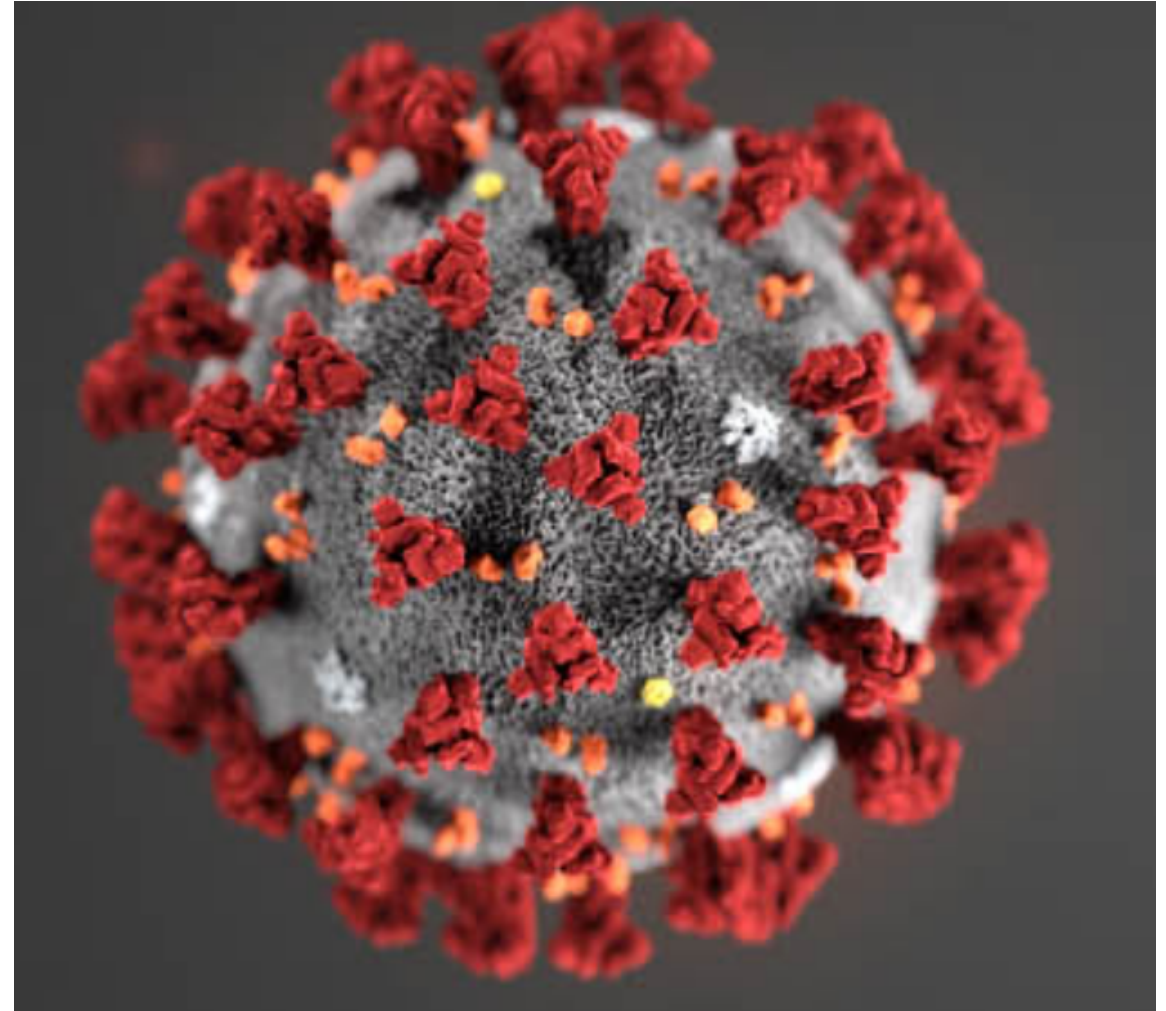


# Temas de discusión

- Human coronaviruses in general, SARS, MERS and the novel coronavirus, SARS-CoV-2
- The emergence of SARS-CoV-2 and its associated disease (COVID-19) in Wuhan, China
- Symptoms and treatment
- Individual-level prevention
- Population-level prevention
- Impact and the future



# Coronaviruses

- Before SARS (2002), coronaviruses were considered relatively inconsequential pathogens that caused common colds
  - Four human coronaviruses are endemic globally and cause 10-30% of upper respiratory tract infections in adults (alpha coronaviruses HCoV 2229E, NL 63, OC 43, HKU 1)
- Widely distributed in mammals and birds
- Since 2002 we've recognized two highly pathogenic strains that causes severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)

# SARS and MERS

- As opposed to the human coronaviruses that are associated with upper respiratory tract infections, SARS and MERS are caused by beta coronaviruses
- Primarily cause lower respiratory tract infection (pneumonia)
- Relatively high case fatality rates

	SARS	MERS
Cases	8098	2494
Deaths	774	858
Case fatality rate	9.5%	34.4%
Controlled	Yes after reached pandemic	No, continued transmission
Other features	58% from nosocomial transmission	70% of cases from nosocomial transmission

# Emergence of the 2019 novel coronavirus (SARS-CoV-2)

- First case (COVID-19) hospitalized 17 December 2019
- Cluster reported on 30 December
- Huanan Wholesale Seafood Market closed 1 January
- COVID-19 isolated 7 January
- COVID-19 sequenced 10 January
- Rapid diagnostic tests developed and distributed
- *Cordon sanitaire* implemented in Wuhan and surrounding cities on 23 January – 59 million people quarantined
- WHO declared Public Health Emergency of International Concern 30 January
- Outbreak grew from a handful of cases exposed at Huanan wholesale seafood market to more than 250,000 cases and 10,000 deaths in less than 3 months with ongoing person-to-person transmission primarily via respiratory droplet



# Respiratory spread

- Data suggest similar transmission as seasonal influenza
  - Droplet - primary, large virus-laden nuclei, <6 feet (OSHA) or <1 m (WHO), don't stay in air
  - Hands
  - Fomites (surfaces)
  - Possible: gastrointestinal
  - While theoretically possible, aerosol transmission unlikely



- Infection control needs to focus on *droplet spread*, which is far and away the most common route of transmission, followed by fomite and possibly GI

