EPIDEMIOLOGY OF CORONA

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PROFESSOR OF INFECTIOUS DISEASE

- Human coronaviruses (HCoVs) have long been considered inconsequential pathogens, causing the "common cold" in otherwise healthy people.
- In the 21st century, 2 highly pathogenic HCoVs—severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)—emerged from animal reservoirs to cause global epidemics with alarming morbidity and mortality
- Coronaviruses are large, enveloped, positivestrand RNA viruses that can be divided into 4 genera: alpha, beta, delta, and gamma, of which alpha and beta CoVs are known to infect humans.
- Four HCoVs (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10% to 30% of upper respiratory tract infections in adults.

- Until recently, HCoVs received relatively little attention due to their mild phenotypes in humans.
- This changed in 2002, when cases of severe atypical pneumonia were described in Guangdong Province, China, causing worldwide concern as disease spread via international travel to more than 2 dozen countries

- The new disease became known as severe acute respiratory syndrome (SARS), and a beta-HCoV, named SARS-CoV, was identified as the causative agent.
- consensus emerged that bats were the natural hosts.
- Common symptoms of SARS included fever, cough, dyspnea, and occasionally watery diarrhea.

- Of infected patients, 20% to 30% required mechanical ventilation and 10% died, with higher fatality rates in older patients and those with medical comorbidities.
- Human-to-human transmission was documented, mostly in health care settings. This nosocomial spread may be explained by basic virology: the predominant human receptor for the SARS S glycoprotein, human angiotensin-converting enzyme 2 (ACE2), is found primarily in the lower respiratory tract, rather than in the upper airway.

- Receptor distribution may account for both the dearth of upper respiratory tract symptoms and the finding that peak viral shedding occurred late (≈10 days) in illness when individuals were already hospitalized.
- SARS care often necessitated aerosol generating procedures such as intubation, which also may have contributed to the prominent nosocomial spread.

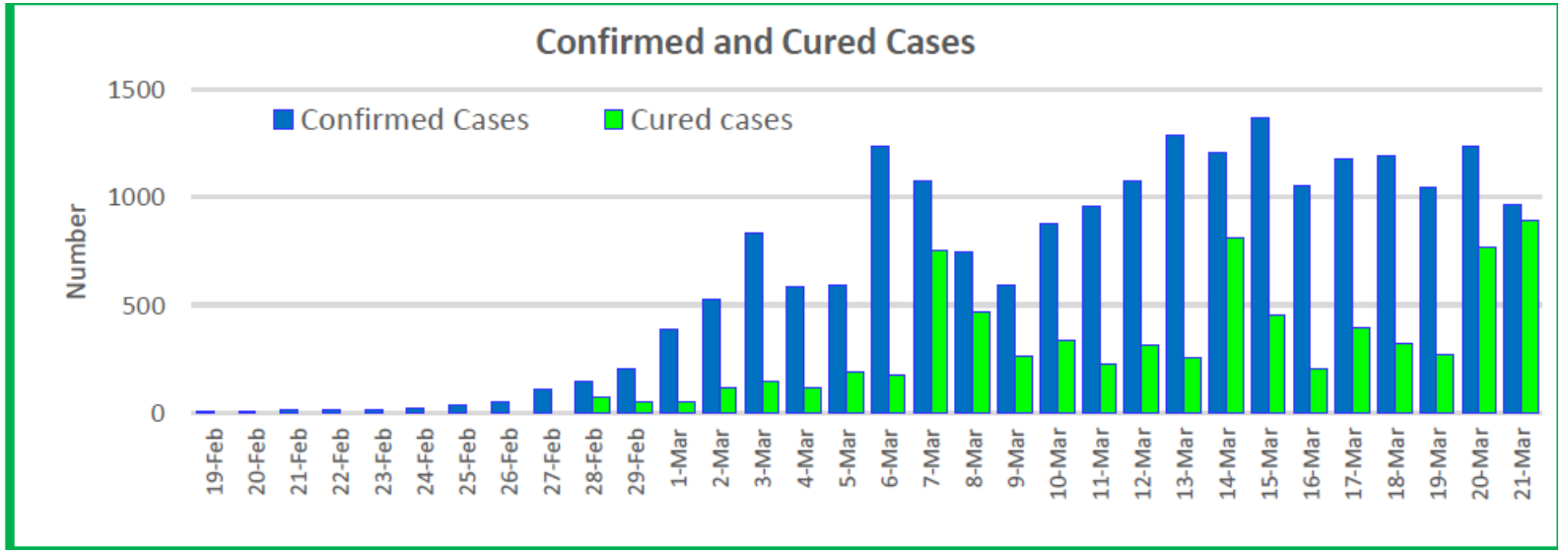
- Several important transmission events did occur in the community, such as the well-characterized mini outbreak in the Hotel Metropole in Hong Kong from where infected patrons traveled and spread SARS internationally.
- Another outbreak occurred at the Amoy Gardens housing complex where more than 300 residents were infected, providing evidence that airborne transmission of SARS-CoV can sometimes occur

