**COVID-19 Bibliography**

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compiled by S. Todd Stolp MD

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4. A thorough video from the Wall Street Journal describing the importance of building ventilation to indoor air quality and viral transmission <https://www.wsj.com/video/ventilation-is-key-to-battling-covid-heres-why/EC6274D1-B4F0-40DF-A8EC-F9BDA7C5D1A1.html>
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N Engl J Med 2020; 383:120-128 July 9, 2020 <https://doi.org/10.1056/NEJMoa2015432> Angiopathy described

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26. Thomas, S et al. Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction Among Ambulatory Patients With SARS-CoV-2 Infection The COVID A to Z Randomized Clinical Trial. JAMA Network Downloaded March 3, 2021 <https://doi.org/10.1001/jamanetworkopen.2021.0369> No benefit demonstrated in this study of zinc and ascorbic acid supplementation for COVID-19 symptoms
27. López-Medina et al Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19 March 4, 2021.A Randomized Clinical Trial. JAMA. Published online March 4, 2021. <https://doi.org/10.1001/jama.2021.3071> Ivermectin did not shorten symptomatic period when administered in earlier COVID-19 infection
28. **Communications**
29. *Putting the Risk of COVID-19 in Perspective,* by David C. Roberts New York Times May 22, 2020 <https://www.nytimes.com/2020/05/22/well/live/putting-the-risk-of-covid-19-in-perspective.html> Defines the risk of death from COVID-19 during the peak of the outbreak in NYC in relative risk terms, using a metric called the “micromort,” which is a one-in-a-million chance of death roughly equivalent to the risk of death that each U.S. citizen faces each day due to nonnatural causes (car accidents, electrocutions, etc..) The risk of death due to COVID-19 between March 15 and May 9th was about one quarter of the risk of childbirth, ten times the risk of undergoing general anesthesia and equivalent to doing 7 parachute jumps, but in this case you are affecting other people and most people would “think twice about forcing their frail grandmothers, or their neighbors, to jump with them.”
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31. Rosenbaum, L Tribal Truce — How Can We Bridge the Partisan Divide and Conquer Covid? NEJM September 23, 2020 Tribal Truce — How Can We Bridge the Partisan Divide and Conquer Covid? <https://doi.org/10.1056/NEJMms2027985> An interesting look at the ethics and sociology behind our expressed messaging
32. Kantor, B N et ak Non-pharmaceutical Interventions for Pandemic COVID-19: A Cross-Sectional Investigation of US General Public Beliefs, Attitudes, and Actions *Frontiers in Medicine* July 2020 Vol. 7 Art. 384 <https://doi.org/10.3389/fmed.2020.00384> Results of a cross-sectional online survey of public beliefs (N=1005) regarding non-pharmaceutical interventions (NPI). 90% reported using some sort of NPI.
33. Callender, B et al The art of medicine COVID-19, comics, and the visual culture of contagion Lancet Vol 396, October 10, 2020 <https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32084-5/fulltext> Interesting view of communication techniques, highlighting comics
34. Wilson, R et al Factors Influencing Risk for COVID-19 Exposure Among Young Adults

Aged 18–23 Years — Winnebago County, Wisconsin, March–July 2020 MMWR Vol. 69 No. 41

<https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6941e2-H.pdf> Informant interviews were conducted during July 9–22 with 13 young adults, nine owners of business

establishments employing and frequented by young adults (e.g., restaurants and bars), and eight community leaders exploring perceptions and misconceptions of public health guidance and how these correlated with legislative and community leader actions (including Wisc Supreme Court invalidation of the Safe At Home Emergency Order) and spread of COVID-19 in Winnebago, Wisconsin

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2. Liu, M et al. Internet Searches for Unproven COVID-19 Therapies in the United States JAMA letter August 2020 Volume 180, Number 8 <https://doi.org/10.1001/jamainternmed.2020.1764> An unsurprising report of the increase in Google searches to purchase Chloroquine and Hydroxychloroquine that followed endorsements by well-known people. A recommendation to counter such unsupported endorsements with organized public messaging is included in the conclusion.
3. Vraga EK, Bode L. Addressing COVID-19 misinformation on social media preemptively and responsively. Emerg Infect Dis. 2021 February 2021 [January 4, 2021]. <https://doi.org/10.3201/eid2701.203139> An interesting experimental design to test the effectiveness of preemptive vs responsive messaging to correct misperceptions promoted by messaging that promotes misinformation. In general, messaging was modestly effective whether preemptive or responsive, although effects were most significant when addressing science principles rather than COVID-19 prevention.
4. Abbasi, Jennifer COVID-19 Conspiracies and Beyond: How Physicians Can Deal With Patients’ Misinformation JAMA News Article (online December 30, 2020) <https://doi.org/10.1001/jama.2020.22018> An interview with a Duke social scientist, Brian Southwell about misinformation in the COVID-19 realm
5. Duplaga, Maiusz. The Determinants of Conspiracy Beliefs Related to the COVID-19 Pandemic in a Nationally Representative Sample of Internet Users. Int J Environ Res Public Health 2020 Oct 26;17(21):7818 <https://doi.org/10.3390/ijerph17217818> The percentage of supporters of particular conspiracy theories in the study sample ranged from 43% to 56%.
6. Druckman, J et al. Affective polarization, local context and public opinion in America, Nature Human Behavior, online November 5, 2020 <https://doi.org/10.1038/s41562-020-01012-5> An in depth look at the influence of political polarization on interpretation of public health messaging and science
7. Sax, Paul E. COVID-19 Frequently Asked Questions NEJM Online (Downloaded January 15, 2021) <https://www.nejm.org/covid-vaccine/faq> Specific answers to FAQs from a Harvard University Infectious Disease specialist, including a number of recommendations regarding public health communications
8. Tyson A﻿, Johnson C﻿, Funk C﻿. US public now divided over whether to get COVID-19 vaccine. Pew Research Center. September 8-13, 2020 <https://www.pewresearch.org/science/2020/09/17/u-s-public-now-divided-over-whether-to-get-covid-19-vaccine/> In this survey vaccine acceptance was lower among Black individuals (32%, 263 of 822); those with lower educational attainment (47%, 676 of 1438 among those with high school or less education) compared with college graduates (56%, 1673 of 2988) or those with a postgraduate education (63%, 1693 of 2668); and among Republican voters (44%, 1817 of 4129)
9. Volpp, K.G. et al. Behaviorally Informed Strategies for a National COVID-19 Vaccine Promotion Program JAMA Network 2021;325(2):125-126. (online December 14, 2020) <https://doi.org/10.1001/jama.2020.24036> Specific recommendations to inform and promote vaccination in a responsible and effective fashion: 1) Make the Vaccine Free and Easily Accessible, 2) Make Access to Valued Settings Conditional on Getting Vaccinated, 3) Use Public Endorsements From Trusted Leaders to Increase Uptake, 4) Provide Priority Access to People Who Sign Up to Get Vaccinated Before Vaccines Are Widely Available, 5) Transform Individual Vaccination Decisions Into a Public Act.
10. Buttenheim, A SARS-CoV-2 Vaccine Acceptance: We May Need to Choose Our Battles Editorial An Int Med September 4, 2020 <https://www.acpjournals.org/doi/10.7326/M20-6206> Selecting the population towards which to focus vaccination messaging
11. Brewer, N.T. et al. Increasing Vaccination: Putting Psychological Science Into Action. Psychol Sci Public Interest. 2017 Dec;18(3):149-207. <https://doi.org/10.1177/1529100618760521> A comprehensive review of the behavioral psychology of antivaccination convictions and messaging strategies to inform such beliefs with vaccine science.
12. Hutchins HJ, Wolff B, Leeb R, et al. COVID-19 mitigation behaviors by age group: United States, April-June 2020. MMWR Morb Mortal Wkly Rep. 2020;69 (43):1584-1590. <https://doi.org/10.15585/mmwr.mm6943e4> The prevalence of reported mitigation behaviors was lowest among younger adults (aged 18–29 years) and highest among older adults (aged ≥60 years).
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14. Wood, S and Schuman, K. Beyond Politics — Promoting Covid-19 Vaccination in the United States N Eng J Med 384;e23 February 18, 2021 <https://doi.org/10.1056/NEJMms2033790> An excellent review of vaccine messaging emphasizing evidence-based tactics and strategies for countering COVID-19 vaccine misinformation and disinformation
15. **Contact Tracing**
16. Cheng, H-Y et al Contact Tracing Assessment of COVID-19 Transmission Dynamics in Taiwan and Risk at Different Exposure Periods Before and After Symptom Onset JAMA Intern Med. 2020;180(9):1156-1163. <https://doi.org/10.1001/jamainternmed.2020.2020> Identifies transmission risks at different points in disease progression in index cases, with zero transmission from 856 symptomatic index patients 6 days or longer after symptom onset
17. Johns Hopkins University Bloomberg School of Public Health Contact Tracing training site, a comprehensive and free on-line five-hour training for prospective contact tracers <https://coronavirus.jhu.edu/contact-tracing>
18. Sachdev, D et al Outcomes of Contact Tracing in San Francisco, California—Test and Trace During Shelter-in-Place, JAMA Int Med November 2, 2020 <https://doi/org/10.1001/jamainternmed.2020.5670> Among 1214 contacts traced from 1394 interviews with cases in San Francisco between April 13 to June 8, 83.8% were successfully notified, 37.6% were tested, and 9.9% (120) were newly diagnosed with COVID-19 (while city-wide testing positivity was 2.2%)
19. CDC Contact Tracing Informational Video for the Public, *Answer the Call* <https://www.youtube.com/watch?v=u3dLoBj3YLo>
20. CDC Contact Tracing Resources, an extensive page of Contact Tracing resources from the CDC including checklist tools for contact tracers

