COVID-19 Pandemic
Epidemiological and Clinical overview

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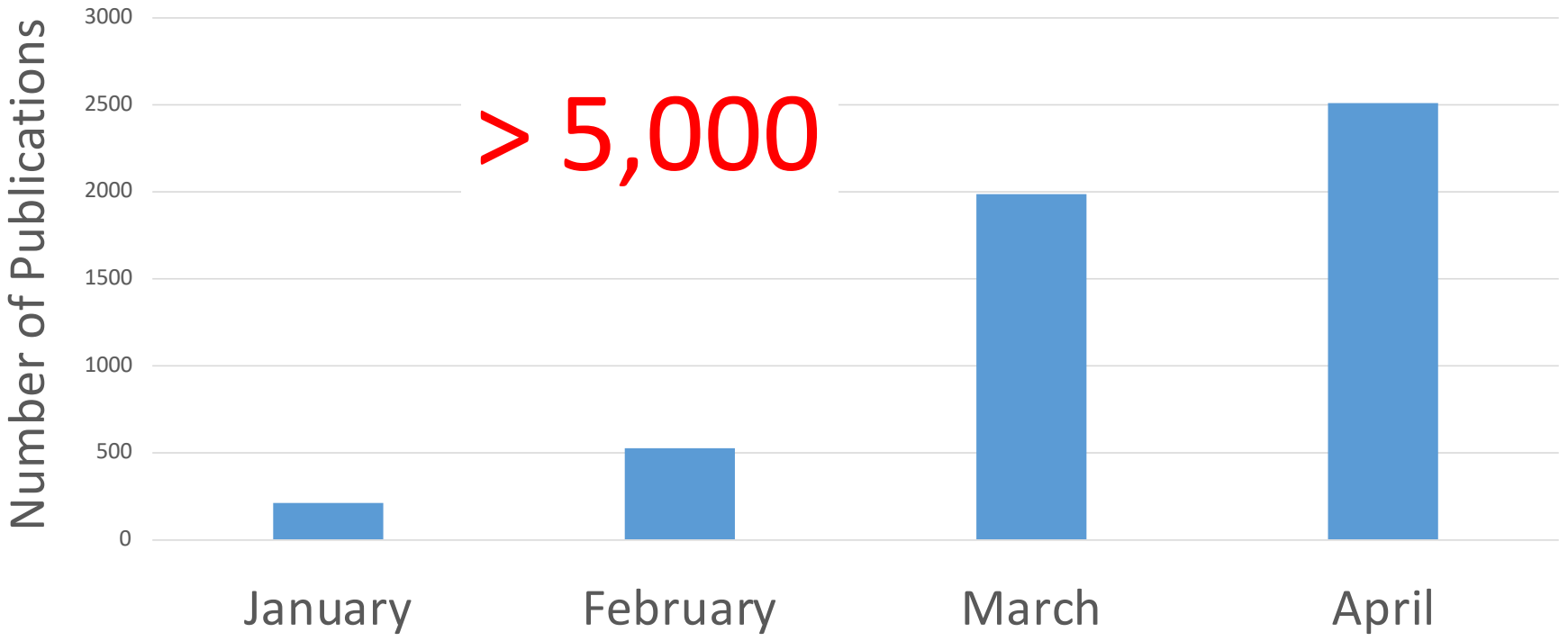
Disclosure: Member of Cleveland Clinic COVID-19 Research prioritization committee

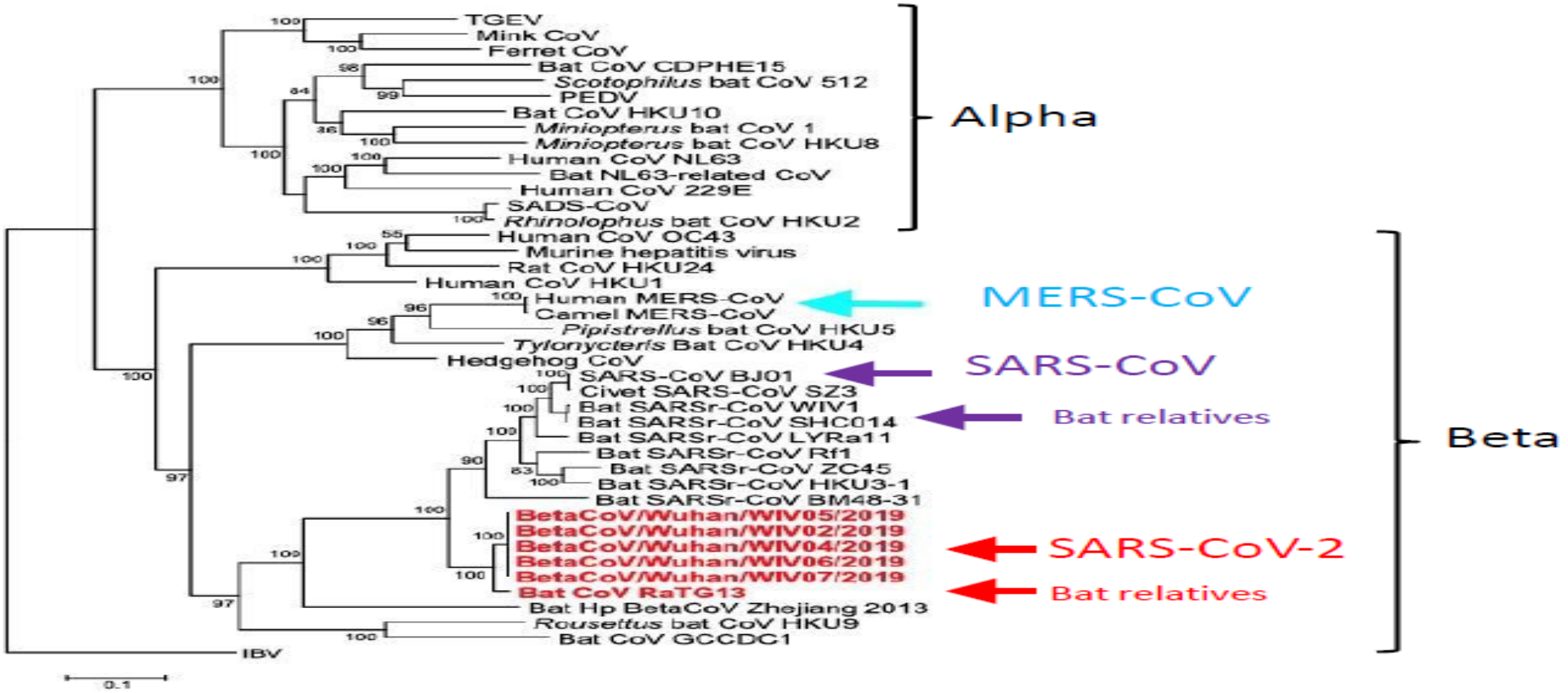
COVID-19 Pub Med Publications since January 2020



Outline

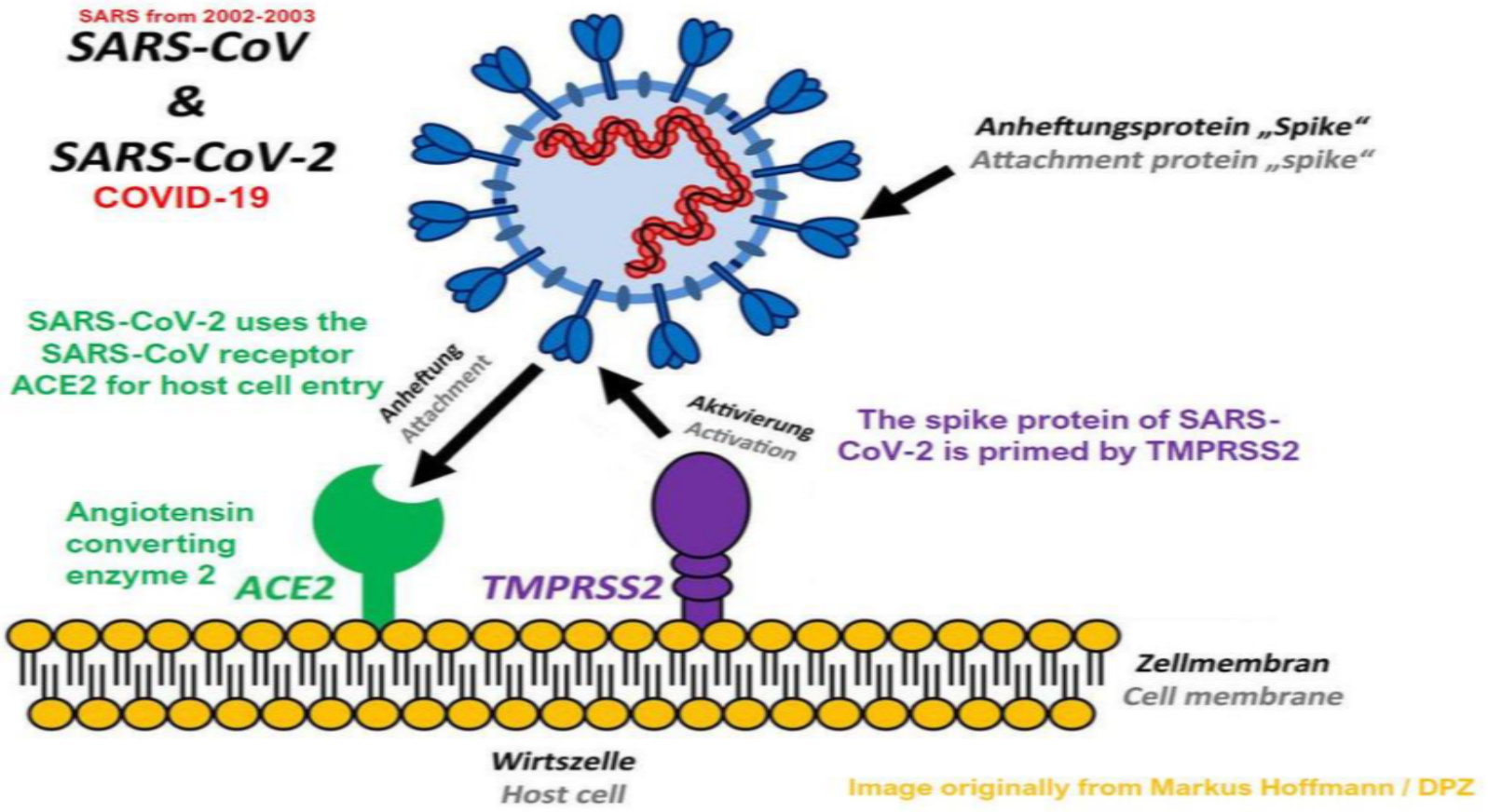
- The virus
- Pathogenesis
- Comparison to other coronavirus outbreaks & a few other infections
- Epidemiology
- Clinical Presentation
- Diagnosis
- Prevention
- Treatment
- Road to recovery

Meet the enemy



https://www.sciencemag.org/news/2020/01/mining-coronavirus-genomes-clues-outbreak-s-origins

Where does it start invading the body?



