

COVID-19 Condition Monograph
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COVID-19

Definition of Condition

COVID-19, an unusually severe disease derived from SARS-CoV-2 infection, is predominantly characterized by excessive immune reaction that affects myriad organ systems, highlighted by a “cytokine storm” that creates devastating, and sometimes deadly inflammation.^{1 2}

It must be noted that up to 45% of all SARS-CoV-2 infections could be asymptomatic, and up to 70% in young persons, yet the potential still exists for body systems to be affected adversely, such as ground glass opacities in the lungs, without these individuals even knowing they have these pathologies.³

Body Systems Affected

Lungs, heart, brain⁴, gastrointestinal system, nervous system⁵, blood vessels, eyes, nasopharynx, epidermis, among others are affected.^{6 7} COVID-19 has also been purported to be a factor in new-onset diabetes.⁸ A large majority of recovered COVID-19 patients report having at least one persistent symptom for weeks or months after the height of infection. Complaints echo myalgic

¹ Yanuck, S. F., Pizzorno, J., Messier, H., & Fitzgerald, K. N. (2020). Evidence Supporting a Phased Immuno-physiological Approach to COVID-19 From Prevention Through Recovery. *Integrative medicine* (Encinitas, Calif.), 19(Suppl 1), 8–35.

² Copaescu, A., Smibert, O., Gibson, A., Phillips, E. J., & Trubiano, J. A. (2020). The role of IL-6 and other mediators in the cytokine storm associated with SARS-CoV-2 infection. *The Journal of allergy and clinical immunology*, 146(3), 518–534.e1. <https://doi.org/10.1016/j.jaci.2020.07.001>

³ Long, Q. X., Tang, X. J., Shi, Q. L., Li, Q., Deng, H. J., Yuan, J., Hu, J. L., Xu, W., Zhang, Y., Lv, F. J., Su, K., Zhang, F., Gong, J., Wu, B., Liu, X. M., Li, J. J., Qiu, J. F., Chen, J., & Huang, A. L. (2020). Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nature medicine*, 10.1038/s41591-020-0965-6. Advance online publication. <https://doi.org/10.1038/s41591-020-0965-6>

⁴ Restivo, D. A., Centonze, D., Alesina, A., & Marchese-Ragona, R. (2020). Myasthenia Gravis Associated With SARS-CoV-2 Infection. *Annals of internal medicine*, L20-0845. Advance online publication. <https://doi.org/10.7326/L20-0845>

⁵ Koralnik, I. J., & Tyler, K. L. (2020). COVID-19: a global threat to the nervous system. *Annals of neurology*, 10.1002/ana.25807. Advance online publication. <https://doi.org/10.1002/ana.25807>

⁶ WebMD:

<https://www.webmd.com/lung/news/20200423/the-great-invader-how-covid-attacks-every-organ>

⁷ Gupta, A., Madhavan, M. V., Sehgal, K., Nair, N., Mahajan, S., Sehrawat, T. S., Bikdeli, B., Ahluwalia, N., Ausiello, J. C., Wan, E. Y., Freedberg, D. E., Kirtane, A. J., Parikh, S. A., Maurer, M. S., Nordvig, A. S., Accilli, D., Bathon, J. M., Mohan, S., Bauer, K. A., Leon, M. B., ... Landry, D. W. (2020).

Extrapulmonary manifestations of COVID-19. *Nature medicine*, 26(7), 1017–1032.

<https://doi.org/10.1038/s41591-020-0968-3>

⁸ Rubino, F., Amiel, S. A., Zimmet, P., Alberti, G., Bornstein, S., Eckel, R. H., Mingrone, G., Boehm, B., Cooper, M. E., Chai, Z., Del Prato, S., Ji, L., Hopkins, D., Herman, W. H., Khunti, K., Mbanya, J. C., & Renard, E. (2020). New-Onset Diabetes in Covid-19. *The New England journal of medicine*, 10.1056/NEJMc2018688. Advance online publication. <https://doi.org/10.1056/NEJMc2018688>

encephalomyelitis, which is known as chronic fatigue syndrome. Common symptoms include brain fog, fatigue, pain, immune issues, and malaise after exercise.^{9 10}

Pathophysiology

Exposure to SARS-CoV-2 occurs most frequently through the air, in respiratory droplets or aerosolized particles. It takes exposure to approximately one million respiratory droplets for 15 minutes to become infected. While the severity of exposure to aerosolized particles is still unknown, they may last in the air for several hours and can travel up to 27 feet.¹¹

SARS-CoV-2 usually infects cells in the nose before moving into the lungs, using angiotensin-converting enzyme 2 (ACE2) protein for entry, eventually entering blood vessels.¹²

If allowed to replicate rapidly, succumbing to COVID-19 disease becomes a multisystem event. The problem is, especially for those who have one or more comorbidities, almost every aspect of the immune arsenal attempts to neutralize SARS-CoV-2. This overactivity, along with the pernicious and impervious nature of SARS-CoV-2, creates the “cytokine storm,” in which the immune system becomes hyper-inflamed, thus destroying healthy tissue. When the lungs become hyper-inflamed, especially, hypoxia ensues and affects oxygen-dependent organs like the heart and brain, leading to a downward spiral in overall organ function. Moreover, when SARS-CoV-2 spreads to blood vessels, the ensuing hyper-inflammation affects almost every organ of the body adversely.¹³

There is a developing theory that in some severe COVID-19 patients, a weakened immune system impairs the ability to fight off SARS-CoV-2, thus clinicians must pay strict attention to a

⁹ Carfi, A., Bernabei, R., Landi, F., & Gemelli Against COVID-19 Post-Acute Care Study Group (2020). Persistent Symptoms in Patients After Acute COVID-19. *JAMA*, 10.1001/jama.2020.12603. Advance online publication. <https://doi.org/10.1001/jama.2020.12603>

¹⁰ Tenforde, M. W., Kim, S. S., Lindsell, C. J., Billig Rose, E., Shapiro, N. I., Files, D. C., Gibbs, K. W., Erickson, H. L., Steingrub, J. S., Smithline, H. A., Gong, M. N., Aboodi, M. S., Exline, M. C., Henning, D. J., Wilson, J. G., Khan, A., Qadir, N., Brown, S. M., Peltan, I. D., Rice, T. W., ... IVY Network Investigators (2020). Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March-June 2020. *MMWR. Morbidity and mortality weekly report*, 69(30), 993–998. <https://doi.org/10.15585/mmwr.mm6930e1>

¹¹ Transmission of SARS-CoV-2: Implications for infection prevention precautions. (n.d.). Retrieved July 28, 2020, from <https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions>

¹² Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.02.20144717v2>

¹³ Gupta, A., Madhavan, M. V., Sehgal, K., Nair, N., Mahajan, S., Sehrawat, T. S., Bikdeli, B., Ahluwalia, N., Ausiello, J. C., Wan, E. Y., Freedberg, D. E., Kirtane, A. J., Parikh, S. A., Maurer, M. S., Nordvig, A. S., Accilli, D., Bathon, J. M., Mohan, S., Bauer, K. A., Leon, M. B., ... Landry, D. W. (2020). Extrapulmonary manifestations of COVID-19. *Nature medicine*, 26(7), 1017–1032. <https://doi.org/10.1038/s41591-020-0968-3>

patient's medical history, symptoms, and bloodwork (especially interleukin 7 levels) to discern what treatments will be needed for this demographic.^{14 15}

Scientists at Oak Ridge National Laboratory suggest the bradykinin hypothesis for many of COVID-19-related symptoms. In a novel study, researchers used artificial intelligence (AI) to analyze gene expression data from cells in lung fluid from COVID-19 patients, which indicated elevated bradykinin levels as the driving force. The AI program then screened thousands of substances and found vitamin D to be one of the most effective at attenuating bradykinin levels.¹⁶

Risk factors for severe illness at any age include: Chronic kidney disease, COPD (chronic obstructive pulmonary disease), immunocompromised state (weakened immune system) from solid organ transplant, serious heart conditions such as heart failure, coronary artery disease, or cardiomyopathies, sickle cell disease, and type 2 diabetes mellitus. The consensus is that obesity¹⁷ (body mass index [BMI] of 30 or higher) is the most common risk factor for severe illness at any age, with research suggesting that high circulating leptin levels are to blame for the connection.¹⁸ Electronic cigarette use, especially in children, greatly increases risk.¹⁹

Risk factors that may increase risk at any age include: Asthma (moderate-to-severe), cerebrovascular disease (affects blood vessels and blood supply to the brain), cystic fibrosis, hypertension or high blood pressure (which is why those taking blood pressure medication seem to be less at risk²⁰), immunocompromised state (weakened immune system) from blood or bone

¹⁴ Remy, K. E., Mazer, M., Striker, D. A., Ellebedy, A. H., Walton, A. H., Unsinger, J., Blood, T. M., Mudd, P. A., Yi, D. J., Mannion, D. A., Osborne, D. F., Martin, R. S., Anand, N. J., Bosanquet, J. P., Blood, J., Drewry, A. M., Caldwell, C. C., Turnbull, I. R., Brakenridge, S. C., Moldwauer, L. L., ... Hotchkiss, R. S. (2020). Severe immunosuppression and not a cytokine storm characterizes COVID-19 infections. *JCI insight*, 5(17), 140329. <https://doi.org/10.1172/jci.insight.140329>

¹⁵ Laterre, P. F., François, B., Collienne, C., Hantson, P., Jeannet, R., Remy, K. E., & Hotchkiss, R. S. (2020). Association of Interleukin 7 Immunotherapy With Lymphocyte Counts Among Patients With Severe Coronavirus Disease 2019 (COVID-19). *JAMA network open*, 3(7), e2016485. <https://doi.org/10.1001/jamanetworkopen.2020.16485>

¹⁶ Garvin, M. R., Alvarez, C., Miller, J. I., Prates, E. T., Walker, A. M., Amos, B. K., Mast, A. E., Justice, A., Aronow, B., & Jacobson, D. (2020). A mechanistic model and therapeutic interventions for COVID-19 involving a RAS-mediated bradykinin storm. *eLife*, 9, e59177. <https://doi.org/10.7554/eLife.59177>

¹⁷ Morbidity and Mortality Weekly Report:

https://www.cdc.gov/mmwr/volumes/69/wr/mm6915e3.htm?s_cid=mm6915e3_w

¹⁸ Rebello, C. J., Kirwan, J. P., & Greenway, F. L. (2020). Obesity, the most common comorbidity in SARS-CoV-2: is leptin the link?. *International journal of obesity* (2005), 1–8. Advance online publication. <https://doi.org/10.1038/s41366-020-0640-5>

¹⁹ Gaiha, S. M., Cheng, J., & Halpern-Felsher, B. (2020). Association Between Youth Smoking, Electronic Cigarette Use, and Coronavirus Disease 2019. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*, 67(4), 519–523. Advance online publication. <https://doi.org/10.1016/j.jadohealth.2020.07.002>

²⁰ Baral, R., White, M., & Vassiliou, V. S. (2020). Effect of Renin-Angiotensin-Aldosterone System Inhibitors in Patients with COVID-19: a Systematic Review and Meta-analysis of 28,872 Patients. *Current atherosclerosis reports*, 22(10), 61. <https://doi.org/10.1007/s11883-020-00880-6>

marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune weakening medicines, neurologic conditions such as dementia, liver disease, pregnancy, pulmonary fibrosis (having damaged or scarred lung tissues), smoking, thalassemia (a type of blood disorder), type 1 diabetes mellitus.²¹

According to the CDC, the older you get, the greater the risk.²² Patients older than 80 were at least 20 times more likely to die from COVID-19 than those in their 50s, and hundreds of times more likely to die than those below the age of 40. One reason for this disparity could be the weakened expression of perforin, a protein that allows cytotoxic proteases to enter cells with the purpose of inducing death in cells that have been hijacked by SARS-CoV-2.²³ In addition, the absence of a vigorous CD8+ T cell immune response in the elderly is indicated.²⁴ Men with the virus had a higher likelihood of dying than women of the same age, as it is believed that estrogen has a protective effect from severe symptoms, as well as contractility.²⁵ Non-whites were at higher risk of dying than white patients.²⁶

²¹ Centers for Disease Control. Retrieved from:

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fneed-extra-precautions%2Fgroups-at-higher-risk.html

²² Centers for Disease Control: Retrieved from:

<https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html>

²³ Cunningham, L., Simmonds, P., Kimber, I., Basketter, D. A., & McFadden, J. P. (2020). Perforin and resistance to SARS coronavirus 2. *The Journal of allergy and clinical immunology*, 146(1), 52–53.

<https://doi.org/10.1016/j.jaci.2020.05.007>

²⁴ Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.21.262329v1>

²⁵ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.30.20164921v2>

²⁶ Williamson, E. J., Walker, A. J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C. E., Curtis, H. J., Mehrkar, A., Evans, D., Inglesby, P., Cockburn, J., McDonald, H. I., MacKenna, B., Tomlinson, L., Douglas, I. J., Rentsch, C. T., Mathur, R., Wong, A., Grieve, R., Harrison, D., ... Goldacre, B. (2020). OpenSAFELY: factors associated with COVID-19 death in 17 million patients. *Nature*, 10.1038/s41586-020-2521-4. Advance online publication. <https://doi.org/10.1038/s41586-020-2521-4>

Other risk factors include ApoE4 gene variant²⁷, ACE2 gene variant²⁸, blood type ‘A’^{29 30}, exposure to higher viral load, impaired glutathione function (GSTP1 variant)³¹, and stress.³² Those taking proton pump inhibitors (PPIs) once daily have exhibited double the risk for COVID-19, while taking PPIs twice daily triples the risk for COVID-19.³³

Allopathic Diagnosis & Treatment

Symptoms

Symptoms are vast and still being discovered. However, the most common symptoms are high fever, stuffy nose, sore throat, dry cough, dyspnea (shortness of breath) or difficulty breathing, prolonged fatigue and malaise, hypoxia, nausea, vomiting, gastrointestinal upset including diarrhea, lost sense of smell or taste, and conjunctivitis.³⁴

While many infected persons are asymptomatic, for those who do exhibit symptoms, the CDC recommends that certain symptoms warrant speaking with your physician or visiting an emergency room. These symptoms are: high fever that either does not abate or fluctuates for

²⁷ Kuo, C. L., Pilling, L. C., Atkins, J. L., Masoli, J., Delgado, J., Kuchel, G. A., & Melzer, D. (2020). APOE e4 genotype predicts severe COVID-19 in the UK Biobank community cohort. *The journals of gerontology. Series A, Biological sciences and medical sciences*, glaa131. Advance online publication. <https://doi.org/10.1093/gerona/glaa131>

²⁸ Nicin, L., Abplanalp, W. T., Mellentin, H., Kattih, B., Tombor, L., John, D., Schmitto, J. D., Heineke, J., Emrich, F., Arsalan, M., Holubec, T., Walther, T., Zeiher, A. M., & Dimmeler, S. (2020). Cell type-specific expression of the putative SARS-CoV-2 receptor ACE2 in human hearts. *European heart journal*, 41(19), 1804–1806. <https://doi.org/10.1093/eurheartj/ehaa311>

²⁹ Ellinghaus, D., Degenhardt, F., Bujanda, L., Buti, M., Albillos, A., Invernizzi, P., Fernández, J., Prati, D., Baselli, G., Asselta, R., Grimsrud, M. M., Milani, C., Aziz, F., Kässens, J., May, S., Wendorff, M., Wienbrandt, L., Uellendahl-Werth, F., Zheng, T., Yi, X., ... Severe Covid-19 GWAS Group (2020). Genomewide Association Study of Severe Covid-19 with Respiratory Failure. *The New England journal of medicine*, 10.1056/NEJMoa2020283. Advance online publication. <https://doi.org/10.1056/NEJMoa2020283>

³⁰ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.12.20152074v1>

³¹ Polonikov A. (2020). Endogenous Deficiency of Glutathione as the Most Likely Cause of Serious Manifestations and Death in COVID-19 Patients. *ACS infectious diseases*, acsinfecdis.0c00288. Advance online publication. <https://doi.org/10.1021/acsinfecdis.0c00288>

³² Shields, G. S., Spahr, C. M., & Slavich, G. M. (2020). Psychosocial Interventions and Immune System Function: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA psychiatry*, 10.1001/jamapsychiatry.2020.0431. Advance online publication. <https://doi.org/10.1001/jamapsychiatry.2020.0431>

³³ Almario, C., Chey, W. & Spiegel, B. (2020). Increased Risk of COVID-19 Among Users of Proton Pump Inhibitors. Retrieved from: [https://journals.lww.com/ajg/Documents/AJG-20-1811_R1\(PUBLISH%20AS%20WEBPART\).pdf](https://journals.lww.com/ajg/Documents/AJG-20-1811_R1(PUBLISH%20AS%20WEBPART).pdf)

³⁴ Centers for Disease Control: <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

several days, shortness of breath or heaviness on the chest, forgetfulness, extreme fatigue or malaise.³⁵

The clearest indicator that one has COVID-19 is loss of taste and/or smell.³⁶ While a combination of loss of taste and smell, extreme fatigue, cough and loss of appetite was the best predictor of having a positive result from the PCR test, loss of taste and/or smell seems to be by far the most abundant single symptom reported.³⁷

King's College London used machine learning from cases in the United Kingdom, United States, and Sweden to determine six distinct symptom clusters that indicate the progression of severe COVID-19 disease:³⁸

1. ('flu-like' with no fever): Headache, loss of smell, muscle pains, cough, sore throat, chest pain, no fever.
2. ('flu-like' with fever): Headache, loss of smell, cough, sore throat, hoarseness, fever, loss of appetite.
3. (gastrointestinal): Headache, loss of smell, loss of appetite, diarrhea, sore throat, chest pain, no cough.
4. (severe level one, fatigue): Headache, loss of smell, cough, fever, hoarseness, chest pain, fatigue.
5. (severe level two, confusion): Headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain.
6. (severe level three, abdominal and respiratory): Headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain, shortness of breath, diarrhea, abdominal pain.

