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Ian T. Liu
University of Colorado Anschutz Medical Campus, Aurora, CO

Vinay Prasad
Department of Epidemiology and Biostatistics, University of California San Francisco

Jonathan D. Darrow
Harvard Medical School, Boston, MA; Bentley University, Waltham, MA; Brigham & Women's Hospital

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Evidence for Community Face Masking to Limit the Spread of SARS-CoV-2: A Critical Review

Ian T. Liu, JD, MS, MPH[†]

Vinay Prasad, MD, MPH[††]

Jonathan J. Darrow, SJD, LLM, JD, MBA[†††]

Abstract

The use of facemasks in community settings has become an accepted public policy response to decrease disease transmission during the COVID-19 pandemic. Yet evidence of facemask efficacy is based primarily on observational studies that are subject to confounding and on mechanistic studies that rely on surrogate endpoints (such as droplet dispersion) as proxies for

† University of Colorado Anschutz Medical Campus, Aurora, CO.

†† Department of Epidemiology and Biostatistics, University of California San Francisco. Dr. Prasad reports grants from Arnold Ventures, royalties from Johns Hopkins University Press and Medscape, honoraria for grand rounds/lectures from universities, medical centers, nonprofits, and professional societies, consulting fees from UnitedHealthcare, speaking fees from eviCore, and funding via Patreon for Plenary Session, a podcast.

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disease transmission. The available clinical evidence of facemask efficacy is of low quality and the best available clinical evidence has mostly failed to show efficacy, with fourteen of sixteen identified randomized controlled trials comparing face masks to no mask controls failing to find statistically significant benefit in the intent-to-treat populations. Of sixteen quantitative meta-analyses, eight were equivocal or critical as to whether evidence supports a public recommendation of masks, and the remaining eight supported a public mask intervention on limited evidence primarily on the basis of the precautionary principle. Although weak evidence should not preclude precautionary actions in the face of unprecedented events such as the COVID-19 pandemic, ethical principles require that the strength of the evidence and best estimates of amount of benefit be truthfully communicated to the public.

Keywords: facemasks, health policy, COVID-19, infectious disease, epidemiology, bioethics

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INTRODUCTION

Until April 2020, World Health Organization COVID-19 guidelines stated that "[c]loth (e.g. cotton or gauze) masks are not recommended under any circumstance."[1] These guidelines were then updated in June 2020 to state that "the widespread use of masks by healthy people in the community setting is not yet supported by high quality or direct scientific evidence."[2] In the surgical theater context, a Cochrane review found "no statistically significant difference in infection rates between the masked and unmasked group in any of the trials."[3] Another Cochrane review, of influenza-like-illness, found "low certainty evidence from nine trials (3507 participants) that wearing a mask may make little or no difference to the outcome of influenza-like illness (ILI) compared to not wearing a mask (risk ratio (RR) 0.99, 95% confidence interval (CI) 0.82 to 1.18)."[4]

These observations may come as a surprise to those in countries, such as the United States, where government leaders, news media, and even public health officials have repeatedly asserted that the widespread use of masks will help to prevent transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19. By September 2020, the U.S. federal government had distributed 600 million face masks for use by the public as part of the response to the pandemic.[5] At the local level, 32 states and numerous

1. WORLD HEALTH ORG., *Advice on the Use of Masks in the Community, During Home Care and in Health Care Settings in the Context of the Novel Coronavirus (2019-nCoV) Outbreak: Interim Guidance* (Jan. 29, 2020), https://apps.who.int/iris/handle/10665/330987 [https://perma.cc/P5LJ-SM4J].

2. WORLD HEALTH ORG., *Advice on the Use of Masks in the Context of COVID-19* (June 5, 2020), https://apps.who.int/iris/handle/10665/332293 [https://perma.cc/Y7WZ-73YD].

3. Marina Vincent & Peggy Edwards, *Disposable Surgical Face Masks for Preventing Surgical Wound Infection in Clean Surgery*, 4 COCHRANE DATABASE SYS. REV. 1, 1 (2016).

4. Tom Jefferson et al., *Physical Interventions to Interrupt or Reduce the Spread of Respiratory Viruses*, 11 COCHRANE DATABASE SYS. REV. 1, 2 (2020).

5. *White House Abandoned HHS Plan to Mail Masks to Every American in April*, KAISER HEALTH NEWS (Sept. 18, 2020), https://khn.org/morning-breakout/white-house-abandoned-hhs-plan-to-mail-masks-to-every-american-in-april/ [https://perma.cc/

municipalities implemented mask mandates,[6] and calls for a nationwide mask mandate garnered significant attention.[7] At the height of the pandemic, New York City instituted a $1000 fine for those who refuse to wear face masks in public,[8] and prominent national leaders stated that "[w]earing masks is not a political statement, it is a scientific imperative."[9] Over 40% of the global population lives in countries that mandated mask-wearing in public areas.[10] As COVID-19 persists, community masking

68CU-5TCJ] ("Documents obtained by The Washington Post and NBC News detail the Department of Health and Human Service's proposal to deliver 650 million cloth masks in April."); *id.* ("A spokesperson for the Department of Health and Human Services told NBC News that 600 million masks have been distributed."); *see also* Helen Branswell et al., *The Trump Administration Haphazardly Gave Away Millions of Covid-19 Masks — To Schools, Broadcasters, and Large Corporations*, STAT NEWS (Aug. 13, 2020), https://www.statnews.com/2020/08/13/the-trump-administration-haphazardly-gave-away-millions-of-masks-to-schools-broadcasters-and-fortune-500-companies/ [https://perma.cc/3DD2-S5QB].

6. *What U.S. States Require Masks in Public?,* #MASKS4ALL, https://masks4all.co/what-states-require-masks/ [https://perma.cc/6FWQ-DKCW] (last visited Jan. 18, 2023); *see also* AUSTIN L. WRIGHT ET AL., TRACKING MASK MANDATES DURING THE COVID-19 PANDEMIC 1 (Univ. Chi. Becker Friedman Inst. 2020).

7. Sheryl G. Stolberg, *Biden's Call for 'National Mask Mandate' Gains Traction in Public Health Circles,* N.Y. TIMES (Oct. 29, 2020), https://www.nytimes.com/2020/10/29/us/politics/trump-biden-mask-mandate.html [https://perma.cc/4S5R-XX9Y].

8. Marisa Peñaloza, *New York City Imposes Fines of Up to $1,000 for Those Who Refuse to Wear Face Masks*. NAT'L PUB. RADIO (Sept. 30, 2020), https://www.npr.org/sections/coronavirus-live-updates/2020/09/30/918704017/new-york-city-imposes-fines-of-up-to-1-000-for-those-who-refuse-to-wear-face-mas [https://perma.cc/5SC7-KMTN].

9. David Shepardson, *Biden Says He Would If Elected Mandate Masks in Interstate Transportation*, REUTERS (Oct. 23, 2020 4:24 PM), https://www.reuters.com/article/us-usa-election-biden-masks/biden-says-he-would-if-elected-mandate-masks-in-interstate-transportation-idUSKBN2782P6 [https://perma.cc/644E-KUCA].

10. *What Countries Require Masks in Public or Recommend Masks?,* #MASKS4ALL, https://masks4all.co/what-countries-require-

policies continue to be the subject of public health and public attention.

These public statements, official policies, and mask requirements have become politically divisive.[11] Non-partisan, evidence-based decision-making is essential to increasing public confidence in appropriate public health interventions. We review the evidence for aerosol transmission of SARS-CoV-2, the mechanistic evidence of how masks may interrupt transmission of respiratory infections and in particular SARS-CoV-2, and the available clinical evidence of the impact of facemask use in community settings on respiratory infection rates, including by SARS-CoV-2.

I. EVIDENCE OF AEROSOL TRANSMISSION OF SARS-COV-2

Airborne diseases can be transmitted from person to person when respiratory secretions containing infectious particles from one person come into contact with the mucosal membranes of another, such as the eyes, nose, or mouth.[12] Such secretions are emitted into the surrounding air when infected individuals cough[13]

masks-in-public/ [https://perma.cc/2LWS-WAV7] (last visited Jan. 18, 2023).

11. Shana K. Gadarian et al., *Partisanship, Health Behavior, and Policy Attitudes in the Early Stages of the COVID-19 Pandemic*, 16 PLOS ONE 1, 10 (2021).

12. Eunice Y. C. Shiu et al., *Controversy Around Airborne Versus Droplet Transmission of Respiratory Viruses: Implication for Infection Prevention*, 32 CURRENT OP. INFECTIOUS DISEASES 372, 373 (2019).

13. Jinho Lee et al., *Quantity, Size Distribution, and Characteristics of Cough-Generated Aerosol Produced by Patients with an Upper Respiratory Tract Infection,* 19 AEROSOL AIR QUALITY RSCH. 840, 840–41 (2019).

or sneeze,[14] or even during the events of daily living irrespective of health status,[15] such as breathing,[16] talking,[17] or singing.[18]

These activities result in the emission of secretions of all sizes.[19] Larger particles greater than a "critical size" behave ballistically,[20] falling to nearby surfaces within a 1-meter radius[21] (although air currents can allow particles to travel beyond this distance[22]), while smaller particles evaporate before falling to the ground.[23] There is no universally accepted threshold delineating these two categories, but by convention droplets are those particles greater than about 10 µm in diameter, while aerosols are

14. ZY Han et al., *Characterizations of Particle Size Distribution of the Droplets Exhaled by Sneeze*, 10 J. ROYAL SOC'Y INTERFACE 1, 1 (2013).

15. Lidia J. Morawska et al., *Size Distribution and Sites of Origin of Droplets Expelled from the Human Respiratory Tract During Expiratory Activities*, 40 J. AEROSOL SCI. 256, 256 (2009).

16. G.R. Johnson et al., *Modality of Human Expired Aerosol Size Distributions*, 42 J. AEROSOL SCI. 839, 843–44 (2011).

17. Valentyn Stadnytskyi et al., *The Airborne Lifetime of Small Speech Droplets and Their Potential Importance in SARS-CoV-2 Transmission,* 117 PROC. NAT'L ACAD. SCI. 11875, 11875 (2020); Sima Asadi et al., *Aerosol Emission and Superemission During Human Speech Increase with Voice Loudness*, 9 SCI. REPORTS 1, 1 (2019).

18. Malin Alsved et al., *Exhaled Respiratory Particles During Singing and Talking*, 54 AEROSOL SCI. & TECH. 1245, 1247–48 (2020).

19. Morawska et al., *supra* note 15.

20. Rajat Mittal et al., *The Flow Physics of COVID-19*, 894 J. FLUID MECHANICS F2-1, F2-1 (2020) (describing critical size); Raymond Tellier et al., *Recognition of Aerosol Transmission of Infectious Agents: A Commentary,* 19 BMC INFECTIOUS DISEASES 1, 2 (2019).

21. WORLD HEALTH ORG., *Infection Prevention and Control of Epidemic- and Pandemic-Prone Acute Respiratory Diseases in Health Care: Interim Guidance* (June 2007), http://www.who.int/csr/resources/publications/WHO_CDS_EPR_2007_6/en [https://perma.cc/AYY6-6V5W].

22. Talib Dbouk & Dimitris Drikakis, *On Coughing and Airborne Droplet Transmission to Humans*, 32 PHYSICS FLUIDS 053310-1, 053310-7 (2020).

23. Mittal et al., *supra* note 20.

those smaller than this size.[24] When smaller particles evaporate,[25] they can stay suspended in the air for long periods of time and be inhaled,[26] potentially causing infection deeper in the respiratory tract and at lower concentrations.[27] Smaller particles are preferentially generated during higher-velocity respiratory events such as coughing and sneezing, with one study finding that 99.9% of particles emitted by subjects with a cold during coughing were <5 µm in diameter,[28] and another finding that more than 97% of the droplets emitted by healthy volunteers in the study were <1 µm in diameter.[29] Exhaled particles <5 µm in diameter have been found to carry the majority of virus in exhaled human breath,[30] and patients with upper respiratory infections emitted significantly greater numbers of particles (5x10^6 compared to 1x10^6, P<0.05) while sick compared to after recovery.[31]

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24. Shiu et al., *supra* note 12, at 375; *see also* J.W. Tang et al., *Factors Involved in the Aerosol Transmission of Infection and Control of Ventilation in Healthcare Premises*, 64 J. HOSP. INFECTION MECHANICS 100, 101 (2006).

25. Lidia J. Morawska, *Droplet Fate in Indoor Environments, or Can We Prevent the Spread of Infection?*, at 9, *in* PROCEEDINGS OF INDOOR AIR 2005: THE 10TH INT'L CONFERENCE ON INDOOR AIR QUALITY AND CLIMATE (2005).

26. Chia C. Wang et al., *Airborne Transmission of Respiratory Viruses*, 373 SCI. NO. 1, 1 (2021).

27. *Id.* at 4. *See* Rachael M. Jones & Lisa M. Brosseau, *Aerosol Transmission of Infectious Disease*, 57 J. OCCUPATIONAL & ENV'T MED. 501, 501–02 (2015).

28. G. R. Johnson et al., *Modality of Human Expired Aerosol Size Distributions*, 42 J. AEROSOL SCI. 839, 844 (2011).

29. Gustavo Zayas et al., *Cough Aerosol in Healthy Participants: Fundamental Knowledge to Optimize Droplet-Spread Infectious Respiratory Disease Management,* 12 BMC PULMONARY MED. 1, 1 (2012); Shinhao Yang et al., *The Size and Concentration of Droplets Generated by Coughing in Human Subjects*, 20 J. AEROSOL SCI. 484, 484 (2007) (finding that 82% of droplet nuclei exhaled during coughing were between 0.74 – 2.12 microns in diameter).

30. Donald K. Milton et al., *Influenza Virus Aerosols in Human Exhaled Breath: Particle Size, Culturability, and Effect of Surgical Masks*, 9 PLOS PATHOGEN 1, 3 (2013).

31. Jinho Lee et al., *Quantity, Size Distribution, and Characteristics of Cough-Generated Aerosol Produced by Patients with an Upper*

The primary mode of transmission (aerosol vs. droplet) for viral respiratory infections, including SARS-CoV-2, is controversial and remains unclear.[32] If aerosol transmission plays a substantial role, the ability of masks to serve as a physical barrier to droplets becomes a less reliable surrogate of efficacy, since air expelled from the lungs necessarily penetrates the mask or flows around its edges, potentially advecting aerosols along with it.

Aerosol transmission has been demonstrated or is considered likely for SARS-CoV,[33] Middle East Respiratory Syndrome (MERS),[34] H1N1 influenza,[35] and respiratory syncytial virus,[36] and a growing body of laboratory, animal, and clinical evidence suggests SARS-CoV-2 is also spread via this mechanism.[37] One

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Respiratory Tract Infection, 19 AEROSOL AIR QUALITY RSCH. 840, 846 (2019).

32. *See* Shiu et al., *supra* note 12, at 372; Mahesh Jayaweera et al., *Transmission of COVID-19 Virus by Droplets and Aerosols: A Critical Review on the Unresolved Dichotomy*, 188 ENV'T RSCH. 1, 1 (2020); *see also* Michael Klompas et al., *Airborne Transmission of SARS-CoV-2: Theoretical Considerations and Available Evidence*, 324 J. AM. MED. ASS'N 441, 441 (2020); *see* Kevin L. Schwartz et al., *Lack of COVID-19 Transmission on an International Flight,* 192 CAN. MED. ASS'N J. E410, E410 (2020); Jan Gralton et al., *The Role of Particle Size in Aerosolised Pathogen Transmission: A Review,* 62 J. INFECTION 1, 1 (2011); Raymond Tellier, *Aerosol Transmission of Influenza A Virus: A Review of New Studies*, 6 J. ROYAL SOC'Y INTERFACE S783, S783 (2009).

33. Ignatius T. Yu et al., *Evidence of Airborne Transmission of the Severe Acute Respiratory Syndrome Virus*, 350 NEW ENG. J. MED. 1731, 1731 (2004).

34. Shenlang Xiao et al., *A Study of the Probable Transmission Routes of MERS-CoV During the First Hospital Outbreak in the Republic of Korea,* 28 INDOOR AIR 51, 51 (2018).

35. Hogna Zhang et al., *Airborne Spread and Infection of a Novel Swine-Origin Influenza A (H1N1) Virus*, 10 VIROLOGY J. 1, 1 (2013).

36. Hemant Kulkarni et al., *Evidence of Respiratory Syncytial Virus Spread by Aerosol. Time to Revisit Infection Control Strategies?* 194 AM. J. RESPIRATORY & CRITICAL CARE MED. 308, 308 (2016).

37. Elizabeth L. Anderson et al., *Consideration of the Aerosol Transmission for COVID-19 and Public Health*, 40 RISK ANALYSIS 902, 902 (2020); Song Tang et al., *Aerosol Transmission of SARS-*

study found SARS-CoV-2 aerosolizes with equal or greater efficiency than both SARS-CoV-1 and MERS-CoV,[38] and retains stability and infectivity for 16 hours in respirable-sized aerosols.[39] Another study found COVID-19 patients exhale millions of SARS-CoV-2 copies into the surrounding air every hour.[40] Even in the early stages of the illness when coughing or sneezing are uncommon, infectious SARS-CoV-2 aerosols have been found in air samples taken at the foot of patient beds in clinical settings.[41] SARS-CoV-2 viral particles have been detected in low-touch areas (e.g. under beds and on unused window ledges) consistent with sustained aerosol distribution, as well as in 58% of air samples taken from hallways outside patient rooms.[42] Evidence of transmission before patients become symptomatic suggests coughing and sneezing are not essential,[43] tending to partially undermine the importance of video evidence showing reductions

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CoV-2? Evidence, Prevention and Control, 144 ENV'T INT'L 1, 1 (2020).

38. Alyssa C. Fears et al., *Persistence of Severe Acute Respiratory Syndrome Coronavirus 2 in Aerosol Suspensions*, 26 EMERGING INFECTIOUS DISEASES INT'L 2168, 2169–70 (2020).

39. *Id.* at 2168.

40. Jianxin Ma et al., *Coronavirus Disease Patients in Earlier Stages Exhaled Millions of Acute Severe Acute Respiratory Syndrome Coronavirus 2 per Hour*, 72 CLINICAL INFECTIOUS DISEASES e652, e652 (2021).

41. Joshua L. Santarpia et al., *The Size and Culturability of Patient-Generated SARS-CoV-2 Aerosol*, J. EXPOSURE SCI. & ENV'T EPIDEMIOLOGY 705, 708 (2020).

42. Joshua L. Santarpia et al., *Aerosol and Surface Contamination of SARS-CoV-2 Observed in Quarantine and Isolation Care*, 10 SCI. REPORTS 1, 3 (2020).

43. *See* Nathan W. Furukawa et al., *Evidence Supporting Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 While Presymptomatic or Asymptomatic*, 26 EMERGING INFECTIOUS DISEASES e1, e1 (2020); Kenji Mizumoto et al., *Estimating the Asymptomatic Proportion of Coronavirus Disease 2019 (COVID-19) Cases on Board the Diamond Princess Cruise Ship, Yokohama, Japan, 2020,* 25 EUROSURVEILLANCE 1, 3–4 (2020); Daniel P. Oran et al., *Prevalence of Asymptomatic SARS-Cov-2 Infection: A Narrative Review*, 173 ANNALS INTERNAL MED. 362, 362 (2020); Seyed M. Moghadas et al., *The Implications of Silent Transmission for the Control of COVID-19 Outbreaks,* 117 PROCEEDINGS NAT'L ACAD. SCI. 17513, 17513 (2020).

in droplet dispersion when individuals cough through masks. Observational evidence of 110 SARS-CoV-2 cases in 11 clusters found transmission rates of COVID-19 that were more than 18 times higher in closed environments, where aerosols can more easily remain concentrated, than in open-air environments.[44] In one published report, an index patient often passed by the open door of the secondary patient's apartment—but never went inside.[45]

Certain "super-spreader" events also suggest that aerosols serve as an important mode of transmission for SARS-CoV-2.[46] For example, a single index patient at a restaurant in Guangzhou, China infected 4 people sitting at his own table, and 5 strangers sitting at adjacent tables up to 4.6 meters (15 feet) away with whom video evidence confirmed that no close contact was shared.[47] In a week where the Netherlands recorded only 493 cases total, one ward of a Dutch nursing home reported 34 cases (17 of 21 residents; 17 of 34 workers), despite mask-wearing requirements for healthcare workers and residents' limited mobility.[48] Researchers isolated SARS-CoV-2 RNA in living room air conditioners at the nursing home and concluded that transmission was likely due to aerosol transmission and

44. Hiroshi Nishiura et al., *Closed Environments Facilitate Secondary Transmission of Coronavirus Disease 2019 (COVID-19)*, MEDRXIV 1, 1–2 (2020).

