



COVID-19 Science and Medicine Updates

Compiled by University of Maine faculty and students

Maine Updates – April 2, 2020:

April 1, 2020 data in Maine (latest CDC posted data this morning):

334 confirmed cases, 80 recovered, 63 hospitalized, 7 deaths

Maine CDC is no longer reporting number of COVID-19 tests that have been processed, and number of negative cases.

<https://www.maine.gov/dhhs/mecdc/infectious-disease/epi/airborne/coronavirus.shtml>

Today is Maine's first day of Governor Mills' Stay Healthy at Home Mandate. This order requires people living in Maine to stay at home at all times unless for an essential job or an essential personal reason, such as obtaining food, medicine, health care, or other necessary purposes. This mandate will last until at least April 30, 2020.

<https://www.maine.gov/governor/mills/news/governor-mills-issues-stay-healthy-home-mandate-2020-03-31>

The Governor also mandated a series of other new restrictions, including:

- For essential businesses and operations that remain open, limiting the number of customers in their buildings at any one time, implementing curbside pickup and delivery options as much as possible, and enforcing U.S. CDC-recommended physical distancing requirements for their customers and employees in and around their facilities.
- Prohibiting the use of public transportation unless for an essential reason or job that cannot be done from home and limiting the number of people traveling in private vehicles to persons within the immediate household unless transporting for essential activities.
- Mandating the continued termination of classroom or other in-person instruction until at least May 1, 2020.
- Mandating that, when out of the home or when at work at an essential business, individuals shall maintain a minimum distance of six feet from other persons.

Legal Enforcement of this Executive Order:

Pursuant to 37-B M.R.S. §786, this Order shall be enforced by law enforcement as necessary and violations are a class E crime subject to up to six months days in jail and a \$1000 fine. In addition, compliance with Section IV of this Order may also be enforced by government officials who regulate licenses, permits or any other authorization to operate a business or occupy a building.

Details of the current executive order:

https://www.maine.gov/governor/mills/sites/maine.gov.governor.mills/files/inline-files/CORRECTED_An%20Order%20Regarding%20Further%20Restrictions%20on%20Public%20Contact%20and%20Movement%2C%20Schools%2C%20Vehicle%20Travel%20and%20Retail%20Business%20Operations.pdf

Previous executive order, listing essential businesses and services:

https://www.maine.gov/governor/mills/sites/maine.gov.governor.mills/files/inline-files/An%20Order%20Regarding%20Essential%20Businesses%20and%20Operations%20_0.pdf

Why the COVID-19 pandemic should avoid encouraging discriminatory behavior

“The Proximal Origin of SARS-CoV-2” Andersen et al, 2020; Nature Correspondence

- Gives evidence that it is highly unlikely that the coronavirus responsible for COVID-19 was manipulated in a laboratory setting

Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: Mental health consequences and target populations. Shigemura et al 2020

<https://onlinelibrary.wiley.com/doi/full/10.1111/pcn.12988>

- Stock prices have dropped in China and Japan, and other parts of the world are also showing some synchronous decline
- Expected mental/physical health consequences:
 - Emotional responses will likely include extreme fear and uncertainty
 - Negative societal behaviors will often be driven by fear and distorted perceptions of risk
 - These experiences might evolve to include a broad range of public mental health concerns, including distress reactions (insomnia, anger, extreme fear of illness even in those not exposed), health risk behaviors (increased use of alcohol and tobacco, social isolation, mental health disorders (PTSD, anxiety disorders, depression, somatization), and lower perceived health
- Particular effort must be directed to vulnerable populations, which includes:
 - The infected and ill patients, their families, and colleagues
 - Chinese individuals and communities
 - Individuals with pre-existing mental/physical conditions
 - Health-care and aid workers, especially nurses and physicians working directly with ill or quarantined persons

“Fear can be more harmful than the severe acute respiratory syndrome coronavirus 2 in controlling the coronavirus disease 2019 epidemic”

Ren et al 2020

<https://www.wjgnet.com/2307-8960/full/v8/i4/652.htm>

- Discrimination and prejudice driven by fear or misinformation has become an issue throughout the world
- Discrimination, prejudice and stigma make those who are ill, potentially with COVID-19, reluctant to get medical help
- Singapore’s Prime Minister Lee Hsien Loong said, “ The virus may have started in China but it doesn’t respect nationality or race. It doesn’t check your passport before it goes into your body and anybody can be infected.”