- Ultimately, classic public health measures brought the SARS pandemic to an end, but not before 8098 individuals were infected and 774 died.
- The pandemic cost the global economy an estimated $30 billion to $100 billion.

- In 2012, another highly pathogenic beta-CoV made the species jump when Middle East respiratory syndrome (MERS) was recognized and MERS-CoV was identified in the sputum of a Saudi man who died from respiratory failure
- Unlike SARS-CoV, which rapidly spread across the globe and was contained and eliminated in relatively short order, MERS has smoldered, characterized by sporadic zoonotic transmission and limited chains of human spread.

- MERS-CoV has not yet sustained community spread; instead, it has caused explosive nosocomial transmission events, in some cases linked to a single superspreader, which are devastating for health care systems
- According to the World Health Organization (WHO), as of November 2019, MERS-CoV has caused a total of 2494 cases and 858 deaths, the majority in Saudi Arabia.
- The natural reservoir of MERS-CoV is presumed to be bats, yet human transmission events have primarily been attributed to an intermediate host, the dromedary camel.

- MERS shares many clinical features with SARS such as severe atypical pneumonia, yet key differences are evident.
- Patients with MERS have prominent gastrointestinal symptoms and often acute kidney failure, likely explained by the binding of the MERS-CoV S glycoprotein to dipeptidyl peptidase 4 (DPP4), which is present in the lower airway as well as the gastrointestinal tract and kidney.
- MERS necessitates mechanical ventilation in 50% to 89% of patients and has a case fatality rate of 36%