45. Juan Wang & Guoqiang Du, *COVID-19 May Transmit Through Aerosol*, 189 IRISH J. MED. SCI. 1143, 1143 (2020).

46. *See* Lidia Morawska & Donald K. Milton, *It Is Time to Address Airborne Transmission of Coronavirus Disease 2019 (COVID-19)*, 71 CLINICAL INFECTIOUS DISEASES 2311, 2311 (2020); Harvey V. Fineberg, *Rapid Expert Consultation on the Possibility of Bioaerosol Spread of SARS-CoV-2 for the COVID-19 Pandemic* (Apr. 1, 2020), https://www.nap.edu/catalog/25769/rapid-expert-consultation-on-the-possibility-of-bioaerosol-spread-of-sars-cov-2-for-the-covid-19-pandemic-april-1-2020 [https://perma.cc/6A9Y-7QFU]; Kevin P. Fennelly, *Particle Sizes of Infectious Aerosols: Implications for Infection Control,* 8 LANCET RESPIRATORY MED. 914, 917–20 (2020).

47. Yuguo Li et al., *Probable Airborne Transmission of SARS-CoV-2 in a Poorly Ventilated Rest.*, 196 BLDG. & ENV'T 1, 2–3 (2020).

48. Peter de Man et al., *Outbreak of Coronavirus Disease 2019 (COVID-19) in a Nursing Home Associated with Aerosol Transmission as a Result of Inadequate Ventilation*, 73 CLINICAL INFECTIOUS DISEASES 170, 170–71 (2020).

recirculation of contaminated air.[49] At a choir rehearsal in Skagit Valley, Washington, a single infected individual spread SARS-CoV-2 to 53 of 59 attendees—a pattern some have concluded is suggestive of aerosol transmission.[50] Super-spreader events could also be explained by transmission via door handles or other fomites,[51] but substantially higher rates of SARS-CoV-2 positivity have been found in exhaled breath samples (26.9%) than in either indoor air samples (3.8%) or surfaces such as cell phones, floors, and computer keyboards (5.4%).[52] A non-clinical study also supported the conclusion that SARS-CoV-2 is transmitted primarily via droplets or aerosols rather than via fomites, based on SARS-CoV-2 transmission to all exposed uninfected hamsters when placed in cages 1.8 cm away from cages with infected hamsters that shared a common air supply for 8 hours.[53] Yet, only 1 of 3 uninfected hamsters contracted SARS-CoV-2 when exposed one-at-a-time for 48 hours to soiled cages (i.e., fomites).[54]

II. Mechanistic Evidence of Facemask Effectiveness

Much of the evidence supporting public mask wearing is based on the surrogate endpoint of droplet dispersion, reductions which are hypothesized to correlate with reductions in disease transmission. This intuition is based on the ability of masks—and indeed any sufficiently dense object or material—to act as a physical barrier that reduces the volume of larger respiratory secretions that are projected directly forward from the mask wearer, or the distance that those droplets travel.[55] Further, a

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49. *Id.*

50. Shelly L. Miller et al., *Transmission of SARS-CoV-2 by Inhalation of Respiratory Aerosol in the Skagit Valley Chorale Superspreading Event*, 31 Indoor Air 314, 315–16 (2021).

51. Klompas et al., *supra* note 32, at 442.

52. Ma et al., *supra* note 40, at e652–53.

53. Sin F. Sia et al., *Pathogenesis and Transmission of SARS-CoV-2 in Golden Hamsters*, 583 Nature 834, 836 (2020).

54. *Id.* at 837.

55. *See* Lucia Bandiera et al., *Face Coverings and Respiratory Tract Droplet Dispersion,* 7 Royal Soc'y Open Sci. 1, 1, 6 fig.2 (2020); *see also* Hiroshi Ueki et al., *Effectiveness of Face Masks in*

robust literature exists documenting the filtration qualities of the various fabrics used to construct face masks.[56]

Such studies examine the ability of fabric to filter particles as they pass through—rather than around—mask material. If aerosols can cause infection, however, then filtering capability is unlikely to be reliable surrogate for infection control, since exhaled air can either leak around a mask's edges or pass through it.[57] Such leakage has been shown to account for the vast majority (~5:1 ratio) of particle penetration of standardized surgical masks,[58] and exhaled air easily passes around the edges of most

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Preventing Airborne Transmission of SARS-CoV-2, 5 MSPHERE 1, 1 (2020).

56. *See e.g.,* Alex Rodriguez-Palacios et al., *Textile Masks and Surface Covers—A Spray Simulation Method and a "Universal Droplet Reduction Model" Against Respiratory Pandemics*, 7 FRONTIERS MED. 1, 1 (2020); Qing-Xia Ma et al., *Potential Utilities of Mask-Wearing and Instant Hand Hygiene for Fighting SARS-CoV-2*, 92 J. MED. VIROLOGY 1567, 1567–68 (2020); Kenneth D. Long et al., *Measurement of Filtration Efficiencies of Healthcare and Consumer Materials Using Modified Respirator Fit Tester Setup*, 15 PLOS ONE 1, 1–2 (2020); Eugenia O'Kelly et al., *Ability of Fabric Face Mask Materials to Filter Ultrafine Particles at Coughing Velocity*, 10 BMJ OPEN 1, 1 (2020); Weixing Hao et al., *Filtration Performances of Non-medical Materials as Candidates for Manufacturing Facemasks and Respirators*, 229 INT'L J. HYGIENE & ENV'T HEALTH 1, 1–2 (2020); Masayoshi Furuhashi, *A Study on the Microbial Filtration Efficiency of Surgical Face Masks—With Special Reference to the Non-woven Fabric Mask,* 25 BULL. TOKYO MED. & DENTAL U. 7, 7 (1978); Saraswati Anindita Rizki & Andree Kurniawan, *Efficacy of Cloth Face Mask in Reducing COVID-19 Transmission: A Literature Rev.*, 1 KESMAS NAT'L PUB. HEALTH J. 43, 44 (2020); Onur Aydin et al., *Performance of Fabrics for Home-Made Masks Against the Spread of COVID-19 Through Droplets: A Quantitative Mechanistic Study*, 40 EXTREME MECH.'S LETTERS 1, 1 (2020).

57. Klompas et al., *supra* note 32. Julian W. Tang et al., *A Schlieren Optical Study of the Human Cough with & Without Wearing Masks for Aerosol Infection Control*, 6 J. ROYAL SOC'Y INTERFACE S727, S732 (2009); Siddhartha Verma et al., *Visualizing the Effectiveness of Face Masks in Obstructing Respiratory Jets*, 32 PHYSICS FLUIDS 061708-1, 061708-2 (2020).

58. Sergey A. Grinshpun et al., *Performance of an N95 Filtering Facepiece Particulate Respirator and a Surgical Mask During Human Breathing: Two Pathways for Particle Penetration,* 6 J. OCCUPATIONAL & ENV'T HYGIENE 593, 593 (2009).

cloth masks.[59] One study of cloth masks simulated leakage and found that a hole equal to ~1% of the mask area decreased mask efficiency by over 60%.[60] Even in professional settings with high-grade, non-cloth masks, a poor fit can allow air to leak.[61] Double-masking reduces, but does not eliminate, such leakage.[62] In a study of N95 respirators, 25% (158 of 643) professional healthcare workers failed to properly fit their mask, despite knowing they were being studied and receiving instructions on how to achieve a proper respirator fit.[63] Unlike respirators, which protect their wearers from airborne particles, surgical masks are intended to

59. *See* Patricia M. Holton et al., *Particle Size-Dependent Leakage and Losses of Aerosols in Respirators*, 48 AM. INDUS. HYGIENE ASS'N J. 848, 848–52, 854 (1987); Ignazio M. Viola et al., *Face Coverings, Aerosol Dispersion and Mitigation of Virus Transmission Risk*, 2 IEEE OPEN J. ENG. MED. & BIOLOGY 26, 30 (2021); Marianne Van der Sande et al., *Professional & Home-Made Face Masks Reduce Exposure to Respiratory Infections Among the General Population*, 3 PLOS ONE 1, 2, 4 (2008); Anna Davies et al., *Testing the Efficacy of Homemade Masks: Would They Protect in an Influenza Pandemic?,* 7 DISASTER MED. & PUB. HEALTH PREPAREDNESS 413, 417 (2013); Eugenia O'Kelly et al., *Comparing the Fit of N95, KN95, Surgical, and Cloth Face Masks and Assessing the Accuracy of Fit Checking*, 16 PLOS ONE 1, 2 (2021).

60. Abhiteja Konda et al., *Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks,* 14 ACS NANO 6339, 6344 (2020).

61. *See* Klaus Willeke et al., New Methods for Quantitative Respirator Fit Testing with Aerosols, 42 AM. INDUS. HYGIENE ASS'N 121, 121 (1981); Angela Weber et al., *Aerosol Penetration and Leakage Characteristics of Masks Used in the Health Care Industry*, 21 AM. J. INFECTION CONTROL 167, 172 (1993) (noting that better-performing respirators can increase breathing resistance, increasing the likelihood that particles could be pulled into the mask through face-seal leaks).

62. Emily E. Sickbert-Bennett et al., *Fitted Filtration Efficiency of Double Masking During the COVID-19 Pandemic,* 181 J. AM. MED. ASS'N INTERNAL MED. 1126, 1126 (2021); Venugopal Arumuru et al., *Double Masking Protection vs. Comfort—A Quantitative Assessment,* 33 PHYSICS FLUIDS 077120, 077120-2 (2021).

63. Quinn Danyluk et al., *Health Care Workers and Respiratory Protection: Is the User Seal Check a Surrogate for Respirator Fit-Testing?,* 8 J. OCCUPATIONAL & ENV'T HYGIENE 267, 268 (2011).

protect those other than the wearer, and have a much looser fit. Cloth masks may be looser still, followed by homemade masks.[64]

Laboratory evidence supports the ability of masks to serve a source-control function. Multiple studies have demonstrated that masks can reduce the number of bacterial colonies that grow on Petri dishes placed in front of subjects who are directed to cough with or without a mask,[65] and one study using reverse-transcription polymerase chain reaction to detect viral particles on such dishes found similar results.[66] In a study of surgical masks against influenza virus, viral RNA was detected in 78% (29 of 37 subjects) of exhaled human breath samples collected from subjects wearing masks, versus 95% (35 of 37 subjects) of those without masks.[67]

Many studies evaluating as-worn face mask efficacy use mannequin heads and compare the number of particles collected inside the mannequin's mask to outside it. Under these conditions, cloth masks have been shown to have highly variable filtration qualities. Cotton mask filtration efficiencies have been

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64. *See* Marianne Van der Sande et al., *Professional and Home-Made Face Masks Reduce Exposure to Respiratory Infections Among the General Population*, 3 PLOS ONE 1, 4 (2008); *see also* Catherine M. Clase et al., *Forgotten Technology in the COVID-19 Pandemic: Filtration Properties of Cloth and Cloth Masks—A Narrative Review*, 95 MAYO CLINIC PROC. 2204, 2215 (2020).

65. *See* Anna Davies et al., *Testing the Efficacy of Homemade Masks: Would They Protect in an Influenza Pandemic?,* 7 DISASTER MED. & PUB. HEALTH PREPAREDNESS 413 (2013); Brewster C. Doust & Arthur B. Lyon, *Face Masks in Infections of the Respiratory Tract*, 71 J. AM. MED. ASS'N 1216 (1918); C. G. Paine, *The Aetiology of Puerperal Infection*, 1 BRIT. MED. J. 243 (1935); R. A. Shooter et al., A Study of Surgical Masks, 47 BRIT. J. SURGERY 246 (1959); V. W. Greene & D. Vesley, *Method for Evaluating Effectiveness of Surgical Masks*, 83 J. BACTERIOLOGY 663 (1962); Louis B. Quesnel, *The Efficiency of Surgical Masks of Varying Design and Composition*, 62 BRIT J. SURGERY 936 (1975); *see also* Charles F. McKhann et al., *Hospital Infections: A Survey of the Problem*, 55 AM. J. INFECTIOUS DISEASES CHILDREN 579 (1938).

66. D. F. Johnson et al., *A Quantitative Assessment of the Efficacy of Surgical and N95 Masks to Filter Influenza Virus in Patients with Acute Influenza Infection,* 49 CLINICAL INFECTIOUS DISEASES 275 (2009).

67. Donald K. Milton et al., *Influenza Virus Aerosols in Human Exhaled Breath: Particle Size, Culturability, and Effect of Surgical Masks*, 9 PLOS PATHOGEN 1, 2 (2013).

measured at between 15–40% when worn on mannequin heads and placed immediately next to an aerosol generator, and this variation in efficiency depends largely on the material used as an insert filter.[68] In an experiment in which 2 mannequins configured to simulate tidal breathing faced each other in a test chamber at greater distances of 25 cm to 100 cm (<10 inches to 3.4 feet), researchers found that placing a cloth mask on the source mannequin blocked more than 50% of virus transmission (P<0.05).[69]

In one study in which cloth masks were placed on mannequins during simulated speaking or coughing, high-speed imaging showed that less than 0.1% of large droplets (>30 µm) escaped.[70] Another mannequin study found similar results, with masks blocking between 50–98% of 5 micron particles but only 0–55% of 0.5 micron particles when breathing outwards.[71] In that study, cloth masks sewn to CDC specifications offered ~18% inward and 0% outward filtration efficacy at the 0.5 micron size, with inward/outward efficiencies improving as particle size increased.[72]

Surgical masks on mannequin heads tend to outperform cloth masks but still demonstrate variable results. One mannequin study found that between 5%–20% of respiratory secretions were captured by standard surgical masks during simulated tidal breathing due to face mask leakage, while better-fitting surgical masks ("SecureFit Ultra") captured ~50% of outward-moving particles.[73] Another study calculated the leakage of inward-moving particles from surgical masks and found that leakage rates

68. W. C. Hill et al., *Testing of Commercial Masks and Respirators and Cotton Mask Insert Materials Using SARS-CoV-2 Virion-Sized Particulates: Comparison of Ideal Aerosol Filtration Efficiency Versus Fitted Filtration Efficiency,* 20 NANO LETTERS 7642, 7645 (2020).

69. Hiroshi Ueki et al., *Effectiveness of Face Masks in Preventing Airborne Transmission of SARS-CoV-2,* 5 MSPHERE 1, 3 (2020).

70. Lucia Bandiera et al., *Face Coverings and Respiratory Tract Droplet Dispersion,* 7 ROYAL SOC'Y OPEN SCI. 1, 6 (2020).

71. Jin Pan et al., *Inward and Outward Effectiveness of Cloth Masks, a Surgical Mask, and a Face Shield*, 55 AEROSOL SCI. & TECH. 718, 728 fig.7 (2021).

72. *Id.*

73. Rajeev B. Patel et al., *Respiratory Source Control Using a Surgical Mask: An In Vitro Study*, 13 J. OCCUPATIONAL & ENV'T HYGIENE 569, 575 fig.6 (2016).

were inversely related to particle size, decreasing from ~78% at 0.3 micron size to ~5% at the 10 micron size.[74] Other fitted filtration studies have reported similar findings.[75] Fewer mannequin studies have been conducted to evaluate the effects of surgical masks on actual viral particles. In one study, researchers aerosolized influenza virus in 0.5 seconds 70 cm in front of a mannequin, collected samples in one minute, and compared the amount of recovered virus from inside and outside the mask.[76] Researchers reported an average 83% reduction in viral particles with a range of 9–98% against particles between 1–200 microns in size, though the study's applicability to long-term mask use in real-life situations is unclear and researchers did not test either cloth masks or surgical masks with ear loops.[77]

Two mechanistic source control studies evaluated the impact of surgical masks against actual SARS-CoV-2 particles. In one study, 7 COVID-19 positive patients were asked to cough five times onto a Petri dish placed 20 cm in front of their mouths—researchers reported that, compared to coughing without a mask, surgical masks were associated with reduced viral load in three cases, increased viral load in two cases, and in two cases they did not detect virus in either sample.[78] In another, surgical masks

74. Gholamhossein Bagheri et al., *Face-Masks Save Us from SARS-CoV-2 Transmission*, ARXIV 5 (2021).

75. *See* Phillip Clapp et al., *Evaluation of Cloth Masks and Modified Procedure Masks as Personal Protective Equipment for the Public During the COVID-19 Pandemic*, 181 J. AM. MED. ASS'N INTERNAL MED. 463, 463 (2020); William G. Lindsley et al., *Efficacy of Face Masks, Neck Gaiters and Face Shields for Reducing the Expulsion of Simulated Cough-Generated Aerosols*, 55 AEROSOL SCI. & TECH. 449, 449 (2021); Amy V. Mueller et al., *Quantitative Method for Comparative Assessment of Particle Removal Efficiency of Fabric Masks as Alternatives to Standard Surgical Masks for PPE*, 3 MATTER 950, 950 (2020); John T. Brooks et al., *Maximizing Fit for Cloth and Medical Procedure Masks to Improve Performance and Reduce SARS-CoV-2 Transmission and Exposure*, 70 MORBIDITY & MORTALITY WKLY. REP. 254, 254 (2021).

76. C. Makison Booth et al., *Effectiveness of Surgical Masks Against Influenza Bioaerosols*, 84 J. HOSP. INFECTION 22, 23 (2013).

77. *Id.* at 25.

78. Min-Chul Kim et al., *Effectiveness of Surgical, KF94, and N95 Respirator Masks in Blocking SARS-CoV-2: A Controlled Comparison in 7 Patients*, 52 INFECTIOUS DISEASES 908, 910 (2020).

eliminated detectable coronavirus particles in both respiratory droplets and aerosols after infected subjects breathed into an air collection device for 30 minutes, but most (60%) respiratory samples of unmasked individuals also failed to contain detectable virions.[79]

Nonetheless, even partial filtration could be beneficial by reducing viral concentration, which may reduce the chance of transmission and the severity of disease.[80] The infective dose for SARS-CoV-2 is not known, but some commentators have speculated a number of between 100 and 700 virions.[81]

III. Clinical and Observational Evidence in the COVID-19 Setting

Laboratory evidence is suggestive, but only high-quality clinical evidence can definitively establish the impact of mask wearing under real-world conditions. Unfortunately, only two randomized controlled trials (RCT) have evaluated the efficacy of community face masking against the spread of COVID-19.

One study of 4862 participants in Denmark ("DANMASK") who reported being outside the home for more than 3 hours per day found no statistically significant difference between a group receiving a recommendation to wear a surgical mask when outside the home and the control group (1.8% (n=42) of the masked intervention group became infected vs. 2.1% (n=53) of the control group).[82] Among other limitations, this study relied on self-

79. Nancy H. Leung et al., *Respiratory Virus Shedding in Exhaled Breath and Efficacy of Face Masks*, 26 NATURE MED. 676, 679 tbl.1b (2020).

80. Monica Gandhi et al., *Masks Do More Than Protect Others During COVID-19: Reducing the Inoculum of SARS-Cov-2 to Protect the Wearer*, 35 GEN. INTERNAL MED. 3063, 3063 (2020).

