



COVID-19 Science and Medicine Updates

Compiled by University of Maine faculty and students

Maine Updates – May 6, 2020

From Maine CDC:

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

Data updated May 5, 2020 at 11:45AM (New: more data categories available!)

Total Cases: 1226

Confirmed cases: 1150

Probably cases: 76

Recovered: 741

Hospitalized: 187

Deaths: 61

Negative test results, updated April 29, 2020 (now published weekly): 19,546

Maine/Penobscot County Data from Maine CDC:

Confirmed: 39

Recoveries: 46

Deaths: 0

Online Dashboard Links:

Desktop version:

<https://arcg.is/1Knarr>

Mobile version:

<https://arcg.is/5qGGr>

News from Maine:

Maine DHHS Issues Emergency Rule to Protect the Health and Safety of Maine Nursing Home Residents and Staff

<https://www.maine.gov/dhhs/press-release.shtml?id=2460746>

From the release:

In partnership with the Long-Term Care Ombudsman Program, DHHS proactively reached out during the week of April 12 to all nursing facilities in Maine about their infection control, visitor screening, and other policies related to COVID-19. After DHHS had initiated and completed this work, the U.S. Centers for Medicare and Medicaid Services required similar action by all states. The findings included that:

- Statewide occupancy of nursing facilities was at 85%, indicating that adequate capacity exists to admit new residents, including those being discharged from hospitals
- 80% of facilities are admitting new residents, with some requiring a negative COVID-19 test prior to admission
- Nearly half (48%) share staff, either across facilities or across units within a facility
- Most reported having a supply of personal protective equipment (PPE), but many were not prepared to estimate how many days' supply they had on hand
- Most reported challenges with maintaining staffing levels

The emergency rule focuses on these areas in need of greater attention, directing nursing facilities and skilled nursing facilities to:

- Within 24 hours, notify facility residents, their family members/guardians, facility staff, Maine CDC and DLC when a resident meets CDC criteria to be designated as a probable or confirmed case
- Amend infection prevention protocols to include consultation with Maine CDC within 24 hours of any probable COVID-19 positive resident or staff, and within 12 hours of any confirmed positive COVID-19 resident or staff, for consideration of universal testing and resident cohorting consistent with CDC consultation and guidance
- Restrict visitation consistent with U.S. CDC guidelines and limit resident departures from the facility to only essential activity, such as medical appointments
- Establish safe and reasonable ways for residents to communicate with family, friends, and loved ones, such as through electronic video conferencing or visitation on-site through closed windows, supplemented with phones if needed. DHHS has received federal approval to provide existing funding to nursing homes for iPads or similar electronic devices and will work with each facility to identify their needs and obtain and distribute the devices consistent with federal guidelines.
- Screen all full- and part-time staff, outside essential health care workers (such as hospice staff, physicians, etc.), and any other individual entering the facility using the most current U.S. CDC screening guidance
- Provide additional personal PPE to staff who work in multiple facilities, based on U.S. CDC guidance
- Stock 72 hours of appropriate PPE at all times and report PPE supplies to Maine CDC
- Ensure adherence to U.S. CDC guidance on the use of PPE and measures to prevent infected individuals from spreading disease
- Conduct cleaning and sanitation consistent with U.S. CDC guidance
- Have an adequate written plan to ensure sufficient staff to care for residents in a crisis
- Have a qualified Infection Preventionist who ensures that staff have received proper training and demonstrated competency in appropriate PPE selection and use, conducts random observations of staff use of PPE, and takes immediate corrective actions to prevent cross-contamination.