Confirmed and Cured Cases
1500
1000
500
0
Number
Confirmed Cases
Cured cases
19-Feb
20-Feb
21-Feb
22-Feb
23-Feb
24-Feb
25-Feb
26-Feb
27-Feb
28-Feb
29-Feb
1-Mar
2-Mar
3-Mar
4-Mar
5-Mar
6-Mar
7-Mar
8-Mar
9-Mar
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18-Mar
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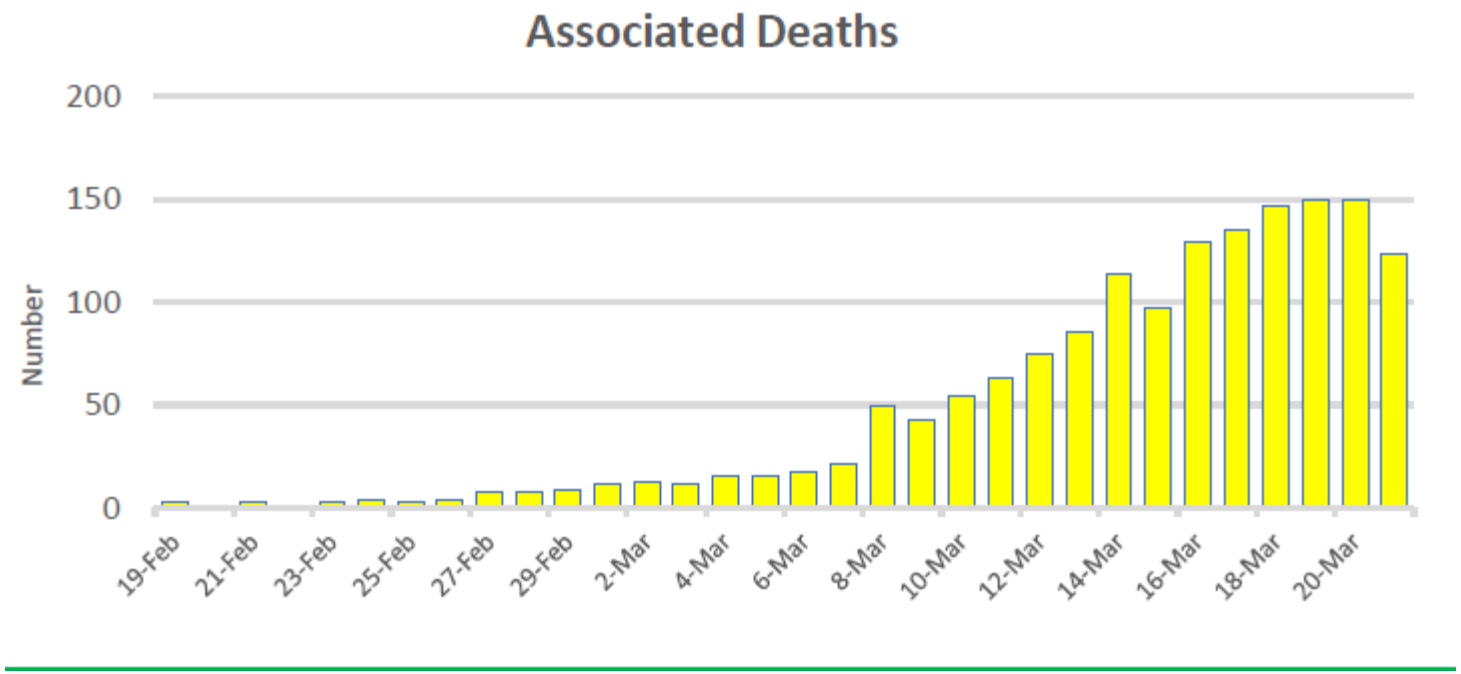
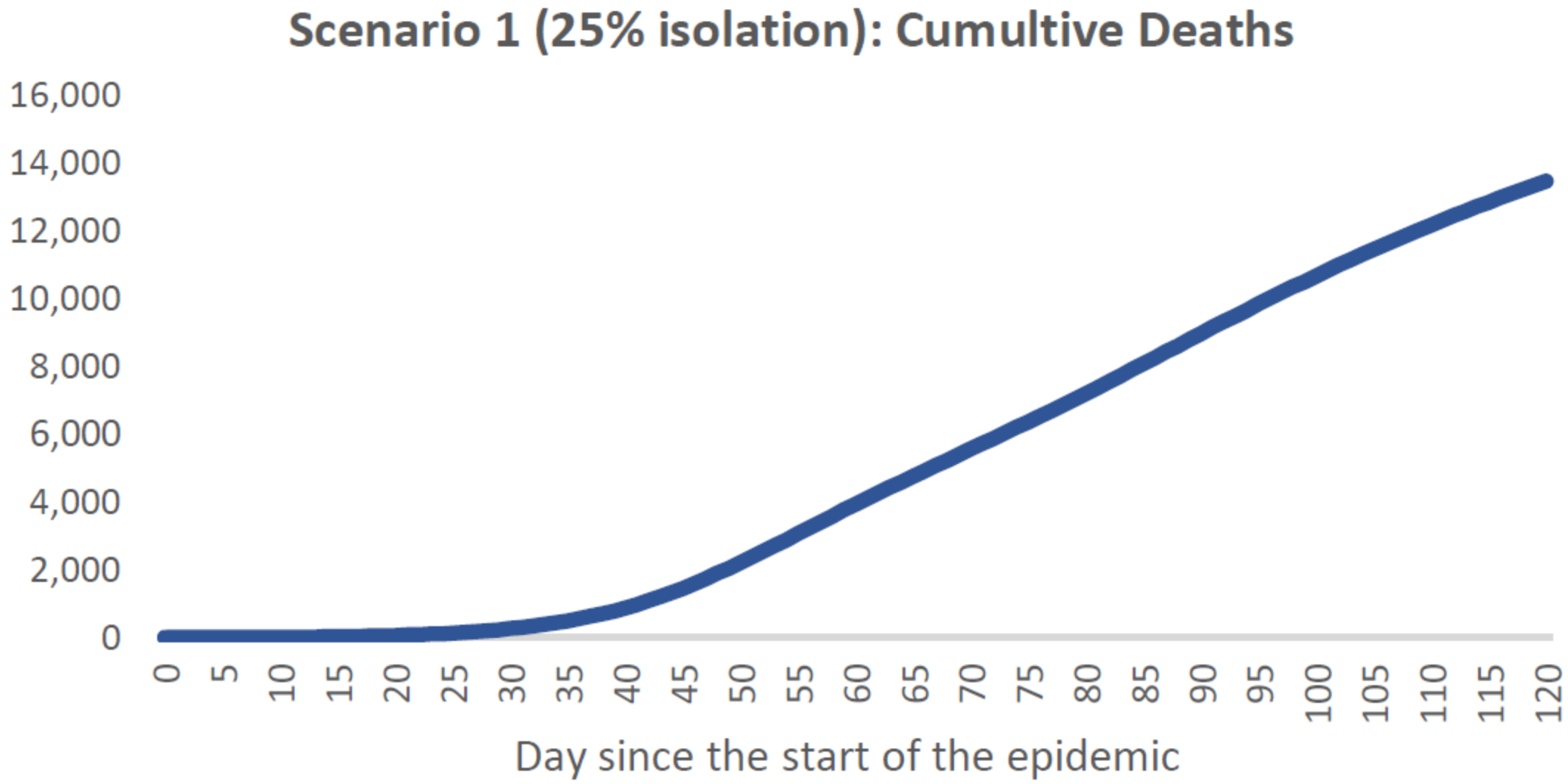