81. Sedighe Karimzadeh et al., *Review of Infective Dose, Routes of Transmission, and Outcome of COVID-19 Caused by the SARS-CoV-2 Virus: Comparison with Other Respiratory Viruses*, 149 EPIDEMIOLOGY & INFECTION 1, 6 (2021).

82. Henning Bundgaard et al., *Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers: A Randomized Controlled Trial*, 174 ANNALS INTERNAL MED. 335, 335 (2021).

reported adherence,[83] was not designed to test the efficacy of masks as source control,[84] and did not consider whether COVID-19 positive participants were infected in the home.[85]

A second, high-quality, cluster-randomized study of more than 342,000 adults spread across 600 villages in rural Bangladesh found that placement in the study's intervention group increased mask-wearing by 28.8% (from 13.3 to 42.3%),[86] with participants in control villages (n=13,893) reporting a 1% higher rate of symptoms of COVID-like illness than participants in intervention villages (n=13,273) (8.6% v. 7.6%; P=0.000).[87] Similar relative rate differences were noted for the study's primary outcome, symptomatic seroprevalence (positive blood test plus COVID-19 symptoms), with control and intervention prevalence rates of 0.80% and 0.71%, respectively (P=0.043).[88] Researchers also reported results by mask type, finding that surgical masks reduced symptomatic seroprevalence rates by 0.09% compared to controls (0.67% vs. 0.76%, P=0.043), but that cloth masks did not offer a statistically significant rate reduction (cloth mask: 0.74%, control: 0.76%, P=0.540).[89] A secondary endpoint of

83. Christine Laine et al., *The Role of Masks in Mitigating the SARS-CoV-2 Pandemic: Another Piece of the Puzzle*, 174 ANNALS INTERNAL MED. 419, 419 (2021).

84. Vinay Prasad, *Here's How to Think About the Danish Mask Study*, MEDPAGE TODAY (Nov. 18, 2020), https://www.medpagetoday.com/blogs/vinay-prasad/89778 [https://perma.cc/8GK5-RWRA].

85. *See Comments on DANMASK-19 Study*, ANNALS INTERNAL MED., https://www.acpjournals.org/doi/10.7326/M20-6817 [https://perma.cc/C73T-8T68] (last visited Sep. 5, 2021); Thomas R. Frieden & Shama Cash-Goldwasser, *Of Masks and Methods*, 174 ANNALS INTERNAL MED. 421, 421 (2021); Henning Bundgaard et al., *Face Masks for the Prevention of COVID-19-Rationale and Design of the Randomised Controlled Trial DANMASK-19*, 67 DANISH MED. J. 1, 7 (2020).

86. Jason Abaluck et al., *The Impact of Community Masking on COVID-19: A Cluster-Randomized Trial in Bangladesh* 7 (Working Paper, Aug. 31, 2021), https://www.poverty-action.org/sites/default/files/publications/Mask_Second_Stage_Paper_20211108.pdf.pdf [https://perma.cc/WBN7-CAHF].

87. *Id.* at 9.

88. *Id.* at 9, 10.

89. *Id.* at 10.

symptoms without serologic confirmation favored face masking generally,[90] but this endpoint is highly susceptible to bias, and the difference in the cloth mask subgroup, although borderline statistically significant, was less than 1% (cloth mask group: 7.9% v. 8.6%, p=0.048). Communities assigned to masking may report symptoms differently, and the more rigorous endpoint of laboratory-confirmed prior SARS-CoV-2 infection found no benefit.

The Bangladesh cluster RCT is applicable to the unique circumstances of the region. Natural immunity at the outset of the study was very low due to low case numbers, vaccination was largely absent, and children and schools were not included. Unfortunately, this trial is limited in its ability to inform regions with higher rates of natural immunity, higher rates of vaccination, or differing school policies.[91]

The remainder of the available clinical evidence is primarily limited to non-randomized observational data, which are subject to confounding variables. Several studies of so-called "natural experiments"[92] found suggestive results of mask effectiveness by comparing case rates in locations implementing mask mandates with those that did not. A widely-cited U.S. study by Lyu et al. of state-wide executive orders requiring masks during the early months of the COVID-19 pandemic found reductions in the average daily county-level growth rate of between 0.9 and 2.0 percentage points during each of a series of 5-day periods beginning 1 day after signing the mask order (days 1–5, 6–10, 11–15, 16–20, and 21+).[93] Yet, declines began sooner than the mean 5.8-day incubation period would suggest could be plausibly

90. *Id.* at 17.

91. A large RCT (n= ~40,000) in Guinea-Bissau on community cloth face mask use against COVID-19 is ongoing. *See Locally Produced Cloth Face Mask and COVID-19 Like Illness Prevention*, U.S. Nat'l Library of Med., https://clinicaltrials.gov/ct2/show/NCT04471766 [https://perma.cc/S8RT-DYGX] (last visited Nov. 16, 2020).

92. Mark Petticrew et al., *Natural Experiments: An Underused Tool for Public Health?*, 119 Pub. Health 751, 752 (2005).

93. Wei Lyu & George L. Wehby, *Community Use of Face Masks and COVID-19: Evidence from a Natural Experiment of State Mandates in the US*, 39 Health Aff. 1419, 1422 (2020).

connected to mask usage,[94] and researchers did not attempt to measure actual mask usage or the impact of mask mandates on mobility. The researchers' estimates that state mandates prevented up to 450,000 cases (and, assuming a 1% case fatality rate, 4,500 deaths) by May 22, 2020 were repeated in news media despite the researchers' statement that their estimates "should be viewed cautiously."[95] However, a widely-cited, non-peer-reviewed analysis from Goldman Sachs based in part on mask mandate data from the Lyu et al. study concluded a national mask mandate could reduce the daily growth rate in infections in states without a mandate from 2.9% to 1%.[96]

Another study of data from 24 counties (23%) in Kansas that abided by the governor's mask mandate (or adopted their own) and 81 counties (77%) that opted out of the mandate found a decline in incidence from 17 to 16 per 100,000 in the former and an increase from 6 to 12 per 100,000 in the latter.[97] However, the choice of opting in or out of the mask mandate suggests different attitudes toward COVID-19 that may have affected other behavioral choices, and six cities in non-mask mandated counties also had mask ordinances in place at the time.[98] In at least 13 (54%) of the 24 mandated counties, mask mandates occurred alongside other mandated or recommended county-level mitigation strategies (e.g., gathering size limitations).[99] Notably, both sets of counties experienced large increases in case rates in the month following the publication of this study.[100]

94. Conor McAloon et al., *Incubation Period of COVID-19: A Rapid Systematic Review and Meta-Analysis of Observational Research*, 10 BMJ OPEN 1, 6 fig.3 (2020).

95. Lyu & Wehby, *supra* note 93, at 1423.

96. J. Hatzius et al., *Face Masks and GDP*, GOLDMAN SACHS (June 29, 2020), https://www.goldmansachs.com/insights/pages/face-masks-and-gdp.html [https://perma.cc/KA99-Z8RJ].

97. Miriam E. Van Dyke et al., *Trends in County-Level COVID-19 Incidence in Counties With and Without a Mask Mandate—Kansas, June 1–August 23, 2020*, 69 MORBIDITY & MORTALITY WKLY. REP. 1777, 1779 tbl. (2020).

98. *Id.*

99. *Id.* at 1778.

100. @youyanggu, Twitter (Dec. 12, 2020), https://twitter.com/youyanggu/status/1339306972189843456. ("A CDC paper last month found that Kansas counties with mask mandates saw a decrease in cases in Aug, while counties without mandates saw an

Other natural experiment studies have similarly taken advantage of differential timing of mask mandates or other interventions to determine the effects of mask wearing on COVID-19 infection rates, generally finding that mask mandates substantially reduced the growth rate of infections and deaths.[101] Although some of these studies attempt to control for behavioral changes by using, e.g., Google mobility data, those data may not capture key aspects of mobility changes, such as selective reductions in mobility by those individuals exhibiting symptoms (e.g., due to increased social stigma of coughing or knowledge that one will face a temperature screening), greater physical distancing within retail establishments or other locations,[102] or the

increase. Since then, both groups saw a huge surge. Counties w/mandates are doing a bit better, but it's difficult to determine causation.").

101. *See, e.g.*, Victor Chernozhukov et al., *Causal Impact of Masks, Policies, Behavior on Early Covid-19 Pandemic in the U.S*, 220 J. ECONOMETRICS 23, 24 (2021); Alexander Karaivanov et al., *Face Masks, Public Policies and Slowing the Spread of Covid-19: Evidence from Canada*, 78 J. HEALTH ECON. 1, 1 (2021); Timo Mitze et al., *Face Masks Considerably Reduce COVID-19 Cases in Germany: A Synthetic Control Method Approach*, 117 PROC. NAT'L ACAD. SCI. 32293, 32293 (2020); M. S. Gallaway et al., *Trends in COVID-19 Incidence After Implementation of Mitigation Measures – Arizona, January 22-August 7, 2020*, 69 MORBIDITY & MORTALITY WKLY. REP. 1460, 1462 (2020); Vincent C. Cheng et al., *The Role of Community-Wide Wearing of Face Mask for Control of Coronavirus Disease 2019 (COVID-19) Epidemic Due to SARS-CoV-2*, 81 J. INFECTION 107, 109 (2020); Xiaowen Wang, et al., *Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers*, 324 J. AM. MED. ASS'N 703, 704 (2020); Heesoo Joo et al., *Decline in COVID-19 Hospitalization Growth Rates Associated with Statewide Mask Mandates — 10 States, March–October 2020*, 70 MORBIDITY & MORTALITY WKLY. REP. 212, 216 (2021); Gery P. Guy 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,* 70 MORBIDITY & MORTALITY WKLY. REP. 350, 350 (2021); Dhaval Adjodah et al., *Association Between COVID-19 Outcomes and Mask Mandates, Adherence, and Attitudes*, 16 PLOS ONE 1, 1–2 (2021).

102. Gyula Seres et al., *Face Mask Use and Physical Distancing Before and After Mandatory Masking: Evidence from Public Waiting Lines* (No. SP II 2020-305), WZB DISCUSSION PAPER 1, 1–3 (2020).

availability of curbside or no-contact pickup. These studies also cannot easily control for non-mobility related measures that may correlate with mask mandates, such as reductions in verbal communication when masks are worn, increased use of sanitary wipes, installation of clear plastic barriers, customer capacity limitations, or adjustments to equipment settings that improve indoor ventilation or air filtration. In cases where mask mandates occurred alongside other public health interventions, such as school or business closure or shelter-in-place restrictions, disambiguating the effects of one component is challenging. Most studies readily admit to limitations such as these.

Country comparisons suffer from similar potential confounding. A multivariate analysis of 196 countries found that only four country-level characteristics correlated in a statistically significant manner with coronavirus mortality rates: duration since first COVID-19 case (coefficient: 0.1782, $P<0.001$), percentage of population over age 60 (coefficient: 0.0691, $P<0.001$), obesity prevalence (coefficient: 0.0196, $P=0.02$), and time since first mask recommendation (coefficient: -0.1266, $P<0.001$).[103] However, the authors concede that "[s]urveys and observational data of mask-wearing by the public [were] unavailable for most countries" and that the simultaneous adoption of health policies can make it "difficult to tease out the relative importance of each."[104]

Another study compared the mask-wearing rate of people in multiple countries from March to April 2020 with coronavirus fatalities and concluded that the mask non-wearing rate in mid-March explained up to 69% of the variation in COVID-related deaths by mid-May.[105] The study's authors also noted that cultural differences may explain much of the differences in infection rates; in Japan, for example, most people do not talk on public transit which may reduce exhaled aerosols[106] and there is evidence to suggest that mask-wearing in Japan also correlates

103. Christopher T. Leffler et al., *Association of Country-Wide Coronavirus Mortality with Demographics, Testing, Lockdowns, and Public Wearing of Masks,* 103 AM. J. TROPICAL MED. & HYGIENE 1, 30 tbl.5 (2020).

104. *Id.* at 31, 33.

105. Daisuke Miyazawa & Gen Kaneko, *Face Mask Wearing Rate Predicts Country's COVID-19 Death Rates*, MEDRXIV 1, 1 (2020).

106. *Id.* at 7.

with other positive hygiene practices, such as hand washing and vaccination.[107]

Several observational studies have attempted to correlate mask-wearing with COVID-19 infection rates in contexts other than state- or country-wide government mask mandates, but suffer from similar potential confounding.[108] For example, studies examining the transmission of SARS-CoV-2 on airplanes have suggested lower rates of secondary cases on flights with masking compared to those without it,[109] but it is unclear whether differences in other factors such as passenger spacing, flight duration, passenger follow-up efforts, cough intensity of infected patients, or pre- or post-flight infection rates played a role. Flight conditions are also atypical in terms of passenger density, air filtration, the presence of pressurized cooling vents, and severely restricted mobility, limiting the ability to generalize any findings to the community context. Of 382 sailors on board the aircraft carrier USS Theodore Roosevelt who volunteered to complete a questionnaire (27% of the 1417 total sailors on board), those self-reporting "face covering" had a lower rate of SARS-CoV-2 infection than those who did not (55.8% vs. 80.8%), but other self-reported behaviors also correlated in a statistically significant manner with lower infection rates, including avoidance of common areas (53.8% vs. 67.5%) and increased distancing from others (54.7% vs. 70.0%).[110] A large U.S. cohort study (n=198,077) found similar results, with individuals who responded via Smartphone app to surveys as "always" wearing facemasks outside the home 62% less likely to report COVID-19 infection, although the study could not exclude the possibility

107. Koji Wada et al., *Wearing Face Masks in Public During the Influenza Season May Reflect Other Positive Hygiene Practices in Japan*, 12 BMC PUB. HEALTH 1, 3 (2012).

108. Chris Kenyon, *Widespread Use of Face Masks in Public May Slow the Spread of SARS CoV-2: An Ecological Study.* MEDRXIV 1, 3 (2020).

109. David O. Freedman & Annelies Wilder-Smith, *In-Flight Transmission of SARS-CoV-2: A Review of the Attack Rates and Available Data on the Efficacy of Face Masks*, 27 J. TRAVEL MED. 1, 6 (2020).

110. Daniel C. Payne et al., S*ARS-CoV-2 Infections and Serologic Responses from a Sample of U.S. Navy Service Members – USS Theodore Roosevelt, April 2020*, 69 MORBIDITY & MORTALITY WKLY. REP. 714, 714 (2020).

that those "always" reporting mask wearing also engaged in other personal risk reduction measures.[111] Similar studies (one in the U.S. and two international) also found correlations between positive responses to mask survey questions and reduced infection rates, and those studies also had similar limitations.[112] A study in Hong Kong found 11 clusters of COVID-19 were related to mask-off settings (i.e. eating, karaoke, religious activities, etc.) while only 3 were related to mask-on (3 clusters) settings (i.e. workplace).[113] However, such mask-off activities may be inherently more risky than the mask-on workplace considered in the study, such as by involving larger numbers of people within a given unit of area, longer durations of contact, or greater face-to-face communication.

Without randomization, natural experiments and other observational evidence provide only weak evidence of effectiveness.[114] Even when they reveal meaningfully different infection rates, the groups being compared may not possess similar characteristics, preventing causal inference. For example, geographic comparisons do not account for the possibility that, in locations where legislators have sufficient political support to enact mask mandates, populations are likely to have different attitudes about COVID-19 that could affect behavior other than

111. Sohee Kwon et al., *Association of Social Distancing and Face Mask Use with Risk of COVID-19*, 12 NATURE COMMC'NS 1, 5 (2021).

112. *See, e.g.*, Benjamin Rader et al., *Mask-Wearing and Control of SARS-CoV-2 Transmission in the USA: A Cross-Sectional Study*, 3 LANCET DIGITAL HEALTH E148, E154 (2021); Gavin Leech et al., *Mass Mask-Wearing Notably Reduces COVID-19 Transmission,* MEDRXIV 1, 6 (2021); Ashwin Aravindakshan et al., *The Impact of Mask-Wearing in Mitigating the Spread of COVID-19 During the Early Phases of the Pandemic,* MEDRVIX 1, 12 (2021).

113. Vincent C. Cheng et al., *The Role of Community-Wide Wearing of Face Mask for Control of Coronavirus Disease 2019 (COVID-19) Epidemic Due to SARS-CoV-2*, 81 J. INFECTION 107, 109 (2020).

114. EUR. CTR. FOR DISEASE PREVENTION & CONTROL, *Using Face Masks in the Community: First Update* (Feb. 15, 2021), https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-face-masks-community-first-update.pdf [https://perma.cc/SD5Q-7PPK].

mask- wearing.[115] Four natural experiment studies measured mask usage rates, but each was based on self-reported surveys which are prone to bias and may not reflect actual behavior. One study, for example, found that while only 12% of individuals surveyed admitted to not wearing a mask, 90% were observed not wearing one, a finding the authors described as a "large and statistically significant discrepancy."[116] Lower case rates following mask mandates could be mediated by differential propensities to respond to new information with, for example, increased hand hygiene, voluntary business restrictions, physical distancing, or reduced time away from home or participation in certain activities. It is possible that mask mandates reduce infection rates by prompting media coverage or statements of public health officials that increase public awareness, or reducing the willingness of individuals to enter public spaces where masks are required rather than reducing transmission when they enter those spaces.[117]

Although some studies attempted to control for potentially confounding variables, it is unlikely that researchers were able to account for all of them or know which were most important, such as simultaneous public health interventions, the publication of new COVID- related research investigations, changes in the capacity to contact trace, the availability and use of more-rapid or less-expensive diagnostics, or attendance at large-scale public gatherings related to social causes, political rallies, or sporting events. Some studies used self-reporting to measure health behaviors (such as social distancing and mask wearing), but mask mandates could increase social pressure to report or overestimate adherence.

115. William F. Maloney & Temel Taskin, *Determinants of Social Distancing and Economic Activity During COVID-19: A Global View*, World Bank Pol'y Rsch. Working Paper 1, 3 (2020).

116. Aleksandra Jakubowski et al., *Self-Reported vs Directly Observed Face Mask Use in Kenya*, 4 J. Am. Med. Ass'n Network Open 1, 3 (2021).

117. *See* Daniel J. McGrail et al., *Enacting National Social Distancing Policies Corresponds with Dramatic Reduction in COVID19 Infection Rates*, 15 PLOS One 1 (2020); *see* Laura Matrajt & Tiffany Leung, *Evaluating the Effectiveness of Social Distancing Interventions to Delay or Flatten the Epidemic Curve of Coronavirus Disease*, 26 Emerging Infectious Diseases 1740 (2020).

Several retrospective cohort studies have attempted to analyze behaviors among people who were either diagnosed with COVID-19 or had known SARS-CoV-2-positive contacts. One such study of 124 families found that family members reported wearing a mask "all the time" after illness onset more frequently in the 83 families without secondary cases than in the 41 families with such secondary cases (45.8% vs. 19.5%, P=.02).[118] However, members of families without secondary cases also more frequently ate separately after illness onset (65.1% vs. 39.0%, P=.008), more frequently self-isolated after illness onset (69.9% vs. 51.2%, P=.05), more frequently self-isolated within 2 days of illness onset (31.3% vs. 14.6%, P=.05), more frequently had more than 1 hour of ventilation (opening of windows) per day (76.5% vs. 57.5%, P=.02), and less frequently had incidents of "close contact" (within 1 meter) with the primary case (8.7% vs. 30.0%, P<0.001),[119] suggesting that many other behavioral factors could be relevant. A retrospective case-control study (n=1050) in Thailand found similar results and had similar limitations.[120] Interviews were conducted one to three months after index patient contact, possibly exacerbating recall bias and sample size selection issues.[121]

Several case reports support the use of masks. A report by the Centers for Disease Control and Prevention described 2 Missouri hair stylists who wore masks while symptomatic with COVID-19 and saw 139 clients, none of whom became ill.[122] However, exposure to the index patient was short (median: 15 minutes), clients faced away, and variables such as hand hygiene,

118. Yu Wang et al., *Reduction of Secondary Transmission of SARS-CoV-2 in Households by Face Mask Use, Disinfection and Social Distancing: A Cohort Study in Beijing, China*, 5 BMJ GLOBAL HEALTH 1, 5 tbl.1 (2020).