Other COVID-19 News:

NOVEL TREATMENTS: Convalescent Plasma

Describe the convalescent plasma treatment:

- Convalescent blood plasma is being explored as a possible treatment for COVID-19. Blood plasma from recently recovered patients may be effective because it contains antibodies to SARS-CoV-2, which could result in a better outlook for patients with COVID-19¹.
 - Convalescent blood plasma would be delivered to ill patients through transfusion.
- There are 3 'pathways for use' of investigational COVID-19 convalescent plasma¹:
 - 1. Clinical Trials
 - 2. Expanded Access: patients with serious or immediately life-threatening COVID-19 who are not eligible or unable to participate in randomized clinical trials.
 - 3. Single Patient Emergency IND: a patient's physician can request a single patient emergency to allow use of an investigational drug for the treatment of an individual patient by a licensed physician upon FDA authorization. This is used if clinical trials or expanded access is unavailable. Patients must meet certain requirements:
 - Lab confirmed COVID-19
 - Severe/life-threatening COVID-19 (one or more of the following):
 - Shortness of breath
 - Respiratory frequency >30/min
 - Blood oxygen saturation <93%
 - Lung infiltrates >50% within 24 to 48 hours
 - Respiratory failure
 - Septic shock
 - Multiple organ dysfunction or failure
 - Informed consent provided by the patient or health care proxy

What is the mechanism of action?

- Anti-SARS-CoV-2 antibodies may mediate their therapeutic effect in a few ways⁵:
 - 1. The antibody can bind to the SARS-Cov-2 virion in the host, which would directly neutralize its infectivity by covering any binding sites. This prevents viral-host interactions that are normally necessary for the virus to replicate and succeed in infection.
 - 2. Complement activation could be triggered by these antibodies. In this mechanism, small complement proteins are activated which leads to stimulation of phagocytes to clear foreign material, inflammation to attract more phagocytes, and activation of the cell-killing membrane attack complex.
 - 3. Non-neutralizing antibodies can bind the pathogen without interfering with its ability to replicate, but may also contribute to prophylaxis and/or recovery.

What is the history of the drug or vaccine?

- Convalescent plasma has previously been studied during other outbreaks including the 2003 SARS-CoV-1 epidemic, 2009-2010 H1N1 influenza pandemic, and 2012 MERS-CoV epidemic¹. It was successful in efficacy and safety².

How do you donate/obtain plasma?

- Must obtain the plasma from an FDA-registered blood establishment that follows donor eligibility criteria and donor qualifications described below¹:
 - Donor eligibility:
 - Documented positive COVID-19 lab test
 - Either complete resolution of symptoms at least 28 days prior to donation OR complete resolution of symptoms at least 14 days prior to donation and negative results for COVID-19
 - Have not been pregnant, or if she has, results must be negative for HLA antibodies
 - SARS-CoV-2 neutralizing antibody titers (if available)
 - Ideal = 1:160
 - Ok = 1:80 if alternative matched unit is unavailable
 - Must keep record of the COVID-19 convalescent plasma units administered to the COVID-19 patient. Records should include unique identification numbers of the units.
- When obtaining plasma, blood goes through a process that separates blood cells from plasma, so you are left with just plasma containing antibodies³.

What is the current published evidence on the drug or vaccine?

- Duan, K., et al. March 18, 2020. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *PNAS*.
 - 10 severely ill patients
 - Each received 1 dose of 200 mL convalescent plasma with neutralizing antibody titers above 1:640 via IV transfusion
 - Transfused in addition to maximum supportive care and antiviral agents
 - Median time from onset of illness to CP transfusion = 16.5 days
 - In 5/10 cases, levels of neutralizing antibody increased rapidly up to 1:640
 - After treatment:
 - All symptoms in the 10 patients largely improved within 1 to 3 days, including fever, cough, shortness of breath, and chest pain
 - Increased lymphocyte counts
 - Decreased C-reactive protein
 - Increase in oxyhemoglobin saturation within 3 days
 - Varying degrees of absorption of lung lesions within 7 days
 - Viral load undetectable after transfusion in 7 patients who had previous viremia (virus in the blood)
 - 2 patients weaned from mechanical ventilation and put on high-flow nasal cannula oxygenation
 - 1 patient discontinued high-flow nasal cannula oxygenation

