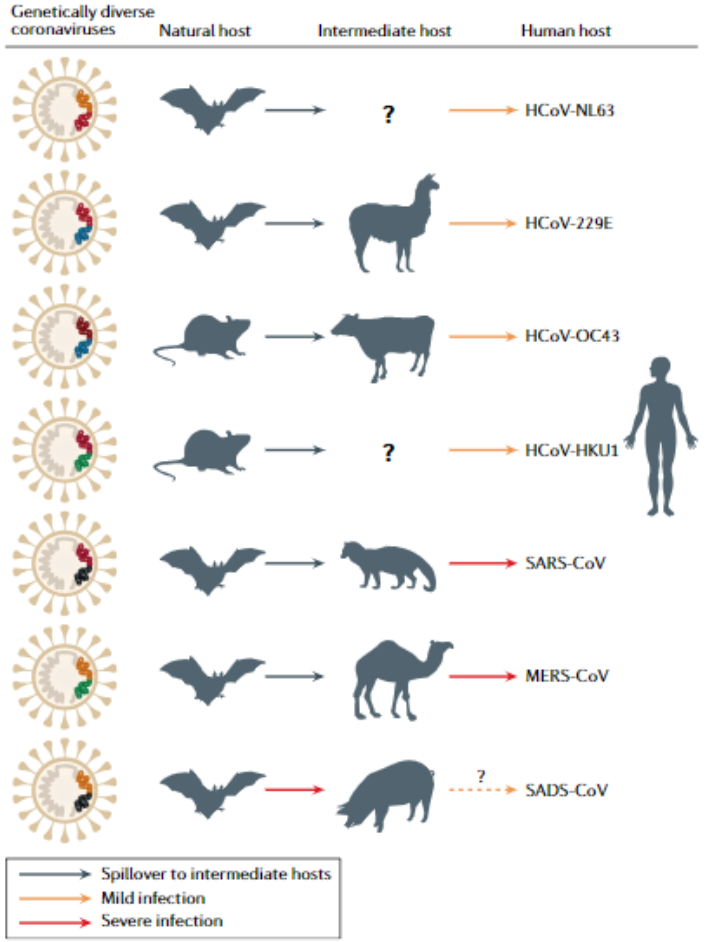


Fig. 2 | **Animal origins of human coronaviruses.** Severe acute respiratory syndrome coronavirus (SARS-CoV) is a new coronavirus that emerged through recombination of bat SARS-related coronaviruses (SARSr-CoVs)[20]. The recombined virus infected civets and humans and adapted to these hosts before causing the SARS epidemic[42,62]. Middle East respiratory syndrome coronavirus (MERS-CoV) likely spilled over from bats to dromedary camels at least 30 years ago[100] and since then has been prevalent in dromedary camels. HCoV-229E and HCoV-NL63 usually cause mild infections in immunocompetent humans. Progenitors of these viruses have recently been found in African bats[133,134], and the camelids are likely intermediate hosts of HCoV-229E[134,135]. HCoV-OC43 and HKU1, both of which are also mostly harmless in humans, likely originated in rodents. Recently, swine acute diarrhoea syndrome (SADS) emerged in piglets. This disease is caused by a novel strain of *Rhinolophus* bat coronavirus HKU2, named SADS coronavirus (SADS-CoV)[14]; there is no evidence of infection in humans. Solid arrows indicate confirmed data. Broken arrows indicate potential interspecies transmission. Black arrows indicate infection in the intermediate animals, yellow arrows indicate a mild infection in humans, and red arrows indicate a severe infection in humans or animals.