119. *Id.* at tbl.2.

120. Pawinee Doung-Ngern et al., *Case-Control Study of Use of Personal Protective Measures and Risk for SARS-CoV 2 Infection, Thailand*, 26 EMERGING INFECTIOUS DISEASES 2607, 2614 (2020).

121. *Id.* at 2609.

122. M. J. Hendrix et al., *Absence of Apparent Transmission of SARS-CoV-2 from Two Stylists After Exposure at a Hair Salon with a Universal Face Covering Policy – Springfield, Missouri, May 2020*, 69 MORBIDITY & MORTALITY WKLY. REP. 930, 930 (2020).

extent of conversation, common surfaces available for touching, disinfection of those surfaces, shared locations where masks were doffed and donned, etc., were not evaluated. The report also suffered from diagnostic limitations: only 67 (48%) clients received PCR tests with the remainder reporting no symptoms, testing was offered on day 5 potentially leading to false negatives due to COVID-19's incubation period, and clients exposed during highest viral shedding time (2-3 days before symptoms appear; number of clients not reported) were not included. These limitations in the absence of prospective design, randomization, and control make causal inference challenging.

IV. Clinical Evidence from Illness Other Than COVID-19

In addition to the two RCTs in the COVID-19 setting, at least 14 RCTs have assessed the relationship between mask-wearing and other respiratory infections (**Table 1**). Five of these took place in communal living settings, eight in household settings, and one in a hospital.

A. Communal Living RCTs

Four of the 5 RCTs examining the effectiveness of mask-wearing in communal settings failed to find statistically significant results. A 3-arm cluster-randomized study of rates of influenza-like illnesses (ILI) among 1178 students in University of Michigan residence halls failed to find a benefit from wearing face masks alone compared to an unmasked control group (11.7% (46/392) vs. 13.8% (51/370); adjusted cumulative rate ratio [RR]: 1.10),[123] but found that masks plus hand hygiene did provide benefit (8.9% (31/349) vs. 13.8% (51/370); RR: 0.78),[124] consistent with findings in an earlier similar cluster-randomized study by the same researchers.[125] A 3-arm study of 995 Hajj pilgrims randomized into health education (n=292, 29%), health

123. Allison E. Aiello et al., *Facemasks, Hand Hygiene, and Influenza Among Young Adults: A Randomized Intervention Trial*, 7 PLOS One 1, 6 tbl.3 (2012).

124. *Id.* at tbl.4.

125. Allison E. Aiello et al., *Mask Use, Hand Hygiene, and Seasonal Influenza-Like Illness Among Young Adults: A Randomized Intervention Trial*, 201 J. Infectious Diseases 491, 491 (2010).

education plus face mask (n=257, 26%), and control (n=446, 45%) groups reported adherence rates of 52% and 81% in its intervention arms, respectively, but found no association between face mask wearing compliance and the chance of developing an acute respiratory infection in 225 individuals within one week of returning (OR: 0.97).[126] In a pilot study of 164 Hajj pilgrims, 53% (28/53) no-mask contacts sleeping immediately adjacent to patients with known ILIs became symptomatic, while only 31% (11/36) of masked contacts did so (P=.04).[127] However, a much larger (n=7687) randomized controlled follow-up study by the same research group not only failed to show a statistically significant benefit for mask wearing, but the per- protocol analysis showed higher point estimates for mask wearers compared to non-mask wearers for both clinical respiratory infections (12% (97/828) vs. 9% (141/1497); odds ratio [OR]: 1.3) and laboratory-confirmed respiratory infections (50% (46/93) vs. 41% (50/122); OR: 1.2).[128] While a subsequent meta-analysis of 13 mostly cohort and cross-sectional studies looking at face mask use among Hajj pilgrims reported a statistically significant decrease in respiratory infections (RR: 0.89; P<.01), it cautioned that facemask effectiveness was still "inconclusive due to great heterogeneity in study [design]" and included only two RCTs in its analysis.[129]

B. Household RCTs

All of the eight RCTs examining the impact of face masks in household settings failed to find statistically significant results in intention-to-treat analyses, with one reporting a significant decrease in a sub-group, per-protocol analysis. Most of these

126. Ebtihal Z. Alabdeen et al., *Effect of Use of Face Mask on Hajj-Related Respiratory Infection Among Hajjis from Riyadh–A Health Promotion Intervention Study,* 12 SAUDI EPIDEMIOLOGY BULL. 27, 27–28 (2005).

127. Osamah Barasheed et al., *Pilot Randomised Controlled Trial to Test Effectiveness of Facemasks in Preventing Influenza-like Illness Transmission Among Australian Hajj Pilgrims in 2011,* 14 INFECTIOUS DISORDERS DRUG TARGETS 110, 113 tbl.1 (2014).

128. Mohammad Alfelali et al., *Facemask Against Viral Respiratory Infections Among Hajj Pilgrims: A Challenging Cluster-Randomized Trial,* 15 PLOS ONE 1, 11 tbl.4 (2020).

129. Osamah Barasheed et al., *Uptake and Effectiveness of Facemask Against Respiratory Infections at Mass Gatherings: A Systemic Review,* 47 INT'L J. INFECTIOUS DISEASES 105, 109 (2016).

studies recruited patients shortly after diagnosis with an ILI, randomized them into a treatment category, and then traced the number of household contacts who then become ill. The studies varied in whether or not the intervention group required mask-wearing for the index patient (source control), other household members, or both groups.

Two RCTs looked at the utility of facemasks as source-control measures to prevent secondary infection in household settings and neither study reported protective effects. One of these took place in France, and found that when index cases wore surgical face masks for the five days following diagnosis, there was no statistically significant difference in transmission compared to households in which index cases did not wear a mask (16.2% (24/148) vs. 15.8% (25/158)).[130] A nearly identical study in China that randomized 245 ILI index cases to mask (n=123) and no mask (n=122) groups—while only requiring mask-wearing until symptom abatement—found no statistically significant effects on intra-household rates of clinical respiratory illness (0.19% (4/2098) vs. 0.29% (6/2036)) or ILI (0.05% (1/2098) vs. 0.15% (3/2036)).[131]

One household RCT conducted in Australia attempted to determine the protective effect of masks for the wearer. The study, involving 245 adults in 145 families in which the index case was a child diagnosed with an ILI and in which parents were randomized to wear a surgical, P2 (an N95 equivalent), or no mask, showed no significant differences in secondary ILI infection rates at the individual level (surgical mask: 19/94 (20%); P2 mask: 14/92 (15%)) compared to the control group (16/100 (16%)).[132] A pre-planned per-protocol analysis found a statistically significant decrease (P=.015) in infection rates among adherent mask users (RR: 0.26),[133] but adherence was low

130. Laetitia Canini et al., *Surgical Mask to Prevent Influenza Transmission in Households: A Cluster of Randomized Trial,* 5 PLOS ONE 1, 5 (2010).

131. Chandini R. MacIntyre et al., *Cluster Randomised Controlled Trial to Examine Medical Mask Use as Source Control for People with Respiratory Illness,* 6 BMJ OPEN 1, 5 tbl.2 (2016).

132. Chandini R. MacIntyre et al., *Face Mask Use and Control of Respiratory Virus Transmission in Households,* 15 EMERGING INFECTIOUS DISEASES 233, 238 tbl.4 (2009).

133. *Id.* at 237.

(38% (36/94) of surgical and 46% (42/92) of P2 mask users reported wearing masks "most or all" of the time on the intervention's first day),[134] and adherent participants may have been more likely to engage in other protective behaviors.

Five RCTs evaluated the effects of mask wearing by all household members on secondary infection rates, with mixed results. A Thai study followed child influenza cases in 442 households with 1147 household members, randomized families into hand -washing (n=292), hand-washing plus face masks (n=291), and control arms (n=302), and reported higher secondary ILI rates based on self-reported symptoms of 17% (50/292) in the hand-washing arm and 18% (51/291) in the hand-washing plus mask arm—compared to only 9% (26/302) in the control arm, and there were no significant differences in the primary outcome measure of laboratory-confirmed secondary influenza.[135]

A pilot study of 198 Hong Kong households found no statistically significant benefit on intra-household secondary influenza infection rates when all household contacts wore masks (5.9%, 12/205) or were educated and given hand hygiene materials (6.6%, 4/61), compared to controls (6.0%, 5/84).[136] A larger, follow-up study by the same group also found no statistically significant benefit for PCR-confirmed secondary influenza infections when all household contacts wore masks and practiced hand hygiene ("M+HH"; 7.0%, 18/258) compared to hand hygiene alone ("HH"; 5.4%, 14/257), or a control arm with neither intervention (10.0%, 28/279; 3-group P value: 0.22).[137]

134. *Id.* at 236.

135. James M. Simmerman et al., *Findings From a Household Randomized Controlled Trial of Hand Washing and Face Masks to Reduce Influenza Transmission in Bangkok, Thailand,* 5 INFLUENZA & OTHER RESPIRATORY VIRUSES 256, 263 tbl.2 (2011).

136. Benjamin J. Cowling et al., *Preliminary Findings of a Randomized Trial of Non-Pharmaceutical Interventions to Prevent Influenza Transmission in Households,* 3 PLOS ONE 1, 7 tbl.2 (2008).

137. Benjamin J. Cowling et al., *Facemasks and Hand Hygiene to Prevent Influenza Transmission in Households: A Cluster Randomized Trial,* 151 ANNALS INTERNAL MED. 437, 442 tbl.3 (2009).

These results were consistent when using two additional clinical definitions of flu (3-group P-values of 0.40 and 0.28).[138]

In a pre-planned, sub-group analysis of households that implemented interventions within 36 hours of symptom onset, 3-group P values reported statistically significant differences under two of three illness criteria, although the M+HH group still underperformed the HH-alone group in most cases (PCR-confirmed: HH 5.4% (7/130), M+HH 4.0% (6/149); Clinical Definition 1: HH 10.8% (14/130), M+HH 18.1% (27/149); Clinical Definition 2: HH 3.1% (4/130), M+HH 4.7% (7/149)).[139] A German study implementing a similar protocol reported protective benefits of masks in its per-protocol analysis, but not its intention-to-treat analysis, finding that compared to the unmasked group, the face mask-only group had a 70% reduced chance (OR: 0.3, P=.04) of secondary infection in household contacts (n=218) against RT-PCR-confirmed influenza, but not influenza-like illness (OR: 0.5, P=.3).[140] A 19-month study of 617 New York City households that randomized families into three cohorts—hand sanitizer ("HS", n=205), HS plus face mask ("HS + mask", n=201), and an educational control group (n=211)—and followed them for 19 months while tracking respiratory infection rates found that the HS + mask group (OR: 0.82; 95% CI 0.70-0.97) outperformed the HS alone group (OR: 1.01; 95% CI 0.85-1.21), compared to the reference educational group.[141]

C. Healthcare Settings

RCT evidence of face mask efficacy in healthcare settings is limited. One small RCT (n=32) of healthcare workers at a Japanese hospital found no statistically significant difference between mean number of days of cold symptoms reported by surgical face mask wearers (mean=16.1 days) and non-wearers

138. *Id.*

139. *Id.*

140. Thorsten Suess et al., *The Role of Facemasks and Hand Hygiene in the Prevention of Influenza Transmission in Households: Results from a Cluster Randomised Trial; Berlin, Germany, 2009-2011,* 12 BMC INFECTIOUS DISEASES 1, 10 tbl.5 (2012).

141. Elaine L. Larson et al., *Impact of Non-Pharmaceutical Interventions on URIs and Influenza in Crowded, Urban Households,* 125 PUB. HEALTH. REP. 178, 186 tbl.5 (2010).

(mean=14.3 days; P=.81) during the winter season.[142] And although surgical masks are ubiquitously worn during surgery because they are believed to prevent infection,[143] multiple studies have reported that the use of surgical masks as source control in operating theaters has not proven to reduce surgical site infection—with a Cochrane meta-analysis reporting mask v. no-mask infection rates of 1.8% (13/706) vs. 1.4% (10/723; P>.05),[144] 0% (0/10) vs. 30% (3/10; P>.05),[145] and 10.5% (33/313) vs. 9.1% (31/340; P>.05)[146] from studies conducted in its literature review.[147]

D. Comparing Types of Masks

At least ten studies evaluate the clinical efficacy of different types of masks, but without a no-mask control group most provide little insight into mask efficacy as a whole. Four RCTs, four meta-analyses, and one prospective cohort study found surgical masks were non-inferior to N95s for protection against respiratory infections,[148] and one found evidence that N95s

142. Joshua L. Jacobs et al., *Use of Surgical Face Masks to Reduce Incidence of the Common Cold Among Health Care Workers in Japan: A Randomized Controlled Trial,* 37 AM. J. INFECTION CONTROL 417, 419 tbl.3 (2009).

143. *See, e.g.,* Neil W. Orr, *Is a Mask Necessary in the Operating Theatre?,* 63 ANNALS ROYAL COLL. SURGEONS ENG. 390 (1981); N.J. Mitchell & S. Hunt, *Surgical Face Masks in Modern Operating Rooms– A Costly and Unnecessary Ritual?*, 18 J. HOSP. INFECTION 239 (1991); M.G. Romney, *Surgical Face Masks in the Operating Theatre: Re-examining the Evidence,* 47 J. HOSP. INFECTION 251 (2001).

144. Th. G. Tunevall, *Postoperative Wound Infections and Surgical Face Masks: A Controlled Study,* 15 WORLD J. SURGERY 383 (1991).

145. Marina Vincent & Peggy Edwards, *Disposable Surgical Face Masks for Preventing Surgical Wound Infection in Clean Surgery,* 4 COCHRANE DATABASE SYS. REV. 1, 8 (2016).

146. *Id.*

147. *Id.*

148. *See* Mark Loeb et al., *Surgical Mask vs N95 Respirator for Preventing Influenza Among Health Care Workers: A Randomized Trial,* 302 AMA 1865, 1870 (2009); Chandini R. MacIntyre et al., *A Randomized Clinical Trial of Three Options for N95 Respirators and Medical Masks in Health Workers,* 187 AM. J. RESPIRATORY & CRITICAL CARE MED. 960, 963 (2013) (finding that surgical mask use was not inferior to targeted N95 use); Lewis J. Radonovich et

provide greater protection than medical masks against self-reported clinical respiratory illness but not ILI.[149] However, a recent review found that evidence that N95s protect healthcare workers from clinical respiratory infections at all is "low-quality."[150] One meta-analysis of particular note, an April 2020 preprint of a Cochrane review of clinical evidence for both surgical and N95 masks, "did not find any differences in the clinical effectiveness of either type of mask in the setting of respiratory

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al., *N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel: A Randomized Clinical Trial,* 322 J. AM. MED. ASS'N 824, 830 (2019); Youlin Long et al., *Effectiveness of N95 Respirators Versus Surgical Masks Against Influenza: A Systematic Review and Meta-Analysis,* 13 J. EVID. BASED MED. 93, 98 (2020); Jessica J. Bartoszko et al., *Medical Masks v. N95 Respirators for Preventing COVID-19 in Healthcare Workers: A Systematic Review and Meta-Analysis of Randomized Trials,* 14 INFLUENZA & OTHER RESPIRATORY VIRUSES 365, 368 (2020); Tom Jefferson et al., *Physical Interventions to Interrupt or Reduce the Spread of Respiratory Viruses* (Review), 11 COCHRANE DATABASE SYS. REV. 1, 6, 7 (2020); Jeffrey D. Smith et al., *Effectiveness of N95 Respirators Versus Surgical Masks in Protecting Health Care Workers from Acute Respiratory Infection: A Systematic Review and Meta-Analysis*, 188 CAN. MED. ASS'N J. 567, 572 (2016); Sabine Haller et al., *Use of Respirator vs. Surgical Masks in Healthcare Personnel and Its Impact on SARS-CoV-2 Acquisition – A Prospective Multicentre Cohort Study*, MEDRXIV 1 (2021), https://www.medrxiv.org/content/10.1101/2021.05.30.21258080v1 [https://perma.cc/8852-RJM7]; Katarzyna Barycka et al., *Comparative Effectiveness of N95 Respirators and Surgical/Face Masks in Preventing Airborne Infections in the Era of SARS-CoV2 Pandemic: A Meta-Analysis of Randomized Trials*, NAT'L LIBRARY MED. (Dec. 15, 2020), https://pubmed.ncbi.nlm.nih.gov/33320847/ [https://perma.cc/Y72H-YBAM].

149. Vittoria Offeddu et al., *Effectiveness of Masks and Respirators Against Respiratory Infections in Healthcare Workers: A Systematic Review and Meta-Analysis*, 65 CLINICAL INFECTIOUS DISEASES 1934, 1938 (2017).

150. Primiano Iannone et al., *The Need of Health Policy Perspective to Protect Healthcare Workers During COVID-19 Pandemic. A GRADE Rapid Review on the N95 Respirators Effectiveness*, NAT'L LIBRARY MED. (2020), https://pubmed.ncbi.nlm.nih.gov/33320847/ [https://perma.cc/733Q-GCFG].

viral infection transmission to healthcare workers,"[151] although the review's final November version omitted this language.[152]

One RCT compared continually worn cloth masks with surgical masks in the healthcare setting, finding cloth masks were associated with ILI infection rates 13-times higher (13/569 or 2.28% for cloth masks; 1/580 or 0.17% for surgical masks) than surgical masks (RR=13.00).[153] The study has been criticized because it provided new surgical masks more frequently than cloth masks and lacked washing protocols for cloth masks,[154] but may provide insight into the effectiveness of community masking where washing protocols are similarly absent and reuse is frequent. A post-hoc, sub-group analysis of this data concluded that the difference in infection rates were largely explained by washing protocols—participants who hand-washed their cloth masks (77%) as opposed to using the hospital laundry (13%) reported infection rates more than twice as high (OR: 2.04) as the hospital laundry group.[155] A mask-comparison study of 1441 Chinese healthcare workers failed to find a statistically significant benefit to either N95 (Clinical Respiratory Illness [CRI]: 3.9%, P=.085; Influenza-like Illness [ILI]: 0.3%, P=.068; Lab- confirmed virus [LCV]: 1.4%, P=.02; Influenza [flu]: 0.3%, P=.051) or surgical face masks (CRI: 6.7%, P=.52; ILI: 0.6%, P=.33; LCV: 2.6%, P=.67; Flu: 1.0%, P=.73), compared to a convenience no-mask group (CRI: ~8.7%; ILI: ~1.7%; LCV: ~3.1%; Flu: ~1.3%)

151. Tom Jefferson et al., *Physical Interventions to Interrupt or Reduce the Spread of Respiratory Viruses. Part 1 – Face Masks, Eye Protection and Person Distancing: Systematic Review and Meta-Analysis*, MEDRXIV1 (2020), https://www.medrxiv.org/content/10.1101/2020.03.30.20047217v2 [https://perma.cc/8KAJ-9DJM].

152. Jefferson et al., *supra* note 148, at 27.

153. Chandini R. MacIntyre et al., *A Cluster Randomised Trial of Cloth Masks Compared with Medical Masks in Healthcare Workers*, 5 BMJ OPEN 1, 6 (2015).

154. Jeremy Howard et al., *Face Masks Against COVID-19: An Evidence Review*, 118 PROCEEDINGS NAT'L ACAD. SCI. 1, 7 (2021); Chandini R. MacIntyre et al., *Community Universal Face Mask Use During the COVID 19 Pandemic—From Households to Travellers and Public Spaces*, 27 J. TRAVEL MED. 1, 2 (2020).