<https://www.cdc.gov/coronavirus/2019-ncov/php/open-america/contact-tracing-resources.html#communication-resources>

1. Braithwaite, I et al, Automated and partly automated contact tracing: a systematic review to inform the control of COVID-19, Lancet, digital health Vol 2 November 2020 <https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30184-9/fulltext> “Well designed prospective studies are needed given gaps in evidence of effectiveness, and to investigate the integration and relative effects of manual and automated systems. Large-scale manual contact tracing is therefore still key in most contexts.”
2. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob Health. 2020;8:e488–96. <https://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(20)30074-7.pdf> Across different initial numbers of cases, the majority of scenarios with an R0 of 1.5 were controllable with less than 50% of contacts successfully traced, but to control the majority of outbreaks for R0 of 2.5 more than 70% of contacts had to be traced, for an R0 of 3·5 more than 90% of contacts had to be traced.
3. **Epidemiology (Including the Great Barrington Declaration)**
4. Wilson NM, Norton A, Young FP, et al. Airborne transmission of severe acute respiratory syndrome coronavirus-2 to healthcare workers: a narrative review. Anaesthesia. 2020. [PMID: 32311771] <https://doi.org/10.1111/anae.15093>
5. Stutt ROJH, Retkute R, Bradley M, Gilligan C, Colvin J. A modelling framework to assess the likely effectiveness of facemasks in combination with ‘lock-down’ in managing the COVID-19 pandemic. Proc. R. Soc. Volume 476, Issue 2238, 2020 <http://doi.org/10.1098/rspa.2020.0376> A look at the effect of masking and lockdowns on mathematical models of the outbreak.
6. Tian, L et al *Calibrated Intervention and Containment of the COVID-19 Pandemic* arXiv.org Submitted March 16, 2020 and last revised April 2, 2020 <https://arxiv.org/abs/2003.07353> Interesting mathematical model projecting the effects of different non-pharmaceutical interventions based upon computer modeling. “…if 70% of the general public wear masks and contact tracing is conducted at 60% efficiency within a 4-day time frame, epidemic growth will be flattened in the hardest hit countries.”
7. Hatfield, K et al *Facility-Wide Testing for SARS-CoV-2 in Nursing Homes — Seven U.S. Jurisdictions, March–June 2020* MMWR Vol69 August 11, 2020 <https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e5.htm?s_cid=mm6932e4_e&deliveryName=USCDC_921-DM35136> “…for each additional day before completion of initial facility-wide testing (after a COVID-19 case was identified in a nursing home), an estimated 1.3 additional cases were identified.”
8. Wang et al Impact of Social Distancing Measures on Coronavirus Disease Healthcare Demand, Central Texas, USA EID Volume 26, Number 10—October 2020 <https://wwwnc.cdc.gov/eid/article/26/10/20-1702-f1> School Closures alone had minimal effect on the epidemic curve in mathematical models from U of Texas
9. Wilson, N et al Case-Fatality Risk Estimates for COVID-19 Calculated by Using a Lag Time for Fatality EID Vol 26, Number 6, June 2020 <https://wwwnc.cdc.gov/eid/article/26/6/20-0320_article> Case fatality estimates, including data on lag time from diagnosis to death i
10. Pollan, M Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study Lancet July 6, 2020 <https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31483-5/fulltext> With a 5% seroprevalence (up to 10% in hotspot urban centers) in Spain, the authors conclude that herd immunity was not yet achieved when non-pharmacologic measures successfully contained the outbreak in Spain.
11. Bilinski, A et al Modeling Contact Tracing Strategies for COVID-19 in the Context of Relaxed Physical Distancing Measures JAMA Netw August 21, 2020 <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2769618> A modeled assessment of the relative benefits of identification of asymptomatic cases, contact tracing and adherence to physical distancing measures.
12. Blackburn, J Infection Fatality Ratios for COVID-19 Among Noninstitutionalized Persons 12 and Older: Results of a Random-Sample Prevalence Study An Int Med, Online September 2, 2020 <https://doi.org/10.7326/M20-5352> An effort to breakdown Infection Fatality Rates for non-institutionalized populations in Indiana showing the expected higher rate of 1.7% IFR for those over 60 and higher rates for racial/ethnic minorities, particularly African Americans, with an overall IFR of 0.26%
13. Bixler, D et al SARS-CoV-2–Associated Deaths Among Persons Aged <21 Years —United States, February 12–July 31, 2020 MMWR data for some variables in case-based surveillance September 18, 2020 Vol. 69 No. 37 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6937e4-H.pdf> “...data on cases and deaths by race/ethnicity are not comparable and case fatality rates by race/ethnicity cannot be calculated.” There were 121 deaths among 391,814 cases in U.S. people under 21 years. A disproportionate percentage of deaths occurred among young adults aged 18–20 years and among Hispanics, Blacks, AI/ANs, and persons with underlying medical conditions.
14. CDC data sets by HHS Region for Tests per 100,000 Population and Test Positivity Rates for School Children <https://stacks.cdc.gov/view/cdc/94151> Variable trends across the U.S. among school children
15. Fineberg, H.V. The Toll of COVID-19 JAMA Editorial October 12, 2020 <https://doi.org/10.1001/jama.2020.20019> A review of the excess death calculations attributable to the COVID-19 pandemic conducted by the NVSS
16. Chau NVV et al Superspreading event of SARS-CoV-2 infection at a bar, Ho Chi Minh City, Vietnam Emerg Infect Dis. downloaded October 15, 20202021 Jan [date cited]. <https://doi.org/10.3201/eid2701.203480> A report of an outbreak in over 200 people at a bar in Vietnam. Crowds in enclosed indoor settings with poor ventilation may be

considered at high risk for transmission.