https://doi.org/10.1038/s41579-018-0118-9

COVID-19 Pandemic Spreading at Unprecedented Pace

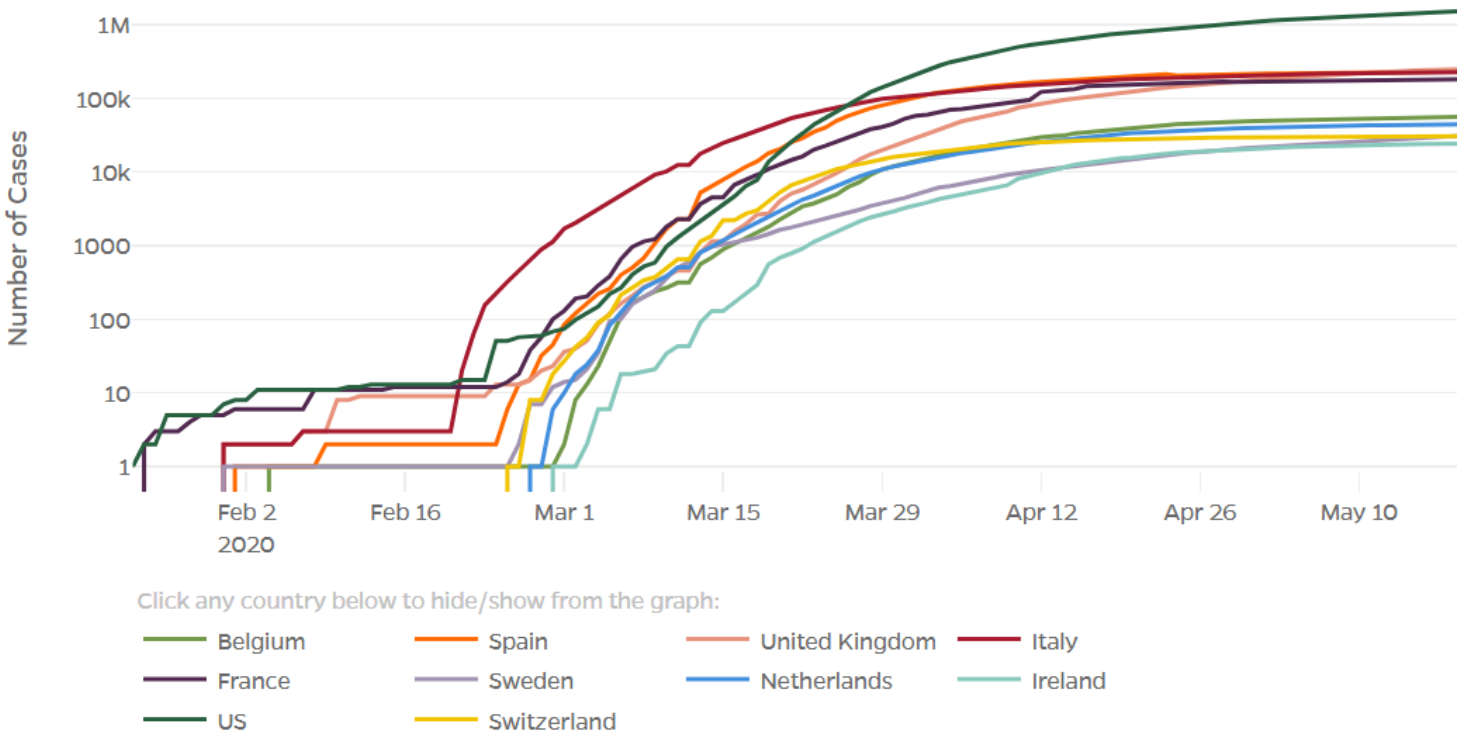
31-Dec-19: a pneumonia of unknown cause detected in Wuhan, China, first reported to WHO Country Office in China

08-Jan-20: pathogen identified as a novel coronavirus 2019

30-Jan-20: outbreak declared a Public Health Emergency of International Concern

12-Feb-20: virus officially named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and WHO officially named the disease caused by it as coronavirus disease 2019 (COVID-19)

11-Mar-20: WHO upgraded the COVID-19 outbreak from epidemic to pandemic



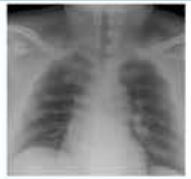
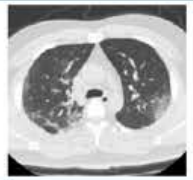
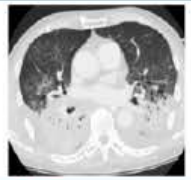
Source: Johns Hopkins University

SARS CoV-2- what we have learned

- Genetically similar to SARS-CoV and bat coronaviruses
- Highly transmissible (Ro= 2.2)
- Detected in upper respiratory tract, especially nose
  - Detected in the first week of illness
  - Detected from asymptomatic and mildly ill patients
- Likely transmitted through droplets, close contacts, fomites, ? airborne
- Asymptomatic infections common, and transmission from asymptomatic and presymptomatic persons occurs
- Causes pneumonia but other syndromes being reported
- High risk groups