Hoffmann M. Cell 2020Cell, DOI: 10.1016/j.cell.2020.02.052

Comparing SARS – MERS – COVID-19

	SARS	MERS	COVID-19
Years	2002 - 2003	2012 →	2019/20 → ?
Pandemic duration	8 months	Sporadic	4.5 months*
Country of onset	China	Saudi Arabia	China
Animal hosts	Bats → civets	Bats → camels	Bats → civets?
Countries affected	26	27	210*
Cases	8,437	2,499	2,235,837*
Deaths (%)	813 (10%)	861 (35%)	153,516 (6.7%)*

*As of April 17th, 2020

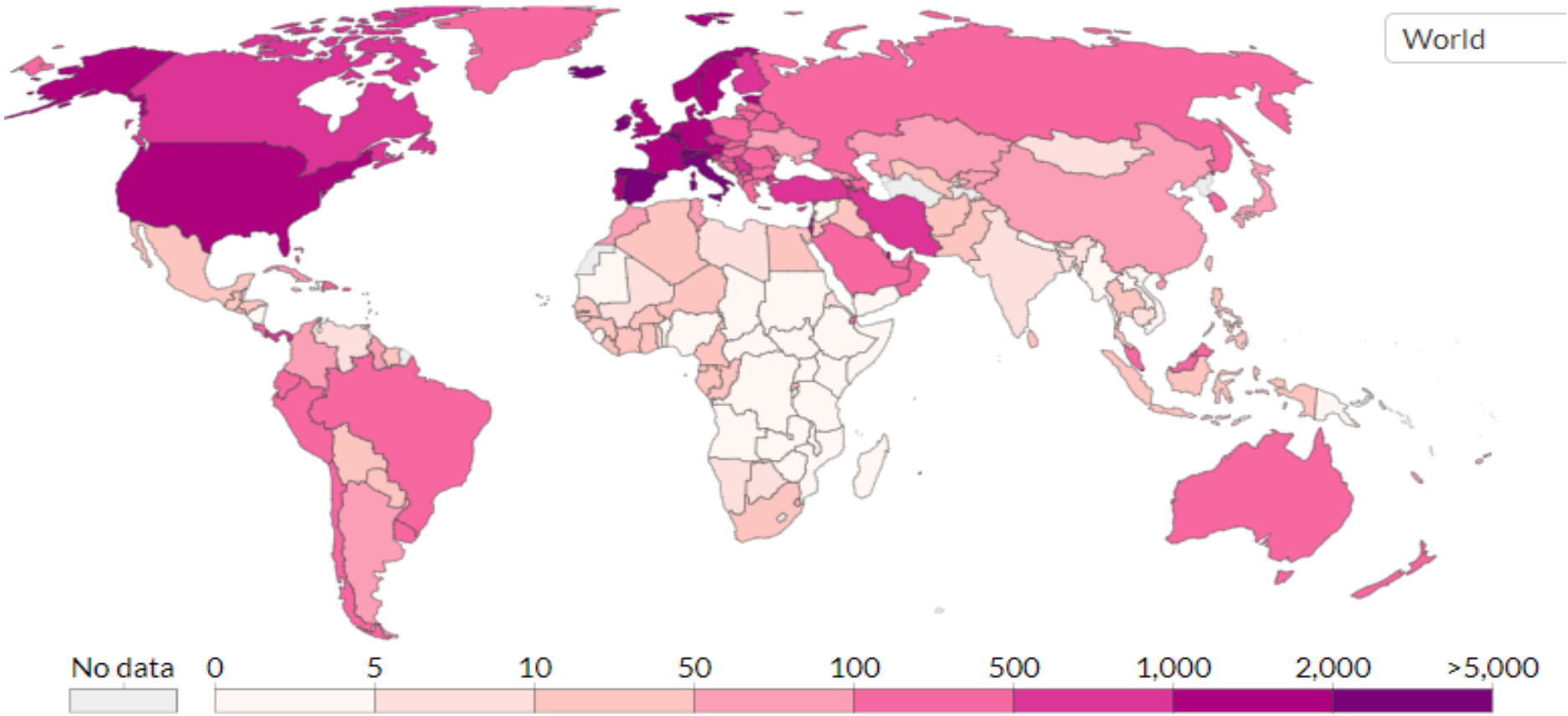
Comparing SARS – MERS – COVID-19

SARS	MERS	COVID-19
8 months to infect 8000 & kill 800	12 months to infect 100 & kill 30	4.5 months to infect 2.2 million & kill 150,000
		

How Contagious is SARS-CoV-2?

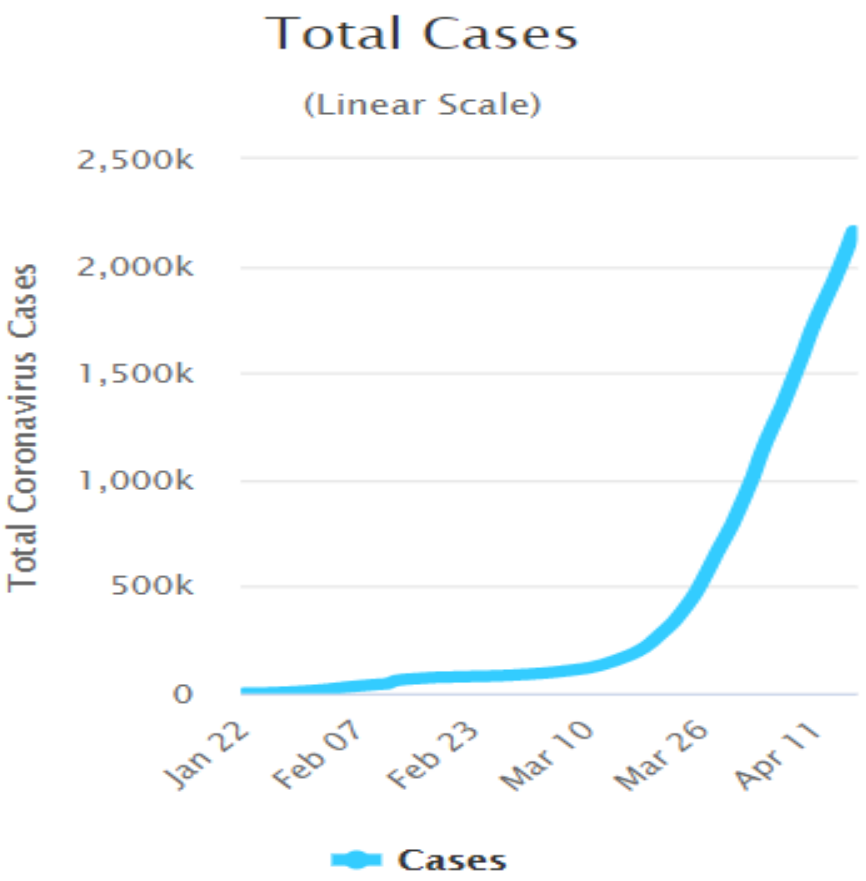
	Reproductive number "R_0 ": How many people can one infected person transmit the infection to a susceptible population?	Secondary household attack rate
SARS-CoV-2	2-3	10%
Influenza	1.2	1-38%
Measles	12-18	≥ 90%
Varicella zoster	10	85%
Tuberculosis	10 per year	≥ 50%

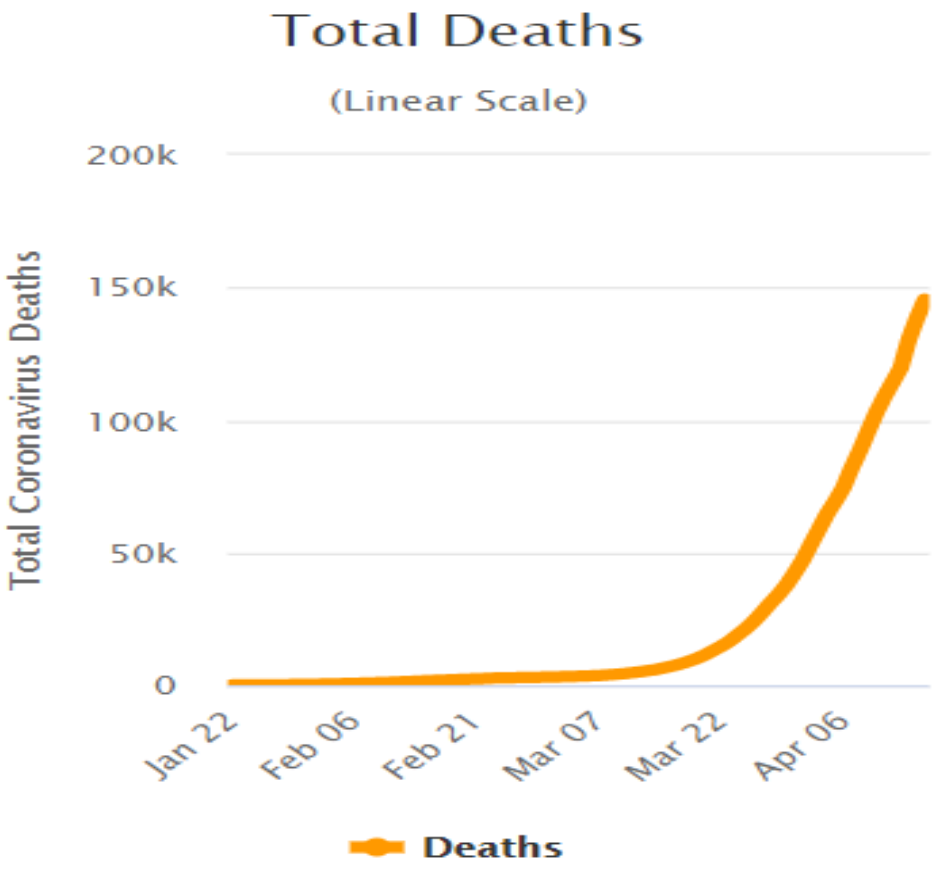
Global Epidemiology



https://ourworldindata.org/grapher/total-confirmed-cases-of-covid-19-per-million-people