³⁵ Scully, E.P., Haverfield, J., Ursin, R.L. et al. (2020). Considering how biological sex impacts immune responses and COVID-19 outcomes. *Nature Reviews Immunology*, <https://doi.org/10.1038/s41577-020-0348-8>

³⁶ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.22.20157263v1>

³⁷ Menni, C., Valdes, A. M., Freidin, M. B., Sudre, C. H., Nguyen, L. H., Drew, D. A., Ganesh, S., Varsavsky, T., Cardoso, M. J., El-Sayed Moustafa, J. S., Visconti, A., Hysi, P., Bowyer, R., Mangino, M., Falchi, M., Wolf, J., Ourselin, S., Chan, A. T., Steves, C. J., & Spector, T. D. (2020). Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nature medicine*, 10.1038/s41591-020-0916-2. Advance online publication. <https://doi.org/10.1038/s41591-020-0916-2>

³⁸ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.12.20129056v1>

Any of the aforementioned needs to be taken even more seriously in persons 65 years of age or older, who represent 80% of hospitalizations and have a 23-fold greater risk of death than those under 65.³⁹ Those under 20 are half as susceptible to getting COVID-19.⁴⁰

Pregnancy, while considered a COVID-19 risk factor, has not shown greater severity compared with non-pregnant patients.⁴¹ While there have been several cases purported regarding transmission of SARS-CoV-2 from pregnant mothers to their fetuses, so far these are rare. One study of 1,000 women showed no evidence of transmission.⁴² Another study has shown protective properties in placental tissue.⁴³ In nursing women, SARS-CoV-2 has not shown to be transmitted to infants.⁴⁴ Alternatively, one study has shown protected antibodies were transmitted from an infected mother to her infant.⁴⁵

Diagnosis

If presenting with what the CDC considers high priority or priority, a COVID-19 viral test to screen for active infection is suggested. Nasal swab or saliva are accepted methods to extract samples.^{46 47 48} High priority is considered hospitalization with older person symptoms, healthcare workers or first responders, and residents of long-term care facilities. Priority is considered anyone with classic symptoms of COVID-19, or those who are suspected through contact tracing have been exposed to someone else with COVID-19.⁴⁹ Guangzhou Institute of Respiratory Health created a calculation tool for predicting critically ill COVID-19 at admission.

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³⁹ Mueller, A. L., McNamara, M. S., & Sinclair, D. A. (2020). Why does COVID-19 disproportionately affect older people?. *Aging*, 12(10), 9959–9981. <https://doi.org/10.18632/aging.103344>

⁴⁰ Davies, N. G., Klepac, P., Liu, Y., Prem, K., Jit, M., CMMID COVID-19 working group, & Eggo, R. M. (2020). Age-dependent effects in the transmission and control of COVID-19 epidemics. *Nature medicine*, 10.1038/s41591-020-0962-9. Advance online publication. <https://doi.org/10.1038/s41591-020-0962-9>

⁴¹ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.17.20161760v1>

⁴² <https://www.medrxiv.org/content/10.1101/2020.08.20.20178657v1>

⁴³ Taglauer, E., Benarroch, Y., Rop, K., Barnett, E., Sabharwal, V., Yarrington, C., & Wachman, E. M. (2020). Consistent localization of SARS-CoV-2 spike glycoprotein and ACE2 over TMPRSS2 predominance in placental villi of 15 COVID-19 positive maternal-fetal dyads. *Placenta*, 100, 69–74. Advance online publication. <https://doi.org/10.1016/j.placenta.2020.08.015>

⁴⁴ Chambers, C., Krogstad, P., Bertrand, K., Contreras, D., Tobin, N. H., Bode, L., & Aldrovandi, G. (2020). Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women. *JAMA*, e2015580. Advance online publication. <https://doi.org/10.1001/jama.2020.15580>

⁴⁵ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.18.20176743v1>

⁴⁶ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.09.20149534v1>

⁴⁷ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.04.16.20067835v1>

⁴⁸ FDA.gov. Retrieved from:

<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-yale-school-public-health>

⁴⁹ Centers for Disease Control: <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>

⁵⁰ Guangzhou Institute of Respiratory Health. Retrieved from: <http://118.126.104.170/>

Testing too early may bring a higher number of false negatives. Patients tested with SARS-CoV-2 in the four days after infection were 67% more likely to test negative, even if they had the virus. When the average patient began displaying symptoms of the virus, the false-negative rate was 38%. The test performed best eight days after infection (on average, three days after symptom onset), but even then had a false negative rate of 20%.⁵¹

Aside from a positive test for active infection, a full blood workup including CBC (looking for elevated neutrophil count⁵² and lymphocyte count below 1000⁵³), Chem Screen, C-reactive protein (elevated level is an indicator), D-Dimer (elevated level is an indicator)⁵⁴, and 25(OH)D especially below 30 ng/mL⁵⁵ may help ascertain the severity of the infection and how it is affecting the body. Knowing the patient's genetic predisposition to inflammatory genes' IL-6, CRP, and TNFa can also be helpful for diagnosing who may be more susceptible to the cytokine storm.⁵⁶

If the patient is complaining of shortness of breath or heaviness on the chest, a lung ultrasound, CT scan, or chest radiography may be performed for detection of COVID-19 abnormalities, including myocarditis, which can still occur in those who are asymptomatic.^{57 58}

Children involving symptoms seen with atypical Kawasaki disease and toxic shock syndrome may be linked to COVID-19 infection.^{59 60}

⁵¹ Kucirka, L. M., Lauer, S. A., Laeyendecker, O., Boon, D., & Lessler, J. (2020). Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure. *Annals of internal medicine*, M20-1495. Advance online publication. <https://doi.org/10.7326/M20-1495>

⁵² Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.08.20141218v1>

⁵³ Wagner, J., DuPont, A., Larson, S., Cash, B., & Farooq, A. (2020). Absolute lymphocyte count is a prognostic marker in Covid-19: A retrospective cohort review. *International Journal of Laboratory Hematology*, 1–5. <https://doi.org/10.1111/ijlh.13288>

⁵⁴ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.24.20139600v1>

⁵⁵ Rhodes, J. M., Subramanian, S., Laird, E., & Kenny, R. A. (2020). Editorial: low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity. *Alimentary pharmacology & therapeutics*, 51(12), 1434–1437. <https://doi.org/10.1111/apt.15777>

⁵⁶ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.17.20155242v1>

⁵⁷ Bernheim, A., Mei, X., Huang, M., Yang, Y., Fayad, Z. A., Zhang, N., Diao, K., Lin, B., Zhu, X., Li, K., Li, S., Shan, H., Jacobi, A., & Chung, M. (2020). Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. *Radiology*, 295(3), 200463. <https://doi.org/10.1148/radiol.2020200463>

⁵⁸ Czawlytko, C., Hossain, R., White, CS. (2020). COVID-19 Diagnostic Imaging Recommendations. *Applied Radiology*, 49(3):10-15.

⁵⁹ Medscape: <https://www.medscape.com/viewarticle/930223>

⁶⁰ Feldstein, L. R., Rose, E. B., Horwitz, S. M., Collins, J. P., Newhams, M. M., Son, M., Newburger, J. W., Kleinman, L. C., Heidemann, S. M., Martin, A. A., Singh, A. R., Li, S., Tarquinio, K. M., Jaggi, P., Oster, M. E., Zackai, S. P., Gillen, J., Ratner, A. J., Walsh, R. F., Fitzgerald, J. C., ... Randolph, A. G. (2020). Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *The New England journal of medicine*, NEJMoa2021680. Advance online publication. <https://doi.org/10.1056/NEJMoa2021680>

Neurological and neuropsychiatric complications such as intracerebral hemorrhage, central nervous system vasculitis, altered mental status, myasthenia gravis, encephalopathy, encephalitis, new-onset psychosis, dementia-like syndromes, and affective disorder have been found in COVID-19 patients of all ages.⁶¹

A serum antibody test for IgA, IgG, and IgM can be performed to learn of past infection. This can help gauge potential severity of symptoms. Initial results suggest that COVID-19 antibodies only remain stable in the blood of the majority of infected individuals for two months after diagnosis and possibly longer. However, antibodies were not detectable in everyone exposed to the virus.⁶²

For asymptomatic individuals who test positive for COVID-19, a complete blood count, blood biochemistry, coagulation function, liver and renal function, infection biomarkers, and chest computed tomography may be measured.⁶³

Treatment

Treatment is trial and error because COVID-19 comes from a novel coronavirus strain and there is still so much we do not know.

The most difficult aspect of treating COVID-19 patients has been breaking the “cytokine storm” or inflammatory cascade.⁶⁴ Treatment varies widely depending upon the country.

For example, in addition to the World Health Organization protocol, Italy includes a nutritional element from a nourishing diet, as well as the IL-6 inhibitor tocilizumab, and the steroid methylprednisolone.⁶⁵ ⁶⁶ China uses a combination of conventional medicine and Chinese

⁶¹ Varatharaj, A., Thomas, N., Ellul, M. A., Davies, N., Pollak, T. A., Tenorio, E. L., Sultan, M., Easton, A., Breen, G., Zandi, M., Coles, J. P., Manji, H., Al-Shahi Salman, R., Menon, D. K., Nicholson, T. R., Benjamin, L. A., Carson, A., Smith, C., Turner, M. R., Solomon, T., ... CoroNerve Study Group (2020). Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *The Lancet. Psychiatry*, S2215-0366(20)30287-X. Advance online publication. [https://doi.org/10.1016/S2215-0366\(20\)30287-X](https://doi.org/10.1016/S2215-0366(20)30287-X)

⁶² Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.07.20124636v2>

⁶³ Long, Q. X., Tang, X. J., Shi, Q. L., Li, Q., Deng, H. J., Yuan, J., Hu, J. L., Xu, W., Zhang, Y., Lv, F. J., Su, K., Zhang, F., Gong, J., Wu, B., Liu, X. M., Li, J. J., Qiu, J. F., Chen, J., & Huang, A. L. (2020). Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nature medicine*, 10.1038/s41591-020-0965-6. Advance online publication. <https://doi.org/10.1038/s41591-020-0965-6>

⁶⁴ Yanuck, S. F., Pizzorno, J., Messier, H., & Fitzgerald, K. N. (2020). Evidence Supporting a Phased Immuno-physiological Approach to COVID-19 From Prevention Through Recovery. *Integrative medicine (Encinitas, Calif.)*, 19(Suppl 1), 8–35.

⁶⁵ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.22.20133413v1>

⁶⁶ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.20.20157503v1>

medicine. Greece has found the older anti-inflammatory drug colchicine helpful.⁶⁷ Pakistan found tocilizumab to be effective and economical.⁶⁸ Israel is using aviptadil, a synthetic form of a natural peptide that the US Food and Drug Administration has fast-tracked to enhance recovery from critical respiratory failure.⁶⁹

Treatment in the United States varies depending upon the hospital. Some hospitals will use ventilators, but only as a last resort. Helmet non-invasive ventilation is a form of continuous positive applied pressure that has emerged for COVID-19 patients who require respiratory support but may not require invasive ventilation.⁷⁰ Others will use supplementary oxygen. Some hospitals use antiviral combinations, including the experimental drug Remdesivir, which is now recommended as a treatment option by the National Institutes of Health to shorten the duration of COVID-19, although some research has shown it to be ineffective, as well as causing cases of liver toxicity have.^{71 72} Other hospitals used the antimalarial chloroquine or hydroxychloroquine, but the FDA revoked its emergency use status and has been banned from use, even though numerous studies outside of the United States purports a benefit, especially when combined with zinc.^{73 74 75 76 77} Anti-inflammatories, especially steroids, have been confirmed as successful

⁶⁷ Deftereos, S. G., Giannopoulos, G., Vrachatis, D. A., Siasos, G. D., Giotaki, S. G., Gargalianos, P., Metallidis, S., Sianos, G., Baltagiannis, S., Panagopoulos, P., Dolianitis, K., Randou, E., Syrigos, K., Kotanidou, A., Koulouris, N. G., Milionis, H., Sipsas, N., Gogos, C., Tsoukalas, G., Olympios, C. D., ... GRECCO-19 investigators (2020). Effect of Colchicine vs Standard Care on Cardiac and Inflammatory Biomarkers and Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019: The GRECCO-19 Randomized Clinical Trial. *JAMA network open*, 3(6), e2013136. <https://doi.org/10.1001/jamanetworkopen.2020.13136>

⁶⁸ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.23.20134072v1>

⁶⁹ Clinicaltrials.gov. Retrieved from: <https://www.clinicaltrials.gov/ct2/show/NCT04311697>

⁷⁰ Medrxiv: Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.29.20141283v1>

⁷¹ National Institutes of Health: <https://www.covid19treatmentguidelines.nih.gov/whats-new/>

⁷² Spinner, C. D., Gottlieb, R. L., Criner, G. J., Arribas López, J. R., Cattelan, A. M., Soriano Viladomiu, A., Ogbuagu, O., Malhotra, P., Mullane, K. M., Castagna, A., Chai, L., Roestenberg, M., Tsang, O., Bernasconi, E., Le Turnier, P., Chang, S. C., SenGupta, D., Hyland, R. H., Osinusi, A. O., Cao, H., ... GS-US-540-5774 Investigators (2020). Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. *JAMA*, 324(11), 1048–1057. <https://doi.org/10.1001/jama.2020.16349>

⁷³ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.16.20175752v1>

⁷⁴ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.09.09.20184143v1>

⁷⁵ COVID-19 RISK and Treatments (CORIST) Collaboration members: (2020). Use of hydroxychloroquine in hospitalised COVID-19 patients is associated with reduced mortality: Findings from the observational multicentre Italian CORIST study. *European journal of internal medicine*, S0953-6205(20)30335-6. Advance online publication. <https://doi.org/10.1016/j.ejim.2020.08.019>

⁷⁶ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.19.20178376v1>

⁷⁷ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.20.20178772v1>

treatments in most cases, especially if the patient shows elevated C-reactive protein level.^{78 79} The steroid dexamethasone is the first drug to reduce COVID deaths, one in eight patients on ventilators, and one in 25 of patients on oxygen.⁸⁰ Recent data suggests an antiparasitic called ivermectin has been shown to inhibit replication of SARS-CoV-2.⁸¹ Medication to prevent blood clots traveling from the legs to the lungs to patients at heightened risk seems to have helped reduce the risk for catastrophic COVID-related death.⁸² Researchers purport that the commonly used medication Heparin could be used as an intervention for excessive clotting.⁸³

The first comprehensive review, while still based upon limited evidence, suggests glucocorticoids being the most effective at reducing mortality. The review purports hydroxychloroquine being most effective for reducing the duration of symptoms, with remdesivir or lopinavir-ritonavir with intermediate effectiveness.⁸⁴

⁷⁸ Keller, M. J., Kitsis, E. A., Arora, S., Chen, J., Agarwal, S., Ross, M. J., . . . Southern, W. (2020). Effect of Systemic Glucocorticoids on Mortality or Mechanical Ventilation in Patients With COVID-19. *Journal of Hospital Medicine*, (2020-07-22 ONLINE FIRST). doi:10.12788/jhm.3497

⁷⁹ WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne, J., Murthy, S., Diaz, J. V., Slutsky, A. S., Villar, J., Angus, D. C., Annane, D., Azevedo, L., Berwanger, O., Cavalcanti, A. B., Dequin, P. F., Du, B., Emberson, J., Fisher, D., Giraudeau, B., Gordon, A. C., Granholm, A., Green, C., Haynes, R., . . . Marshall, J. C. (2020). Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. *JAMA*, 10.1001/jama.2020.17023. Advance online publication. <https://doi.org/10.1001/jama.2020.17023>

⁸⁰ University of Oxford. Retrieved from: <https://www.recoverytrial.net/news/low-cost-dexamethasone-reduces-death-by-up-to-one-third-in-hospitalised-patients-with-severe-respiratory-complications-of-covid-19>

⁸¹ Bray, M., Rayner, C., Noël, F., Jans, D., & Wagstaff, K. (2020). Ivermectin and COVID-19: A report in Antiviral Research, widespread interest, an FDA warning, two letters to the editor and the authors' responses. *Antiviral research*, 178, 104805. Advance online publication. <https://doi.org/10.1016/j.antiviral.2020.104805>