1. Dominguez, S et al Isolation, propagation, genome analysis and epidemiology of HKU1 betacoronaviruses J Gen Virol. 2014 Apr; 95(Pt 4): 836–848. <https://doi/org/10.1099/vir.0.059832-0> The prevalence of HKU1 betacoronavirus RNA detection, which may have some homology with antigens in SARS-CoV-2, in over 15000 specimens collected between 2009 and 2013 was 0.5%
2. Viner, RM et al Susceptibility to SARS-CoV-2 Infection Among Children and Adolescents Compared With Adults, JAMA Pediatrics online September 25, 2020 <https://doi.org/10.1001/jamapediatrics.2020.4573> “In this meta-analysis, there is preliminary evidence that children and adolescents have lower susceptibility to SARS-CoV-2, with an odds ratio of 0.56 for being an infected contact compared with adults. There is weak evidence that children and adolescents play a lesser role than adults in transmission of SARS-CoV-2 at a population level. This study provides no information on the infectivity of children.”
3. Ng, OT et al SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study, Lancet (online November 2, 2020) <https://doi.org/10.1016/S1473-3099(20)30833-1> A retrospective cohort study of close contacts of confirmed COVID-19 cases in Singapore, identified between Jan 23 and April 3, 2020, analyzing transmission risk factors in and outside of households
4. Brown, K et al Association Between Nursing Home Crowding and COVID-19 Infection and Mortality in Ontario, Canada JAMA Int Med (online November 9, 2020) <https://doi.org/10.1001/jamainternmed.2020.6466> In this cohort of Canadian nursing homes, crowded homes were more likely to experience larger and deadlier COVID-19 outbreaks. Shared bedrooms and bathrooms in nursing homes were associated with larger and deadlier COVID-19 outbreaks.
5. Selden, T and Berdahl, T COVID-19 And Racial/Ethnic Disparities In Health Risk, Employment, And Household Composition *Health Affairs* Vol. 39, No. 9 July 14, 2020 <https://www.healthaffairs.org/doi/10.1377/hlthaff.2020.00897> Racially stratified employment risk factors as an explanation for disparity in incidence and fatality rates, with essential work outside the home accounting for higher incidence for Black and Hispanic populations and higher age group accounting for higher White fatality rates in some areas (although age-controlled fatality rates are higher in Black and Latinx populations)
6. Liotti, F et al Assessment of SARS-CoV-2 RNA Test Results Among Patients Who Recovered From COVID-19 With Prior Negative Results JAMA Internal Med November 12, 2020 <https://doi/org/10.1001/jamainternmed.2020.7570> After a mean (SD) time from COVID-19 diagnosis to follow-up was 48.6 (13.1) days in 32 patients (Table) and 57.7 (16.9) days in 144 patients 0.6% of patients continued to have positive replicable virus
7. Chang, S et al Mobility network models of COVID-19 explain inequities and inform reopening, Nature (Accelerated Article Preview) November 10, 2020 <https://doi.org/10.1038/s41586-020-2923-3> ‘Our model predicts that a small minority of “superspreader” POIs account for a large majority of infections and that restricting maximum occupancy at each POI is more effective than uniformly reducing mobility.’
8. **The “Great Barrington Declaration” and proposals for Herd Immunity**

* Omer, S et al Herd Immunity and Implications for SARS-CoV-2 Control JAMA Network, October 19, 2020 <https://jamanetwork.com/journals/jama/fullarticle/2772167> A review of factors that affect Herd Immunity. Arguments against the “Great Barrington Declaration” proposal
* Barry, John M What Fans of ‘Herd Immunity’ Don’t Tell You *The New York Times*, October 19, 2020 <https://www.nytimes.com/2020/10/19/opinion/coronavirus-herd-immunity.html> An interesting discussion of the ethical and epidemiologic implications of the so-called “Great Barrington Declaration.” (See next item)
* *The Great Barrington Declaration* A public policy proposal by a group of credentialed signatories supporting a strategy called “Focused Protection,” by allowing low risk groups to return to normal activities to seek herd immunity in communities around the world. Ongoing debate addresses exactly how that could be accomplished and the number of deaths that would result (see previous NY Times perspective piece)<https://gbdeclaration.org/>
* You Tube presentation moderated by the Editor of JAMA of the debate regarding the Great Barrington Declaration, clarifying its proposals and risks posed by its recommendations <https://youtu.be/2tsUTAWBJ9M>

1. Cheng, H-Y et al Contact Tracing Assessment of COVID-19 Transmission Dynamics in Taiwan and Risk at Different Exposure Periods Before and After Symptom Onset JAMA Intern Med. 2020;180(9):1156-1163. <https://doi.org/10.1001/jamainternmed.2020.2020> Identifies transmission risks at different points in disease progression in index cases, with zero transmission from 856 symptomatic index patients 6 days or longer after symptom onset
2. Wang, E et al, COVID-19, Decarceration, and the Role of Clinicians, Health Systems, and Payers A Report From the National Academy of Sciences, Engineering, and Medicine JAMA Network, November 16, 2020 <https://doi.org/10.1001/jama.2020.22109> “According to the COVID Prison Project, by August 2020, 90 of the largest 100 cluster outbreaks in the United States have occurred in prisons and jails.”
3. Firestone, M et al COVID-19 Outbreak Associated with a 10-Day Motorcycle Rally in a

Neighboring State — Minnesota, August–September 2020 MMWR Vol. 69 November 20, 2020 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6947e1-H.pdf> “The impact of gatherings as a source of virus transmission underscores the importance of reducing the number of attendees at gatherings, using face masks, and encouraging physical distancing”