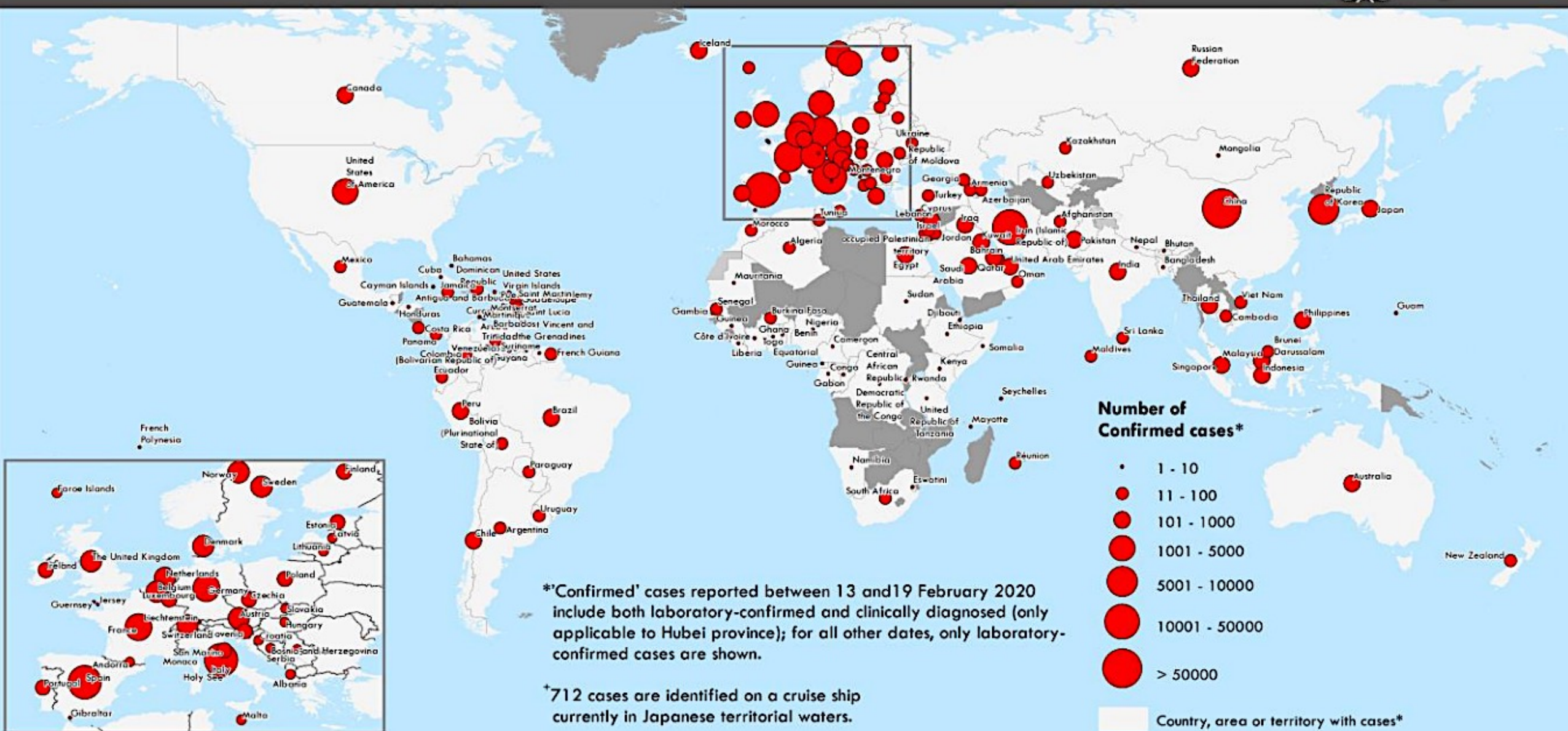
# Epizootology of COVID-19

- Genetic sequence close to bat strains of coronavirus
- Suggestion of a secondary host, which acquired COVID-19 from bats and transmitted it to humans at Huanan Wholesale Seafood Market
- Possible candidate is the *pangolin*, a mammal whose scales used in traditional medicine
  - Most illegally trafficked animal in the world





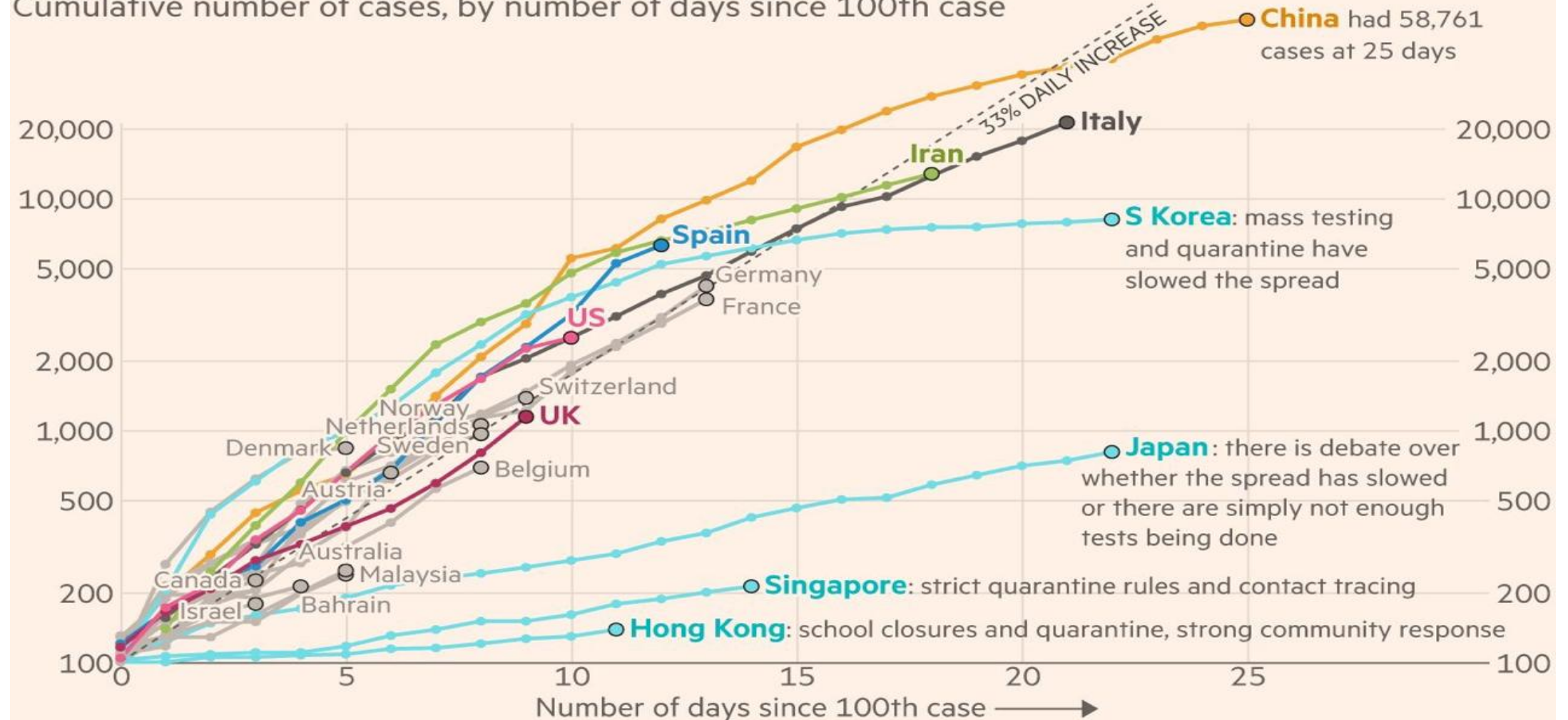
# Distribution of COVID-19 cases as of 18 March 2020