Clinical features and timeline of signs and symptoms in COVID-19

Typical features according to current publications
Age Mean (SD) 55,5 (13·1), Male (68%)
Exposure to Huanan seafood market in Wuhan, China (49%)
Chronic medical underlying illness (51%)
Admission to Intensive Care Unit (23%)

INCUBATION PERIOD and ONSET OF SYMPTOMS 3 DAYS AGO

	FIRST WEEK				SECOND WEEK			
SETTING	WARD Illness day 4	WARD Illness day 5	WARD Illness day 6	WARD Illness day 7	WARD/ICU Illness day 8	ICU Illness day 9	ICU Illness day 10	ICU Illness day 11
REPEATED SAMPLING OF THE NASOPHARYNX AND TRACHEAL ASPIRATES (IF INTUBATED) BY rRT-PCR FOR THE COVID-19	Initial important viral shedding		Decrease of the viral shedding sometimes associated with transient respiratory deterioration		Respiratory failure, increase of the viral shedding and viremia or Decrease of the viral shedding, and superinfections			Duration of viral excretion unknown
OXYGEN THERAPY AND MECHANICAL VENTILATION	NO		Consider oxygen support	FNC	FNC followed by MV	MV		MV
ORGAN FAILURE	**Typical signs according to current publications** Fever, cough, and shortness of breath (15%) bilateral pneumonia (75%), lymphopenia (35%), thrombocytopenia (12%), prothrombin time decreased (30%), elevated liver enzyme levels (about 30%)		Deterioration of respiratory status with most often spontaneous recovery		ARDS If shock beware of superinfections ⚠ Possible renal failure Neurological failure unlikely Hemostasis disorders			YES
CO-INFECTION/SUPERINFECTION	NOT LIKELY				Consider a possible HAP/VAP and other nosocomial infections (see text for diagnostic procedures)			Profound immune paralysis and late onset infections
ANTIBIOTICS	NO				Consider antibiotic therapy			YES
ANTIVIRAL AGENTS	NO				Consider antiviral agents if deterioration[a]			

LONG TERM INFO PENDING

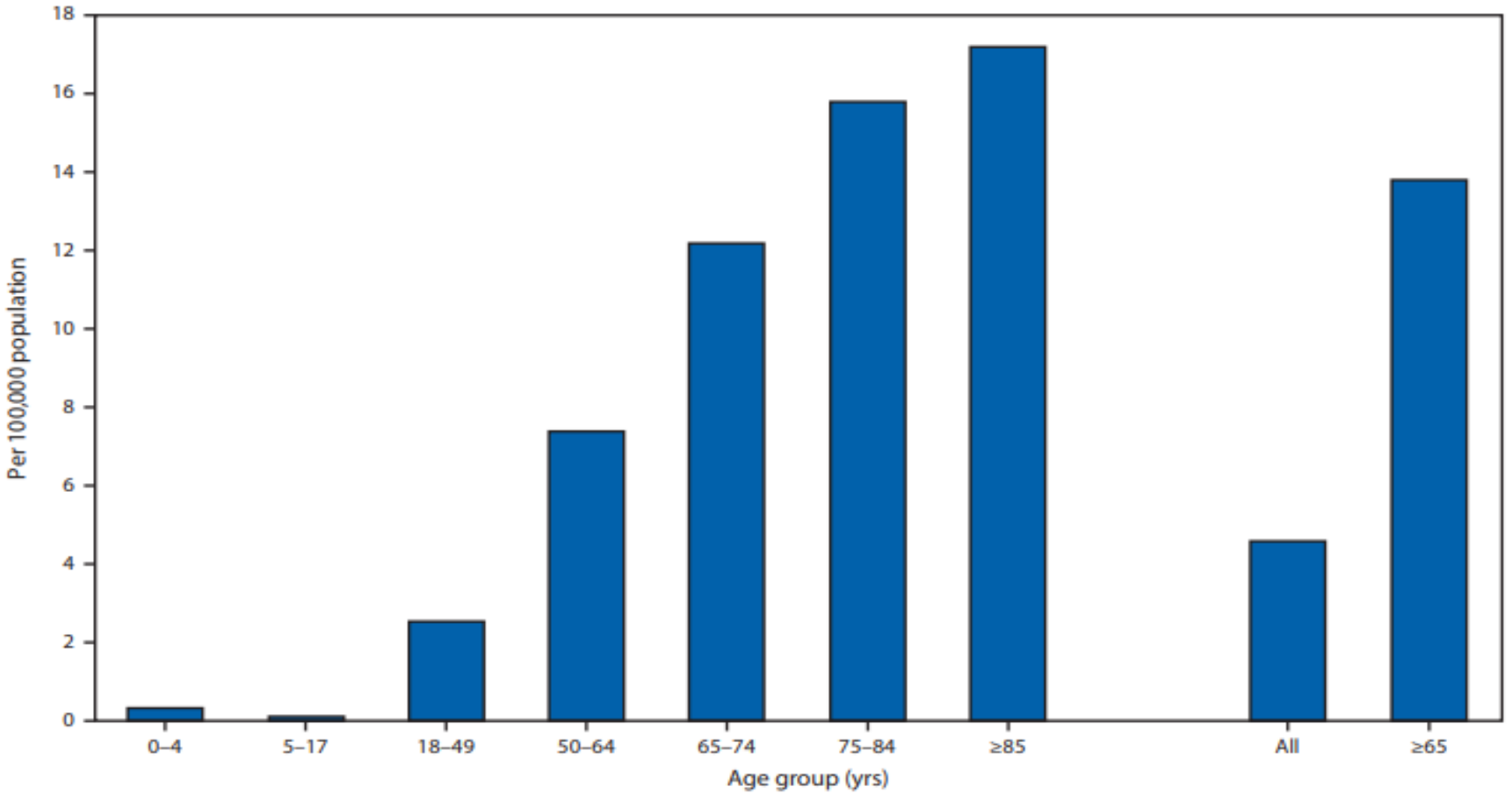
FNC = flow nasal cannula; HFNC = high flow nasal cannula; HAP = healthcare-associated pneumonia; VAP = ventilator-associated pneumonia; MV = Mechanical ventilation;
[a] The use of immunomodulation including corticosteroids is unlikely but debated