- No severe adverse effects observed
- Optimal dose and time point at which to administer still needs further investigation
- Limitations to study:
 - Patients received other standard care, including antivirals, and some received glucocorticoid therapy
 - CP was not administered until a median of 16.5 days from onset of symptoms
 - CP may actually be more effective if administered before this
- Shen, C., et al. March 27, 2020. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA*.
 - 5 severely ill patients
 - All patients had severe respiratory failure
 - 4 patients without coexisting diseases received plasma around hospital day 20
 - 1 patient with hypertension and mitral valve insufficiency received plasma around day 10
 - All patients improved approximately 1 week post-transfusion
 - Normalization of body temperature and improvement in sequential organ failure assessment scores
 - Additionally, patients' neutralizing antibody titers increased and respiratory samples tested negative for SARS-CoV-2 between 1 and 12 days post-transfusion
 - However, they also had been treated with lopinavir/ritonavir and interferon
 - Not compared with outcomes in a control group of patients who did not receive transfusion

What is the timeline for obtaining the convalescent plasma treatment?

- ***BENEFIT***: Convalescent plasma can be available TODAY
 - This treatment doesn't require time to develop as it is already available from recovered COVID-19 patients.

What do you see as the limitations for this drug/vaccine?

- Could be hard to acquire in large quantities
 - Can we produce these antibodies/serum in an animal model or in cell culture? We can't necessarily rely on people getting sick and donating their plasma afterwards.
- Safety of transfusions - there is always some risk involved⁴
 - Fever
 - Allergic reaction
 - Lung injury
- Counting on people to voluntarily donate! We can't force people to do this.
- Regulations on donors
 - It takes a long time for someone to be eligible to donate plasma after they have cleared the illness
 - How long can people donate plasma before their antibody titers have dropped too much?
 - Lots of screening involved to ensure a donor is qualified

1. <https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma>
2. Duan, K., et al. March 18, 2020. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *PNAS*.
3. <https://www.mayoclinic.org/diseases-conditions/coronavirus/expert-answers/convalescent-plasma/faq-20484383>
4. <https://www.wsj.com/video/why-blood-from-coronavirus-survivors-could-be-a-lifeline-for-the-sick/A2B7F562-2101-4D27-8F4A-DBDB07B35009.html>
5. Bloch, E., et al. 2020. Deployment of convalescent plasma for the prevention and treatment of COVID-19. *JCI*.
6. Shen, C., et al. March 27, 2020. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA*.

NOVEL TREATMENTS: Favipiravir

Favipiravir to treat COVID-19

- Favipiravir is an antiviral therapeutic that is currently being investigated as a potential therapy for COVID-19.
- Favipiravir is marketed under the name Avigan by Fujifilm Toyama Chemical in Japan and functions as an RNA polymerase inhibitor, preventing the replication of the virus.
- Treatment of Favipiravir for other RNA viruses have been previously shown to be effective, including influenza A, B, and C, as well as more recently, viral hemorrhagic fevers including Ebola and Lassa viruses for which there are multiple clinical trials underway.
- Favipiravir is an approved therapy for influenza in Japan though it is only used when other antiviral agents are not effective or for use in treating new or reemerging influenza viruses. Because of this, the Japanese government has a stockpile of the drug.
- A clinical study completed in March in China demonstrated significant patient improvement in comparison to control treated patients; recovery was reported in 4 days in comparison to 11 days for the control patients.
- However, another clinical trial in China has reported that patients do not recover more quickly in comparison to control groups, though they seem to have alleviated symptoms.
 - This suggests that further research is necessary to understand the benefit, if any, of therapeutic treatment with Favipiravir to treat COVID-19. It is currently thought that Favipiravir should be administered early in infection for the most therapeutic benefit
- Japan has committed to sending Favipiravir to over 40 countries for COVID-19 testing in clinical trials.
 - Twenty of those countries have been offered Favipiravir free-of-charge by the Japanese government.
 - Favipiravir is currently in two Phase 2 clinical trials in Massachusetts at health centers.
 - One of the sites, the University of Massachusetts Medical School, the department chair for the school of medicine is quoted, “We expect the drug will enhance clearance of the virus and shorten the

duration of COVID-19 illness, previous studies of this drug have indicated that it enhances clearance of influenza. We expect results in approximately one to two months.”