Most western countries are on the same coronavirus trajectory. Hong Kong and Singapore have so far limited the spread; S Korea is slowing its progress

Cumulative number of cases, by number of days since 100th case

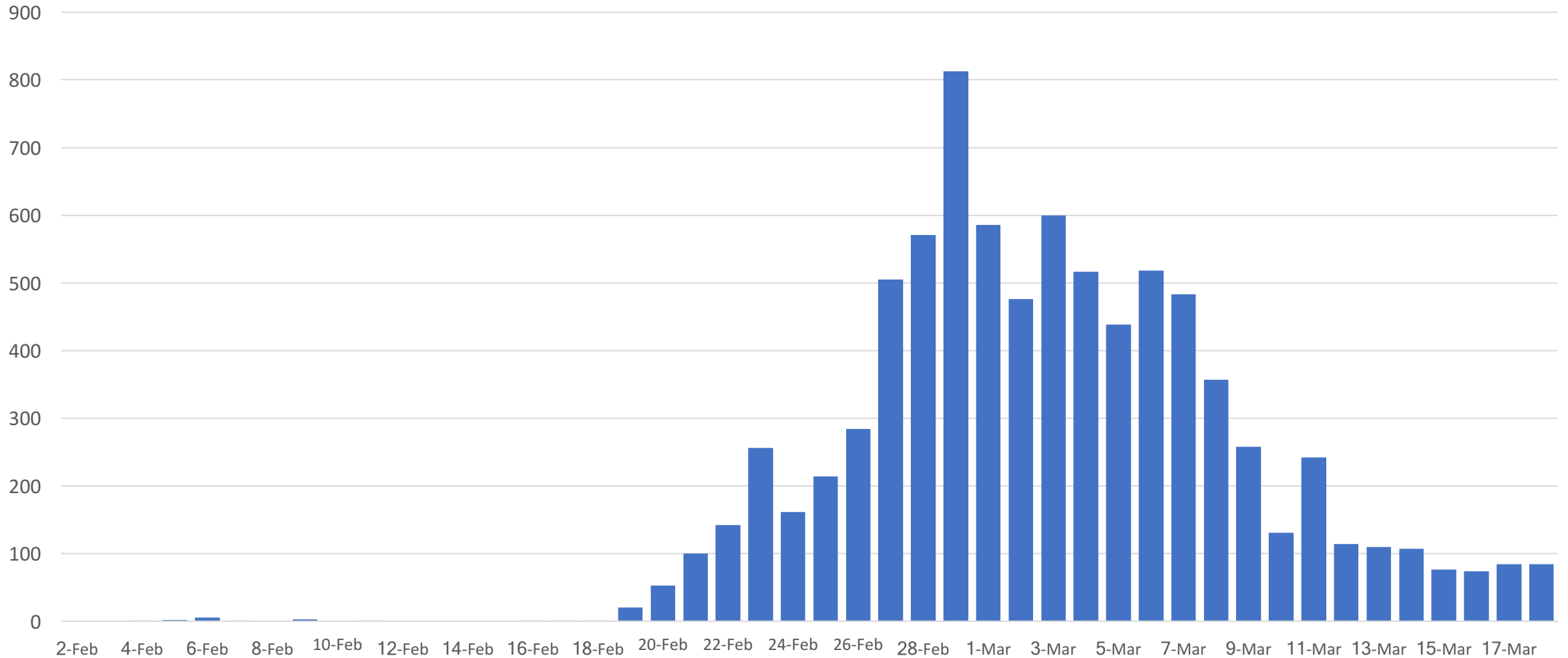


FT graphic: John Burn-Murdoch / @jburnmurdoch

Source: FT analysis of Johns Hopkins University, CSSE. Data updated March 14, 19:00 GMT

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# COVID-19 cases by date of report, Republic of Korea, 2020