Severe symptoms including respiratory failure begin in second week
May be due to cytokine storm

Bouadma L, et al. Intensive Care Medicine. 2020 Feb 26:1-4.

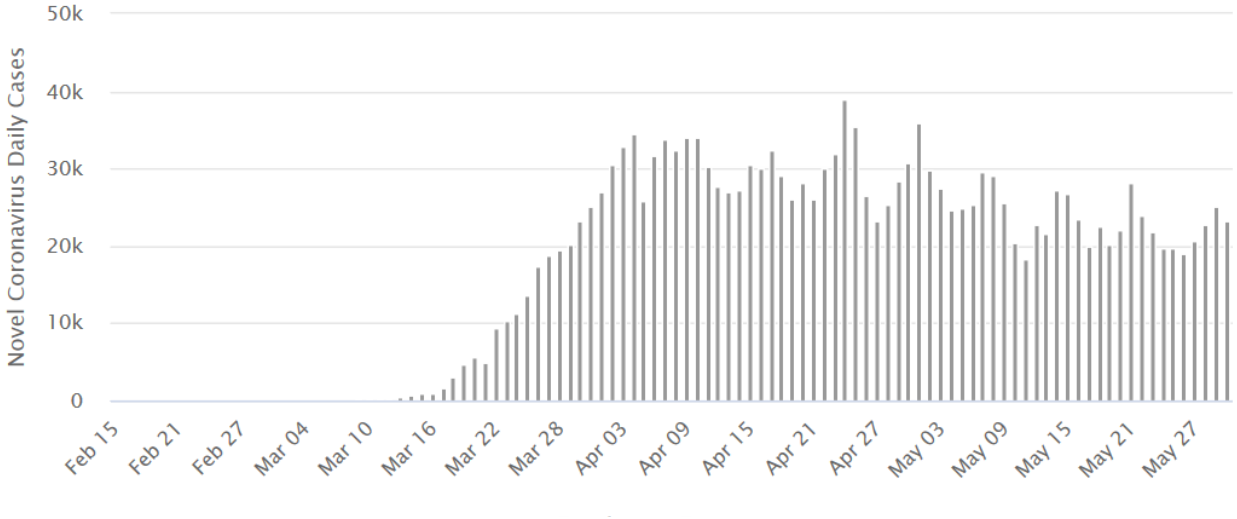
Age distribution, United States

FIGURE 1. Laboratory-confirmed coronavirus disease 2019 (COVID-19)–associated hospitalization rates,* by age group — COVID-NET, 14 states,† March 1–28, 2020