- Favipiravir has not been demonstrated to cause serious side effects when used as an influenza treatment or in clinical trials for COVID-19.
 - However, it is not recommended for individuals who are pregnant due to the possibility of fetal death or birth defects (determined in animal model systems).

Sources:

<https://www.sciencedirect.com/science/article/pii/S2095809920300631>

<https://www.medrxiv.org/content/medrxiv/early/2020/04/15/2020.03.17.20037432.full.pdf>

https://www.istage.ist.go.jp/article/ddt/14/1/14_2020.01012/article/-char/ja/

<https://www.cnbc.com/2020/05/04/fujifilms-flu-drug-favipiravir-sent-to-43-nations-for-covid-19-trials.html>

<https://www.ukrinform.net/rubric-society/3003115-covid19-japanese-pharmacists-have-good-news.html>

NOVEL TREATMENTS: Remdesivir Update

- Remdesivir, an investigational antiviral drug produced by Gilead Sciences, was given Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) on May 1, 2020.
- The EUA for remdesivir is a major advance against the fight of COVID-19, as there are currently no approved therapies or treatments for this disease.
- Remdesivir can be administered intravenously in a healthcare setting to patients with severe COVID-19 disease, defined as low blood oxygen levels, required oxygen therapy, or use of mechanical ventilators.
- The EUA is not the same as a full FDA approval, as the drug is still the focus of numerous clinical studies, including two Phase 3 clinical trials in progress to determine optimal dosing duration.
- A double-blinded, placebo-controlled study with >1000 patients, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) (Trial ID NCT04280705), showed a reduction in disease severity cutting recovery time in the hospital by 4 days (31% improvement). The mortality rate of 8% (drug group) compared to 12% (control group) was not statistically significant.
- Data from other clinical studies demonstrated no clinical improvement, including a clinical trial in China with 237 patients (Trial ID NCT04257656) that was terminated early and a Gilead uncontrolled trial (NCT04292899) with 397 patients.
- Gilead Sciences CEO Daniel O’Day announced a donation of 1.5 million doses to patients at no cost to patients.

Sources:

<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-potential-covid-19-treatment>

<https://www.gilead.com/purpose/advancing-global-health/covid-19/remdesivir-clinical-trials>

<https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gileads-investigational-antiviral-remdesivir-receives-us-food-and-drug-administration-emergency-use-authorization-for-the-treatment-of-covid19>

Why global shutdowns haven't occurred for previous viral outbreaks:

- In the past 20 years, other viruses have posed a significant threat to human health including influenza, Ebola, and SARS viruses. While those viruses have caused significant deaths, they haven't had the same level of societal and economic disruption that we have seen for COVID-19.

SARS and MERS

- SARS and MERS, two other coronaviruses responsible for outbreaks of approximately 2500 and 8000 cases, respectively, did not cause the same level of devastation that we are seeing for COVID-19 because they aren't spread as easily as COVID-19.
 - SARS and MERS are more commonly spread through households, between patients and healthcare workers, or in the case of MERS, primarily through contact with infected dromedary camels. Further, these viruses are not spread asymptotically.
 - "By and large, except for a couple of mass transmission events, almost all of the transmission of SARS was within the healthcare setting, when you have an aerosol generating event like intubating someone, or dialysis. So basically, you could control SARS by improving infection control and prevention in the hospitals" - Stephen Morse, Infectious Disease Epidemiologist, Columbia University's Mailman School of Public Health.