# COVID-19 cases by date of report, China, March 2020

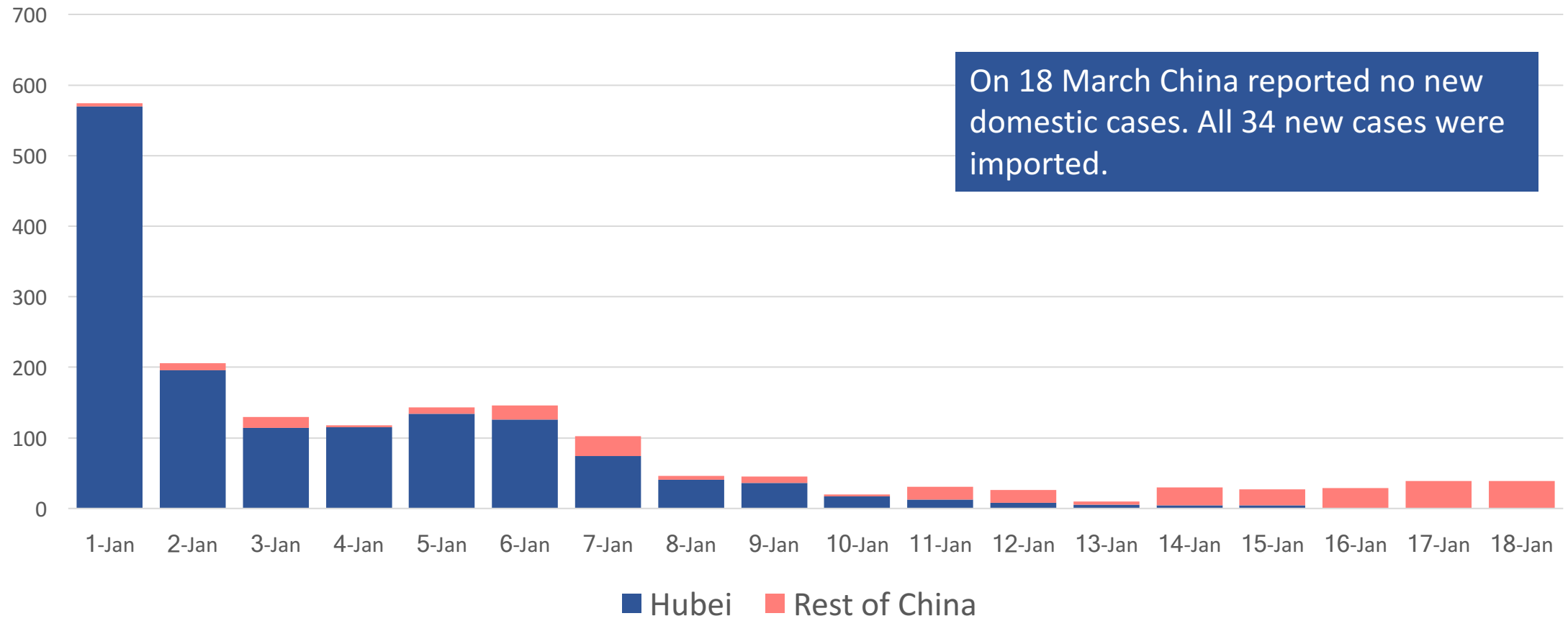
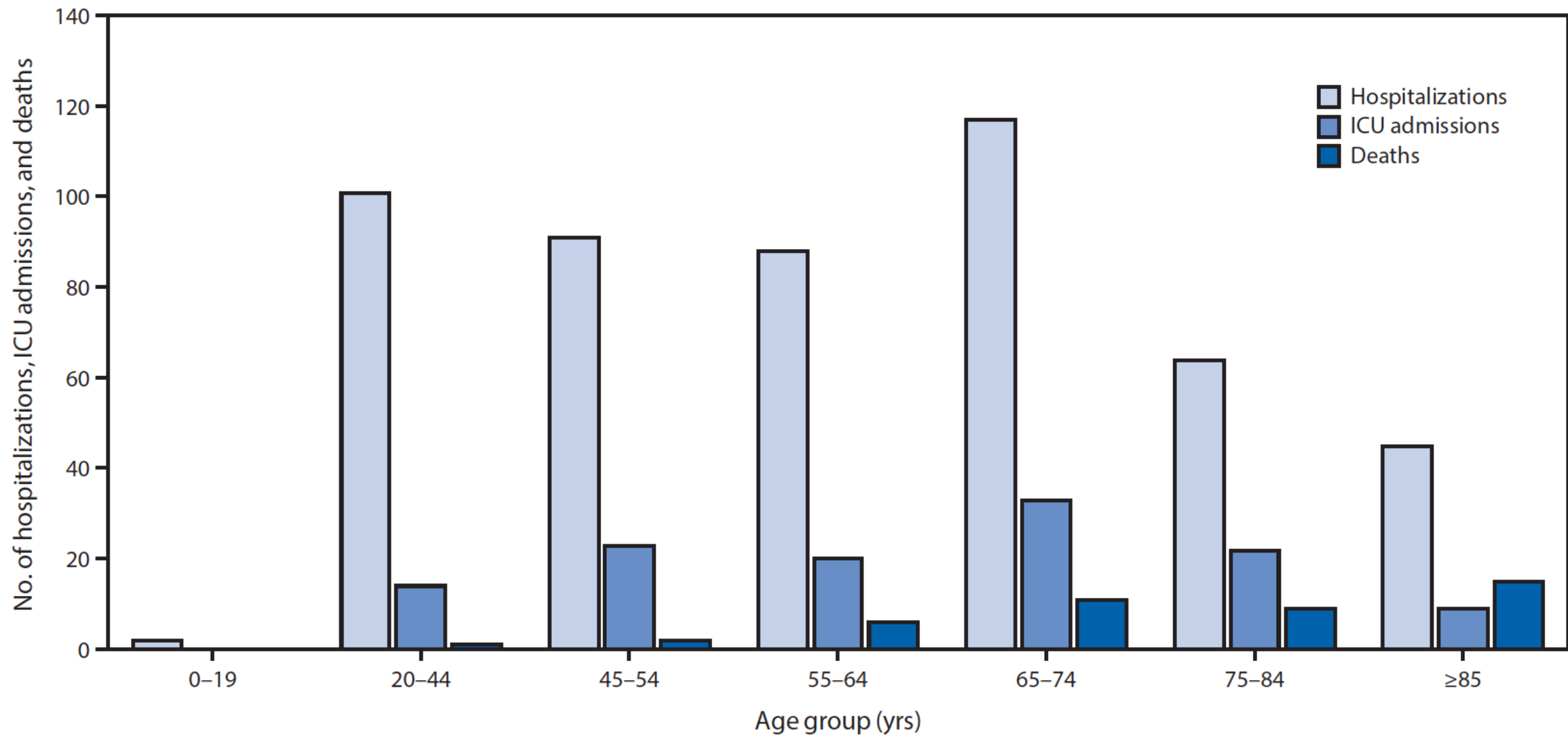


FIGURE 2. COVID-19 hospitalizations,\* intensive care unit (ICU) admissions,† and deaths,§ by age group — United States, February 12–March 16, 2020



\* Hospitalization status missing or unknown for 1,514 cases.

† ICU status missing or unknown for 2,253 cases.

§ Illness outcome or death missing or unknown for 2,001 cases.