⁸² Gao, C., Cai, Y., Zhang, K., Zhou, L., Zhang, Y., Zhang, X., Li, Q., Li, W., Yang, S., Zhao, X., Zhao, Y., Wang, H., Liu, Y., Yin, Z., Zhang, R., Wang, R., Yang, M., Hui, C., Wijns, W., McEvoy, J. W., . . . Li, F. (2020). Association of hypertension and antihypertensive treatment with COVID-19 mortality: a retrospective observational study. *European heart journal*, 41(22), 2058–2066. <https://doi.org/10.1093/eurheartj/ehaa433>

⁸³ Kim, S. Y., Jin, W., Sood, A., Montgomery, D. W., Grant, O. C., Fuster, M. M., Fu, L., Dordick, J. S., Woods, R. J., Zhang, F., & Linhardt, R. J. (2020). Characterization of heparin and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) spike glycoprotein binding interactions. *Antiviral research*, 181, 104873. Advance online publication. <https://doi.org/10.1016/j.antiviral.2020.104873>

⁸⁴ Siemieniuk, R. A., Bartoszko, J. J., Ge, L., Zeraatkar, D., Izcovich, A., Pardo-Hernandez, H., Rochweg, B., Lamontagne, F., Han, M. A., Kum, E., Liu, Q., Agarwal, A., Agoritsas, T., Alexander, P., Chu, D. K., Couban, R., Darzi, A., Devji, T., Fang, B., Fang, C., . . . Brignardello-Petersen, R. (2020). Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ (Clinical research ed.)*, 370, m2980. <https://doi.org/10.1136/bmj.m2980>

One multi-country study performed found a dual histamine-receptor blockade with cetirizine and famotidine appeared to reduce pulmonary symptoms and may have other benefits in patients with COVID-19.⁸⁵

Many hospitals have found that simple techniques such as putting severe hypoxic patients in the prone position for improved oxygenation to be extremely helpful in lieu of ventilators, which have an extremely high death rate.⁸⁶

Transfusions of plasma from recovered COVID-19 patients into critically ill patients has shown promise in several patient trials with no adverse side effects and is considered a safe treatment option for patients with severe COVID-19 disease.^{87 88}

Research suggests the same inflammatory pathways that lead to Rheumatoid arthritis may affect alveolar structures in COVID-19. Preventing the cytokine storm may be ameliorated, and increase survival, by using treatments to inhibit IL-6, IL-1 β or TNF or targeting cytokine signalling via Janus kinase inhibition.^{89 90 91}

Several studies are now examining low radiation therapy after several patients were able to go off oxygen through marked improvement in inflammation.⁹²

A multi-country study found that adding vitamin D to immunomodulatory drugs, especially steroids, can down-regulate hyper-inflammation in severe COVID-19 patients, which helps ameliorate the cytokine storm.⁹³

⁸⁵ Hogan li, R. B., Hogan lii, R. B., Cannon, T., Rappai, M., Studdard, J., Paul, D., & Dooley, T. P. (2020). Dual-histamine receptor blockade with cetirizine - famotidine reduces pulmonary symptoms in COVID-19 patients. *Pulmonary pharmacology & therapeutics*, 63, 101942. Advance online publication. <https://doi.org/10.1016/j.pupt.2020.101942>

⁸⁶ Elharrar, X., Trigui, Y., Dols, A. M., Touchon, F., Martinez, S., Prud'homme, E., & Papazian, L. (2020). Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure. *JAMA*, 323(22), 2336–2338. Advance online publication. <https://doi.org/10.1001/jama.2020.8255>

⁸⁷ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.05.08.20095471v1>

⁸⁸ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.23.20160796v1>

⁸⁹ Schett, G., Manger, B., Simon, D., & Caporali, R. (2020). COVID-19 revisiting inflammatory pathways of arthritis. *Nature reviews rheumatology* (2020). <https://doi.org/10.1038/s41584-020-0451-z>

⁹⁰ van de Veerdonk, F. L., & Netea, M. G. (2020). Blocking IL-1 to prevent respiratory failure in COVID-19. *Critical care (London, England)*, 24(1), 445. <https://doi.org/10.1186/s13054-020-03166-0>

⁹¹ Del Valle, D. M., Kim-Schulze, S., Hsin-Hui, H., Beckmann, N. D., Nirenberg, S., Wang, B., Lavin, Y., Swartz, T., Madduri, D., Stock, A., Marron, T., Xie, H., Patel, M. K., van Oekelen, O., Rahman, A., Kovatch, P., Aberg, J., Schadt, E., Jagannath, S., Mazumdar, M., ... Gnjatic, S. (2020). An inflammatory cytokine signature helps predict COVID-19 severity and death. *medRxiv : the preprint server for health sciences*, 2020.05.28.20115758. <https://doi.org/10.1101/2020.05.28.20115758>

⁹² Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.03.20116988v1>

⁹³ Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.07.18.210161v1>

In rare cases, some physicians and hospitals find that a mix of allopathic and integrative therapies work best. Paul Marik, MD, from Eastern Virginia medical School, created a COVID-19 protocol that spans from mild to severe symptoms that include targeted medications and nutrients together.⁹⁴ Richard Bartlett, MD has found success using the nebulized corticosteroid budesonide (pulmicort), macrolide antibiotic, low dose aspirin, and zinc.⁹⁵

Patients should understand and continue with targeted COVID-19 disease treatment as lingering symptoms can last for weeks, if not months after twice testing negative.⁹⁶

One major question scientists have been trying to answer is immunity, to what degree, and can one catch COVID-19 more than once. These answers to these questions are still coming to fruition. From what the research tells us so far, antibody immunity wanes in many COVID patients after several months, and one can catch COVID-19 more than once, albeit in almost every case the symptoms are milder, which indicates an adaptive immunity via memory B and T cells.^{97 98 99 100}

When to Refer

Any patient who has one or more comorbidities, or anyone older than 60 years of age, should seek out their physician if they even feel the slightest symptoms or have been exposed to a person with a positive result for SARS-CoV-2 infection. In a person without any of the aforementioned, if they exhibit one or a combination of the following, should seek out their

⁹⁴ Critical Care COVID-19 Protocol. Retrieved from: https://www.evms.edu/media/evms_public/departments/internal_medicine/Marik-Covid-Protocol-Summary.pdf

⁹⁵ SARS-CoV-2 and The Case for Empirical Treatment. Retrieved: <https://americacanwetalk.org/wp-content/uploads/2020/07/ColumnByDrBartlettReCOVID-5.pdf>

⁹⁶ Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March–June 2020. (2020, July 24). Retrieved July 28, 2020, from <https://www.cdc.gov/mmwr/volumes/69/wr/mm6930e1.htm>

⁹⁷ Patel, M. M., Thornburg, N. J., Stubblefield, W. B., Talbot, H. K., Coughlin, M. M., Feldstein, L. R., & Self, W. H. (2020). Change in Antibodies to SARS-CoV-2 Over 60 Days Among Health Care Personnel in Nashville, Tennessee. *JAMA*, 10.1001/jama.2020.18796. Advance online publication. <https://doi.org/10.1001/jama.2020.18796>

⁹⁸ Gudbjartsson, D. F., Norddahl, G. L., Melsted, P., Gunnarsdottir, K., Holm, H., Eythorsson, E., Arnthorsson, A. O., Helgason, D., Bjarnadottir, K., Ingvarsson, R. F., Thorsteinsdottir, B., Kristjansdottir, S., Birgisdottir, K., Kristinsdottir, A. M., Sigurdsson, M. I., Arnadottir, G. A., Ivarsdottir, E. V., Andresdottir, M., Jonsson, F., Agustsdottir, A. B., ... Stefansson, K. (2020). Humoral Immune Response to SARS-CoV-2 in Iceland. *The New England journal of medicine*, 10.1056/NEJMoa2026116. Advance online publication. <https://doi.org/10.1056/NEJMoa2026116>

⁹⁹ Wu, F., Liu, M., Wang, A., Lu, L., Wang, Q., Gu, C., Chen, J., Wu, Y., Xia, S., Ling, Y., Zhang, Y., Xun, J., Zhang, R., Xie, Y., Jiang, S., Zhu, T., Lu, H., Wen, Y., & Huang, J. (2020). Evaluating the Association of Clinical Characteristics With Neutralizing Antibody Levels in Patients Who Have Recovered From Mild COVID-19 in Shanghai, China. *JAMA internal medicine*, 10.1001/jamainternmed.2020.4616. Advance online publication. <https://doi.org/10.1001/jamainternmed.2020.4616>

¹⁰⁰ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.11.20171843v2>

physician: shortness of breath, heaviness of the chest, diarrhea, high fever that does not abate and fluctuates wildly, forgetfulness, and severe fatigue or malaise.¹⁰¹

Integrative Perspective of Causes

Close contact with a person who is infected is the main cause of transmission. Cough or sneeze is more strongly associated with contraction of SARS-CoV-2, but a person speaking loudly and forcefully can transmit saliva droplets.¹⁰² As recently as July 9th, the World Health Organization is considering changing the main aspect of transmission SARS-CoV-2 as aerosol, which means the virus could stay on droplets in the air for a number of hours.¹⁰³ This would render indoor areas with poor ventilation as major areas of transmission, such as cruise ships and old buildings.

¹⁰⁴

An infected person who has the virus can also leave remnants on surfaces, although transmission is more difficult. The surfaces most likely to transmit are door handles, phone or computer interfaces, and more. Some public health experts urge anyone with a mobile phone to decontaminate their devices daily with either 70 percent isopropyl alcohol or by sanitizing with (ultraviolet) devices.¹⁰⁵

SARS-CoV2 can enter the body through the eyes (because the eyes contain the ACE2 protein receptors), mouth, nose, and ears, mostly through touch by infected hands or inundation from a SARS-CoV-2 cloud.¹⁰⁶

Breathing through the nose and exhaling through your mouth is a preferred way to breathe for extra viral infection protection. Nitric oxide, which helps oxygenate the blood and thus reduces the ability of viruses to replicate, is produced only in the nasal cavity, so mouth breathers do not

¹⁰¹ Centers for Disease Control:
<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

¹⁰² Centers for Disease Control:
<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/activities.html>

¹⁰³ New WHO guidance calls for more evidence on airborne transmission. Retrieved from:
<https://www.reuters.com/article/us-health-coronavirus-who-airborne/new-who-guidance-calls-for-more-evidence-on-airborne-transmission-idUSKBN24A2E5>

¹⁰⁴ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.08.20148775v1>

¹⁰⁵ Kampf, G., Todt, D., Pfaender, S., & Steinmann, E. (2020). Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *The Journal of hospital infection*, 104(3), 246–251.
<https://doi.org/10.1016/j.jhin.2020.01.022>

¹⁰⁶ Wu, P., Duan, F., Luo, C., Liu, Q., Qu, X., Liang, L., & Wu, K. (2020). Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA ophthalmology*, 138(5), 575–578. Advance online publication.
<https://doi.org/10.1001/jamaophthalmol.2020.1291>

produce enough nitric oxide.¹⁰⁷ Implementing breathing exercises for prevention or if symptomatic have been touted as helpful.¹⁰⁸

Dietary sugar, including added sugar, sweets, sugary beverages, or any other sugary product that is not naturally occurring (i.e. fruit) weakens the immune system more than any foodstuff.¹⁰⁹

Inferior nutritional status is often missing in public health discussions regarding an optimally functioning immune system for preventing COVID-19.¹¹⁰ Numerous vitamins, including vitamins A, B6, B12, C, D, E, and folate; and trace elements, including zinc, iron, selenium, magnesium, and copper, among others, play important and complementary roles as immunomodulatory agents in supporting both the innate and adaptive immune systems.¹¹¹ Deficiencies or suboptimal status in micronutrients negatively affect immune function and can decrease resistance to infections. Vitamin D deficiency has been the focus of copious COVID-19 research to the degree that public health experts are calling for universal screening, and medical

¹⁰⁷ Ignarro, Louise. Retrieved from:

<https://www.oregonlive.com/coronavirus/2020/06/the-science-behind-why-this-is-the-safest-way-to-breathe-to-avoid-coronavirus.html>

¹⁰⁸ Hamzelou J. (2020). Can breathing exercises help protect you from covid-19?. *New scientist* (1971), 246(3279), 10–11. [https://doi.org/10.1016/S0262-4079\(20\)30789-2](https://doi.org/10.1016/S0262-4079(20)30789-2)

¹⁰⁹ American Nutrition Association: <https://theana.org/COVID-19>

¹¹⁰ Calder, P. C., Carr, A. C., Gombart, A. F., & Eggersdorfer, M. (2020). Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. *Nutrients*, 12(4), 1181. <https://doi.org/10.3390/nu12041181>

¹¹¹ Gasmi, A., Tippairote, T., Mujawdiya, P. K., Peana, M., Menzel, A., Dadar, M., Benahmed, A. G., & Bjørklund, G. (2020). Micronutrients as immunomodulatory tools for COVID-19 management. *Clinical immunology (Orlando, Fla.)*, 108545. Advance online publication. <https://doi.org/10.1016/j.clim.2020.108545>

associations are asking for mandatory supplementation during the pandemic.^{112 113 114 115 116 117 118}
119 120 121 122

Stress can impair immune function in more ways than one. Along with the direct effect, stress can lead to overeating or a migration to comfort food.¹²³ Hence, stress weakens the body's initial defenses when they are most needed to fight off initial SARS-CoV-2 exposure. Increases in levels of the inflammatory cytokine interleukin-6 (IL-6) correspond to increased levels of worrying.¹²⁴ This can be specifically detrimental for many that have one or more mutations of the IL-6 gene. After subjects did a 10-minute relaxation induction task that focused on deep breathing, there were significant reductions in levels of IL-6. This is further evidence of the important mind-body connection and its influence from stress.

¹¹² Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.24.20138644v1>

¹¹³ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.01.20144329v1>

¹¹⁴ ASBMR. Joint Guidance On Vitamin D in the Era of COVID-19 From the ASBMR, AACE, ENDOCRINE SOCIETY, ECTS, NOF, AND IOF. Retrieved from: <https://www.asbmr.org/ASBMRStatementsDetail/joint-guidance-on-vitamin-d-in-era-of-covid-19-fro>

¹¹⁵ Meltzer, D. O., Best, T. J., Zhang, H., Vokes, T., Arora, V., & Solway, J. (2020). Association of Vitamin D Status and Other Clinical Characteristics With COVID-19 Test Results. *JAMA network open*, 3(9), e2019722. <https://doi.org/10.1001/jamanetworkopen.2020.19722>

¹¹⁶ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.09.04.20188268v1>

¹¹⁷ Verdoia, M., & De Luca, G. (2020). Potential role of hypovitaminosis D and Vitamin D supplementation during COVID-19 pandemic. *QJM : monthly journal of the Association of Physicians*, hcaa234. Advance online publication. <https://doi.org/10.1093/qjmed/hcaa234>

¹¹⁸ Medscape. Retrieved from: <https://www.medscape.com/viewarticle/937567>

¹¹⁹ Brenner, H., Holleczeck, B., & Schöttker, B. (2020). Vitamin D Insufficiency and Deficiency and Mortality from Respiratory Diseases in a Cohort of Older Adults: Potential for Limiting the Death Toll during and beyond the COVID-19 Pandemic?. *Nutrients*, 12(8), 2488. <https://doi.org/10.3390/nu12082488>

¹²⁰ Somasundaram, N. P., Ranathunga, I., Ratnasamy, V., Wijewickrama, P., Dissanayake, H. A., Yogendranathan, N., Gamage, K., de Silva, N. L., Sumanatilleke, M., Katulanda, P., & Grossman, A. B. (2020). The Impact of SARS-Cov-2 Virus Infection on the Endocrine System. *Journal of the Endocrine Society*, 4(8), bvaa082. <https://doi.org/10.1210/jendso/bvaa082>

¹²¹ Stohs, S. J., & Aruoma, O. I. (2020). Vitamin D and Wellbeing beyond Infections: COVID-19 and Future Pandemics. *Journal of the American College of Nutrition*, 1–2. Advance online publication. <https://doi.org/10.1080/07315724.2020.1786302>

¹²² Vyas, N., Kurian, S. J., Bagchi, D., Manu, M. K., Saravu, K., Unnikrishnan, M. K., Mukhopadhyay, C., Rao, M., & Miraj, S. S. (2020). Vitamin D in Prevention and Treatment of COVID-19: Current Perspective and Future Prospects. *Journal of the American College of Nutrition*, 1–14. Advance online publication. <https://doi.org/10.1080/07315724.2020.1806758>

¹²³ Muscogiuri, G., Barrea, L., Savastano, S., & Colao, A. (2020). Nutritional recommendations for CoVID-19 quarantine. *European journal of clinical nutrition*, 74(6), 850–851. <https://doi.org/10.1038/s41430-020-0635-2>

¹²⁴ Medscape: https://www.medscape.com/viewarticle/928287#vp_1

Lack of humidity indoors during the winter months or in very dry climates allows greater transmission of SARS-CoV-2.^{125 126 127} SARS-CoV-2 virus lasts longer on various surfaces during cold weather months, so extra vigilance should be taken for cleaning during fall and winter.¹²⁸

Specialized Integrative Analysis

The primary interface between ourselves and SARS-CoV-2 is our immune system. SARS-CoV-2's initial entry is in the throat and nasopharynx area via the nose, mouth, or eyes. If SARS-CoV-2 gets to the lungs and blood vessels, the potential for devastation grows.