The Swine Flu

- In the Spring of 2009, a novel strain of influenza emerged with the capability to cause a global pandemic, this novel H1N1 strain, the swine flu, was the same type of influenza virus responsible for the 1918 Spanish Flu pandemic and is thought to have infected 1 billion people in 2009-2010 alone
 - The 1918 Spanish Flu was responsible for approximately 50 million deaths.
 - The 2009 H1N1 is easily spread from person-to-person and has an R_0 of 1.4 to 1.6, less than COVID-19 which is estimated to be 1.5 to 3.5. While the R_0 value was lower for the swine flu it was still very contagious, also capable of spread before the onset of symptoms.
 - The swine flu did not overwhelm our healthcare systems or largely impact the economy because the infection turned out to be mild and not as deadly as expected. The case fatality ratio for swine flu varies but is thought to have been less than 0.1%. Even with this

low case fatality, the swine flu spread very easily between people, suggesting that for COVID-19, a more infectious virus with a higher case fatality ratio, could very easily overwhelm our healthcare system and cause widespread devastation without measures to limit the spread.

Ebola Virus

- Ebola virus first emerged in 1976 in Western Africa, with the most recent significant outbreak recorded in 2014, resulting in approximately 11,000 deaths between 2014 and 2016.
 - Ebola virus causes a severe disease characterized as a hemorrhagic fever, resulting in fever, fatigue, vomiting, and diarrhea. Ebola affects the overall vascular system causing multisystem organ failure and breakdown resulting in bleeding from all body orifices. Given the severity of symptoms, the average case fatality ratio is approximately 50%.
 - Infected individuals do not start spreading Ebola virus prior to symptom onset and transmission is through direct contact with bodily fluids like blood, sweat, and urine. Because of this, Ebola is not as easily transmitted as COVID-19, which is capable of transmission through respiratory droplets.
 - Because Ebola virus causes such severe symptomatology, it is relatively easy to identify individuals who may be infected, making it easier to isolate and protect healthcare workers, resulting in limited spread.

Perspectives for COVID-19

- Each of the viruses described lacks at least one key element that could cause it to tip into a global pandemic, the likes of which we are currently experiencing for COVID-19.
- Because of this, COVID-19 is described as a “perfect storm” for a virus outbreak.
 - It causes mild enough disease that some individuals may not know that they have it or attribute it to an alternative illness like influenza or the common cold, leading to increased public exposure and risk of infection for healthcare workers and first responders, resulting in pressure on our healthcare system.
 - COVID-19 is capable of spreading from person-to-person before the presentation of symptoms. It is also spread very easily from person-to-person. This means that individuals who may not know that they are infected can be out in public infecting others, those who may be more at risk for fatality than yourself, this is why social distancing is so important, even if you do not believe you are ill.
 - Because of this, COVID-19 has resulted in stricter containment procedures.

Helpful/informative video: <https://abcnews.go.com/ThisWeek/video/social-distancing-us-flattening-curve-70110270>

Source:

<https://triplebyte.com/blog/modeling-infectious-diseases>
https://fivethirtyeight.com/features/why-did-the-world-shut-down-for-covid-19-but-not-ebola-sars-or-swine-flu/?ex_cid=story-facebook
<https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html>
<https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html>
<https://www.afro.who.int/health-topics/ebola-virus-disease>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4358015/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4535930/>
<https://www.cdc.gov/vhf/index.html>

COVID and Climate Change

- Cities that normally experience high air pollution (New York, Lebanon etc.) have seen a dip in air pollutant levels since the beginning of the COVID-19 pandemic.

<https://www.bbc.com/future/article/20200326-covid-19-the-impact-of-coronavirus-on-the-environment>

<https://www.bbc.com/news/science-environment-51944780>

- A drop in global CO₂ emissions by 0.3% may be seen in 2020.

<https://www.bbc.com/future/article/20200326-covid-19-the-impact-of-coronavirus-on-the-environment>

<https://theconversation.com/how-changes-brought-on-by-coronavirus-could-help-tackle-climate-change-133509>

- The attenuation of emissions due to COVID-19 is projected to be less dramatic than the emissions reduction seen in 2008-09, during the financial crisis.