1. James, A et al High COVID-19 Attack Rate Among Attendees at Events at a Church — Arkansas, March 2020, MMWR Vol. 69 No. 20 May 22, 2020 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6920e2-H.pdf> Thirty-five confirmed cases, three deaths occurred in attendees at a church, with 26 additional cases in secondary contacts and one additional death. No information available on specific risk behaviors or masking.
2. Pray, I et al COVID-19 Outbreak at an Overnight Summer School Retreat — Wisconsin, July–August 2020 MMWR Vol. 69 No. 43 October 30, 2020 <https://doi.org/https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6943a4-H.pdf> Assuming that compliance with a “7-day quarantine” was impeccable, this outbreak occurred despite the “7-day quarantine” following a negative SARS-CoV-2 PCR in a Wisconsin camp.
3. Biggerstaff M, Cowling BJ, Cucunubá ZM, Dinh L, Ferguson NM, Gao H, et al., for the WHO COVID-19 Modelling Parameters Group. Early insights from statistical and mathematical modeling of key epidemiologic parameters of COVID-19. Emerg Infect Dis. 2020 [cited November 25]. <https://doi.org/10.3201/eid2611.201074> An excellent article addressing estimated epidemiologic parameters for SARS-CoV-2 through a partial review of various studies (“partial” because the outbreak continues to evolve and peer review of the data in many cases had not been completed at the time of this analysis)
4. Faust, J.S. et al. All-Cause Excess Mortality and COVID-19–Related Mortality Among US Adults Aged 25-44 Years, March-July 2020 JAMA Research Letter December 16, 2020 <https://doi.org/10.1001/jama.2020.24243> From March 1, 2020, to July 31, 2020, a total of 76 088 all-cause deaths occurred among US adults aged 25 to 44 years, which was 11 899 more than the expected 64 189 deaths (incident rate ratio, 1.19 [95% CI, 1.14-1.23], and 38% of these were recorded as due to COVID-19.
5. Woolf, S et al. COVID-19 as the Leading Cause of Death in the United States. JAMA Network Viewpoint December 17, 2020 <https://doi.org/10.1001/jama.2020.24865> A sobering look at the toll of COVID-19 using relative risk figures
6. Chen, Y.H. et al. Excess Mortality in California During the Coronavirus Disease 2019 Pandemic, March to August 2020. JAMA Int Med Published Online: December 21, 2020. <https://doi.org/10.1001/jamainternmed.2020.7578>
7. **Ethics**
8. Powell, t et al COVID in NYC: What We Could Do Better Am Journ of Bioethics 2020, Vol. 20, No. 7, 62-66 <https://doi.org/10.1080/15265161.2020.1764146> A look at the NYC response to the COVID-19 pandemic and ethical dilemmas that emerged
9. Abbott, J et al Ensuring Adequate Palliative and Hospice Care During COVID-19 Surges September 21, 2020 Online <https://doi.org/10.1001/jama.2020.16843> Addressing the importance of palliative end-of-life care during the pandemic surge
10. Rosenbaum, L Tribal Truce — How Can We Bridge the Partisan Divide and Conquer Covid? NEJM September 23, 2020 Tribal Truce — How Can We Bridge the Partisan Divide and Conquer Covid? <https://doi.org/10.1056/NEJMms2027985> An interesting look at the ethics and sociology behind our expressed messaging
11. Lynn, Joanne Playing the Cards We Are Dealt: COVID‐19 and Nursing Homes J. of the Amer. Geriatrics Soc Vol. 68 Iss. 8 May 30, 2020 <https://doi.org/10.1111/jgs.16658> Some questions raised regarding geriatric patients in SNFs in this article early in the outbreak, although speculation about such things as long term immunity and effectiveness of isolation and quarantine are debateable.
12. Barry, John M What Fans of ‘Herd Immunity’ Don’t Tell You *The New York Times*, October 19, 2020 <https://www.nytimes.com/2020/10/19/opinion/coronavirus-herd-immunity.html> An interesting discussion of the ethical and epidemiologic implications of the so-called “Great Barrington Declaration.” (See next item)
13. *The Great Barrington Declaration* A public policy proposal by a group of credentialed signatories supporting a strategy called “Focused Protection,” by allowing low risk groups to return to normal activities to seek herd immunity in communities around the world. Ongoing debate addresses exactly how that could be accomplished and the number of deaths that would result (see previous NY Times perspective piece)<https://gbdeclaration.org/>
14. Becker, Carolyn. Relationships Between Academic Medicine Leaders and Industry—Time for Another Look? November 10, 2020 JAMA. 2020;324(18):1833-1834. <https://doi.org/10.1001/jama.2020.21021> Some important economic conflicts of interest are discussed regarding the interface between public service and personal gain, some of which contribute to loss of public trust in the health care system
15. McClung, N et al, The Advisory Committee on Immunization Practices’ Ethical Principles for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020, MMWR Vol. 69 November 23, 2020 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6947e3-H.pdf> ACIP COVID-19 Vaccines Work Group
16. **Masking and Respirator Use (See related subject of Aerosol/Airborne transmission)**
17. World Health Organization. Shortage of personal protective equipment endangering health workers worldwide. 3 March 2020. Accessed at [www.who.int/news-room/detail/03-03-2020-shortage-of-personal-protective-equipment-endangering-health-workers-worldwide](http://www.who.int/news-room/detail/03-03-2020-shortage-of-personal-protective-equipment-endangering-health-workers-worldwide) on 15 April 2020 Served as argument against the use of surgical masks or N-95 masks for the general public during the early period of the outbreak
18. ECRI. Clinical evidence assessment: safety of extended use and reuse of N95 respirators. March 2020. Accessed at <https://assets.ecri.org/PDF/COVID-19-Resource-Center/COVID-19-Clinical-Care/COVID-ECRI-N95-Respirators-updated.pdf> on 10 April 2020. Reuse of N-95 respirators is feasible
19. Stutt ROJH, Retkute R, Bradley M, Gilligan C, Colvin J. A modelling framework to assess the likely effectiveness of facemasks in combination with ‘lock-down’ in managing the COVID-19 pandemic. Proc. R. Soc. Volume 476, Issue 2238, 2020 <https://royalsocietypublishing.org/doi/10.1098/rspa.2020.0376>
20. Leung, N et al, Respiratory virus shedding in exhaled breath and efficacy of face masks, *Nature Medicine,* Vol 26, May 2020: 676-680 <https://doi.org/10.1038/s41591-020-0843-2>

Frequently quoted study assessing the effectiveness of cloth masks and respirators

1. Abhitejo Konda et al, Aerosol Filtration Efficiency of Cloth Masks, *American Chemical Society*: April 21, 2020 <https://dx.doi.org/10.1021/acsnano.0c03252> Specific look at cloth masks
2. Wilson NM, Norton A, Young FP, et al. Airborne transmission of severe acute respiratory syndrome coronavirus-2 to healthcare workers: a narrative review. Anaesthesia. 2020. [PMID: 32311771] doi:10.1111/anae.15093 Aerosol transmission of SARS-CoV-2 likely, advising airborne precautions for healthcare workers
3. Sickbert-Bennet, E Filtration Efficiency of Hospital Face Mask Alternatives Available for Use During the COVID-19 Pandemic JAMA Int Med Published online August 11, 2020. doi:10.1001/jamainternmed.2020.4221 Reuse of N95 respirators after ethylene oxide and hydrogen peroxide sterilization is acceptable
4. Dugdale CM and Walensky RP. Filtration efficiency, effectiveness, and availability of N95 face masks for COVID-19 prevention. JAMA Intern Med 2020 Aug 11; [e-pub]. <https://doi.org/10.1001/jamainternmed.2020.4218> Surgical masks worn by both caregiver and patient were as effective as N-95 respirators in preventing transmission
5. Ngonghala, C et al Mathematical assessment of the impact of non-pharmaceutical interventions on curtailing the 2019 novel Coronavirus Mathematical Biosciences Volume 325, July 2020, 108364 [https://www.sciencedirect.com/science/article/pii/S0025556420300560#](https://www.sciencedirect.com/science/article/pii/S0025556420300560)! Combining face-masks and social-distancing is more effective in COVID-19 control
6. Eikenberry, S et al To mask or not to mask: Modeling the potential for face mask use by the general public to curtail the COVID-19 pandemic Infectious Disease Modelling April 21, 2020 <https://doi.org/10.1016/j.idm.2020.04.001> We therefore estimate that inward mask efficiency could range widely, anywhere from 20 to 80% for cloth masks, with ≥50% possibly more typical (and higher values are possible for well-made, tightly fitting masks made of optimal materials), 70–90% typical for surgical masks, and >95% typical for properly worn N95 masks.
7. Doung-ngern, P et al Case-Control Study of Use of Personal Protective Measures and Risk for Severe Acute Respiratory Syndrome Coronavirus 2 Infection, Thailand Emerg Inf Dis. Volume 26, Number 11 November 2020 <https://doi.org/10.3201/eid2611.203003> An indication that cloth masks may indeed protect the wearer
8. Balazy, A et al Do N95 Respirators provide 95% protection level against airborne viruses, and how adequate are surgical masks? APIC 2006 <https://doi.org/10.1016/j.ajic.2005.08.018> A specific look at the filtering capacity of N95 respirators
9. Dugdale, Caitlin et al Filtration Efficiency, Effectiveness, and Availability of N95 Face Masks for COVID-19 Prevention JAMA Int Med August 11, 2020 <https://doi.org/10.1001/jamainternmed.2020.4218> If both caregiver and patient are wearing surgical masks during encounters, this does not constitute an exposure despite the fact that an N95 respirator was not in use.
10. Gallaway, MS et al Trends in COVID-19 Incidence After Implementation of Mitigation Measures — Arizona, January 22–August 7, 2020 MMWR October 9, 2020 Vol. 69 No. 40 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6940e3-H.pdf> Another study supporting the effectiveness of non-pharmaceutical measures, although relative benefits of each measure remaining difficult to assess
11. Lyu, W and Wehby, L Community Use Of Face Masks And COVID-19: Evidence From A Natural Experiment Of State Mandates In The US Health Affairs 39, No. 8 August 2020 1419–1425 <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2020.00818> Addressing the correlation between masking mandates and declining COVID-19 incidence
12. Howard, J et alFace Masks Against COVID-19: An Evidence Review, Europe PMC July 11 2020 Preprint <https://doi.org/10.20944/preprints202004.0203.v3> Support for masking in European literature
13. Wang, et al Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers (HCW) JAMA Research Letter Vol. 324, No. 7 <https://doi.org/10.1001/jama.2020.12897> Mass General Brigham health care system found a correlation between implementation of testing and masking requirments and declining COVID-19 incidence
14. Sunjaya, AP et al Rational for universal face masks in public against COVID-19 Respirology Asian Pacific Society of Respirology (2020) 25, 678–679 <https://doi.org/10.1111/resp.13834> An early review of masking as a public health intervention to mitigate SARS-CoV-2 spread
15. Leffler, CT et al Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks. Update August 4, 2020. medRxiv preprint