Global Epidemiology





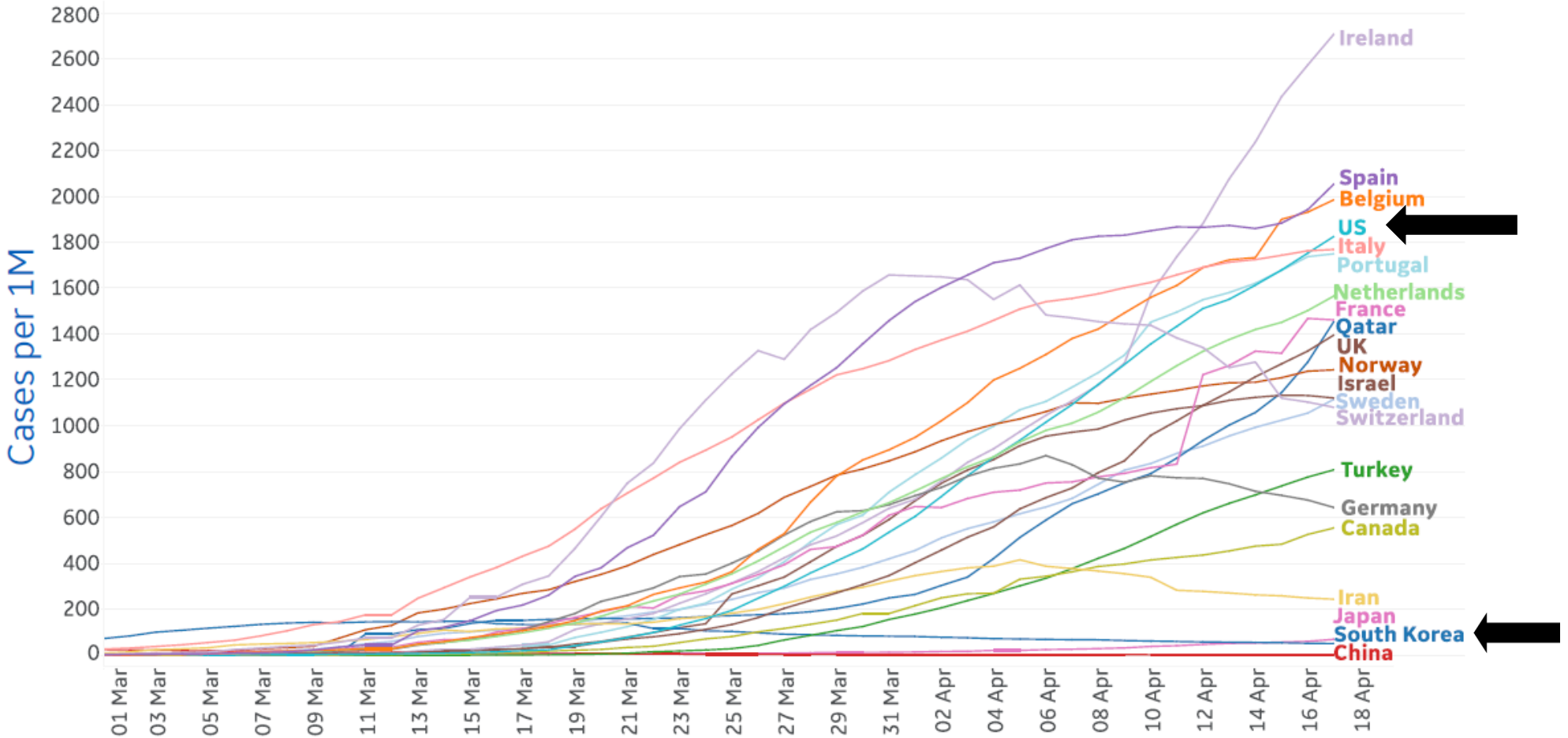
https://www.worldometers.info/coronavirus/