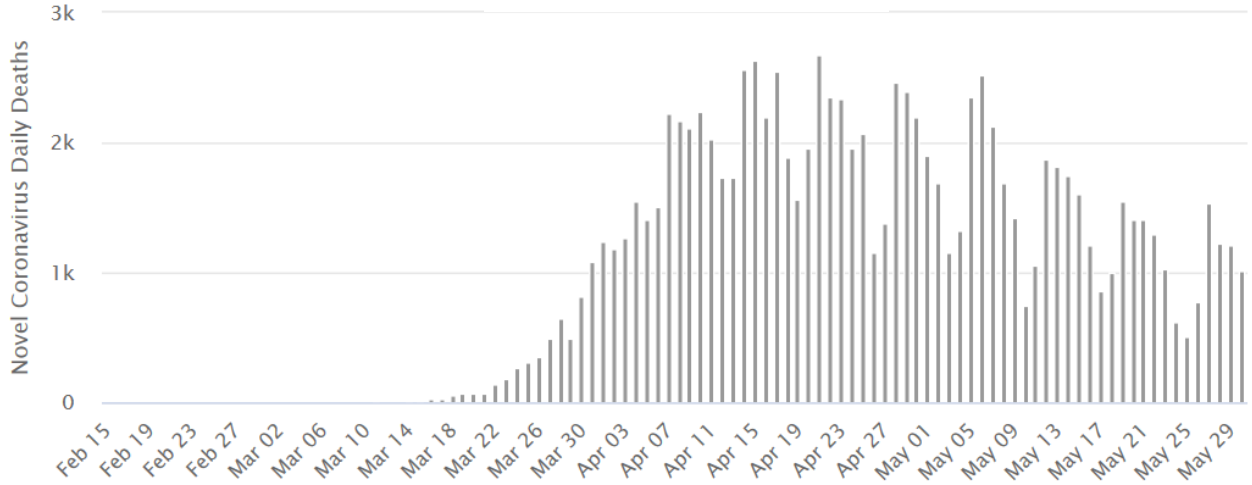


COVID-19 cases and deaths by day, United States, May 31, 2020

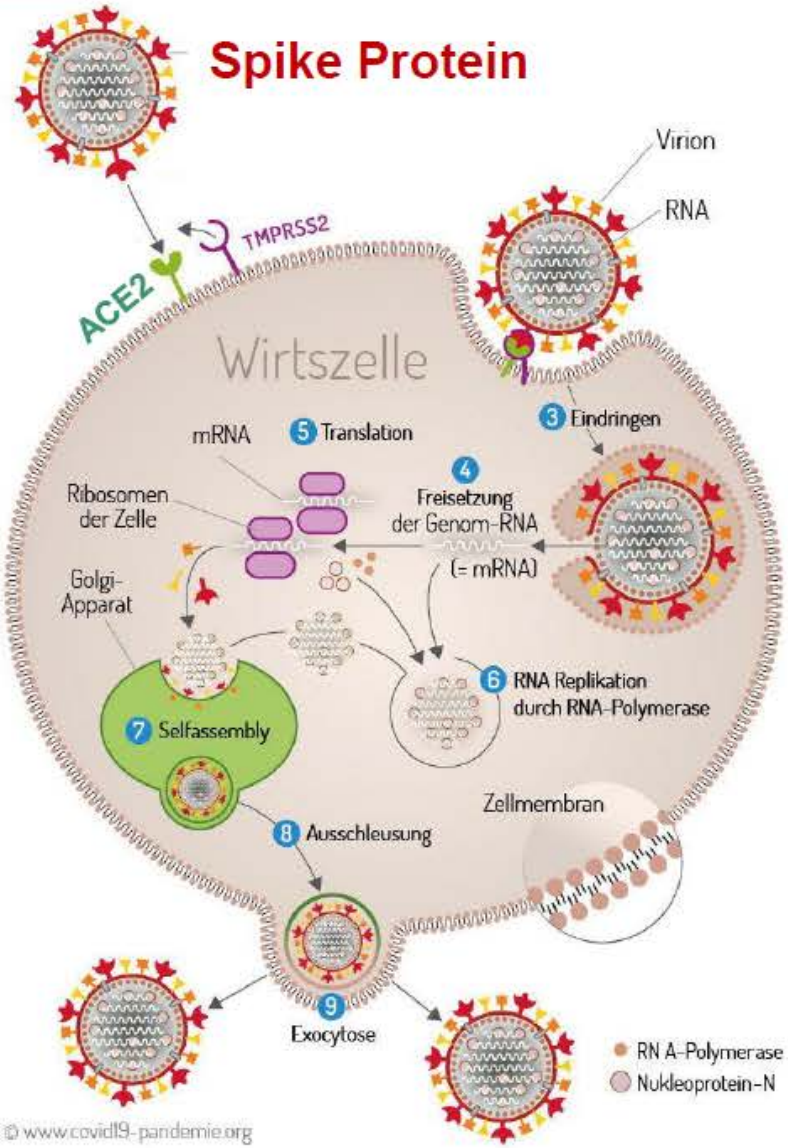
Cases per day

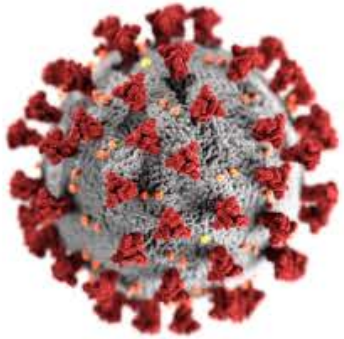


Deaths per day

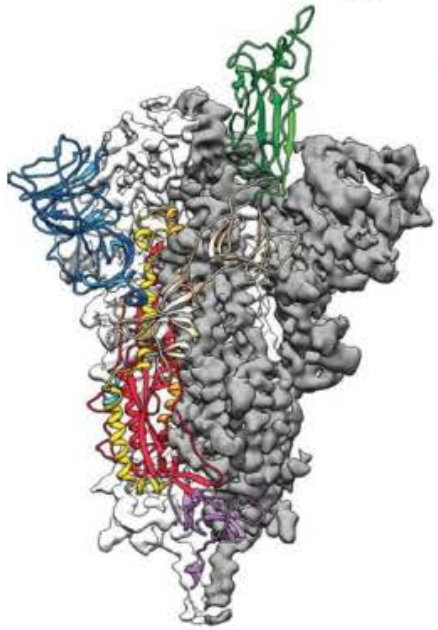


SARS-CoV-2 Spike and Receptor Binding Domain





SARS-COV-2
(3D Model)



SARS-COV-2
Spike Protein 3D Structure
(Wrapp et al., 2020, Science)

BIONTECH