<https://www.medrxiv.org/content/10.1101/2020.05.22.20109231v5> “Societal norms and government policies supporting the wearing of masks by the public, as well as international travel controls, are independently associated with lower per-capita mortality from COVID-19”

1. Snyder, A and O’Reilly, E Where the Science Stands on Using Face Masks Against Coronavirus *Science* June 25, 2020 <https://www.axios.com/coronavirus-face-mask-science-e9df446b-e7fb-447b-a980-67a9cf73556a.html> A news summary report regarding recent research on masking for SARS-CoV-2
2. Chughtai, A et al Effectiveness of Cloth Masks for Protection Against Severe Acute Respiratory Syndrome Coronavirus, EID Vol. 26, No. 10, October 2020 <https://wwwnc.cdc.gov/eid/article/26/10/20-0948_article> Addresses the importance of correct use of cloth masks
3. Wilson, RF et al Factors Influencing Risk for COVID-19 Exposure Among Young Adults Aged 18-23 Years – Winnebago County, Wisconsin, March – July 2020 MMWR Vol 69 early release October 9, 2020 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6941e2-H.pdf> Conflicting messages and peer pressure to not wear a mask was influential to youth who became infected
4. Seidelman  J﻿, Lewis  S﻿, Advani  S﻿,  et al.  Universal masking is an effective strategy to flatten the SARS-2-CoV healthcare worker epidemiologic curve. ﻿ *Infect Control Hosp Epidemiol*. Published online June 24, 2020. doi:[10.1017/ice.2020.313](http://dx.doi.org/10.1017/ice.2020.313) Universal masking of all HCWs significantly reduced the rate of healthcare-acquisition of SARS-CoV-2
5. Chan, N et al Peripheral Oxygen Saturation in Older Persons Wearing Nonmedical Face Masks in Community Settings, JAMA Network, October 30, 2020 <https://doi.org/10.1001/jama.2020.21905> Limited study that does not support the concern that three layer cloth masks contribute to oxygen desaturation in otherwise healthy older persons
6. Van Dyke, M et al Trends in County-Level COVID-19 Incidence in Counties With and Without a Mask Mandate — Kansas, June 1–August 23, 2020 MMWR Vol. 69 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6947e2-H.pdf> “Countywide mask mandates appear to have contributed to the mitigation of COVID-19 transmission in mandated counties.”
7. Clapp, P et al. Evaluation of Cloth Masks and Modified Procedure Masks as Personal Protective Equipment for the Public During the COVID-19 Pandemic. JAMA Int Med Published online December 10, 2020 <https://doi.org/10.1001/jamainternmed.2020.8168> The comparative effectiveness of the 7 consumer-grade and 5 medical masks that were tested was essentially the same, based upon the OSHA Fitted Filtration Efficiency (FFE), a measure of how much the masks protect the wearer from airborne particles.
8. Brooks, J et al. Maximizing Fit for Cloth and Medical Procedure Masks to Improve Performance and Reduce SARS-CoV-2 Transmission and Exposure, 2021 MMWR February 19, 2021 Vol 70, No. 7 <https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7007e1-H.pdf> There are multiple simple ways to achieve better fit of masks to more effectively slow the spread of COVID-19.
9. Schumm, M et al. Filtering Facepiece Respirator (N95 Respirator) Reprocessing: A Systematic Review. JAMA March 3, 2021 <https://doi.org/10.1001/jama.2021.2531> Ultraviolet germicidal irradiation, moist heat, and microwave-generated steam processing of filtering facepiece respirators are effective means for decontamination and are simple to implement.
10. Guy GP Jr., Lee FC, Sunshine G, et al. Association of State-Issued Mask Mandates and Allowing On-Premises Restaurant Dining with County-Level COVID-19 Case and Death Growth Rates — United States, March 1–December 31, 2020. MMWR Morb Mortal Wkly Rep. ePub: 5 March 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7010e3> Reviews the correlation between mask mandates, restaurant lockdowns and distancing measures and decreased SARS-CoV-2 transmission and deaths between March and December 2020.
11. **Mental Health**
12. Czeisler, ME et al Mental Health, Substance Use, and Suicidal Ideation During the COVID-19

Pandemic — United States, June 24–30, 2020 MMWR Vol. 69, No. 32 August 14, 2020 <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6932a1-H.pdf> A fairly intuitive report about the metrics monitoring mental health during the pandemic, identifying young adults, racial/ethnic minorities, essential workers and unpaid adult caregivers as high risk populations

1. Amsalem, D et al The Coronavirus Disease 2019 (COVID-19) Outbreak and Mental Health — Current Risks and Recommended Actions [COMMENTARY] JAMA June 24, 2020 <https://www.notion.so/The-Coronavirus-Disease-2019-COVID-19-Outbreak-and-Mental-Health-Current-Risks-and-Recommended-A-eadcfab550a84b20a4cb3cc213dd1e3c> Effects on increasing consumption of digital media
2. Serafini, G et al The psychological impact of COVID-19 on the mental health in the general population QJM: An International Journal of Medicine, Volume 113, Issue 8, 30 June 2020August 2020, Pages 531–537, <https://doi.org/10.1093/qjmed/hcaa201> A General review of the psychological impacts of quarantine on the population and sources of resilience
3. Summers-Gabr, N Rural–Urban Mental Health Disparities in the United States During COVID-19 2020, Am Psych Assoc Vol. 12, No. S1, S222–S224 <http://dx.doi.org/10.1037/tra0000871S222> Addressing the urban-rural disparity in access to broadband internet as a specific social distancing risk factor
4. Shim, R Mental Health Inequities in the Context of COVID-19JAMA Netw Open.2020; 3(9):e2020104. doi:10.1001/jamanetworkopen.2020.20104 <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770142> Addresses disparities in access to mental health resources, considering internet access as a social determinant of health
5. Patrick et al Well-being of Parents and Children During the COVID-19 Pandemic: A National Survey Pediatrics (Prepublication) 2020 <https://doi.org/10.1542/peds.2020-016824> Identifies factors, most of which are intuitive, contributing to worsening measures of mental and behavioral health, with 27% of parents reporting worsening mental health and 14% reporting worsening mental health for their children in June 2020
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“Even under conditions of moderate transmission (<10 cases per 100,000 people), however, we believe that primary schools should be recognized as essential services…and that school reopening plans should be developed and financed accordingly. The safest way to open schools fully is to reduce or eliminate community transmission…Such measures along with universal mask wearing must be implemented now in the United States if we are to bring case numbers down to safe levels for elementary schools to reopen this fall nationwide.”

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Conclusions and Relevance: “Between March 9, 2020, and May 7, 2020, school closure in

the US was temporally associated with decreased COVID-19 incidence and mortality; states

that closed schools earlier, when cumulative incidence of COVID-19 was low, had the largest

relative reduction in incidence and mortality. However, it remains possible that some of the

reduction may have been related to other concurrent nonpharmaceutical interventions.”

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After describing principles of flexibility, the AAP states, “AAP strongly advocates that all policy considerations for the coming school year should start with a goal of having students physically present in school.” No scientific citations are included in the Guidance document.

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* In mid-April 2020, over 1.5 billion students, representing 91% of the global population of enrolled students from preschool through higher education, were prevented from attending school in person due to COVID-19–related school closures
* “School closures due to coronavirus have impacted at least 124,000 U.S. public and private schools and affected at least 55.1 million students” enrolled in grades K through 12.” (*EdWeek*)
* As of March 27, over 80% of public schools were providing meal services to students—almost twice the percentage that were providing any educational services. By mid-April, about 80% of school districts had teaching plans in place, and 57 to 61% of districts had organized to distribute digital devices or Internet access—but a full 94% were distributing meals to students and families.
* “But we should also remember our revealed preferences in the first two months of massive school closures: schools’ essential value is in providing care even when they cannot provide academics; it is not in providing academics in the absence of care.”