GE Healthcare

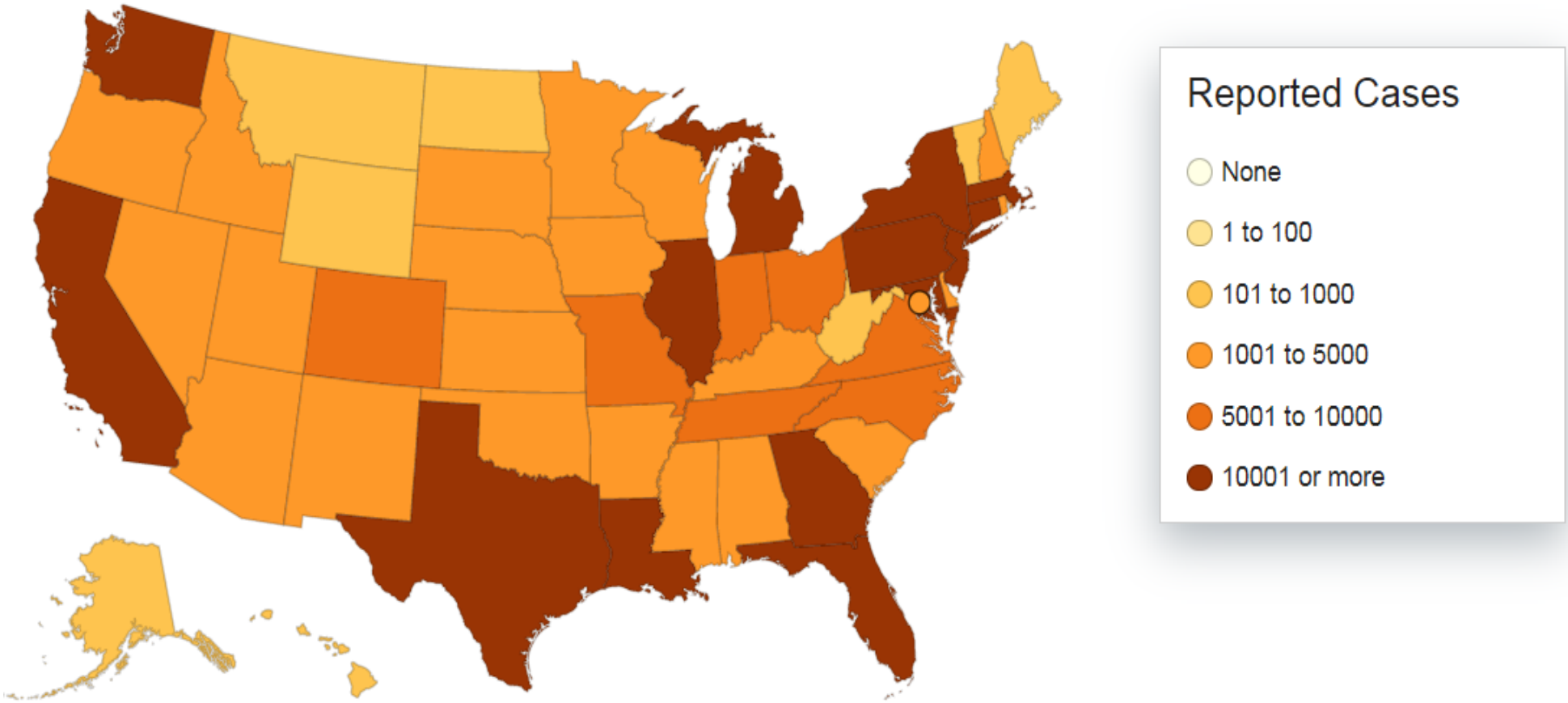
Active Cases by Country

Since 1 March 2020

Updated 18 April 2020, 1:00 GMT

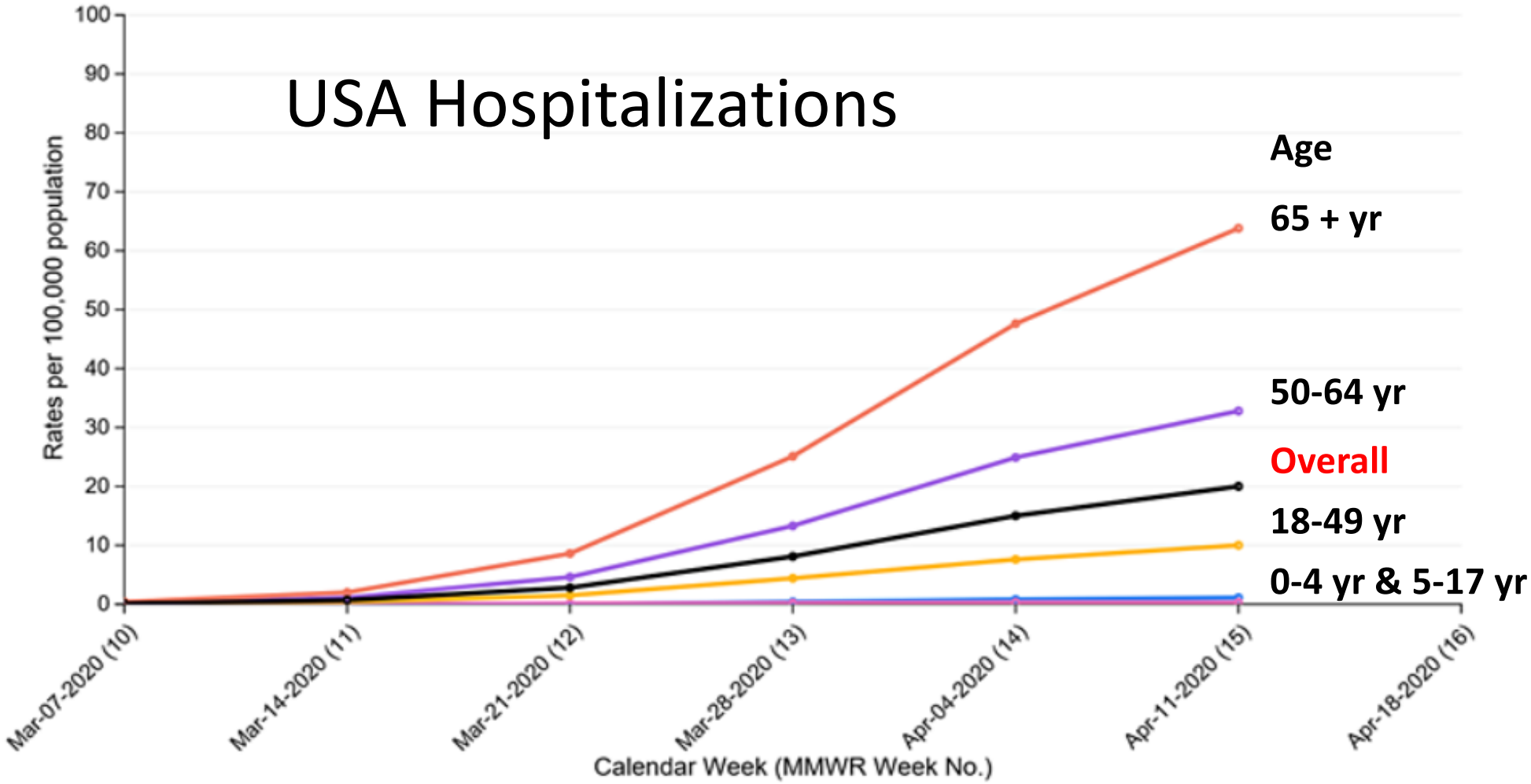


USA Epidemiology

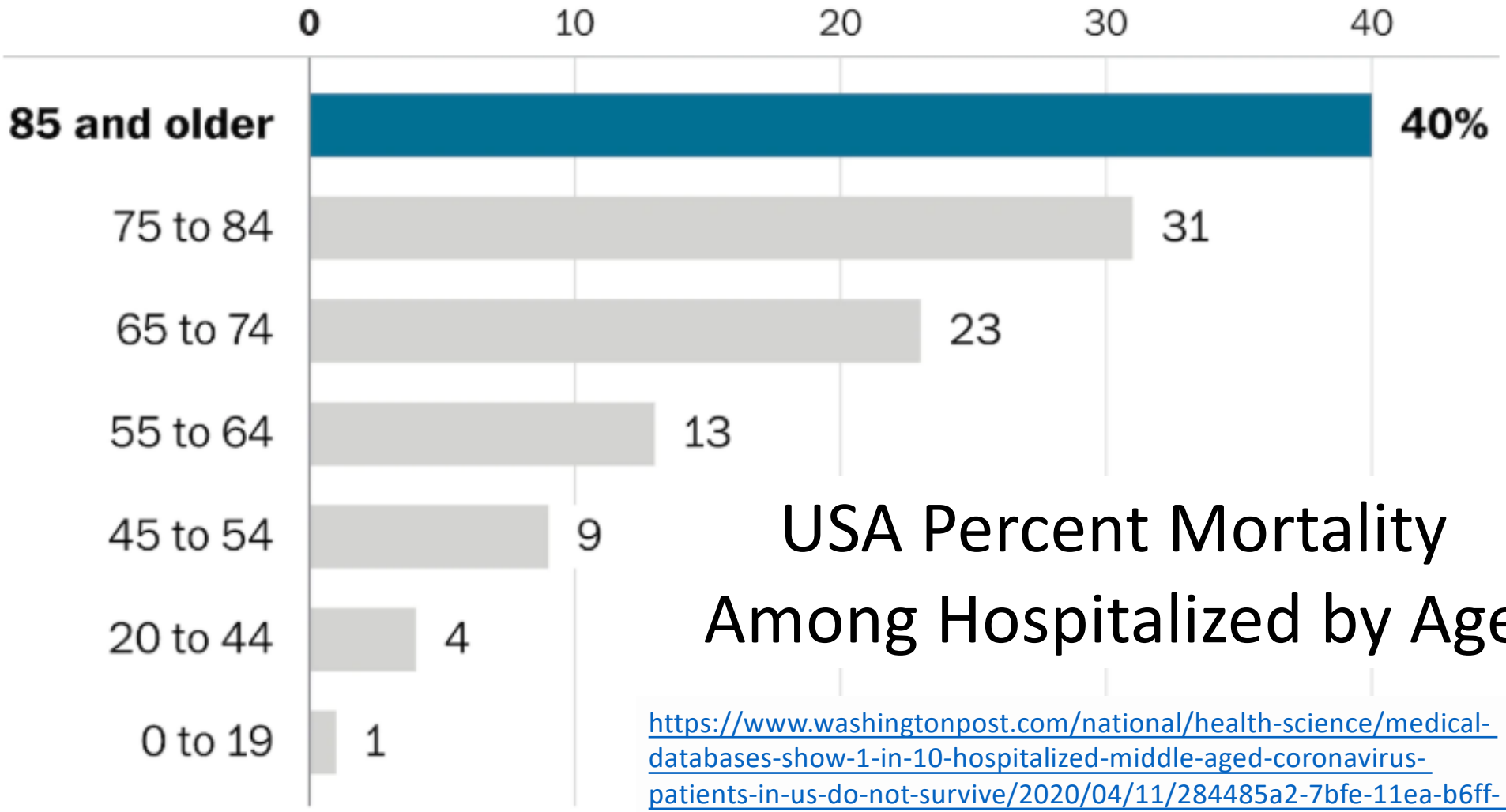


https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html#anchor_1586782138

USA Hospitalizations



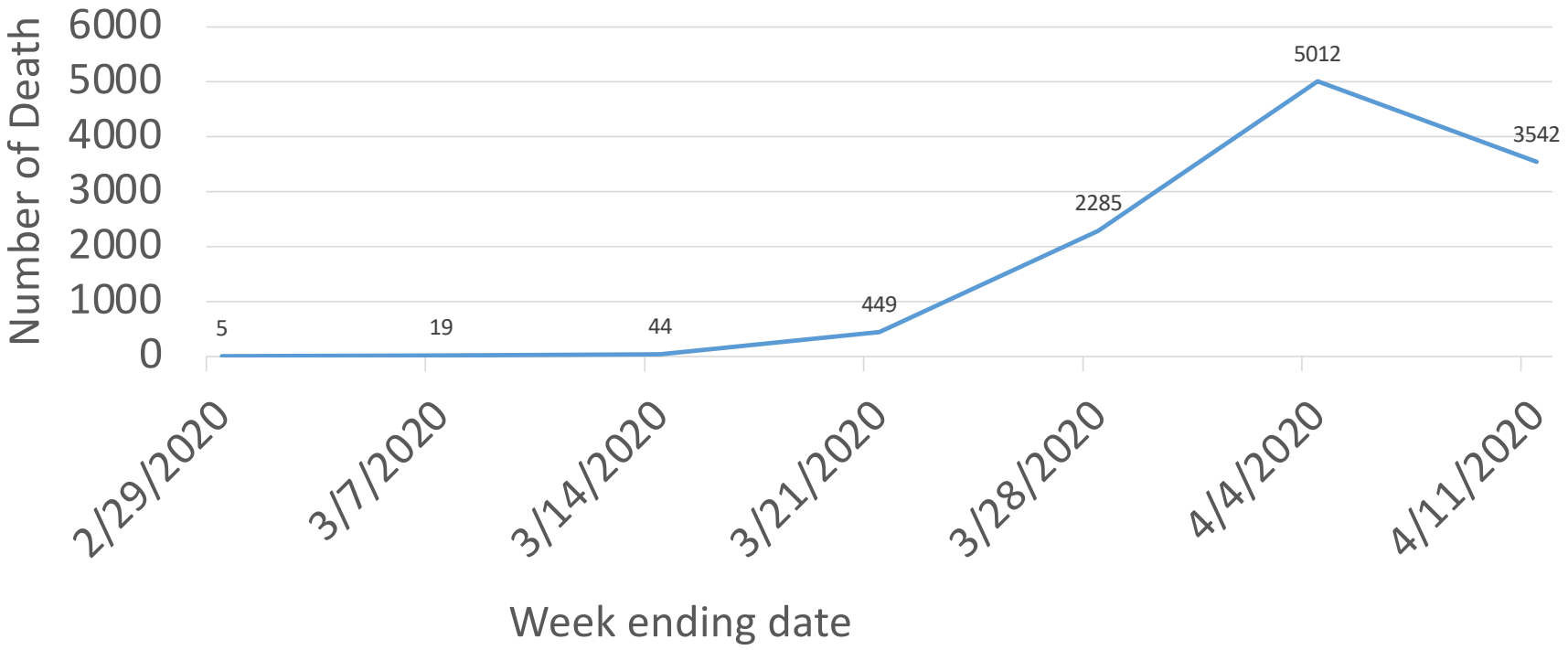
https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html



USA Percent Mortality Among Hospitalized by Age

https://www.washingtonpost.com/national/health-science/medical-databases-show-1-in-10-hospitalized-middle-aged-coronavirus-patients-in-us-do-not-survive/2020/04/11/284485a2-7bfe-11ea-b6ff-597f170df8f8_story.html

USA Number of Deaths Over Time



https://www.cdc.gov/nchs/data/health_policy/Provisional-Death-Counts-COVID-19-Pneumonia-and-Influenza.pdf

Focusing on Health Care Settings

What Constitutes Close contact?