SARS-CoV-2 draws the innate immune response of T-antibodies, IgM, other IgGs, and neutrophils more than lymphocytes. It seems particularly deadly in adults because it may be able to evade these initial innate immune responses, whereas children rely more on their adaptive immune response.¹²⁹

Pyroptosis, a novel form of inflammatory cell death, may be a cause of the increased virulence of COVID-19. Pyroptosis initiates the upregulation of inflammasome NLRP3. Chronic activation of pyroptosis can occur with proinflammatory, high-sugar and -processed food diets, gut dysbiosis, stress, toxins, drugs, etc. Chronic activation has been noted in inflammatory diseases such as type 2 diabetes, obesity, autoimmune disease, cardiovascular disease, and cancer.¹³⁰

Discerning between COVID-19, cold, allergy, strep or flu can be difficult initially because many of the symptoms are similar, including fatigue, fever, headache, aches and pains, diarrhea and gastrointestinal upset.

¹²⁵ Sajadi, M. M., Habibzadeh, P., Vintzileos, A., Shokouhi, S., Miralles-Wilhelm, F., & Amoroso, A. (2020). Temperature, Humidity, and Latitude Analysis to Estimate Potential Spread and Seasonality of Coronavirus Disease 2019 (COVID-19). *JAMA network open*, 3(6), e2011834. <https://doi.org/10.1001/jamanetworkopen.2020.11834>

¹²⁶ Paez, A., Lopez, F. A., Menezes, T., Cavalcanti, R., & Pitta, M. (2020). A Spatio-Temporal Analysis of the Environmental Correlates of COVID-19 Incidence in Spain. *Geographical analysis*, 10.1111/gean.12241. Advance online publication. <https://doi.org/10.1111/gean.12241>

¹²⁷ Ward, M. P., Xiao, S., & Zhang, Z. (2020). Humidity is a consistent climatic factor contributing to SARS-CoV-2 transmission. *Transboundary and emerging diseases*, 10.1111/tbed.13766. Advance online publication. <https://doi.org/10.1111/tbed.13766>

¹²⁸ Biorxiv. Retrieved: <https://www.biorxiv.org/content/10.1101/2020.08.30.274241v1>

¹²⁹ Nikolich-Zugich, J., Knox, K. S., Rios, C. T., Natt, B., Bhattacharya, D., & Fain, M. J. (2020). SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. *GeroScience*, 42(2), 505–514. <https://doi.org/10.1007/s11357-020-00186-0>

¹³⁰ Fusco, R., Siracusa, R., Genovese, T., Cuzzocrea, S., & Di Paola, R. (2020) Focus on the Role of NLRP3 Inflammasome in Diseases. *International Journal of Molecular Sciences*, (21) 4223. <https://doi.org/10.3390/ijms21124223>

SARS-CoV-2 is the only coronavirus with a furin cleavage site, which is why scientists believe neutralizing this is the key to stopping it.¹³¹ Not even distant relatives of SARS-CoV-2 have it, and the coronaviruses that do have it share only 40% of SARS-CoV-2's genome. Lifestyle intervention is critical for attenuating this cleavage site from SARS-CoV-2.¹³²

Nutritional and lifestyle intervention is critical to enhance immunity in viral infections such as COVID-19.¹³³ Whey protein is one foodstuff shown to have an antiviral effect against SARS-CoV-2.¹³⁵

The amount of SARS-CoV-2 exposure, or viral load, often warrants how serious the COVID-19 infection may be. Ascertaining this from the patient can assist in treatment decisions.¹³⁶

There are four phases in the timeline of COVID-19. Knowing the phases and what self-treatment they require is important as SARS-CoV-2 puts our immune system at odds. We need early activation but not continued overactivity.¹³⁷

Phase One - Prevention

Prevention means you are prepping your immune system for peak surveillance to detect SARS-CoV-2, as well as reducing daily levels of inflammation, to improve outcomes if you become infected.

Phase Two - Infection

If you happen to be infected with SARS-CoV-2, support for infection emphasizes specialized immune activity against infection.

Phase Three - Escalating Inflammation

¹³¹ Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.26.268854v1>

¹³² SSRN. Retrieved from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3612934

¹³³ Jayawardena, R., Sooriyaarachchi, P., Chourdakis, M., Jeewandara, C., & Ranasinghe, P. (2020). Enhancing immunity in viral infections, with special emphasis on COVID-19: A review. *Diabetes & metabolic syndrome*, 14(4), 367–382. Advance online publication. <https://doi.org/10.1016/j.dsx.2020.04.015>

¹³⁴ Frates, E. P., & Rifai, T. (2020). Making the Case for "COVID-19 Prophylaxis" With Lifestyle Medicine. *American journal of health promotion : AJHP*, 34(6), 689–691. <https://doi.org/10.1177/0890117120930536c>

¹³⁵ Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.17.254979v1>

¹³⁶ Liu, Y., Yan, L. M., Wan, L., Xiang, T. X., Le, A., Liu, J. M., Peiris, M., Poon, L., & Zhang, W. (2020). Viral dynamics in mild and severe cases of COVID-19. *The Lancet. Infectious diseases*, 20(6), 656–657. [https://doi.org/10.1016/S1473-3099\(20\)30232-2](https://doi.org/10.1016/S1473-3099(20)30232-2)

¹³⁷ Yanuck, S. F., Pizzorno, J., Messier, H., & Fitzgerald, K. N. (2020). Evidence Supporting a Phased Immuno-physiological Approach to COVID-19 From Prevention Through Recovery. *Integrative medicine (Encinitas, Calif.)*, 19(Suppl 1), 8–35.

If SARS-CoV-2 over-stimulates the immune response to the point that you are symptomatic, support is focused on anti-inflammatory measures.

Phase Four - Recovery

Once you are not symptomatic, support should still be focused on resolving inflammation, inhibiting tissue damage, curtailing losses of function, and restoring and reoptimizing function.

Because patients have been observed to relapse into the Escalating Inflammation Phase, it is essential to communicate with your health professional to continue following the protocol well into what may appear to be the Recovery Phase.

In-depth strategies to support the four phases are below. Public health measures such as wearing a mask, social distancing, not touching your face, washing your hands, and the like were not included in this monograph, as most are aware of these measures.

Integrative Support Protocols

Before explaining how important diet and lifestyle choices are, five critical care physicians developed and are using an integrative protocol for hospitalized COVID-19 patients called MATH+. ¹³⁸ The protocol calls for the use of intravenous methylprednisolone, vitamin C and subcutaneous heparin within six hours of admission into the hospital, along with high-flow nasal oxygen. Optional additions include thiamine, zinc and vitamin D. They have successfully used this protocol to prevent severe COVID-19 symptoms of hyperinflammation, hypercoagulation and hypoxia.

Two extremely economical things every home and office can do to lower the transmission of COVID-19 are opening up windows to improve air flow and letting more natural light into a room, creating a healthier environment. ¹³⁹

Diet and Lifestyle Choices

Nutrient support via an anti-inflammatory diet and targeted vitamins, minerals, and antioxidants are important to stave off infection, but critical if one presents with severe COVID-19 to stave off death. ¹⁴⁰

¹³⁸ U.S. Senate Committee on Homeland Security and Governmental Affairs. Retrieved from: <https://www.hsgac.senate.gov/imo/media/doc/Testimony-Kory-2020-05-06-REVISED.pdf>

¹³⁹ Dietz, L., Horve, P. F., Coil, D. A., Fretz, M., Eisen, J. A., & Van Den Wymelenberg, K. (2020). 2019 Novel Coronavirus (COVID-19) Pandemic: Built Environment Considerations To Reduce Transmission. *mSystems*, 5(2), e00245-20. <https://doi.org/10.1128/mSystems.00245-20>

¹⁴⁰ Bousquet, J., Anto, J. M., Iaccarino, G., Czarlewski, W., Haahtela, T., Anto, A., Akdis, C. A., Blain, H., Canonica, G. W., Cardona, V., Cruz, A. A., Illario, M., Ivancevich, J. C., Jutel, M., Klimek, L., Kuna, P., Laune, D., Larenas-Linnemann, D., Mullol, J., Papadopoulos, N. G., ... ARIA group (2020). Is diet partly

Public health experts are imploring populations all over the world to keep good glucose control to avoid infection. Being extra vigilant regarding sugars and sugar control to avoid peaks and valleys is crucial, especially for those with blood sugar disorders, and those who are hospitalized with COVID-19.¹⁴¹ ¹⁴² Higher glucose levels lead to higher inflammatory cytokine activity, which if not mitigated, may lead to severe COVID-19.¹⁴³

Alcohol may put people at increased risk for the coronavirus, weakening the body's immune system and leaving drinkers at risk for other risky behaviors that could increase the likelihood of contracting coronavirus. While alcohol does work as a disinfectant on surfaces, excessive alcohol consumption can actually make the body less capable of handling SARS-CoV-2. Crucially, alcohol, especially in strong concentrations and large amounts, can be a vasoconstrictor, leaving one more susceptible to serious COVID-19 symptoms.¹⁴⁴

Eat copious amounts of fruit and vegetables. Not only do they provide fluid and electrolytes, their phytochemicals protect the throat and lungs, and most importantly help maintain your acid/alkaline balance. It is much tougher for viruses to take hold when the body's pH level is between 6.8 and 7.2, which is slightly alkaline. Being too acidic or too alkaline is also not ideal. Cruciferous vegetables from the Brassica family also help boost our Th1 immune antibodies.¹⁴⁵ Leafy greens rich in vitamin K can help promote optimal coagulation as those with accelerated COVID-19 severity seem to have low vitamin K levels.¹⁴⁶

responsible for differences in COVID-19 death rates between and within countries?. Clinical and translational allergy, 10, 16. <https://doi.org/10.1186/s13601-020-00323-0>

¹⁴¹ Korytkowski, M., Antinori-Lent, K., Drincic, A., Hirsch, I. B., McDonnell, M. E., Rushakoff, R., & Muniyappa, R. (2020). A Pragmatic Approach to Inpatient Diabetes Management during the COVID-19 Pandemic. *The Journal of clinical endocrinology and metabolism*, dgaa342. Advance online publication. <https://doi.org/10.1210/clinem/dgaa342>

¹⁴² Demasi M. (2020). COVID-19 and metabolic syndrome: could diet be the key?. *BMJ evidence-based medicine*, bmjebm-2020-111451. Advance online publication. <https://doi.org/10.1136/bmjebm-2020-111451>

¹⁴³ Wang, Q., Fang, P., He, R., Li, M., Yu, H., Zhou, L., Yi, Y., Wang, F., Rong, Y., Zhang, Y., Chen, A., Peng, N., Lin, Y., Lu, M., Zhu, Y., Peng, G., Rao, L., & Liu, S. (2020). O-GlcNAc transferase promotes influenza A virus-induced cytokine storm by targeting interferon regulatory factor-5. *Science advances*, 6(16), eaaz7086. <https://doi.org/10.1126/sciadv.aaz7086>

¹⁴⁴ World Health Organization:

<https://www.euro.who.int/en/health-topics/disease-prevention/alcohol-use/news/news/2020/04/alcohol-does-not-protect-against-covid-19-access-should-be-restricted-during-lockdown>

¹⁴⁵ The Institute for Functional Medicine:

<https://www.ifm.org/news-insights/the-functional-medicine-approach-to-covid-19-virus-specific-nutraceutical-and-botanical-agents/?fbclid=IwAR24Kg3-s4SA3170UnwoKuZIO9gKKup8iFNU7XKMtEmCohMWI5SCwpZ3uDQ>

¹⁴⁶ Dofferhoff, A., Piscaer, I., Schurgers, L., Walk, J., van den Ouweland, J., Hackeng, T., Lux, P., Maassen, C., Karssemeijer, E., Wouters, E., & Janssen, R. (2020). Reduced Vitamin K Status as a Potentially Modifiable Prognostic Risk Factor in COVID-19. Preprints, 2020040457; doi: 10.20944/preprints202004.0457.v1.

Drink a lot of fluid (warm or hot) to avoid dehydration. Electrolytes, especially potassium, are crucial. One of the things that happens with infection in severe cases is hypokalemia.¹⁴⁷ Sodas, juices, and sweetened coffee or tea drinks are not recommended. A sip of warm water every 20 minutes may wash any existing viruses down the throat down into the gastric juices of the stomach where they have trouble surviving the ultra-acidic environment.

Healthy sleep supports antiviral immune response. Disordered sleep promotes inflammation. Data shows that patients hospitalized with COVID-19 are often those who slept the least.¹⁴⁸ Six to eight hours of sleep is ideal.

Psychosocial interventions such as cognitive behavioral therapy (CBT) are associated with positive changes in immune system function, and decreases in harmful immune function that persisted for at least 6 months following treatment for participants randomly assigned to CBT psychosocial intervention versus a control group.¹⁴⁹

Exercise and movement is essential for prevention of COVID-19 and has been shown to reduce symptomatic days if you do get COVID-19.^{150 151} The key is not to do too much or too little. It is also essential to move around, even if you just get up every 20 minutes or so. To decrease inflammation, the right exercise intensity is critical with moderate levels effective at lowering inflammatory markers, while overtly intense exercise does not. Caution should be used when considering the form and duration of exercise during the pandemic.

Spending time outdoors not only lowers transmission of SARS-CoV-2¹⁵², but being outdoors, especially in nature, has multimodal beneficial effects.

The state of the gut microbiome has been shown to contribute either positively or negatively to SARS-CoV-2 infection. Both the lung and the GI tract have a microbiome. The complex relationship between them and the immune system is emerging. Disrupted balance of GI

¹⁴⁷ Lippi, G., South, A. M., & Henry, B. M. (2020). Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). *Annals of clinical biochemistry*, 57(3), 262–265. <https://doi.org/10.1177/0004563220922255>

¹⁴⁸ Vallat, R., Shah, V. D., Redline, S., Attia, P., & Walker, M. P. (2020). Broken sleep predicts hardened blood vessels. *PLoS biology*, 18(6), e3000726. <https://doi.org/10.1371/journal.pbio.3000726>

¹⁴⁹ Shields, G. S., Spahr, C. M., & Slavich, G. M. (2020). Psychosocial Interventions and Immune System Function: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA psychiatry*, e200431. Advance online publication. <https://doi.org/10.1001/jamapsychiatry.2020.0431>

¹⁵⁰ Alkhatib A. (2020). Antiviral Functional Foods and Exercise Lifestyle Prevention of Coronavirus. *Nutrients*, 12(9), E2633. <https://doi.org/10.3390/nu12092633>

¹⁵¹ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.21.20179499v1>

¹⁵² Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.04.04.20053058v1>

microbiome bacteria has been shown to be a source of systemic inflammation. Consuming ample dietary fiber helps the gut and perpetuates beneficial lung health. Optimal diet, but also pre- and -probiotic supplementation may be warranted for this.¹⁵³ Probiotic strains of lactobacilli and bifidobacteria exhibited an ameliorating impact on the clinical conditions of hospitalized patients positive for SARS-CoV-2 infection.¹⁵⁴

If where one resides does not offer the ability to breathe pristinely clean air, such as big cities or areas with power plants,¹⁵⁵ one can assure their domicile has clean air by installing a HEPA filter.¹⁵⁶ This is especially important during hot weather months where one must be indoors with air conditioning.¹⁵⁷ In addition, a humidifier in the winter is essential, as viruses are not as virulent when there is more moisture in the air.¹⁵⁸ ¹⁵⁹ Keeping your humidifier set to 25-40% is ideal. Research suggests that every degree Celsius increase in daily average temperature results in a 2.88% decrease in new daily COVID-19 cases.¹⁶⁰

In those that need to be hospitalized, many hospitals around the world are using intravenous nutrients, such as vitamin C and glutathione, with positive case reports.¹⁶¹ A clinical trial that started in February will be completed this fall regarding the effectiveness of IV vitamin C therapy in COVID-19-related pneumonia.¹⁶² A case report found IV glutathione, glutathione precursors (N-acetyl-cysteine), and alpha lipoic acid may represent a novel treatment approach for addressing "cytokine storm syndrome" and respiratory distress in patients with COVID-19 pneumonia.¹⁶³

¹⁵³ Dhar, D., & Mohanty, A. (2020). Gut microbiota and Covid-19- possible link and implications. *Virus research*, 285, 198018. <https://doi.org/10.1016/j.virusres.2020.198018>

¹⁵⁴ D'ettore, G., Ceccarelli, G., Marazzato, M., Campagna, G., Pinacchio, C., Alessandri, F., . . . Mastroianni, C. M. (2020). Challenges in the Management of SARS-CoV2 Infection: The Role of Oral Bacteriotherapy as Complementary Therapeutic Strategy to Avoid the Progression of COVID-19. *Frontiers in Medicine*, 7. doi:10.3389/fmed.2020.00389

¹⁵⁵ Medrxiv. Retrieved from: <https://doi.org/10.1101/2020.04.05.20054502>

¹⁵⁶ Institute of Labor Economics. Retrieved from: <http://ftp.iza.org/dp13367.pdf>

¹⁵⁷ ASHRAE Epidemic Task Force. Retrieved from: <https://www.ashrae.org/file%20library/technical%20resources/covid-19/ashrae-building-readiness.pdf>

¹⁵⁸ American Lung Association: <https://www.lung.org/media/press-releases/state-of-the-air-2020>

¹⁵⁹ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.18.20177444v3>

¹⁶⁰ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.29.20164152v1>

¹⁶¹ Waqas Khan, H. M., Parikh, N., Megala, S. M., & Predeteanu, G. S. (2020). Unusual Early Recovery of a Critical COVID-19 Patient After Administration of Intravenous Vitamin C. *The American journal of case reports*, 21, e925521. <https://doi.org/10.12659/AJCR.925521>

¹⁶² Clinicaltrials.gov: <https://clinicaltrials.gov/ct2/show/NCT04264533>

¹⁶³ Horowitz, R. I., Freeman, P. R., & Bruzzese, J. (2020). Efficacy of glutathione therapy in relieving dyspnea associated with COVID-19 pneumonia: A report of 2 cases. *Respiratory medicine case reports*, 30, 101063. Advance online publication. <https://doi.org/10.1016/j.rmcr.2020.101063>

Just eating a healthy diet will not suffice. You need supplemental support.^{164 165 166 167}

Supplements for All Four COVID-19 Timeline Phases

VITAMIN C (Ascorbic Acid)

Critical for almost every cellular function.¹⁶⁸

Dosage: 500mg - 700 mg twice daily for adults; 250mg - 350 mg twice daily for children.