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2. Choe et al, Are We Ready for Coronavirus Disease 2019 Arriving at Schools?J Korean Med Sci. 2020 Mar 23;35(11):e127 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7086087/pdf/jkms-35-e127.pdf> Speculative report on school closures as a containment strategy in South Korea
3. Park YJ, Choe YJ, Park O, Park SY, Kim YM, Kim J, et al. Contact tracing during coronavirus disease outbreak, South Korea, 2020. Emerg Infect Dis. 2020 Oct [date cited]. <https://doi.org/10.3201/eid2610.201315> Support for school closures as a mitigation strategy.
4. Heald-Sergeant, T et al Age-related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients With Mid to Moderate Coronavirus Disease 2019 (COVID-19) JAMA Pediatrics July 30, 2020 Children under 5 years carried as much or more SARS-CoV-2 viral load as older children and adults.
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<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2769634> A survey of parents highlighting issues that will affect decisions to return children to school

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the context of COVID-19 August 21, 2020 <https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC_Masks-Children-2020.1> A thorough synopsis of the experience with masking the pediatric population around the world

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Masks, class sizes and hygiene are important, but low community spread is key.

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    Vol. 368, Issue 6496, pp. 1163 <https://doi.org/10.1126/science.abd2220> Outlines a number of concerns regarding potential synergies between influenza and SARS-CoV-2 outbreaks
13. Gandhi, M et al Masks Do More Than Protect Others During COVID-19: Reducing the Inoculum of SARS-CoV-2 to Protect the Wearer J Gen Intern Med. 2020 Jul 31 : 1–4. <https://doi.org/10.1007/s11606-020-06067-8> [Epub ahead of print] Citations for one small study and several news articles to support the theory that low dose viral exposures may result in asymptomatic infection with immunity
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*Science* 15 Dec 2020 <https://doi.org/10.1126/science.abd9338> In this analysis of COVID-19 data from 41 countries school and university closures, limited gatherings to 10 people and shutting businesses substantially cut transmission. Stay-at-home orders were less effective when these other mitigations were in place.

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5. **Testing, Screening and Diagnosis**
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7. **Johns Hopkins Serology-based Testing website** describing different types of serologic assays for COVID-19,including those approved in the U.S. and in other countries and manufacturers sensitivity and specificity data <https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html>
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10. Ulhaq, Z et al Interleukin-6 as a potential biomarker of COVID-19 progression Médecine et Maladies Infectieuses Volume 50, Issue 4, June 2020, Pages 382-38 <https://www.sciencedirect.com/science/article/pii/S0399077X20300883?via%3Dihub> Supports the Roche Diagnostics Elecsys IL-6 test EUA to identify SARS-CoV-2 positive patients at risk of severe COVID-19, a debatable clinical management tool
11. Kucirka et al. Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARSCoV-2 Tests by Time Since Exposure. Annals of Internal Medicine. May 13, 2020 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240870/> Molecular testing false-negative rate is lowest 3 days after onset of symptoms (approximately 8 days after exposure)
12. Rao et al. A Narrative Systematic Review of the Clinical Utility of Cycle Threshold Values in the Context of COVID-19. Infect Dis Ther. July 2020. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7386165/> Cycle Threshold (Ct) in a PCR assay is not an approved measure of viral burden at this time, even if it may correlate with SARS-CoV-2 RNA in the sample and have value in specific investigational settings.
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14. FDA Website listing EUA-authorized Serology Test performance, including sensitivities, specificities and PPV/NPVs <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance>
15. Pan et al Potential false-negative nucleic acid testing results for Severe Acute Respiratory Syndrome Coronavirus 2 from thermal inactivation of samples with low viral loads *Clinical Chemistry* April 4, 2020 <https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa091/5815979> Thermal inactivation of specimens at 56°C has been recommended to inactivate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) before NAT. This study suggests that thermal inactivation adversely affected the efficiency of RT-PCR for SARS-CoV-2 detection, potentially leading to increased false negative results.
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17. Wyllie, A et al Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs medRxiv April 22, 2020 (This was subsequently published in NEJM at <https://www.nejm.org/doi/pdf/10.1056/NEJMc2016359?articleTools=true>) <https://www.medrxiv.org/content/10.1101/2020.04.16.20067835v1> A study of 44 inpatients with severe COVID-19 disease, 29 with paired NP swabs and self-collected saliva specimens, suggesting that saliva was at least as effective for screening inpatients with severe disease
18. Abdalhamid, B., et al. 2020. Assessment of Specimen Pooling to Conserve SARS CoV-2 Testing Resources. American Journal of Clinical Pathology, Volume 153. <https://doi.org/10.1093/ajcp/aqaa064>
19. COVID-19 Testing Task Force website <https://testing.covid19.ca.gov/>
20. Gudbjartsson, D Humoral Immune Response to SARS-CoV-2 in Iceland NEJM Vol. 383 No. 10

<https://www.nejm.org/doi/full/10.1056/NEJMoa2026116?query=TOC> Crossectional longitudinal study of the Icelandic population showing that antiviral antibodies did not decline over the 4 months between serological testing campaigns