CDC. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) – United States, February 12–March 16, 2020. MMWR 2020 Mar 18 [Early release].

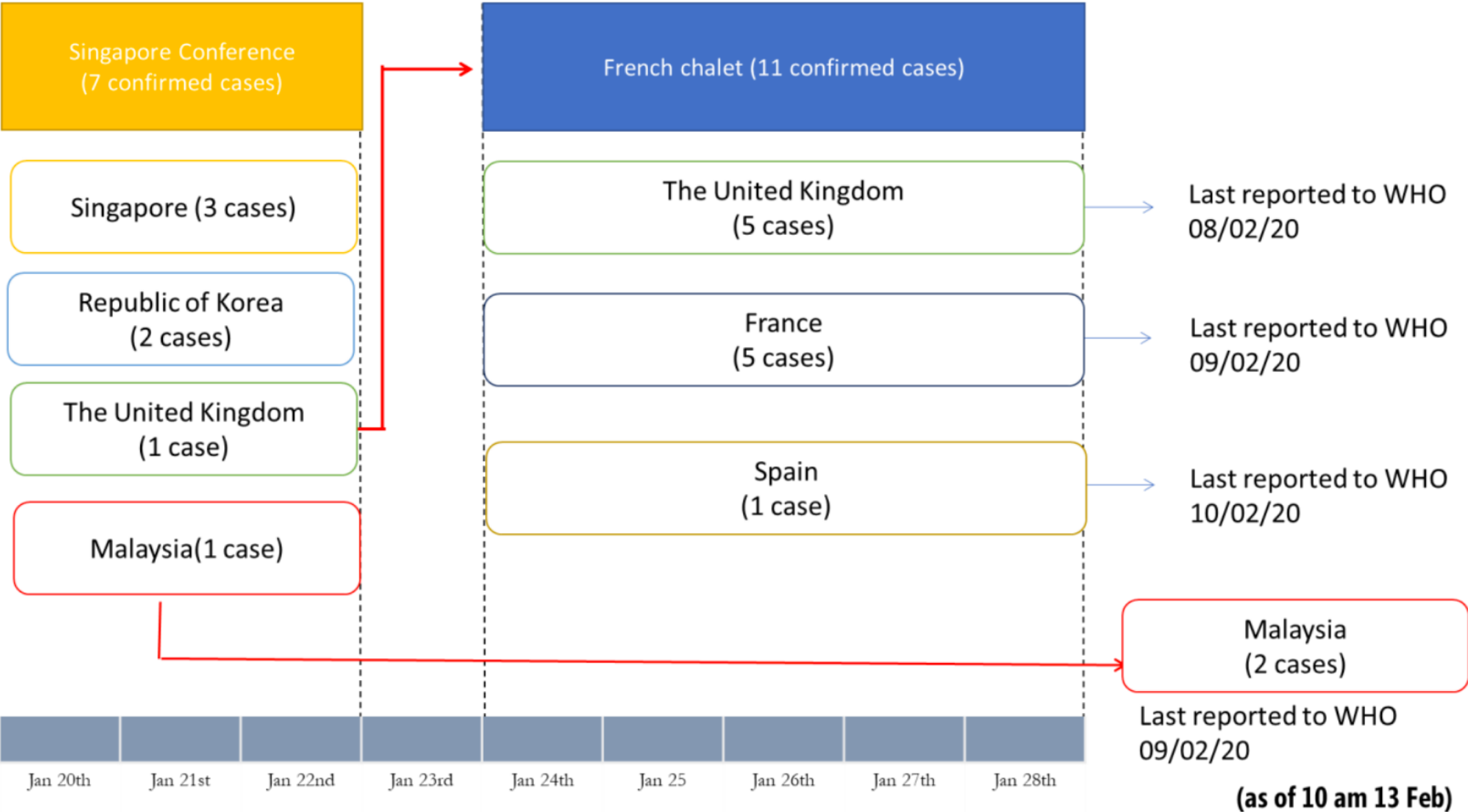


# Cases in California, 19 March 2020

- 870 cases and 16 deaths
  - At least 60 local transmissions
- Testing still lagging
- California bans gatherings of >50 people
- Disneyland announces closure
- >11 900 self monitoring who returned to the U.S. through LAX or SFO
- 49 local health jurisdictions involved in self monitoring
- 8 316 tests done in 21 public health labs
- 21 public health, several university labs and 2 commercial labs with test kits - moving to 5 500 tests per day

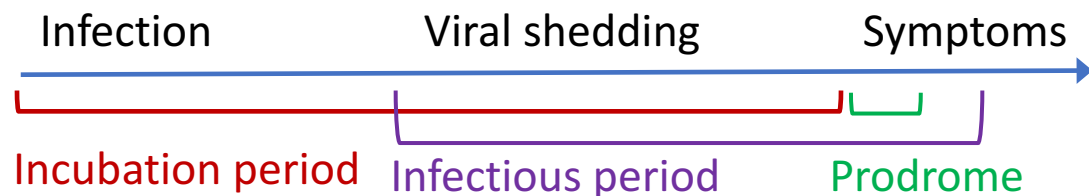


Figure 2. Description of the known transmission chain of event originating in Singapore (Event Number 1, Table 1), as of 10 am 13 Feb 2020