Which groups are more at risk for COVID-19?

Reports from around the world indicate anyone, at any age and even healthy individuals, can experience severe co-morbidities or mortality as a result of COVID-19. More data is needed to definitively determine which groups are more at risk, and whether or not there is an underlying genetic risk. Below are summaries of current research regarding who may be more at risk for COVID-19 complications.

<https://www.cdc.gov/coronavirus/2019-ncov/specific-groups/high-risk-complications.html>

- Older adults and people of any age who have serious underlying medical conditions might be at higher risk for severe illness
- 65 years and older
 - 8 out of 10 deaths in U.S. have been adults 65 years old or older

CDC data among adults with confirmed COVID-19 reported in the U.S.:

Age	Estimated percent requiring hospitalization	Estimated percent requiring admission to intensive care unit	Estimated percent who died
65-84 years old	31-59%	11-31%	4-11%
85 years old or older	31-70%	6-29%	10-27%

- Those living in a nursing home or long-term care facility
- Individuals with chronic lung disease or moderate to severe asthma
- Individuals with serious heart conditions
- Individuals who are immunocompromised
 - Cancer treatment
 - Bone marrow or organ transplantation
 - Immune deficiencies
 - Poorly controlled HIV or AIDS
 - Prolonged use of corticosteroids or other immune weakening medications
- Individuals with severe obesity at any age (BMI >40)
- Diabetes
- Renal failure
- Liver disease
- Potentially individuals who are pregnant - data on COVID-19 has not shown an increased risk but typically pregnant individuals are at risk with severe viral illness

“Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta analysis” (Ma et al, 2020) pre-print 3/17/2020

Objectives: summarize and analyze the clinical characteristics and identify the predictors of disease severity and mortality

Methods: Meta-analysis up to February 25, 2020 of various databases: Pubmed, Web of Science Core Collection, Embase, Cochrane, & MedRxiv

Results:

- Analysis of a total of 30 studies including 53,000 patients with COVID-19 included
- Mean age = 49.5 years old; 55% male
- Majority of studies in Wuhan, China (13, 43.3%) and other cities in China (11, 36.7%)
 - 2 from nationwide and 3 from other countries including the US, Australia, and Korea
 - Avoided overlap by using the nationwide study of Chinese CDC including 44672 confirmed cases only for identifying COVID-19 related death risk factors
- Pooled incidence of severity = 20.2%
 - Higher in Wuhan subgroup than outside Wuhan (36.9% vs 10.9%)
- Pooled incidence of mortality = 3.1%
 - Higher in Wuhan subgroup than outside Wuhan (9.5% vs 0.2%)

Predictor for disease severity included:

Condition	Odds ratio (OR)	95% confidence interval (CI)
Old age (≥50 years old)	2.61	2.29-2.98
Male	1.248	1.195-1.521
Smoking	1.734	1.146-2.626
Any comorbidity	2.635	2.098-3.309
Chronic kidney disease (CKD)	6.017	2.192-16.514
Chronic obstructive pulmonary disease (COPD)	5.323	2.613-10.847
Cerebrovascular disease	3.219	1.486-6.972
Tumor	3.21	1.42-7.24
Diabetes	2.49	1.82-3.4
Hypertension	2.06	1.61-2.62

Increased lactate dehydrogenase (LDH), C-reactive protein (CRP), and D-dimer and decreased blood platelet and lymphocytes count were highly associated with severe COVID-19.