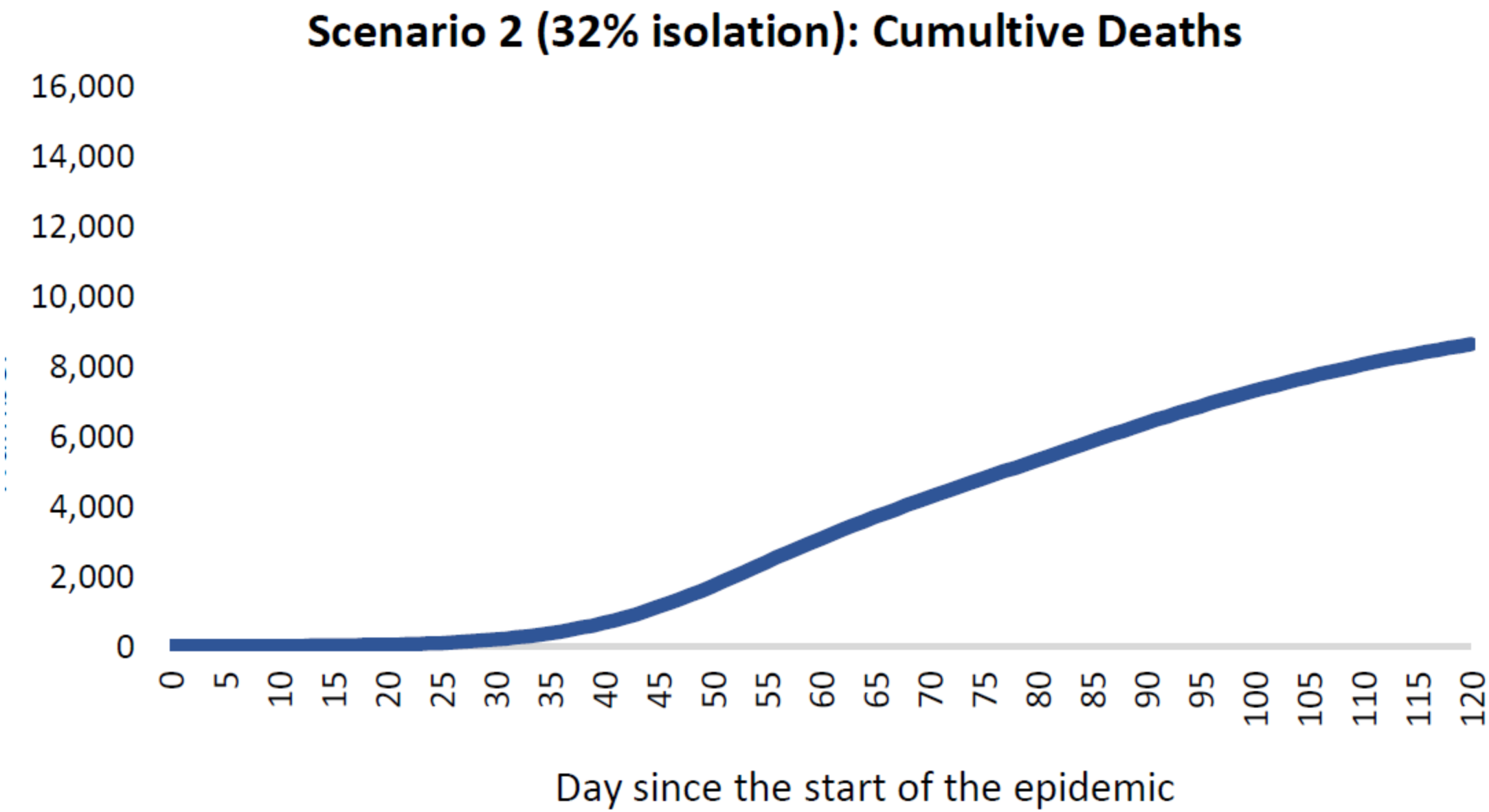
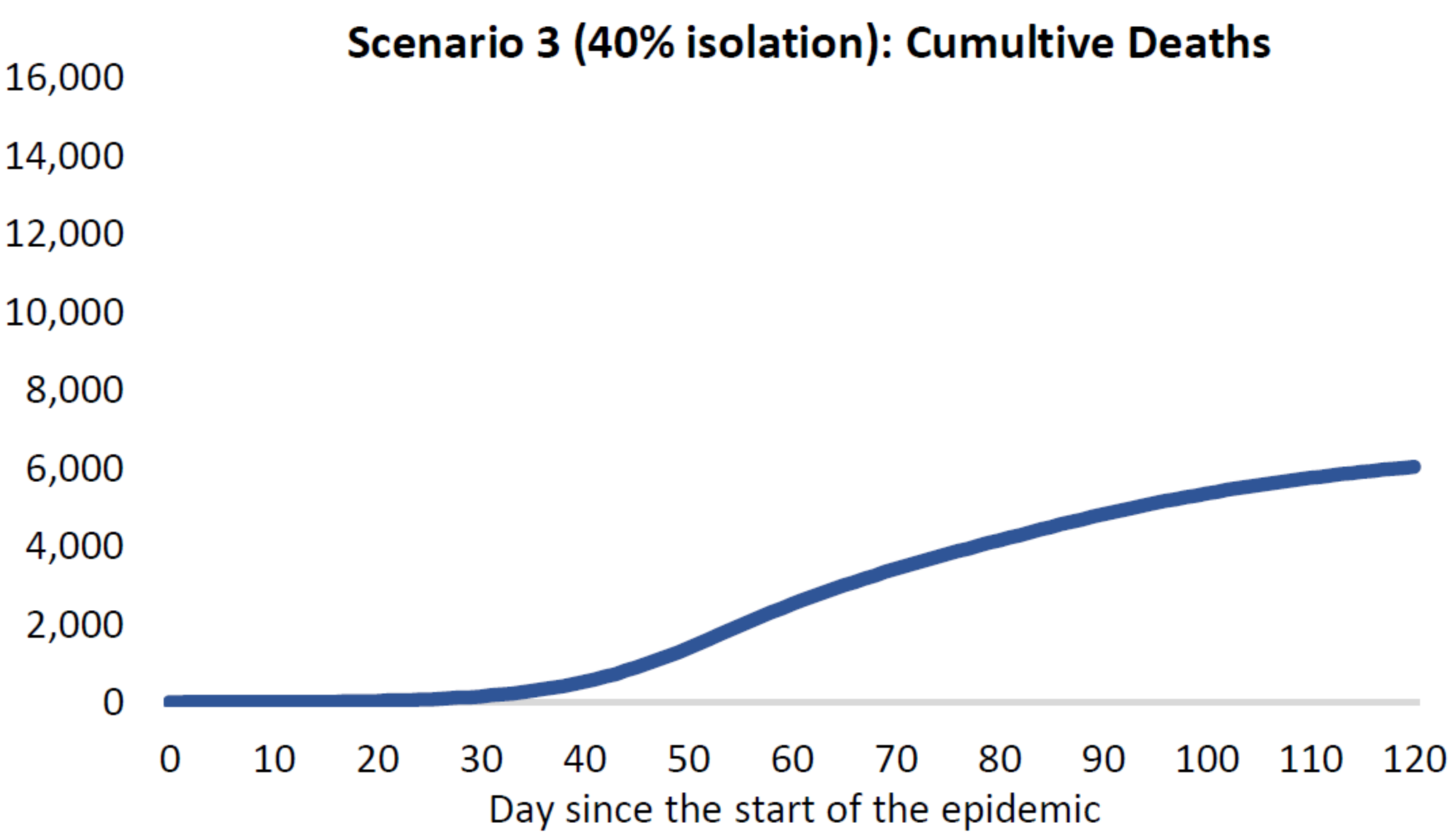
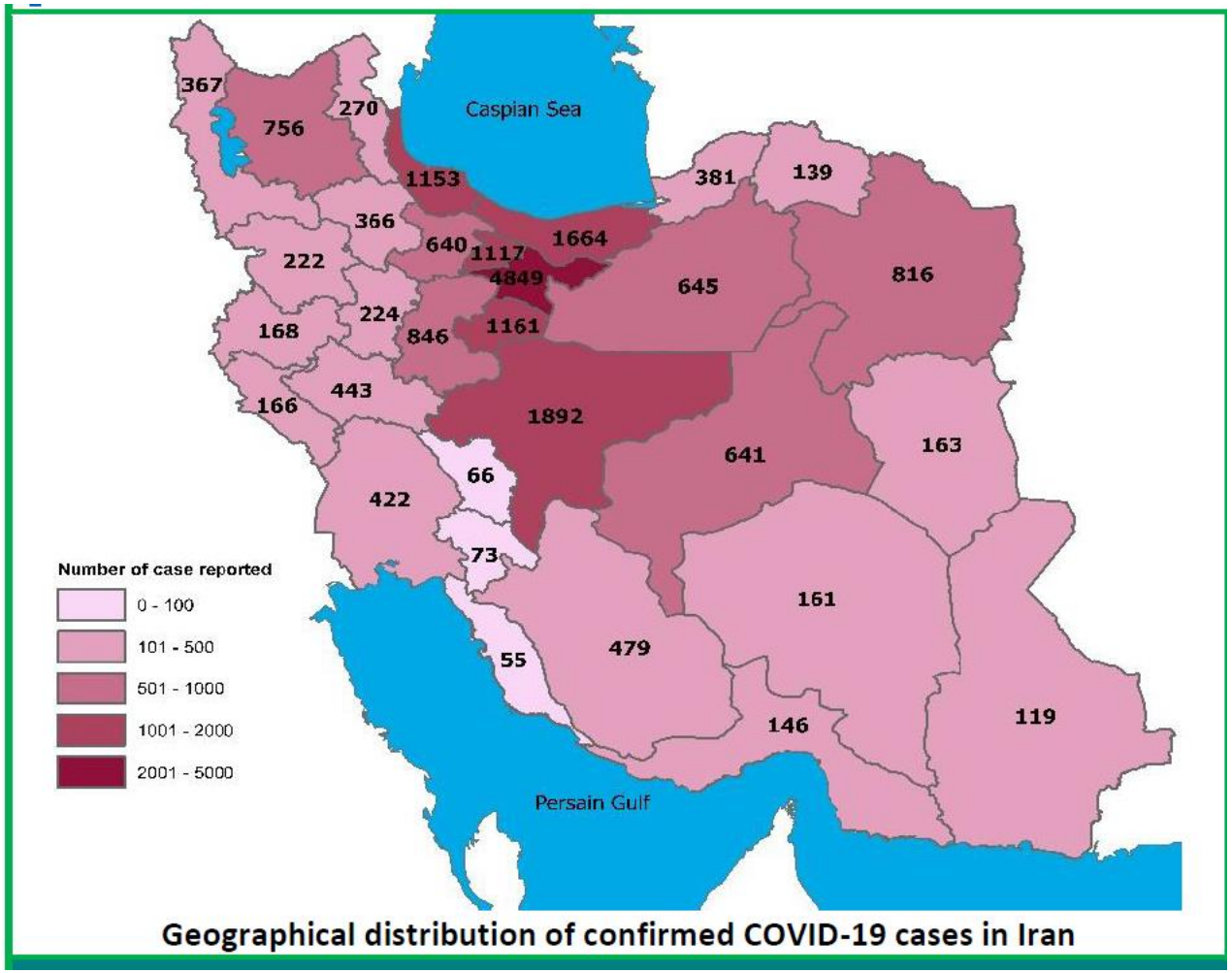
20-Mar
21-Mar