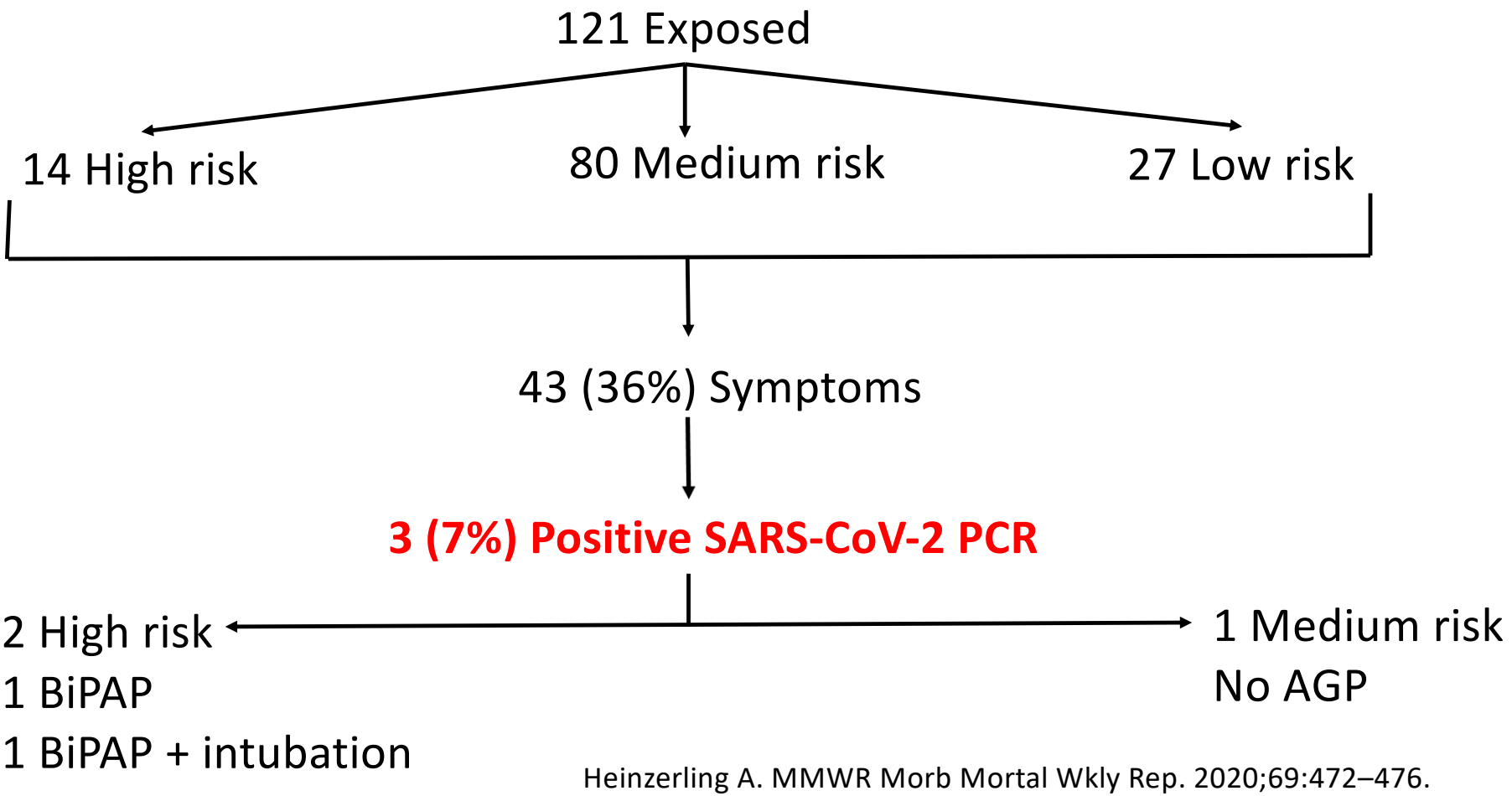
a) Being within approximately 6 feet (2 meters), of a person with COVID-19 for a prolonged period of time (such as caring for or visiting the patient); or

b) Having unprotected direct contact with infectious secretions or excretions of the patient (e.g., being coughed on, touching used tissues with a bare hand).

https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html

Exposure Risk Categories in Health Care Settings

Transmission to Health Care Personnel in California



Heinzerling A. MMWR Morb Mortal Wkly Rep. 2020;69:472–476.

Infected USA Health Care Workers' Exposure Settings

Only health care	780 (55%)
Only household	384 (27%)
Only community	187 (13%)
Multiple	72 (5%)

No data on health care workers' specialties

CDC COVID-19 Response Team. MMWR Morb Mortal Wkly Rep 2020;69:477–481.

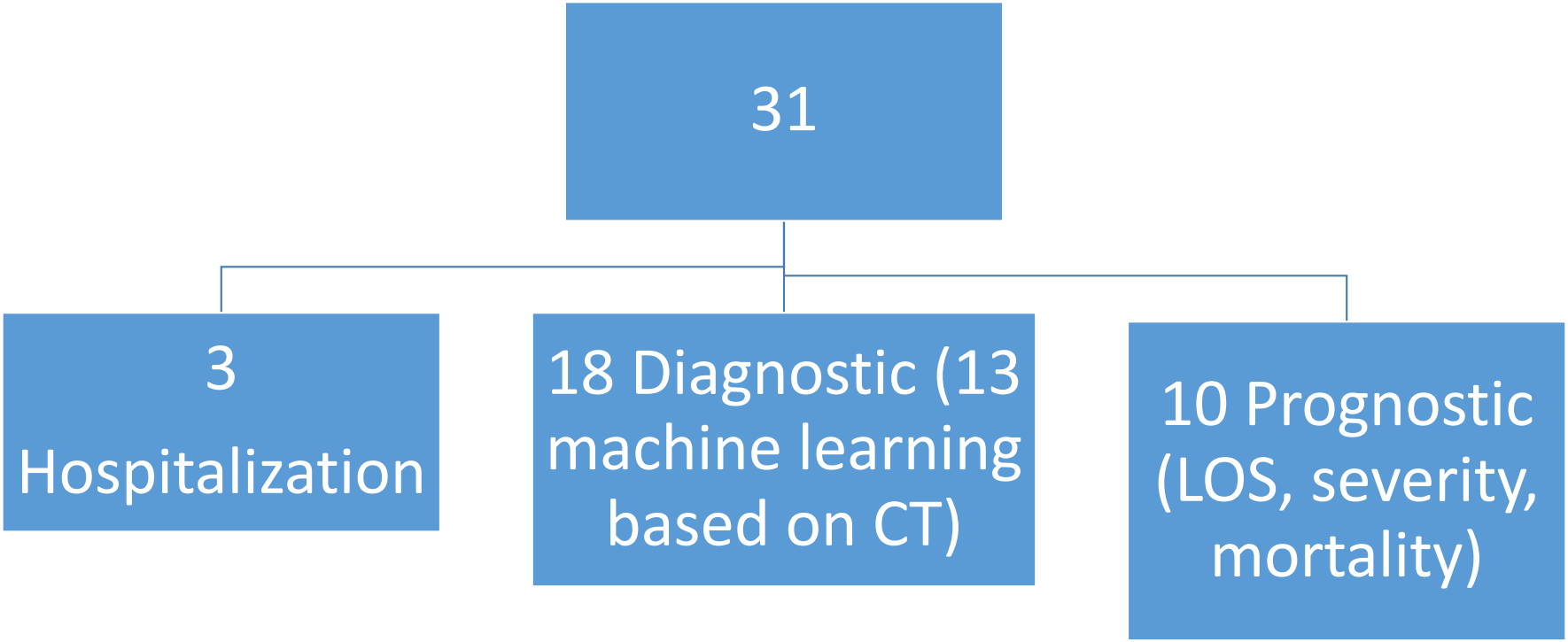
Medical Specialties of 23 Health Care Workers who died from COVID-19 in China

- 13 physicians:
  - 5 practiced in community health centers or in private clinics
  - 3 practiced Chinese medicine
  - 2 internal medicine physicians
  - 2 physicians in respiratory medicine
  - 1 was a gastroenterologist
- 8 were surgeons
  - 3 ophthalmologic surgeons
- 1 electrocardiography technician
- 1 nurse

No anesthesiologists listed

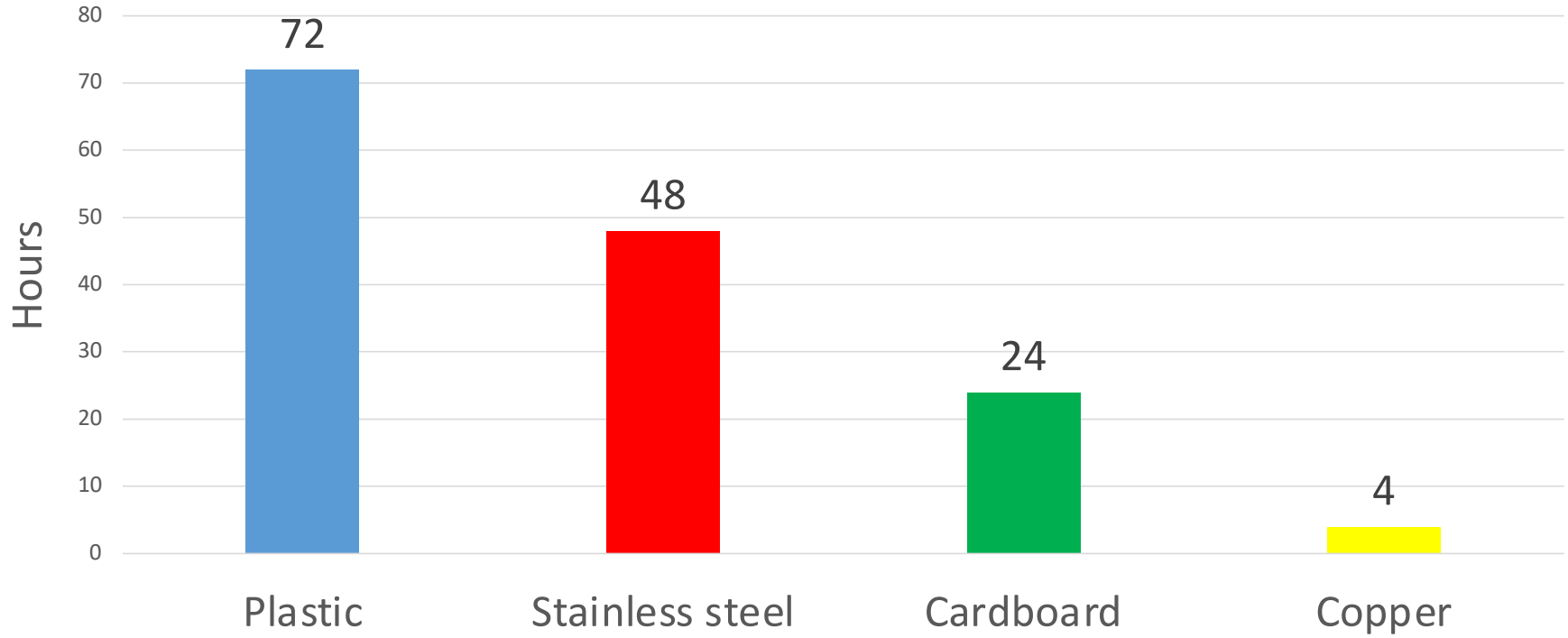
Zhan M. N Engl J Med; April 15, 2020 DOI: 10.1056/NEJMc2005696