Calculating relative risks (RR) in regards to COVID-19 related death, the following were found to be independent prognostic factors for the COVID-19 related death:

Condition	Relative risks	95% CI
Old age (≥60 years old)	9.45	8.09-11.04
Cardiovascular disease	6.75	5.40-8.43

Hypertension	4.48	3.69-5.45
Diabetes	4.43	3.49-5.61

- Onset-to-admission time closely correlated with case severity rate (4.99% per increase in days) and case fatality rate (1.97% per increase in days)
 - Suggests shortening the onset-to-admission time favored COVID-19 related outcomes
- Pooled case fatality rate of severe patients (N=1374) was significantly higher than non-severe patients (N=4326)
- Mean incubation period = 7.10 days (95% CI, 6.06-8.14 d)
 - w/ no statistical difference between severe and non-severe cases
- Mean time from symptom onset to hospital admission = 6.18 days (95% CI, 5.23-7.12 d)
 - Longer in severe cases than that in non-severe cases (6.56 days vs 4.81 days, P=0.023) and in Wuhan than outside (7.23 days vs 4.86 days, P=0.027)

Symptoms:

Symptom	Percent	95% CI
Fever*	79.1%	68.0-90.3%
Cough*	58.0%	42.0-74.0%
Fatigue*	29.3%	23.4-35.3%
Diarrhea	5.7%	3.9-7.5%
Nausea or vomiting	2.0%	1.9-2.9%

*dominant symptoms

Prevalence of comorbidities:

Condition	Prevalence	95% CI	Additional info
Any comorbidity	37.1%	28.1-46.1%	Higher in severe cases vs non-severe (54.9% vs 27.6%, P=0.006) & higher in Wuhan than other areas (45.1% vs 28.8%, P=0.01)
Hypertension	19.0%	13.2-24.9%	
Diabetes	8.2%	6.3-10.0%	
Cardiovascular diseases (CVD)	2.7%	1.4-4.1%	

- Hypertension, diabetes, CVD, cerebrovascular diseases, chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD) were significantly more common in severe cases as compared with non-severe cases (all for P<0.05)

Potential antivirals to combat COVID-19

- Currently, there are no FDA approved drugs that are specifically used for COVID-19 <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html#r1> (3/21/20)
- Below are existing anti-viral medications that are being investigated for potential to mitigate COVID-19

Remdesivir

- Remdesivir is an intravenous antiviral drug that inhibits viral replication. It is not approved by the FDA but it can be obtained if the patient takes part in a clinical trial, or in some cases where clinical trials are not available, some patients may be treated with remdesivir “on an uncontrolled compassionate use basis” <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html#r1> (3/21/20).
- It has shown efficacy against the novel COVID-19 (Wang et al. - 2/4/20) and against similar viruses that cause SARS and MERS (Sheahan et al. - 1/10/20) in initial clinical trials.
- Mechanism of action: Inhibits replication by inhibiting the viral RNA-dependent RNA polymerase (Gordon et al. - 2/24/20).

Choloroquine and hydroxychloroquine...

- These are broadly used antimalarial drugs taken orally. Studies on patients are promising but there have been no randomized control trials on these drugs. Hydroxychloroquine is often paired with azithromycin <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html#r1> (3/21/20).
- Studies in China and the United States have shown promising initial results for patients that took either chloroquine or hydroxychloroquine (Wang et al. - 2/4/20, Gautret et al. - 3/17/20).
- HQC and QC are associated with a number of adverse health effects like QT prolongation and retinopathy, therefore patients especially with pre-existing conditions should be aware of these side effects <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html#r1> (3/21/20).
- Mechanism of action: these drugs inhibit the virus’s ability to enter the cell by changing the chemical makeup of the glycoprotein spikes on the outside of the virus (Liu et al. - 3/18/20).
- These drugs are currently in limited supply in the US, for those who require them for other medical conditions, due to unfounded public interest in these potential treatments for COVID-19

Ritonavir/lopinavir...

- These drugs were originally developed for HIV and are taken orally.
- A study in 2015 showed efficacy against MERS virus (Chan et al. - 1/15/15), however the first clinical trial did not show as much promise. More clinical trials will follow <https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments> (3/22/20).
- Mechanism of action: protease inhibitors - inhibits the protease activity (breakdown of proteins) of the virus <https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments> (3/22/20).

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