155. Chandini R. MacIntyre et al., *Contamination and Washing of Cloth Masks and Risk of Infection Among Hospital Health Workers in Vietnam: A Post Hoc Analysis of a Randomised Controlled Trial*, 10 BMJ OPEN 1, 4 (2020).

using four different disease outcomes (except for greater protections from N95s as compared to no masks with lab-confirmed viruses), but all point estimates favored mask-wearing.[156] The no-mask comparison group was a non-randomized convenience group composed of individuals from nine different hospitals, limiting the ability to draw reliable conclusions.

E. Observational Studies of SARS-CoV-1 and Pandemic Influenza

Fourteen non-randomized observational studies conducted during the 2003 SARS-CoV-1 ("SARS") and 2009 H1NI epidemics provide mixed correlational evidence for the efficacy of face masks against the spread of viral infections, but suffer from various types of potential bias and other limitations. Three SARS case-control studies and one H1NI cross-sectional survey were undertaken outside the healthcare setting. One case-control study of patients in Beijing found that just 27% (26/94) of probable cases "always" wore a mask when going outside, compared to 43% (121/281) of uninfected controls (RR 0.3),[157] but controls were identified by sequential digit dialing to achieve "neighborhood matching," a method that may be likely to identify individuals who leave the home less frequently. Similarly, a case-control study of probable SARS-positive patients in Hong Kong found that cases wore masks less frequently than controls (27.9% (92/330) vs. 58.7% (387/660)), but identified controls through random digit dialing. In addition, cases in the Hong Kong study were less likely than controls to report disinfecting living quarters thoroughly (46.6% (154/330) vs. 74.5% (492/660)) and washing hands >11 times a day (18.4% (61/330) vs. 33.7% (223/660)), suggesting possible confounding.[158] A survey of 7,448 Korean school-aged children during the H1N1 pandemic found that, of

156. Chandini R. MacIntyre et al., *A Cluster Randomized Clinical Trial Comparing Fit-Tested and Non-Fit-Tested N95 Respirators to Medical Masks to Prevent Respiratory Virus Infection in Health Care Workers: RCT of Face Masks in Health Workers*, 5 INFLUENZA & OTHER RESPIRATORY VIRUSES 170, 176 (2011).

157. Jiang Wu et al., *Risk Factors for SARS Among Persons Without Known Contact with SARS Patients, Beijing, China*, 10 EMERGING INFECTIOUS DISEASES 210, 213 (2004).

158. Joseph T. Lau et al., *SARS Transmission, Risk Factors, and Prevention in Hong Kong*, 10 EMERGING INFECTIOUS DISEASES 587, 590 (2004).

466 respondents reporting "continuous" mask use, only 3% (14) were diagnosed with H1N1, compared to 5.8% (164/2819) of irregular users and 5.7% (239/4164) of non-users (P=.04), but the authors cautioned that the cross-sectional design precluded confirmation of a causal relationship.[159] A study in Vietnam (n=65) during the SARS-CoV-1 outbreak found that 7 of 154 (or 1 in 22) unmasked people who had known contact with a SARS-positive index case contracted SARS, compared to none (of 9) people who reported wearing a mask,[160] but a 1 in 22 chance yields a 72% probability that, of a sample of 7 non-mask-wearing individuals, none would contract the disease.

Due primarily to ease of recruitment and outbreak patterns, the 10 remaining studies recruited SARS and H1N1-positive workers in healthcare settings. Six case-control studies were conducted during the SARS-CoV-1 epidemic. A study of 758 healthcare workers caring for patients with SARS at a hospital in Guangzhou, China found that those reporting that they wore 2 multi-layer cotton masks were diagnosed with SARS 10.9% (59/541) of the time compared to 27.6% (32/116) for those reporting wearing 1 multi-layer mask (P<0.001),[161] but there was no unmasked comparison group and the researchers concluded that they "did not find that wearing double layers of . . . multilayered cotton masks . . . [was] associated with being protected from SARS."[162] A univariate analysis of 477 Beijing hospital workers found that 5.5% (15/274) of those reporting that they wore 16-layer cotton surgical masks also had SARS compared to 17.7% (36/203) for those not reporting wearing this type of mask (P<0.001), but the same study failed to show efficacy for 12-layer cotton surgical masks (6.5% (8/123) vs. 12.1% (43/354), P=.07), N95 masks (6.1% (2/33) vs. 11.0%

159. Choon O. Kim et al., *Is Abdominal Obesity Associated with the 2009 Influenza a (H1N1) Pandemic in Korean School-Aged Children?,* Nat'l Library Med. (Dec. 8, 2011), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779813/ [https://perma.cc/5J63-UHXH].

160. P. A. Tuan et al., *SARS Transmission in Vietnam Outside of the Health-Care Setting,* 135 Epidemiology & Infection 392, 397 (2007).

161. Wei-Qing Chen et al., *Which Preventive Measures Might Protect Health Care Workers from SARS*?, 9 BMC Pub. Health 1, 5 (2009).

162. *Id.* at 7.

(49/444), P=.37), or disposable masks (11.6% (11/95) vs. 10.5% (40/382)).[163] A case-control study of 29 SARS-positive cases and 98 non-SARS controls at a hospital in Hanoi, Vietnam reported that cases wore masks less frequently than controls (32% (8/25) vs. 38.9% (35/90); P=.01).[164] Yet, the authors cautioned that recall bias is particularly relevant where an exposure (mask usage) has a strong intuitive causal link with outcome, also noting that the results were likely less accurate than would be obtained in a blinded or matched case-control study.[165] A case-control study of 13 SARS-infected and 241 non-infected staff members at various Hong Kong hospitals found that cases wore masks much less often than controls (15% (2/13) vs. 70% (169/241); P=.0001).[166] In a study of 320 subjects hospitals in Hanoi, Vietnam, a multivariate logistic regression analysis of 85 (27%) of those subjects found a 12.6-fold protective effect associated with continuous mask-wearing compared to no mask wearing (aOR: 12.6, P<.01), but it is unclear how the 85 subjects were selected and whether the selection process created a risk of bias, and interviews were conducted 7 or more months after the beginning of the SARS epidemic, creating a risk of reporting bias.[167]

Four observational studies of healthcare workers were conducted during the H1N1 influenza pandemic. A case-control study at a hospital in Hong Kong found that in the 4 cases neither the index patients nor the exposed persons wore a mask (or could not recall whether they wore a mask), while among controls approximately two-thirds of index patients wore masks (0% (0/4)

163. Wei Liu et al., *Risk Factors for SARS Infection Among Hospital Healthcare Workers in Beijing: A Case Control Study*, 14 TROPICAL MED. & INT'L HEALTH 52, 55 (2009) (raw numbers back-calculated from Table 2 data).

164. Hiroshi Nishiura et al., *Rapid Awareness and Transmission of Severe Acute Respiratory Syndrome in Hanoi French Hospital, Vietnam*, 73 AM. J. TROPICAL MED. & HYGIENE 17, 20 (2005).

165. *Id.* at 22.

166. W. H. Seto et al., *Effectiveness of Precautions Against Droplets and Contact in Prevention of Nosocomial Transmission of Severe Acute Respiratory Syndrome (SARS),* 361 LANCET 1519, 1520 (2003).

167. Ayako Nishiyama et al., *Risk Factors for SARS Infection Within Hospitals in Hanoi, Vietnam*, 61 JAPANESE J. INFECTIOUS DISEASES 388, 389 (2008).

vs. 63.9% (532/832), P=.01).[168] Similarly, a case-control study at a hospital in Kobe, Japan found that 96% (79/82) of controls "always" wore masks but only 80% (4/5) of cases, a difference that was not statistically significant.[169] A case-control study of healthcare workers in Beijing during the H1N1 pandemic did not show a benefit associated with continuous mask-wearing: 71.6% (146/204) of controls wore masks most of their working time vs. 72.5% (37/51) of cases.[170]

A Cochrane meta-analysis of 7 of the above case-control studies conducted during the SARS-CoV-1 epidemic found that 39.4% (268/681) of cases reported mask wearing compared to 62.0% (1573/2535) of controls.[171] The authors concluded that "simple mask-wearing was highly effective (OR 0.32)," but also cautioned that 6 of the 7 studies had a medium or high risk of bias, and these 6 studies provided over 96% of the total number of cases and controls in the meta- analysis.[172] A more recent meta-analysis of 8 studies from the H1N1 influenza pandemic concluded that, overall, "facemask use was not significantly protective," and also cautioned that most studies included in the analysis had a moderate to high risk of bias.[173] Specific biases mentioned in these meta-analyses included, among others, selection bias, reporting bias, publication bias, and ascertainment bias, as well as concerns over non-specific definitions of what constituted "exposure,"

168. Vincent C. Cheng et al., *Prevention of Nosocomial Transmission of Swine-Origin Pandemic Influenza Virus A/H1N1 by Infection Control Bundle,* 74 J. HOSP. INFECTION 271 (2010).

169. Takao Toyokawa et al., *Seroprevalence of Antibodies to Pandemic (H1N1) 2009 Influenza Virus Among Health Care Workers in Two General Hospitals After First Outbreak in Kobe, Japan*, 63 J. INFECTION 281, 286 tbl.5 (2011).

170. Yi Zhang et al., *Associated with the Transmission of Pandemic (H1N1) 2009 Among Hospital Healthcare Workers in Beijing, China,* 7 INFLUENZA & OTHER RESPIRATORY VIRUSES 466, 469 (2013).

171. Tom Jefferson et al., *Interventions for the Interruption or Reduction of the Spread of Respiratory Viruses*, 7 COCHRANE DATABASE SYS. REV. 1, 108 (2011) (Analysis 1.3).

172. *Id.* at 11.

173. Patrick Saunders-Hastings et al., *Effectiveness of Personal Protective Measures in Reducing Pandemic Influenza Transmission: A Systematic Review and Meta-Analysis*, 20 EPIDEMICS 1, 6 (2017).

potential confounding of unmeasured protective (or harmful) behaviors, and lack of an adequate description of controls. Additionally, the infection dynamics of SARS-COV-1 and pandemic influenza differ from SARS-CoV-2, limiting the extent of insight these studies can provide. Ten of the 14 available studies evaluated exposures only in high-risk healthcare settings, which may differ from community interactions in duration, proximity, and frequency. Considered in view of available RCT evidence, such weaknesses place observational mask data in a skeptical light.

V. META-ANALYSIS

We identified 32 systematic reviews and meta-analyses evaluating the effects of community face masking against respiratory viral transmission. Of 16 quantitative meta-analyses (**Table 2**), 8 were critical or equivocal as to whether existing evidence was sufficient to support a public recommendation of masks, and the remaining 8 supported a public mask intervention on the basis of existing evidence primarily due to the precautionary principle—i.e., based on the assumption that masks might help and are unlikely to harm—and on the basis of observational or other indirect evidence. Of the 15 solely qualitative reviews identified by the authors, seven concluded that evidence for the use of community masking was weak,[174]

174. *See* Roger Chou et al., *Masks for Prevention of Respiratory Virus Infections, Including SARS-CoV-2, in Health Care and Community Settings: A Living Rapid Review*, 173 ANNALS INTERNAL MED. 542, 553 (2020) ("[T]he evidence on mask use and risk for SARS-CoV-2 infection is very sparse."); Monica Taminato et al., *Homemade Cloth Face Masks as a Barrier Against Respiratory Droplets–Systematic Review*, 33 ACTA PAULISTA ENFERMAGEM 1, 8 (2020) ("[A]ny face mask, regardless of filtering efficiency . . . will have a marginal impact if not used in connection to other measures, such as . . . social distancing . . . and regular hand hygiene."); Samir Benkouiten et al., *Non-pharmaceutical Interventions for the Prevention of Respiratory Tract Infections During Hajj Pilgrimage*, 12 TRAVEL MED. & INFECTIOUS DISEASE 429, 437 (2014) (characterizing the results of face mask studies in preventing respiratory illnesses as "contradictory"); Ali Mostafaei et al., *Can Wearing a Face Mask Protect from COVID-19? A Systematic Review*, 14 IRANIAN J. MED. MICROBIOLOGY 101, 104 (2020) (describing the level of evidence that facemasks alone provide protection against respiratory infection as "low to moderate"); Faisal bin-Reza et al., *The Use of Masks and Respirators to Prevent*

seven cautiously concluded that mask benefits outweigh risks in various settings, often conceding that the evidence was only of low to moderate quality,[175] and one unequivocally concluded that

Transmission of Influenza: A Systematic Review of the Scientific Evidence, 6 Influenza & Other Respiratory Viruses 257, 265 (2012) ("[T]here is a limited evidence base to support the use of masks and/or respirators in healthcare or community settings."); Benjamin J. Cowling et al., *Face Masks to Prevent Transmission of Influenza Virus: A Systematic Review*, 138 Epidemiology & Infection 449, 455 (2010) ("There is little evidence to support the effectiveness of face masks to reduce the risk of infection."); Amir Qaseem et al., *Use of N95, Surgical, and Cloth Masks to Prevent COVID-19 in Health Care and Community Settings: Living Practice Points From the American College of Physicians (Version 1)*, 173 Annals Internal Med. 642, 646 tbl.4 (2020) ("The evidence is very uncertain about the effectiveness of cloth masks . . . compared with no masks on the risk for SARS-CoV-1 infection."); *see also id.* at 647 ("The CDC does not consider cloth masks as PPE [personal protective equipment] in health care settings, given the lack of evidence of their effectiveness against transmission of SARS-CoV-2.").

175. *See* Jeremy Howard et al., *Face Masks Against COVID-19: An Evidence Review,* 118 Proc. Nat'l Acad. Sci. 1, 6 (2021) ("The positive impact of public mask wearing . . . is 'scientifically plausible but uncertain'."); Mehr Jain et al., *Efficacy and Use of Cloth Masks: A Scoping Review*, 12 Cureus 1, 10 (2020) ("Cloth masks are shown to have limited inward protection in healthcare settings where viral exposure is high but may be beneficial for outward protection in low-risk settings and use by the general public where no other alternatives to medical masks are available."); Milena Santos et al., *Are Cloth Masks a Substitute to Medical Masks in Reducing Transmission and Contamination? A Systematic Review,* 34 Brazilian Oral Rsch. 1, 15 (2020) ("Cloth masks seem to provide some degree of protection" but "the quality of evidence about efficiency is very low to moderate."); Chandini R. MacIntyre & Abrar A. Chughtai, *A Rapid Systematic Review of the Efficacy of Face Masks and Respirators Against Coronaviruses and Other Respiratory Transmissible Viruses for the Community, Healthcare Workers and Sick Patients*, 104 Int'l J. Nursing Stud. 1, 5 (2020) (Use of masks as source control is "a sensible recommendation given the suggestion of protection."); Mary Abboah-Offei et al., *A Rapid Review of the Use of Face Mask in Preventing the Spread of COVID-19*, 3 Int'l J. Nursing Stud. Advances 1, 26 (2020) ("[T]he efficacy of some face mask types . . . such as . . . cloth has not been established."); P. B. Smith et al., *A Scoping Review of Surgical Masks and N95 Filtering Facepiece Respirators: Learning from the Past to Guide the Future of Dentistry*, 131 Safety Sci. 1, 6 (2020) ("Current sterilization measures are not sufficient to permit routine reuse of facemasks.");

facemasks were beneficial.[176] Despite their varying conclusions, these 15 qualitative reviews are largely redundant of one another and chiefly evaluate evidence already discussed above.

The meta-analyses largely analyzed the same RCTs as one another but used different methodologies and sometimes included different non-RCT observational studies. None of these studies considered the SARS-CoV-2 virus specifically, and most looked at surgical—not cloth—face mask use in community settings.

VI. EVIDENCE SUGGESTIVE OF FACE MASK HARM

Although high-quality evidence may eventually support recommendations to wear masks that are currently based on the precautionary principle or optimistic interpretations of observational data that have potentially important limitations, it is important to consider the alternate possibility: that community masking may accelerate the transmission of infectious disease. Although some evidence suggests masks may cause non-infection-related harms such as breathing difficulties,[177] psychological burdens,[178] impaired communication,[179] skin irritation or

Maria C. de Camargo et al., *Effectiveness of the Use of Non-woven Face Mask to Prevent Coronavirus Infections in the General Population: A Rapid Systematic Review*, 25 CIENCIA & SAUDE COLETIVA 3365, 3374 (2020) ("The results regarding masks effectiveness were conflicting.").

176. Madhu Gupta et al., *The Use of Facemasks by the General Population To Prevent Transmission of COVID 19 Infection: A Systematic Review*, MEDRXIV (2020), https://www.medrxiv.org/content/10.1101/2020.05.01.20087064v1.full.pdf [https://perma.cc/AYL9-JTL8].

177. *See* Jian H. Zhu et al., *Effects of Long-Duration Wearing of N95 Respirator and Surgical Facemask: A Pilot Study*, 4 J. LUNG PULMONARY & RESPIRATORY RSCH. 97, 97 (2014) (discussing nasal resistance as a result of physiology changes due to N95s); Mina Bakhit et al., *Downsides of Face Masks and Possible Mitigation Strategies: A Systematic Review and Meta- Analysis,* 11 BMJ OPEN 1, 9 tbl.2 (2021).

178. Jennifer L. Scheid et al., *Commentary: Physiological and Psychological Impact of Face Mask Usage during the COVID-19 Pandemic*, 17 INT'L J. ENV'T RSCH. & PUB. HEALTH 6655 (2020).

179. Divya Swaminathan & Shoba S. Meera, *Masks Mask Communication – Communicating with Children in Health Care Settings*, 88 INDIAN J. PEDIATRICS 283 (2021); Katharina Hufner et

breakdown,[180] and headaches,[181] the most concerning potential harm to health is an increased rate of disease spread.

A number of studies have found higher point estimates of infection among mask wearers, some of which were statistically significant (**Table 3**). A study of healthcare workers returning from the Hajj reported that intermittent use of face masks was associated with a higher rate of acute respiratory tract infections than not wearing masks (34% (42/122) vs. 22% (4/18)), but also found that using masks "all the time" was associated with a lower infection rate (16% (18/110)).[182] Another Hajj study reported that "[u]nvaccinated pilgrims in the Facemask group had a higher rate of CRI than their counterpart in the Control group (13% versus 10%, P=0 · 03)."[183]

Multiple household studies have found higher instances of respiratory sickness in masked intervention groups than in unmasked controls. In one household source-control medical mask trial, point estimates of the primary outcome measure of ILI in the intention-to-treat analysis were higher in the surgical mask group than in the no mask group (22.3% (21/94) vs. 16.0% (16/100)), but the results were not statistically significant and adherence was poor.[184] In a study of 509 households comprised of 2,788 individual members, households in the hand sanitizer group

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al., *On the Difficulties of Building Therapeutic Relationships When Wearing Face Masks*, 138 J. PSYCHOSOMATIC RSCH. 110226 (2020).

180. Elisheva Rosner, *Adverse Effects of Prolonged Mask Use Among Healthcare Professionals During COVID-19*, 6 J. INFECTIOUS DISEASE EPIDEMIOLOGY 1 (2020); Jeff Donovan & Sandy Skotnicki-Grant, *Allergic Contact Dermatitis from Formaldehyde Textile Resins in Surgical Uniforms and Nonwoven Textile Masks*, 18 DERMATITIS 40, 40 (2007).

181. Jonathan J. Ong et al., *Headaches Associated with Personal Protective Equipment—A Cross-Sectional Study Among Frontline Healthcare Workers During COVID-19*, 60 HEADACHE: THE J. HEAD & FACE PAIN 864, 864 (2020) (finding that most healthcare workers in the study develop "de novo PPE-associated headaches" as a result of wearing PPE including facemasks).

182. Saeed Al-Asmary et al., *Acute Respiratory Tract Infections Among Hajj Medical Mission Personnel, Saudi Arabia*, 11 INT'L J. INFECTIOUS DISEASE 268, 270 tbl.2 (2007).