<https://www.bbc.com/future/article/20200326-covid-19-the-impact-of-coronavirus-on-the-environment>

- Even though emissions are down, it is possible they could rebound as soon as travel restrictions are lifted and industry resumes. There is potential people will be more frivolous with their carbon usage after the pandemic, rationalizing their usage with the small dip in CO₂ emissions seen recently. Such dips in emissions only slow climate change; for real mitigation of climate change, policy will need to be established guaranteeing the use of clean energy.

<https://www.bbc.com/future/article/20200326-covid-19-the-impact-of-coronavirus-on-the-environment>

<https://theconversation.com/how-changes-brought-on-by-coronavirus-could-help-tackle-climate-change-133509>

Wastewater Testing for COVID-19

- One alternative to patient testing may be wastewater testing, given that humans infected with SARS-CoV-2 are shedding virus in stool samples

<https://www.biorxiv.org/content/10.1101/2020.04.24.059667v1>

<https://www.medrxiv.org/content/10.1101/2020.03.29.20045880v1>

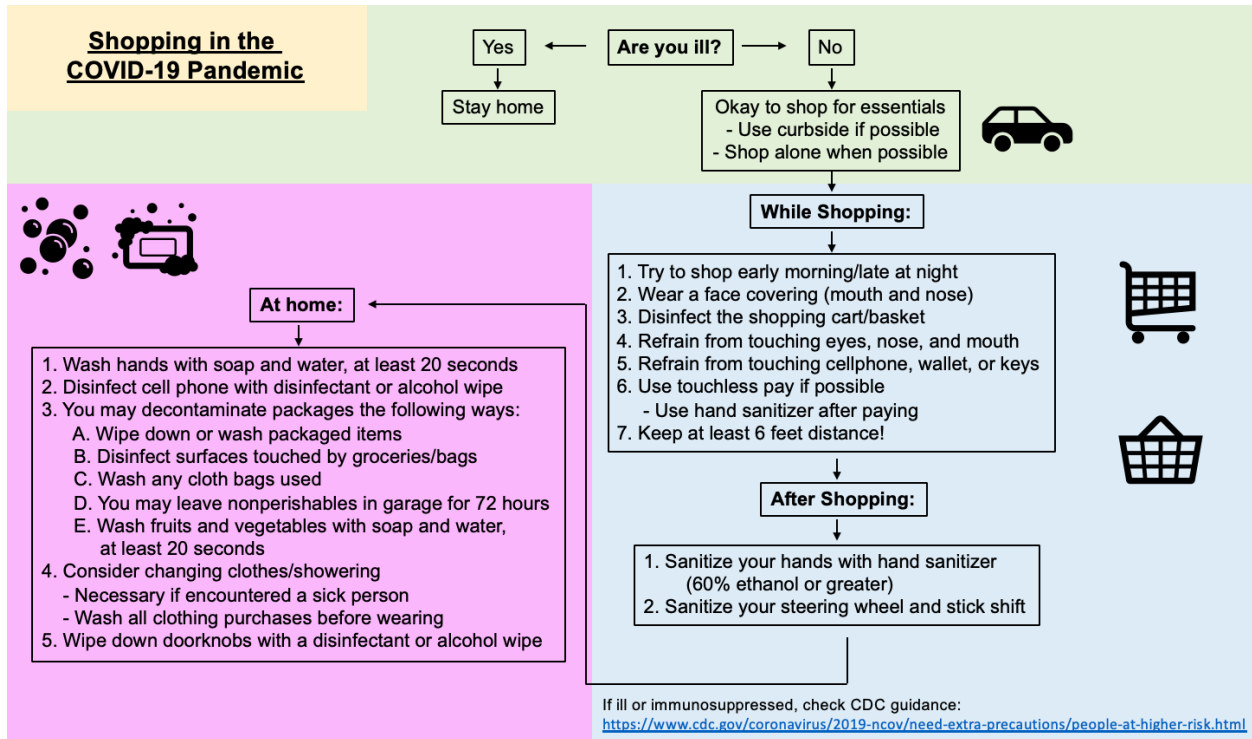
- Research suggests sewage tests could be a good early warning sign if the virus returns to communities in the future. Since wastewater plants may receive influent from up to 1 million people, there is a need to quantify the typical amount of virus particles excreted in feces, and this could then be extrapolated to estimate the number of infected people in a population. Currently, the number of infected individuals can not be estimated from wastewater testing.