Associated Deaths
200
150
100
50
0
Number
19-Feb
21-Feb
23-Feb
25-Feb
27-Feb
29-Feb
2-Mar
4-Mar
6-Mar
8-Mar
10-Mar
12-Mar
14-Mar
16-Mar
18-Mar
20-Mar


Scenario 1 (25% isolation): Cumultive Deaths
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
120
Day since the start of the epidemic


Scenario 2 (32% isolation): Cumultive Deaths
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
120
Day since the start of the epidemic


Scenario 3 (40% isolation): Cumultive Deaths
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
0
10
20
30
40
50
60
70
80
90
100
110
120
Day since the start of the epidemic



Geographical distribution of confirmed COVID-19 cases in Iran

	Spain*		Canada**		Nederland***		China****		Italy*****		Germany[Y]	
	Total case	%	Total case	%	Total case	%	Total case	%	Total case	%	Total case	%
<20	741	0.8	220	4	173	1.1	965	2	1868	1.5	2624	2.8
20–29	4,629	5.2	658	13	974	6.2	3619	8	33,248	26.7	66,896	70.3
30–39	8,761	9.9	847	16	1251	8	38,680	87				
40–49	13,421	15.2	881	17	1582	10.1						
50–59	16,577	18.8	1023	19	2590	16.5			44,581	35.8		
60–69	14,933	16.9	855	16	2450	15.5					18,307	19.3
70–79	14,300	16.2	468	9	3013	19.8			44,830	36		
80–89	14,828	16.8	309	6	3550	22.8	1408	3			7357	7.7
Total	88,190	100.0	5261		15723	100	72,314	100	124,527	100	94,850	100

Reporting country	Total confirmed cases	Total deaths	Case fatality rate
France	94,382	14,374	15.23
Italy	156,363	19,901	12.73
The United Kingdom	84,283	10,612	12.59
Belgium	29,647	3600	12.14
Netherlands	25,587	2737	10.70
Spain	166,019	16,972	10.22
Sweden	10,483	899	8.58
İran	71,686	4474	6.24
Brazil	20,727	1124	5.42
China	83,597	3351	4.01
USA	524,514	20,444	3.90
Switzerland	25,220	858	3.40

Box. Key Findings From the Chinese Center for Disease Control and Prevention Report

72 314 Cases (as of February 11, 2020)

- Confirmed cases: 44 672 (62%)
- Suspected cases: 16 186 (22%)
- Diagnosed cases: 10 567 (15%)
- Asymptomatic cases: 889 (1%)

Age distribution (N = 44 672)

- ≥80 years: 3% (1408 cases)
- 30-79 years: 87% (38 680 cases)
- 20-29 years: 8% (3619 cases)
- 10-19 years: 1% (549 cases)
- <10 years: 1% (416 cases)

Spectrum of disease (N = 44 415)

- Mild: 81% (36 160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

Case-fatality rate

- 2.3% (1023 of 44 672 confirmed cases)
- 14.8% in patients aged ≥80 years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0% in critical cases (1023 of 2087)

Health care personnel infected

- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

JAMA | Original Investigation

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

Safiya Richardson, MD, MPH; Jamie S. Hirsch, MD, MA, MSB; Mangala Narasimhan, DO; James M. Crawford, MD, PhD; Thomas McGinn, MD, MPH; Karina W. Davidson, PhD, MASc; and the Northwell COVID-19 Research Consortium

RESULTS A total of 5700 patients were included (median age, 63 years [interquartile range {IQR}, 52-75; range, 0-107 years]; 39.7% female). The most common comorbidities were hypertension (3026; 56.6%), obesity (1737; 41.7%), and diabetes (1808; 33.8%). At triage, 30.7% of patients were febrile, 17.3% had a respiratory rate greater than 24 breaths/minute, and 27.8% received supplemental oxygen. The rate of respiratory virus co-infection was 2.1%. Outcomes were assessed for 2634 patients who were discharged or had died at the study end point. During hospitalization, 373 patients (14.2%) (median age, 68 years [IQR, 56-78]; 33.5% female) were treated in the intensive care unit care, 320 (12.2%) received invasive mechanical ventilation, 81 (3.2%) were treated with kidney replacement therapy, and 553 (21%) died. Mortality for those requiring mechanical ventilation was 88.1%. The median postdischarge follow-up time was 4.4 days (IQR, 2.2-9.3). A total of 45 patients (2.2%) were readmitted during the study period. The median time to readmission was 3 days (IQR, 1.0-4.5) for readmitted patients. Among the 3066 patients who remained hospitalized at the final study follow-up date (median age, 65 years [IQR, 54-75]), the median follow-up at time of censoring was 4.5 days (IQR, 2.4-8.1).

Comorbidities	
Total No.	5700
Cancer	320 (6)
Cardiovascular disease	
Hypertension	3026 (56.6)
Coronary artery disease	595 (11.1)
Congestive heart failure	371 (6.9)
Chronic respiratory disease	
Asthma	479 (9)
Chronic obstructive pulmonary disease	287 (5.4)
Obstructive sleep apnea	154 (2.9)
Immunosuppression	
HIV	43 (0.8)
History of solid organ transplant	55 (1)
Kidney disease	
Chronic[c]	268 (5)
End-stage[d]	186 (3.5)
Liver disease	
Cirrhosis	19 (0.4)
Chronic	
Hepatitis B	8 (0.1)
Hepatitis C	3 (0.1)
Metabolic disease	
Obesity (BMI ≥30)	1737 (41.7)
No.	4170
Morbid obesity (BMI ≥35)	791 (19.0)
No.	4170
Diabetes[e]	1808 (33.8)

(continued)

CASE FATALITY

- A yet unanswered question that adds to uncertainty around the outbreak involves the case-fatality rate (CFR), defined as the percentage of deaths among all cases.
- Presently, global mortality is reported at 4.7% but this varies widely by location from a high of 10.8% in Italy to a low of 0.7% in Germany.
- Several factors influence the CFR including a reliable estimate of the total number of cases.