183. Alfelali et al., *supra* note 128, at 8.

184. MacIntyre et al., *Face Mask Use and Control of Respiratory Virus Transmission in Households*, *supra* note 132, at 238 tbl.4.

included significantly more members without any reported upper respiratory symptoms compared to the hand sanitizer plus face mask group (57.6% (545/946) vs. 38.7% (363/938), P<0.01).[185] In the Thai study discussed previously, there were higher point estimates of the primary outcome measure of laboratory-confirmed secondary infections among members in the hand washing plus mask group compared to the control group (23% (66/291) vs. 19% (58/302), n.s.), higher rates of such infections at the household level (35% vs. 22%), and in an analytic subset of 348 households with 885 members (with 94 co-index households removed), a statistically significant increase in ILI for those in the mask group (OR: 2.15, P=0.004) that the researchers described as "twofold in the opposite direction from the hypothesized protective effect."[186]

In a cluster-randomized trial of cloth masks compared with medical masks in healthcare workers, rates of ILI in the cloth mask intervention arm, where 56.8% of workers wore a mask more than 70% of the time, were more than 3 times higher compared to the "standard practice" control arm, where 23.6% did so (2.3% (13/569) vs. 0.7% (3/458)).[187] Researchers noted that because the Institutional Review Board deemed it unethical to ask participants not to use a mask (presumably because of beliefs about the effectiveness of masks in preventing infection), they were unable to include a no-mask control group.[188]

VII. Discussion

Taken as a whole, the available mechanistic and clinical evidence leaves substantial uncertainty as to whether, to what extent, and under what circumstances community-wide use of face masks helps to reduce infection rates of SARS-CoV-2. The voluminous mechanistic evidence clearly demonstrates that masks reduce some measures of droplet transmission, such as the distance that larger droplets travel, and it is known that such droplets contain SARS-CoV-2. Images showing respiratory

185. Larson et al., *supra* note 141, at 189.

186. Simmerman et al., *supra* note 135, at 262.

187. Chandini R. MacIntyre et al., *A Cluster Randomised Trial of Cloth Masks Compared with Medical Masks in Healthcare Workers*, 5 BMJ Open 1, 6 tbl.2 (2015).

188. *Id.* at 2.

droplets expelled during sneezing or coughing have been used to elicit visceral reactions of the public, and a series of articles in the New York Times featured Virginia Tech professor Linsey Marr explaining in simple language how mask fibers "create a haphazard obstacle course through which air . . . must navigate," thus filtering the air.[189]

However, such surrogates of efficacy have not been demonstrated to correlate with infection outcomes and therefore fail to show that masks reduce the true measure of interest, namely, the spread of respiratory illness. It is also not clear that these studies have adequately replicated real-world conditions even as to the surrogate of droplet transmission. Mannequin faces are unmoving and tend to be tested under conditions that generate particle sizes and air speeds that may not reflect the variable nature of human speech or breathing. For example, in a study co-authored by Linsey Marr, a constant rate of air flow was used, mannequin heads were placed in a chamber designed to minimize disruptions to air flow, and masks sometimes covered the mannequins' eyes.[190] Mannequins were also placed only 13 inches apart, relevant perhaps for crowded subway cars, but far closer than traditional conceptions of personal space would allow.[191] In real life it also is considered socially unacceptable to cough directly into someone's face at close range without at least averting the head or covering the cough. Although evidence is limited, one study comparing coughing into a mask versus the crook of the elbow demonstrated similar results in both the size and number of expelled droplets.[192]

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189. Katherine J. Wu, *One Mask Is Good. Would Two Be Better?*, N.Y. Times (Jan. 12, 2021), https://www.nytimes.com/2021/01/12/health/coronavirus-masks-transmission.html [https://perma.cc/VT5A-R6LY].

190. Jin Pan, Charbel Harb, Weinan Leng & Linsey C. Marr, *Inward and Outward Effectiveness of Cloth Masks, a Surgical Mask, and a Face Shield*, MedRxiv 1, 10 (2021).

191. Vikas Mehta, *The New Proxemics: COVID-19, Social Distancing, and Sociable Space*, 25 J. Urban Design 669 (2020) (noting that traditional notions of personal space span 4 to 12 feet for acquaintances).

192. Gustavo Zayas et al., *Effectiveness of Cough Etiquette Maneuvers in Disrupting the Chain of Transmission of Infectious Respiratory Diseases*, 13 BMC Pub. Health 1, 8 (2013).

Clinical evidence also fails to demonstrate that face masks are an effective intervention against the spread of respiratory illness. There have been 2 large-scale RCTs evaluating the use of facemasks at limiting the spread of SARS-CoV-2.[193] One failed to show a statistically significant benefit to those randomized to wear high-quality surgical masks in both the intention-to-treat and per protocol (i.e., excluding those who reported not wearing masks as specified in the protocol) analyses.[194] The other failed to find a statistically significant benefit to cloth masks, but found an 11% relative reduction in COVID-19 prevalence for surgical masks that was marginally statistically significant, with the confidence interval spanning 0% to 22%.[195] In the latter trial, absolute reductions in COVID-19-like illness associated with mask-wearing were only 1% (reduced from 8.6% in control villages to 7.6% in intervention villages), while absolute reductions in symptomatic seroprevalence were less than 0.1% (from 0.76% in control villages to 0.68% in intervention village),[196] raising questions about whether resources devoted to mask production, awareness, utilization, and enforcement could be deployed to greater public health benefit if directed at alternate interventions, such as vaccination, contact-tracing, or isolation.

This study also does not apply to children, as they were excluded.[197] Further, it showed that mask compliance waned drastically after the study period was complete and may not extrapolate to settings disparate from rural Bangladesh, which at the time of this study had no available vaccination and very low rates of natural immunity.[198]

In non-healthcare settings, of the 14 RCTs identified by the authors that evaluated face mask efficacy compared to no-mask controls in protecting against respiratory infections other than

193. Bundgaard et al., *Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers, supra* note 82; Abaluck et al., *supra* note 86, at 1.

194. Bundgaard et al., *Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers, supra* note 82, at 3, 5.

195. Abaluck et al., *supra* note 86, at 20.

196. *Id.* at 9–10.

197. *Id.* at 21–22.

198. *Id.* at 16.

COVID-19, 13 failed to find statically significant benefits from facemask use under intention-to-treat analyses.[199] In communal living settings, four of five RCTs failed to show statistically significant benefits to masking, and the promising results of the fifth study were not confirmed when its authors sought to replicate the results in a much larger follow-up trial.[200] Of eight RCTs that evaluated face mask efficacy against respiratory illness transmission in non- healthcare household settings, all eight failed to find a statistically significant benefit for the use of face masks alone compared to controls in their intention-to-treat analyses, and only three found statistically significant benefit in highly selective sub-group analyses (**Table 1**).[201]

199. Allison E. Aiello et al., *Facemasks, Hand Hygiene, and Influenza Among Young Adults: A Randomized Intervention Trial*, 7 PLOS ONE 1, 6 (2012); Allison E. Aiello et al., *A Randomized Intervention Trial of Mask Use and Hand Hygiene to Reduce Seasonal Influenza-Like Illness and Influenza Infections Among Young Adults in a University Setting*, 14 INT'L J. INFECTIOUS DISEASES e320 (2010); Ebtihal Z. Abdin & Abdul Coudhry, *Effect of Use of Face Mask on Hajj-Related Respiratory Infection Among Hajjis from Riyadh: A Health Promotion Intervention Study*, 12 SAUDI EPIDEMIOLOGY BULL. 27, 27–28 (2005); Osamah Barasheed et al., *Pilot Randomised Controlled Trial to Testing Facemasks Effectiveness in Preventing Influenza-Like Illness Transmission Among Hajj Pilgrims,* 14 INFECTIOUS DISORDERS DRUG TARGETS 110, 113 tbl.1 (2014); Mohammad Alfelali et al., *Facemask Against Viral Respiratory Infections Among Hajj Pilgrims: A Challenging Cluster-Randomized Trial*, 15 PLOS ONE 1, 7 (2020); Canini et al., *supra* note 130, at 5; Chandini R. MacIntyre et al., *Cluster Randomised Controlled Trial to Examine Medical Mask Use as Source Control for People with Respiratory Illness*, 6 BMJ OPEN 1, 1 (2016); Chandini R. MacIntyre et al., *Face Mask Use and Control of Respiratory Virus Transmission in Households*, 15 EMERGING INFECTIOUS DISEASES 233, 238 tbl. 4 (2009); Simmerman et al., *supra* note 135, at 256; Benjamin J. Cowling et al., *Preliminary Findings of a Randomized Trial of Non-Pharmaceutical Interventions to Prevent Influenza Transmission in Households*, 3 PLOS ONE 1, 5 tbl.1 (2008); Cowling et al., *Facemasks and Hand Hygiene to Prevent Influenza Transmission in Households: A Cluster Randomized Trial*, *supra* note 137, at 442 tbl. 3 (2009); Suess et al., *supra* note 140, at 10 tbl.5; Larson et al., *supra* note 141, at 186 tbl.5.

200. Barasheed et al., *supra* note 127; Alfelali et al., *supra* note 128.

201. Canini et al., *supra* note 130; MacIntyre et al., *Cluster Randomised Controlled Trial to Examine Medical Mask Use as Source Control for People with Respiratory Illness*, *supra* note 131; MacIntyre et

While there is observational evidence that facemasks protect against SARS-CoV-1 and SARS-CoV-2, especially in healthcare settings, this evidence is confounded by other variables. Study limitations and potential confounders are often stated by study authors, but tend to be truncated or omitted when study results are reported to the public.[202]

We are not the first to evaluate the body of available evidence regarding mask use and conclude that the evidence fails to clearly support a benefit from mask wearing. Of 16 quantitative meta-analytical analyses evaluating facemask use in non-healthcare, non-mass gathering settings, only two reported statistically significant benefits of facemask use alone compared to no-mask controls, and those results were largely due to inclusion of the observational SARS-CoV-1 data discussed above.

Some Evidence Suggests Masks Cause Higher Infection Rates

Studies of other respiratory illnesses raise the possibility that masks could actually cause higher infection rates under some circumstances, although as with the evidence for masks in general, the existing evidence fails to clearly support this hypothesis and the point estimates of harm could simply be the result of chance. However, the explanation of chance is similarly applicable to the non-significant point estimates of benefit found in some studies, which have frequently been interpreted as supportive of mask efficacy on the rationale that the studies had insufficient statistical power.[203]

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al., *Face Mask Use and Control of Respiratory Virus Transmission in Households*, *supra* note 132; Simmerman et al., *supra* note 135; Cowling et al., *Preliminary Findings of a Randomized Trial of Non-Pharmaceutical Interventions to Prevent Influenza Transmission in Households*, *supra* note 136; Cowling et al., *Facemasks and Hand Hygiene to Prevent Influenza Transmission in Households: A Cluster Randomized Trial*, *supra* note 137; Suess et al., *supra* note 140; Larson et al., *supra* note 141.

202. Apoorva Mandavilli, *The Price for Not Wearing Masks: Perhaps 130,000 Lives*, N.Y. TIMES (Oct. 23, 2020), https://www.nytimes.com/2020/10/23/health/covid-deaths.html [https://perma.cc/B4RP-E9KL].

203. Julii Brainard et al., *Community Use of Face Masks and Similar Barriers to Prevent Respiratory Illness Such as COVID-19: A Rapid Scoping Review*, 25 EUROSURVEILLANCE 1, 12 (2020) ("This is especially true if studies can be well powered to produce more definitive results . . . ."); Chandini R. MacIntyre et al., *A Rapid Systematic Review of the Efficacy of Face Masks and Respirators*

The World Health Organization has noted the possibility that mask wearing could accelerate disease spread by providing a false sense of security that induces individuals to forego standard sanitary measures,[204] although this concern is contested[205] and the evidence is mixed. In one study, mask wearing was associated with reductions of physical distancing when the experimenter asked passersby for directions, particularly if the experimenter was wearing clothes suggestive of high social status.[206] Another study, however, have found passersby increased distance from an experimenter standing on the side of a pathway if the

Against Coronaviruses and Other Respiratory Transmissible Viruses for the Community, Healthcare Workers and Sick Patients, 104 Int'l J. Nursing Stud. 1, 4 (2020) ("[The trial] may have been underpowered."); Chandini R. MacIntyre et al., *Cluster Randomised Controlled Trial to Examine Medical Mask Use as Source Control for People with Respiratory Illness*, 6 BMJ Open 1, 8 (2016) ("This study . . . may have been underpowered . . . ."); Mandy Wang et al., *A Cluster-Randomised Controlled Trial to Test the Efficacy of Facemasks in Preventing Respiratory Viral Infection Among Hajj Pilgrims*, 5 J. Epidemiology & Glob. Health 181, 182 (2015) (discussing the previous largest cluster-randomized trial in the area, noting that "[t]he authors pointed to concerns about . . . the under-powering of the study . . . "); Canini et al., *supra* note 130, at 6 ("[T]he lack of statistical power prevents us [from drawing] a formal conclusion."); Allison E. Aiello et al., *Facemasks, Hand Hygiene, and Influenza Among Young Adults: A Randomized Intervention Trial*, 7 PLOS One 1, 7 (2012) ("It is possible that either lack of power to detect small effects from mask use alone or that the amount of time masks were worn was not sufficient alone to provide a reduction in illness.").

204. World Health Org., Advice on the Use of Masks in the Community, During Home Care and in Health Care Settings in the Context of the Novel Coronavirus (2019-Ncov) Outbreak, at 1 (Interim Rprt. Jan. 29, 2020).

205. Eleni Mantzari et al., *Is Risk Compensation Threatening Public Health in the Covid 19 Pandemic?*, 370 BMJ 1 (2020).

206. Martin Aranguren, *Face Mask Use Conditionally Decreases Compliance with Physical Distancing Rules Against COVID-19: Gender Differences in Risk Compensation Pattern*, Annals Behav. Med. (2021); *see also* Alice Cartaud et al., *Wearing a Face Mask Against COVID-19 Results in a Reduction of Social Distancing*, 15 PLOS One 1, 1 (2020) (online experiment in which subjects must assess whether the distance to a happy, angry, neutral, or masked virtual character is appropriate).

experimenter was wearing a mask, particularly if the mask was homemade and accompanied by goggles.[207]

Mask use could also lead to higher infection rates by encouraging other behavioral changes, such as by providing perceived license to engage in high-risk activities. As with physical distancing, the evidence is mixed. In the United States, a review of location data aggregated from multiple phone apps found that mask mandates were associated with 20-30 minutes of increased daily time outside the home and increase restaurant visitation,[208] while in Germany a review of Google's location data showed small reductions in visits to grocery stores and small decreases in time spent outside the home following mask mandates.[209] Both studies relied on mask mandates rather than actual mask wearing,[210] and neither used randomization nor measured physical distancing.

Even if masks do not affect individual behavior choices for ordinary activities such as visiting grocery stores or working from home, they could lower social inhibitions for engaging in potentially high-risk outlier events such as political rallies, civic demonstrations, professional conferences, and sporting events.[211] They could also provide businesses and government leaders with political cover to "reopen the economy safely," including the reopening of restaurants, bars, health facilities, schools, and other locations where large numbers of people congregate.

Masks could also accelerate disease spread in other ways. For example, the auditory difficulties engendered by masks combined with their obfuscation of lip movements could cause wearers to

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207. Massimo Marchiori, *COVID-19 and the Social Distancing Paradox: Dangers and Solutions*, ARXIV 1, 6 (2020).

208. Youpei Yan et al., *Do Face Masks Create a False Sense of Security? A Covid-19 Dilemma*, MEDRXIV 1, 15–16 (2020).

209. Roxanne Kovacs et al., *Compulsory Face Mask Policies Do Not Affect Community Mobility in Germany* 4–5 (Econstor, Working Paper, 2020).

210. *Id.* at 15; Yan et al., *supra* note 208, at 4.

211. William F. Maloney & Temel Taskin, *Determinants of Social Distancing and Economic Activity During COVID-19: A Global View* 11 (World Bank Group, Pol'y Rsch. Working Paper, 2020) ("[W]earing masks makes individuals feel more in control and protected and hence, the net impact is to increase mobility.").

talk more loudly (which yields greater numbers of droplets[212]), lean to the side of plastic barriers while speaking, or approach more closely to hear or be heard, undermining the reductions in droplet movement that masks provide. This concern is particularly relevant for the aged or others who have impaired hearing and who may also be at higher risk of severe COVID- 19 infection.[213] Although masks appear to reduce the distance traveled by larger droplets, one study found that neck gaiter-type masks can disperse large droplets into a multitude of smaller droplets, which the authors noted "might be counterproductive."[214]

Increased facial touching is also a concern.[215] In one study, 75% of participants reported mask discomfort,[216] and another study reported that 20% of mask wearers experience facial itch,[217] both of which may lead to increased facial touching. Although some studies have reported decreased facial touching associated with mask wearing, these studies had important limitations, such as lacking randomization and blinding,[218] not including indoor

212. Phillip Anfinrud et al., *Visualizing Speech-Generated Oral Fluid Droplets with Laser Light Scattering*, 382 NEW ENG. J. MED. 2061, 2062 (2020).

213. Joshua Chodosh et al., *Face Masks Can Be Devastating for People with Hearing Loss*, 370 BMJ 1, 1 (2020).

214. Emma P. Fischer et al., *Low-Cost Measurement of Face Mask Efficacy for Filtering Expelled Droplets During Speech*, 6 SCI. ADVANCES 1, 3 (2020).

215. Terri Rebmann et al., *Physiologic and Other Effects and Compliance with Long-Term Respirator Use Among Medical Intensive Care Unit Nurses*, 41 AM. J. INFECTION CONTROL 1218, 1218 (2013).

216. Canini et al., *supra* note 130, at 5.

217. Jacek. C. Szepietowski et al., *Face Mask-Induced Itch: A Self-Questionnaire Study of 2,315 Responders During the COVID-19 Pandemic*, 100 ACTA DERMATO-VENEREOLOGICA 1, 2 (2020).

218. Tiffany L. Lucas, *Frequency of Face Touching With and Without a Mask in Pediatric Hematology/Oncology Health Care Professionals*, 67 PEDIATRIC BLOOD & CANCER 1 (2020).

spaces,[219] and excluding subjects who touched their faces to don, doff, or adjust their masks.[220]

Contamination of the hands can occur when masks are removed or reused.[221] Mask studies may therefore overestimate mask benefit and underestimate harm, since most provide subjects with fresh masks at frequent intervals, sometimes including multiple masks per day.[222] By contrast, it is unclear how often cloth masks are washed during community use, leading to the possibility that they are inadvertently serving as homemade disease cultures with the potential to contaminate surfaces when they are temporarily removed. Clean masks can come in contact with contaminated surfaces such as restaurant tables, bathroom shelving, handbag contents, or coat pockets and then be placed on the face.[223] For healthy individuals, the dampness of an otherwise clean cloth mask may increase the likelihood of contact contamination and the need for mask adjustment.

VIII. CONCLUSION

We reviewed the mechanistic, observational, and clinical evidence relevant to the use of cloth face masks in community settings to limit the spread of respiratory infections, and in

219. Yong Jian Chen et al., *Comparison of Face-Touching Behaviors Before and During the Coronavirus Disease 2019 Pandemic*, 3 J. AM. MED. ASS'N NETWORK OPEN (2020).

220. Lasse S. Liebst et al., *Face-Touching Behaviour as a Possible Correlate of Mask-Wearing: A Video Observational Study of Public Place Incidents During the COVID-19 Pandemic*, TANSBOUNDARY & EMERGING DISEASES (2021).