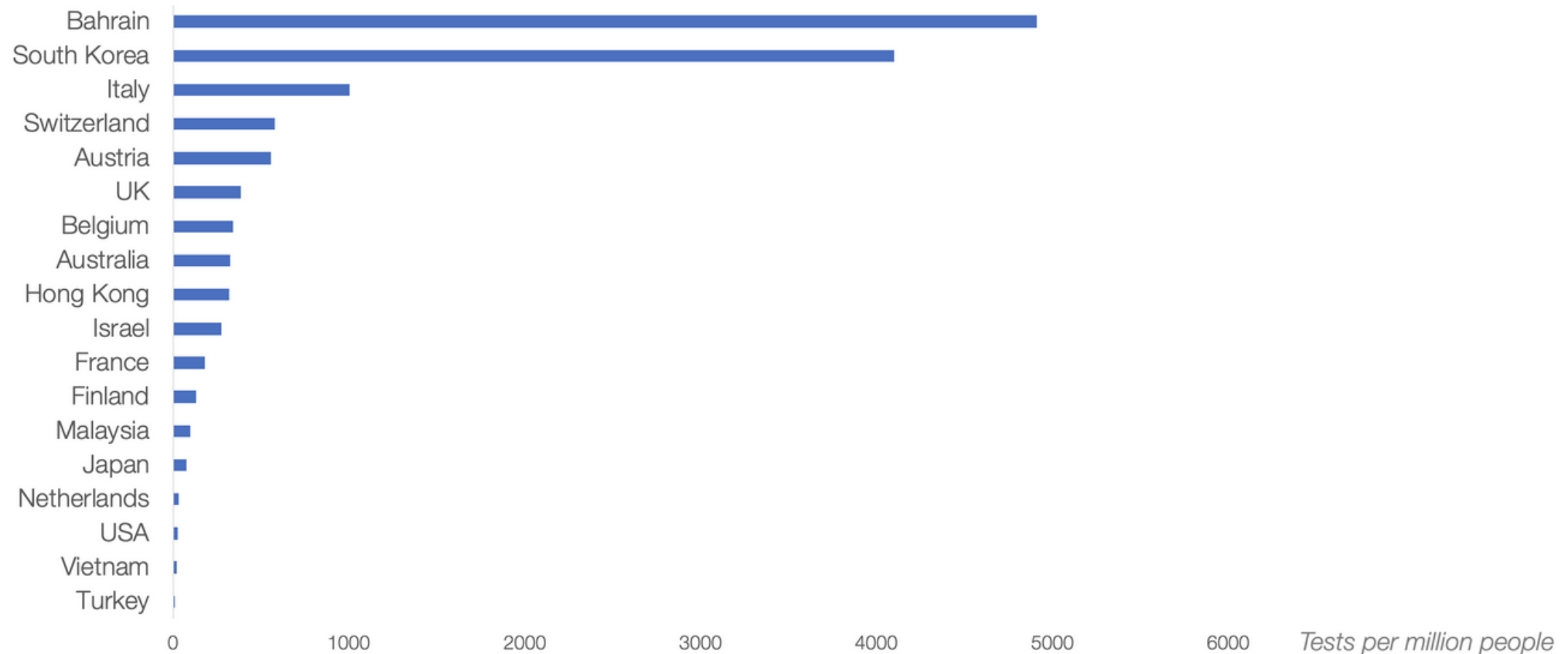


# Current understanding of clinical COVID-19

- Most likely single introduction to humans then person-to-person spread
- $R_0$  2.68 (95% confidence interval 2.47-2.86)
- Doubling time 6.4 days
- Incubation period 5.2 days (may be as long as 14)
- Median age 49-56 years, cases very rare in infants and children
- Virus shedding can occur 24-48 hours before onset of symptoms and continues for 7-12 days in mild/moderate, >14 days in severe disease
- Nonspecific symptoms: fever and dry cough in majority, one-third dyspnea
- 5% of patients with develop ARDS and require intensive care, 20% may need hospitalization for clinical reasons
  - Particularly true for those with comorbid conditions, like diabetes or hypertension



# COVID-19 testing per million inhabitants by country\*



\*As of 9 March 2020

Source: Tomas Pueyo analysis from data aggregated by Worldometers: <https://www.worldometers.info/coronavirus/covid-19-testing/>  
Per country sources available at Worldometers or at:  
<https://docs.google.com/spreadsheets/d/17YyCmjb2Z2QwMiRRwAb7W0vQoEAIL9Co0ARsl03dSlw/edit#gid=508476959>

# New therapeutics and vaccine

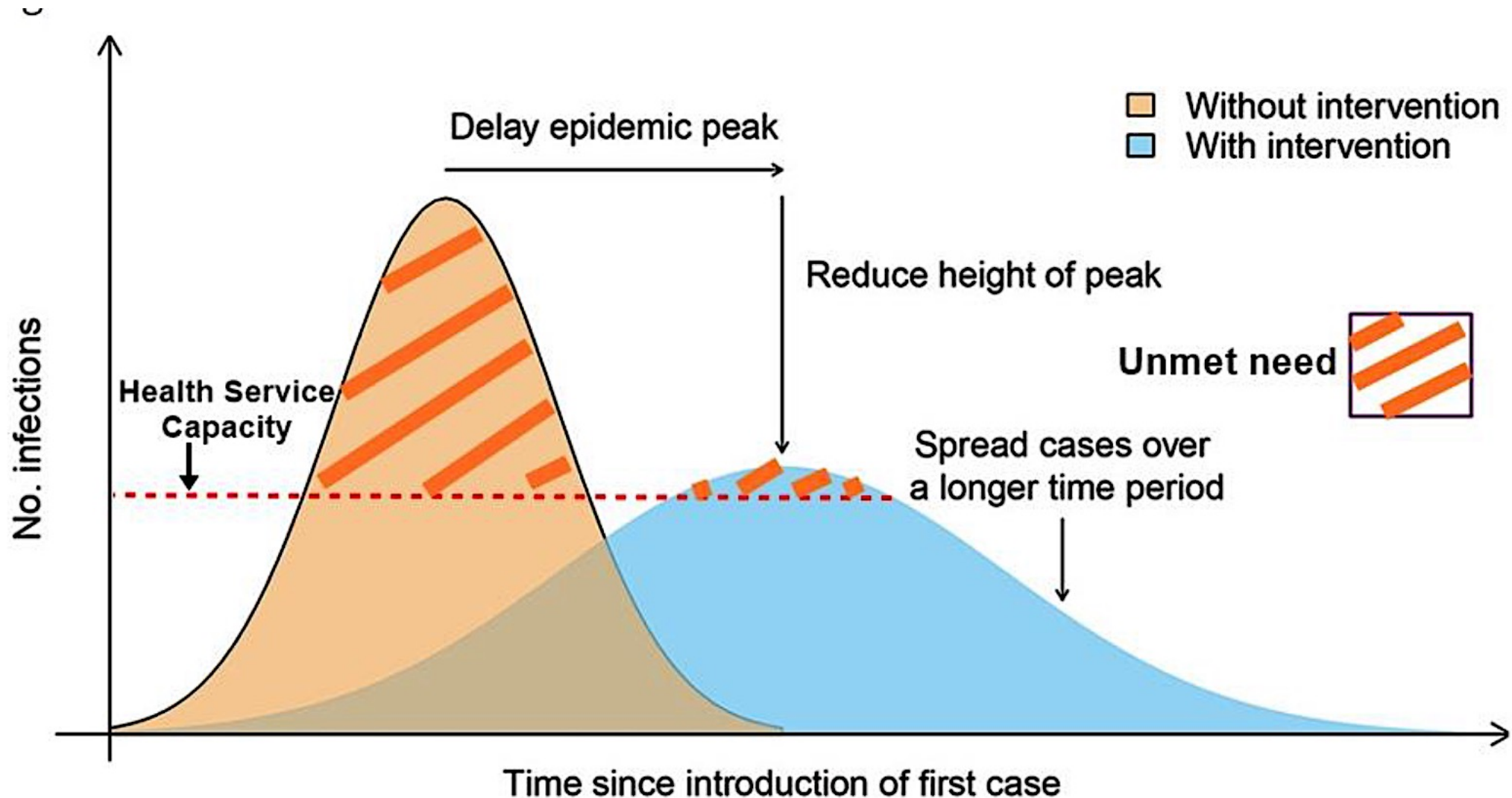
- Remdesivir (Gilead)
  - Broad spectrum antiviral compound with in vitro activity against SARS-CoV-2 and MERS
  - Nucleotide analogue
  - Phase 2 trials have begun at University of Nebraska National Quarantine Unit, where sickest COVID-19 patients evacuated from Asia are hospitalized
- Lopinivir/ritonavir combination therapy under study in China
  - Targets SARS-CoV-2's protease enzyme
  - RCT found no effect (18 March)
- Moderna Therapeutics shipped first vials of a COVID-19 vaccine to NIAID for initial testing on February 25 (one of three candidate vaccines)
  - 42 days after initial sequencing were made available
- NIAID will likely begin early clinical safety trials in April
  - It will take 1.5 years to fully test