1. Johns Hopkins COVID-19 Molecular Testing page <https://www.centerforhealthsecurity.org/resources/COVID-19/molecular-based-tests/> A thorough treatment and clear description of EUA-approved and available molecular COVID-19 tests, including LOD (Limits of Detection) and PPA (positive percent agreement) as a proxy for sensitivity and NPA (negative percent agreement) as a proxy for specificity.
2. Sung, H et al Nationwide External Quality Assessment of SARS-CoV-2 Molecular Testing, South Korea Vol 26 No 10 October 2020 <https://wwwnc.cdc.gov/eid/article/26/10/20-2551_article> A procedure for testing the sensitivities for commercial testing is presented. This study found there to be a range of sensitivities and specificities for SARS-CoV-2 commercial testing in Korea, from acceptable (PowerCheck 2019 nCoV kit) to less so (AllPlex kit).
3. Joung, J et al Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing NEJM Letter, Sept 16, 2020 <https://doi.org/10.1056/NEJMc2026172> A one-hour CRISPR-based test that combines a the extraction and amplification steps in the assay and provides reasonably acceptable sensitivity (93.1%) and specificity (98.5%) compared to PCR molecular tests.
4. Higgins, T et al SARS-CoV-2 Nasopharyngeal Swab Testing—False-Negative Results From a Pervasive Anatomical Misconception JAMA Network September 17, 2020 <https://doi.org/10.1001/jamaoto.2020.2946> An important reminder regarding proper nasopharyngeal swab collections
5. Morley, G et al Sensitive Detection of SARS-CoV-2–Specific Antibodies in Dried Blood Spot Samples Vol. 26, No. 12, December 2020 <https://doi.org/10.3201/eid2612.203309> Opportunity for a more simple collection procedure for running a highly sensitive and specific serological test
6. Makaronidis J, Mok J, Balogun N, Magee CG, Omar RZ, Carnemolla A, et al. (2020) Seroprevalence of SARS-CoV-2 antibodies in people with an acute loss in their sense of smell and/or taste in a community-based population in London, UK: An observational cohort study. PLoS Med 17(10): e1003358. <https://doi.org/10.1371/journal.pmed.1003358> Anosmia was a more specific screening tool for COVID-19 than ageusia
7. Schwarzkopf, S et al Cellular Immunity in COVID-19 Convalescents with PCR-Confirmed Infection but with Undetectable SARS-CoV-2–Specific IgG Vol. 27, No. 1 January 2021 (On line October 2020) <https://wwwnc.cdc.gov/eid/article/27/1/20-3772_article> 78% of PCR-positive volunteers with undetectable antibodies showed T cell immunity against SARS-CoV-2
8. Larremore, D et al Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance medRxiv September 8, 2020 <https://www.medrxiv.org/content/10.1101/2020.06.22.20136309v3.full.pdf> Interesting study supporting that frequency of testing and test turnaround time is more critical than test sensitivity to effective surveillance
9. Wang, H et al Performance of Nucleic Acid Amplification Tests for Detection of Severe Acute Respiratory Syndrome Coronavirus 2 in Prospectively Pooled Specimens, EID Volume 27, Number 1, January 2021 <https://doi.org/10.3201/eid2701.203379> “tested 1,648 prospectively pooled specimens by using 3 nucleic acid amplification tests for severe acute respiratory syndrome coronavirus 2:…Positive percent agreement (PPA) of pooled versus individual testing ranged from 71.7% to 82.6% for pools of 8 and from 82.9% to 100.0% for pools of 4.”
10. Wölfel, R., Corman, V.M., Guggemos, W. et al. Virological assessment of hospitalized patients with COVID-2019. Nature 581, 465–469 (2020). <https://doi.org/10.1038/s41586-020-2196-x> Comparative viral loads and specimen sources are analyzed for SARS-CoV and SARS-CoV-2. A novel technique is used for determining replicative virus by identifying viral mRNA, used to identify persistent active infection in 0.6% of patients in a JAMA article (<https://doi/org/10.1001/jamainternmed.2020.7570>)
11. Jones A, Fialkowski V, Prinzing L, Trites J, Kelso P, Levine M. Assessment of Day-7 Postexposure Testing of Asymptomatic Contacts of COVID-19 Patients to Evaluate Early Release from Quarantine — Vermont, May–November 2020. MMWR Morb Mortal Wkly Rep 2021;70:12–13. <http://dx.doi.org/10.15585/mmwr.mm7001a3> Vermont’s policy to test asymptomatic exposed patients at 7 days and if negative to release from quarantine was successful, with no negative patients at 7 days subsequently testing positive, although there was only a small number (16%) that underwent subsequent testing after a negative test at seven days.
12. Pilarowski, G et al. Field performance and public health response using the BinaxNOWTM Rapid SARS-CoV-2 antigen detection assay during community-based testing . Clin Inf Dis. 26 December 2020 <https://doi.org/10.1093/cid/ciaa1890> Among 3,302 persons tested for SARS-CoV-2 by BinaxNOWTM and RT-PCR in a community setting, rapid assay sensitivity was 100%/98.5%/89% using RT-PCR Ct thresholds of 30, 35 and none. “We returned rapid antigen test results via secure messaging within an hour of testing. Persons with a positive rapid antigen test received a follow-up phone call within 2 hours.”
13. Bastos, M. L. et al The Sensitivity and Costs of Testing for SARS-CoV-2 Infection With Saliva Versus Nasopharyngeal Swabs: A Systematic Review and Meta-analysis. An Int Med, January 12, 2021 <https://doi.org/10.7326/M20-6569> Saliva sampling seems to be a similarly sensitive and less costly alternative that could replace nasopharyngeal swabs for collection of clinical samples for SARS-CoV-2 testing, although this study did not look at test specificity
14. Butler-Laporte, G et al Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2: A Systematic Review and Meta-analysis JAMA Intern Med. Published online January 15, 2021 <https://doi.org/10.1001/jamainternmed.2020.8876> Another study indicating that salivary PCR (NAAT) testing is comparable to nasopharyngeal swab testing sensitivity and specificity
15. Prince-Guerra, J.L. et al. Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 Infection at Two Community-Based Testing Sites — Pima County, Arizona, November 3–17, 2020 MMWR Vol 70(3) January 22, 2021 <http://dx.doi.org/10.15585/mmwr.mm7003e3> In this evaluation, using real-time RT-PCR as the standard, the sensitivity of the BinaxNOW antigen test was lower among specimens from asymptomatic persons (35.8%) than among specimens from symptomatic persons (64.2%). Specificity (99.8%–100%) was high in specimens from both asymptomatic and symptomatic groups.
16. Shuren, J and Stenzel, T. The FDA’s Experience with Covid-19 Antibody Tests N Engl J Med February 18, 2021; 384:592-594 <https://doi.org/10.1056/NEJMp2033687> A description of the steps taken to maximize available of serological tests for COVID-19, followed by the removal of a large number of poorly performing tests from the market after the market was flooded with flawed tests that did not adhere to regulations
17. **Treatment**
18. **Bamlanivimab**
19. U.S. FDA News Release, Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19 <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibody-treatment-covid-19> Studies of bamlanivimab have not yet been published in the refereed literature, but the FDA news release included the following: “While the safety and effectiveness of this investigational therapy continues to be evaluated, bamlanivimab was shown in clinical trials to reduce COVID-19-related hospitalization or emergency room visits”
20. *The Medical Letter* An EUA for Bamlanivimab—A Monoclonal Antibody for COVID-19 JAMA. Published online December 11, 2020. <https://doi.org/10.1001/jama.2020.24415> A monoclonal antibody approved for mild to moderate COVID-19. Bamlanivimab is not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. A benefit of bamlanivimab treatment has not been shown in patients hospitalized due to COVID-19.” Also, “The data supporting this EUA for bamlanivimab are based on an interim analysis from a phase two randomized, double-blind, placebo-controlled clinical trial in 465 non-hospitalized adults with mild to moderate COVID-19 symptoms.” Health Care Provider information on bamlanivimab is available at <https://www.fda.gov/media/143603/download>
21. Center for Drug Evaluation and Research (CDER) Review, Emergency Use Authorization (EUA) for bamlanivimab 700mg IV <https://www.fda.gov/media/144118/download>
22. ACTIV-3/TICO LY-CoV555 (bamlanivimab) Study Group. A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19 N Eng J Med December 22, 2020, <https://doi.org/10.1056/NEJMoa2033130> This monoclonal antibody trial demonstrated no benefit for hospitalized patients compared to placebo.
23. Chen, P et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19 N Eng J Med October 28, 2020 <https://doi.org/10.1056/NEJMoa2029849>

The BLAZE-1 trial included a primary endpoint of viral load at day 11, a benefit not achieved by the intervention, although a secondary endpoint - progression to hospitalization – did suggest modest benefit (1.6% in intervention group, 6.3% in the placebo group). In a post hoc analysis examining hospitalization among patients who were 65 years of age or older and among those with a BMI of 35 or more, the percentage who were hospitalized was 4% (4 of 95) in the LY-CoV555 group and 15% (7 of 48) in the placebo group.

1. Gottlieb, R et al. Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19: A Randomized Clinical Trial

JAMA. Published online January 21, 2021. <https://doi.org/10.1001/jama.2021.0202> Treatment with bamlanivimab and etesevimab combination therapy, but not bamlanivimab monotherapy, resulted in a reduction in SARS-CoV-2 log viral load at day 11 in patients with mild to moderate COVID-19. The comparison of the monotherapy groups against the final results for the placebo group led to changes in the effect sizes, and the loss of previously reported statistical significance for decreased viral load in the group that received 2800 mg of bamlanivimab that was reported in the Chen article (see previous report) describing early findings of the BLAZE-1 trial.