**During Inflammation Phase, increase to 2,000mg - 4,000mg if tolerated digestively.

ZINC

Zinc deficiency is believed to be a risk factor for COVID-19.¹⁶⁹ Oral tablets/capsules along with zinc lozenges/zinc sulfate solution have been proven to be effective in blocking coronavirus (and most other viruses) from multiplying in your throat and nasopharynx.^{170 171}

Loss of smell (anosmia) and distorted sense of taste (dysgeusia), the most frequent complaint in those with COVID-19, are classic symptoms of zinc deficiency.

It is especially important that you take zinc if you have the SLC30A genetic mutation that impedes absorption. Mutation(s) of the gene increases risk for the viral infections varicella

¹⁶⁴ McAuliffe, S., Ray, S., Fallon, E., Bradfield, J., Eden, T., & Kohlmeier, M. (2020, June 18). Dietary micronutrients in the wake of COVID-19: An appraisal of evidence with a focus on high-risk groups and preventative healthcare. Retrieved June 27, 2020, from <https://nutrition.bmj.com/content/early/2020/06/17/bmjnph-2020-000100>

¹⁶⁵ BourBour, F., Mirzaei Dahka, S., Gholamalizadeh, M., Akbari, M. E., Shadnoush, M., Haghighi, M., Taghvaye-Masoumi, H., Ashoori, N., & Doaei, S. (2020). Nutrients in prevention, treatment, and management of viral infections; special focus on Coronavirus. *Archives of physiology and biochemistry*, 1–10. Advance online publication. <https://doi.org/10.1080/13813455.2020.1791188>

¹⁶⁶ Jovic, T. H., Ali, S. R., Ibrahim, N., Jessop, Z. M., Tarassoli, S. P., Dobbs, T. D., Holford, P., Thornton, C. A., & Whitaker, I. S. (2020). Could Vitamins Help in the Fight Against COVID-19?. *Nutrients*, 12(9), E2550. <https://doi.org/10.3390/nu12092550>

¹⁶⁷ Shakoor, H., Feehan, J., Dhaheri, A. S., Ali, H. I., Platat, C., Ismail, L. C., . . . Stojanovska, L. (2021). Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? *Maturitas*, 143, 1-9. doi:10.1016/j.maturitas.2020.08.003

¹⁶⁸ American Nutrition Association: <https://theana.org/COVID-19>

¹⁶⁹ Singh, S. (2020). Covariation of Zinc Deficiency with COVID19 Infections and Mortality in European Countries: Is Zinc Deficiency a Risk Factor for COVID-19? *Journal of Scientific Research*, 64(02), 153-157. doi:10.37398/jsr.2020.640222

¹⁷⁰ The Institute for Functional Medicine:

<https://www.ifm.org/news-insights/the-functional-medicine-approach-to-covid-19-virus-specific-nutraceutical-and-botanical-agents/?fbclid=IwAR24Kg3-s4SA3170UnwoKuZIO9gKKup8iFNU7XKMtEmCohMWI5SCwpZ3uDQ>

¹⁷¹ Mossink, J. P. (2020). Zinc as nutritional intervention and prevention measure for COVID–19 disease. *BMJ Nutrition, Prevention & Health*. doi:10.1136/bmjnph-2020-000095

(chicken pox), zoster (shingles), herpes, coronavirus (common cold), influenza, hepatitis, viral warts, stomach flu, HPV, and now COVID-19.

Dosage: 20mg - 30mg capsules/tablets with a 60mg maximum daily for adults (so if you take a multi with extra zinc you should be good). 15mg - 30mg for children. Always take oral zinc with a protein meal.

For lozenges, let them dissolve in the back of your throat and nasopharynx.

For children who cannot swallow a pill, a 15 mg. zinc sulfate solution can be added to water.

There is also a 2 mg zinc sulfate solution that can be gargled and swallowed twice daily by anyone as a preventive or for sore throats.

****During Infection and Inflammation Phase, take at least 60mg supplemental zinc until Recovery Phase.**

MONOLaurin (glycerol monostearate)

Similar to how washing our hands with soap kills viruses, monolaurin does a similar thing in our bodies at the cellular level. A natural antiviral derived from coconut, glycerol monostearate mirrors the immune property monolaurin, found in human breast milk. Monolaurin kills viruses by breaking down their phospholipid layer, leading to apoptosis (cell death). As a natural emulsifier, it takes the fight to viruses on the cellular level because of its natural foaming properties.

Monolaurin also inactivates lipid-coated viruses by binding to the lipid-protein envelope of the virus, thereby preventing it from attaching and entering host cells, making infection and replication impossible.¹⁷² Monolaurin can also disintegrate the protective viral envelope, killing the virus (SARS-CoV-2 has this viral envelope). Monolaurin can balance out T-cell antibody and cytokine overactivity.¹⁷³

Dosage: 600mg daily for adults and teens; 300mg for young children.

¹⁷² Schlievert, P. M., Kilgore, S. H., Kaus, G. M., Ho, T. D., & Ellermeier, C. D. (2018). Glycerol Monolaurate (GML) and a Nonaqueous Five-Percent GML Gel Kill Bacillus and Clostridium Spores. *mSphere*, 3(6), e00597-18. <https://doi.org/10.1128/mSphereDirect.00597-18>

¹⁷³ Zhang, M. S., Tran, P. M., Wolff, A. J., Tremblay, M. M., Fosdick, M. G., & Houtman, J. (2018). Glycerol monolaurate induces filopodia formation by disrupting the association between LAT and SLP-76 microclusters. *Science signaling*, 11(528), eaam9095. <https://doi.org/10.1126/scisignal.aam9095>

****During Infection and Inflammation Phase, increase to 2400mg daily for adults and teens, 1200mg daily for children.**

****Contraindicated in those with coconut intolerance.**

VITAMIN D3

Having optimal vitamin D levels can reduce severity of COVID-19 symptoms and mortality by 50%.^{174 175 176} Countries such as the United Kingdom and France have mandated vitamin D3 supplementation for the pandemic.

It is especially important to have enough vitamin D3 if you had a low level previously or you have genetic mutations of specific vitamin D genes that impede absorption. An optimal D3 level is between 50-75 ng/ML.¹⁷⁷

Dosage: 5000IU (125 mcg) - 10,000IU (250 mcg) daily for adults until herd immunity is reached; 1000IU (25 mcg) - 5000IU (125 mcg) for children.

VITAMIN A (not beta carotene)

Vitamin A is critical not only because it helps vitamin D absorption, and vice versa, but it is a crucial immune nutrient for numerous viruses.¹⁷⁸ It is even more critical to take supplemental vitamin A if you have a genetic mutation that blocks your ability to turn beta carotene into vitamin A (BCMO1).

Dosage: 3000IU (900mcg) - 5000IU (1500mcg) daily for adults; 500IU (150mcg) - 1500IU (600mcg) daily for children. Note micrograms, not milligrams.

****During Infection and Inflammation Phase, double the dose.**

¹⁷⁴ Medrxiv: <https://www.medrxiv.org/content/10.1101/2020.04.08.20058578v4>

¹⁷⁵ Kaufman, H. W., Niles, J. K., Kroll, M. H., Bi, C., & Holick, M. F. (2020). SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. *PloS one*, 15(9), e0239252. <https://doi.org/10.1371/journal.pone.0239252>

¹⁷⁶ Entrenas Castillo, M., Entrenas Costa, L. M., Vaquero Barrios, J. M., Alcalá Díaz, J. F., López Miranda, J., Bouillon, R., & Quesada Gomez, J. M. (2020). "Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study". *The Journal of steroid biochemistry and molecular biology*, 203, 105751. Advance online publication. <https://doi.org/10.1016/j.jsbmb.2020.105751>

¹⁷⁷ Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.14.20152728v1>

¹⁷⁸ Iddir, M., Brito, A., Dingo, G., Fernandez Del Campo, S. S., Samouda, H., La Frano, M. R., & Bohn, T. (2020). Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis. *Nutrients*, 12(6), E1562. <https://doi.org/10.3390/nu12061562>

MELATONIN

Aside from exhibiting preventive characteristics against SARS-CoV-2, melatonin helps restorative sleep, which is important for recharging your immune system. Cleveland Clinic recently launched a COVID-19 Risk Calculator, in which one major risk factor was low melatonin levels.¹⁷⁹ Scientists around the world are calling for more clinical trials regarding melatonin as treatment for COVID-19.¹⁸⁰

Dosage: 3mg - 10mg daily for adults 20 minutes before bed; 0.5mg - 3mg for children.

QUERCETIN

Flavonoids have antiviral properties.¹⁸¹ Quercetin helps transport zinc into the cell. In a new study looking for agents that could bind to SARS-CoV-2 viral spike protein and inhibit its activity, researchers found quercetin was the fifth most effective of 77 agents.^{182 183}

Dosage: 500mg daily (250mg with breakfast and dinner) for adults; 125mg - 250mg for children.

EPA/DHA FISH OIL

Fish or cod liver oil are natural anti-inflammatory agents which are necessary to extinguish initial immune overactivity when presented with an infectious agent.

Dosage: 1200mg - 2400 mg. daily total for adults; 600mg - 1200mg for children.

**During Inflammation and Recovery Phase, double your daily dose or take SPMs (see below).

**If you are on blood thinners, please speak with your physician.

REDUCED GLUTATHIONE OR N-ACETYL CYSTEINE (NAC)

The glutathione pathway is critical for assuring proper oxygen efficiency without extra inflammation. Much of the human population have genetic mutations that warrant supplemental

¹⁷⁹ Cleveland Clinic: <https://riskcalc.org/COVID19/>

¹⁸⁰ Kleszczyński, K., Slominski, A. T., Steinbrink, K., & Reiter, R. J. (2020). Clinical Trials for Use of Melatonin to Fight against COVID-19 Are Urgently Needed. *Nutrients*, 12(9), E2561. <https://doi.org/10.3390/nu12092561>

¹⁸¹ Ninfali, P., Antonelli, A., Magnani, M., & Scarpa, E. S. (2020). Antiviral Properties of Flavonoids and Delivery Strategies. *Nutrients*, 12(9), E2534. <https://doi.org/10.3390/nu12092534>

¹⁸² McKee, D. L., Sternberg, A., Stange, U., Laufer, S., & Naujokat, C. (2020). Candidate drugs against SARS-CoV-2 and COVID-19. *Pharmacological research*, 157, 104859. <https://doi.org/10.1016/j.phrs.2020.104859>

¹⁸³ Colunga Biancatelli, R., Berrill, M., Catravas, J. D., & Marik, P. E. (2020). Quercetin and Vitamin C: An Experimental, Synergistic Therapy for the Prevention and Treatment of SARS-CoV-2 Related Disease (COVID-19). *Frontiers in immunology*, 11, 1451. <https://doi.org/10.3389/fimmu.2020.01451>

use. However, some do not have the glutathione genetic mutation (GSTP1), in which supplementation can then be harmful.

In this case especially, knowing your genetics is very important. NAC is the precursor to glutathione. Some health professionals prefer NAC to glutathione. We have always preferred glutathione in reduced form.

Dosage for NAC: 900mg through all phases for adults; speak with a pediatrician for children.

Dosage for Reduced Glutathione: 100mg - 200mg for adults; speak with a pediatrician for children.

**During Inflammation and Recovery Phases, increase glutathione to 500mg or NAC to 1800mg.

MAGNESIUM GLYCINATE

Magnesium is critical for over 300 bodily functions, but during the pandemic is most helpful for stress, anxiety, and restful sleep. Hypomagnesia, which can lead to hypokalemia, one of the pathologies of severe COVID-19, may be avoided with optimal magnesium supplementation.¹⁸⁴

Dosage: 350mg daily for adult women; 400mg daily for adult men; 100mg - 200mg for children. Best taken upon waking and before bed.

MULTIVITAMIN/MINERAL

Foundational support to fill in other nutrient cracks as well as provide immune support.¹⁸⁵ Some multis may contain sufficient amounts of the aforementioned nutrients.

Dosage: brand and amount is too broad to recommend here.

Supplements for Infection Phase

(at first sign of symptoms)

ANDROGRAPHIS

¹⁸⁴ Wallace T. C. (2020). Combating COVID-19 and Building Immune Resilience: A Potential Role for Magnesium Nutrition?. *Journal of the American College of Nutrition*, 1–9. Advance online publication. <https://doi.org/10.1080/07315724.2020.1785971>

¹⁸⁵ Fantacone, M. L., Lowry, M. B., Uesugi, S. L., Michels, A. J., Choi, J., Leonard, S. W., Gombart, S. K., Gombart, J. S., Bobe, G., & Gombart, A. F. (2020). The Effect of a Multivitamin and Mineral Supplement on Immune Function in Healthy Older Adults: A Double-Blind, Randomized, Controlled Trial. *Nutrients*, 12(8), 2447. <https://doi.org/10.3390/nu12082447>

Andrographis is a herb with a long history of use in both Ayurveda and Traditional Chinese Medicine for treating viral infections, particularly of the upper respiratory tract, and relieving cold and flu symptoms. The bitter herb is a powerful immune modulator, down to the andrographolides in the plant which are thought to enhance the production of white blood cells, to support the release of interferon, and to promote the healthy activity of the lymphatic system.

186

Dosage: 1800mg (divided equally at three meals) for adults; halve for children.

**During Prevention Phase, 200 mg is optional.

GRAPEFRUIT SEED EXTRACT

GSE oral tablet/capsule and via liquid or throat spray if symptoms begin.

Dosage: 250mg - 500 mg for adults; 125mg - 250 mg for children

**During Prevention Phase, 125mg - 250mg is optional.

**Do not take with certain heart medications, especially statins.

POTASSIUM

COVID-19 depletes potassium at an alarming rate. During infection phase, high potassium foods may not be enough. We suggest speaking with your physician before taking supplemental potassium, especially if you are on meds for hypertension or other heart-related issues.

Dosage: 99mg - 200 mg; not advised for children unless authorized by a pediatrician.

Supplements for Escalating Inflammation and Recovery Phases

The goal for these two phases is to stop your immune system from harming your own tissue, as well as heal enough to achieve homeostasis.

SPECIALIZED PRO-RESOLVING MEDIATORS (SPMs)

This anti-inflammatory agent is naturally occurring in fish oil in small amounts, but you'd have to take a ton of fish oil to get what is provided in a therapeutic dose of SPM supplement. Resolvins and other SPMs stimulate clearance of debris and counter pro-inflammatory cytokine production, a process called inflammation resolution. SPMs exhibit antiviral activity at nano doses in the

¹⁸⁶ Yanuck, S. F., Pizzorno, J., Messier, H., & Fitzgerald, K. N. (2020). Evidence Supporting a Phased Immuno-physiological Approach to COVID-19 From Prevention Through Recovery. *Integrative medicine (Encinitas, Calif.)*, 19(Suppl 1), 8–35.

setting of influenza without being immunosuppressive. SPMs also promote antiviral antibodies and lymphocyte activity, highlighting their potential use in the treatment of COVID-19.

Resolvins also prevent pathological thrombosis and promote clot removal, which is emerging as a key pathology of COVID-19 infection. Thus, SPMs may promote the resolution of inflammation in COVID-19, thereby reducing acute respiratory distress syndrome (ARDS) and other life-threatening complications associated with robust viral-induced inflammation.¹⁸⁷

Dosage: 2g - 4g for adults; 1g - 2g for children (note this is grams, not milligrams).

CURCUMIN

Not recommended for anyone who has GERD, salicylate intolerance, or is overly acidic.

Dosage: 1000mg for adults; 250mg for children.

BROMELAIN

Australian researchers are currently testing bromelain as an antiviral agent, and have found bromelain render SARS-CoV-2 spike protein inactive.¹⁸⁸ Bromelain also showed to reduce SARS-CoV-2 activity in vivo.¹⁸⁹ Do not use it if you have a pineapple intolerance.

Dosage: 600mg - 2400 mg for adults; 200mg - 800mg for children.