Prediction Models for Diagnosis and Prognosis of COVID-19 infection



"Poorly reported, at high risk of bias, and their reported performance is probably optimistic." Wynants L. BMJ 2020; 369 :m1328

Environmental Stability of SARS-CoV-2

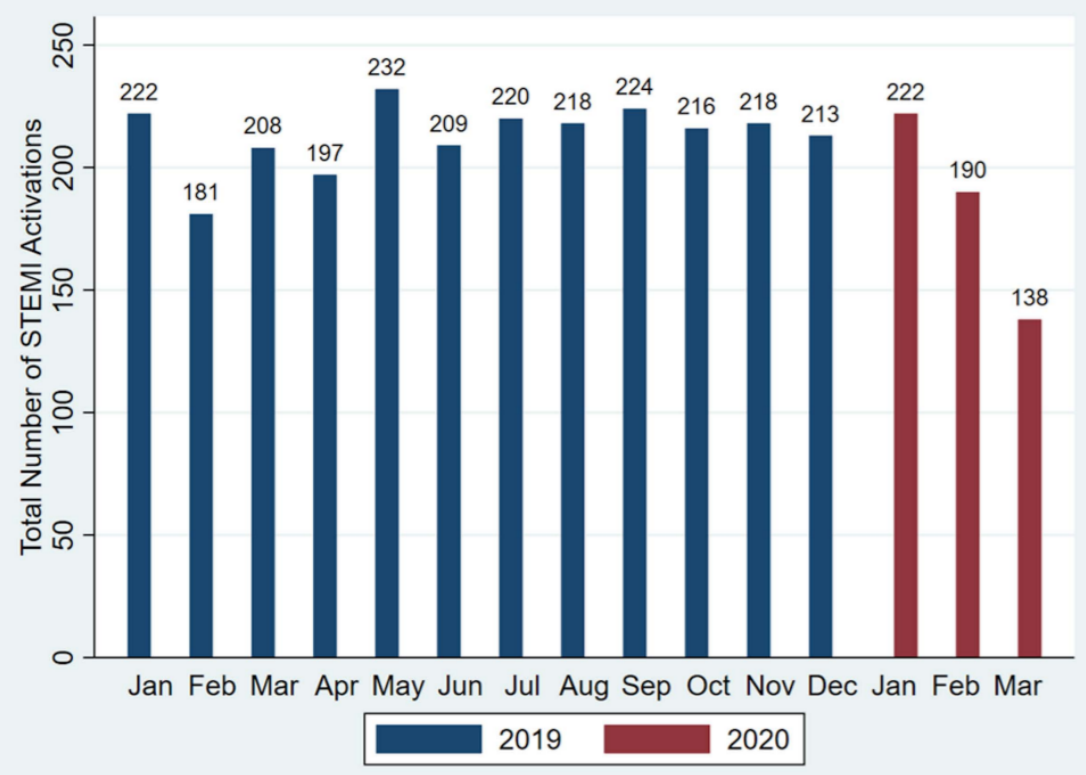


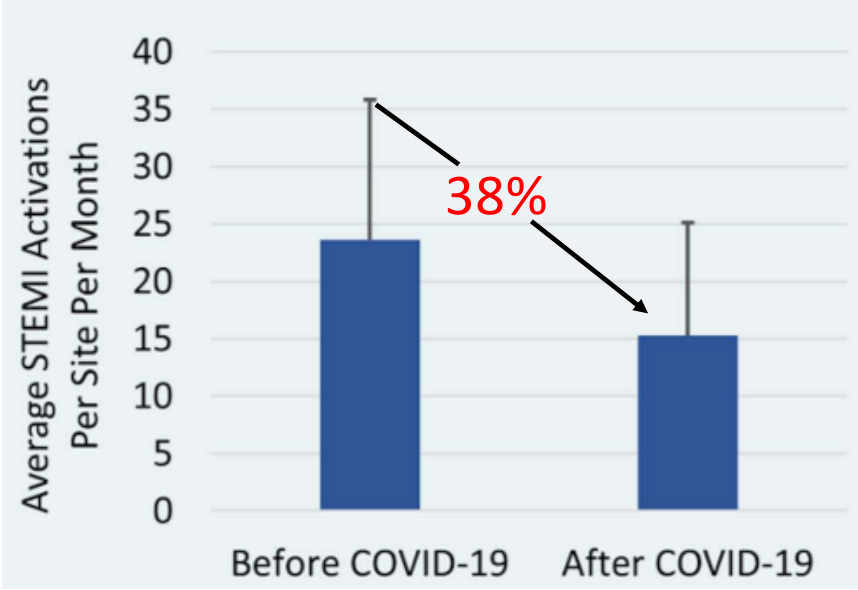
van Doremalen N. N Engl J Med 2020; 382:1564-1567

Clinical Presentation

- Mild 80%, moderate 15%, severe 5%
- Influenza-like illness (fever, cough, dyspnea [4-8 days from onset])
  Huang C. The Lancet, 2020,395(10223):497 - 50
- Nausea, diarrhea, abdominal pain (20%)
  Cheung KS. *Gastroenterology* 2020 (https://doi.org/10.1053/j.gastro.2020.03.065)
- Loss of sense of smell & taste (60%??)
  Menni C. MedRxiv 2020.04.05.20048421; doi (not peer-reviewed)
- Acute respiratory distress syndrome
  Matthay MA. Lancet Respiratory Medicine DOI:https://doi.org/10.1016/S2213-2600(20)30127-2
- Encephalopathy, agitation, confusion & corticospinal tract signs (14%)
  Hemls J. N Engl J med DOI: 10.1056/NEJMc2008597
- Hypercoagulable state
  Zhou F. Lancet 2020;395(10229):1054-1062

Collateral Damage: Reduction in ST-Segment Elevation Cardiac Catheterization Laboratory Activations in the United States during COVID-19 Pandemic





Garcia S. J Amer Col Cardiol 2020, doi: https://doi.org/10.1016/ j.jacc.2020.04.011

Asymptomatic / Presymptomatic SARS-CoV-2 infection

1%

1.8%

1/23/20 – 3/16/20

243 cases

157 locally acquired

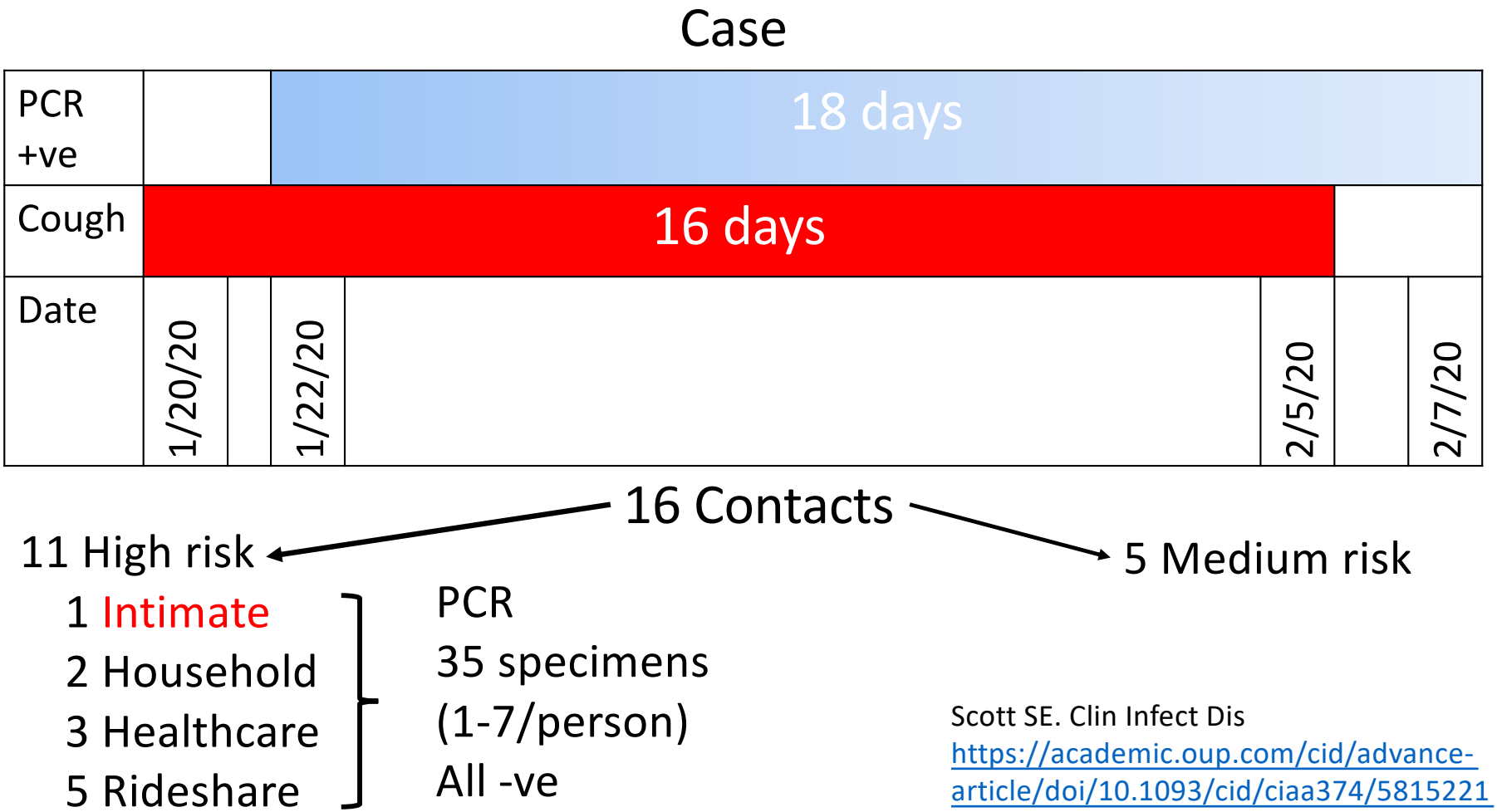
10 (6.4%)

Transmission occurred from an asymptomatic / presymptomatic person to a secondary patient before the source patient developed symptoms, with no evidence that the secondary patient had been exposed to anyone else with COVID-19.