IS PCR ALWAYS POSITIVE?WHAT IS THE MEANING OF ANEGATIVE PCR?

- Given the lack of a reference standard for diagnosing COVID-19, the sensitivity and specificity of diagnostic testing are unknown.
- In addition, inadequate sample collection may reduce test sensitivity
- Individuals with chest computed tomography findings compatible withCOVID-19,and a negative reverse transcriptase (RT)–PCR result for SARSCoV-2, tested positive on subsequent testing, suggesting that certain patients (eg,with compatible radiological findings) might require repeat testing with specimens collected from multiple sites in the respiratory tract

- It is likely that lower respiratory samples (eg,minibronchial alveolar lavage) are more sensitive than a nasopharyngeal swab
- It is important to emphasize that, depending on the clinical presentation, a negative RT-PCR result does not exclude COVID-19.

CAN PATIENTS BECOME REINFECTED?

- Reports from China and Japan have indicated that some patients with COVID-19 who were discharged from the hospital after a negative RT-PCR result were readmitted and subsequently tested positive on RT-PCR
- It is unclear from the available information if these were true reinfections or the tests were falsely negative at the time of initial discharge.
- However, while other coronaviruses demonstrate evidence of reinfection, this usually does not happen form any months or years. Therefore, it is unlikely that these were true cases of reinfection.

- Some reassuring evidence comes from a challenge study among rhesus macaques. After initial challenge and clearance ofSARS-CoV-2, the animals were rechallenged with the virus but were not infected.

HOW LONG DOES IMMUNITY LAST?

- Presently, there is no validated immune correlate of protection for SARSCoV-,ie,antibody level or another immunological marker associated with protection from infection nor disease.
- In a study that included 82 confirmed and 58 probable cases of COVID-19 from China, the median duration of IgM detection was 5 days (interquartile range, 3-6), while IgG was detected at a median of 14 days (interquartile range, 10-18) after symptom onset

- Data from SARS-CoV-1 indicate that titers of IgG and neutralizing antibodies peaked at 4 months after infection, with a subsequent decline through at least 3 years after infection.

HOW DOES SARS-COV-2 SPREAD?

- Current evidence suggests that SARS-CoV-2isprimarily transmitted through droplets (particles5-10μm in size).
- Person-to-person transmission occurs when an individual with the infection emits droplets containing virus particle swhile coughing, sneezing, and talking.
- These droplets land on the respiratory mucosa or conjunctiva of another person, usually within a distance of 6 ft (1.8m) but perhaps farther

- The droplets can also settle on stationary or movable objects and can be transferred to another person when they come in contact with these fomites
- The available evidence suggests that the virus can remain infectious on inanimate surfaces at room temperature for up to9 days.
- This time is shorter at temperatures greater than 30° C.

- Transmission through aerosols, particles smaller than 5 μm, can also occur under specific circumstances such as endotracheal intubation,bronchoscopy, suctioning, turning the patient to the prone position, or disconnecting the patient from the ventilator.

WHEN CAN SOCIAL DISTANCING MEASURES BE LIFTED?

- social-distancing measures can help reduce the overall number of infections and help spread out cases over a longer period of time, thus allowing health systems to better manage the surge of additional patients.

- long-term social distancing can have detrimental effects on physical and mental health outcomes as well as the economy.

- 1) An aggressive program of testing to identify asymptomatic and mild cases combined with proactive contact tracing and early isolation as well as quarantine of contacts
- 2) A focus on reducing home-based transmission.
- 3) Even a treatment that only shortens an intensive care unit stay by 20% to 30% can have a substantial benefit on health system capacity

WHEN WILL A VACCINE BE AVAILABLE?

- The ultimate strategy for controlling this pandemic will depend on a safe and efficacious vaccine against SARS-CoV-2.
- However, only 3 vaccine candidates are currently in phase 1 human trials: a messenger RNA vaccine and 2 adenovirus vector-based vaccines.
- The estimated timeline for availability of an initial vaccine is between early and mid-2021.