1. **Baricitinib**
2. Kalil, A.C. et al. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19. N Eng J Med December 11, 2020 <https://doi.org/10.1056/NEJMoa2031994> Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status, notably among patients receiving high-flow oxygen or noninvasive mechanical ventilation for which groups the hazard ratios were 0.4 and 0.55 respectively.
3. **Casirivimab-Imdevimab**
4. Weinreich, D et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19 N Eng J Med December 17, 2020 <https://doi.org/10.1056/NEJMoa2035002> The REGN-COV2 antibody cocktail (AKA Regeneron REGN10933 and REGN10987 AKA Casirivimab-Imdevimab monoclonal antibody to the spike protein) reduced viral load, with a greater effect in patients whose immune response had not yet been initiated.
5. FDA EUA for Casirivimab-Imdevimab, authorized November 21, 2020 <https://www.fda.gov/media/143891/download> To treat mild to moderate COVID-19 in adults and pediatric patients >12 years of age but not adults or pediatric patients who are hospitalized or who require oxygen therapy due to COVID-19
6. Baum A, Ajithdoss D, Copin R, et al. REGN-COV2 antibodies prevent and treat SARS-CoV-2 infection in rhesus macaques and hamsters. Science Nov 27;370(6520):1110-1115 <https://pubmed.ncbi.nlm.nih.gov/33037066/> Initial testing of REGN-CoV cocktail (REGN10933 and REGN10987, AKA Casirivimab-Imdevimab) in macaque monkeys and hamsters suggested a dose-related therapeutic and prophylactic impact on viral replication and lung pathology
7. **Convalescent Plasma**
8. Libster, R et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults N Eng J Med Vol. 69 December 17, 2020 <https://doi.org/10.1056/NEJMoa2033700> “Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.”
9. Simonovich, V et al. A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia N Eng J Med November 24, 2020 <https://doi.org/10.1056/NEJMoa2031304> No significant differences were observed in clinical status or overall mortality between 228 patients with severe pneumonia treated with convalescent plasma and 105 patients who received placebo.
10. **Dexamethasone**
11. Horby, PW et al *Effect of Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report* RECOVERY study <https://doi.org/10.1101/2020.06.22.20137273> 33% improvement in mortality with use of dexamethasone in ventilation assisted patients admitted to the hospital with severe COVID-19, 20% improvement in mortality for oxygen supplemented patients without invasive ventilation assistance, but no benefit for randomized admissions with COVID-19
12. **Fluvoxamine**
13. Lenze, E et al, Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19: A Randomized Clinical Trial JAMA Network November 13, 2020 <https://doi.org/10.1001/jama.2020.22760> A weakly powered study suggesting that the SSRI and σ-1 Receptor agonist Fluvoxamine may help symptomatic patients have a lower likelihood of clinical deterioration over 15 days.
14. **Hydroxychloroquine**
15. Horby, PW et al, Effe*ct of Hydroxychloroquine in Hospitalized Patients with COVID-19: Preliminary results from a 5 multi-centre, randomized, controlled trial*, RECOVERY Trial MedRxiv Preprint, June 5, 2020 <https://doi.org/10.1101/2020.07.15.20151852>

* Primary study that concluded that Hydroxychloroquine was ineffective in hospitalized patients with a Covid-19 diagnosis
* Statements of Professor Peter Horby and Professor Martin Landray on June 5, 2020 regarding the decision to cease enrolling patients into the hydroxychloroquine arm of the RECOVERY trial in the UK:

‘A total of 1542 patients were randomised to hydroxychloroquine and compared with 3132 patients randomised to usual care alone. There was no significant difference in the primary endpoint of 28-day mortality (25.7% hydroxychloroquine vs. 23.5% usual care; hazard ratio 1.11 [95% confidence interval 0.98-1.26]; p=0.10). There was also no evidence of beneficial effects on hospital stay duration or other outcomes.’

1. Boulware, D.R. A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19, NEJM June 3, 2020 DOI: 10.1056/NEJMoa2016638 <https://www.nejm.org/doi/pdf/10.1056/NEJMoa2016638?articleTools=true>

Hydroxychloroquine did not prevent illness after high-risk or moderate-risk exposure to COVID-19. Strong argument against the Risch argument (below) that Hydroxychloroquine is effective when given early in the course of COVID-19 infection

1. National Institutes of Health. NIH halts clinical trial of hydroxychloroquine: study shows treatment does no harm, but provides no benefit [news release]. 20 June 2020. Accessed at www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine on 6 July 2020.
2. Cavalcanti, AB Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19 NEJM July 23, 2020 DOI: 10.1056/NEJMoa2019014 Among patients hospitalized with mild-to-moderate Covid-19, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days
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5. Do not use chloroquine or hydroxychloroquine alone or in combination with azithromycin as a treatment of patients with COVID-19.
6. Two published studies were retracted in June 2020 (*The Lancet* retracted the paper titled Hydroxychloroquine or Chloroquine With or Without a Macrolide for Treatment of COVID-19: A Multinational Registry Analysis and The New England Journal of Medicine retracted the paper titled Cardiovascular Disease, Drug Therapy, and Mortality in COVID-19, both due to questions about the data procured from 169 hospitals around the world by Surgisphere, a data compiling company used in the studies).
7. Harvey A. Risch, *Early Outpatient Treatment of Symptomatic, High-Risk Covid-19 Patients Should be Ramped-Up Immediately as Key to the Pandemic Crisis* Oxford University Press on behalf of the Johns Hopkins Bloomberg School of Public Health. Yale epidemiologist supporting the use and further research into Hydroxychloroquine in combination with Azithromycin and Zinc in **outpatients** as prevention and or treatment prior to the first 48 hours of symptoms. Some of the data from the studies upon which he bases his conclusions have been deemed unreliable. These studies include:

* 1450 (405) symptomatic Zelenko Patients, 1045 considered low risk not treated, 405 treated with HCQ+AZ+Zinc X 5 days; COVID diagnosis made based upon clinical symptoms
* 1061 Marseilles patients, tested positive and treated for at least 3 days followed for 9 days; “good clinical outcome and virological cure were seen in 973 patients (92%), 5 died (~0.5%) and remainder in various stages of recovery”
* 42 patients in Marseilles France, Non randomized study with questionable data according to third party analysis

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2. Philippe Gautret et al, Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial, International Journal of Antimicrobial Agents, 56 (2020) 105949 https://doi.org/10.1016/j.ijantimicag.2020.105949 Only 20 cases in the series from France
3. Arnold et al, (from the Center for Emerging and Reemerging Infectious Diseases (CERID) at University of Washington Seattle) Clin Transl Sci (2020) 13, 642–645; March 27, 2020; accepted: April 6, 2020. <http://doi.org/10.1111/cts.12797> Reviews the in vitro studies and concludes “Improved HCQ PK models are needed to increase our confidence in predicting HCQ efficacy”
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N Engl J Med February 4, 2021; 384:417-427 <https://doi.org/10.1056/NEJMoa2021801> Postexposure therapy with hydroxychloroquine did not prevent SARS-CoV-2 infection or symptomatic Covid-19 in healthy persons exposed to a PCR-positive case patient

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5. Beigel, JH *Remdesivir for the Treatment of Covid-19— Preliminary Report* NEJM <https://doi/org/10.1056/NEJMoa2007764> Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection
6. WHO Solidarity trial consortium, Repurposed antiviral drugs for COVID-19 –interim WHO SOLIDARITY trial results, medRxiv preprint server, October 15, 2020 <https://doi.org/10.1101/2020.10.15.20209817> Lack of overall mortality, initiation of ventilation and duration of hospital stay benefit was demonstrated in hospitalized patients in the SOLIDARITY trial.
7. **Tocilizumab**
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10. FDA EUA Fact Sheet for Health Care Providers for the Pfizer-BioNTech vaccine <https://www.fda.gov/media/144413/download>
11. CDC COVID-19 Response Team. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States, December 14–23, 2020 MMWR January 15, 2021 Vol. 70, No. 2 <https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7002e1-H.pdf> As of December 23, 2020, a reported 1,893,360 first doses of Pfizer-BioNTech COVID-19 vaccine had been administered in the United States, and reports of 4,393 (0.2%) adverse events after receipt of Pfizer BioNTech COVID-19 vaccine had been submitted to the Vaccine Adverse Event Reporting System (VAERS). Twenty-one cases were determined to be anaphylaxis (a rate of 11.1 per million doses administered), including 17 in persons with a documented history of allergies or allergic reactions
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10. Baden, L et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine N Eng J Med December 30, 2020 <https://doi.org/10.1056/NEJMoa2035389> Summary of the Phase 3 Trial data published in NEJM
11. CDC COVID-19 Response Team. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020–January 10, 2021 MMWR Vol. 70 January 22, 2021; <https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7004e1-H.pdf> As of January 10, 2021, a reported 4,041,396 first doses of Moderna COVID-19 vaccine had been administered in the United States, and reports of 1,266 (0.03%) adverse events after receipt of Moderna COVID-19 vaccine were submitted to the Vaccine Adverse Event Reporting System (VAERS), 10 cases determined to be anaphylaxis for a rate of 2.5 cases of anaphylaxis per million Moderna COVID-19 vaccine doses
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NEJM February 17, 2021 <https://doi.org/10.1056/NEJMc2102179>

While no reduction in neutralizing effect against the B.1.1.7 variant was noted by using a pseudovirus model, there was a 2.7 fold reduction in neutralization against the B.1.351 variant and a 6.5 fold reduction in neutralization of a combination of all mutations with the Moderna mRNA-1273 vaccine.

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