ASTAXANTHIN

Finding ways to enhance nitric oxide production may be helpful tampering inflammation by supporting ACE2 homeostasis. In lieu of intravenous nitric oxide, astaxanthin is a safe supplement.¹⁹⁰

Dosage: 8mg for adults; 4mg for children

Supplements for Sleep and Adrenal Support

¹⁸⁷ Panigrahy, D., Gilligan, M. M., Huang, S., Gartung, A., Cortés-Puch, I., Sime, P. J., Phipps, R. P., Serhan, C. N., & Hammock, B. D. (2020). Inflammation resolution: a dual-pronged approach to averting cytokine storms in COVID-19?. *Cancer metastasis reviews*, 1–4. Advance online publication. <https://doi.org/10.1007/s10555-020-09889-4>

¹⁸⁸ Health Times. Retrieved from:

<https://healthtimes.com.au/hub/diseases/24/news/aap/researchers-in-australia-are-testing-a-treatment-for-covid19/5238/>

¹⁸⁹ Medrxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.09.16.297366v1>

¹⁹⁰ Adusumilli, N. C., Zhang, D., Friedman, J. M., & Friedman, A. J. (2020). Harnessing nitric oxide for preventing, limiting and treating the severe pulmonary consequences of COVID-19. *Nitric oxide : biology and chemistry*, 103, 4–8. Advance online publication. <https://doi.org/10.1016/j.niox.2020.07.003>

RHODIOLA ROSEA

For adrenal and mood support.

Dosage: 100mg - 200 mg for adults and teens; not recommended for children.

VALERIAN ROOT, L-THEANINE, LAVELA OIL, HEMP OIL

For extra sleep assistance if melatonin is not enough. Hemp Oil should only be used if none of the other sleep supplements are effective. None of these should be used if taking sleep medication.

Dosage varies widely depending upon brand and source.

Other Integrative Therapies for COVID-19

Far Infrared Sauna Therapy (if you have at home) or sauna bathing can lower blood pressure.¹⁹¹

Hyperbaric Oxygen Therapy is already being used in some hospitals in patients with hypoxia (lacking oxygen) and also to prevent using ventilators.¹⁹²

Acupuncture and Traditional Chinese Medicine¹⁹³ have shown success in treating symptoms of COVID-19 in or out of the hospital setting.¹⁹⁴

Chiropractic has been found to be particularly useful during lockdown as lack of movement has caused many more cases of back trouble.¹⁹⁵

¹⁹¹ Laukkanen, J. A., Laukkanen, T., & Kunutsor, S. K. (2018). Cardiovascular and Other Health Benefits of Sauna Bathing: A Review of the Evidence. *Mayo Clinic proceedings*, 93(8), 1111–1121. <https://doi.org/10.1016/j.mayocp.2018.04.008>

¹⁹² Thibodeaux, K., Speyrer, M., Raza, A., Yaakov, R., & Serena, T. E. (2020). Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a retrospective case series. *Journal of wound care*, 29(Sup5a), S4–S8. <https://doi.org/10.12968/jowc.2020.29.Sup5a.S4>

¹⁹³ Shahzad, F., Anderson, D., & Najafzadeh, M. (2020). The Antiviral, Anti-Inflammatory Effects of Natural Medicinal Herbs and Mushrooms and SARS-CoV-2 Infection. *Nutrients*, 12(9), E2573. <https://doi.org/10.3390/nu12092573>

¹⁹⁴ Liu, W. H., Guo, S. N., Wang, F., & Hao, Y. (2020). Understanding of guidance for acupuncture and moxibustion interventions on COVID-19 (Second edition) issued by CAAM. *World journal of acupuncture-moxibustion*, 30(1), 1–4. Advance online publication. <https://doi.org/10.1016/j.wjam.2020.03.005>

¹⁹⁵ ACA. Retrieved from: <https://www.acatoday.org/News-Publications/Coronavirus-COVID-19>

Ceiling fixtures emitting a safe form of ultraviolet light called far-UVC seem to be efficient at killing airborne coronaviruses.¹⁹⁶

Chewing gum sweetened with xylitol may have an inhibitory effect on SARS-CoV-2 as shown in cell cultures.¹⁹⁷

Concluding Thought

One of the most honest accounts of the coronavirus saga was uttered recently by WHO official Mike Ryan: "This virus may become just another endemic virus in our communities, and this virus may never go away." SARS-CoV-2 could become a long-term fact of life that must be managed, not an enemy that can be permanently eradicated. The sooner we come to this realization, and not pine away for a "moon shot vaccine," as Mr. Ryan put it, we will be able to function as a society.

We can successfully live with SARS-CoV-2, as we have with myriad viruses, including other coronaviruses, over millennia. The best way to do that is to take better care of ourselves.

¹⁹⁶ Buonanno, M., Welch, D., Shuryak, I., & Brenner, D. J. (2020). Far-UVC light (222 nm) efficiently and safely inactivates airborne human coronaviruses. *Scientific reports*, 10(1), 10285. <https://doi.org/10.1038/s41598-020-67211-2>

¹⁹⁷ Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.19.225854v1>

References

- ACA. Retrieved from: <https://www.acatoday.org/News-Publications/Coronavirus-COVID-19>
- Adusumilli, N. C., Zhang, D., Friedman, J. M., & Friedman, A. J. (2020). Harnessing nitric oxide for preventing, limiting and treating the severe pulmonary consequences of COVID-19. *Nitric oxide : biology and chemistry*, 103, 4–8. Advance online publication. <https://doi.org/10.1016/j.niox.2020.07.003>
- Alkhatib A. (2020). Antiviral Functional Foods and Exercise Lifestyle Prevention of Coronavirus. *Nutrients*, 12(9), E2633. <https://doi.org/10.3390/nu12092633>
- Almario, C., Chey, W. & Spiegel, B. (2020). Increased Risk of COVID-19 Among Users of Proton Pump Inhibitors. Retrieved from: [https://journals.lww.com/ajg/Documents/AJG-20-1811_R1\(PUBLISH%20AS%20WEBP ART\).pdf](https://journals.lww.com/ajg/Documents/AJG-20-1811_R1(PUBLISH%20AS%20WEBP ART).pdf)
- American Lung Association. Retrieved from: <https://www.lung.org/media/press-releases/state-of-the-air-2020>
- American Nutrition Association. Retrieved from: <https://theana.org/COVID-19>
- ASBMR. Joint Guidance On Vitamin D in the Era of COVID-19 From the ASBMR, AACE, ENDOCRINE SOCIETY, ECTS, NOF, AND IOF. Retrieved from: <https://www.asbmr.org/ASBMRStatementsDetail/joint-guidance-on-vitamin-d-in-era-of-covid-19-fro>
- ASHRAE Epidemic Task Force. Retrieved from: <https://www.ashrae.org/file%20library/technical%20resources/covid-19/ashrae-building-readiness.pdf>
- Baral, R., White, M., & Vassiliou, V. S. (2020). Effect of Renin-Angiotensin-Aldosterone System Inhibitors in Patients with COVID-19: a Systematic Review and Meta-analysis of 28,872 Patients. *Current atherosclerosis reports*, 22(10), 61. <https://doi.org/10.1007/s11883-020-00880-6>
- Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.07.18.210161v1>

Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.17.254979v1>

Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.19.225854v1>

Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.21.262329v1>

Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.26.268854v1>

Biorxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.08.30.274241v1>

Bernheim, A., Mei, X., Huang, M., Yang, Y., Fayad, Z. A., Zhang, N., Diao, K., Lin, B., Zhu, X.,

Li, K., Li, S., Shan, H., Jacobi, A., & Chung, M. (2020). Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. *Radiology*, 295(3), 200463. <https://doi.org/10.1148/radiol.2020200463>

Bousquet, J., Anto, J. M., Iaccarino, G., Czarlewski, W., Haahtela, T., Anto, A., Akdis, C. A., Blain, H., Canonica, G. W., Cardona, V., Cruz, A. A., Illario, M., Ivancevich, J. C., Jutel, M., Klimek, L., Kuna, P., Laune, D., Larenas-Linnemann, D., Mullol, J., Papadopoulos, N. G., ... ARIA group (2020). Is diet partly responsible for differences in COVID-19 death rates between and within countries?. *Clinical and translational allergy*, 10, 16. <https://doi.org/10.1186/s13601-020-00323-0>

BourBour, F., Mirzaei Dahka, S., Gholamalizadeh, M., Akbari, M. E., Shadnoush, M., Haghighi, M., Taghvaye-Masoumi, H., Ashoori, N., & Doaei, S. (2020). Nutrients in prevention, treatment, and management of viral infections; special focus on Coronavirus. *Archives of physiology and biochemistry*, 1–10. Advance online publication. <https://doi.org/10.1080/13813455.2020.1791188>

Bray, M., Rayner, C., Noël, F., Jans, D., & Wagstaff, K. (2020). Ivermectin and COVID-19: A report in *Antiviral Research*, widespread interest, an FDA warning, two letters to the editor and the authors' responses. *Antiviral research*, 178, 104805. Advance online publication. <https://doi.org/10.1016/j.antiviral.2020.104805>

Buonanno, M., Welch, D., Shuryak, I., & Brenner, D. J. (2020). Far-UVC light (222 nm) efficiently and safely inactivates airborne human coronaviruses. *Scientific reports*, 10(1), 10285. <https://doi.org/10.1038/s41598-020-67211-2>

Brenner, H., Holleczeck, B., & Schöttker, B. (2020). Vitamin D Insufficiency and Deficiency and

Mortality from Respiratory Diseases in a Cohort of Older Adults: Potential for Limiting the Death Toll during and beyond the COVID-19 Pandemic?. *Nutrients*, 12(8), 2488. <https://doi.org/10.3390/nu12082488>

Calder, P. C., Carr, A. C., Gombart, A. F., & Eggersdorfer, M. (2020). Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. *Nutrients*, 12(4), 1181. <https://doi.org/10.3390/nu12041181>

Carfi, A., Bernabei, R., Landi, F., & Gemelli Against COVID-19 Post-Acute Care Study Group (2020). Persistent Symptoms in Patients After Acute COVID-19. *JAMA*, 10.1001/jama.2020.12603. Advance online publication. <https://doi.org/10.1001/jama.2020.12603>

Centers for Disease Control. Retrieved from: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html?>

Centers for Disease Control: Retrieved from: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html>

Centers for Disease Control. Retrieved from: <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>

Centers for Disease Control. Retrieved from: <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/activities.html>

Centers for Disease Control. Retrieved from: <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

Centers for Disease Control. Retrieved from: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6924e2.htm>

Chambers, C., Krogstad, P., Bertrand, K., Contreras, D., Tobin, N. H., Bode, L., & Aldrovandi, G. (2020). Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women. *JAMA*, e2015580. Advance online publication. <https://doi.org/10.1001/jama.2020.15580>

Cleveland Clinic. Retrieved from: <https://riskcalc.org/COVID19/>

Clinicaltrials.gov. Retrieved from: <https://clinicaltrials.gov/ct2/show/NCT04264533>

Clinicaltrials.gov. Retrieved from: <https://www.clinicaltrials.gov/ct2/show/NCT04311697>

Colunga Biancatelli, R., Berrill, M., Catravas, J. D., & Marik, P. E. (2020). Quercetin and Vitamin C: An Experimental, Synergistic Therapy for the Prevention and Treatment of SARS-CoV-2 Related Disease (COVID-19). *Frontiers in immunology*, 11, 1451. <https://doi.org/10.3389/fimmu.2020.01451>

Copaescu, A., Smibert, O., Gibson, A., Phillips, E. J., & Trubiano, J. A. (2020). The role of IL-6 and other mediators in the cytokine storm associated with SARS-CoV-2 infection. *The Journal of allergy and clinical immunology*, 146(3), 518–534.e1. <https://doi.org/10.1016/j.jaci.2020.07.001>

COVID-19 RISK and Treatments (CORIST) Collaboration members: (2020). Use of hydroxychloroquine in hospitalised COVID-19 patients is associated with reduced mortality: Findings from the observational multicentre Italian CORIST study. *European journal of internal medicine*, S0953-6205(20)30335-6. Advance online publication. <https://doi.org/10.1016/j.ejim.2020.08.019>

Critical Care COVID-19 Protocol. Retrieved from: https://www.evms.edu/media/evms_public/departments/internal_medicine/Marik-Covid-Protocol-Summary.pdf

Cunningham, L., Simmonds, P., Kimber, I., Basketter, D. A., & McFadden, J. P. (2020). Perforin and resistance to SARS coronavirus 2. *The Journal of allergy and clinical immunology*, 146(1), 52–53. <https://doi.org/10.1016/j.jaci.2020.05.007>

Czawlytko, C., Hossain, R., White, CS. (2020). COVID-19 Diagnostic Imaging Recommendations. *Applied Radiology*, 49(3):10-15.

D'ettorre, G., Ceccarelli, G., Marazzato, M., Campagna, G., Pinacchio, C., Alessandri, F., . . . Mastroianni, C. M. (2020). Challenges in the Management of SARS-CoV2 Infection: The Role of Oral Bacteriotherapy as Complementary Therapeutic Strategy to Avoid the Progression of COVID-19. *Frontiers in Medicine*, 7. doi:10.3389/fmed.2020.00389

Davies, N. G., Klepac, P., Liu, Y., Prem, K., Jit, M., CMMID COVID-19 working group, &

- Eggo, R. M. (2020). Age-dependent effects in the transmission and control of COVID-19 epidemics. *Nature medicine*, 10.1038/s41591-020-0962-9. Advance online publication. <https://doi.org/10.1038/s41591-020-0962-9>
- Deftereos, S. G., Giannopoulos, G., Vrachatis, D. A., Siasos, G. D., Giotaki, S. G., Gargalianos, P., Metallidis, S., Sianos, G., Baltagiannis, S., Panagopoulos, P., Dolianitis, K., Randou, E., Syrigos, K., Kotanidou, A., Koulouris, N. G., Milionis, H., Sipsas, N., Gogos, C., Tsoukalas, G., Olympos, C. D., ... GRECCO-19 investigators (2020). Effect of Colchicine vs Standard Care on Cardiac and Inflammatory Biomarkers and Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019: The GRECCO-19 Randomized Clinical Trial. *JAMA network open*, 3(6), e2013136. <https://doi.org/10.1001/jamanetworkopen.2020.13136>
- Del Valle, D. M., Kim-Schulze, S., Hsin-Hui, H., Beckmann, N. D., Nirenberg, S., Wang, B., Lavin, Y., Swartz, T., Madduri, D., Stock, A., Marron, T., Xie, H., Patel, M. K., van Oekelen, O., Rahman, A., Kovatch, P., Aberg, J., Schadt, E., Jagannath, S., Mazumdar, M., ... Gnjjatic, S. (2020). An inflammatory cytokine signature helps predict COVID-19 severity and death. *medRxiv : the preprint server for health sciences*, 2020.05.28.20115758. <https://doi.org/10.1101/2020.05.28.20115758>
- Demasi M. (2020). COVID-19 and metabolic syndrome: could diet be the key?. *BMJ evidence-based medicine*, bmjebm-2020-111451. Advance online publication. <https://doi.org/10.1136/bmjebm-2020-111451>
- Dhar, D., & Mohanty, A. (2020). Gut microbiota and Covid-19- possible link and implications. *Virus research*, 285, 198018. <https://doi.org/10.1016/j.virusres.2020.198018>
- Dietz, L., Horve, P. F., Coil, D. A., Fretz, M., Eisen, J. A., & Van Den Wymelenberg, K. (2020). 2019 Novel Coronavirus (COVID-19) Pandemic: Built Environment Considerations To Reduce Transmission. *mSystems*, 5(2), e00245-20. <https://doi.org/10.1128/mSystems.00245-20>
- Dofferhoff, A., Piscaer, I., Schurgers, L., Walk, J., van den Ouweland, J., Hackeng, T., Lux, P., Maassen, C., Karssemeijer, E., Wouters, E., & Janssen, R. (2020). Reduced Vitamin K Status as A Potentially Modifiable Prognostic Risk Factor in COVID-19. *Preprints*, 2020040457; doi: 10.20944/preprints202004.0457.v1.
- Elharrar, X., Trigui, Y., Dols, A. M., Touchon, F., Martinez, S., Prud'homme, E., & Papazian, L.