Note: there are 94 trials registered at [clinicaltrials.gov](https://clinicaltrials.gov) and 423 at ICTRP

## Two strategic goals

- Limit new cases by decreasing  $R_e$ , the effective reproductive number
- Flatten and prolong the outbreak to (1) assure adequacy of health care resources and (2) buy time for antivirals and eventually vaccine

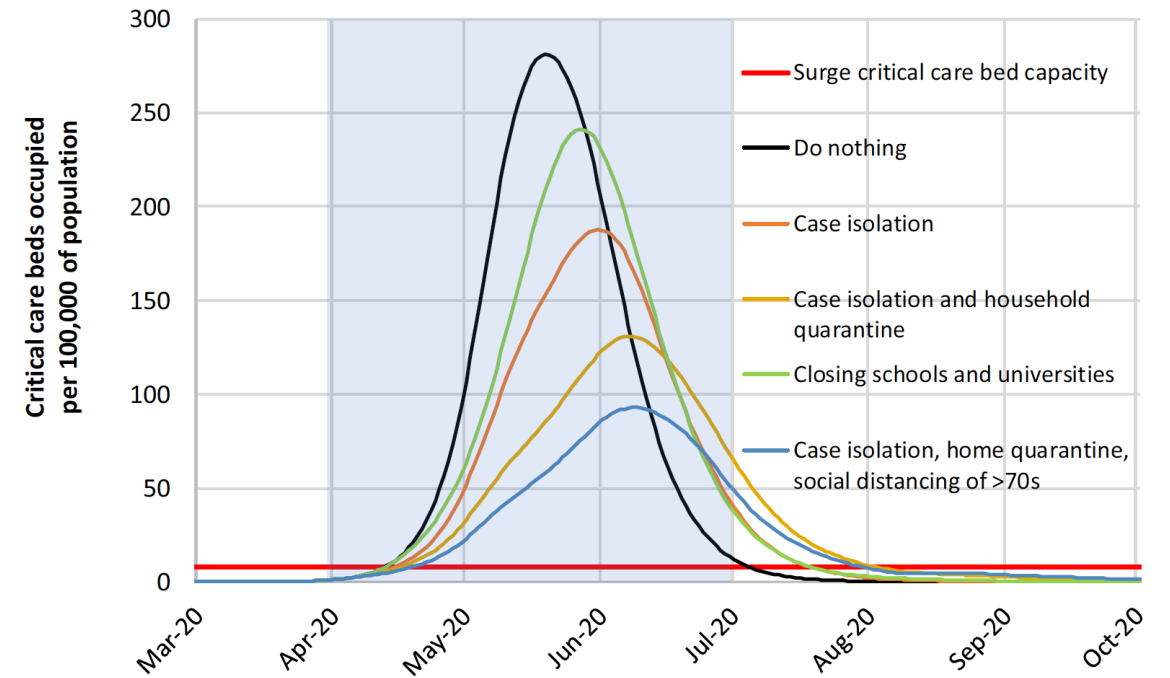
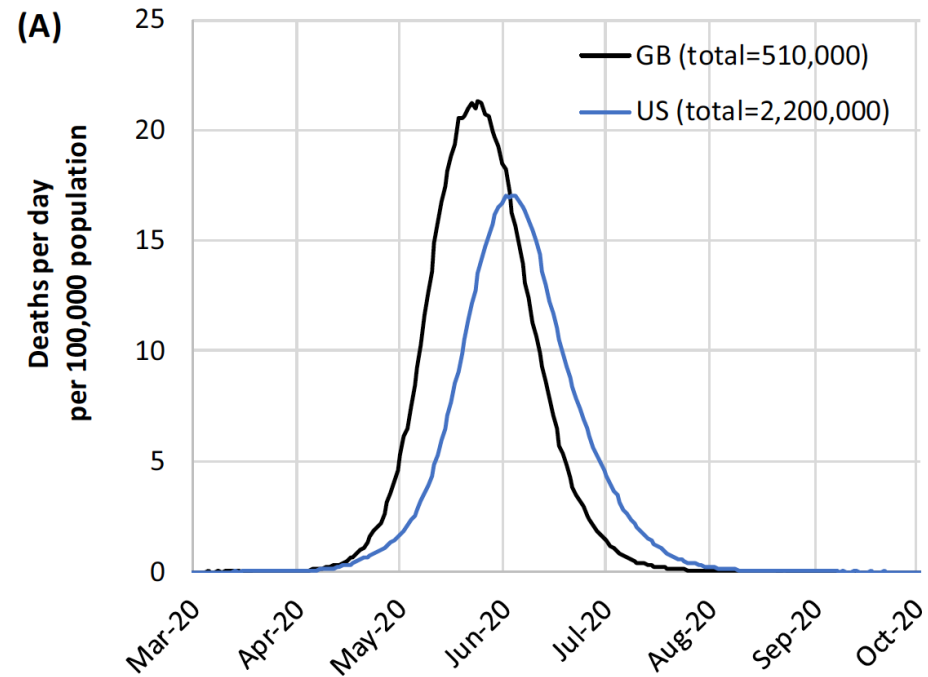
# Effects of pandemic mitigation on health care needs