Ng O-T. N Engl J Med 2020; 382:1476-1478
Hoehl S. N Engl J Med 2020; 382:1278-1280

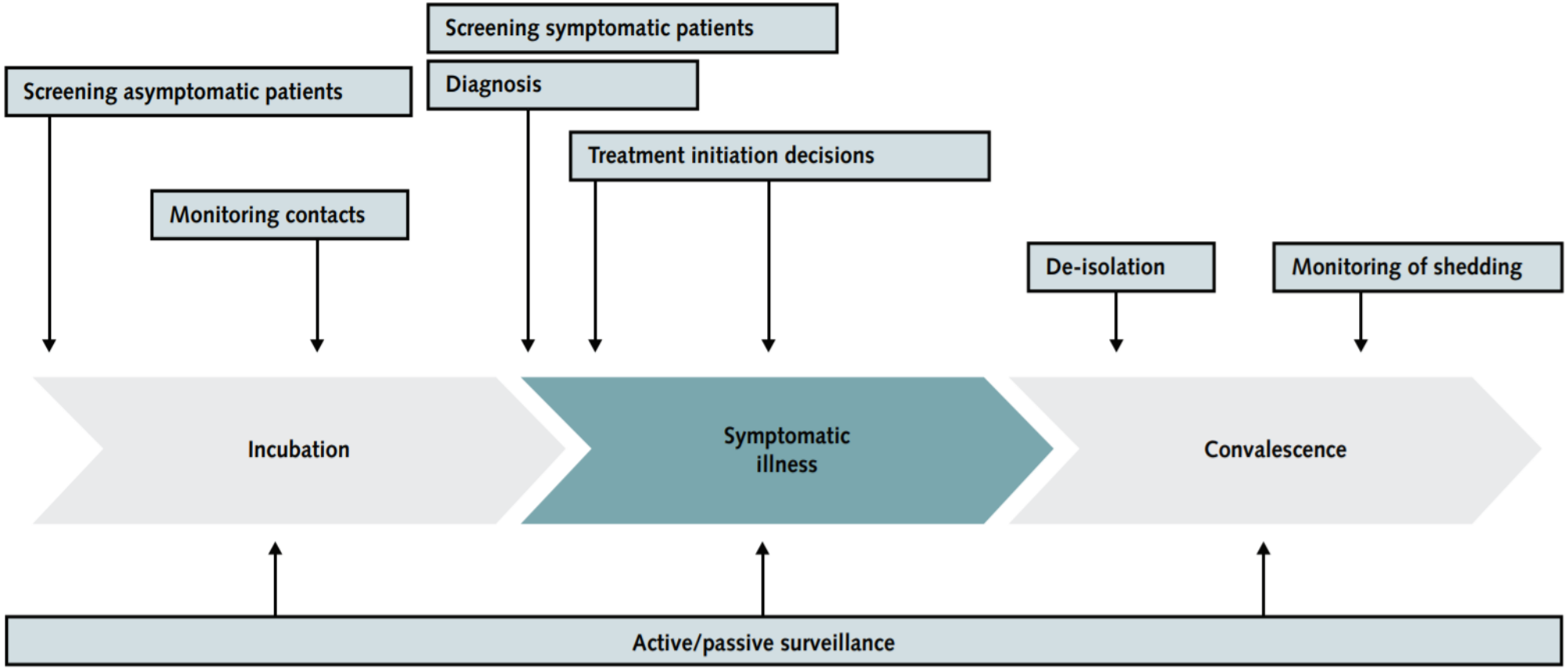
Wei WE. MMWR Morb Mortal Wkly Rep 2020;69:411–415.

Study of a case with mild illness & 16 contacts in USA



Scott SE. Clin Infect Dis
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa374/5815221

Diagnostic tests: a continuum of care

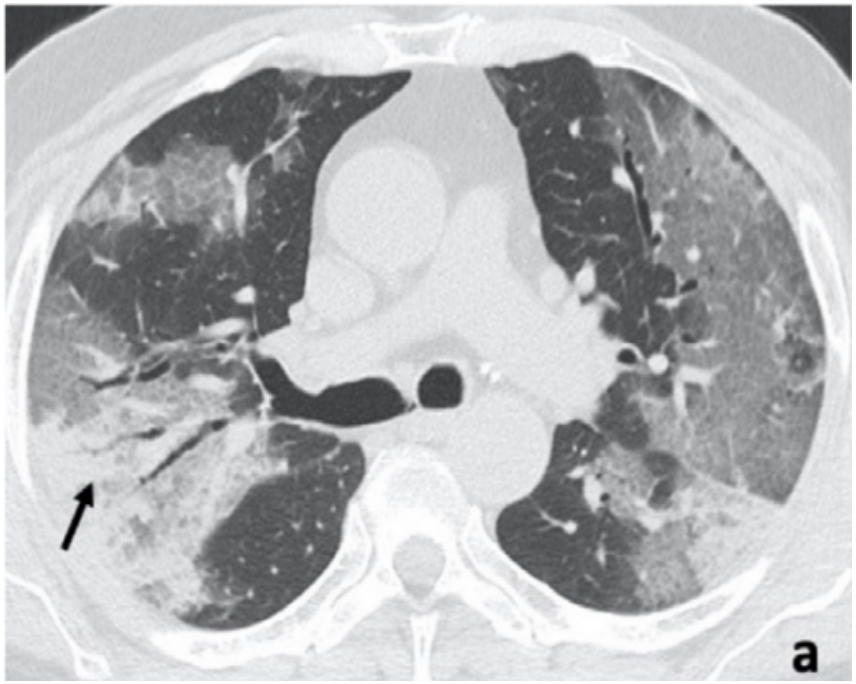


Cheng MP. Ann Intern Med. doi:10.7326/M20-1301

		Selected Use Case			
		Screening during incubation/asymptomatic phase	Diagnosis of symptomatic disease	Screening for viral shedding in convalescence phase for de-isolation decisions	Epidemiologic surveillance
Assay Type	Laboratory-based RT-PCR or NAAT assay	Unknown/insufficient negative predictive value	Current reference standard	Unknown/insufficient negative predictive value	Passive surveillance Unknown/insufficient negative predictive value for case finding
	POC sample-to-answer NAAT assay	Unknown/insufficient negative predictive value	Likely comparable to reference standard	Unknown/insufficient negative predictive value	Passive surveillance Unknown/insufficient negative predictive value for case finding
	Antigen detection POC*	Unknown/insufficient negative predictive value	Yet to be developed	Likely insufficient negative predictive value	Likely lower sensitivity than NAAT will hamper predictive value with low prevalence
	Serology IgM/IgG detection (POC or laboratory based)*	Likely false-negative in early disease	Likely false-negative in early disease†	Typically do not mirror disease activity	Serosurveys could assess individual and population immunity*

Cheng MP. Ann Intern Med. doi:10.7326/M20-1301

Chest CT



CT Features	% present
Ground Glass Opacity	100%
Multilobe involvement	93%
Bilateral distribution	91%
Posterior Involvement	93%
Peripheral GGO location	89%
Subsegmental vessel enlargement (> 3 mm)	89%

Diagnostic Performance with RT-PCR as the standard of reference: Sensitivity 97%, Specificity 56%, Positive predictive value 59%, Negative predictive value 96%, **Accuracy 72%**

Caruso D. Radiology
https://pubs.rsna.org/doi/pdf/10.1148/radiol.2020201237

Laboratory abnormalities

Table 2: Main laboratory abnormalities in patients with unfavorable progression of coronavirus disease 2019 (COVID-19).

– Increased white blood cell count
– Increased neutrophil count
– Decreased lymphocyte count
– Decreased albumin
– Increased lactate dehydrogenase (LDH)
– Increased alanine aminotransferase (ALT)
– Increased aspartate aminotransferase (AST)
– Increased total bilirubin
– Increased creatinine
– Increased cardiac troponin
– Increased D-dimer
– Increased prothrombin time (PT)
– Increased procalcitonin
– Increased C-reactive protein (CRP)

Lippi G. Clin Chem Lab Med. DOI: https://doi.org/10.1515/cclm-2020-0198.