- (2020). Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure. *JAMA*, 323(22), 2336–2338. Advance online publication. <https://doi.org/10.1001/jama.2020.8255>
- Ellinghaus, D., Degenhardt, F., Bujanda, L., Buti, M., Albillos, A., Invernizzi, P., Fernández, J., Prati, D., Baselli, G., Asselta, R., Grimsrud, M. M., Milani, C., Aziz, F., Kässens, J., May, S., Wendorff, M., Wienbrandt, L., Uellendahl-Werth, F., Zheng, T., Yi, X., ... Severe Covid-19 GWAS Group (2020). Genomewide Association Study of Severe Covid-19 with Respiratory Failure. *The New England journal of medicine*, 10.1056/NEJMoa2020283. Advance online publication. <https://doi.org/10.1056/NEJMoa2020283>
- Entrenas Castillo, M., Entrenas Costa, L. M., Vaquero Barrios, J. M., Alcalá Díaz, J. F., López Miranda, J., Bouillon, R., & Quesada Gomez, J. M. (2020). "Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study". *The Journal of steroid biochemistry and molecular biology*, 203, 105751. Advance online publication. <https://doi.org/10.1016/j.jsbmb.2020.105751>
- Fantacone, M. L., Lowry, M. B., Uesugi, S. L., Michels, A. J., Choi, J., Leonard, S. W., Gombart, S. K., Gombart, J. S., Bobe, G., & Gombart, A. F. (2020). The Effect of a Multivitamin and Mineral Supplement on Immune Function in Healthy Older Adults: A Double-Blind, Randomized, Controlled Trial. *Nutrients*, 12(8), 2447. <https://doi.org/10.3390/nu12082447>
- Gaiha, S. M., Cheng, J., & Halpern-Felsher, B. (2020). Association Between Youth Smoking, Electronic Cigarette Use, and Coronavirus Disease 2019. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*, 67(4), 519–523. Advance online publication. <https://doi.org/10.1016/j.jadohealth.2020.07.002>
- Gao, C., Cai, Y., Zhang, K., Zhou, L., Zhang, Y., Zhang, X., Li, Q., Li, W., Yang, S., Zhao, X., Zhao, Y., Wang, H., Liu, Y., Yin, Z., Zhang, R., Wang, R., Yang, M., Hui, C., Wijns, W., McEvoy, J. W., ... Li, F. (2020). Association of hypertension and antihypertensive treatment with COVID-19 mortality: a retrospective observational study. *European heart journal*, 41(22), 2058–2066. <https://doi.org/10.1093/eurheartj/ehaa433>
- Gasmi, A., Tippairote, T., Mujawdiya, P. K., Peana, M., Menzel, A., Dadar, M., Benahmed, A.

G., & Björklund, G. (2020). Micronutrients as immunomodulatory tools for COVID-19 management. *Clinical immunology (Orlando, Fla.)*, 108545. Advance online publication. <https://doi.org/10.1016/j.clim.2020.108545>

Gudbjartsson, D. F., Norddahl, G. L., Melsted, P., Gunnarsdottir, K., Holm, H., Eythorsson, E., Arnthorsson, A. O., Helgason, D., Bjarnadottir, K., Ingvarsson, R. F., Thorsteinsdottir, B., Kristjansdottir, S., Birgisdottir, K., Kristinsdottir, A. M., Sigurdsson, M. I., Arnadottir, G. A., Ivarsdottir, E. V., Andresdottir, M., Jonsson, F., Agustsdottir, A. B., ... Stefansson, K. (2020). Humoral Immune Response to SARS-CoV-2 in Iceland. *The New England journal of medicine*, 10.1056/NEJMoa2026116. Advance online publication. <https://doi.org/10.1056/NEJMoa2026116>

Gupta, A., Madhavan, M. V., Sehgal, K., Nair, N., Mahajan, S., Sehrawat, T. S., Bikdeli, B., Ahluwalia, N., Ausiello, J. C., Wan, E. Y., Freedberg, D. E., Kirtane, A. J., Parikh, S. A., Maurer, M. S., Nordvig, A. S., Accili, D., Bathon, J. M., Mohan, S., Bauer, K. A., Leon, M. B., ... Landry, D. W. (2020). Extrapulmonary manifestations of COVID-19. *Nature medicine*, 26(7), 1017–1032. <https://doi.org/10.1038/s41591-020-0968-3>

FDA.gov. Retrieved from:

<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-yale-school-public-health>

Feldstein, L. R., Rose, E. B., Horwitz, S. M., Collins, J. P., Newhams, M. M., Son, M., Newburger, J. W., Kleinman, L. C., Heidemann, S. M., Martin, A. A., Singh, A. R., Li, S., Tarquinio, K. M., Jaggi, P., Oster, M. E., Zackai, S. P., Gillen, J., Ratner, A. J., Walsh, R. F., Fitzgerald, J. C., ... Randolph, A. G. (2020). Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *The New England journal of medicine*, NEJMoa2021680. Advance online publication. <https://doi.org/10.1056/NEJMoa2021680>

Frates, E. P., & Rifai, T. (2020). Making the Case for "COVID-19 Prophylaxis" With Lifestyle Medicine. *American journal of health promotion : AJHP*, 34(6), 689–691. <https://doi.org/10.1177/0890117120930536c>

Fusco, R., Siracusa, R., Genovese, T., Cuzzocrea, S., & Di Paola, R. (2020) Focus on the Role of NLRP3 Inflammasome in Diseases. *International journal of molecular sciences*, (21) 4223. <https://doi.org/10.3390/ijms21124223>

Garvin, M. R., Alvarez, C., Miller, J. I., Prates, E. T., Walker, A. M., Amos, B. K., Mast, A. E.,

- Justice, A., Aronow, B., & Jacobson, D. (2020). A mechanistic model and therapeutic interventions for COVID-19 involving a RAS-mediated bradykinin storm. *eLife*, 9, e59177. <https://doi.org/10.7554/eLife.59177>
- Hamzelou J. (2020). Can breathing exercises help protect you from covid-19?. *New scientist* (1971), 246(3279), 10–11. [https://doi.org/10.1016/S0262-4079\(20\)30789-2](https://doi.org/10.1016/S0262-4079(20)30789-2)
- Health Times. Retrieved from:
<https://healthtimes.com.au/hub/diseases/24/news/aap/researchers-in-australia-are-testing-a-treatment-for-covid19/5238/>
- Hogan Ii, R. B., Hogan Iii, R. B., Cannon, T., Rappai, M., Studdard, J., Paul, D., & Dooley, T. P. (2020). Dual-histamine receptor blockade with cetirizine - famotidine reduces pulmonary symptoms in COVID-19 patients. *Pulmonary pharmacology & therapeutics*, 63, 101942. Advance online publication. <https://doi.org/10.1016/j.pupt.2020.101942>
- Horowitz, R. I., Freeman, P. R., & Bruzzese, J. (2020). Efficacy of glutathione therapy in relieving dyspnea associated with COVID-19 pneumonia: A report of 2 cases. *Respiratory medicine case reports*, 30, 101063. Advance online publication. <https://doi.org/10.1016/j.rmcr.2020.101063>
- Iddir, M., Brito, A., Dingo, G., Fernandez Del Campo, S. S., Samouda, H., La Frano, M. R., & Bohn, T. (2020). Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis. *Nutrients*, 12(6), E1562. <https://doi.org/10.3390/nu12061562>
- Institute of Labor Economics. Retrieved from: <http://ftp.iza.org/dp13367.pdf>
- Jayawardena, R., Sooriyaarachchi, P., Chourdakis, M., Jeewandara, C., & Ranasinghe, P. (2020). Enhancing immunity in viral infections, with special emphasis on COVID-19: A review. *Diabetes & metabolic syndrome*, 14(4), 367–382. Advance online publication. <https://doi.org/10.1016/j.dsx.2020.04.015>
- Jovic, T. H., Ali, S. R., Ibrahim, N., Jessop, Z. M., Tarassoli, S. P., Dobbs, T. D., Holford, P., Thornton, C. A., & Whitaker, I. S. (2020). Could Vitamins Help in the Fight Against COVID-19?. *Nutrients*, 12(9), E2550. <https://doi.org/10.3390/nu12092550>
- Kampf, G., Todt, D., Pfaender, S., & Steinmann, E. (2020). Persistence of coronaviruses on

- inanimate surfaces and their inactivation with biocidal agents. *The Journal of hospital infection*, 104(3), 246–251. <https://doi.org/10.1016/j.jhin.2020.01.022>
- Kaufman, H. W., Niles, J. K., Kroll, M. H., Bi, C., & Holick, M. F. (2020). SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. *PloS one*, 15(9), e0239252. <https://doi.org/10.1371/journal.pone.0239252>
- Keller, M. J., Kitsis, E. A., Arora, S., Chen, J., Agarwal, S., Ross, M. J., . . . Southern, W. (2020). Effect of Systemic Glucocorticoids on Mortality or Mechanical Ventilation in Patients With COVID-19. *Journal of hospital medicine*, (2020-07-22 ONLINE FIRST). doi:10.12788/jhm.3497
- Kim, S. Y., Jin, W., Sood, A., Montgomery, D. W., Grant, O. C., Fuster, M. M., Fu, L., Dordick, J. S., Woods, R. J., Zhang, F., & Linhardt, R. J. (2020). Characterization of heparin and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) spike glycoprotein binding interactions. *Antiviral research*, 181, 104873. Advance online publication. <https://doi.org/10.1016/j.antiviral.2020.104873>
- Kleszczyński, K., Slominski, A. T., Steinbrink, K., & Reiter, R. J. (2020). Clinical Trials for Use of Melatonin to Fight against COVID-19 Are Urgently Needed. *Nutrients*, 12(9), E2561. <https://doi.org/10.3390/nu12092561>
- Koralnik, I. J., & Tyler, K. L. (2020). COVID-19: a global threat to the nervous system. *Annals of neurology*, 10.1002/ana.25807. Advance online publication. <https://doi.org/10.1002/ana.25807>
- Korytkowski, M., Antinori-Lent, K., Drincic, A., Hirsch, I. B., McDonnell, M. E., Rushakoff, R., & Muniyappa, R. (2020). A Pragmatic Approach to Inpatient Diabetes Management during the COVID-19 Pandemic. *The Journal of clinical endocrinology and metabolism*, dgaa342. Advance online publication. <https://doi.org/10.1210/clinem/dgaa342>
- Kucirka, L. M., Lauer, S. A., Laeyendecker, O., Boon, D., & Lessler, J. (2020). Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure. *Annals of internal medicine*, M20-1495. Advance online publication. <https://doi.org/10.7326/M20-1495>
- Kuo, C. L., Pilling, L. C., Atkins, J. L., Masoli, J., Delgado, J., Kuchel, G. A., & Melzer, D.

- (2020). APOE e4 genotype predicts severe COVID-19 in the UK Biobank community cohort. *The journals of gerontology. Series A, Biological sciences and medical sciences*, glaa131. Advance online publication. <https://doi.org/10.1093/gerona/glaa131>
- Laterre, P. F., François, B., Collienne, C., Hantson, P., Jeannet, R., Remy, K. E., & Hotchkiss, R. S. (2020). Association of Interleukin 7 Immunotherapy With Lymphocyte Counts Among Patients With Severe Coronavirus Disease 2019 (COVID-19). *JAMA network open*, 3(7), e2016485. <https://doi.org/10.1001/jamanetworkopen.2020.16485>
- Laukkanen, J. A., Laukkanen, T., & Kunutsor, S. K. (2018). Cardiovascular and Other Health Benefits of Sauna Bathing: A Review of the Evidence. *Mayo Clinic proceedings*, 93(8), 1111–1121. <https://doi.org/10.1016/j.mayocp.2018.04.008>
- Lippi, G., South, A. M., & Henry, B. M. (2020). Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). *Annals of clinical biochemistry*, 57(3), 262–265. <https://doi.org/10.1177/0004563220922255>
- Liu, W. H., Guo, S. N., Wang, F., & Hao, Y. (2020). Understanding of guidance for acupuncture and moxibustion interventions on COVID-19 (Second edition) issued by CAAM. *World journal of acupuncture-moxibustion*, 30(1), 1–4. Advance online publication. <https://doi.org/10.1016/j.wjam.2020.03.005>
- Liu, Y., Yan, L. M., Wan, L., Xiang, T. X., Le, A., Liu, J. M., Peiris, M., Poon, L., & Zhang, W. (2020). Viral dynamics in mild and severe cases of COVID-19. *The Lancet. Infectious diseases*, 20(6), 656–657. [https://doi.org/10.1016/S1473-3099\(20\)30232-2](https://doi.org/10.1016/S1473-3099(20)30232-2)
- Long, Q. X., Tang, X. J., Shi, Q. L., Li, Q., Deng, H. J., Yuan, J., Hu, J. L., Xu, W., Zhang, Y., Lv, F. J., Su, K., Zhang, F., Gong, J., Wu, B., Liu, X. M., Li, J. J., Qiu, J. F., Chen, J., & Huang, A. L. (2020). Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nature medicine*, 10.1038/s41591-020-0965-6. Advance online publication. <https://doi.org/10.1038/s41591-020-0965-6>
- McKee, D. L., Sternberg, A., Stange, U., Laufer, S., & Naujokat, C. (2020). Candidate drugs against SARS-CoV-2 and COVID-19. *Pharmacological research*, 157, 104859. <https://doi.org/10.1016/j.phrs.2020.104859>
- McAuliffe, S., Ray, S., Fallon, E., Bradfield, J., Eden, T., & Kohlmeier, M. (2020, June 18).

Dietary micronutrients in the wake of COVID-19: An appraisal of evidence with a focus on high-risk groups and preventative healthcare. Retrieved June 27, 2020, from <https://nutrition.bmj.com/content/early/2020/06/17/bmjnph-2020-000100>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.04.04.20053058v1>

Medrxiv. Retrieved from: <https://doi.org/10.1101/2020.04.05.20054502>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.04.08.20058578v4>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.04.16.20067835v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.05.08.20095471v1>

Medrxiv. Retrieved from; <https://www.medrxiv.org/content/10.1101/2020.05.31.20114991v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.03.20116988v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.07.20124636v2>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.12.20129056v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.22.20133413v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.23.20134072v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.24.20139600v1>

Medrxiv: Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.24.20138644v1>

Medrxiv: Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.06.29.20141283v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.01.20144329v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.02.20144717v2>

Medrxiv: Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.08.20141218v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.08.20148775v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.09.20149534v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.12.20152074v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.14.20152728v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.17.20155242v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.20.20157503v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.22.20157263v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.23.20160796v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.29.20164152v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.07.30.20164921v2>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.11.20171843v2>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.17.20161760v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.16.20175752v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.18.20176743v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.18.20177444v3>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.19.20178376v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.20.20178657v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.20.20178772v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.08.21.20179499v1>

Medrxiv. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.09.16.297366v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.09.04.20188268v1>

Medrxiv. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.09.09.20184143v1>

Medscape: Retrieved from: https://www.medscape.com/viewarticle/928287#vp_1

Medscape. Retrieved from: <https://www.medscape.com/viewarticle/930223>

Medscape. Retrieved from: <https://www.medscape.com/viewarticle/937567>

Meltzer, D. O., Best, T. J., Zhang, H., Vokes, T., Arora, V., & Solway, J. (2020). Association of Vitamin D Status and Other Clinical Characteristics With COVID-19 Test Results. *JAMA network open*, 3(9), e2019722. <https://doi.org/10.1001/jamanetworkopen.2020.19722>

Menni, C., Valdes, A. M., Freidin, M. B., Sudre, C. H., Nguyen, L. H., Drew, D. A., Ganesh, S., Varsavsky, T., Cardoso, M. J., El-Sayed Moustafa, J. S., Visconti, A., Hysi, P., Bowyer, R., Mangino, M., Falchi, M., Wolf, J., Ourselin, S., Chan, A. T., Steves, C. J., & Spector, T. D. (2020). Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nature medicine*, 10.1038/s41591-020-0916-2. Advance online publication. <https://doi.org/10.1038/s41591-020-0916-2>

Morbidity and Mortality Weekly Report, Retrieved from: https://www.cdc.gov/mmwr/volumes/69/wr/mm6915e3.htm?s_cid=mm6915e3_w

Mossink, J. P. (2020). Zinc as nutritional intervention and prevention measure for COVID-19 disease. *BMJ nutrition, prevention & health*. doi:10.1136/bmjnph-2020-000095

Mueller, A. L., McNamara, M. S., & Sinclair, D. A. (2020). Why does COVID-19 disproportionately affect older people?. *Aging*, 12(10), 9959–9981. <https://doi.org/10.18632/aging.103344>

Muscogiuri, G., Barrea, L., Savastano, S., & Colao, A. (2020). Nutritional recommendations for CoVID-19 quarantine. *European journal of clinical nutrition*, 74(6), 850–851. <https://doi.org/10.1038/s41430-020-0635-2>

National Institutes of Health. Retrieved from: <https://www.covid19treatmentguidelines.nih.gov/whats-new/>