<https://www.nature.com/articles/d41586-020-00973-x>

- Wastewater testing can also be a surveillance tool to monitor increase or decrease prevalence of COVID-19 infections in a community and determine active viral load in a community
<https://www.medscape.com/viewarticle/929626>
- Since wastewater testing is limited to communities, or potentially to isolated buildings, there is no way to determine who is infected or if they were just visiting a given area when their infected stool entered the system. Therefore, wastewater testing is not a replacement for recommended test-trace-isolate strategies that identify infected individuals and their contacts, followed by quarantine and isolation procedures.
- Example of a commercial provider of wastewater testing for SARS-CoV-2: BioBot: <https://www.biobot.io/covid19>

Shopping infographic

Created by UMaine and free to print/distribute:



RESOURCES AND RECOMMENDED READINGS:

Clinical and Administrative Guidance on COVID-19 shared by UW Hospitals:

As an early hot-spot in the US, Washington has been providing leadership and guidance around handling clinical cases of COVID-19. Documents are shared at this site, and constantly updated:

<https://covid-19.uwmedicine.org/Pages/default.aspx>

UMaine's Fogler Library COVID-19 Lib Guide:

<https://libguides.library.umaine.edu/coronavirus/maine>

Calculate your Pandemic Footprint, based on your behaviors:

<https://www.pandemic-footprint.com/>

NIH is Enrolling for a New Study to Quantify Undetected Cases of Coronavirus

Blood samples from healthy volunteers are needed, learn more here:

<https://www.niaid.nih.gov/news-events/nih-begins-study-quantify-undetected-cases-coronavirus-infection>

Maine Small Business Resources during COVID

<http://www.mainestreamfinance.org/covid-19-updates/small-business-updates-and-resources-during-covid-19-outbreak/>

COVID-19 Literature Searches MLA Net (Medical Library Association)

<https://www.mlanet.org/page/covid-19-literature-searching>

CDC Research Guide

<https://www.cdc.gov/library/researchguides/2019novelcoronavirus/databasesjournals.html>

LitCOVID:

<https://www.ncbi.nlm.nih.gov/research/coronavirus/>

Nature – Pick of the papers (COVID)

<https://www.nature.com/articles/d41586-020-00502-w>

Mayo Clinic

<https://news.mayocliniclabs.com/covid19/>

Reputable Online Resources with COVID-19 Data:

IHME Health Data and Projections:

<https://covid19.healthdata.org/united-states-of-america>

<https://covid19.healthdata.org/united-states-of-america/maine>

- *Now including more data for Maine!*

Johns Hopkins

<https://coronavirus.jhu.edu/map.html>

Comparison of COVID testing results, false positive and false negative rates across platforms:

<https://covidtestingproject.org/>

COVID-19 Projections Using Machine Learning. Taking a data-driven approach rooted in epidemiology to forecast infections, deaths, and recovery timelines of the COVID-19 / coronavirus epidemic in the US and around the world

<https://covid19-projections.com/about/>

COVID-19 Simulator

<https://www.covid19sim.org/>

Questions about the production of these bulletins?

Contact kristy.townsend@maine.edu

All bulletins posted publicly online at:

<https://umaine.edu/coronavirus/umaine-science-and-medicine-updates/>

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