221. Tyler M. Brady et al., *Transfer of Bacteriophage MS2 and Fluorescein from N95 Filtering Facepiece Respirators to Hands: Measuring Fomite Potential*, 12 J. OCCUPATIONAL & ENV'T HYGIENE 898, 904 (2017); Lisa Casanova et al., *Virus Transfer from Personal Protective Equipment to Healthcare Employees' Skin and Clothing*, 14 EMERGING INFECTIOUS DISEASES 1291, 1292–93 (2008).

222. *See, e.g.,* Allison E. Aiello et al., *Facemasks, Hand Hygiene, and Influenza Among Young Adults: A Randomized Intervention Trial*, 7 PLOS ONE 1, 2 (2012); Alfelali et al.*, supra* note 128, at 4.

223. Nikolaos I. Stilianakis & Yannis Drossinos, *Dynamics of Infectious Disease Transmission by Inhalable Respiratory Droplets*, 7 J. ROYAL SOC'Y INTERFACE 1, 1355 (2010); Alex W. H. Chin et al., *Stability of SARS-CoV-2 in Different Environmental Conditions*, 1 LANCET MICROBE e10 (2020).

particular the novel SARS-CoV-2 coronavirus. In each area, we found existing evidence inadequate to demonstrate clear benefit (or harm). Mechanistic evidence shows a clear benefit as measured by laboratory surrogates, but it is not clear to what extent those surrogates are relevant to the clinical question of infection rate or offset by behavioral factors. Uncontrolled observational studies are confounded by numerous known and unknown variables, and most considered mask mandates or self-reported mask wearing as the key variable rather than actual mask usage. The infection dynamics of SARS-CoV-2 differ from SARS-CoV-1 and other respiratory illnesses, meaning that much of the evidence, even if suggestive, has uncertain relevance to SARS-CoV-2. Recommendations to impose mask mandates based on the precautionary principle fail to account for the possibility that masks cause harm[224] or that masks may have varying benefits and risks in different settings.

Notwithstanding the lack of evidence, in the midst of a pandemic policymakers and public health officials cannot wait until high-quality evidence is generated. However, if they determine based on limited evidence that community masking policies are appropriate, it is an ethical imperative to refrain from portraying the evidence as stronger than it actually is.

Estimates of lives that could potentially be saved, if provided, must be carefully balanced with appropriate disclosure of study limitations and uncertainties. Some models supporting community face masking suggest large beneficial effects,[225] but these models are based on assumptions that face masks reduce SARS-CoV-2 transmission by 40–50%[226]— assumptions that are

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224. Trisha Greenhalgh et al., *Face Masks for the Public During the COVID-19 Crisis*, 369 BMJ 1 (2020).

225. Steffen E. Eikenberry 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*, 5 INFECTIOUS DISEASE MODELLING 293, 304 (2020); Richard O. J. H. Stutt et al., *A Modelling Framework to Assess the Likely Effectiveness of Facemasks in Combination with 'Lock-Down' in Managing the COVID-19 Pandemic*, 476 PROC. ROYAL SOC'Y 1, 2 (2020).

226. EMMANUELA GAKIDOU ET AL., GLOBAL PROJECTIONS OF LIVES SAVED FROM COVID-19 WITH UNIVERSAL MASK USE, MEDRXIV 1, 16 (2020); IHME Covid Forecasting Team*, Modeling COVID-19 Scenarios for the United States*, 27 NATURE MED. 94, 94–95 (2021); Tatiana Filonets et al., *Investigation of the Efficiency of Mask*

not adequately supported by existing data. More generally, given the low quality of evidence, the absence of statistically significant benefit indicated by most randomized controlled trials, and the possible harm suggested by a few studies, scientists and public health officials must take care not to apply a double standard to available studies—emphasizing projections of lives saved when evidence suggests benefit, while focusing on study limitations rather than outcomes when the evidence suggests harm or the absence of benefit.

Overconfident portrayal of evidence could also stifle research agendas, making it difficult to reevaluate previously-held but insufficiently supported positions.[227] Early in the pandemic, pressure exerted on public officials to offer immediate solutions led to rhetoric that outpaced the evidence. Once officials or others became publicly committed to a position on masks, it became difficult to advocate for high-quality evidence generation, leading to a situation in which, despite the prevalence of masking policies, only two randomized trials have been performed to address the question of face mask efficacy for SARS-CoV-2. Until it is clear whether and in what circumstances masks provide net benefit (or cause net harm), ethical concerns should not foreclose Institutional Review Boards from approving trials that are randomized, blinded, and controlled. Reliance on randomized evidence is not only a common practice for other clinical interventions[228] (there have been at least 28 randomized controlled trials around the world of hydroxychloroquine, for example[229]), but is a fundamental point of distinction between modern medicine and that of centuries past.

Wearing, Contact Tracing, and Case Isolation During the COVID-19 Outbreak, 10 J. CLINICAL MED. 1, 5 (2021).

227. Dyani Lewis, *COVID-19 Rarely Spreads Through Surfaces. So Why Are We Still Deep Cleaning?*, 590 NATURE 26, 26 (2021).

228. Margaret McCartney, *We Need Better Evidence on Non-Drug Interventions for COVID-19*, 370 BMJ 1, 1 (2020).

229. Cathrine Axfors & Andreas M. Schmitt, *Mortality Outcomes with Hydroxychloroquine and Chloroquine in COVID-19 From an International Collaborative Meta-Analysis of Randomized Trials*, 12 NATURE COMMC'NS 1, 1 (2021).

The well-known distinction between absence of evidence and evidence of absence applies to the COVID-19 context.[230] If face masks save lives—or even if it is reasonably likely that they do––such measures are appropriate and compassionate. Simultaneously, higher quality evidence can be gathered. This rationale applies to all unproven interventions, and has served as a basis for the FDA's expanded access program and the various Right-to-Try laws.[231] Yet as with medicines, the use of unproven non-drug technologies is not without potential harm. Users of the technology can acquire a false sense of security that causes the substitution of unproven or less effective measures for measures for which better evidence may be available, such as physical distancing, improved indoor ventilation, and vaccination.[232] If later evidence proves the intervention useless or harmful, the experience can undermine public trust.[233] The technology itself may cause harm through mechanisms that are not yet well understood, or cause economic, environmental or other harms that indirectly impact health. For example, although masks are individually inexpensive, the collective costs of producing and distributing an adequate and continuous supply of masks to a global community of 7.8 billion people is not trivial, nor are the environmental harms that result when they are discarded.[234]

230. Shuo Feng et al., *Rational Use of Face Masks in the COVID-19 Pandemic*, 8 LANCET RESPIRATORY MED. 434, 435 (2020).

231. *See generally* Jonathan J. Darrow et al., *Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs*, 372 NEW ENG. J. MED. 279, 279 (2015) (describing the FDA's expanded access program).

232. Graham P. Martin et al., *Science, Society, and Policy in the Face of Uncertainty: Reflections on the Debate Around Face Coverings for the Public During COVID-19*, 30 CRITICAL PUB. HEALTH 1, 1 (2020).

233. Brit Trogen et al., *Adverse Consequences of Rushing a SARS-CoV-2 Vaccine: Implications for Public Trust*, 323 J. AM. MED. ASS'N 2460, 2460 (2020).

234. Kajanan Selvaranjan et al., *Environmental Challenges Induced by Extensive Use of Face Masks During COVID-19: A Review and Potential Solutions*, 3 ENV'T CHALLENGES 1, 1 (2021); V.C. Shruti et al., *Reusable Masks for COVID-19: A Missing Piece of the Microplastic Problem During the Global Health Crisis*, 161 MARINE POLLUTION BULL. 1, 2 (2020).

More than a century after the 1918 influenza pandemic, examination of the efficacy of masks has produced a large volume of mostly low- to moderate-quality evidence that has largely failed to demonstrate their value in most settings. Ideally, high-quality evidence will eventually provide clarification. When repeated attempts are undertaken to demonstrate an expected or desired outcome, there is a risk of declaring the effort resolved once results consistent with preconceived notions are generated, regardless of the number or extent of previous failures. Scientists and public health officials should exercise caution to ensure that this potential bias does not lead to a cessation of research once the first high-quality study demonstrating mask efficacy is reported.

Table 1. RCT Evidence for the Efficacy of Face Masks Against Respiratory Virus Transmission.

	Authors (Year) [Context]	**Intention-To-Treat (ITT) Outcomes [Statistical Significance in ITT Outcome]**	**Selected Secondary Outcomes**
1	Aiello et al.[235] (2010) [U. Mich. dorms]	Influenza-like illness (ILI) was cumulatively reported in 26.2% (99/378) of the mask group, 25.1% (92/367) of mask plus hand hygiene (HH), and 32.1% (177/552) of controls. Neither group's reductions were statistically significant before (mask v. control, P=.25; mask plus HH P=.10) or after adjustment for covariates (mask v. control, P=.19; mask plus HH, P=.08). [Statistical Significance: No]	Reported statistically significant point reductions in adjusted ILI for both mask and mask + HH groups compared to controls in study weeks 3-6 (RRs of 0.49–0.72 with P values from 0.01–0.05).
2	Aiello et al.[236] (2012) [U. Mich. dorms]	ILI was cumulatively reported in 11.7% (46/392) of the mask group, 8.9% (31/349) of mask plus hand hygiene (HH), and 13.8% (51/370) of controls. Neither group's reductions were statistically significant before (mask v. control, P=.52; mask plus HH, P=.10) or after adjustment for covariates (mask v.	Like the 2010 study, reported statistically significant point reductions in adjusted ILI for the mask + HH group compared to controls in study weeks 3-6 (RRs of 0.25–0.40 with P values from 0.01–0.03).

235. Allison E. Aiello et al., *Mask Use, Hand Hygiene, and Seasonal Influenza-Like Illness Among Young: A Randomized Intervention Trial*, 201 Int'l J. Infectious Diseases 491, 493–96 (2010).

236. Allison E. Aiello et al., *Facemasks, Hand Hygiene, and Influenza Among Young Adults: A Randomized Intervention Trial*, 7 Plos One 1, 3–6 (2012).

		control, P=.42; mask plus HH, P=.13). [Statistical Significance: No]	However, no statistically significant point reductions were reported for the mask group only.
3	Abdin et al.[237] (2012) [U. Mich. dorms]	Study of acute respiratory infection (ARI) in 995 Hajj pilgrims with a compliance rate of 81% in its health education plus face mask arms found "no association [ ] observed between compliance with face mask wearing and developing ARI (OR 0.97, 95% CI 0.73 -1.28)." [Statistical Significance: No]	N/A
4	Barasheed et al.[238] (2014) [Hajj pilgrims]	Pilot study that reported 53% (28/53) of masked contacts who slept next to known sick patients subsequently developed ILIs compared to 31% (11/36) of masked contacts (P=0.04). [Statistical Significance: Yes]	Reported a statistically significant decrease in ILIs among the subgroup of masked contacts who reported wearing their masks >8 hours/day (P=0.01) compared to both controls and contacts who reported mask use <8 hours/day.

237. Ebtihal Z. Abdin et al., *Effect of Use of Face Mask on Hajj Related Acute Respiratory Infection Among Hajjis from Riyadh - A Health Promotion Intervention Study*, 12 SAUDI EPIDEMIOLOGY BULL. 27, 27–28 (2005).

238. Osamah Barasheed et al., *Pilot Randomised Controlled Trial to Test Effectiveness of Facemasks in Preventing Influenza-Like Illness Transmission Among Australian Hajj Pilgrims in 2011,* 14 INFECTIOUS DISORDERS DRUG TARGETS 110, 113 (2014).

5	Alfelali et al.[239] (2020) [Hajj Pilgrims]	Follow-up study to Barasheed et al.'s pilot RCT above; reported no statistically significant difference in viral respiratory infections (VRIs) among masked tents (41.6%, 149/358) compared to control tents (43.8%, 128/292; P=.18). [Statistical Significance: No]	In a per-protocol analysis (that only considered daily mask wearers in the intervention group and non-mask wearers in the control group), failed to find statistically significant differences "against laboratory-confirmed viral respiratory infections (OR 1.2, 95% CI 0.9–1.7, p = 0.26) nor against clinical respiratory infection (OR 1.3, 95% CI 1.0–1.8, p = 0.06)."
6	Canini et al.[240] (2010) [Households in France]	Study where index cases in households wore surgical masks for five days following diagnosis; reported secondary ILI case rates of 16.2% (24/148) in the mask group versus 15.8% (25/158) in the control group with no statistical difference (P=1.00). [Statistical Significance: No]	Also reported no decreases in ILIs in households where masks were worn within 24 hours of symptom onset, (18.1% (15/83) masked vs. 15.7% (7/108) control; P=0.70) and found no association between various measures of mask

239. Mohammad Alfelali et al., *Facemask Against Viral Respiratory Infections Among Hajj Pilgrims: A Challenging Cluster-Randomized Trial*, 15 Plos One 1, 7 (2020).

240. Laetitia Canini et al., *Surgical Mask to Prevent Influenza Transmission in Households: A Cluster Randomized Trial*, 5 Plos One 1, 5 (2010).

			adherence and incidence of ILI among household contacts (P=0.098–0.31).
7	Macintyre et al.[241] (2009) [Households in Australia]	Reported no significant differences between surgical or P2 (N95 equivalent) masks for secondary ILI infection rates at the individual (surgical mask: 20% (19/94), P=0.46; P2 mask: 15% (14/92), P=1.0; control: 16% (16/100)) or household levels (surgical mask: 32% (15/47), P=0.50; P2 mask: 22% (10/46), P=0.81; control: 24% (12/50)). [Statistical Significance: No]	Per-protocol analysis found a statistically significant decrease (RR: 0.26, P=.015) in infection rates among adherent mask users but adherence was low (only 38% (36/94) of surgical and 46% (42/92) of P2 mask users reported wearing masks "most or all" of the time on the intervention's first day).
8	Macintyre et al.[242] (2016) [Households in China]	Study where index cases in households wore surgical masks for seven days following diagnosis, using three different primary outcomes: clinical respiratory illness (CRI), lab-confirmed viral infection (LCVI), and influenza-like illness (ILI). Reported lower outcome rates for masked groups in all outcomes, with	In a per-protocol analysis, reported a statistically significant hazard ratio (HR) decrease for CRIs in masked groups (HR: 0.22, 95% CI 0.06–0.86), but not for ILIs (HR: 0.18, 0.02–1.73) or LCVIs

241. Chandini R. MacIntyre et al., *Face Mask Use and Control of Respiratory Virus Transmission in Households*, 15 EMERGING INFECTIOUS DISEASES 233, 238 (2009).

242. Chandini R. MacIntyre et al., *Cluster Randomised Controlled Trial to Examine Medical Mask Use as Source Control for People with Respiratory Illness*, 6 BMJ OPEN 1, 5–7 (2016).

		none reaching statistical significance. For CRI, mask group rates of 0.19% (4/2098) versus 0.29% (6/2036) for controls (RR: 0.65, 95% CI 0.18–2.29). For LCVI, mask group rates of 0.05% (1/2098) versus 0.05% (1/2036) for controls (RR: 0.97, 95% CI .06–15.5). For ILI, mask group rates of 0.05% (1/2098) versus 0.15% (3/2036) for controls (RR: 0.03–3.11). [Statistical Significance: No]	(HR: 0.11, 95% CI 0.01–4.40).
9	Simmerman et al.[243] (2011) [Households in Thailand]	Reported no statistically significant differences on lab-confirmed, intra-household secondary influenza infection between handwashing (23%, 66/292), handwashing plus masks (23%, 66/291), and control groups (19%, 58/302; 3-group adjusted Chi-square: 0.63). Using ILI secondary attack rate as a prima ry measure, reported increases in ILI rates in handwashing (17%, 50/292) and handwashing plus mask groups (18%, 51/291) compared to controls (9%, 26/302; 3-group adjusted Chi-square: 0.01). [Statistical Significance: No]	None notable.

243. James M. Simmerman et al., *Findings from a Household Randomized Controlled Trial of Hand Washing and Face Masks to Reduce Influenza Transmission in Bangkok, Thailand*, 5 INFLUENZA & OTHER RESPIRATORY VIRUSES 256, 263 (2011).

10	Cowling et al.[244] (2008) [Households in Hong Kong]	Reported no statistically significant benefit on intra-household secondary influenza infection rates when all household contacts wore masks (5.9%, 12/205) or were educated and given hand hygiene materials (6.6%, 4/61), compared to controls (6.0%, 5/84; P=0.99). Also found no differences (P=0.52–1.0) using three different clinical definitions of influenza. [Statistical Significance: No]	Reported no statistically significant variation in secondary infection rates when interventions were implemented within 36 hours of symptom onset using lab or clinical influenza diagnostic criteria (P=0.44–0.69).
11	Cowling et al.[245] (2009) [Households, /Hong Kong]	Follow-up study of Cowling et al. (2008) above; reported no statistically significant benefit for PCR-confirmed secondary influenza infections when all household contacts wore masks and practiced hand hygiene ("MH"; 7.0%, 18/258) compared to hand hygiene alone ("HH"; 5.4%, 14/257), or a control arm with neither intervention (10.0%, 28/279; 3-group P value: 0.22). Also found no differences using two different clinical diagnostic criteria (3-group P-values of 0.40 and 0.28). [Statistical Significance: No]	In a pre-planned, sub-group analysis of households that implemented interventions within 36 hours of symptom onset, 3-group P values reported statistically significant differences under two of three illness criteria, although the MH group still underperformed the HH-alone group in most cases (PCR-confirmed: HH 5.4% (7/130), MH 4.0%

244. Benjamin J. Cowling et al., *Preliminary Findings of a Randomized Trial of Non-pharmaceutical Interventions to Prevent Influenza Transmission in Households*, 3 PLOS ONE 1, 7 (2008).

245. Benjamin J. Cowling et al., *Facemasks and Hand Hygiene to Prevent Influenza Transmission in Households: A Cluster Randomized Trial*, 151 ANNALS INTERNAL MED. 437, 442 (2009).

			(6/149); Clinical Definition 1: HH 10.8% (14/130), MH 18.1% (27/149); Clinical Definition 2: HH 3.1% (4/130), MH 4.7% (7/149)).
12	Suess et al.[246] (2007) [Households in Germany]	Reported no statistically significant differences, with lab-confirmed secondary infection rates of 9% (6/69) in the mask, 15% (10/67) in the mask plus hand hygiene (MH), and 23% (19/82) in the control group (P=0.18), and secondary clinical ILI rates of 9% (6/69) in the mask, 9% (6/67) in the MH group, and 17% (14/82) in controls (P=0.37). [Statistical Significance: No]	In a per-protocol analysis, found a statistically significant decrease in the OR of the masked group compared to controls (OR: 0.3, P=0.04) in lab-confirmed influenza, but not clinical ILI cases (OR: 0.5, P=0.3).
13	Larson et al.[247] (2010) [Households in New York City]	Reported unadjusted secondary URI/ILI/influenza rates of 0.137 for education, 0.144 for education plus hand sanitizer (HS), and 0.124 for education plus mask plus hand sanitizer (MHS) with no reported P values, but "a significant decrease . . . [in MHS] compared with the Education group." In the	In a secondary adjusted model, reported intervention group as significantly impacting infection rate with a 3-group P value of 0.02 between the MHS group (OR: 0.82; 95% CI 0.70-0.97), the HS alone

246. Thorsten Suess et al., *The Role of Facemasks and Hand Hygiene in the Prevention of Influenza Transmission in Households: Results from a Cluster Randomised Trial; Berlin, Germany, 2009–2011*, 12 BMC INFECTIOUS DISEASES 1, 10 (2012).