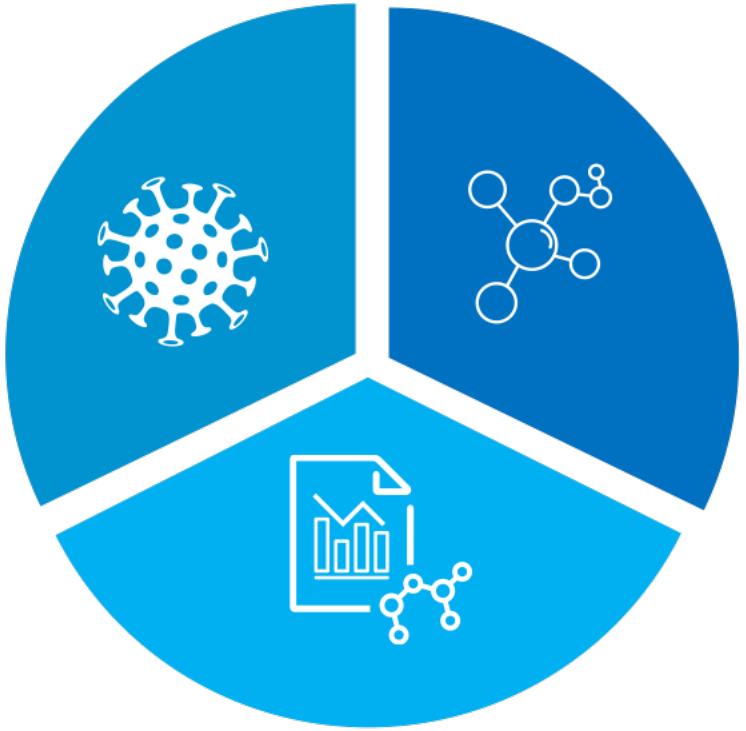
Pfizer's Robust Response to Develop Potential Vaccines and Treatments for COVID-19

Leveraging expertise from across our organization

Vaccine

Developing a Vaccine to Potentially Prevent Infections using mRNA technology

Collaboration with BioNTech



Antiviral

Advancing Our Protease Inhibitors

Exploratory

Pfizer Existing Pipeline Assets

Pfizer | Breakthroughs that change patients' lives