- New WHO guidance calls for more evidence on airborne transmission. Retrieved from:
<https://www.reuters.com/article/us-health-coronavirus-who-airborne/new-who-guidance-calls-for-more-evidence-on-airborne-transmission-idUSKBN24A2E5>
- Nicin, L., Abplanalp, W. T., Mellentin, H., Kattih, B., Tombor, L., John, D., Schmitto, J. D., Heineke, J., Emrich, F., Arsalan, M., Holubec, T., Walther, T., Zeiher, A. M., & Dimmeler, S. (2020). Cell type-specific expression of the putative SARS-CoV-2 receptor ACE2 in human hearts. *European heart journal*, 41(19), 1804–1806.
<https://doi.org/10.1093/eurheartj/ehaa311>
- Nikolich-Zugich, J., Knox, K. S., Rios, C. T., Natt, B., Bhattacharya, D., & Fain, M. J. (2020). SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. *GeroScience*, 42(2), 505–514.
<https://doi.org/10.1007/s11357-020-00186-0>
- Ninfali, P., Antonelli, A., Magnani, M., & Scarpa, E. S. (2020). Antiviral Properties of Flavonoids and Delivery Strategies. *Nutrients*, 12(9), E2534.
<https://doi.org/10.3390/nu12092534>
- Paez, A., Lopez, F. A., Menezes, T., Cavalcanti, R., & Pitta, M. (2020). A Spatio-Temporal Analysis of the Environmental Correlates of COVID-19 Incidence in Spain. *Geographical analysis*, 10.1111/gean.12241. Advance online publication.
<https://doi.org/10.1111/gean.12241>
- Patel, M. M., Thornburg, N. J., Stubblefield, W. B., Talbot, H. K., Coughlin, M. M., Feldstein, L. R., & Self, W. H. (2020). Change in Antibodies to SARS-CoV-2 Over 60 Days Among Health Care Personnel in Nashville, Tennessee. *JAMA*, 10.1001/jama.2020.18796. Advance online publication. <https://doi.org/10.1001/jama.2020.18796>
- Panigrahy, D., Gilligan, M. M., Huang, S., Gartung, A., Cortés-Puch, I., Sime, P. J., Phipps, R. P., Serhan, C. N., & Hammock, B. D. (2020). Inflammation resolution: a dual-pronged approach to averting cytokine storms in COVID-19?. *Cancer metastasis reviews*, 1–4. Advance online publication. <https://doi.org/10.1007/s10555-020-09889-4>
- Polonikov A. (2020). Endogenous Deficiency of Glutathione as the Most Likely Cause of Serious Manifestations and Death in COVID-19 Patients. *ACS infectious diseases*, acsinfecdis.0c00288. Advance online publication.
<https://doi.org/10.1021/acsinfecdis.0c00288>

Rebello, C. J., Kirwan, J. P., & Greenway, F. L. (2020). Obesity, the most common comorbidity in SARS-CoV-2: is leptin the link?. *International journal of obesity* (2005), 1–8. Advance online publication. <https://doi.org/10.1038/s41366-020-0640-5>

Remy, K. E., Mazer, M., Striker, D. A., Ellebedy, A. H., Walton, A. H., Unsinger, J., Blood, T.M., Mudd, P. A., Yi, D. J., Mannion, D. A., Osborne, D. F., Martin, R. S., Anand, N. J., Bosanquet, J. P., Blood, J., Drewry, A. M., Caldwell, C. C., Turnbull, I. R., Brakenridge, S. C., Moldwawer, L. L., ... Hotchkiss, R. S. (2020). Severe immunosuppression and not a cytokine storm characterizes COVID-19 infections. *JCI insight*, 5(17), 140329. <https://doi.org/10.1172/jci.insight.140329>

Restivo, D. A., Centonze, D., Alesina, A., & Marchese-Ragona, R. (2020). Myasthenia Gravis Associated With SARS-CoV-2 Infection. *Annals of internal medicine*, L20-0845. Advance online publication. <https://doi.org/10.7326/L20-0845>

Rhodes, J. M., Subramanian, S., Laird, E., & Kenny, R. A. (2020). Editorial: low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity. *Alimentary pharmacology & therapeutics*, 51(12), 1434–1437. <https://doi.org/10.1111/apt.15777>

Rubino, F., Amiel, S. A., Zimmet, P., Alberti, G., Bornstein, S., Eckel, R. H., Mingrone, G., Boehm, B., Cooper, M. E., Chai, Z., Del Prato, S., Ji, L., Hopkins, D., Herman, W. H., Khunti, K., Mbanya, J. C., & Renard, E. (2020). New-Onset Diabetes in Covid-19. *The New England journal of medicine*, 10.1056/NEJMc2018688. Advance online publication. <https://doi.org/10.1056/NEJMc2018688>

Sajadi, M. M., Habibzadeh, P., Vintzileos, A., Shokouhi, S., Miralles-Wilhelm, F., & Amoroso, A. (2020). Temperature, Humidity, and Latitude Analysis to Estimate Potential Spread and Seasonality of Coronavirus Disease 2019 (COVID-19). *JAMA network open*, 3(6), e2011834. <https://doi.org/10.1001/jamanetworkopen.2020.11834>

SARS-CoV-2 and The Case for Empirical Treatment. Retrieved: <https://americacanwetalk.org/wp-content/uploads/2020/07/ColumnByDrBartlettReCOVID-5.pdf>

Schett, G., Manger, B., Simon, D., & Caporali, R. (2020). COVID-19 revisiting inflammatory

- pathways of arthritis. *Nature reviews rheumatology* (2020).
<https://doi.org/10.1038/s41584-020-0451-z>
- Schlievert, P. M., Kilgore, S. H., Kaus, G. M., Ho, T. D., & Ellermeier, C. D. (2018). Glycerol Monolaurate (GML) and a Nonaqueous Five-Percent GML Gel Kill *Bacillus* and *Clostridium* Spores. *mSphere*, 3(6), e00597-18.
<https://doi.org/10.1128/mSphereDirect.00597-18>
- Scully, E.P., Haverfield, J., Ursin, R.L. et al. (2020). Considering how biological sex impacts immune responses and COVID-19 outcomes. *Nature reviews immunology*,
<https://doi.org/10.1038/s41577-020-0348-8>
- Shahzad, F., Anderson, D., & Najafzadeh, M. (2020). The Antiviral, Anti-Inflammatory Effects of Natural Medicinal Herbs and Mushrooms and SARS-CoV-2 Infection. *Nutrients*, 12(9), E2573. <https://doi.org/10.3390/nu12092573>
- Shakoor, H., Feehan, J., Dhaheri, A. S., Ali, H. I., Platat, C., Ismail, L. C., . . . Stojanovska, L. (2021). Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? *Maturitas*, 143, 1-9.
[doi:10.1016/j.maturitas.2020.08.003](https://doi.org/10.1016/j.maturitas.2020.08.003)
- Shields, G. S., Spahr, C. M., & Slavich, G. M. (2020). Psychosocial Interventions and Immune System Function: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA psychiatry*, 10.1001/jamapsychiatry.2020.0431. Advance online publication. <https://doi.org/10.1001/jamapsychiatry.2020.0431>
- Siemieniuk, R. A., Bartoszko, J. J., Ge, L., Zeraatkar, D., Izcovich, A., Pardo-Hernandez, H., Rochweg, B., Lamontagne, F., Han, M. A., Kum, E., Liu, Q., Agarwal, A., Agoritsas, T., Alexander, P., Chu, D. K., Couban, R., Darzi, A., Devji, T., Fang, B., Fang, C., . . . Brignardello-Petersen, R. (2020). Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ (Clinical research ed.)*, 370, m2980.
<https://doi.org/10.1136/bmj.m2980>
- Singh, S. (2020). Covariation of Zinc Deficiency with COVID19 Infections and Mortality in European Countries: Is Zinc Deficiency a Risk Factor for COVID-19? *Journal of Scientific Research*, 64(02), 153-157. [doi:10.37398/jsr.2020.640222](https://doi.org/10.37398/jsr.2020.640222)
- Somasundaram, N. P., Ranathunga, I., Ratnasamy, V., Wijewickrama, P., Dissanayake, H. A.,

Yogendranathan, N., Gamage, K., de Silva, N. L., Sumanatilleke, M., Katulanda, P., & Grossman, A. B. (2020). The Impact of SARS-Cov-2 Virus Infection on the Endocrine System. *Journal of the Endocrine Society*, 4(8), bvaa082.
<https://doi.org/10.1210/jendso/bvaa082>

Spinner, C. D., Gottlieb, R. L., Criner, G. J., Arribas López, J. R., Cattelan, A. M., Soriano Viladomiu, A., Ogbuagu, O., Malhotra, P., Mullane, K. M., Castagna, A., Chai, L., Roestenberg, M., Tsang, O., Bernasconi, E., Le Turnier, P., Chang, S. C., SenGupta, D., Hyland, R. H., Osinusi, A. O., Cao, H., ... GS-US-540-5774 Investigators (2020). Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. *JAMA*, 324(11), 1048–1057.
<https://doi.org/10.1001/jama.2020.16349>

SSRN. Retrieved from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3612934

Stohs, S. J., & Aruoma, O. I. (2020). Vitamin D and Wellbeing beyond Infections: COVID-19 and Future Pandemics. *Journal of the American College of Nutrition*, 1–2. Advance online publication. <https://doi.org/10.1080/07315724.2020.1786302>

Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March–June 2020. (2020, July 24). Retrieved from:
<https://www.cdc.gov/mmwr/volumes/69/wr/mm6930e1.htm>

Taglauer, E., Benarroch, Y., Rop, K., Barnett, E., Sabharwal, V., Yarrington, C., & Wachman, E. M. (2020). Consistent localization of SARS-CoV-2 spike glycoprotein and ACE2 over TMPRSS2 predominance in placental villi of 15 COVID-19 positive maternal-fetal dyads. *Placenta*, 100, 69–74. Advance online publication.
<https://doi.org/10.1016/j.placenta.2020.08.015>

Tenforde, M. W., Kim, S. S., Lindsell, C. J., Billig Rose, E., Shapiro, N. I., Files, D. C., Gibbs, K. W., Erickson, H. L., Steingrub, J. S., Smithline, H. A., Gong, M. N., Aboodi, M. S., Exline, M. C., Henning, D. J., Wilson, J. G., Khan, A., Qadir, N., Brown, S. M., Peltan, I. D., Rice, T. W., ... IVY Network Investigators (2020). Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March-June 2020. *MMWR. Morbidity and mortality weekly report*, 69(30), 993–998.
<https://doi.org/10.15585/mmwr.mm6930e1>

The Institute for Functional Medicine. Retrieved from:

<https://www.ifm.org/news-insights/the-functional-medicine-approach-to-covid-19-virus-specific-nutraceutical-and-botanical-agents/?fbclid=IwAR24Kg3-s4SA3170UnwoKuZIO9gKKup8iFNu7XKMtEmCohMWI5SCwpZ3uDQ>

Thibodeaux, K., Speyrer, M., Raza, A., Yaakov, R., & Serena, T. E. (2020). Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a retrospective case series. *Journal of wound care*, 29(Sup5a), S4–S8.
<https://doi.org/10.12968/jowc.2020.29.Sup5a.S4>

Transmission of SARS-CoV-2: Implications for infection prevention precautions. (n.d.).

Retrieved from:

<https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions>

University of Oxford. Retrieved from:

<https://www.recoverytrial.net/news/low-cost-dexamethasone-reduces-death-by-up-to-one-third-in-hospitalised-patients-with-severe-respiratory-complications-of-covid-19>

U.S. Senate Committee on Homeland Security and Governmental Affairs. Retrieved from:

<https://www.hsgac.senate.gov/imo/media/doc/Testimony-Kory-2020-05-06-REVISED.pdf>

Vallat, R., Shah, V. D., Redline, S., Attia, P., & Walker, M. P. (2020). Broken sleep predicts hardened blood vessels. *PLoS biology*, 18(6), e3000726.
<https://doi.org/10.1371/journal.pbio.3000726>

van de Veerdonk, F. L., & Netea, M. G. (2020). Blocking IL-1 to prevent respiratory failure in COVID-19. *Critical care (London, England)*, 24(1), 445.
<https://doi.org/10.1186/s13054-020-03166-0>

Varatharaj, A., Thomas, N., Ellul, M. A., Davies, N., Pollak, T. A., Tenorio, E. L., Sultan, M., Easton, A., Breen, G., Zandi, M., Coles, J. P., Manji, H., Al-Shahi Salman, R., Menon, D. K., Nicholson, T. R., Benjamin, L. A., Carson, A., Smith, C., Turner, M. R., Solomon, T., ... CoroNerve Study Group (2020). Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *The Lancet. Psychiatry*, S2215-0366(20)30287-X. Advance online publication.
[https://doi.org/10.1016/S2215-0366\(20\)30287-X](https://doi.org/10.1016/S2215-0366(20)30287-X)

Verdoia, M., & De Luca, G. (2020). Potential role of hypovitaminosis D and Vitamin D

supplementation during COVID-19 pandemic. QJM : monthly journal of the Association of Physicians, hcaa234. Advance online publication.
<https://doi.org/10.1093/qjmed/hcaa234>

Vyas, N., Kurian, S. J., Bagchi, D., Manu, M. K., Saravu, K., Unnikrishnan, M. K., Mukhopadhyay, C., Rao, M., & Miraj, S. S. (2020). Vitamin D in Prevention and Treatment of COVID-19: Current Perspective and Future Prospects. *Journal of the American College of Nutrition*, 1–14. Advance online publication.
<https://doi.org/10.1080/07315724.2020.1806758>

Wagner, J., DuPont, A., Larson, S., Cash, B., & Farooq, A. (2020). Absolute lymphocyte count is a prognostic marker in Covid-19: A retrospective cohort review. *International journal of laboratory hematology*, 1–5. <https://doi.org/10.1111/ijlh.13288>

Wallace T. C. (2020). Combating COVID-19 and Building Immune Resilience: A Potential Role for Magnesium Nutrition?. *Journal of the American College of Nutrition*, 1–9. Advance online publication. <https://doi.org/10.1080/07315724.2020.1785971>

Wang, Q., Fang, P., He, R., Li, M., Yu, H., Zhou, L., Yi, Y., Wang, F., Rong, Y., Zhang, Y., Chen, A., Peng, N., Lin, Y., Lu, M., Zhu, Y., Peng, G., Rao, L., & Liu, S. (2020). O-GlcNAc transferase promotes influenza A virus-induced cytokine storm by targeting interferon regulatory factor-5. *Science advances*, 6(16), eaaz7086.
<https://doi.org/10.1126/sciadv.aaz7086>

Waqas Khan, H. M., Parikh, N., Megala, S. M., & Predeteanu, G. S. (2020). Unusual Early Recovery of a Critical COVID-19 Patient After Administration of Intravenous Vitamin C. *The American journal of case reports*, 21, e925521.
<https://doi.org/10.12659/AJCR.925521>

Ward, M. P., Xiao, S., & Zhang, Z. (2020). Humidity is a consistent climatic factor contributing to SARS-CoV-2 transmission. *Transboundary and emerging diseases*, 10.1111/tbed.13766. Advance online publication. <https://doi.org/10.1111/tbed.13766>
Ward, M. P., Xiao, S., & Zhang, Z. (2020). Humidity is a consistent climatic factor contributing to SARS-CoV-2 transmission. *Transboundary and emerging diseases*, 10.1111/tbed.13766. Advance online publication. <https://doi.org/10.1111/tbed.13766>

WebMD. Retrieved from:

<https://www.webmd.com/lung/news/20200423/the-great-invader-how-covid-attacks-every-organ>

WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne, J., Murthy, S., Diaz, J. V., Slutsky, A. S., Villar, J., Angus, D. C., Annane, D., Azevedo, L., Berwanger, O., Cavalcanti, A. B., Dequin, P. F., Du, B., Emberson, J., Fisher, D., Giraudeau, B., Gordon, A. C., Granholm, A., Green, C., Haynes, R., ... Marshall, J. C. (2020). Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. *JAMA*, 10.1001/jama.2020.17023. Advance online publication. <https://doi.org/10.1001/jama.2020.17023>

Williamson, E. J., Walker, A. J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C. E., Curtis, H. J., Mehrkar, A., Evans, D., Inglesby, P., Cockburn, J., McDonald, H. I., MacKenna, B., Tomlinson, L., Douglas, I. J., Rentsch, C. T., Mathur, R., Wong, A., Grieve, R., Harrison, D., ... Goldacre, B. (2020). OpenSAFELY: factors associated with COVID-19 death in 17 million patients. *Nature*, 10.1038/s41586-020-2521-4. Advance online publication. <https://doi.org/10.1038/s41586-020-2521-4>

World Health Organization. Retrieved from:

<https://www.euro.who.int/en/health-topics/disease-prevention/alcohol-use/news/news/2020/04/alcohol-does-not-protect-against-covid-19-access-should-be-restricted-during-lock-down>

Wu, F., Liu, M., Wang, A., Lu, L., Wang, Q., Gu, C., Chen, J., Wu, Y., Xia, S., Ling, Y., Zhang, Y., Xun, J., Zhang, R., Xie, Y., Jiang, S., Zhu, T., Lu, H., Wen, Y., & Huang, J. (2020). Evaluating the Association of Clinical Characteristics With Neutralizing Antibody Levels in Patients Who Have Recovered From Mild COVID-19 in Shanghai, China. *JAMA internal medicine*, 10.1001/jamainternmed.2020.4616. Advance online publication. <https://doi.org/10.1001/jamainternmed.2020.4616>

Wu, P., Duan, F., Luo, C., Liu, Q., Qu, X., Liang, L., & Wu, K. (2020). Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA ophthalmology*, 138(5), 575–578. Advance online publication. <https://doi.org/10.1001/jamaophthalmol.2020.1291>

Yanuck, S. F., Pizzorno, J., Messier, H., & Fitzgerald, K. N. (2020). Evidence Supporting a Phased Immuno-physiological Approach to COVID-19 From Prevention Through Recovery. *Integrative medicine (Encinitas, Calif.)*, 19(Suppl 1), 8–35.

Zhang, M. S., Tran, P. M., Wolff, A. J., Tremblay, M. M., Fosdick, M. G., & Houtman, J. (2018).

Glycerol monolaurate induces filopodia formation by disrupting the association between LAT and SLP-76 microclusters. *Science signaling*, 11(528), eaam9095.

<https://doi.org/10.1126/scisignal.aam9095>