Respiratory Copathogens

Pathogen	% positive
Rhinovirus/enterovirus	6.9%
Respiratory Syncytial virus	5.2%
Other coronaviridae	4.3%
Metapneumovirus	1.7%
Influenza A	0.9%
Parainfluenza virus 1	0.9%
Parainfluenza virus 3	0.9%
Parainfluenza virus 4	0.9%
Total	20%

Kim D. *JAMA.* Published online April 15, 2020. doi:10.1001/jama.2020.6266

Prevention

- Hand washing
- Social distancing
- Cough & sneeze etiquette
- Masking
- Disinfecting surfaces
- Stay home if sick
- Beware of unsubstantiated claims

https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/index.html






Monday, March 16, 2020

NIH clinical trial of investigational vaccine for COVID-19 begins

- mRNA-1273
- Phase 1 clinical trial (safety & immunogenicity)
- Healthy volunteers, 18-45 years
- Washington Seattle
- 6 weeks

Expected availability for public use 12-18 months

https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins

How to treat COVID-19

- Mild: supportive care
- Moderate / severe:
  - Supportive care
  - No FDA approved medications / biological products

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

Hospitalization	Hydroxychloroquine/chloroquine in the context of a clinical trial
	Convalescent plasma in the context of a clinical trial
	Hydroxychloroquine/chloroquine + azithromycin only in the context of a clinical trial
	Combination of lopinavir/ritonavir only in the context of a clinical trial
	Tocilizumab only in the context of a clinical trial
Hospitalization for pneumonia	Against the use of corticosteroids
Hospitalization for ARDS	Corticosteroids in the context of a clinical trial

Bhimraj A. Clin Infect Dis https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

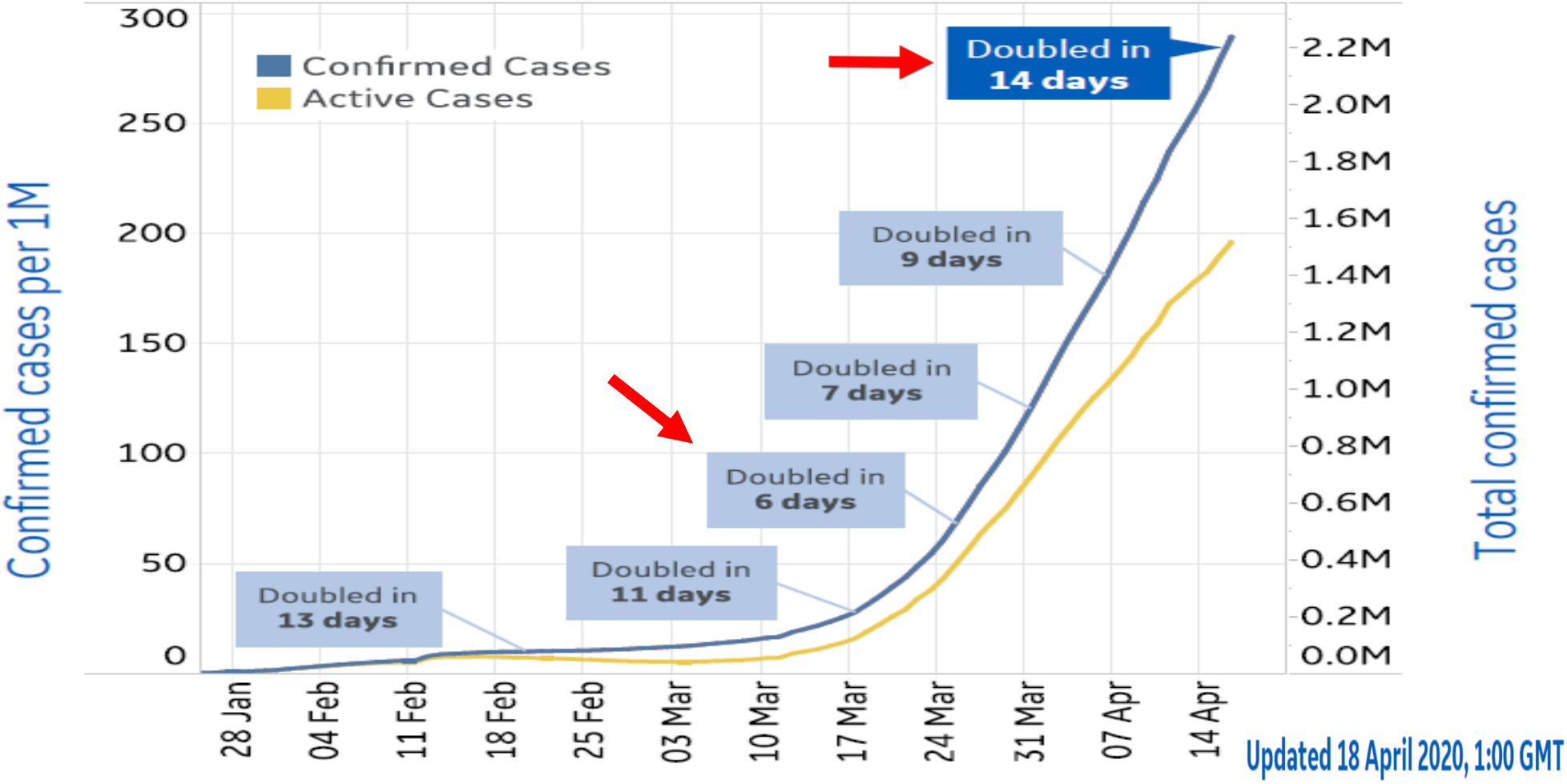
IDSA Guidelines on the Treatment and Management of Patients with COVID-19: "Other"

- Darunavir/cobicistat: No
- Lopinavir-ritonavir + interferon beta or other antivirals: "being evaluated"
- Convalescent plasma for prophylaxis: "study opened"
- Ribavirin: No. Inconclusive or harm for SARS-CoV-1 and MERS-CoV
- Oseltamivir: No. Neuraminidase enzyme not found in coronaviruses
- Intravenous immunoglobulin: No. Studies needed in communities with increasing numbers of people recovering from COVID-19
- Remdesivir: Awaiting studies. Termination of viral RNA transcription (Ebola virus, MERS-CoV & SARS-CoV-1). Compassionate-use in COVID-19 pneumonia: improvement 68%, mortality 13% & acceptable toxicity profile.
- Should NSAIDS be stopped? No
- Should ACE and ARBs be stopped? No

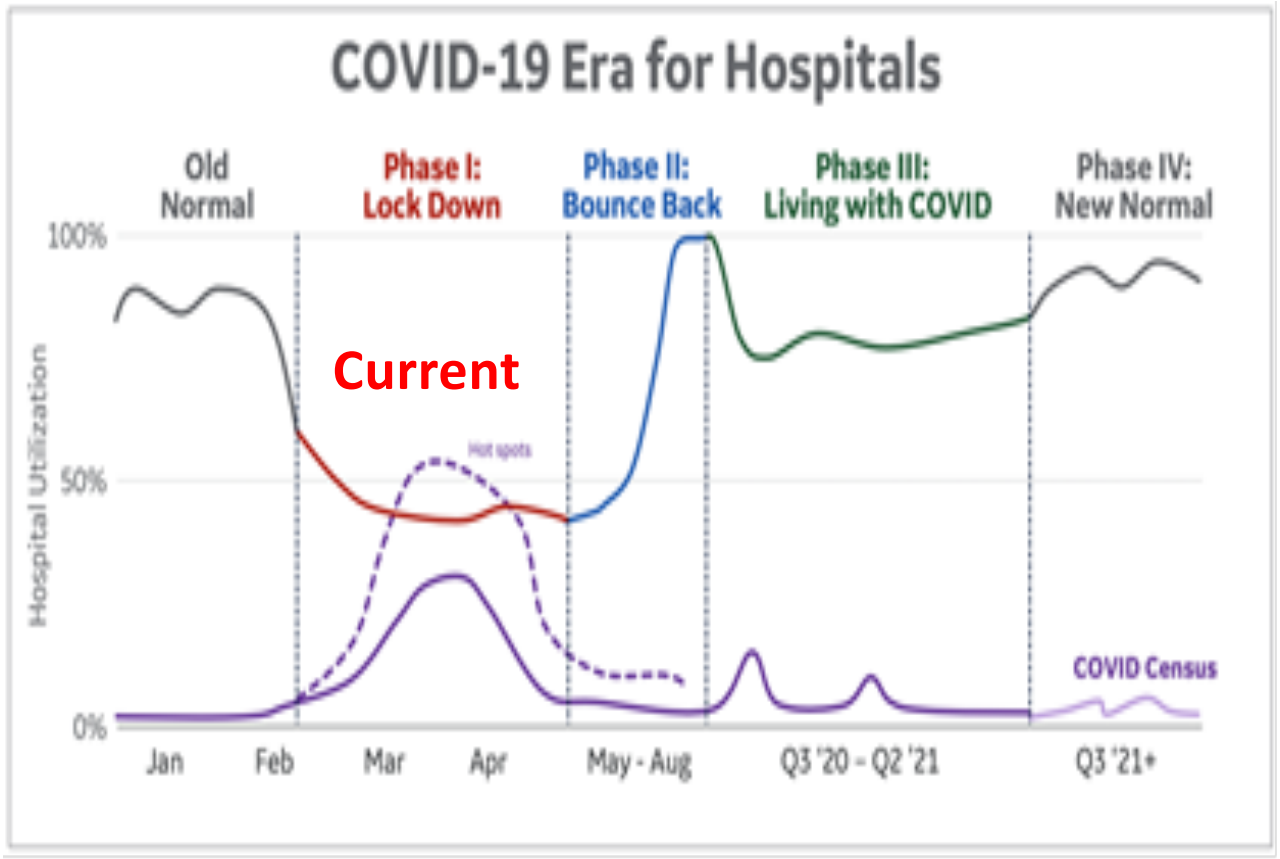
Bhimraj A. Clin Infect Dis https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management

A Reason for Hope: Doubling of Doubling Time

GE Healthcare



Road to Recovery. Responsible “Bounce Back”



1. Widespread Testing
2. Cohorting
3. Restructured waiting rooms
4. Risk-stratified catch-up
5. Maintain appropriate physical distancing
6. Employee support
7. PPE supply chain
8. Effective Treatment & Prevention

https://www.idsociety.org/contentassets/9ba35522e0964d51a47ae3b22e59fb47/idsa-recommendations-for-reducing-covid-19-distancing_16apr2020_final-.pdf

GE Healthcare

Take Away Points

- Information moving at the speed of light
- Beginning to understand the virus biology & epidemiology
- Mostly human to human droplet transmission
- Proportion of asymptomatic / presymptomatic transmission unclear
- Prevention through behavioral measures + vaccine development
- Treatment supportive + clinical trials
- Reason for hope and road to recovery