247. Elaine L. Larson et al., *Impact of Non-pharmaceutical Interventions on URIs and Influenza in Crowded, Urban Households*, 125 PUB. HEALTH REP. 178, 186 (2010).

		primary multivariate regression analysis, found "no significant differences in rates of infection by intervention group" with P values ranging from 0.19–0.89. [Statistical Significance: No]	group (OR: 1.01; 95% CI 0.85-1.21), and the educational reference group.
14	Jacobs et al.[248] (2009) [Hospital workers in Japan]	Reported no statistically significant difference between mean number of days of cold symptoms reported by surgical face mask wearers (mean=16.1 days) and non-wearers (mean=14.3 days; P=0.81) during the winter season. [Statistical Significance: No]	In a univariate analysis, reported the only significantly predictive factor of mean days with cold symptoms was living with children under 16 years old (P=0.02).
15	Bundgaard et al.[249] (2021) [adult community members in Denmark]	The primary outcome of SARS-CoV-2 infection (either laboratory-confirmed, or a hospital-based diagnosis) occurred in 42 (1.8%) of 2392 participants in the mask group and 53 (2.1%) of 2470 in the control group (P=0.38). [Statistical Significance: No]	Nine participants (0.5%) were positive for at least 1 of the 11 respiratory viruses other than SARS-CoV-2, compared with 11 participants (0.6%) in the control group (P=0.87).
16	Abaluck et al. (2021)[250]	The primary outcome of symptomatic SARS-CoV-2	Excluding surgical mask villages,

248. Joshua L. Jacobs et al., *Use of Surgical Face Masks to Reduce the Incidence of the Common Cold Among Health Care Workers in Japan: A Randomized Controlled Trial*, 37 Am. J. Infection Control 417, 419 (2009).

249. Bundgaard et al., *Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers, supra* note 82, at 3.

250. Jason Abaluck et al., *The Impact of Community Masking on COVID-19: A Cluster-Randomized Trial in Bangladesh* 7 (Working Paper, Aug. 31, 2021), https://www.poverty-

	[cluster-randomized communities in Bangladesh]	seroprevalence was 0.76% in control villages and 0.68% in intervention (i.e., both cloth and surgical mask) villages. [Statistical Significance: Yes]	symptomatic SARS-CoV-2 seroprevalence was 0.76% in control villages and 0.74% in cloth mask villages (P=0.54).

action.org/sites/default/files/publications/Mask_Second_Stage_Paper_20211108.pdf.pdf [https://perma.cc/WBN7-CAHF].

Table 2. Quantitative Meta-analytical Evidence for the Efficacy of Community Masking Against Respiratory Viral Infections.

Authors & Year	Total Studies [Non-Healthcare Settings] (RCTs) Key findings	[Characterization] Supporting text
Gómez-Ochoa et al.[251] 2021	5 [5] (5) Brief letter to the editor that reanalyzed the data from the Chaabna et al. meta-analysis, but only included studies that used face mask use alone compared against a control group. The authors found no significant differences between medical facemasks use only and controls in the odds of developing laboratory-confirmed influenza (9.6% (27/274) vs. 9.7% (50/515)) and influenza-like illness (13.7% (58/423) vs. 14.9% (100/673)).	[critical] "Because of these divergent results and the lack of high-quality research . . . , strong recommendations for facemask use in the community context should be issued with caution . . . ."
Aggarwal et al.[252] 2020	9 [9] (9) Using results from 9 non-healthcare RCTs, found that mask use, both with hand hygiene (P=.714) and without (P=.226), was not associated with lower rates of ILI infection in community settings.	[equivocal] "Available evidence does not confirm a protective effect of face mask usage alone in a community setting against influenza-like illnesses (and potentially, the COVID-19)."

251. Sergio A. Gómez-Ochoa & Taulant Muka, *Meta-Analysis on Facemask Use in Community Settings to Prevent Respiratory Infection Transmission Shows No Effect*, 103 INT'L J. INFECTIOUS DISEASE 257, 257 (2021).

252. Nishant Aggarwal et al., *Facemasks for Prevention of Viral Respiratory Infections in Community Settings: A Systematic Review and Meta-Analysis*, 103 INDIAN J. PUB. HEALTH 192, 197–98 (2020).

Brainard et al.[253] 2020	31 [61] (12) Did not report any statistically significant results when analyzing RCT data. Reported that mask use was not associated with statistically significant reductions in ILIs when used by a well person (11.2% (116/1032) vs. 12.1% (127/1046), P=.68), when used as source control by an ill person in a home setting (5.6% (25/450)) vs. 6.2% (28/453), P=.87), or when used by all parties in a home with a sick individual (11.0% (79/715) vs. 12.0% (107/890, P=.43). Authors reported significant reductions in multiple observational study types including cross-sectional (22.3% (2771/12418) vs. 34.1% (7287/21353), P=.003, case control (18.4% (128/694) vs. 40.5% (327/807), P=.02), and pre-post (3.3% (15/454) vs. 10.3% (95/920), P<.001), but not in cohort studies (13.8% (248/1795) vs. 20.4% (640/3131), P=.52).	[supportive] "Available evidence does not confirm a protective effect of face mask usage alone in a community setting against influenza-like illnesses (and potentially, the COVID-19.)" [supportive] "The quality of the evidence is problematic . . . [o]ur best estimate is that the effect of wearing a face mask is between the effects seen in RCTs and the effects seen in cohort studies, or around 6 to 15% reduction in disease transmission."[254]
Chaabna et al.[255] 2020	12 [12] (10) Reported a significant protective effect of medical	[supportive] "There is no available direct evidence in

253. Julii Brainard et al., *Community Use of Face Masks and Similar Barriers to Prevent Respiratory Illness Such As COVID-19: A Rapid Scoping Review*, 25 Eurosurveillance 1, 1 (2020).

254. *See* Julii S. Brainard et al., *Facemasks and Similar Barriers to Prevent Respiratory Illness Such as COVID-19: A Rapid Systematic Review*, MedRxiv 1, 1 (2020).

255. Karima Chaabna et al., *Facemask Use in Community Settings to Prevent Respiratory Infection Transmission: A Rapid Review and Meta-Analysis*, 104 Int'l J. Infectious Disease 198, 205 (2021).

	facemask use when evaluated in conjunction with other interventions (e.g. handwashing) (6.8% (273/4029) vs. 9.8% (458/4677), 95% CI 0.54–0.81). Did not report data for facemask use alone compared to control groups.	humans . . . for recommending cloth facemask use" but "[o]verall . . . there is enough evidence to show that medical facemasks are effective in community settings . . . ."
Chu et al.[256] 2020	172 [3] (0) Using data from six observational studies on SARS-CoV-1, reported a statistically significant reduction in infections associated with face masks (adjusted OR: 0.33) compared to no mask controls. Four of the studies were in healthcare settings and one of the studies reported aerosol generating procedures. In a separate analysis, the authors reported statistical reductions in non-health-care settings on the basis of three observational studies from the SARS-CoV-1 epidemic (15.2% (37/244) vs. 21.0% (101/481); OR: 0.56).	[supportive] "[D]irect evidence is limited" but "[t]he use of face masks was protective for both healthcare workers and people in the community . . . , with both the frequentist and Bayesian analyses lending support to face mask use irrespective of setting . . . ."
Jefferson et al.[257] 2020	15 [7] (15) Analyzing 15 RCTs, found no reductions in ILIs (RR 0.93, 95% CI 0.83-1.05) or influenzas (RR 0.84, 95% CI 0.61-1.17) for masks in the general population	[equivocal] "We are uncertain whether wearing masks or N95/P2 respirators helps to

256. Derek K. Chu et al., *Physical Distancing, Face Masks, and Eye Protection to Prevent Person-to-Person Transmission of SARS-CoV-2 and COVID-19: A Systematic Review and Meta-Analysis*, 395 LANCET 1973, 1984 (2021).

257. Tom Jefferson et al., *Physical Interventions for the Interruption or Reduction of the Spread of Respiratory Viruses*, 7 COCHRANE DATABASE SYS. REV. 1, 108 (2011).

	or healthcare workers (RR 0.37, 95% CI 0.05-2.50).	slow the spread of respiratory viruses."
Liang et al.[258] 2020	21 [8] (6) Using data from both observational and RCT studies, the authors reported a significant protective effect on lab-confirmed respiratory viral infection (5.9% (307/5217) vs. 12.1% (419/3469), P<.00001). In non-healthcare settings, using RCT and observational data, the authors reported statistically significant effects (6.1% (111/1812) vs 11.3% (227/2008), P=.002) with moderate heterogeneity between the studies (I^2=45%, P=.08). The authors did not consider RCT-only data, although if they had, between-group differences would have declined (5.4% (44/816) vs. 7.8% (77/989)).	[supportive] "The present systematic review and meta-analysis showed the general efficacy of masks in preventing the transmission of RVIs [respiratory viral infections]."
Ollila et al.[259] 2020	5 [5] (5) Analyzing data from 5 RCTs, reported strong and statistically significant results in favor of face mask efficacy at maximum follow up (7.8% (297/3793) vs. 18.4% (704/3830); RR: 0.608). However, for 2 of the 5 papers studied the authors utilize data from face mask + other intervention arms instead of	[supportive] "[Four] out of 17 studies supported the use of masks in the intention-to-treat analysis." "Despite . . . small effect sizes in the individual studies, the findings did support use of face masks."

258. Mingming Liang et al., *Efficacy of Face Mask in Preventing Respiratory Virus Transmission: A Systematic Review and Meta-Analysis*, 36 Travel Med. & Infectious Disease 1, 7 (2020).

259. Hanna M. Ollila et al., *Face Masks Prevent Transmission of Respiratory Diseases: A Meta-Analysis of Randomized Controlled Trials*, MedRxiv 1, 12 (2020).

	available data from face mask-only arm. These risk ratios are considerably different (0.78 and 0.88 instead of 1.10 and 0.92, respectively) and the involved groups constitute 14.3% (542/3793) and 16.4% (629/3830) of each treatment group, which would likely alter the final result.	
Perski et al.[260] 2020	21 [11] (11) Authors considered 10 observa tional studies and 11 RCTs (only one of which found a reduction in self - reported ILIs in participants wearing face masks) and, using a Bayesian analysis, reported a "moderate likelihood of a small effect for the wearing of face masks" in reducing self-reported ILI (cumulative posterior odds=3.61), but determined that evidence was equivocal as to clinically- and laboratory-confirmed infections (cumulative posterior odds of 1.07 and 1.22, respectively).	[equivocal] RCT evidence was "equivocal on whether facemask wearing in community settings reduces the transmission of clinically- or laboratory-confirmed viral respiratory infections." "RCTs and observational studies have found an effect on self-reported symptoms, but this may be the result of reporting bias and confounding."
Wang et al.[261] 2020	15 [15] (5) Using 15 non-healthcare studies (10 observational and 5 RCTs), authors reported a slightly decreased pooled odds ratio (OR: 0.96, 95% CI 0.8–1.15)	[critical] "Our review found that SMs [surgical masks] were not associated to ARI

260. Olga Perski et al., *Face Masks to Prevent Community Transmission of Viral Respiratory Infections: A Rapid Evidence Review Using Bayesian Analysis*, QEIOS 1, 15 (2020).

261. Min X. Wang et al., *Effectiveness of Surgical Face Masks in Reducing Acute Respiratory Infections in Non-Healthcare Settings: A Systematic Review and Meta-Analysis*, 7 FRONTIERS MED. 1, 20 (2020).

	but the results were not statistically significant.	[acute respiratory illnesses] incidence, indicating that SMs may be ineffective . . . when worn by an uninfected individual in the general community. However, given the weak methodologies across studies assessed and the possibility of residual confounding, an absence of evidence cannot be simply regarded as an evidence of absence."
Xiao et al.[262] 2020	14 [14] (14) Incorporating data from 10 RCTs in non-healthcare settings, reported no statistically significant effect for the use of masks on laboratory-confirmed influenza (2.3% (29/1276) vs. 3.3% (51/1567), P=.25).	[critical] "We did not find evidence that surgical-type face masks are effective in reducing laboratory-confirmed influenza transmission, either when worn by infected persons (source control) or by persons in the general community to reduce their susceptibility."
Li et al.[263] 2021	6 [1] (0) Using data from 6 COVID-19 case-control studies—5 in healthcare settings—to report a significantly-reduced risk of	[supportive] "Face masks reduced the risk of COVID-19 infection by 70% for health care workers,"

262. Jingyi Xiao et al., *Nonpharmaceutical Measures for Pandemic Influenza in Nonhealthcare Settings—Personal Protective and Environmental Measures*, 26 EMERGING INFECTIOUS DISEASES 967, 972 (2020).

263. Yanni Li et al., *Face Masks To Prevent Transmission of COVID-19: A Systematic Review and Meta-Analysis*, 49 AM. J. INFECTION CONTROL 900, 905 (2021).

	infection (11.4% (82/718) vs. 20.0% (202/1008); OR: 0.38). However, in the only non-HCW study considered the results were non-significant (12.8% (29/227) vs. 16.9% (102/602); OR: 0.72, 95% CI: 0.46–1.12).	but the "included original studies did not make . . . adjustments for possible confounding factors, such as . . . hand hygiene" and the two most heavily weighted studies involved exclusively N95 masks or primarily non-cloth masks.
Tabatabaeizadeh[264] 2020	4 [1] (0) Authors used data from 4 observational COVID-19 studies to conclude that mask-wearing is correlated with statistically significant risk ratio decrease of 0.12. However, 70.8% (n=5442) of the study's total participants (n=7688) came from a single paper where participants used N95 respirators, not facemasks.	[supportive] "[U]se of the face mask was associated significantly with a decrease [sic] risk of SARS-CoV-2 infection" but "[t]he non-randomized design of the included studies in this meta-analysis" was an "important limitation."
Coclite et al.[265] 2021	13 [13] (3) Authors used data from 3 RCTs and 10 observational papers to conduct two separate meta -analyses. Concluded that neither RCT data (11.7% (187/1598) vs. 11.2% (272/2419); RR: 0.97,	[supportive] "We found very low-certainty evidence that wearing a face mask is associated with a reduced risk of primary infection in

264. Seyed-Amer Tabatabaeizadeh, *Airborne Transmission of COVID-19 and the Role of Face Mask to Prevent It: A Systematic Review and Meta-Analysis*, 26 Eur. J. Med. Rsch. 1, 5 (2021).

265. Daniela Coclite et al., *Face Mask Use in the Community for Reducing the Spread of COVID-19: A Systematic Review*, 7 Frontiers Med. 1, 8–11 (2021).

	P=0.85) nor any of the observational data (cross-sectional: 20.2% (1302/6438) vs. 17.2% (1714/9975); RR: 0.90, 95% CI: 0.74–1.10) (case-control: 19.9% (138/694) vs. 40.5% (327/807); RR: 0.59, 95% CI: 0.34–1.03) (prospective: 20.5% (88/429) vs. 58.4% (310/531); RR: 0.55, 95% CI: 0.11–2.75)) were statistically significant.	RCTs as well as in observational studies." "The results . . . support[] the use of face masks for reducing the transmission and acquisition of respiratory viral infections in the community."
Abdullahi et al.[266] 2020	2 [3] (5) Considering data from 2 RCTs and 3 observational studies in the SARS-CoV-1 and influenza contexts, authors failed to find a statistically significant benefit of face mask use (18.7% (142/758) vs. 33.1% (480/1451); RR: 0.78, P=0.52).	[equivocal] "On the intervention on face masks, there are contested discussions . . . . However, WHO acknowledges that the wearing of masks by the general public has been impactful in reducing previous severe pandemics."
Nanda et al.[267] 2021	7 [7] (7) Incorporating data from 7 RCTs (all previously discussed) evaluating ILI transmission, found no significant difference in infection between mask and no-mask groups (2.8% (37/1301) vs. 3.6% (57/1592); RR: 1.00, P=0.93).	[equivocal] "The available preclinical findings limited clinical and indirect evidence suggests biological plausibility that face masks may reduce the spread of SARS-CoV-2. The available

266. Leila Abdullahi et al., *Community Interventions in Low- and Middle-Income Countries to Inform COVID-19 Control Implementation Decisions in Kenya: A Rapid Systematic Review*, 15 PLOS ONE 1, 22 (2020).

267. Akriti Nanda et al., *Efficacy of Surgical Masks or Cloth Masks in the Prevention of Viral Transmission: Systematic Review, Meta-Analysis, and Proposal for Future Trial*, 14 J. EVIDENCE-BASED MED. 97, 110 (2021).

		clinical trial evidence shows no significant difference in limiting transmission [of] respiratory viral illnesses, but the evidence is of poor quality.”

Table 3. Studies Suggesting an Association of Face Masks with High Rates of Infection

Authors	Year	Study Type (N)	Results Suggestive of Harm	Conclusions
Alfelali et al.[268]	2019	Cluster-randomized trial (7,687)	Unvaccinated pilgrims had higher CRI (clinical respiratory infection) rates than counterparts in the control group (13% versus 10%, P=0.03).	"[A]llocation to facemask use was not associated with reduced laboratory-confirmed viral respiratory infections or clinical respiratory infections."
MacIntyre et al.[269]	2015	Cluster-randomized trial (1607)	Rates of ILI in cloth mask intervention arm were more than 3 times higher compared to the "standard practice" control arm (2.3% (13/569) vs. 0.7% (3/458)).	Future research should examine "cloth masks, but until such research is carried out cloth masks should not be recommended." The authors "recommend that infection control guidelines be updated about cloth mask use [referring to its risks] to protect the occupational health and safety of [healthcare

268. Mohammad Alfelali et al., *Facemask Against Viral Respiratory Infections Among Hajj Pilgrims: A Challenging Cluster-Randomized Trial*, 15 Plos One 1, 7 (2020).

269. Chandini R. MacIntyre et al., *A Cluster Randomised Trial of Cloth Masks Compared with Medical Masks in Healthcare Workers*, 5 BMJ Open 1, 8 (2015).

				workers]."
Simmerman et al.[270]	2011	Cluster-randomized trial (885)	More laboratory-confirmed secondary infections among members in the hand washing plus mask group compared to the control group (23% (66/291) vs. 19% (58/302), n.s.), higher rates at the household level (35% vs. 22%) and, in a separate sub-group analysis, higher rates of ILI among those in the mask group (OR: 2.15, P=0.004) that the researchers described as "twofold in the opposite direction from the hypothesized protective effect."	Reported that "[i]nfluenza transmission was not reduced by interventions to promote hand washing and face mask use."
Larson et al.[271]	2010	Cluster-randomized trial (509 households)	Households in the hand sanitizer group included significantly more members	Did not have sufficient data to support mask wearing but nevertheless concluded that "[m]ask wearing is a promising

270. James M. Simmerman et al., *Findings from a Household Randomized Controlled Trial of Hand Washing and Face Masks to Reduce Influenza Transmission in Bangkok, Thailand*, 5 Influenza & Other Respiratory Viruses 256 (2011).

271. Larson et al., *supra* note 141, at 189.

			without any reported upper respiratory symptoms compared to the hand sanitizer plus face mask group (57.6% (545/946) vs. 38.7% (363/938), P<0.01).	non-pharmaceutical intervention . . . ”
MacIntyre et al.[272]	2009	Cluster-randomized trial (145)	Point estimates of the primary outcome measure of ILI were higher in the surgical mask group than in the no mask group (22.3% vs. 16.0%), but the results were not statistically significant.	Authors “found that distributing masks during seasonal winter influenza outbreaks is an ineffective control measure characterized by low adherence” and stated that masks may only have efficacy “where a larger adherence may be expected, such as during a severe influenza pandemic or other emerging infection.”
Al-Asmary et al.[273]	2007	Nested case-control (375)	Intermittent use of face masks associated	“The common practice among

272. Chandini R. MacIntyre et al., *Face Mask Use and Control of Respiratory Virus Transmission in Households*, 15 Emerging Infectious Diseases 233, 238 (2009).

273. Saeed Al-Asmary et al., *Acute Respiratory Tract Infections Among Hajj Medical Mission Personnel, Saudi Arabia*, 11 Int’l J. Infectious Disease 268, 271 (2007).

			with a higher rate of acute respiratory tract infections than not wearing masks (34% (42/122) vs. 22% (4/18)).	pilgrims and medical personnel of using surgical facemasks to protect themselves against ARI [acute respiratory infections] should be discontinued.”