# Modeling outcomes

Projected daily mortality due to COVID-19, US and UK



Critical care bed capacity for COVID-19 by mitigation strategies, UK

# Will it work?

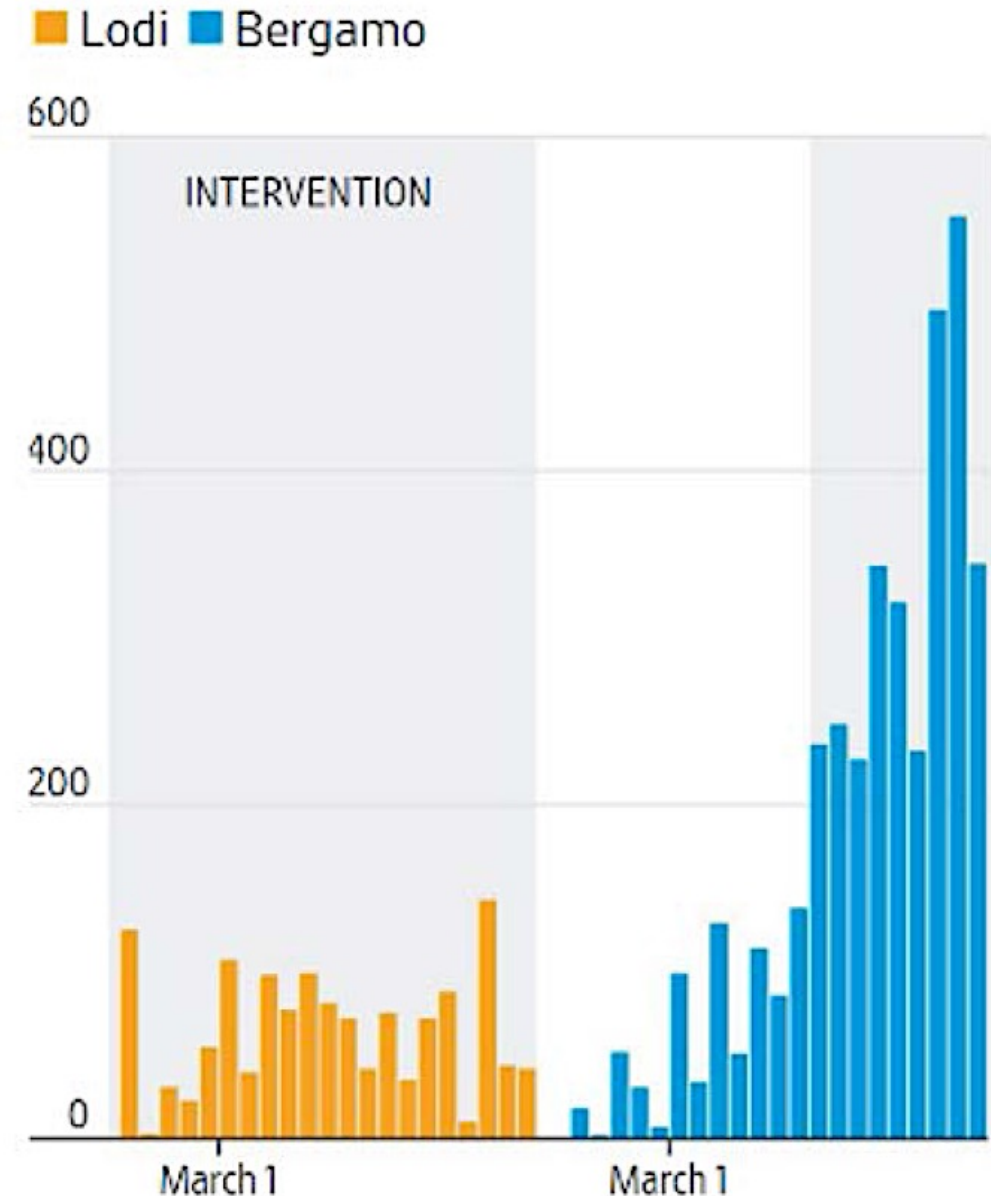
- Two adjacent Italian provinces in Lombardy region
- One (Lodi) began shelter-in-place on 26 February
- Other (Bergamo) began shelter-in-place on 9 March
- Empirical evidence that shelter in place orders can blunt transmission and new disease

STATISTICHE SUL CORONAVIRUS

## Coronavirus, i dati di Lodi lo dimostrano: le misure di «lockdown» rallentano il contagio

Negli ultimi tre giorni, in particolare dal 6 al 9 marzo, in provincia di Lodi il tasso di diffusione del contagio ha rallentato la sua corsa rispetto alle settimane precedenti

Figure 1. COVID-19 cases in Lodi and Bergamo regions in Italy



# How will this end?

- Containment – didn't happen
  - Keep large bulk of infection in China (currently 89%)
  - But large new clusters in Iran, Italy and South Korea with regional spread
  - New clusters of transmission will aggressive follow up, isolation and quarantine
  - Spring weather may give us a break
  - Key: rapid response to suspected cases
  - Can Italy and the EU contain their outbreaks?
- Pandemic spread – this is where we are now
  - Spread outside of China and sustained person-to-person transmission in other countries
    - Iran, Italy and South Korea
    - U.S. (New York, Washington, California)
  - Attack rate somewhere between <1% and 20% (40-70% in worst case scenarios with no controls)
  - Potentially very taxing on healthcare system (5% with critical disease)
  - Endemic cause of viral pneumonia?
  - Summer Olympics in Tokyo – what will happen?



smartwater

GRAND LAKE

DOUBLE FEATURE COMING SOON:  
DEATH OF THE CORONAVIRUS  
PLUS, END OF DONALD TRUMP